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J.N. Maina

The Gas Exchangers

Structure, Function, and Evolution of the Respiratory Processes

With 108 Figures and 33 Tables

Springer

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"Biologists are seeking to integrate studies of morphology, development, physiology, ecology, systematics, and behaviour in order to understand how species and lineages deal with their environments and how they have diversified." Wake (1990)

Dedication

This book would not have been written without the patience, understanding, and support of my wife, Wanjuku, and our children, Ndegwa, Wanjiru, and Kireru. I am particularly indebted to them for their forbearance when the work was a major preoccupation. They kept urging me on especially when the "spirit was willing but the body weak" by firmly and persistently inquiring when "the book" would be ready. I dedicate the work to them.

It has been both a challenge and pleasure writing this book. I hope that the reader will partake in some of it.

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Johannesburg, March 1998 *J.N. Maina*

Preface

> *"Amongst animals, diversity of form and of environmental circumstances have given rise to a multitude of different adaptations subserving the relatively unified patterns of cellular metabolism. Nowhere else is this state of affairs better exemplified than in the realm of respiration". Jones (1972).*

The field of comparative respiratory biology is expanding almost exponentially. With the ever-improving analytical tools and methods of experimentation, its scope is blossoming to fascinating horizons. The innovativeness and productivity in the area continue to confound students as well as specialists. The increasing wealth of data makes it possible to broaden the information base and meaningfully synthesize, rationalize, reconcile, redefine, consolidate, and offer empirical validation of some of the earlier anecdotal views and interpretations, helping resolve the issues into adequately realistic and easily perceptible models. Occasional reflections on the advances made, as well as on the yet unresolved problems, helps chart out new grounds, formulate new concepts, and stimulate inquiry. Moreover, timely assessments help minimize isolation among investigators, averting costly duplication of effort. This exposition focuses on the diversity of the design of the gas exchangers and gives a critical appraisal of the plausible factors that have motivated or constrained the evolvement of respiration. The cause-and-effect relationship between the phylogenetic, developmental, and environmental factors, conditions, and states which at various thresholds and under certain backgrounds conspired in molding the gas exchangers is argued. Convergence as well as divergence, retrogression and progression, parallel as well as serial developments have occurred in this stochastic process manifest with recurrent catastrophic crises. Gould (1994) asserts that "life's pathways are more contingent and chancy than predictable and directional". Such a caveat notwithstanding, with judicious use of data, an integrative multidisplinary approach into the evolvement of the gas exchangers should help develop a conceptual framework of the appropriation and synthesis of the myriad parameters and components involved in the assembly of the gas exchangers. The repertoire of the functional mechanisms conceived, the investments made to support such developments, the losses incurred, and the gains reaped in the course of the development of respiration can be grasped. The adaptive attributes common to or unique to broadly defined groups of organisms can be adduced. On that basis, the connectivity, the diversity, and the chronology of the changes that occurred during and after the incorporation of molecular O_2 into the respiratory process can be gauged. To place the historical developments of respiration in their proper perspective, an ecopaleobiological approach has been adopted. Borrowing heavily from works of others, pertinent past and present states, events, and circumstances have been associated. I have been consciously eclectic in order to remain both brief and focused on the subject matter. The embracing approach adopted provides instructive parametric insights into the permutations and spatial and temporal vectorial shifts of the causative factors during the genesis of the respiratory processes. This should explain how and why particular respiratory traits were acquired, some lost, and the means by which solutions to attendant challenges were found as the respiratory machines were forged. In evolutionary terms, contemporary animals are living edifices of past events and developments. They give us a narrow, nebulous window through which to espy and presage the assaults that life has endured and the changes which may have occurred. Kardong (1995) observes that "the architectural design of an organism expresses something about the processes that produced, it, the history out of which it came, and the functions its parts perform."

To present a truly comparative account, detailed considerations of individual animal species have been avoided. Instead, broad taxonomic groups are considered. The shared and dissimilar strategies, principles, mechanisms, and themes are instead rationalized. Data on individual species are given only to explain a feature, a process, a concept, or a theory. Effort has been made to balance out physiology with morphology, the latter having been largely relegated to the background in practically all earlier publications on the subject. This approach is adopted in the firm belief that morphology is not simply a synonym of anatomy, i.e., a description of the structure, topography, and composition of inert biological entities for their own sake. The discipline delves into the logical basis of form, casting back on the true spirit of the etymology of the word. Perceptively, Thompson (1959, p.14) expressed this notion as follows: "morphology is not only a study of material things and of the forms of material things, but has its dynamical aspect, under which we deal with the interpretation, in terms of force, of the operations of Energy."

This book was written with a broad readership in mind. Graduate students as well as established biologists, be they zoologists, physiologists, morphologists, paleontologists, or ecologists who work or may contemplate working on materials and aspects of respiration in whole organisms will find it useful. Scientists in Earth Sciences with an interest in the interactive developmental processes between the physical and biological realms will find the book of certain interest and perhaps stimulating. No apology is made that a rather lengthy section of the work has been devoted to the biophysical aspects of the respiratory media, habitats, and the accretion of molecular O_2. The "history" of the evolution of the respiratory processes and that of gas exchangers in particular would be in great default without a clear grasp of the setting in which the changes occurred, the intractable challenges faced, and the successes and failures encountered as animals strived not only to survive but also to establish themselves and flourish in alien habitats. Some of the aspects covered here have taken me outside the limits of my personal experience and expertise. In such cases, I well realize that I may not have articulated the issues with the competence required by the specialists in those fields. Should any infelicities of judgment, inference, or omission have occurred, I beg the reader's indulgence, and would be most grateful if such aspects were pointed out to me. While consciously avoiding teleology, a rather difficult thing for one to do especially when rationalizing design, I have not hesitated to use explicative interpretations and suppositions where firm data are lacking. Fishman (1983) observed that "the understanding of biological systems rests on a combination of mechanisms, which deal with beginnings, and teleology, which deals with the concept of purpose and end", while Jones (1972) asserts that "frank and self-controlled (teleological) speculation is an essential part of the comparative approach". In such a long process, and one which has to be studied indirectly (due to lack of fossilized materials of soft tissues like the gas exchangers), it has to be conceded that "background noise", discernible as anomaly between the expected outcome and the reality, is to be anticipated. Evolutionary reconstruction of the history of a natural process is one of the most challenging problems that biologists have been called upon to solve. The skepticism with which such accounts are received was voiced by Rancour-Laferriere (1985), who stated that "anyone who attempts to narrate the evolution of something over geologic time is telling a story". Although, given the limitations imposed by the wide gaps in the fossil records, such skepticism is warranted, I consider such sentiments extreme and perhaps somewhat misplaced. When presenting a chronological account of a classical natural event, a measure of subjectivity should be allowed. More often than not, the best that can be accomplished is to build as complete a case as possible – based on intuitive sense, logical inferences, and known facts. A historically realistic model or a simulation of what could have happened should be fabricated and tested. This should show that, given specified conditions and circumstances, particular events were not only inevitable but most likely occurred. In the general purview of biology, Stebbins (1984) realistically observes that "the only law that holds without exception in biology is that exceptions exist for every law". I have explicitly stated where experimental facts are lacking and personal view has been proffered. I hope that such thoughts will provide areas for consideration and debate.

Due to limitation of space, it is not possible to give an encyclopedic review of the utterly immense aspects of the evolution and comparative respiratory morphology and physiology of the gas exchangers in a single work. There are excellent accounts, monographs, treatises, and perspectives on different areas of these aspects, especially on the vertebrates. The key publications are included in the reference list; they should be consulted where particular details are desired. While offering a synthesis of more recent findings, this account is meant to complement such comprehensive publications and not supersede them. I have purposely placed particular emphasis on the respiratory processes of the invertebrates, a group on which relatively less is known. In doing so, I hoped to avoid the conventional "prejudice" (against the group) and the parochial but somewhat legitimate interest and popular emphasis on the vertebrate aspects. In most people, mention of the word animal conjures up a vertebrate in their mind. With real setbacks, mammals in particular (a highly specialized taxon in most respects) have been used as the focal point (model group) in discussing comparative pulmonary structure and function. A prospective look at the design of the gas exchangers, i.e., from the lowest to the highest forms rather than retrospectively (i.e., back in time) has been made here in order to hopefully better fit the developments into the natural polarity of evolutionary change. This approach perhaps offers a more satisfactory causal explanation of the early developments in respiration. Moreover, reading evolution backwards has its intrinsic bias in that one inevitably sees an outcomes as the only possible result from a series of events. Nature is extremely complex and too unpredictable to be read easily. I hope that a satisfactory balance in the presentation has been achieved here. The designs of the gas exchangers in the so-called primitive animals (a very unfortunate term which has come to be equated with crude, mediocre, or imperfect, just as complex, superior, and advanced have come to be taken to mean better or efficient) are most instructive in understanding the structure and the operations of the more sophisticated processes of respiration. Tenney and Boggs (1985) observed that "the great events in respiratory system evolution can be appreciated best in lower classes". The diversity of the stratagems adopted for procuring molecular O_2 and eliminating CO_2 among animals having different lifestyles, occupying different habitats, and which have acquired remarkable morphological eccentricities are most evident when the underlying cost-benefit analysis and the compromises, the trade-offs (and even payoffs?), and the alternative solutions to the respiratory imperatives are comparatively examined. The protracted transactions and the transformations that went into the design and adoption of particular respiratory schemes and the perceivable limitations or capacities inherent in different gas exchangers can be recognized. A heuristic approach in biology reveals subtle areas of convergence, homology, analogy, and homeostasis, providing an explanation of the mechanisms which yielded particular states and phenomena. Nature, however, does not yield its secrets willingly. They have to be patiently gleaned and teased through protracted, well-planned inquiries and meticulous attention to details. A multidisplinary approach in such studies allows a broad understanding of a problem and offers robust answers.

The chapters in this account are sequenced to survey the respiratory events as they are conceived to have more or less chronologically unfolded. It is hoped that this approach offers a more logical understanding of the developments. Chapter 1 examines the fundamental attributes of life and its evolution on Earth, the accretion and fluctuations of O_2 and CO_2 in the biosphere, and the enigmatic nature of molecular O_2 in respiration and evolution of life itself and the intricate role it has played in the ecological adaptations of the animal life. Chapter 2 surveys the forms and designs of the gas exchangers, the underlying engineering principles which form the basis of their manifold plans and constructions, and argues out the factors which have imposed the different architectural contrivances. Chapter 3 considers the biophysical dictates of water and air as respiratory media and livable habitats, the adaptive respiratory needs for survival in unique environments and circumstances, the effects of the different respiratory milieus and habitats on the fabrication of the gas exchangers, the essence of the diverse respiratory stratagems adopted by different animal taxa, and the effect of gravity on the design and function of gas exchangers. Chapter 4 looks at the structure and function of the archetype aquatic gas exchanger - the gills - and considers the placenta as an ephemeral liquid-to-liquid gas exchanger. Chapter 5 examines the limitations and constraints which confronted animals during the switch from water- to air breathing and the pivotal import of transitional (bimodal) breathing in the traumatic process of terrestrial invasion. Chapter 6 outlines a cost-benefit analysis of what went into the utilization of the atmospheric O_2 and the structural and functional prescriptions in the evolved air-breathing organs and structures. I must regardless concede that in this treatise, not all aspects and issues pertaining to the evolution of respiration and the form and function of the gas exchangers have been covered and those which are may not have been exhausitively discussed and satisfactorily resolved. Based on personal preferences on the subject matter and keeping in perspective the restriction of space, many elisions were made. Only the weighed imperatives were included. My objective will have been more than adequately met if the discourse provides areas for reflection, points for discussion, or, better still, aspects for further investigations on the many yet gray areas.

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Chapter 1

Perspectives on Life and Respiration: How, When, and Wherefore

> *"A reconstruction of the remote past must necessarily be based upon inference, rarely from systematically collected data, more often from an inadequate number of facts which chance has placed in the way of competent investigators who can recognize their significance. As time goes on some gaps are filled, others remain forever empty, but the picture as a whole becomes progressively clearer." Beadle (1974).*

1.1 Life: Diversity, Complexity, and Uniformity Fabricated on Simplicity

Humankind has always been fascinated by the spectacle of extreme states and phenomena. The *Guinness Book of Records*, which after the *Holy Bible* is alleged to be the second most widely read book, is according to the publishers compiled "in hope of providing a means for peaceful setting of arguments about record performances". Though not given much attention outside the professional realms, the elegance and constellation of life on Earth is enchanting, bewildering, and intellectually intriguing. More than 284 000 species of plants, 750 000 species of insects, and 280 000 species of other animals have been catalogued (e.g., Dixon 1994; Service 1997). Of this plethora, vertebrates represent only one phylum and a mere 50 000 species or so (e.g., Pough et al. 1989). Nature's fortitude for survival is remarkable. For example, albeit the tumultuous crises which preceded the Tertiary period when colossal population clashes occurred and many species were wiped out, by the end of the period, there were as many as 2500 families of animals (Benton 1995). From molecular sequence studies of different microcosms (e.g., Pace et al. 1985; Ward et al. 1990; Winker and Woese 1991; Olsen and Woese 1993), it is becoming unequivocally evident that, compared with the Metazoa and the Metaphyta (i.e., the visible world), the microbial domain (i.e., the microworld) presents a more complex biodiversity than was hitherto thought, and quantitatively remains largely unknown to us (e.g., Embley et al. 1994; Lovejoy 1994). The existing numerical data on the taxonomic diversity of animal life differ remarkably. It is envisaged that life's copious tree comprises between 5 and 50 million species of animals (e.g., May 1988, 1990, 1992; Hammond 1992). This hopelessly wide range owns up to the fact that we know very little of the actual richness and geographical patterning of contemporary animal life (e.g., Wilson 1992; Colwell and Coddington 1994). Since most of the crucial environmental processes are driven by the microbial activities which involve biochemical nutrient recycling operations such as nitrogen fixation, sulfur oxidation and reduction, ammonification, methanogenesis, and methane oxidation (e.g., Capone et al. 1997), it can legitimately be anticipated that the microorganismal biomass (which must form the base of life) should overwhelm that of plants and animals. The methanogenic bacteria which occur in the hindguts of many arthropods contribute substantially to the loading of the atmosphere with methane (e.g., Hackstein and Stumm 1994). Fenchel (1992) estimated that a 1 cm^3 core of coastal marine sediment contains 4×10^{10} bacterial cells, 10^4 heterotrophic flagellates and amoebae, 10^8 chlorophyll a-containing microorganisms, and about 2000 ciliates. Expressing a personal view on the ambitious program named Systematics Agenda 2000, which envisages that all the Earth's species will be discovered, described, and classified in the next 25 years (Anonymous 1993), Wicksten (1994) doubts that "the world's organisms will be described within the next century – if ever"! The same may be said on the Fifty-Year Plan (e.g., Raven and Wilson 1992). Applying the lengthy traditional methods of identifying and cataloguing species, May (1990), Hawksworth (1991), and Hammond (1992) envisage that it will take a couple of centuries to gain an adequate understanding of species diversity on Earth. With speciation being a continuous process (e.g., Butlin and Tregenza 1997; Smith et al. 1997), there may not be an actual end to the task. From the microbes to the whales, living animals differ in mass by at least 21 orders of magnitude (McMahon and Bonner 1983; Schmidt-Nielsen 1984; Brown 1995). The staggering numerical density, specific diversity, and allometric disparity is a clear testimony of the tenacity, resiliency, richness, and innovativeness of nature's designs for survival. It remains a great challenge to the biologists to fully explain the factors which drive and determine specific patterning (Hutchison 1959; Brown 1981; Cracraft 1994; Butlin and Tregenza 1997).

Until the enunciation of the theory of evolution through natural selection (Darwin and Wallace 1858; Darwin 1859), the complexity of life on Earth was scientifically inexplicable. Since then, the kaleidoscopy has been perceived as integral to the dynamic process of evolution (e.g., Ruthen 1993), with the degree of profuseness and variability a mark of success and suitability to an environment. The spatial and temporal distribution of species is set by definite physical, biological, and environmental controls. Through the about 4 billion years (billion = 1 thousand million years = 10^9) of existence on Earth, living forms have adopted behavioral strategies, developed biochemical and functional capacities, and appropriated certain devices which enable them to occupy species-specific niches. Such stable states have been attained amidst profound ambient changes that have included variations in the rotation of the Earth, changes in the Earth's orbit, fluctuations in the average surface temperature, physical displacements of the continental plates, pulses in the O_2 and CO_2 levels, and fluctuations in the availability of important nutrients (e.g., Hayes et al. 1976; Hunt 1979; Ben-Avraham 1981; Boucot and Gray 1982; Walker et al. 1983; Bray 1985; Raymo and Ruddiman 1992). In their different ecological settings, the nature, dynamics, and heterogeneity of environments detail the dissimilitude of animal life: form and function are molded by the physical and biotic factors in the ecotopes. Based on the separate traits they have acquired through interfacing with environments, animal life can be grouped into aquatic, terrestrial, and aerial assemblages. Finer divisions place them into, e.g., nocturnal, diurnal, fossorial, pelagic, arboreal, benthonic types, etc. Since environments are dynamic spaces (e.g., Schaffer and Kot 1986; Doebeli 1993; Rand and Wilson 1993), organisms must equally be phenotypically fluid to continually adapt to the external cues (e.g., Stearns 1982;

Prosser 1986). While freely interacting with the environment, organisms must not compromise their physical and biological integrity as self-sustaining, self-regulating dynamical entities. Energy must be obtained from the environment to regulate their internal states and defend homeostasis. To steady the environmental oscillations, strictly, organisms are a process in a nonsteady state (e.g., Levins and Lewontin 1985; Wainright 1988). As urged by Simpson (1953), when considering adaptation, "it is equally or more useful to focus neither on environment nor on organisms but on the complex interrelationship in which they are not really separable". The term comprehensive selective regime was used by Baum and Larson (1991) to define the combination of all the environmental and organismic factors which prescribe how natural selection acts on organismal variations. Chronobiology (circadian rhythmicity), a process which has evolved to sense and counterbalance the nuances of the environment, pervades all levels of biological organization from molecular, cellular, to organismal (e.g., Aschoff and Pohl 1970; Bünning 1973; Sweeney 1987; Ishii et al. 1989; Prinzinger and Hinninger 1992; Lloyd and Rossi 1993; Martin and Palumbi 1993; Page 1994). Through a mechanism termed endogenous clock or pacemaker (e.g., Sassone-Corsi 1996), circadian rhythmic activities occur even under constant environmental conditions (e.g., Aldrich and McMullan 1979; Prinzinger and Hinninger 1992). In such cases, it is thought that the property helps organisms anticipate the exigencies of life through programmed cyclic regulation of specific target genes. The common inhibitory neurotransmitter in the central nervous system, GABA (γ-aminobutyric acid), has been implicated in circadian rhythmicity (e.g., Wagner et al. 1997).

Life occurs in backgrounds which after cursory glance can resolutely be dismissed as being implicitly inhospitable. Nature, however, appears to abhor a vacuum. Practically every nook and cranny on Earth is filled with some kind of life. Animals which have adapted to extreme environmental circumstances have particularly intrigued biologists (e.g., Madigan and Marrs 1997). Habitats such as the subzero temperature glaciers (e.g., Arrigo et al. 1997), the fiercely hot bubbling hydrothermal (volcanic) vents in the deep seas (e.g., Meredith 1985; Jonnston et al. 1986), the highly desiccating tropical deserts, the fresh (nearly ion-free) water, the hypersaline lakes, the remote virtually anoxic reducing muds, and submarine environments where the hydrostatic pressures may exceed 1000 atmospheres have all been variably conquered and occupied. Life has been found at a depth of about 4 km below the surface of the Earth where the temperature is 75 °C (Ehrlich 1996; Frederickson and Onstott 1996) and in the ice-free, cold, dry valleys of the Antarctica, regions considered to be the closest terrestrial analogs of the Martian and other extraterrestrial planetary environments (Friedmann 1982; Friedmann and Ocampo 1976). While few, if any, multicellular organisms can tolerate a temperature above 50 °C (Huey and Kingsolver 1993), some microbes, i.e., the so-called hyperthermophiles, thrive at and above 100 °C (Madigan and Marrs 1997), the boiling point of water at sea level. In their quest to secure new habitats, organisms have devised design-specific solutions to the vast threats which have resolutely besieged them. These have ranged from momentous changes such as variations in solar insolation (e.g., Newman and Rood 1977; Frils-Christensen and Lassen 1991) and volcanic activity to minor spatial and temporal shifts in temperature and levels of respiratory gases in their immediate habitats. Such changes have had dramatic effects on the form, distribution, and lifestyles of animal life. Hippopotamuses are reported to have roamed the Yorkshire Dales some 125 000 years before present (Shackleton 1993) and in northern Africa, the Sahara-Sahel boundary crept northwards by 10° of latitude between 18 and 8 thousand years before present (Petit-Maire 1991). The overall fitness of an organism in a particular environmental setting is an aggregate effect of the different adaptive strategies an animal has requisitioned during its evolutionary existence (Kozlowski 1993). This arsenal confers the adaptive capacity to withstand adverse changes in the environment and, if necessary, to actively carve out and exploit new, more hospitable and resourceful habitats.

From the smallest known entities, the fundamental subatomic particles such as quarks, to the observable universe (the largest entity of which humankind has knowledge), a scale which ranges from under 10^{-15} to 10^{27} (Ronan 1991), nature is governed by four fundamental forces. These are gravity, electromagnetism, the weak force (the force responsible for radioactive decay), and the strong nuclear force (the force that holds the nucleus of an atom together). Gravity, of which the carrier particle (the graviton) is still undiscovered, is the weakest of the forces (strength 10^{-38}) but has an infinite range. The weak nuclear force, of which the carriers are the electrically charged W^+ and the W^- and the neutral Z° particles, has a range of 10^{-15} and a strength of 10^{-13}, the electromagnetic force, of which the carrier particles are photons, has an infinite range, a strength of 10^{-2}, and operates between electrically charged particles, while the strong nuclear force which acts on the quarks is powerful (strength $= 1$) but has a range of only 10^{-12}. By studying the universal properties of matter, science strives to understand and test how these characteristics contrived matter culminating in the phenomenon of life. It is hoped that the principles which govern organismal existence, design[1], behavior, function, and life-style can be better grasped as a part of such a broad fundamental and integrative approach. The quest for the elusive grand unified theory (e.g., Hawking 1993; Weinberg 1994), an attempt to integrate a number of independent mathematical equations which seek to demonstrate that three of the fundamental forces of nature (electromagnetism, and the weak and strong nuclear forces) are essentially performances of the same superforce, continues with zeal and zest. After unification with gravity, the theoretical physicists contemplate advancing the "theory of everything", an encompassing principium which should explain the formation of the Universe at the Big Bang, the subsequent existence of the material world, and perhaps the development of life (Moore 1990a; Maynard-Smith and Szathmary 1996; Ronan 1991) and the end of it all at the Big Crunch. Though some measure of success has been achieved, especially in harmonizing the weak and electromagnetic forces, from what is

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[1] The term design, which is borrowed from engineering, is used in this book in a sense to mean "creative natural arrangement of parts (= components) in a device (= gas exchanger) for a particular purpose (respiration)". Vogel (1988) defined biological design as "functionally competent arrangement of parts resulting from natural selection".

known presently, the cosmos abounds with mystery and deliberately shuns order and conformity. While the Newtonian laws apply in the intermediate scales of biology, at subatomic (the so-called nanoworld) level, quantum mechanics reigns, and at the cosmological level, relativity holds true. Recently, a concept dubbed new physics was professed to be highly rewarding in analyzing the dynamics of the life processes (Davies 1989; Stonier 1990). The approach is based on arguments that: (1) life is transmitted through what are bits of information (algorithms) inscribed in the genome and (2) the frequency and amplitude of biological events are regulated through ultrafast integrated information processing. Applying an electronic analogy, Lloyd and Rossi (1993) asserted that "the living state is an ensemble of oscillators" and that information processing may be the "common denominator" (the missing link?) in the formulation of a "unifying theory". Inasmuch as our understanding of biological processes (especially neurobiology) continues to accumulate with the advances in computer technology, this supposition appears to be credible (e.g., Adams 1979; Kawasaki 1993). Other lines of inquiries attempting to simplify and explain biological order and diversity include the so-called life-history theory (e.g., Charnov 1993; Ruthen 1993) and the synthetic theory of biological organization (e.g., Eigen and Schuster 1979; Fontana and Buss 1993). According to these concepts, it is argued that for a given organism, if the fundamental parameters which govern and regulate resource procurement, utilization, regeneration, and self-perpetuation in a particular environment are known, it would be possible to model the life patterns which optimize fitness (Charnov 1997; Godfray 1997). Reductionism and all mechanistic approaches to biology endeavor to explain natural phenomena by manipulating fewer and simpler components that are responsive to exact simple physical laws (e.g., Popper 1968, 1969). However, when dealing with complex natural dynamical entities like organisms (e.g., Mann 1982; Brown 1993), it is not only difficult to correctly identify such components but also practically impossible to predict the outcomes of their myriad nonlinear interactions. Due to the hierarchical organization of biological systems from atomic, molecular, cellular, tissues, organs, organisms, through populations and communities to ecosystems, boundary conditions exist (Brown 1994): it is practically impossible to predict the outcomes from one level of organization to another (Polanyi 1968). Despite the caveats, the rationale behind the rather esoteric reductionistic investigations in biology includes among others the warranted recognition that although biological systems may evolve through means different from those that accrete the physical ones, their forms and states are fundamentally governed by the universal, permeative properties of matter and energy (e.g., Nagel 1961; Brooks 1994). The structure and the mechanistic chemical juxtaposition of organic molecules is a programmed process which generates exact structural configurations and arrangements which yield stable states. Life cannot violate the immutable laws of physics and chemistry during its development. Thompson (1959, p. 8) points out that "the forces which operate in the body are of the same character as are the inorganic forces". He envisages that mathematics and physics will greatly contribute in explaining biological phenomena even though they may not fully account for certain aspects that he consigns to the "soul". As cautioned by Giebisch et al. (1990) and Nurse (1997), when dealing with an intricate process such as life, reductionistic approaches may fail simply due to the fact that the underlying assumption that encompassing properties of an organism can be understood by studying its individual parts could be fatally flawed. The aggregate expression of the functional processes in an organism is not necessarily equal to that expressed by the intact animal. Thompson (1959, p. 41) observed that "the life of the body is more than the sum of the properties of the cells of which it is composed" and Hoagland and Dodson (1995) note that "an organism is greater than the sum of its parts". The total of the O_2 consumption of the individual tissues of the body, for example, may be lower (e.g., Weymouth et al. 1944; Itazawa and Oikawa 1983; Oikawa and Itazawa 1993) or higher (e.g., Terroine and Roche 1925; Crandall and Smith 1952; Vernberg 1954; Lilja 1997) than that of the whole animal. Based on a similar observation, Von Bertalanffy and Estwick (1953) proposed that the decrease in the mass-specific metabolic rate of an intact animal is regulated by "factors lying in the organism as a whole which do not appear in tissues excised from the intact animal". Brown (1994) contends that "while physical scientists seek precise answers to relatively simple problems, biologists on the whole seek approximate answers to very complex problems".

In what may be deemed convergence between natural and human engineering designs, modern research into natural configurations has led to the fascinating discipline of bionics (= *bio*mecha*nics*) (e.g., Nachtigall 1991; Witt and Lieckfeld 1991). Astonishing parallels in the "plans" and "constructions" of living organisms with technical principles abound. Though nature uses essentially the same structural materials as those used by human beings (i.e., materials found on Earth), while it is possible to mimic them, it is virtually impossible to exactly duplicate natural designs. During the long period of evolution, through progressive and yet recursive trial-and-error processes (e.g., Schaeffer 1965a), nature has honed and produced perfect or near-perfect innovations. Natural solutions for complex problems are often strikingly simple and fascinating (e.g., Hayes 1994): minimal resources are committed in configuring highly cost-effective structures. Amidst the remarkable diversity of form at the organismal level, however, the differences that distinguish the various kinds of life in the macroscopic and microscopic worlds disappear down the organizational cascade as similarities preponderate. From the perspective of structural chemistry, at the molecular and atomic levels, there are no differences between the living and nonliving worlds: organic molecules are made up of essentially the same elements (atoms) which comprise the inorganic ones but are arranged into complexes with unique properties. Life's diversity can be attributed to differences in the characters and arrangements of protein molecules which constitute more than half of the nonwater mass in a cell (Hoagland and Dodson 1995). Though the number of molecules which formed with the accrual of the Earth (inorganic evolution) and development of life (organic evolution) (Kirschner 1994; Weinberg 1994) is immense and to this bounty chemists keep on throwing in new ones, from this vast collection, life has been extremely selective on what it has appropriated. Of the about 8 million now known chemical compounds (e.g., Morgan 1995), only a very small number has been incorporated in the evolved biochemistry. Proteins, some of the largest and most complex molecules known and perhaps the most important organic factors, as they form enzymes which catalyze chemical reactions, are configured around only 20 different amino acids. From the infinite three-dimensional possible dispositions, the forms and behaviors of proteins are limitless (e.g., Ronan 1991). Amazingly, the amino acids are produced through a code which is written in only four molecules (the nucleotide bases) which present 64 possible arrangements in triplets, the codons: 61 codons are distributed among 20 amino acids, the other 3 serving as stop codons. Proteins are intrisically dynamic molecules. Flauenfelder et al. (1991) pointed out that evolution occurs through changes in the primary sequence of proteins, a process which leads to changes in the structure and the conformational energy landscapes. From the well over 100 known elements, about 99% of the living matter is fundamentally made up of four elements, i.e., C, O_2, N_2, and H_2. Of the 28 selected elements in the human body, H_2 and O_2 are the most abundant, respectively comprising 63 and 25.5% of it. Carbon is central to life. It forms chains and rings that can be elaborated into an immense number of complex compounds and makes up about 1% of the mass of the Earth. Carbon-based fuels contribute about 75% of the energy that is currently used on Earth. Methane is the most abundant organic molecule in the Universe (Ancilotto et al. 1997).

Succinctly put, biology uses a characteristic set of elements and compounds to carry out an infinite array of processes. It is bewildering that the most complex state of organization that matter has consummated has been fabricated through remarkable simplicity, essentially during a chemical circumstance which entailed microscopic architecture around the carbon atom. Though the chemical constituents of living organisms have been recognized and the biochemical processes which support life are now reasonably well understood, the actual origin of life remains a mystery (Szathmàry 1997). It is now known that organic molecules abound in the cosmos. Such molecules could have been seeded on Earth from space (e.g., Ronan 1991; Cohen 1995), landing at the right place at the right time. The recent report by NASA scientists on chemical fingerprints of extremely primitive life in a 4.5-billion-year-old piece of Martian rock (Kerr 1996a; McKay et al. 1996) may in future totally change our concept and the very definition of life.

1.2 The Earth: a Highly Dynamic Planet

Though from space it looks serene and motionless, the Earth is a perpetually metamorphosing planet. Life, the most complex organization of matter, has astonishingly evolved against a highly dynamic setting. Geometrically about a sphere (but strictly an ellipse) some 12700 km in diameter, a mass of about 6×10^{21} tonnes and a volume of about 1.1×10^{12} km^3, it spins round on an inclined axis (23.5° to the perpendicular of the plane of its orbit) at a speed of about 28 km/s (at the equator), moving around the sun (from a distance of 150 million km) along a slightly elliptical orbit about 300 million km in length at an incredible speed in excess of 1700 km/s. The rotation is completed in 23 h and 56 min and the revolution (around the sun) takes 365.25 days: the rotation causes day and night while the revolution occasions seasons. Different places on the Earth's surface move at different speeds, the speed at the equator being the greatest. The spin greatly influences the shape (e.g., Dixon 1987), distorting the spherical figure to a slightly flattened shape and creating many irregularities on the surface: the polar diameter is about 43 km less than the equatorial one. In what has been called the Colioris Effect, due to the rotation, in the Northern Hemisphere a mass of air around a high pressure area is deflected in a clockwise direction and counterclockwise around a low pressure one: in the Southern Hemisphere there is an opposite effect. A centrifugal acceleration which tends to oppose gravity makes the value of gravity at the equator ($9.780\,m\,s^{-2}$) 0.35% less than that of $9.832\,m\,s^{-2}$ at the poles: the maximum gravity ($10.5\,m\,s^{-2}$) is reached at the boundary of the liquid core some 2900 km below the Earth's surface. Near the surface, gravity decreases by about $0.003\,m\,s^{-2}\,km^{-1}$ distance above sea level. While the angular momentum in an elliptical orbit remains constant, according to Kepler's Second Law of Planetary Motion, at periastron (when the radius of the orbit is small) the speed is faster and at apastron (when the radius of the orbit is greater), the speed is slower. The giant outer gas planets, namely Jupiter, Saturn, Uranus, and Neptune (the Jovian planets), have solid cores surrounded by cold atmospheres of light gases such as methane, ammonia, helium, and hydrogen. The Earth, like the other three inner planets, i.e., Mercury, Venus, and Mars (terrestrial planets), is made up of a dense iron-nickel core (some 3400 km in radius at a temperature of 3700 °C), a rocky mantle 2900 km thick, and an outer shell, the crust (lithosphere) some 50 km thick. The light gases were lost from the terrestrial planets due to the fact that: (1) they are closer to the sun and hence received more heat that highly excited the gas molecules and (2) their smaller gravitational forces were not adequate to retain the fast-moving molecules. Compelling an escape velocity of 11.8 km/s, the Earth has been able to hold onto most of its gases except for the very light ones like hydrogen, neon, krypton, and argon. Hydrogen, produced by photodissociation of water vapor in the stratosphere, is presently estimated to be escaping from the Earth's atmosphere at a rate of 3×10^8 atoms $cm^{-2}\,s^{-1}$ (Donahue 1966; Joseph 1967; Hunten 1973; Hunten and Strobel 1974; Hunten and Donahue 1976). A planet or a satellite has to be more than 10% of the mass of the Earth to be able to hold its atmosphere. About two thirds of the Earth's surface is covered with water. The gravitational pulls of the Moon and the Sun cause tides and the movement of the air masses weather. Water (hydrosphere), air (atmosphere), and the superficial layer of the lithosphere (the soil) constitute the biosphere. They are the theaters in which life has experimented and developed.

1.3 Factors that Encouraged the Evolution of Life on Earth

Whether by default or design, the Earth is peculiarly well conditioned for habitation, at least by the kind of life which we know. As prescribed by nature, organisms adapt and evolve into environments: they do not carve them out to suit themselves. The fundamental factors which "allowed" life to develop on Earth included: (1) an O_2-rich atmosphere with the moderate level being just appropriate for the respiratory needs for life (Urey 1959), (2) location at a right distance from the sun (orbiting between the terribly hot Venus and the hard frozen Mars) for the temperature to support presence of water in both liquid and vapor form, (3) the accretion of the giant planets like Jupiter, Saturn, Uranus, and Neptune drastically reduced the number of comets and other debris in orbit, minimizing the devastating effects of collision with the Earth (Weidenschilling and Marzari 1996), (4) the presence of atmospheric gases like CO_2 provided a mild greenhouse effect which kept the planet warm, (5) the mass of the Earth (and hence its gravity) is just right to hold and prevent loss of most atmospheric gases to the outer space without undue pressure on life, and (6) the Earth's magnetosphere is adequately strong to prevent sputtering of the atmospheric gases by the constant bombardment of energized ions. Jupiter's largest moon, Ganymede, with a magnetic field about one tenth that of Earth but greater than that of Mercury, Venus, and Earth's moon (Gurnett et al. 1996), has a thin atmosphere (Stevenson 1996) with O_2 in a frozen state (Vidal et al. 1997). Though Mars, with its distant orbit which is 50% farther from the Sun than Earth, now presents a desolate, cold, and dry surface with a small ice cap especially at its north pole, in the past the planet appears to have experienced episodes during which an atmosphere may have existed to create a greenhouse effect adequate to generate ample liquid water on the surface (Kargel and Strom 1996): over time, the planet has lost large quantities of CO_2 as well as O_2 and H_2, gases derived from breakdown of atmospheric water by sunlight, leaving a thin 7-km-thick gaseous envelope. The planet's atmosphere has been worn out (sputtered) by energetic O^+ ions created from escaping O_2 and hurled back to the atmosphere by the solar wind fields (Johnson and Liu 1996). The highly rarefied Martian atmosphere compares with that of Earth at an altitude of 50 km, the atmospheric pressure being less than 1% of that on Earth. It cannot be completely ruled out that under similar or different circumstances a kind of life could have evolved elsewhere in the Universe (e.g., Powell 1993). Possible past occurrence of primitive life on Mars has been advanced (e.g., Kerr 1996b; McKay et al. 1996) and existence of life in other celestial bodies argued (e.g., Chyba 1997).

The Earth's atmosphere weighs about 500 million million tonnes. About 50% of it is in the lower layers about 5 km from the Earth's surface. The troposphere, the part of the atmosphere where the air is well mixed, extends up to an altitude of about 10 km above sea level and constitutes 80% of the total mass of the atmosphere. Barometric pressure is a consequence of the Earth's gravitational pull on the air which envelopes it. From the surface of the Earth, barometric pressure drops exponentially. However, at a given altitude, the actual pressure depends on factors such as latitude, season, and the prevailing weather conditions (e.g., Bouverot 1985). For every 5.5-km ascent from sea level (where the barometric pressure is 1013 mbar), the barometric pressure drops by a half and the temperature drops at a rate of 1 °C for every 150 m. Beyond 500 km, the atmosphere (exosphere) is highly rarefied and contains free atoms of O_2, H_2, and helium. The most important respiratory gases in air are O_2 and CO_2. At normal pressures, N_2 is considered to be physiologically inert, but at high pressures it is harmful to life.

1.4 Oxygen: a Vital Molecular Resource for Life

The Lord God formed the man from the dust of the ground and breathed into his nostrils the breath of life, and the man became a living being. (Genesis 2:7)

There are few, if any, processes in biology which are as encompassing and critical for life as respiration. For most animals, procuring O_2 from outside and delivering it to the tissues and voiding CO_2 produced from tissue oxidative metabolism are some of the main tasks of respiration. Laitman et al. (1996) assert that "the acquisition and processing of O_2 and its by-products is the primary mission of any air-breathing vertebrate". Just now (as you read this line) you are breathing O_2 and would die in a couple of minutes without it. Beyond about 3 min of cessation of breathing, irreparable damage, especially of the central nervous system, could occur even after successful resuscitation, and after about 6 min one would be declared brain dead. From a practical standpoint, this bespeaks the importance and urgency of procuring molecular O_2 at the right time and in the right quantities. In the course of evolution, preference would have been given to the organs and systems which support such crucial process. Though other cells such as the neurons (e.g., Schömig et al. 1987), endothelial cells (e.g., Mertens et al. 1990), and smooth muscle cells (e.g., Paul 1989) can cover energy deficits by anaerobic glycolysis, except for the hearts of the freeze-tolerant animals which stop at subzero temperatures (e.g., Storey and Storey 1986, 1988), the continuous mechanical performance of the myocardial cells is totally dependent on transient changes in cytosolic Ca^{2+} (interacting with contractile proteins) and sustained oxidative production of energy in the mitochondria (e.g., Driedzic and Gesser 1994; Piper et al. 1994). While there are assertions that life can exist without O_2, such states can only exist in the simplest forms of life (Hochachka et al. 1973; Herreid 1980; Fenchel and Finlay 1990a, 1991a, 1994). Intestinal parasites are alleged to live without molecular O_2 and intertidal molluskan facultative anaerobes remain for days without it (Ghiretti 1966). In adverse conditions, adaptively, some animals enter latent (ametabolic) states where in cryptobiosis (Hochachka and Guppy 1987), the most extreme of such conditions, life virtually stops. However, even in such states, an infinitesimal amount of energy must be produced by the cells to sustain the crucial molecular processes of life such as protein turnover and ion flux. Even before the discovery of O_2 was made by Priestley and the composition of air demonstrated by Lavoisier (see Perkins 1964 for an account of these elegant discoveries), it was recognized that breathing, the mechanical pumping of air in and out of the body, a process which occurred in the majority of animals, was essential for life. For a long time and until recently, a test for death was the failure of breathing and the common method of killing was by strangulation. Presently, the phrase "the breath of life" is commonly used to indicate the need for continuous movement of air in and out of the body to support life. The comprehensive need for O_2 for life was termed the call for oxygen by August Krogh (Krogh 1941).

Generation, storage, and utilization of energy are processes central to the activities and the very existence of living cells, just as they are relevant to the proper economic management of the Earth's resources. Excess energy is largely conserved in form of carbohydrate and lipid molecules to be utilized in event of deficit. The acquisition and utilization of energy in life occurs according to Maxwell's Laws of Thermodynamics. According to the first law, the amount of energy in the Universe is fixed: no more of it can be created nor can the existing amount be destroyed but can be converted from one form to another. In face of the steadily decreasing amount of freely usable (accessible) energy in the Universe (according to the Second Law of Thermodynamics), the natural state of matter is chaos (e.g., Prigogine and Stengers 1984). Since living systems constitute highly organized complex states of matter, from a casual glance, it would seem that life runs uphill in a downhill Universe, i.e., it proceeds counter to the natural dissipation of energy. In such a case, life would appear to negate the Second Law of Thermodynamics. This, however, is not the case. In fact, instead of threatening life, the Second Law of Thermodynamics actually guarantees it. Unlike the closed thermostatic state of the ordinary (controlled) chemical reactions, living systems are open thermodynamic processes which access energy from outside (especially from the sun) to steady entropy (chaos) through effervescent repair and rebuilding at the molecular level. Generally, organisms are efficient conduits of energy in the vastness of the Universe. Evolution by natural selection is thought to be driven by competition for the dwindling amount of energy in the Universe (e.g., Blum 1955). Much of the energy on Earth is conserved in the covalent bonds, especially of the large organic molecules such as glucose, fatty acids, starch, and glycogen. Intricate interdependency exists in nature where, directly or indirectly, living things rely on each other in appropriating raw materials and harnessing energy. Over time, evolution has modified morphological design and physiological processes to eliminate or reduce unnecessary expenditure of energy. More optimal states are established to better manage the finite resources. Superfluous structures are eliminated and hence support of unused or underutilized capacities is avoided.

No molecule has been as pervasive in its influence on life and paradoxical in its roles as O_2. In all evolved complex animal life, O_2 is the most important molecular factor contracted from the ambient milieu. The metabolic rate of an organism correlates with the efficiency of procuring it. Nature has been particularly inventive in the development of gas exchangers and the respiratory processes. The many examples of convergence show that permeative forces have been involved in programming the design of the gas exchangers. Regarding the procurement and utilization of energy, living things are essentially open thermodynamic systems in a self-regulating steady state. A continuous influx and efflux of matter and energy occur as the necessary physiological and behavioral adjustments are made to maintain homeostasis. Such a dynamic state ensures that, though intimately relating to its immediate environment, an organism remains a viable, discrete entity. While life can be defined as a process of capturing and utilizing energy and raw materials, empirically, death is the cessation of all such activities, i.e., when energy production falls to zero. In such a state, the energy in a body is at equilibrium with that in the environment. For individual animals, the continuity of respiration is terminated at death, and for a species at extinction. Animals will generally live for weeks without food, days without water, but only minutes without O_2. Activities such as feeding, thermoregulation, locomotion, and even reproduction (e.g., Hurst and McVean 1996) can be adjusted, delayed, or abandoned altogether, depending on species and circumstances (McNamara and Houston 1996).

Energy is decisive in all biological events from molecular, biochemical, ecological to evolutionary levels (e.g., Bennett 1988). It is required for building, servicing, and maintaining the general infrastructural integrity of an organism as well as driving the physiological processes and fortifying homeostasis against external perturbations. The rate of respiration indicates the speed at which an animal uses its resources to meet the demands placed on it by the environment and the lifestyle it leads. Those species capable of maintaining a high rate of O_2 to CO_2 exchange ratio in relation to the volume and the complexity of the protoplasmic mass are able to establish stable tissue fluid gas concentrations under different environmental circumstances and metabolic states. It is unequivocally evident from the design of the gas exchangers that such specialized taxa are the most successful. From the earliest recorded fossils, which are 3.8 to 3.5 million years old (Schopf 1978, 1993; Mojzsis et al. 1996), to the first well-documented composite organisms, the ediacaran Metazoa which occurred more than 600 million years ago (e.g., Gould 1989; Knoll 1991; Levinton 1992; Runnegar 1992), for over 80% of its tenure on Earth, life remained exclusively unicellular (Gould 1994) and anaerobic. It is thought that lack of O_2 in most of the Precambrian may have been the main factor which repressed further progress (Knoll 1991): the so-called Cambrian explosion, when the biota underwent remarkable diversity, has been associated with the presence of and the increasing levels of molecular O_2.

1.5 Anaerobic Metabolism and Adaptive Success in Animals

The capacity to procure, transport, and utilize large amounts of O_2 has bestowed a monumental selective advantage on the evolution and adaptive radiation of the terrestrial vertebrate fauna. Predator avoidance correlates with the level of energy expenditure and the kind of food eaten (e.g., McNab 1966). Terrestrial species with low metabolic rates rely heavily on burrows or passive integumental structures such as shells, plates, and spines for protection. The evolution of efficiently ventilated and perfused gas exchangers and carrier-mediated O_2 transport systems appear to have been fundamental for supporting energetically demanding life-styles. Metabolic rate expresses the integral speed at which energy is mobilized, transformed, and utilized by an organism for biological activities (e.g., Kleiber 1965; Calder 1987; Brown et al. 1993; Lundberg and Persson 1993) and hence expresses the vitality of life (e.g., Zeuthen 1970; Calder 1984). In mammals, factors such as enzymatic activities (Emmett and Hochachka 1981), enzyme contents of tissues (Drabkin 1950), O_2 consumption (R.E. Smith 1956), and protein turnover (Munro and Downie 1964) reflect the effect of body size on metabolism. An inverse correlation between the specific metabolic rate (amount of O_2 consumed per gram body mass per unit time) of animal species and their life spans has been established (e.g., Adelman et al. 1988; Shigenaga et al. 1989). Dwarf mice live much longer than normal ones by as much as 350 days for males and 470 days for females (Brown-Borg et al. 1996).

Thompson (1959, p. 42) forthrightly stated that "size of body is no mere accident". Metabolic rate determines vital aspects such as life patterns, population fluctuations, behavioral ecology, and reproductive efficiency (e.g., Prothero 1986; Calder 1987; DeAngelis et al. 1991; Dunham 1993; McNamara and Houston 1996). In the modern ecosystems, the chance of extinction is directly proportional to body size (e.g., Carroll 1988). Diverse factors such as phylogeny, habitat, ambient temperature, O_2 consumption, food intake, latitude, climate, season, body size, shape, level of development, degree of activity, sex, and age to varying extents determine the metabolic rate (e.g., Zeuthen 1953; Else and Hubert 1985; Crews et al. 1987; Labra and Rosenmann 1994). Unlike metabolic substrates, e.g., carbohydrates and fats, which can be stored in large quantities in the body, except in a few heterothermic and anaerobic parasites (e.g., Ghiretti 1966), O_2 has to be derived from the external environment in the necessary measures. In the human being, about 12000 l of air are filtered by the lung everyday (Burri 1985). The amount of O_2 dissolved in blood or plasma is insufficient for tissue requirements even at rest. The quantity falls far short of the amount which would be required to service physical activity when the uptake may increase by as much as 30 times during vigorous exercise, e.g., flight (Thomas 1987). A human being at rest requires 200 to 250 ml O_2 min^{-1} but during maximal exercise the amount increases to about 5.5 l min^{-1} (Comroe 1974; Weibel et al. 1987a). A 70-kg human being has only 1.55 l of O_2 in the body at any one moment, 370 ml being in the alveolar gas, about 280 in the arterial blood, about 600 in the capillary and venous blood, 60 ml dissolved in body tissues, and 240 ml bound to the muscle myoglobin (Farhi 1964): the total amount is adequate to support life for only 6 minutes, but irreparable damage starts to occur within about 3 min of cessation of breathing. Snyder (1983) observed that the amount of O_2 dissolved in tissue (about 0.8 ml/kg) is sufficient to support aerobic metabolism for only a few seconds. However, in the champion divers, e.g., the Weddell seal, *Leptonychotes weddelli* (Kooyman 1985), in a 450-kg animal, the O_2 stored in the muscles can support aerobic metabolism at a rate of 4.2 ml O_2 kg^{-1} min^{-1} for about 15 min. At an estimated O_2 consumption rate of 1.6 ml O_2 per kg, a 20-tonne sperm whale, *Physeter catodon* can dive for 50 min while maintaining aerobic metabolism (Butler 1991a). The body stores of CO_2 in solution and in form of HCO_3^- ions exceed those of O_2 (Farhi and Rahn 1955). It is perhaps owing to its intrinsically great toxicity (e.g., Fenchel and Finlay 1990b) (Sect. 1.16.1) that animals have not evolved capacities of storing appreciable amounts of O_2 in the body tissues and cavities: the rate of O_2 uptake from the environment is approximately equal to its utilization. The infinitesimal amounts held in the bodies of most organisms, either chemically bound or in solution, are able to support aerobic requirements for only a short period of time. In some fish with physoclistic swim bladders, however, O_2 is held in the swim bladder at high pressures and concentrations (Saunders 1953). Such stores can be utilized during hypoxia (Randall and Daxboeck 1984) with adequate tissue oxygenation being sustained for several hours.

1.6 Evolved Mechanisms and Strategies of Procuring Molecular O_2

Respiration has been pivotal in all the evolutionary and adaptive changes which have occurred in animal life. This is evinced by the fact that to a fair measure, the functional competencies of the gas exchangers correspond with the general phylogenetic statuses of animals. Respiration encompasses an impressive arsenal of biomechanical, physiological, and behavioral strategies and mechanisms that are involved in making available to an organism a sample of the external respiratory milieu from which molecular O_2 is extracted and into which CO_2 is voided. External respiration involves movement of two vectorial quantities in opposite directions, namely, influx of O_2 from the environment and efflux of CO_2 from the organism. Oxygen is delivered to the tissue cells across a panoply of structural compartments through self-regulating convective and diffusive processes. The operation starts with convective delivery of O_2 by a respiratory medium (water and/or air) to the gas-exchanging site, diffusion across the tissue barrier, binding to carrier pigments, convective transport by blood circulation, and ultimately diffusion from the blood into the cells (Figs. 1,2,3). In a steady nonlimiting state, servomechanically, the flow of O_2 from the environment across the steps to the mitochondria is constant (Weibel 1982; Wagner 1993). Mitochondria contain all enzymes associated with the processes of oxidative phosphorylation in their inner and cristae membranes and the enzymes of the TCA cycle in the mitochondrial matrix. The influx of O_2 into the mitochondria, the terminal O_2 sink which determines the flow of O_2 across the lung through the cardiovascular system (e.g.,

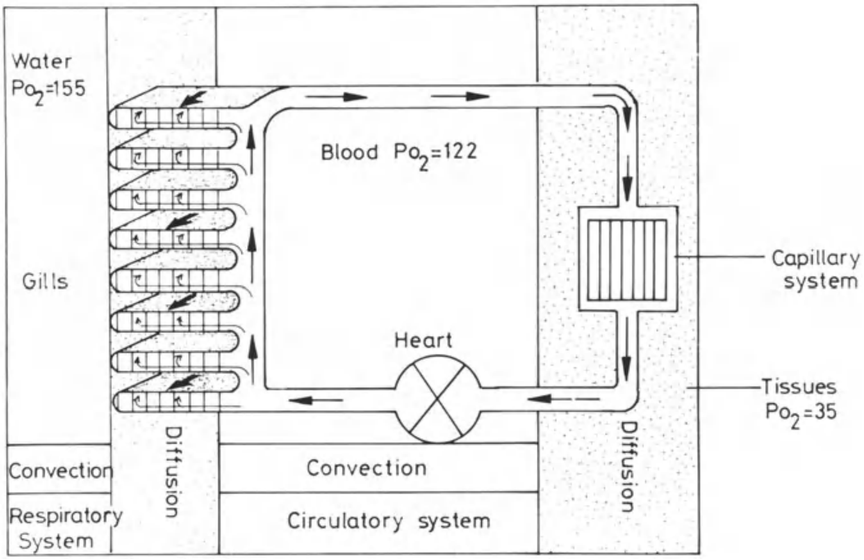


Fig. 1. Sites of convective and diffusive gas transfer in an aquatic breather. Water and blood spatially relate in a countercurrent manner at the gills. (After Satchell 1971)

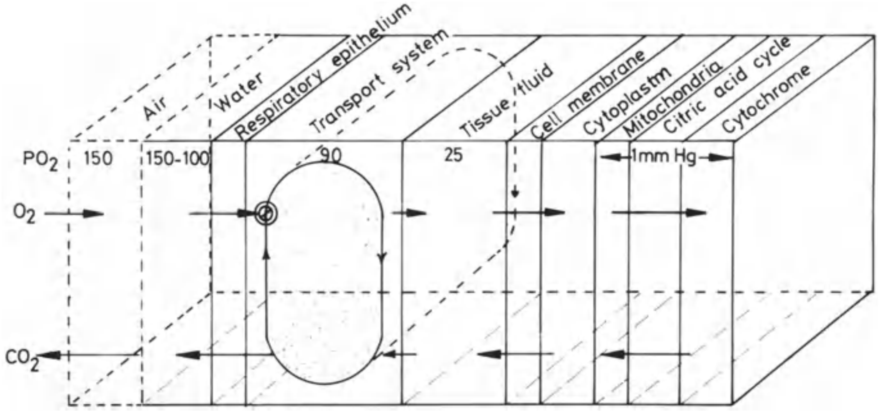


Fig. 2. The intricate stratified arrangement of the gas exchange components in the diffusional pathway of O_2 from the external milieu to the mitochondria. The partial pressure of O_2 gradually decreases towards the tissue cells. CO_2 is greatest in the tissues and is eliminated in the opposite direction to that of O_2. (After Hughes 1978)

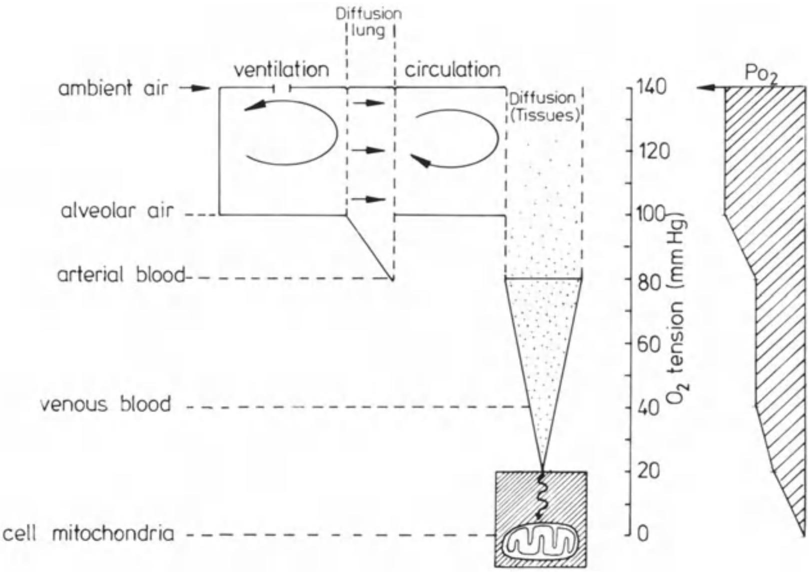


Fig. 3. Cascade process of delivery of O_2 from the ambient milieu in an air breather with a convective lung. The ventilatory and circulatory systems maintain a partial pressure gradient across the air/blood interface. The PO_2 decreases towards the tissue cells and the mitochondria. The utilization of O_2 in the mitochondria maintains the flow. The components of the pathway are quantitatively sized to optimize flow. (Wood and Lenfant 1976)

Suarez 1992), is set by the phosphorylation potential of the tissue cells (Folkow and Neil 1971; Taylor et al. 1987a, 1989) especially in the skeletal muscle mass, which constitutes about 50% of the body mass in mammals and as much as 80% in fish (Goldspink 1985): the PO_2 drops from about 20 kPa in water or air to almost zero in the vicinity of the mitochondria of the outlying tissues (Wittenberg and Wittenberg 1987, 1989; Graiger et al. 1995). Between the capillaries of the heart muscle and the mitochondria, the PO_2 drop is 2.7 kPa (Tamura et al. 1989) and that between the cytosol and the mitochondria is less than 0.03 kPa (Wittenberg and Wittenberg 1987, 1989; Clark et al. 1987). In a rat (mean body mass 266 g), the total mitochondrial surface area in the liver, kidney, heart, brain, and lung is $460\,m^2$ and in a 1.8-kg bandicoot the value is $5520\,m^2$ for the same organs (Else and Hubert 1985). The drop in the PO_2 between the capillaries and the surrounding tissues is inversely proportional to the permeability of the tissue to O_2 (Meng et al. 1992). In exercising human gastrocnemius muscle, the O_2 tension decreases with the intensity of contraction, indicating that O_2 may be a limiting factor for mitochondrial respiration (Fellenius et al. 1984): under such conditions, the PO_2 in the extracellular fluid may decrease by 70% and in the cells by 30% of the resting values. To increase the flow of O_2 from water to the tissues, the heart muscle of the hemoglobinless Antarctic icefish is profusely supplied with blood (Fitch et al. 1984; Johnston and Harrison 1985): the muscle mitochondrial volume density rivals that of the insect flight muscles (Londraville and Sidell 1990) but myoglobin is lacking in significant quantities (Douglas et al. 1985; Feller and Gerdy 1987; Sidell et al. 1987). The complexity of the O_2 conduction line differs between animals. It depends on factors such as body size, environment occupied, and lifestyle. In the Protozoa, O_2 diffuses across the cell membrane into the protoplasm. The simple invertebrates lack a circulatory system while the more complex ones and the vertebrates have a circulatory system which convectively transports O_2 from the respiratory site(s) to the body tissue cells. In insects (Sect. 6.6.1), O_2 is delivered directly to the tissue cells by the trachea. Internal respiration entails utilization of O_2 at cellular level to generate the high energy molecule adenosine triphosphate (ATP), with CO_2 and water as secondary products. Expulsion of CO_2 occurs in the opposite direction to that of O_2, i.e., from the tissue cells to the gas exchanger, driven by the same mechanisms (Hills 1996) but carried through somewhat different processes (e.g., Davenport 1974; Heisler 1989): CO_2 excretion occurs through a passive process along an electrochemical gradient from the site of production (Bidani and Crandall 1988; Nikinmaa 1990).

Depending on the function(s) they carry, organ systems have different needs for O_2 (Else and Hubert 1983). By default, the gas exchangers are the only organs in which a conflict of interests can occur. For efficient uptake of O_2, the designs must effect transfer O_2 with minimal utilization of it. Without compromising their functional integrity, as little tissue as possible must be committed in the construction of the gas exchangers. In the avian lung, the bodies of the extremely thin epithelial cells which line the air capillaries are confined to the atria and to a lesser extent in the infundibulae, which are non gas exchange sites (Figs. 88,90). In its thinnest sections, the blood-gas barrier of the avian lung consists of an endothelial, an epithelial, and a common basement membrane (Maina and King 1982a): interstitial spaces are largely lacking (Figs. 29,40). On average, the vertebrate lung is estimated to utilize as much as 10% of the total body O_2 consumption (Slonim and Hamilton 1971).

While O_2 transfer in simple organisms occurs by simple diffusion across the entire body surface, in the more complex ones this takes place at specialized sites where tissue barriers are crossed. In spite of the intrinsic differences in the structural complexities, after about 2 billion years of evolution of aerobic metabolism, the transfer of molecular O_2 in all evolved gas exchangers still occurs by passive diffusion – only ways have changed but means have remained essentially the same. Aerobic metabolism must have evolved at a critical point when the ambient PO_2 was just adequate to drive the gas across the cell membranes of the amphiaerobes. The gradual increase of the PO_2 in the bioshere lead to reduction in the respiratory effort, supporting greater metabolic capacity. The delivery of O_2 to the cells/tissues appears to have been machanistically optimized right from the point of incorporation of molecular O_2 into the aerobic processes. For a substance that is needed continuously throughout life, the alternative method of acquisition, i.e., by active means, as was envisaged to occur in the vertebrate lungs at the turn of this century (see, e.g., Haldane 1922), is improbable. To support respiration driven through active acquisition of O_2 would obligate an enormous investment in energy, rendering the entire process uneconomical and perhaps untenable within the present designs of the gas exchangers and the activities which animals perform. Gas exchangers are largely multifunctional organs. Many play nonrespiratory functions which are in some cases equal to, if not more important than, respiration (Sect. 6.10). Fish and crustacean gills, for example, serve indispensable osmoregulatory roles, are the principal pathway for ammonia and urea excretion, and are involved in the regulation of levels of some blood chemical factors, e.g., hormones (e.g., Zadunaisky 1984; Gilles and Pequeux 1985; C.M. Wood et al. 1989, 1994). The human lungs are important sites for elaboration, metabolism, and regulation of the concentrations of various active pharmacological agents in the body (e.g., Slonim and Hamilton 1971). The lung removes from circulation or destroys such chemical factors as prostaglandins, serotonin, and bradykinin, converts angiotensin I to angiotensin II, and synthesizes lipids such as the pulmonary surfactant (Sect. 6.10): the high O_2 consumption of the vertebrate lung can be attributed to these metabolic processes. While the design requirements for gas exchange demand minimal tissue infrastructure, there must be a critical mass necessary to carry out the nonrespiratory roles. The definitive organization of the gas exchangers must integrate these rather constraining needs. The gas exchangers are unique in that there are no tissue cells which are ubiquitous to them as hepatocytes are to the liver, osteocytes to bone, or neurons to nervous tissue. A cell membrane with no distinct specializations (Figs. 4,5) as in the Protozoa and in many simple Metazoa is the most elementary gas exchanger (e.g., Mangum 1994). The unconventionalized designs of the gas exchangers can be ascribed to the fact that the simple passive process of diffusion of the respiratory gases does not oblige a specific structural plan. Based on the fundamental feature that at a respiratory site all that need exist is an O_2 concen-

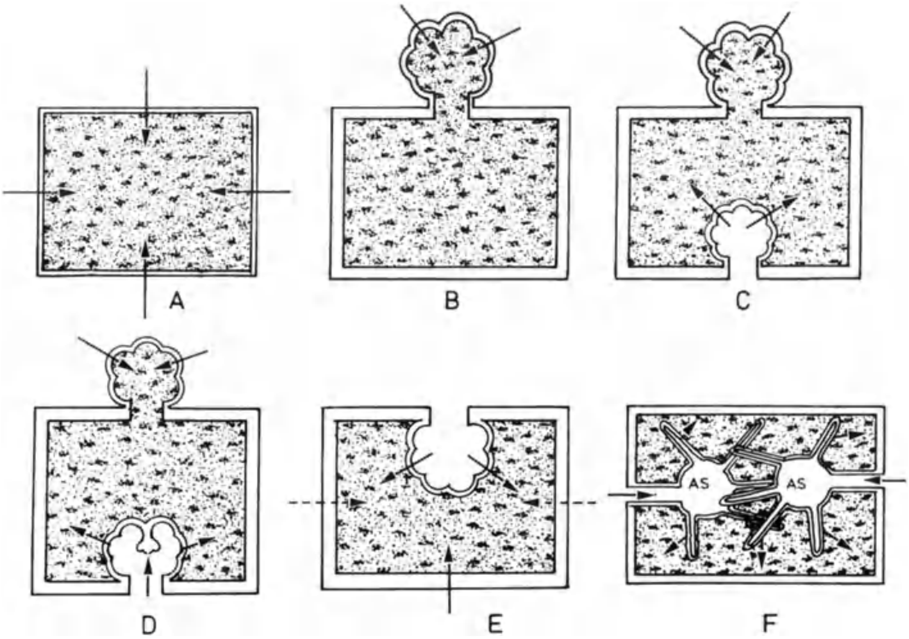
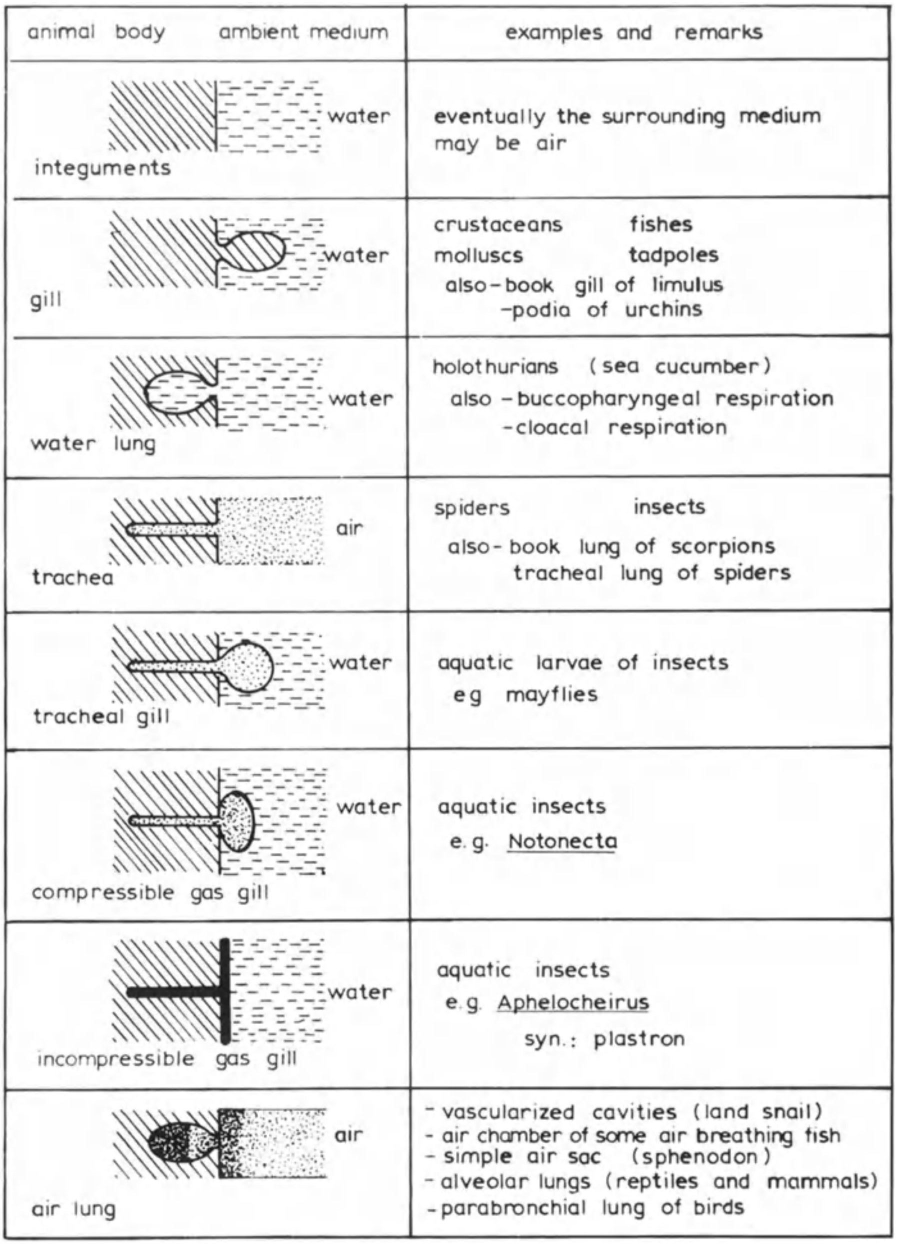


Fig. 4A–F. Basic designs of gas exchangers. The least specialized gas exchanger (**A**) is found in the unicells where the transfer (shown with →) occurs by diffusion across a plain cell membrane. In the more complex animals, gas exchangers have formed either as evaginations (**B**) generally called gills and specialized for aquatic breathing, or invaginations (**C–F**) generally called lungs for aerial breathing. **B** An example of a unimodal aquatic breather. **C** A bimodal breather with an "unspecialized" accessory respiratory organ. **D** A bimodal breather with a "specialized" accessory respiratory organ. **E** A terrestrial air breather with the lung (an invagination) as the exclusive gas exchanger [in amphibians diffusion across the skin (shown with →) is an important respiratory pathway in appropriate environments]. **F** Insect tracheal system where air is delivered directly to the tissue cells across the air sacs, *AS*, especially in the larger species. (Maina 1994)

tration differential (a partial pressure gradient), exquisite experiments have been used to identify morphologically obscure respiratory sites by use of O_2-sensitive bioindicators. Suitable flagellates such as *Polytoma* (Thorpe 1932) and a protozoa such as *Bodo* (Fox 1921) have been utilized as markers of areas of rapid O_2 influx in the *Simulium* and larval *Omorgus* (Ichneumonidae), respectively, and in *Cryptochaetum* (Agromyzidae). Terebellid worms (e.g., Weber 1978) and sea anamones, e.g., *Metridium senile* (Sassaman and Mangum 1972; Schick 1991) present some localized areas of the body where the thickness of the skin is drastically reduced. In the large scyphozoan, *Cyanea capillata*, and the tube anemone, *Ceriantheopsis americanus*, it is still debatable whether the skin over the body column plays any significant role in respiration (Sassaman and Mangum 1974; Mangum 1994). Up to now, gas exchangers still remain to be discovered!



animal body	ambient medium	examples and remarks
integuments	water	eventually the surrounding medium may be air
gill	water	crustaceans fishes molluscs tadpoles also - book gill of limulus -podia of urchins
water lung	water	holothurians (sea cucumber) also - buccopharyngeal respiration -cloacal respiration
trachea	air	spiders insects also - book lung of scorpions tracheal lung of spiders
tracheal gill	water	aquatic larvae of insects eg mayflies
compressible gas gill	water	aquatic insects e.g. *Notonecta*
incompressible gas gill	water	aquatic insects e.g. *Aphelocheirus* syn.: plastron
air lung	air	- vascularized cavities (land snail) - air chamber of some air breathing fish - simple air sac (sphenodon) - alveolar lungs (reptiles and mammals) - parabronchial lung of birds

Fig. 5. Scheme showing the different anatomical designs of gas exchangers in water and air breathers and specialized modes of gas exchange. The organization of gas exchangers is mainly determined by the kind of respiratory medium utilized, habitat occupied, lifestyle, and the evolutionary level of development of a particular organism. (Dejours 1988)

1.7 Explicating the Process of Evolution of Respiration: Limitations

Reconstructing the pathways and the stages through which gas exchangers have evolved is an undertaking beset with many difficulties. The main obstacle lies in the uncertainty of our grasping the nature, the severity, and the direction of the changes which occurred in what was a highly dynamic biosphere of the ancient Earth. There is a particularly glaring lack of fossilized materials of the gas exchangers except on one Devonian species, *Bothriolepis* (e.g., Denison 1941; Wells and Dorr 1985). Soft tissues are very seldom adequately geologically preserved. When it occurs, however, by their very nature of being delicate, the materials are reduced from their three-dimensional form to two-dimensional films through intense heat and compression (e.g., Behrensmeyer and Kidwell 1985), making their recognition and interpretation very difficult and unreliable.

Air breathing has only evolved in the lineages of the two osteichthyan (bony) fishes, the actinopterygian (ray-finned fishes), e.g., bichirs, gar, and bowfin and sarcopterygian (lobe-finned fishes), e.g., lungfishes (Romer 1972; Pough et al. 1989; Cloutier and Forey 1991). Though a very distant point in evolution, this, nevertheless, provides a focal point for seeking convergence and divergence of the animal groups from which air breathers evolved. The near total extinction of the crossopterygian fishes (the sole survivor being the coelacanth, *Latimeria chalumnae*), a group thought to be a direct progenitor of the tetrapods (e.g., Pough et al. 1989; Gorr et al. 1991), makes the discernment of the evolution of the respiratory processes much harder. More often than not, one has to more or less rely on circumstantial evidence. From molecular genetic studies, it has now been proved that the popular phrase that “ontogeny recapitulates phylogeny” is too simplistic for developmental biology (on its own) to be reliably meaningful in reconstructing phylogenies (e.g., Humburger 1980; Alberch 1985; De Queiroz 1985; Gans 1985; Northcutt 1990; Marshall and Schultze 1992). Neoteny and/or pedomorphy (e.g., Semlitsch and Wilbur 1989; Wake and Roth 1989) are but two characteristics which manifest nonconforming developments. Morphological, experimental embryological, physiological, biomechanical, paleontological, molecular, and biochemical investigations need to be integrated to effectively elucidate evolutionary transformations, mechanisms, and pathways. In amphibians in particular, dramatic changes in form, location, and function of the gas exchangers and the circulatory system occur during metamorphosis (e.g., Infantino et al. 1988; Hou and Burggren 1991; Burggren and Bemis 1992; Newman 1992; Burggren and Infantino 1994; Fig. 47). These entail radical modifications of the ventilatory mechanisms and transformations of the respiratory organs, changes which must be accompanied by appropriate neurophysiological reorganizations for proper motor functional control and coordination (Burggren et al. 1990).

Albeit the glaring lack of data, the evolutionary and adaptive developments of the gas exchangers can be patched together by collateral evidence gathered by studies of: (1) animals which have adapted to atypical habitats, (2) those that possess transitional respiratory features, (3) those at different phylogenetic levels of development, (4) those which have unique behavioral lifestyles, and (5) those which show peculiar developmental changes. Study of the ancient air-breathing fish such as the Dipnoi, Holostei, and Polypterida should provide a fertile ground for such inferential studies. For biologists, there is always some unique kind of satisfaction when a previously unknown phenomenon or state of natural history fits into a theoretical prediction. The excitement of discovering the so-called living fossils, rare animals which fill the evolutionary gaps, is great. The capture of the Carboniferous actinistian, the coelacanth *Latimeria chalumnae* in 1938 (see R.E. Smith 1956; Thomson 1986; Fricke 1988; Cloutier and Forey 1991; Bruton et al. 1992), a group thought to be long extinct, is a classical instance. It is now, however, profitable to recognize that since the first successful engineering of transgenic mice by Gordon et al. (1980), it is no longer necessary to formulate a scientific question to suit a biological system. These days, it is possible to specifically design an organism (e.g., a transgenic organism) to best answer a particular question (e.g., Cory and Adams 1988; Adams and Cory 1991; Taketo et al. 1991; Ho 1994). Such new experimental paradigms, which hitherto were not possible to configure, provide useful tools for analytical manipulations at molecular, organismal, and ecological levels. When adopted, they should contribute greatly in the advancement of comparative respiratory biology.

The diversity of the organization of the gas exchangers was highlighted in Maina (1994). In this account, the essence of the contrast is discussed with particular focus on: (1) the conditions under which the respiratory processes evolved, (2) the physical characteristics of the media in which these changes occurred, and (3) the different strategies which animals adopted to extract O_2 from the external milieus. The simplest respiratory organs are generally found in the aquatic animals or those organisms which subsist in cryptozoic (humidic) habitats. In their rudimentary form, they occur in the form of permeable, moist, well-vascularized surface membranes, e.g., the integument of the invertebrates such as the earthworms and planaria and in vertebrates such as the eel and the frog, e.g., *Rana*. At the more advanced stages, cardiorespiratory coupling developed to enhance the transfer of O_2 to the complex highly aerobic tissues. In those aquatic animals where the integument is the main respiratory pathway and in fish which have lost the bucco-pharyngeal ventilatory capacity of the gills (e.g., mackerel), locomotion provides an important respiratory activity.

1.8 Plans and Performance Measures of the Gas Exchangers

Over and above the simple diffusive respiration of the unicellular organisms and the lower invertebrates, the gills and lungs are distinctively suited for respiration in water and air, respectively. Owing mainly to the remarkable differences between the two fluid respiratory media (Sect. 3.2), on very rare occasions the two organs are contrived to operate in both respiratory media with equal efficiency. With the progressive organizational complexity of animals, forms, and processes such as closed circulation, double circulation, convective movement of the respiratory media, and presence of respiratory pigments in the body fluids and erythrocytes evolved to match the intensifying demands. Such transformations invite interpretations and speculations. Compared with the more recent enhancements, the ancient elements of the respiratory improvements would have been optimized and conserved in due course. Both the physical characteristics of the respiratory media and the respiratory needs have determined the definitive functional designs of the gas exchangers. The various schemes of the respiratory systems, however, are not congruous with the classic concept of Darwinian radiative animal evolution, which is artistically presented as a branching tree with birds and mammals sitting somewhere at the top. Unlike the brain, which shows progressive development reaching the pinnacle in the human being, the gas exchangers of mammals do not present the ultimate pulmonary design. The structural and functional attributes of a gas exchanger cannot be easily predicted based on any single phylogenetic factor in a simple and direct way.

The importance of O_2 in the survival of organisms is reflected in the dramatic effect that hypoxia and hyperoxia have on the structure and function of the gas exchangers. Parameters such as blood O_2 carrying capacity, O_2 affinity, and myoglobin concentration in tissues can change within a matter of hours in response to aspects such as sojourn at high altitude or after being subjected to severe exercise. In the respiratory system, the working capacities at all steps, be they convective or diffusive, must be appropriately sized and regulated for optimal function. Decrease in size and increase in activity calls for more elaborate gas exchangers and more efficient means of O_2 uptake and transport. Amidist these permutations, certain conflicts, compromises, and tradeoffs occur. For example, whereas intucking of the gas exchangers was essential for avoidance of desiccation on land, affording better protection against trauma, and achieving a more extensive respiratory surface area (Figs. 4,5), such organs could only be ventilated tidally, a pattern functionally inferior to the continuous unidirectional process which is possible in the evaginated gas exchangers (Figs. 6,18). In the erythrocytes, the main organic phosphate 2,3-diphosphoglycerate (2,3-DPG) and CO_2 combine with the same basic groups of the hemoglobin competing with each other (Davenport 1974). The effects of 2,3-DPG and CO_2 on the hemoglobin dissociation curve are not additive: the shift brought about by the two factors together is less than the sum of each separately. The avian trachea presents a good example illustrating the nature and extents of the compromises and structural adjustments effected to enhance the efficiency of the gas exchangers. To attain flight, birds totally committed the forelimbs for this singular function. Ipso facto (i.e., to substitute for the roles which the forelimbs played), birds evolved a long neck (and with it a long trachea) for defense, procuring food, construction of the nests, and preening. For animals of the same body mass, the avian trachea is three times longer than that of a mammal (Hinds and Calder 1971). In order to compensate for what may have led to a greater resistance to air flow (as resistance to air flow in a tube is directly proportional to the length but inversely proportional to the radius to the fourth power in laminar flow – and to the 4.75 power if the flow is turbulent), the avian trachea acquired a diameter 1.3 times greater than that of mammals (Hinds and Calder 1971): air flow in the trachea of the ostrich has been shown to be laminar (Schmidt-Nielsen et al. 1969). The net effect of these adjustments, i.e., increase in the diameter and the length of the trachea in birds, ensued in an overall resistance similar to that of the trachea of a mammal of the same size. In gaining a large tracheal volume and hence a large tracheal dead space (TDS) which is 4.5 times greater than in a mammal (Hinds and Calder 1971), it could

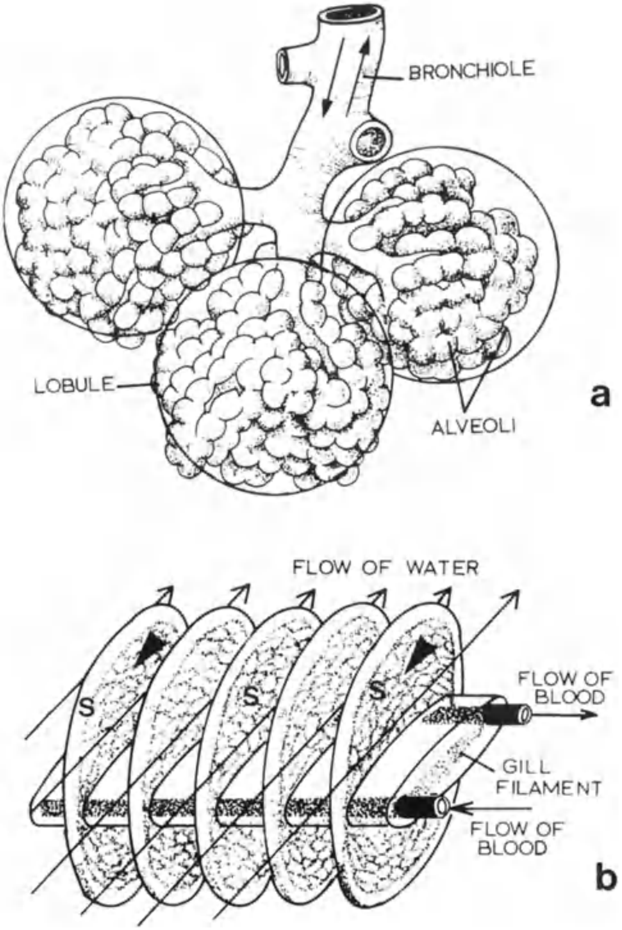


Fig. 6a,b. Spatial arrangement of the respiratory media in an invaginated gas exchanger (**a**) and an evaginated one (**b**). Except for the highly specialized bird lung, the gas exchange zone of the invaginated gas exchangers is ventilated tidally (⇆, **a**) while the evaginated ones are ventilated unidirectionally (→, **b**). *s* Secondary lamellae. In the fish gills (**b**), the direction of the flow of the blood in the secondary lamellae (➤) runs counter to that of the water in the interlamellar space (→). (Kylstra 1968)

conceivably be concluded that natural selection imparted an impediment on the function of the avian respiratory system. This, however, is not the case. The lower respiratory frequency (RF) of birds, which is 0.32 to 0.42 times that of a mammal of equal size, countered the limitations caused by the large TDS. Moreover, the lower RF has afforded room for remarkable configurations of the trachea (e.g., Forbes 1882). Extreme trachea lengths occur in birds such as the trumpet bird, *Phonygammus keraudrenii*, the magpie goose, *Anseranas semipalmata*, and the whooping crane, *Grus americana* (Clench 1978; McLelland 1989). Although

P. keraudrenii has the same body mass as a common flicker (*Colaptes auratus*), which has a trachea only 38 mm long, its trachea may be over 800 mm in length and compares with that of the much larger ostrich, *Struthio camelus* (Clench 1978). In *G. americana*, the overall tracheal length is 1.5 m (Welty 1979). Tracheal coiling has been taken to be an acoustic adaptation for lowering the pitch or amplifying sound (e.g., Greenewalt 1968; Gaunt et al. 1987). Furthermore, tracheal loops have been said to increase the tracheal respiratory surface area enhancing evaporative water loss during panting (e.g., Prange et al. 1985) without running a risk of respiratory alkalosis (Schmidt-Nielsen et al. 1969; Bech and Johansen 1980). Compared with birds with straight trachea, those with tracheal convolutions or other tracheal prolongations adaptively have relatively wider tracheal diameters (Hinds and Calder 1971). Perhaps to play similar roles, trachea diverticula have been reported in snakes (Young 1992).

Miscellaneous tissues and organs such as the cell membrane, skin, buccal cavity, gastrointestinal tract, gills, and lungs variably serve as respiratory sites. Because they characterize the more phylogenetically advanced animals, the air-breathing organs (lungs) are assumed to be the better (more efficient) gas exchangers. Except in the bimodal breathers (Chap. 5), gas exchangers are refined to operate best in only one respiratory medium. The human being at the epitome of evolution soon succumbs when the lungs are flooded with liquid (Sect. 6.11). In all respiratory organs, be they water or air breathing, O_2 dissolves in a thin film of water as it traverses the tissue barrier (Sect. 6.1). The flux of the respiratory gases occurs under the prevailing partial pressure gradients across the water or air-blood barrier and is maintained by utilization (O_2) and production (CO_2) in the tissue cells and the physical movements of the external and internal respiratory media. There has been protracted debate as to whether the diffusion of O_2 across the cell membrane is entirely passive or is facilitated (e.g., Longmuir and Bourke 1959; Scholander 1960; Burns and Gurtner 1973; Wittenberg 1976). Hemoglobin, myoglobin, and a specific carrier (cytochrome P_{450}) have been implicated in facilitated diffusion of O_2 in tissues such as the lung, placenta, and the liver (Kreuzer 1970; Wittenberg and Wittenberg 1989). The significance of facilitated diffusion of O_2 in tissues is not well known. The process may, however, be consequential in states of reduced O_2 flow across the blood-gas barrier, e.g., in cases of interstitial edema (Burns et al. 1975, 1976), and in hypoxic conditions (Longmuir 1976).

In both aquatic and terrestrial animals, the complexity of the gas exchangers correlates with the mode of life, habitat occupied, environment, and the general metabolic capacities (e.g., Hughes and Morgan 1973; Gehr et al. 1981; Maina et al. 1989a; Hughes 1995). In nature, the high metabolic needs of the endotherms have not been satisfied except by air breathing. The diffusion of O_2 occurs at a rate of $2.3 \times 10^{-5}\,cm^2\,s^{-1}$ (Grote 1967) across an extremely thin, expansive blood-gas barrier. The process is completed within 250 to 500 ms (West 1974). For the typical O_2 uptake of 200 ml per min, a concentration gradient of only 0.057 kPa (a value which is negligible compared with the prevailing inspired air-arterial blood PO_2 gradient of about 6.7 kPa in the mammalian lung) is all that is necessary. The requisite structural and functional attributes of an efficient respiratory organ are an extensive surface area, a thin partitioning between the respiratory media, and efficient ventilatory and perfusive mechanisms to maintain the highest possible pressure gradient across the barrier. In simple animals, the extensive surface area (per unit body volume) is more than adequate for gas transfer, while in the larger ones respiration is restricted to specialized sites. Such areas are brought about by outfolding (evagination) or intucking (invagination = cavitation = sacculation) of a part of the body surface (Figs. 4,5). The organs in the first category have been termed gills and those in the second lungs. The gills (Chap. 4) are the archetype aquatic respiratory organs while the lungs (Chap. 6) are the model ones for air breathing: the bimodal (transitional) breathers (Chap. 5) have evolved organs which are used to extract molecular O_2 from both water and air. In the multicellular organisms, the consequential features which must be presented either singly or in combination for an organ to be designated a gas exchanger include: (1) movement of the external respiratory medium, (2) the PO_2 must be lower and the CO_2 higher in the effluent respiratory medium than in the influent one (e.g., Qasim et al. 1960), and (3) perceptible structural modifications such as infolding or outfolding and internal subdivision of the respiratory surface. Vestiges of lungs which are used for water breathing and a number of gills modified for air breathing exist, but these are rare.

1.9 The Early Anoxic Earth and the Evolution of Life

Of all concepts which have been enunciated in biology, that of evolution is probably the most important and encompassing. Dobzhansky (1973) declares that "nothing in biology makes sense, except in right of evolution". Wainright (1988) asserts that "evolution is the single most important and inclusive concept in biology". Its practical utility in biology is summed up by Nelson (1978) as follows: "the concept of evolution is an extrapolation, or an interpretation, of the order liness of ontogeny". Although debate still continues even on the validity of the concept itself and the mechanisms through which it occurs, no other plausible principle can: (1) satisfactorily organize and explain the diversity of the existing life forms, (2) account for and align the preserved fossils and the extinct forms with the extant species, and (3) explain in the context of the contemporary species the paintings and sculptures made within recorded history by the early human beings. Fossils bespeak terminated (failed?) experiments in evolution. Living things have a shared biology. The theory of evolution is grounded on the fundamental belief that life has a common origin (e.g., Brown and Doolittle 1995): through natural selection, animals and plants have progressively developed and genomically diverged in the continuum of time. However unpalatable it may sound, from congruent evidence derived from multiple proteins (Baldauf and Palmer 1993), animals and fungi are sister groups with plants constituting a more distant evolutionary lineage! Cladistic classifications attempt to reconstruct the evolutionary histories and establish relationships between different taxa from study of states of shared derived characters (e.g., Benton 1995; Huelsenbeck and Rannala 1997). Molecular genetic sequences form the basis of many modern phylogenetic reconstructions (e.g., Stewart et al. 1987; Dean and Golding 1997). To delve into the origin of life and understand the subsequent inputs and changes which culminated in the formation of the modern ecosystems for which utilization of molecular O_2 was central, different scientific disciplines like biology, astronomy, atmospheric physics, geophysics, astrophysics, geochemistry, inorganic and organic chemistry, oceanography, and geology should be integrated. An interdisplinary approach better illumines the convergence of experimental and analytical data, connecting events across temporal and spatial scales. Scientific disciplines gradually diffuse into each other. The often aggressively defended boundaries are more apparent than real. They are often created for self-interests and preservation and have profoundly hindered advances in ratiocinative thought.

The age of the Universe is estimated at between 10 to 20 billion years (e.g., Schopf 1980; Peebles et al. 1994). For a long time after its accretion, some 4.5 billion years ago, the Earth was in a state of perpetual physical and chemical turbulence (Schopf 1978, 1993; Mojzsis et al. 1996). The surface temperature was in excess of 1500 K and the high pressure primary atmosphere consisted of water vapor ($\sim 8 \times 10^{22}$ mol), CO_2 ($\sim 5 \times 10^{21}$ mol), N_2 ($\sim 3 \times 10^{20}$ mol), H_2S ($\sim 9 \times 10^{20}$ mol), and SO_2 ($\sim 7 \times 10^{19}$ mol) (Matsui and Abe 1986). With the cooling to below 650 K, the water vapor condensed, forming highly acidic primitive oceans. The minerals in the lithosphere soon neutralized the acids and the dissolved SO_2 formed sulfates and sulfides. Through outgassing (Allegre and Schneider 1994), the secondary atmosphere came to comprise mainly CO_2, N_2, water vapor, and traces of CH_4, NH_3, and SO_2. This composed the incipient neutral atmosphere which was essentially similar to the present one of Venus and Mars. Subsequently, the H_2O vapor was photochemically dissociated into H_2 and H^+, converting the secondary atmosphere into a reducing one. Some of the other most important changes to have occurred during the evolution of life on Earth have been: (1) variations in temperature and solar insolation (e.g., Foley et al. 1994; D'Hondt and Arthur 1997), (2) changes in the orbit (Imbrie et al. 1989), (3) plate tectonics (e.g., Raymo and Ruddiman 1992), (4) variations in the gaseous composition of the atmosphere (from a neutral, i.e., one where CO_2 and N_2 predominated to a highly reducing one where H_2 was the principal gas and finally an oxidizing one – with accretion of O_2) (e.g., Tappan 1974; Chappellaz et al. 1992), (5) decrease in the rate of rotation (e.g., Scrutton 1978), and (6) small fluctuations of the atmospheric pressure (e.g., Hinton 1971) and gravitational forces (e.g., Carey 1976; McElhinny et al. 1978). It is widely postulated that the chemical evolution of life occurred by combination and transformation of a vast range of simple inorganic molecules such as carbon monoxide, CO_2, N_2, H_2, and H_2O into complex biologically relevant organic compounds. This process is envisaged as having been induced by enormous energy influx probably from solar radiation, heat, meteorite impact events, radioactive decay, electrical discharges, and thunder shock waves (Calvin 1956). Though organic molecules themselves may have been extraterrestrial in origin (e.g., Cohen 1995), life is thought to have been fabricated in a chemically reducing atmosphere (e.g., Chang et al. 1983; Cloud 1983a,b; Jenkins 1991), probably around geothermal springs (e.g., Stong 1979) or on the surface of catalytic iron sulfide crystals (Russell and Daniel 1992; Kaschke and Russell 1994; Russell et al. 1994). Through long intricate condensation, polymerization and oxidation-reduction reactions of organic molecules such as amino acids, sugars, and other suitable molecules (the so-called primordial broth, or organic soup), the high-energy phosphate bonds (for intracellular energy transfer), specificity of protein molecules as organic catalysts, genetic coding of the nucleotides, and membrane ionic transfer processes developed (e.g., Bar-Nun and Shaviv 1975). Biogenesis of self-repairing, self-constructing, highly dynamic molecules resulted in the first living entity called protobiont by Oparin (1953) and concept organism by Chapman and Ragan (1980). This microscopic unit is the simplest ancestral prokaryote which possessed the most basic requisites for life. Organic evolution had to await the development of genetic and protein-synthesizing pathways. Interestingly, Lee et al. (1996) have described a self-replicating peptide. Organic molecules like amino acids, protein-like polymers, and nucleic acid polymers have been synthesized in the laboratory by passing an electric are through a mixture of gases such as CH_4, NH_3, H_2, and H_2O vapor, i.e., by simulating what are thought to have been the atmospheric conditions and circumstances which existed in the primeval past (see e.g., Sagan 1994).

1.10 Abundance of Molecular O_2 in the Earth's Biosphere

Of the nine solar system planets (eight – should Pluto finally turn out to be merely a piece space junk as recently suggested!), only the Earth has a veritable atmosphere suitable for life. While the atmosphere of Earth contains only tiny amounts of CO_2, those of Venus and Mars contain 96.5 and 98% CO_2, respectively. The atmospheres of Jupiter and Saturn are composed essentially of H_2 and helium. Mercury strictly lacks an atmosphere. The present atmosphere of Earth compares with that of Mars some 300 to 400 million years ago (Kargel and Strom 1996). Saturn's giant moon, Titan, has an atmosphere ten times larger than that of Earth and a surface pressure of 1.5 atm (Samuelson et al. 1981; Lorenz et al. 1997). The atmosphere is made up predominantly of molecular N_2 (82.2%), Ar (11.6%), 6% CH_4, and 0.2% H_2. Like Earth, Titan has a greenhouse effect (McKay et al. 1991; Lorenz et al. 1997). The greenhouse effect on Venus, which is caused by CO_2, generates surface temperatures of around 455 °C. Life evolved on Earth nearly 4 billion years ago (Schopf 1980; Balter 1996). The first obligatory aerobic eukaryotic cells appeared between 2.0 to 1.5 billion years ago (e.g., Reader 1986; Schopf and Walter 1983) and the first multicellular organisms about 600 million years ago, i.e., at the beginning of the Cambrian period (Nursall 1959; Cloud 1983a). The tenure of life on Earth constitutes only about 15% of biogeologic history. The complex organisms have existed for an even shorter period, i.e., about 5% of it (Figs. 7,8).

1.11 Shift from Anaerobiotic to Aerobiotic State in the Early Earth

The oxidative state of the Earth's biosphere has corresponded with the measure of the sources of O_2 and the abundance of inorganic and organic reduced com-

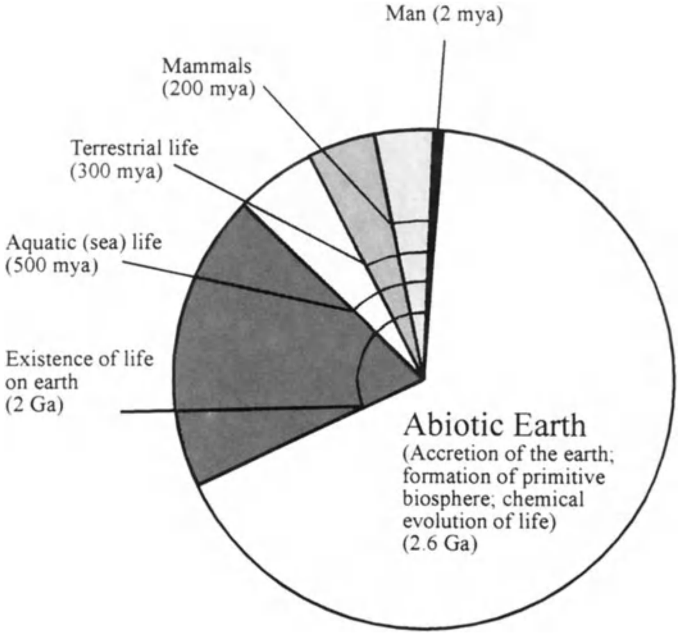


Fig. 7. Scheme showing the relatively very short period over which terrestrial and in general air-breathing organisms have lived on Earth. The dates (in *parentheses*) are averages from different publications

pounds. The appearance of an oxygenic environment entailed a change from an inefficient to a more advanced energetically O_2-dependent and metabolically highly versatile oxidizing ecosystems. Anaerobic fermentation is a highly inefficient source of energy as much of it is left locked in molecules such as alcohols and organic acids, end-products which must be removed before they accumulate to toxic levels. Fermentation of a molecule of glucose results in production of only 2 molecules of adenosine triphosphate (ATP) which contain only about 15 kcal of available energy, while in aerobic respiration 36 molecules of ATP equivalent to 263 kilocalories of utilizable energy are produced. Stated differently, to obtain the same amount of energy through fermentative respiration, a greater quantity of carbohydrate molecules must be utilized. The Pasteur effect, named in honor of Louis Pasteur (1822 to 1895), who first described the fermentation of yeast independent of O_2, has been defined in the broadest terms as "the stimulation of carbohydrate consumption by reduced O_2 tension" (Schmidt and Kamp 1996). The products of aerobic respiration are water and CO_2, two innocuous molecules which are easily eliminated into any environment at minimal risk and cost. While the energy derived from fermentative processes is just adequate to support life, aerobic respiration provided excess energy, which organisms invested towards attaining greater structural and functional complexity, resulting in greater success compared with their predecessors. Without O_2, life would probably not have developed above that of the unicellular fermentative prokaryotes.

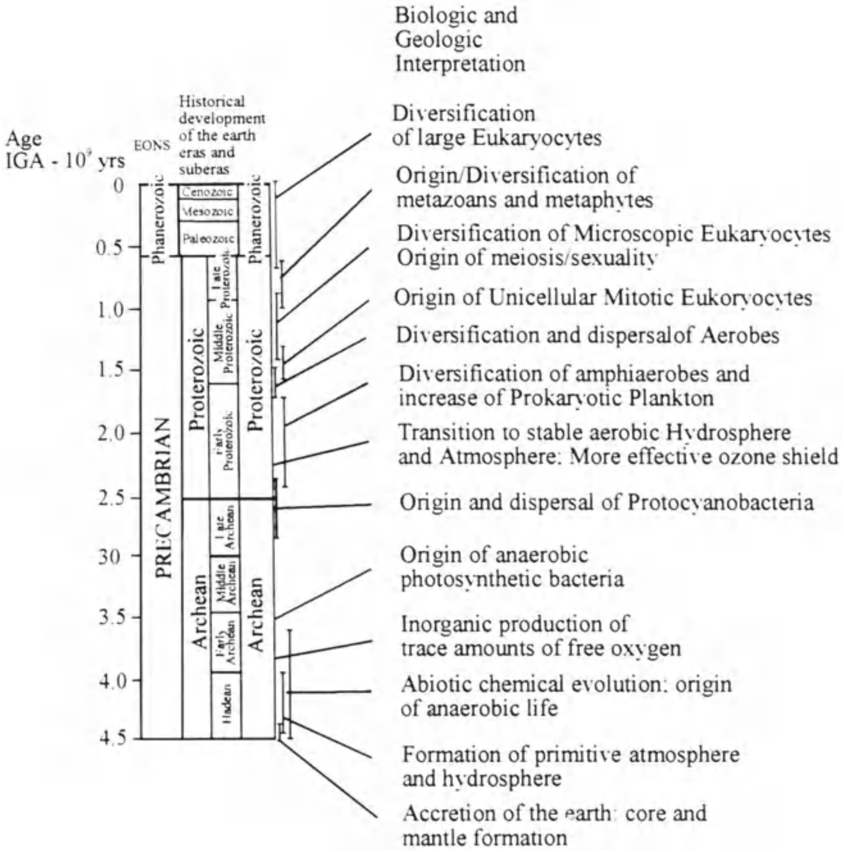


Fig. 8. Summary of the major biotic developments during the geological periods. (Schopf et al. 1983)

Oxygenic biochemistry has evolved regularly in the past in response to the changing levels of molecular O_2 in the biosphere (e.g., Fox et al. 1980). These conditions have changed from neutral to reducing state and varied from anoxia, hypoxia, and hyperoxia (relative to the present) by no means chronologically in that order (e.g., Frakes 1979; Hendry 1993; Fig. 9). Changes in atmospheric O_2 have paralleled biotic developments (Figs. 8,9). Until about 1 to 2 billion years ago, the atmosphere consisted essentially of carbon monoxide, NH_3, CH_4, H_2, H_2O vapor, and other simple hydrocarbons (Schopf 1978, 1983; Owens et al. 1979; Chapman and Schopf 1983; Grieshaber et al. 1994). Chemical evolution of life occurred within such a reducing atmosphere after the surface of the Earth had cooled to a level compatible with synthesis of the labile organic molecules (Chang et al. 1983). It has been argued by, among others, Oparin (1938) that the present conditions on Earth are no longer suitable for compounding life from inorganic

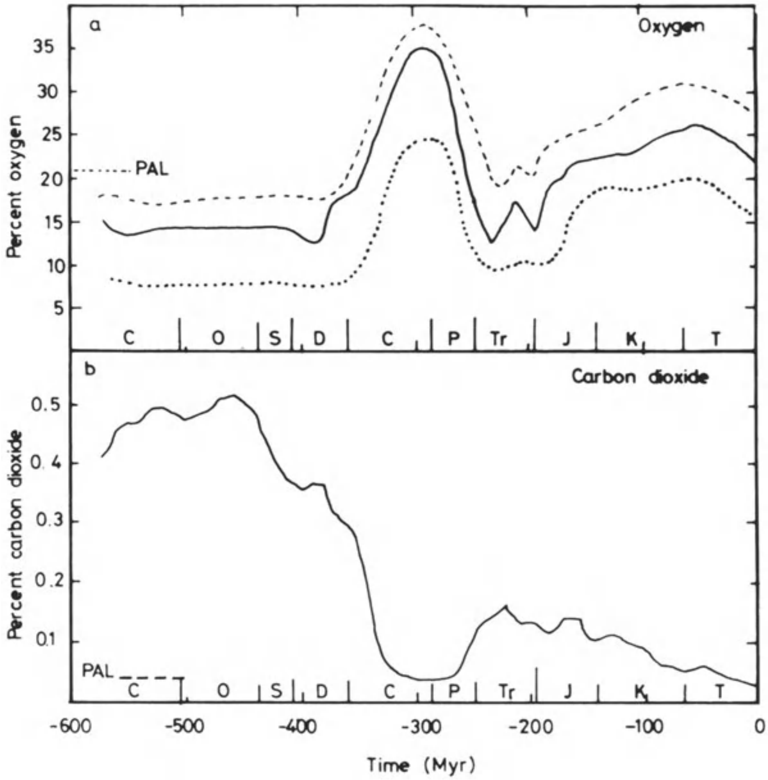


Fig. 9. Changes in the levels of O_2 and CO_2 in the late Paleozoic. Oxygen levels have fluctuated from a low of about 15% (reached towards the end of the Paleozoic, i.e., 250 million years ago) peaking at 35% by the late Carboniferous (268 mya). The present atmospheric level (PAL) of 21% is shown with a *dotted line*. CO_2 level was highest in the Ordovician-Silurian, dropped remarkably during the Devonian-Carboniferous, and increased in the late Permian. The PAL of CO_2 of about 0.036% is shown with a *dotted line*. Note that the relative levels of the two gases fluctuate in an inverse manner. *C* Cambrian; *O* Ordovician; *S* Silurian; *D* Devonian; *C* Carboniferous; *P* Permian; *Tr* Triassic; *J* Jurassic; *K* Cretaceous; *T* Tertiary. (After Graham et al. 1995; reprinted by permission from *Nature*, Vol. 375, pp. 117–120, copyright 1995 Macmillan Magazines Ltd.)

matter because the atmosphere is too highly oxidizing. Anaerobic microorganisms flourished in water in excess of 500 million years before O_2 production started (Fenchel and Finlay 1994). At the middle of the Precambrian era, a group of prokaryotes, the cyanobacteria (blue-green algae), evolved chlorophyll a, acquiring means of utilizing solar energy for the process of photosynthesis (e.g., Owens et al. 1979; DiMagno et al. 1995; Nisbet et al. 1995; Boussaad et al. 1997). Photosynthesis is the one large-scale process that abundantly converts simple inorganic compounds (CO_2, H_2O, and tiny amounts of minerals) into complex energy-rich organic carbohydrate (CH_2O) molecules. It is the source of all living matter on Earth and in that case all biological energy (Rabinowitch and Govindjee

1965). It is interesting to note that the discovery of flourishing hydrothermal vent communities in the 1970s (e.g., Meredith 1985) demonstrated that life could exist on Earth totally independent of solar radiation. The accumulation of O_2 (a product of the photosynthetic process) in the atmosphere resulted in the transformation of the Earth's nascent biotic ecosystems from an anaerobic to an aerobic state. This initiated decisive biological changes (Table 1). For successful progression of life from water to land, due to the harmful effects of the UV light, the presence of O_2, which generated a protective ozone layer in the atmosphere, was necessary. Compared with the present state, the solar UV light flux was more fierce and perhaps invariably lethal during the first 500 million years of the Earth's evolution (Gaustad and Vogel 1982).

Oxygen enrichment of the atmosphere resulted in an increase from 3 to 10% up to 100% of the present atmospheric level in the late Proterozoic and early Cambrian epochs (about 0.54 billion years ago) (Des Marais et al. 1992; Canfield and Teske 1996). It is believed that this led to the so-called Cambrian explosion, an event that was characterized by dramatic biotic developments which included: (1)

Table 1. Comparison of physical properties of the present O_2 atmosphere (21% O_2) with those of the relatively hyperoxic late Carboniferous (35% O_2) and relatively hypoxic end-Permian (15% O_2). (Graham et al. 1995)

	21% O_2 present	35% O_2 285 mya	15% O_2 250 mya	
Respiratory gases				Biological significance
Oxygen				
O_2 partial pressure (kPa)	21.2	35.3	15.1	Respiration, lignin biosynthesis
Krogh's maximum radius (cm)	0.11	0.14	0.09	Size limit for diffusion dependence
Water O_2 content (ml^{-1})	6.9	7.4	4.9	Aquatic respiration
Carbon dioxide				
Carbon dioxide partial pressure (kPa)	0.03	0.03	0.09	Effects on photosynthesis, moisture content and global energy balance
Water CO_2 content (ml^{-1})	0.31	0.31	0.31	Aquatic pH effects, acid-base balance and ion regulation
Air properties				
Density ($kg\,m^{-3}$)	1.29	1.56	1.12	Flight and respiratory mechanics, wind shear
Dynamic viscosity ($kg\,m^{-1}s^{-1}$)	18.2×10^{-6}	+	–	Boundary layer thickness
Specific heat ($js^{-1}deg^{-1}$)	1.006	+	–	Heat capacity and relative humidity
Thermal conductivity ($js^{-1}m^{-1}deg^{-1}$)	2.4×10^{-2}	+	–	Earth thermal budget, climate

+ and – indicate increase and decrease, respectively, relative to the present 21% O_2 atmosphere; mya, million years ago.

the evolution of the multicellular life (Conway-Morris 1993), (2) synthesis of the structural protein collagen which is widely distributed in the metazoans (Towe 1970), and (3) remarkable adaptive radiation and ecological diversification of the animal life (Conway-Morris 1993; Canfield and Teske 1996; Knoll 1996). In general, episodes of rapid evolutionary change correspond with occurrences of speciation (e.g., Gould and Eldridge 1977; Stanley 1979). In water, the surge in the O_2 level accelerated the biodegradation of the dissolved iron and the organic (bacterial and algal) matter. Precipitation of the resultant complexes to the bottom increased the level of oxygenation of the surface waters (Logan et al. 1995), making them more habitable. Without the ancient cyanobacteria, the Earth would still be having little, if any, reactive molecular O_2: like the atmospheres of Mars and Venus, CO_2 would still be the predominant atmospheric gas. In *Rhodobacter sphaeroides*, a metabolically versatile photosynthetic bacterium able to operate under a wide variety of environmental states, a decrease in O_2 availability leads to induction of the membranous photosynthetic apparatus (Yeliseev et al. 1997): the expression of gene-encoding components of the photosynthetic complexes, e.g., structural polypeptides, bacteriochlorophyll, and carotenoids, is closely directed by O_2 tension and light intensity. The momentous point at the end of the Early Proterozoic (some 2.0 to 1.5 billion years ago) (e.g., Kasting and Walker 1981), when the Earth changed from a mainly anoxic hydrosphere and atmosphere to an oxic one is marked by the time at which: (1) the production of banded iron abruptly stopped, (2) deposition of the highly oxidizable uraninite stopped, and (3) the first occurrence of blue-green algae of which the cells included thick-walled heterocysts which may have shielded the O_2-sensitive nitrogenase enzymes, as the modern ones do. It was not until after the oxidization of the reducing gases and mineralogic factors, when photosynthetic O_2 discharge into the biosphere finally exceeded the turnover rate of the reduced matter, that O_2 became a vital and permanent factor in a stable aerobic atmosphere. The transition from reducing to oxidizing oceans and atmosphere may have been accelerated by a declining discharge of reducing gases and oxidizable substrates through less tectonic activity (Walker 1978). Depending on ecological settings, the transitional point may have differed profoundly in different parts of the Earth.

The extensive invasion of land by plants during the Devonian enhanced the rate of production of O_2. This shifted the base of photosynthesis from water to land (McLean 1978; Knoll 1979, 1991) with the productivity of O_2 on land exceeding that of the oceans by a factor of 2 (Holland 1978). Practically all the molecular O_2 which was produced during the Earth's history, much of which is now held in diverse organic sinks, arose from green plant type and blue-green algal cyanobacterial photosynthesis (van Valen 1971; Walker 1974). The O_2 we respire today was de facto "excreted" by the cyanobacteria some 2 billion years ago during what is often called the age of the blue-green algae. As the level of O_2 in water rose and by diffusion the gas was transferred to the atmosphere, the terrestrial obligate anaerobes of the time perished with only a few, e.g., tetanus bacteria, surviving until today. Some molecular O_2 could, however, have been produced inorganically through UV light-induced photodissociation of water vapor in the primitive atmosphere after which H_2 was lost into the interplanetary space. Such a small quantity of O_2 would not have been of any biochemical consequence, as much of it would have been rapidly taken up by the unoxidized volcanically produced gases and mineralogic factors. However, a modicum level of photolytic (nonbiological) molecular O_2 may have nurtured the evolution of biological aerotolerance to O_2 in the elementary biota (Fay 1965; Holm-Hansen 1968) through development of specific biochemical pathways of mopping up and detoxifying intracellular O_2. This would have imparted a selective advantage to such moderately adapted microorganisms (e.g., Schopf and Walter 1983). Based on 16S ribosomal RNA sequencing of the prokaryotes (Fox et al. 1980), it has been shown that under modicum level of O_2, these fledgling life forms gave rise to the aerobic eukaryotes. The threshold for this transition (about 0.2% or 0.002 atm) has been incorrectly termed the Pasteur point as it resembles the Pasteur effect (e.g., Dejours 1975), the level of O_2 at which amphiaerobes change from anaerobic (fermentation) to aerobic metabolism. At that critical point, an organism converts from low efficiency fermentation to high efficiency aerobic energy-yielding catabolism. The actual point in time when this process occurred varied between organisms and environmental circumstances.

1.12 Accretion of Molecular O_2

As a general rule, the ecological resources available to organisms in any environment are finite (Hutchison 1959; MacArthur and Levine 1967; Levine 1976; Brown 1981). Environments cannot endure if they are continuously depleted of resources. Life will last only if and as long as there is frugal utilization and coherent cycling and revitalization of materials and energy (Smil 1997). Hydrologic and atmospheric O_2-CO_2 recycling are but two of the many global natural rotations of resources (e.g., McLean 1978). The changes in the partial pressures of O_2 and CO_2 in the biosphere are some of the most fascinating parameters which have influenced the direction and pace of development of life on Earth (Berkner and Marshall 1965; Rutten 1970). To stabilize and set optimal tolerable limits, at least since the Devonian, environmental PO_2 regulation was brought under direct biological control. This occurred through transfer between the biological sources (photosynthesis) and sinks (aerobic respiration) (Fig. 10). In effect, but not in mechanism, the processes of respiration and photosynthesis are diametrical: the former yields CO_2 and the latter O_2. Plants (photosynthetic autotrophs) and animals (heterotrophs) are involved in a continuous, intricate process of resource recycling, maintaining constant levels of CO_2 and O_2 in the atmosphere (Fig. 10). Using sunlight, atmospheric O_2 is continuously replenished by aquatic and terrestrial plant life and CO_2 and H_2O are produced by the respiratory processes. The end products of the way of life of each group become food for the other. The sun is the decisive source of the energy which drives this global animal-plant continuum of resource recycling. Averaged globally, the Earth receives $343\,W\,m^{-2}$ of energy from the sun in form of short wavelength radiation. About one third of it is reflected back into space by the atmosphere and the remainder ($240\,W/m^2$) is absorbed by the Earth's surface and the atmosphere. About one third ($103\,W/m^2$)

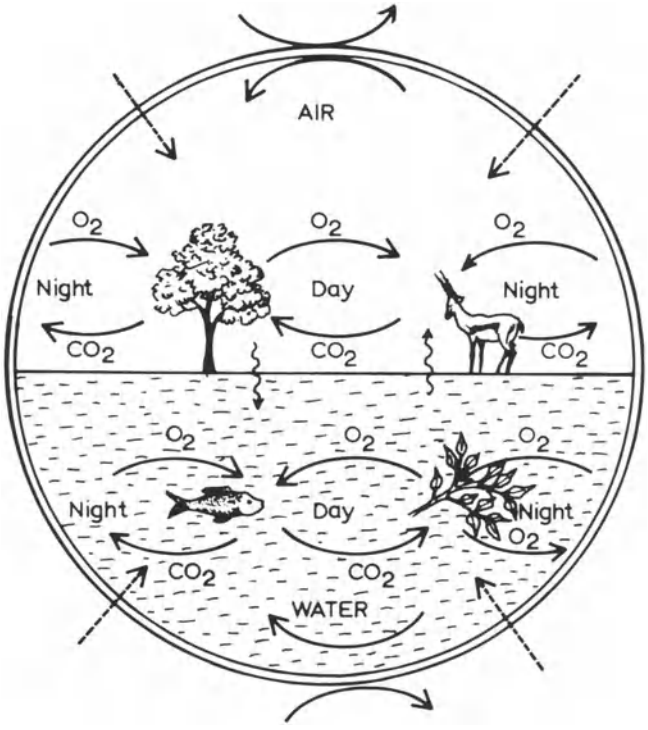


Fig. 10. Scheme showing the processes which regulate the O_2 levels in a closed habitat and the dynamics of gas transfer between water and air. The rather constant atmospheric O_2 and CO_2 levels are maintained by the cyclic balance between the photosynthetic and respiratory processes and supported by the fast diffusion rates of gases in air

of the net incoming solar radiation is reflected by the Earth's surface to the atmosphere (the Earth's albedo) in form of long wave-length radiation where it is absorbed by the greenhouse gases (e.g., water vapor, CO_2, ozone, methane, and nitrous oxide) and the clouds maintaining the surface temperature about 33 °C warmer than it would otherwise be without them (= the natural greenhouse effect). Oxygen and CO_2 are exchanged in air and to an extent with water by diffusion. Without a self-regulating O_2 and CO_2 recycling mechanism, life on Earth would have been short-lived. In the modern atmosphere, nitrogen constitutes 78.09%, O_2 20.95%, and CO_2 0.03%, the rest being composed of rare gases such as argon, hydrogen, krypton, xenon, etc. The present so-called normoxic atmospheric level of O_2 (21% by volume = about 0.2 atm) is strictly hyperoxic and far in excess of the optimum respiratory needs for life. Strictly, the modern terrestrial animals are exposed to an oxidative stress. According to the available data on amphiaerobic eukaryotic yeasts, systemic aerobic biochemistry can occur at values of 0.04% O_2 by volume (about 0.0004 atm) and organismic aerobiosis can occur at O_2 concentrations as low as 0.2 to 0.4% (i.e., 0.002 to 0.004 atm) (e.g., Rogers and Stewart 1973; Jahnke and Klein 1979). It is probably not coincidental that the Pasteur point is about 0.2% O_2 by volume, a value equal to the minimum O_2 level able to support organismal aerobiosis (Chapman and Schopf 1983). Adaptations to withstanding the harmful effects of the reactive factors of molecular O_2 was of particular importance in those life forms which produced the gas itself or were immobile and hence unable to escape from microhabitats with high concentrations of it. Unlike animals which normally operate under rather constant and somehow manageable O_2 tensions, green plants which produce the molecule itself had to evolve a complex range of molecular factors for protection against oxidative attack. Chloroplasts are the main source of antioxidants which include vitamins C and E (Crawford et al. 1994). Furthermore, while the land plants are exposed to air (21% O_2 by volume), the roots are located in the soil which, depending on type and firmness, may be virtually anoxic at depth (Currie 1962, 1984). In the marine angiosperms (Teal and Kanwisher 1966; Armstrong 1970), O_2 is known to diffuse from the roots, creating aerobic zones in the immediate area. This provides a unique microhabitat for some marine creatures such as the eulamellibranch bivalve, *Lucina floridana* (Britton 1970).

By the start of the Paleozoic era (about 600 million years ago), the PO_2 in the water and air had risen to the modest level of 0.2 kPa, i.e., one hundredth (= 0.2% O_2 by volume) of the modern sea level value. When the first vertebrates (ostracoderms) appeared some 550 million years ago (e.g., Forey and Janvier 1994), the PO_2 was only 0.9 kPa and by the Silurian-Permian periods, some 450 to 250 million years ago, the PO_2 had risen to 4.7 kPa when the amphibians ventured onto land (McClanahan et al. 1994). The terrestrial arthropods and amphibians were well entrenched on land by the Devonian period, by which time the PO_2 had risen to 10.7 kPa. The critical environmental threshold (10% of the present-day O_2 level) was crossed late in the Proterozoic era (Canfield and Teske 1996). The present level of 21 kPa was not reached until the Carboniferous period (350 million years ago) when the first reptiles appeared on land (e.g., Carroll 1988). The level of atmospheric O_2 has fluctuated greatly in the Phanerozoic (e.g., Tappan 1974; Cloud 1983a; Berner and Canfield 1989; Graham et al. 1995; Fig. 9). During the late Paleozoic, over a period of about 120 million years, O_2 rose to a hyperoxic level of 35% (compared to the present atmospheric level of 21%) and then dropped precipitously to a hypoxic low of 15% (Berner and Canfield 1989; Landis and Snee 1991). These changes were duplicated in the water (e.g., Hosler 1977; Solem 1985; Dejours 1994) and had a dramatic influence on the aquatic life (Table 1), inducing relocation to land. The greater availability of O_2 during the Mid-Devonian to Carboniferous hyperoxic episode would have made it possible for organisms, e.g., the arthropods, to attain larger body sizes (Graham 1994). Furthermore, the abundance of O_2 resulted in higher metabolic capacities and greater accessibility to resources instigating vast radiation of the animal life.

1.13 CO_2 Pulses in the Biosphere

The atmospheric and aquatic levels of CO_2 have undergone remarkable fluctuations in the past (e.g., Bender 1984; Shackleton and Pisias 1985; Walker 1985;

Barnola et al. 1987; Berger and Spitzy 1988; Jasper and Hayes 1990). The partial pressure of CO_2 is presumed to have been 100 to 1000 times more in the antediluvian Earth than now (Walker 1983). It is envisaged that CO_2, CH_4, and NH_3 produced a greenhouse effect which sustained liquid water (e.g., Owens et al. 1979; Kasting 1997; Sagan and Chyba 1997). The solar luminosity during that time was 25 to 30% lower than at present (e.g., Newman and Rood 1977). Models of the early Earth after the end of the heavy bombardment suggest that the PCO_2 may have been as high as 10 bar (Walker 1977, 1983). From analysis of air trapped in the ice cores, Raynaud et al. (1993) observed that the atmospheric CO_2 decreased from about 290 to 190 $\mu mol\,mol^{-1}$ over a period of about 10000 years during the last interglacial-glacial maxima. Whereas the atmospheric partial pressures of nitrogen and helium remained fairly constant across the Phanerozoic, those of neon, krypton, and argon may have increased through mantle and crustal degassing (Holland 1984; Warneck 1988). Carbon dioxide and O_2 oscillations have occurred in reverse manner (e.g., Delmas et al. 1980; Neftel et al. 1982; Graham et al. 1995; Fig. 9). This is due to the fact that over geological time, photosynthetic carbon fixation in the oceans has surpassed the respiratory oxidation of carbon (Holland 1984; Berner 1991; Walker 1987; Falkowski 1997): the difference between the two values has reflected the net increase in O_2 and reduction of CO_2 from the Earth's atmosphere. During the Devonian period (400 to 360 million years ago), the spread of rooted vascular plants to the elevated areas of the dry land may have enhanced chemical weathering leading to removal of CO_2 from the atmosphere (Berner 1997; Fig. 9). Mechanisms of phosphorus-mediated redox stabilization of the atmospheric and marine O_2 levels (e.g., Redfield 1958; Broecker 1982; Cappellen and Ingall 1996) and nitrogen fixation and denitrification in sequestration of CO_2 in the oceans over geological time scales have been described by McElroy (1983), Codispoti and Christensen (1985), Shaffer (1990), and Falkowski (1997). During the past 2 million years, reduction in the atmospheric CO_2 level has correlated with increases in the deposition of organic carbon from the surface waters to the marine sediments (e.g., Sarnthein et al. 1988; Mix 1989; Hansell et al. 1997): carbon is traded between the atmosphere, the oceans, and the terrestrial biosphere, and in geological time scales between the sediments and the sedimentary rocks. The equatorial Pacific Ocean is the greatest oceanic source of CO_2 to the atmosphere and is also the main site of organic carbon discharge to the deep sea (Murray et al. 1994).

The highest levels of CO_2 in the biosphere occurred in the Ordovician and Silurian, mainly owing to massive tectonic activities (Holland 1984). Between the late Miocene, Pliocene, and early Pleistocene (i.e., between 10 and 2 million years ago), the concentration of CO_2 fluctuated within 280 and 370 ppm by volume (van der Burgh et al. 1993). By the Carboniferous, the level had dropped almost to the present one of 0.036% subsequently rising threefold by the end of the Permian (Graham et al. 1995). In the Archean, CO_2 level may have been 100 times greater than it is today (Walker et al. 1983). In the geological recent past, the atmospheric concentration of O_2 has been fairly constant but that of CO_2 is estimated to have increased from 0.029 to 0.033% within a period of 50 years, i.e., between 1900 and 1950 (Callender 1940) owing to combustion of fossil fuels. From the start of this century, anthropogenic emission of CO_2 (mainly from activities such as burning fossil fuel, cement production, and changes in land use) has led to its increase in mole fraction from 0.00030 to 0.00034 (Revelle 1982). Between the years 1980 and 1989, the average annual anthropogenic production of CO_2 is estimated to have been 7.1 billion tonnes (Bolin et al. 1994). Since the industrial revolution, the concentration of CO_2 has risen from 280 to 350 ppm by volume (ppmv), the highest value reached in the last 160 000 years (Bazzaz and Fajer 1992; Bolin et al. 1994). Estimations at the Mauna Loa observatory in Hawaii indicated about 20% real rise in CO_2 levels between the years 1957 and 1987 (Barnola et al. 1987). Owing to the greenhouse effect, the present global temperature change correlates with the logarithm of the atmospheric CO_2 concentration (Thomson 1995). It is projected that through anthropogenic emissions, global concentrations of CO_2 will double by the end of the 21st century, a process which may cause a temperature rise of about 3 °C, resulting in serious ecological consequences (e.g., Bazzaz and Fajer 1992; Azar and Rodh 1997). If CO_2 emission were held at the present level, this would lead to a nearly constant rate of increase in the atmospheric concentrations for at least two centuries, stabilizing at 500 ppmv by the end of the 21st century, i.e., about twice the level of the time before the industrial revolution, which was about 280 ppmv (Bolin et al. 1994). Photosynthesis can be stimulated by increased level of CO_2: an inverse relationship between stomatal frequency in the leaves of C_3 plants and anthropogenic increase in atmospheric CO_2 concentration has been demonstrated (e.g., Wagner et al. 1996). Under optimal conditions of water and nutrient supply, there is a potential increase in photosynthesis by 20 to 40% when the level of CO_2 rises (Youvan and Marrs 1987). Undisturbed forests are important terrestrial sinks of CO_2 (Grace et al. 1995). The view that an atmosphere enriched with CO_2 will accelerate photosynthesis resulting in a "greener planet" and that the greenhouse effect will be brought under control by increased withdrawal of CO_2 from the atmosphere by the luxuriant plant growth has been deemed highly simplistic and short-sighted (e.g., Bazzaz and Fajer 1992). Presently, CO_2 is the most important gas in the causation of global warming by the greenhouse effect, a state which may lead to irreversible changes in plant physiology and pattern of the vegetation cover (Betts et al. 1997).

Although CO_2 is well mixed in the atmosphere, variations in its concentration in air over land and that over the oceans and between the Northern and Southern Hemispheres are well recognized. In the more industrial Northern Hemisphere, the concentration of CO_2 rises in winter and declines in summer mainly in response to seasonal growth in land vegetation (e.g., Chapin et al. 1996; Keeling et al. 1996): the seasonal cycle (peak to trough) is 15 to 20 ppmv in the far north. The equilibrium PCO_2 between air and seawater increases three times when temperature rises from 0 to 30 °C. The surface temperature of the sea modifies the CO_2 content of the oceanic biosphere, making the cold polar air contain as much as 20 ppm less CO_2 than the warmer continental and tropical air. In spite of such fluctuations, the composition of the atmosphere is considered to be reasonably homogenous. This is mainly attributable to the greater turbulence of air resulting from temperature differentials in various parts of the Earth and the high diffusivity of atmospheric gases at these temperatures. This accounts for the simplicity of the composition of the atmosphere and, for that matter, of any gas mixture. With as little information as temperature and barometric pressure, it is possible to accurately predict and estimate the changes in the tensions and concentrations which occur in a gas phase when O_2 is consumed and CO_2 released during respiration. Except for special microhabitats such as burrows and dens of mammals, reptiles, and birds, caves of freely roosting bats, within colonies of insects, and in pouches of marsupials (e.g., Mitchell 1964; Boggs et al. 1984; White et al. 1984), where relatively high levels of CO_2 and NH_3 and low concentrations of O_2 may occur, deviations in the basic composition of atmospheric gases are only naturally encountered at high altitude due to changes in barometric pressure. The rise in the atmospheric O_2 and the drop in that of CO_2 were major factors in the development of the modern respiratory organs. In the derelict aquatic habitats, high concentrations of CO_2 in water constituted a decisive driving force for transition to air breathing (Chap. 5). High atmospheric levels of O_2 led to a greater emphasis of the lungs for gas exchange, influenced the transition from buccal pumping to suctional breathing (Liem 1985; Brainerd 1994), and perhaps occasioned the change from O_2- to a CO_2-regulated respiratory control mechanism. The reduced water loss to O_2 extraction ratio was an important benefit derived from occupying a normoxic atmosphere. The early Paleozoic aquatic animals and subsequently the early amphibians subsisted in hypoxic conditions similar to the inimical ones which presently occur in habitats such as in burrows, tropical swamps, ocean sediments, and high altitudes. The present-day bimodal breathers and the developing amphibians face challenges similar to those which confronted the pioneers of transition from water- to air breathing.

1.14 The Overt and Covert Roles of O_2 in Colonization and Extinctions of Biota

Except for the recent past when the Earth presented much the same kind of climate as it does now (e.g., Boucot and Gray 1982), the planet is replete with recurrent catastrophic crises of varying magnitudes, a number of which have more or less directly or indirectly corresponded with the levels of O_2 in the biosphere. Five major episodes, in addition to numerous minor ones, have occurred. They took place at the end of the Ordovician, late Devonian, end of Permian, end of Triassic, and end of Cretaceous (e.g., Benton 1993; Weinberg 1994). Fairly fortuitously, life has navigated through these hazards, but at an enormous cost. About 99.99% of all animal species which have ever evolved on Earth are now extinct (Pough et al. 1989). During the mid-Paleozoic Mass Extinction, dubbed "the mother of all extinction" by Erwin (1993), an event which occurred towards the end of the Permian period (e.g., Robinson 1991; Allegre and Schneider 1994), adverse tectonic activity which lasted through the Triassic to the early Jurassic culminated in an abrupt temperature decline. Concurrently, a sudden drop in sea level occurred. The land submerged under water decreased from 30 to 5%, leading to exposure of expansive organic sediment (Erwin 1996). This resulted in increased utilization of O_2 in oxidative processes with an attendant upsurge in the discharge of CO_2 into the atmosphere. The consequence was an extremely severe hypoxia which was exacerbated by hypercarbia (Benton 1995; Wignall and Twitchett 1996): a worldwide deep sea anoxic outcome which occurred across the Permo-Triassic (or Paleozoic and Mezozoic) boundary (~250 million years ago) which lasted for 20 million years has been described by Isozaki (1997). The mid-Paleozoic crisis led to a near-annihilation of the marine biota (e.g., Tappan 1974; Weinberg 1994). Even under such dire circumstances, the level of O_2 in air was greater than that in water, making air breathing an evolutionary advantage. Nearly 90% of the aquatic animals succumbed (e.g., McGhee 1989) and on land, more than two thirds of the reptilian and amphibian species perished (Erwin 1993, 1994). In the only mass extinction which insects have had to endure, a sign of the severity of the prevailing conditions, 30% of the orders died (Erwin 1996). In all taxa, the particularly vulnerable groups were those which had preadapted to the earlier hyperoxic milieu of the Carboniferous. It has, however, been argued, e.g., Graham et al. (1995), that lack of O_2 per se was not the primary factor which precipitated this immense demise, since the drop in O_2 from the peak levels is envisaged to have been very gradual, occurring over a long period of time during which the animals should have adapted to the change. However, Erwin (1996) pointed out that the actual active period of extinction may have been as short 1 million years, if not less. In the late Triassic extinction (about 200 million years ago), 20% of the families of animals died out, eliminating some 50% of the species (Benton 1993). Animals such as the ammonoids and bivalves were severely decimated and the cocodonts disappeared. Contrary to expectation, no frequency or periodicity has been evident in the seven mass extinctions (i.e., in the Early Cambrian, Late Ordovician, Late Devonian, Late Permian, Early Triassic, Late Triassic, and End Cretaceous) which have occurred in the last 250 million years (Benton 1995): the episodes are separated by between 20 and 60 million years.

The ecological disaster which has caught most of the attention of scientists and the public, even though far less severe, is that of the dinosaurs and their contemporaries, the plesiosaurs and pterosaurs. This occurred between the Cretaceous and Tertiary (65 million years ago). The global faunal diversity was reduced by 60 to 80% (Raup and Jablonski 1993). Geological (terrestrial) as well as cosmic (extraterrestrial) events have been associated with the demise (e.g., Hallam 1987; Stanley 1987; Kerr 1988; Powell 1993). Based on a high concentration of iridium in some rock deposits at the end of the Cretaceous, a large asteroid or a comet about 10 km in diameter is thought to have impacted on Earth off the Yucatan Peninsula (Mexico) (e.g., Sheehan et al. 1991). The mass of dust thrown into the atmosphere blocked out the sun's rays, suppressed photosynthesis (perhaps causing a drop in the level of O_2 in both air and water), and occasioned severe changes in the Earth's climate. As in the "mid-Paleozoic Mass Extinction", sea level fluctuated by about 50 to 200 m over a period of 0.2 to 1 million years (Haq et al. 1987; Kerr 1996b; Stoll and Schrag 1996). The definite cause of the drop in sea level during the Cretaceous, a period during which the climate is predicted to have been fairly stable, where the equatorial temperatures were equal to the present ones (Herman and Spicer 1996), and the poles were ice-free (Barron et al. 1981), is still debatable.

1.15 Oxygen: a Paradoxical Molecule

Most profoundly, molecular O_2 has influenced the geology of the Earth and pervasively directed the trajectory and forward momentum of evolution of life. Since the first appearance of the gas in the biosphere in appreciable quantity some 2 billion years ago (e.g., Owens et al. 1979), the history of life is literally inscribed on this single molecule. The buildup of O_2 and evolution of oxygenic respiration (following the radical conversion of the incipient high CO_2-low O_2 atmosphere to low CO_2-high O_2 atmosphere) led to the transformation of the early simple anaerobic cells to the versatile eukaryotic ones which subsequently accreted into the aerobic, multicellular organisms (Siever 1979; Allegre and Schneider 1994; Orgel 1994). The transformation enhanced the efficiency of carbon and nutrient recycling, leading to a climactic increase in the organic biomass. Margulis (1979) envisages that the toxicity of the O_2 molecule enforced symbiotic associations on anaerobic bacteria, leading to development of eukaryotic cells. Symbiotic relationships are known to evolve under extreme circumstances (e.g., Childress et al. 1989; Rennie 1992). The presence and the resolutely increasing levels of O_2 may explain the short period (in evolutionary terms) of 700 million years which it took for the growth and change of the eukaryotic cells to multicellular organisms compared with the over 2 billion years which passed before the aerobic eukaryotic cells developed from the anaerobic prokaryotes (Gould 1994; Fig. 8).

In virtually all the solar system planets and their satellites, free atmospheric O_2 for which there are no known primary (geochemical) sources, is found in high concentration only on Earth. As a molecular factor, however, O_2 is not unique to our biosphere. Jupiter's moons Europa and lo, for example, have surface and atmospheric water, gaseous sodium, and small quantities of O_2 (Brown and Hill 1996; Kerr 1997), a state which is similar to that of Earth some 4 billion years ago. Due to its high reactivity with other elements at both the temperatures of the formation of the magma (500 to 1200 °C) and at ordinary surface temperatures, O_2 is the most abundant element of the average crustal rocks, followed by silicon, aluminum, and iron (Chapman and Schopf 1983). This notwithstanding, O_2 is a somewhat alien factor to life. A reducing (nonoxidizing) environment was a prerequisite for the chemical evolution of life from the first organic molecules in the primitive atmosphere (e.g., Cloud 1974, 1988; Miller and Orgel 1974; Tappan 1974; Schidlowski 1975; Chang et al. 1983). It is an intellectually intriguing contradiction that life, which evolved in absence of O_2, is now tractably dependent on it. Oxygen is a necessary resource for body growth and development (e.g., Adelman and Smith 1970; Priede 1977; Armstrong et al. 1992). Extended exposure to hypoxia in newborn and young mammals causes a decrease in body growth (e.g., Timiras et al. 1957; LaManna et al. 1992). While animals that are well adapted to high altitude, like the Ilama and many small rodents and birds, are known to reproduce successfully up to an altitude of 5 km, human fetal growth is retarded at altitudes beyond 3 km above sea level (e.g., Haas et al. 1980; Mayhew et al. 1990).

1.16 The Rise of the Level of Molecular O_2: a Curse or a Blessing?

1.16.1 The Deleterious Reactive Radicals of Molecular O_2

Although the aerobic life-style confers great advantages, as metabolism using O_2 yields 20 times more free metabolic energy than an anaerobic one, utilization of O_2 is accompanied by great danger (Pryor 1986; Joenje 1989; Sies 1991). Even under ordinary conditions, due to continuous formation of free radicals (chemically highly reactive molecules with an unpaired electron) which are intermediates of a number of biochemical reactions, O_2 is a highly toxic substance. Its utilization by aerobes is harmful in both the short and long terms (e.g., Comroe et al. 1945; Clark and Lambertsen 1971; Fridovich 1978; Halliwell 1978; Hill 1978; Slater 1984; Sies and Cadenas 1985). Physical exercise increases formation of reactive O_2 species but in the long term, endurance training improves antioxidant handling (Sen 1995). Strictly, molecular O_2 is not the toxic agent but rather its reactive derivatives (Cochrane 1991). Inflammatory cells (neutrophils, eosinophils, and macrophages), catalase negative bacteria, inhaled environmental pollutants (e.g., ozone and nitrous oxide), and even epithelial cells (e.g., intracellular production from mitochondrial respiration and xenobiotic drug metabolism) are potential sources of reactive O_2 species (Bast et al. 1991; Kinnula et al. 1992; Cohn et al. 1994). The oxidants have been associated with pathogenesis of respiratory disorders such as adult respiratory distress syndrome, emphysema, asthma, and pollutant-precipitated diseases (Adler et al. 1990; Barnes 1990). During ordinary aerobic respiration, complete reduction of a molecule of O_2 to H_2O requires four electrons which are sequentially utilized in the process:

$$O_2 \xrightarrow{e^-} O_2^- \xrightarrow{e^-} H_2O_2 \xrightarrow{e^-} OH^- \xrightarrow{e^-} H_2O.$$

Various active intermediates, highly reactive chemical species with one or more unpaired electrons, are produced. These include the superoxide anion radical (O_2^-), hydrogen peroxide (H_2O_2), hydroxyl radical (OH^-), and singlet oxygen ($^1O_2$). The oxidant by products of metabolism cause extensive damage to DNA, proteins, and other macromolecules (Borteux 1993; Epe 1995). Degenerative diseases associated with aging such as arteriosclerosis, Parkinson's disease, diabetes, cancer, decline in the immune system, and senility have been associated with the oxidative damages caused by molecular O_2 (e.g., Fraga et al. 1990; Wagner et al. 1992; Ames et al. 1993; Gutteridge 1993; Halliwell 1994). The assault by the reactive O_2 radicals on cell functional and structural integrity is intense. It is estimated that about 2 to 3% of the O_2 taken up by aerobic cells results in production of O_2^- radical and H_2O_2 (Chance et al. 1979). Approximately 10^{12} O_2 molecules are handled by a rat cell daily (Chance et al. 1979). This results in about 2×10^{10} (i.e., 2%) O_2^- and H_2O_2 active (partially reduced) species. Frage et al. (1990) estimated that there are about 9×10^4 attacks on the DNA per day per cell in a rat. Under a steady state, about 10% of protein molecules may undergo carbonyl modifications (Fridovich 1978; Ames et al. 1993; Orr and Sohal 1994). Ames et al. (1993) envisaged that O_2 free radicals are responsible for 10000 or so DNA base modifications per cell per day. Such sustained attacks can easily overwhelm the cell's repair mechanisms. All cells have evolved a number of repair endonucleases which specifically recognize and repair the damages caused by the reactive species (Lindal 1990; Demple and Harrison 1994). When the biodegradative processes surpass the biosynthetic ones, the cumulative damages may result in significant loss in the cell functional capacity (Stadtman 1992). Oxygen free radical-mediated lipid peroxidation, for example, could easily lead to loss of membrane integrity and hence compromise the normal cellular activities. A substantial memory recovery was achieved by chronically treating old gerbils (15 to 18 months) with a free radical spin-trapping compound *N-tert*-butyl-β-phenylnitrone (Carney et al. 1991). The process resulted in a substantial decrease in the amount of oxidized protein in the brain and an increase in the amounts of glutamine synthetase and neutral protease activities. Oxygen, and particularly the resultant OH^- radical, increase the lethal effects of ionizing radiation (Von Sonntag 1987; Ames et al. 1993). Lipid peroxidation results in mutagenic factors (e.g., epoxides and alkoxyls) and $^1O_2$.

The formation of reactive O_2 species inside cells constitutes a serious threat to the functional and structural integrity of the cellular genome (Lindal 1990; Epe 1995). It is envisaged that control of O_2 toxicity could have necessitated the evolution of the nucleus and the nuclear membrane in the eukaryotic cells to minimize external affronts by molecular O_2 (e.g., Margulis 1981). The nucleus constitutes an anoxic and fairly safe location for the deoxyribonucleic acid (DNA). The DNA nearer to the nuclear membrane and that in the O_2-rich cytoplasm are more susceptible to damage. The mitochondrial DNA (mtDNA) is particularly more exposed to O_2 toxicity compared with the nuclear DNA (nDNA) (Gupta et al. 1990; Dyer and Ober 1994). The mtDNA from the rat liver causes more than ten times the level of oxidative DNA damage than does nDNA from the same tissue (Richter et al. 1988). This may be due to factors such as lack of mtDNA repair enzymes, lack of histones protecting mtDNA, and the proximity of mtDNA to oxidants produced during oxidative phosphorylation. A high turnover of mitochondria ensures removal of the damaged organelles (which generate greater quantities of oxidants) but overall, oxidative lesions accumulate in the mtDNA at a greater rate than in the nDNA (Ames et al. 1993). Generally, mitochondria are protected from injury by: (1) the complex extracellular O_2 diffusion pathway where at the cellular level the PO_2 will have dropped to almost zero and (2) by clustering, a process which reduces the area available for influx of O_2 into individual mitochondria (Gnaiger 1991). The PO_2 in blood capillaries of the cardiac muscle is ten times greater than in isolated mitochondria (Tamura et al. 1989). Clustering accounts for the difference in the O_2 uptake capacities between isolated liver mitochondria and the intact ones in the hepatocytes (Jones 1986). Connett et al. (1985) estimated that the PO_2 in the red muscle cell is about 0.07 kPa. Mitochondria in living tissues are estimated to operate at low O_2 levels, frequently below 2% of air saturation of a PO_2 of 0.5 kPa (Wittenberg and Wittenberg 1987, 1989; Graiger et al. 1995). Respiration in the mitochondria is not affected until the PO_2 drops to below 0.01 to 0.1 kPa (Oshino et al. 1974; Sugano et al. 1974). Just as in high quantities, lack of O_2 is equally injurious. In those tissues that are intolerant to hypoxia, e.g., the brain and the heart muscle, mitochondria undergo irreversible structural failures where the membrane potentials decline, and the degree and capacity of molecular coupling is lowered (Zimmer et al. 1985).

1.16.2 Senescence: the Effects of Molecular O_2

Senescence is a progressive and irrevocable loss of functional capacity due to degeneration of somatic cells in the last part of life. It has been associated with the use of O_2 by the cells even under normal physiological conditions (e.g., Floyd 1991; Ames et al. 1993; Sohal and Weindruch 1996). As part of the metabolic processes, aerobic organisms generate potentially destructive O_2 species which cause serious oxidative damage to biological macromolecules (e.g., Fridovich 1978). The damage occurs in form of peroxidation of membrane polysaturated fatty acid chains, alteration in DNA protein bases configuration, and carbonylation and loss of sulfhydryls in proteins. Changes due to aging directly or indirectly affect the O_2 uptake process itself (Horvath and Borgia 1984). A senile lung is defined as one which presents dilation of the air spaces without tissue destruction (e.g., Hyde et al. 1977; Pinkerton et al. 1982; Snider et al. 1985; Dios-Escolar et al. 1994). Studies on the effects of age on lung structure have, however, been inconlusive (e.g., Thurlbeck 1980). The impedement has been due to the fact that the effects of environmental pollution and lifestyle have been difficult to fully assess and exclude from the various studies. No aging structural changes in the lung were observed in the growing specific-pathogen-free inbred male BALB/cNNia mice between 38 days and 28 months by Masahiko et al. (1984). In adult humans, arterial O_2 tension decreases by an average of 0.28 to 0.54 kPa each decade while the alveolar PO_2 remains constant or increases slightly (Dill et al 1963; Sorbini et al. 1968). Pulmonary diffusing capacity decreases by 5 to 8% in each decade of life (Cohen 1964). With aging, the surface area of the erythrocytes decreases and the cells become more susceptible to osmotic changes and mechanical disruption while there is reduction in enzymatic activity, e.g., hexokinase, glucose-6-phosphate dehydrogenase, and lactate dehydrogenase (Prankerd 1961). Compared with young rats, old rats have a lower hind limb muscle respiratory capacity and whole body maximal O_2 consumption (Cartee and Farrar 1987). In both animals and plants, paraquat (methyl viologen), a commonly used herbicide, and antibiotics such as streptonigrin which enhance the rate of O_2 radical (O_2^-) production, are more toxic under aerobic than anaerobic conditions. Longevity correlates inversely with the rate of mitochondrial production of the O_2^-, H_2O_2, and OH^- species. In a number of mammals, the severity of oxidative DNA damage appears to correlate with the metabolic rate (Adelman et al. 1988; Shigenaga et al. 1989). Restriction of calorific intake, a process which lowers metabolic stress, reduces age-related changes and prolongs the life span of mammals (Sohal and Weindruch 1996). Overexpression of superoxide dismutase and catalase, antioxidative enzymes which respectively remove O_2^- and H_2O_2, extends the life span of *Drosophila melanogaster* (Orr and Sohal 1994). Reduction in production of active O_2 species in transgenic *Drosophila melanogaster* leads to a 30% increase in the metabolic potential (Orr and Sohal 1994). In two human diseases associated with premature aging, Werner syndrome and progeria, oxidized protein residues increase at a faster rate than normally (Stadtman 1992). The gradual decay of the cell integrity with age is an indication that the antioxidant defenses of the aerobic cells are inefficient in face of sustained assault by the reactive O_2 metabolites. Oxidative lesions on DNA increase with age (Ames et al. 1993): at the age of 2 years, a rat cell has about 2 million lesions per cell. This is about twice that of a young rat. Exogenous oxidant loading from activities such as smoking may deplete the endogenous antioxidant levels in the cells, such stress compromising the cell defenses (Csillag and Aldhous 1992).

Notwithstanding the deleterious effects of the endogenous reactive species, not all effects of the active species are harmful. Leukocytes and other phagocytic cells destroy bacteria or virus-infected cells by subjecting them to a lethal discharge of nitric oxide (NO), O_2^-, H_2O_2, OH^- and OCl^-, a potent oxidant mixture (Baldridge and Gerard 1933; Seifert and Schultz 1991; Stamler et al. 1992). Like O_2, among gases, NO (which, unlike O_2, is elaborated in animal tissues but in very small quantities; De Belder et al. 1993; Ballingand et al. 1995) is an enigmatic molecule. In the atmosphere, NO is a toxic chemical but in small regulated quantities in the body, it plays vital physiological, pharmacological, and immunological roles. It participates in processes such as blood pressure control (through smooth muscle relaxation), platelet inhibition, neurotransmission, destruction of pathogens, penile erection, and has even been associated with learning and long-term memory (Culotta and Koshland 1992; Koshland 1992; Stamler et al. 1992; De Belder et al. 1993; Ballingand et al. 1995). Nitric oxide and, amazingly, carbon monoxide (one of the most feared gases) are the first gases known to physiologically regulate levels of guanosine 3,5-monophosphate and thus act as biological messengers and signaling molecules in mammals (Moncada et al. 1991; Toda and Okamura 1991; Galla 1993; Verma et al. 1993; Katušic and Cosentino 1994). Above certain thresholds, active radicals of NO such as nitrosonium cation (NO^+), nitric oxide ($NO^\cdot$), and nitroxyl anion (NO^-), similar to the redox states of O_2 (i.e., O_2^-, H_2O_2, and OH^-), form and oxidize biological molecules.

Evolution does not appear to have found any direct, enduring solution for neutralizing the harmful active species of molecular O_2. However, to ameliorate the effects, cellular biochemistry has been configured such that the most important processes are the reductive ones: biological oxidations entail removal of H_2 rather than addition of O_2. The increasing susceptibility of the cells to oxidative effects of the reactive O_2 radicals with age may be caused by several factors. These include: (1) an increase in the O_2 delivery rate to the cells as may occur with changes in the amounts of allosteric effectors which determine the O_2 binding capacity by the hemoglobin, (2) increased availability of the Fe(II) or Cu(II), metals which are catalytically involved in the production of the highly damaging O_2-free species by changes in the efficacy of metal binding proteins and chelating agents, (3) an age-dependent increase in the production of the reactive O_2 metabolites, (4) an intrinsic decline in the production of the endogenous antioxidant scavenger enzymes and metabolite defenses, (5) loss of capacity to biodegrade the products of cell oxidation, and (6) decrease in the capacity to mobilize and repair the damages caused by the active radicals. In the life cycles of practically all complex organisms, the integrity of the tissue cells appears to be guaranteed only up to the useful reproductive period. It is possible that reproduction takes such a heavy toll of an animal's resources that the necessary amount needed for maintenance of the integrity of the somatic cells is irrevocably compromised.

1.16.3 Biological Defenses Against O_2 Toxicity

Of the four fundamental elements of life, the so-called biogenetic elements, carbon, hydrogen, oxygen, and nitrogen, O_2 is a geochemical and biochemical anomaly. Although a structural component of biological tissues and an integral part of biochemical reactions, in combined as well as free diatomic state, depending on the organism and level of concentration, O_2 is a toxic factor. The accretion of molecular O_2 changed the entire global environment and dramatically influenced the nature and tempo of all subsequent evolutionary developments in life. Most animals die after extended exposure to 100% O_2 (1 atm), the endothelial lining of the lung being the main site of injury (e.g., Matalon and Egan 1981; Crapo et al. 1984; Block et al. 1986; Crapo 1986). Rats die between 60 to 72 h after exposure to 100% O_2 (Crapo 1987). Exposure of 21-day-old rats to >95% O_2 for 8 days induces cholinergic hyperresponsiveness as well as hypertrophy of the airway epithelial and smooth muscle layers (Hershenson et al. 1994). More than 50% of 72-h-old chick embryos die on exposure to 3 h of 5 atm of O_2 and 20 to 30% of those which hatch have deformities of the brain, eyes, upper jaw, legs, feet, and heart (Pizarello and Shircliffe 1967). In mammals, on exposure to hyperbaric O_2 (partial pressure of O_2 in the inspired air greater than 1 atm), nervous acute O_2 poisoning occurs. This is expressed in form of epileptiform convulsions (Barthelemy 1987). Nitrogenases, the enzymes necessary for the fixation of nitrogen (e.g., Leigh 1997), are inhibited by as little as 0.1% free O_2 (Postgate 1987). Many nitrogenous bacteria occupy anaerobic habitats, e.g., cells of leguminous plants under the soil. The reactivity of O_2 makes it a rather biologically enigmatic molecule (Cochrane 1991). It readily reacts with the reduced (H-rich) biochemical factors to produce energy (in aerobic respiration) and its highly reactive radicals oxidize and destroy enzymes. The reactive side products such as superoxides, peroxides, hydroxyl radicals, and $^1O_2$ are biologically toxic to strict anaerobes and at even moderate concentrations are highly toxic to aerobes (Fridovich 1976, 1978; Halliwell 1978). Practically all organic compounds tend to be easily oxidized and are hence potentially unstable in the presence of molecular O_2 (Miller and Orgel 1974). Adaptively, the epithelial cells which line the respiratory organs contain antioxidant enzymes which prevent initiation of pulmonary pathology after contact with oxidants such as ozone, nitrous oxide, and oxidants produced by local inflammatory reactions (Kinnula et al. 1992; Cohn et al. 1994).

It is overtly anomalous that life started in an O_2-free environment and subsequently became so heavily dependent on it. The stubbornly increasing levels of O_2 left the cells with no alternative but to somehow accommodate it or face certain annihilation. Its rather small molecular size and hence high intracellular diffusivity and a correct redox potential endeared O_2 to utilization as an electron acceptor in the biochemical energy production of the tricarboxylic chain processes. Interestingly, in myocardial cells, when energy depletion in a cell, e.g., in the case of ischaemia or hypoxia, is extended beyond the stage when reoxygenation leads to spontaneous recovery, in what has been termed the oxygen paradox (e.g., Piper et al. 1994), reoxygenation may intensify tissue damage (Hearse et al. 1973; Ganote 1983; Gorge et al. 1991) presumably due to excessive production of active free radical (McCord 1988; Turrens et al. 1991): life's biochemistry has not achieved a capacity of totally taming molecular O_2.

As a part of antioxidant defense system, gas exchangers (e.g., Crapo and McCord 1976) and some organisms, e.g., bacterial aerobes like *Escherichia coli* (Gregory and Fridovich 1973) possess a battery of simple nonenzymatic molecules and complex enzymes which scavenge the oxidative O_2 radicals (Forman and Fisher 1981; Freeman and Crapo 1982; Halliwell and Gutteridge 1985; Sies 1991). The former include glutathione, ascorbate, urate, bilirubin, ubiquinol, β-carotene, and tacopherol, while the latter comprise superoxide dismutase (SD), catalase, and glutathione peroxidase. Superoxide dismutase converts the superoxide radical (O_2^-) to H_2O_2 plus O_2 (e.g., Crapo and Tierney 1974; Fridovich 1975; Cassini et al. 1993) and catalases and peroxidases convert H_2O_2 to H_2O and O_2. Experimentally, rats are protected from O_2 toxicity by intravenous injection of liposome-entrapped catalase and superoxide dismutase (Turrens et al. 1984). Hyperoxia increases release of reactive O_2 species in the mitochondia (Turrens et al. 1982a,b). Adaptively, in old rats, even though glutathione synthesis is decreased, the tissue regeneration capacity appears to be increased to cope with oxidative stress (Ohkuwa et al. 1997). In rat lungs, on hyperoxic exposure, gene expression plays an important role in controlling manganese containing superoxide dismutase activity (Ho et al. 1996). Interestingly, molecular H_2, has been reported to destroy active O_2 radicals (Jones 1996). Aerobiosis could not have arisen directly from anaerobiosis. It was imperative that preadaptations for tolerating O_2 toxicity would have required time to evolve. It is speculated that photochemically produced O_2 at low manageable levels may have nurtured some degree of aerotolerance (Walker et al. 1983), a feature which would have imparted a selective advantage when a stable oxygenic atmosphere formed. The envisaged chronological order through which molecular O_2 was incorporated into the biochemical processes is: (1) development of defensive mechanisms (though it is difficult to explain how these could have been configured in absence of O_2 itself), (2) production of O_2 by the cyanobacteria, and (3) incorporation and utilization of O_2 at the cellular level. The transition to an aerobic environment brought about and required evolution of higher redox potential biochemistry (e.g., Williams and Da Silva 1978). This necessitated evolution of new catalysts which were based on transitional metals. It has been estimated that the befitting redox potential of the primitive oceans may have been about $-350\,\mathrm{mV}$ (Osterberg 1974). Though O_2 is mainly utilized for energy production, many other nonrespiratory processes like collagen synthesis, oxidation of amino acids, and tanning of cuticle (in many insects) require molecular O_2. In the facultative invertebrate anaerobes, growth is arrested with reduction in the level of O_2 (e.g., Hammen 1969, 1976). To avoid oxidation of nitrogenase enzymes, the nitrogen-fixing cyanobacteria have evolved a novel method of coexistence ensuring intracellular anoxia. Special cells called heterocytes which lack the full complement of photosynthetic pigments and are hence incapable of producing O_2 have developed thick cell walls covered by a mucinous coat to limit O_2 inflow: these cells are endowed with the appropriate enzymes for destroying the harmful O_2 radicals.

1.17 The Evolution of Complex Metabolic Processes

The evolution of the eukaryotes from prokaryotes (some 2 billion years ago), the attainment of capacity for sexual reproduction (some 1 billion years ago) and, subsequently, development of complex multicellular life about 600 million to 1 billion years ago (Schopf and Oehler 1976; Schopf 1978; Wray et al. 1996) were pivotal points in the development and proliferation of animal life (Romer 1967). It is conjectured that mitochondria, the power houses of cells, evolved from free-living eubacteria-like endosymbionts which more than a billion years ago (e.g., Palmer 1997) invaded the eukaryotic cells (e.g., Margulis 1970, 1979; Vogel 1997). This is vindicated by the fact that organelles such as chloroplasts and mitochondria contain RNA and DNA which are different from those in the nuclei of the eukaryotic cells and in most ways resemble those of certain bacteria. The closest contemporary "relatives" of the mitochondria are the rickettsial group of the α-proteobacteria (Yang et al. 1985; Lang et al. 1997). The rat mitochondrial outer membrane localizes benzodiazepine receptor (MBR) which is expressed in wild-type and $TspO^-$ (tryptophan-rich sensory protein) strains of the facultative photoheterotroph, *Rhodobacter sphaeroides* (Yeliseev et al. 1997): functionally, MBR substitutes for $TspO^-$ and negatively regulates the expression of photosynthesis genes in response to O_2. This provides further evolutionary support for the origin of mammalian mitochondrion from a photosynthetic precursor. Since it was fully elucidated in the 1960s, the genetic code was thought to be universally identical as any mutations were deemed fatal – the frozen accident hypothesis of Crick (1966). Intellectually, this was a satisfying expectation as it supported the concept of a common origin of life and the parsimony of life in conservation of highly important factors. It is now known that the coding system in mitochondria in various mammalian phyla, certain bacteria, ciliated protozoa, mycoplasma, algae, and yeasts differs from the "universal code", in use of certain codons (e.g., Barrell et al. 1979; Anderson et al. 1981; Jukes 1985; Yamao et al. 1985; Jukes and Osawa 1993). It is envisaged that the universal code may be an evolutionary descendent of the mitochondrial-type code (Osawa et al. 1992) which shows extreme features of genomic economization perhaps to save space (Kurland 1992). By incorporating the endosymbionts, a process called secondary endosymbiosis, the eukaryotic cells did not, so to speak, have to reinvent respiration and photosynthesis through the long and costly trial-and-error process of genetic evolution. The origin of aerobic metabolism involved only extension and refinement of the preexisting anaerobic processes (the O_2-independent primitive glycolytic fermentation) by development of catalysts (enzymes) (Keevil and Mason 1978; Gunsalus and Sligar 1978; White and Coon 1980) which acted on the new addition to the energetically more efficient citric acid (Krebs) cycle (Williams and Da Silva 1978; Chapman and Schopf 1983; Schopf 1989). In advanced eukaryotes (e.g., vertebrates and plants), O_2 is involved in the sequence of chemical reactions only at the terminal stages, i.e., the most recently evolved sections of the pathway. The anaerobic bacteria are capable of effecting only the glycolytic pathway. With time, molecular O_2 has been incorporated in the biochemical synthetic pathways of compounds such as phenols, polyunsaturated fatty acids, amino acids, cytochromes, and bile pigments (in vertebrates) and elsewhere only in the relatively advanced organisms of particular lineages. The O_2-dependent metabolites of the aerobes have amply been used only to refine in a biochemical, structural, and functional manner the earlier established anaerobic systems: no totally new molecular complexes have evolved (e.g., Rohmer et al. 1979; Chapman and Ragan 1980).

1.18 Oxygen and CO_2 as Biochemical Factors in Respiration

The development of aerobic biochemistry is of fundamental interest to respiratory and evolutionary biologists. Compared with CO_2, O_2 is the more important factor in respiration. No permanent change especially of structural nature has been reported on exposure of living tissue to extended hypercapnia. In total anoxia, e.g., when breathing pure N_2, a human being loses consciousness within 30 to 40 s and permanent brain damage may occur. On breathing 30% CO_2 in O_2, a period of dyspnea occurs and loss of consciousness ensues. Complete resuscitation without any permanent damage can occur. Carbon dioxide-induced acidotic narcosis (Sieker and Hickam 1956) has been applied to treat some psychiatric disorders (e.g., Meduna 1950). Unequivocally, O_2 procurement is the primary goal of respiration and CO_2 elimination and hence acid-base regulation are secondary roles. A complex neurohormonal system has evolved especially in vertebrates (e.g., Fedde and Kuhlmann 1978; Ballintijn 1982) to monitor O_2 levels in blood. A reduction of the PO_2 in the ambient air results in a drop of that in blood. Below a certain threshold level, the arterial PO_2 chemoreceptors send impulses to the respiratory center in the brain stem from where ventilatory rate is adjusted. Although the brain constitutes one of the so-called noble organs (the others being the heart and the lung), which are structurally and functionally highly protected against O_2 fluctuations (e.g., Zapol et al. 1979; Freedman et al. 1980), the blood-brain barrier is highly permeable to respiratory gases. The actual mechanism through which molecular CO_2 acts on the respiratory centers, if it does at all, has been highly debated since H^+ and HCO_3^- ions exist in equilibrium with carbonic acid (H_2CO_3) (e.g., Crone and Lassen 1970; Bradbury 1979). Hyperoxia-induced hypercapnia, which may result in total cessation of ventilation in the trout (e.g., Dejours 1973), in the crayfish (Massabuau et al. 1984), and in the green crab (Jouve-Duhamel and Truchot 1983), shows that at least in water breathers, animals are insensitive to or are incapable of responding to elevated CO_2 in face of O_2 assault. Hypercapnea does not appear to affect ventilation in hyperoxic water breathers (Dejours 1988). However, in the only discordant view, Thomas et al. (1983) reported data to the contrary on the rainbow trout (*Oncorhynchus mykiss*): marked increase in ventilation was observed in specimens made hypercapnic even under hyperoxia. Except in the fossorial animals which adaptively tolerate high CO_2 levels, whether in moderate hypoxia, normoxia, or hyperoxia, air breathers increase ventilatory rate after inhalation of CO_2-enriched air: the hypercapnia-induced hyperventilation enhances CO_2 clearance, reduces arterial hypercapnia, and establishes normal pH. In a hypoxic environment, increased ventilation and heart rate, processes which are energetically costly to maintain, are not only unproductive but harmful. Faced with such a crises, reduction of metabolism is a beneficial process to overcome hypoxia (e.g., Hochachka 1988). Hypothermic hypometabolism in a squirrel results in an 88% saving on energy (Wang 1978).

1.19 Homeostasis: the Role of Respiration

Respiration plays an integral part in regulation of the blood pH. To a large extent, respiratory activity is driven to meet the need. The PCO_2 of the arterial blood is the most important factor which governs respiration (Davenport 1974). The goal of regulating breathing is to minimize respiratory work while maintaining stable and optimal levels of respiratory gases and pH. The arterial blood O_2 concentrations are appropriately adjusted and the levels of CO_2 and H^+ ions in blood kept within the physiological range. At the normal steady-state respiratory rate, the alveolar and arterial PCO_2 are adjusted around a value of 5.3 kPa. The respiratory system presents a metabolic servomechanism designed to match pulmonary and metabolic gas exchange rates without altering the internal chemical concentrations of the body fluids. The error-correcting feedback signals are provided by the concentrations of O_2, CO_2, and H^+ in the arterial blood. In the higher vertebrates, birds and mammals and to an extent terrestrial reptiles, pulmonary ventilation is used to regulate the rate of CO_2 elimination, a role played by the gills in aquatic breathers. The gas exchanger and the circulatory system effect these processes at rates corresponding with the prevailing metabolic demands. Uptake of O_2 affects body fluid homeostasis especially the acid-base status to a very small extent through release of H^+ ions (after conversion of HCO_3^- ions to CO_2 on the binding of O_2 to hemoglobin – the Haldane effect) in the gas exchanger (e.g., Davenport 1974; Heisler 1989). In contrast, CO_2 is the main product of aerobic metabolism. It is involved in chemical reactions which affect the acid-base status of the body fluids. In a watery solution, on accumulation, CO_2 is a weak acid and has to be buffered to keep the body fluid pH relatively constant. Through carbonic anhydrase catalysis and chloride shift, the largest fraction of total CO_2 is carried in form of HCO_3^- ions in both blood plasma and the erythrocytes (Davenport 1974). This roughly constitutes about 90 to 95% of the total CO_2 in blood. At the gas exchanger, the HCO_3^- ions are converted back into CO_2, which diffuses out into the external medium (e.g., Perry and Laurent 1990). To ascertain CO_2 diffusion equilibrium, the amounts of carbonic anhydrase in the erythrocytes are much higher in the small than in the larger mammals up to an order of magnitude (Larimer and Schmidt-Nielsen 1960; Lindstedt 1984). Although hypoxia may be brought about by deficiency of O_2 in the environment or excessive utilization of it

Table 2. Comparison of blood respiratory features of the trout (*Salmo gairdneri*), the tadpole and adult bullfrog (*Rana catesbeiana*), and the snapping turtle (*Chelydra serpentina*) to show the differences in water and air breathers

	Trout[a]	Bullfrog[b]		Bullfrog		Turtle[c]
		Tadpole	Adult	Tadpole	Adult	
T (°C)	20	20	20	23	23	20
PCO_2 (mmHg)[d]	2.42	1.95	13.4	4.36	18.9	25.2
pH	7.80	7.83	7.90	7.80	7.70	7.76
HCO_3^- ($mEql^{-1}$)	4.63	4.0	32	8.0	27.5	49.0

[a] Trout - Randall and Cameron (1973).
[b] Tadpole and adult bullfrog - Erasmus et al. (1970/71) at 20 °C and Just et al. (1973) at 23 °C.
[c] Snapping turtle - Howell et al. (1970).
[d] To convert to kPa multiply by 0.133.

Table 3. Some physiological characteristics of typical aquatic and terrestrial animals. (Dejours 1988)

Parameter	Aquatic	Terrestrial
Respiration	Skin and/or gills	Tracheae or lungs
PCO_2/PO_2[a]	Low ratio	High ratio
(HCO_3^{-1})	Low	High
N end products	Mainly ammonia	Mainly urea and/or uric acid and other purine derivatives
Water turnover	High or very high	Low or very low
Temperature	Poikilothermy (most of them)	Homeothermy (some of them)
Locomotion	Swimming	Running, flying

[a] PO_2 and PCO_2 designate the difference in PO_2 and PCO_2 values between body fluids and ambient milieu.

by an organism, O_2 has no direct effect on the acid-base status. However, the increased ventilatory rate which befalls an animal in an attempt to supply the required amounts of O_2 may lead to respiratory acidosis due to increased metabolic CO_2 production or respiratory alkalosis due to excessive flushing out of CO_2 from the gas exchanger. There is no systemic difference in pH among the water-, bimodal-, and air breathers. Since the PCO_2 is higher in air breathers than in water breathers, that of the bimodal breathers falling in between, the adjustments in the pH are made by body fluid bicarbonate concentrations which increase with the degree of air breathing (Tables 2,3).

A truly comparative account on respiration must not only endeavor to examine how different organs and organ systems have been refined and integrated for the purpose of exchange of O_2 and CO_2 but must also explore these states and phenomena outside the purview of the so-called model animals. In the class Agnatha, the most frequently studied species is the Atlantic hagfish, *Myxine* *glutinosa* (e.g., Strathmann 1963), in the elamobranchs the commonly studied species are a variety of dogfish, e.g., *Scyliorhinus canicula*, *Squalus suckleyi*, *Squalus acanthias*, and skates; among the bony fish (class: Pisces) studies have been made largely on the subclass Teleosti, the most highly studied species being the cod (*Gadus morhua*), eel (*Anguilla anguilla*), goldfish (*Carassius auratus*), trout (*Onchorhynchus mykiss*, formerly *Salmo gairdneri*), and the sea raven (*Hemitripterus americanus*). In amphibians, the common grass frog (*Rana pipiens*), European frog (*Rana temporaria*), and the marine toad (*Bufo marinus*), all of which are anurans, are taken to be representative of the diverse class Amphibia. Within the class Reptilia, particular interest has been shown in the painted turtles, which fall either into the genus *Pseudemys* or *Chrysemys*. The laboratory white rat (*Rattus rattus*) and the guinea pig (*Carvia porcellus*) have been used widely among mammals, while in birds, the domestic fowl (*Gallus gallus* variant *domesticus*), muscovy duck (*Cairina moschata*), and the guinea fowl (*Numida meleagris*) have been used extensively. These few animals, most of which have been selected more for convenience and availability than for any concrete morphological or physiological merit, are far from being genuinely representative of the many taxa in the Animal Kingdom. Most of the discrepancies in the conclusions and observations that abound in comparative biology have arisen from unwarranted extrapolations of observations based on a handful of unrepresentative animals.

Chapter 2

Essence of the Designs of Gas Exchangers – the Imperative Concepts

> *"To understand completely respiratory adaptations to the environment, it is an implicit but fundamental requirement that we understand how such adaptations evolved, not just how they operate in living animals." Burggren (1991)*

2.1 Innovations and Maximization of Respiratory Efficiency

Gas exchangers have developed and tractably adapted with the respiratory requirements of whole organisms in different states and habitats. The environmental factors that have profoundly influenced the general phenotype have simultaneously shaped the designs of the gas exchangers. On that account, the functional constructs of the gas exchangers cannot be understood without recognizing both these drives as well as the underlying physical principles that govern organismal biology. Form is a gestalt of structure. The importance of morphology and physiology as investigative approaches towards conceptual understanding of comparative evolution by natural selection cannot be overstated (Cracraft 1983; Duncker 1985; Greenberg 1985; Huey 1987). It should, nonetheless, be cautioned that it is oftentimes possible to mislead these aspects (especially morphology) in accurate reconstruction of phylogeny. For example, the so-called cryptic species (e.g., Bruna et al. 1996) or sibling species (e.g., Mayr 1942) are morphologically identical but genetically different. Such mismatched animals can be utilized to investigate the ecological and evolutionary events and mechanisms which enforce congruent morphologies. Until recently, morphological characteristics were the primary and practically the only means of organizing and classifying animals (e.g., Eldredge 1993; Rieppel 1993). Molecular genetics now offers a powerful means of supplementing morphological observations and validating phylogenetic relationships between different animals (e.g., Sibley and Ahlquish 1990; Graur 1993; Larson and Chippindale 1993; Luckett and Hartenberger 1993; Blair 1994; Hedges and Sibley 1994; Janke et al. 1994; Averof and Akam 1995; Penny and Hasegwa 1997). Considering the remarkable diversity of animal life, the different habitats occupied, lifestyles led, and the disparate metabolic potentials, unless autamorphic features of respiration are emphasized, the uniformity of the gas exchange and transport mechanisms between species is astonishing. A reductionistic (mechanistic) perception of a gas exchanger is that of a construction where an external medium and an internal one are separated by a barrier and a concentration gradient of O_2 and CO_2 occurs between the two compartments. This overly simplistic concept provides a useful conceptual framework for understanding the fundamental comparative principles of respiratory biology. The ultimate design of the gas exchanger must present those useful features which natural selection has selected, rigorously tested, and genomically conserved.

Energy is integral for building, servicing, and supporting the tissue infrastructure of organisms. To maximize the finite quantity available to them, cost-effective designs are essential. This calls for a logical plan of the constituent parts of the body. The most economic designs are those which demand least cost to construct, operate, and maintain while yielding the best possible results. Rosen (1967) deems optimization to be synonymous with "quest for minimum cost", Howell (1983) considers minimization of cost as "a pragmatic replacement for maximization of fitness", and Cannon (1939) termed optimal design simply "the wisdom of the body". Integrated arrangement occurs in the cardiopulmonary system of the fox (Longworth et al. 1989): though having among the highest mass-specific O_2 consumption in mammals (3.05 ml O_2 per second per kg), the animal has only an ordinary mass-specific morphometric pulmonary diffusing capacity (Weibel et al. 1983). The high unit O_2 flux across the blood-gas barrier is achieved by a large PO_2 gradient which drives O_2 from the alveolus to the capillary blood. At VO_{2max} (3.6 ml $O_2 s^{-1}$ per kg), the fox raises the alveolar PO_2 to 16 kPa by hyperventilating and maintains a low mean capillary PO_2 (12 kPa) by having a short capillary transit time (0.31 of a second) due to a high mass specific cardiac output (25 ml $s^{-1} kg^{-1}$). In the horse lung, at VO_{2max}, the capillary transit time is 0.4 to 0.5 of a second and the capillary blood is equilibrated with alveolar air after 75% of the transit time (Constantinopol et al. 1989). Among the evolved respiratory steps, the shape of the mammalian erythrocytes gives a good example of the multidimensionality in the enhancement of functional efficiency through morphological and biochemical refinements (Edsall 1972). With few exceptions, e.g., in the camel (Cohen 1978), where the cells are ellipsoidal, in mammals, the resting or minimum energy configuration is that of a biconcave disk (Nikinmaa 1990). The shape affords a high surface-to-volume ratio, with the definitive erythrocyte surface area of about 163 μm^2 being 70% larger than the surface of a spherical cell of equal volume. The camel's erythrocytes are subjected to considerable changes in the osmotic pressure of the plasma when the animal goes for 6 to 8 days without drinking water (Schmidt-Nielsen et al. 1957; Schmidt-Nielsen 1990).

Energy production by oxidative phosphorylation has been an irrevocable and continuous process since the evolution of the O_2-utilizing pathways in the primordial facultatively aerobic prokaryotic and eukaryotic unicells (Fig. 8). By way of binary division, unicellular organisms and sex cells of higher animals have been transmitted for millennia of generations. Though in finite amounts, these cells require O_2 for subdivision. The O_2 consumption of a single unfertilized mouse egg cell is 0.37 $\mu l\ O_2 mg^{-1} h^{-1}$, a value which increases to 0.38 after fertilization (Mills and Brinster 1967). In the pea, *Pisum sativum*, mitosis is only completed above an O_2 level of 0.004 of an atmosphere (Amoore 1961). Since the transition from anaerobiosis to aerobiosis, the function of the gas exchangers has remained essentially the same, i.e., taking up O_2 from the external milieu and discharging metabolically produced CO_2 into the same. The survival and adaptability of an organism are dependent on availability of the necessary resources and the capacity of the genotype to manipulate them (Phillipson 1981). In the Metazoa, molecular O_2 is a critical factor in energy production. For such an important procss, the strategies of procuring O_2 should have been differently optimized very early after the inauguration of aerobic metabolism. The past history of an organism sets the boundaries and the scope of its future development and the present constraints define its prevailing operational latitudes. Working on genetic variation, natural selection shapes and hones biological structures, increasing their fitness. Excessive design and redundancy are expunged, eliminating superfluousity and hence avoiding the unnecessary cost of supporting underutilized capacities. Astute designs are particularly necessary in those organs like the respiratory ones which must remain stable in face of changing needs and circumstances. The cost effectiveness of a gas exchanger can be gauged from the difference between the energy expended to secure molecular O_2 and that required by an organism for sustenance: optimization of the respiratory process endeavors to increase the net balance of O_2.

The modern gas exchangers are recent products of long-standing evolutionary developments in the ancestral animals. They give us an opening to conceive what may have evolved in the past. The environment has directed and regulated the amplitude and frequency of the adaptive changes which have occurred in the respiratory organs. Environments are highly dynamical systems (Peitgen and Richter 1986; Wainright 1988) which affect the development of organisms in complex and multidimensional ways. Even clonal populations show phenotypic variability. Dubbed Dollo's Law of irreversibility of Evolution (see Meyer 1988), it is considered statistically improbably that an organism can follow exactly the same evolutionary pathway in either direction, i.e., during progressive and retrogressive transformations. This is because environments "evolve" moment by moment. As soon as they are vacated, they are immediately taken over by other animals (e.g., Harvey 1993). The hypothesis frequently called Gause's Principle (see Moore 1990a) asserts that no two species can occupy the same niche. The pneumonate gastropods, a group which displays remarkable subtlety in respiratory strategies (Sect. 5.6.1), constitute an excellent prototype showing the effect environment has on the design of the gas exchangers. With realization or air breathing, the mantle cavity was transformed into a lung (Fig. 59) as the gills (ctenidia) gradually regressed: some species in the group have readopted water breathing through regrowth of similar but not identical structures (Cheatum 1934; Yonge 1952).

2.2 Safety Factors and Margins of Operation of Gas Exchangers

While biological systems largely function at a steady (unstressed) state, occasionally momentary severe conditions call for large adjustments in the level of operation. Highly trained human athletes and some elite animal species such as the horse and the dog (Snow 1985) can increase their O_2 consumption above rest 20- to 30-fold (e.g., Seeherman et al. 1981; Jones et al. 1989). To accommodate such adjustments, the relevant biological systems are intrinsically malleably designed and constructed (e.g., di Prampero 1985). In the case of the gas exchangers, maximal gas transfer is effected at the maximum O_2 consumption (VO_{2max}) when further increase in exercise does not result in a corresponding increase in O_2 uptake across the gas exchanger (e.g., Taylor et al. 1981, 1987a; Weibel et al. 1987b): supplementary energy is supplied anaerobically, with the accumulating lactic acid eventually inhibiting exercise (Margaria 1976; Taylor et al. 1981, 1989). Vo_{2max} increases with increasing PO_2 in the inspired air (e.g., Margaria et al. 1972; Welch and Pedersen 1981), transfusion of erythrocytes (e.g., Ekblom et al. 1975; Buick et al. 1984), and endurance exercise training (Saltin and Gollnick 1983; Saltin 1985). The scale of adjustment which enables a biological system to cope with functional loads is said to constitute a reserve capacity (=safety factor). Such capacities could strictly be viewed as "excessive constructions" over and above those necessary for minimum operation (Gans 1979). Biological designs appear to be configured for the worst-case scenarios and when these extremes are exceeded, death or irreparable damage occurs. In the Australian agamid lizard, *Amphibolurus nuchalis*, intense endurance exercise results in a decrease (rather than an increase) in the maximal O_2 consumption by a factor of 18% and pathological changes in the muscles and joints (Garland et al. 1987). Muscle fiber necrosis has been reported in human marathon runners (Hikida et al. 1983).

In engineering schemes (e.g., Gordon 1978; Petroski 1985), a safety factor is defined as the ratio between the load that just causes failure of a device (i.e., the component's maximal capacity (=strength = performance) to the maximum load that the device is anticipated to bear during operation. Within certain extents, biological systems change harmonically with the fluctuating strains and stresses to which they are subjected (e.g., Gilbert 1988). In composite systems (as are biological tissues), theoretically there should be room for infinite design creativity. Physical (constructional) and biological (phylogenetic, developmental, functional, and ecological) constraints, however, limit the number of possible outcomes (phenotypes) (Thompson 1959; Alberch 1980; Alexander 1985) delimiting the most optimal ultimate configuration(s). Increasing the operational safety margin calls for commitment of greater resources for construction and maintenance. From a perspective of cost-benefit analysis, through refinement brought about by natural selection acting on the phenotype, the measure of the safety factors contrived into different biological systems is aligned with specified needs (Diamond and Hammond 1992; Weibel et al. 1998). Excess functional capacities and extravagant structures precipitate unnecessary costs in form of energy required for maintenance of the infrastructure and operation. For an organ such as the brain, which consumes as much as 25% of the total resting O_2 consumption (Dejours 1990), optimal structure and function with inbuilt malleability is critical. Three-week exposure of rats to hypobaric hypoxia (0.5 of an atmosphere) causes an increase in the brain blood flow by 71% and microvessel density in the frontopolar cerebral cortex by 76% (LaManna et al. 1992). Lack of space in the body may be an important factor in determining the location and the definitive sizes of different organs (e.g., Diamond 1998). The unilateral development of normally paired organs such as the lung in, e.g., snakes and caecilians (e.g., Renous and Gasc 1989), animals with long cylindrical bodies, may be a consequence of a 'crowding-out effect. In bats (Maina et al. 1982a), the capacity to procure the large amounts of O_2 needed for flight has mainly been attained by development of remarkably large lungs (Maina and King 1984; Maina et al. 1991): compared with the thoracic cavity, the abdominal cavity is remarkably small. The gastrointestinal (GIT) system is simple (Makanya and Maina 1994; Makanya et al. 1995), and the transit time of the ingesta through the GIT is short (Klite 1965; Morrison 1980). Animals evolve just enough of what they need to overcome natural loads (Gans 1988): perfection and elegance are not pursued for their own sake. In what Taylor et al. (1987b) termed shared adaptive effort, unless there are certain underlying constraints, animals prefer to use compensatory combinations of multiple factors to achieve a greater broad-based safety margin of operation rather than few thinly stretched ones (e.g., Maina 1998). Gans (1985) envisaged that "it is the rule rather than the exception that each role utilizes multiple structures and that each structure inevitably supports multiple roles". In different species, biological functions are carried out in a variety of different ways (Brown 1994), indicating that "successful adaptations to particular conditions differ from species to species and from one group to another". This phenomenon has been called multiple realisability by Kitcher (1984) and Brooks (1994). Unless the "coupling", the "working", and the environment in which a gas exchanger operates are well understood (e.g., Connett et al. 1990; Wasserman 1994), respiratory safety margins may be perceived as overadaptations or even redundancies (e.g., Cannon 1939). By way of illustration, in mammals, the morphometric (DLo_2m) and the physiological (DLo_2p) diffusing capacities of the lung for O_2 differ by a factor of 2 (Gehr et al. 1978; Weibel et al. 1983). While the difference between the two values may be attributed to intrinsic deficiencies and assumptions in the model used to estimate the DLo_2m, an aspect discussed by Crapo et al. (1986, 1988) and recently critically reviewed by Weibel et al. (1993), it is thought that the disparity may register a fabricated functional reserve which is utilized during extreme circumstances (Weibel 1984a, 1990; Weibel and Taylor 1986). In a similar study which suggested the existence of a safety factor in the design of gas exchangers, Weibel and Taylor (1986) and Karas et al. (1987a) observed that the athletic animals (dog and pony) had a 2.5-fold greater maximum O_2 consumption (Vo_{2max}) compared with the less athletic ones (goat and calf): the latter group utilized one third of their pulmonary diffusing capacity while the former used three quarters of it at Vo_{2max}. The estimations made by Wagner and West (1972) and Hill et al. (1973) indicated that the blood-gas barrier of the human lung, which is normally 0.62 μm thick (Gehr et al. 1978), would have to be increased four to ten times before it became a limiting factor for end capillary PO_2 equilibration.

Among animals, different structures, organs, and organ systems possess different functional reserves and redundancies (Alexander 1981, 1982b, 1996; Gans 1985, 1988; Karasov and Diamond 1985; Diamond et al. 1986; Karasov et al. 1986; Toloza et al. 1991; Diamond 1998). The human intestine has a factor of 2 to 2.5, leg bones of mammals 3, breast of most mammals 2, shell of a squid 1.3 to 1.4, and lung of a small dog 1.25. Calculations indicate that at VO_{2max}, in contrast to other animals like the pony, dog, calf, and goat (Karas et al. 1987b; Taylor et al. 1987b), the fox uses almost all the capillary transit time for O_2 equilibration, i.e., under extreme effort the fox virtually exhausts the capillary length in O_2 transfer. In the normal placenta at full term, for example, about 21% of the total volume comprises nonparenchymal tissue which is not involved in either gas exchange or metabolite transfer (Aherne and Dunnill 1966). The lung of the shrew, the smallest extant and most highly metabolically active mammal (Morrison et al. 1959; Fons and Sicart 1976; Gehr et al. 1980; Sparti 1992), is elegantly refined for gas exchange. The alveoli are as small as 30 μm in diameter (Tenney and Remmers 1963), the alveolar surface area density is $2800\,cm^2\,cm^{-3}$, and the harmonic mean thickness of the blood-gas barrier is only 0.25 μm. This gives a mass pulmonary morphometric diffusing capacity of $0.143\,ml\ O_2\,s^{-1}\,mbar^{-1}\,g^{-1}$ compared with the values of 0.08 and 0.05 in the rat and man, respectively. Based on the geometry and profusity of the pulmonary blood capillaries in the alveolar septa of the lung of the shrew, Weibel (1979, 1984a) observed a resemblance between the honeycomb arrangement of the alveoli of the shrew with the intimately intertwined air- and blood capillaries of the bird lung (Maina 1982a, 1988a; Figs. 88, 89). The physiological diffusing capacities of the chorioallatois estimated by Piiper et al. (1980) of $8.7 \times 10^{-5}\,ml\ O_2\,s^{-1}\,mbar^{-1}$and that of $7.5 \times 10^{-5}\,ml\ O_2\ s^{-1}\,mbar^{-1}$ by Tazawa and Mochizuki (1976) compare with the morphometric diffusing capacities of O_2 of a 16-day-old chicken egg of $8.5 \times 10^{-5}\,ml\ O_2\,s^{-1}\,mbar^{-1}$ estimated by Wangensteen and Weibel (1982). Wangensteen and Weibel (1982) and Weibel (1984a) interpreted this similarity to bespeak the underlying optimization of gas transfer capacity across the chicken egg shell. While this may apply to individual eggs, egg shell conductance differs remarkably between and within species (Tazawa 1987). In the African parrot, *Enicognathus ferrugineus*, in a single clutch, the shell conductances may differ by a factor of 7 (Bucher and Barnhart 1984). Similar variations have been reported in the turkey, *Melleagris gallopavo* (Rahn et al. 1981; Tullet 1981), and in the chicken, *Gallus domesticus* (Tullet and Deeming 1982; Tazawa et al. 1983a; Visschedijk et al. 1985), eggs. Although large differences in the air cell PO_2 and PCO_2 must occur between the low and high conductance eggs, the O_2 consumption during the last stages of incubation are the same in both kinds of eggs (Tazawa 1987). This must allude to occurrence of either underutilized capacity (functional reserve) in the high conductance eggs or possible compensatory adjustments in the blood-gas uptake and transport variables to promote O_2 availability in the low conductance eggs. High conductance eggs should withstand environmental changes in O_2 levels better than the low conductance ones, improving chances of survival in hypoxic environments. The morphometric diffusing capacity of the human placenta (DPo_2m) was estimated to range between 0.05 to 0.08 ml O_2 per s per mbar (Mayhew et al. 1984). Based on estimations of O_2 consumption in the pregnant human uterus and the PO_2 in the maternal and fetal blood streams, Metcalfe et al. (1967) estimated the physiological diffusing capacity of the placenta (DPo_2p) to lie between 0.014 to $0.018\,mlO_2\,s^{-1}\,mbar^{-1}$. However, calculations based on diffusing capacities of CO_2 in pregnant women (Forster 1973) yielded a higher value of $0.025\,ml\ O_2\,s^{-1}\,mbar^{-1}$. Based on a mathematical model which simulated the effects of uterine contractions on placental O_2 exchange, Longo et al. (1969) estimated a DPo_2p of $0.038\,ml\ O_2\,s^{-1}\,mbar^{-1}$. The present data indicate that the DPo_2p of the human placenta lies between 0.025 to $0.038\,ml\ O_2\,s^{-1}\,mbar^{-1}$, a value which is lower than the DPo_2m by a factor of about 2. As may apply to the mammalian lung, the difference between the DPo_2m and the DPo_2p may constitute a reserve which is exploited by the placenta during extreme circumstances (Mayhew et al. 1984). The reserve is brought about by factors such as vascular shunts, placental O_2 consumption, and regional inequalities of perfusion (Metcalfe et al. 1967; Mayhew et al. 1984, 1990). Lack of uniformity in the thickness of the villous membrane may lead to local inhomogeneities of diffusional resistances across the sporadically attenuated barrier (Mayhew et al. 1984; Jackson et al. 1985). Like other gas exchangers, the placenta is a multifunctional organ which must present a compromise design (Sect. 4.7). Though fundamentally constructed for gas exchange, the organ plays important endocrine roles and constitutes an important barrier which protects the fetus from harmful agents and factors in the maternal blood. In some situations, fetotropic viruses such as rubella virus, cytomegalovirus, hepatitis B virus, human immunodeficiency virus, enterovirus, and Theiler's murine encephalomyelities virus are prevented from affecting the fetus (e.g., Alford et al. 1964; Hayes and Gibas 1971; Maury et al. 1989; Garcia et al. 1991; Abzug 1994). It is material to note that the maximum morphometric pulmonary diffusing capacity of the lung for O_2 (DLo_2m) of 2.38 ml $O_2\,s^{-1}\,mbar^{-1}$ (Gehr et al. 1978) is about 30 times greater than the morphometric diffusing capacity of the placenta (DPo_2m) of 0.08 ml $O_2\,s^{-1}\,mbar^{-1}$. This should constitute an enormous functional reserve which guarantees O_2 supply to the fetus under different respiratory conditions and circumstances.

The trade-offs necessary for the development of optimal designs and functional reserves are manifest in many gas exchanges. For example, the completely aquatic lobster, *Homarus vulgaris*, which shows neither evidence for terrestrial adaptations nor propensity for air breathing when stranded on the beach (a real hazard for intertidal animals) will breath air, maintaining its O_2 uptake at near-aquatic levels (Thomas 1954). Facultative air breathing appears to be an acquired adaptive feature which allows solely aquatic animals to withstand a transient, stressful physiological condition. In eggs, high porosity compromises fitness by increasing water loss, but the same process improves it by enhancing the conductance of the egg shell to respiratory gases. In the mammalian lung, while intense subdivision of the pulmonary parenchyma provides a greater respiratory surface area, according to the Young-Laplace relationship ($P = T\,r^{-1}$), where P is the recoil pressure, T surface tension, and r the radius of curvature at the air-liquid interface, the decrease in the diameter (with the resultant increase in the surface radius of curvature of the alveolus) engenders greater surface tension. At an invariable recoil pressure, this increases the disposition of the alveoli to collapse as well as the energy needed to inflate them with air during inspiration (e.g., Wilson 1981; Wilson and Bachofen 1982). On expiration, the alveolar surface tension reaches a value close to zero (Schürch et al. 1985). The design of the lung of the shrew, e.g., *Microsorex hoyi* which weighs as little as 2.3 g (Lasiewski 1963a,b), has been greatly improved and probably driven to the very limit of a functionally operable mammalian lung. On the lung of the minute shrew, Weibel (1979) pointed out that "it may well be that a limit of bioengineering feasibility has been reached at all levels of the respiratory system". The same may apply for the lungs of the 2-g Cuban bee humming bird, and the Thai bumblebee bat (Suarez 1992). To maintain extremely small sizes especially during the larval stages of development, endothermy, a high-cost approach to life, is out of reach of the ectothermic air breathing vertebrates such as amphibians and reptiles. The smallest amphibian is the arrow-poison frog, *Sminthilus limbatus*, which in adulthood measures only 11 mm from nose to anus. In biological systems, through compromises, concessionary states are established by harmonizing the composite fitness components with the limiting ones. In the fish gills, the two main parameters that can be adjusted to increase transbranchial O_2 diffusion are respiratory surface area and the partial pressure gradient of O_2: the former can be increased through lamellar recruitment (e.g., Booth 1978) and the latter by increasing ventilatory and perfusion rates. Adjustments of these parameters leads to what has been called osmorespiratory compromise. While improving gas exchange, increasing the gill surface area results in osmoregulatory problems engendered by increased ionic loss and influx of water in the freshwater teleosts or water loss and ionic loading in the marine teleosts (Perry and Laurent 1993). It has been demonstrated by, e.g., Randall et al. (1972), Wood and Randall (1973), and Gonzalez and McDonald (1992), that increased O_2 consumption is accompanied by increase in Na^+ flux, a process that calls for increased energy expenditure. It was envisaged by, e.g., Satchell (1984) and Nilsson (1986), that fish oblige the osmorespiratory compromise by limiting the surface area and increasing the partial pressure gradient of O_2, a process which increases O_2 flux without provoking problems of ionic transfer. Part et al. (1984) demonstrated nonrespiratory areas in perfused gills of the rainbow trout, *Oncorhynchus mykiss*, supporting the long-held proposition that fish are able to regulate the surface area of the gills for the purposes of gaseous and osmotic exchange (e.g., Randall 1982; Butler and Metcalfe 1983). To enhance gas exchange, the more energetic species of fish appear to rely more on increasing the respiratory surface area while the less energetic ones utilize hemodynamic adjustment (Perry and McDonald 1993). In the rainbow trout, at rest, only 60% of the gill lamellae are perfused (Booth 1978). During exercise, the blood perfusing the gills is shunted from the less well-ventilated basal channels to the more central ones (Nilsson 1986). The complex anatomy of the circulatory system of the gills where the vascular arrangement has been differentiated into respiratory and nonrespiratory pathways (e.g., Gannon et al. 1973; Dunel-Erb and Laurent 1980a; Butler and Metcalfe 1983; De Vries and De Jager 1984) has been associated with the plasticity of the gills for varying the exposure of blood to water. In the European eel, *Anguilla anguilla*, the volume of the blood in the nonrespiratory vasculature of the gills comprises 5% of the total blood volume in the body (Bennett 1988). Interestingly, though the blood of the dogfish, *Scyliorhinus canicula*, like that of the other elasmobranchs, is almost isosmotic to seawater (Burger and Bradley 1951) and hence gill perfusion does not affect ionic flux across the water-blood barrier significantly, both kinds of vascular circuits were reported (Metcalfe and Butler 1986). Unlike the teleosts (Pettersson and Nilsson 1979), the gills of the dogfish, *S. canicula*, lack nervous control of blood flow across the gills (Metcalfe and Butler 1984).

The existence of safety margins in biology is well shown in some physiological processes. Oxygen regulators, for example, operate between two levels, a critical and a limiting one. In the lugworm, *Arenicola marina*, the critical PO_2 is near air saturation at 16 kPa (Toulmond 1975) but the anaerobic processes do not start until the PO_2 drops to 6kPa (Schöttler et al. 1983). Between the two levels, an organism can maintain aerobic metabolism by rearranging and/or mobilizing different physiological factors. In extreme circumstances, the metabolic level of activity is reduced (Hochachka 1988). In principle, the function of a biological system is facilitated by a structure that is correct for the settings where function occurs. As animals establish themselves in relatively more stable environments, adopt more successful designs and acquire more efficient behavioral, physiological, and biochemical responses to external perturbations, flexibility for genetic change and transformation is gradually blunted. While prokaryotic organisms exhibit remarkable capacity to change metabolism in response to changes in substrate and environmental conditions, cells and tissues of eukaryotic organisms, particularly the higher animals, are considered less responsive since they live in more stable environments (e.g., Golspink 1985). Whether a catastrophic event occurs or not, in all species, the capacity to survive inevitably decays with geological time. Schopf (1984) estimated that the average species' longevity may be as short as 200 000 years. No vertebrate species has avoided extinction for more than a few million years (Carroll 1988). Effective adaptive changes demand selection and refinement of only those features which are favorable in a particular milieu. Apparently, not all features presented by an organism are intrinsically adaptive (e.g, Futuyuma 1986): most organisms present anachronistic features. These features may arise when a particular selective pressure drive stops midstream (e.g., if an environmental stress factor abates) or if a certain structure is diverted to configure a totally different one from that initiated. The common perception that "biological innovations tend to appear soon after environmental conditions become favorable to them" (e.g., Cloud 1974) is a gross oversimplification of the evolutionary process. Strictly, organisms are not passive participants totally subservient to the drifts of the environment: they identify the evolutionary pathways they wish to follow, set their own selective pressures, and actively engage the environment in determining the direction, rate of progress, and nature of change (e.g., Gillis 1991). Only the traits that require a driving force (e.g., natural selection) to establish and impart a performance advantage are adaptations (e.g., Baum and Larson 1991). For example, at the various stages of their evolution, invagination, compartmentalization, and ventilation of the gas exchangers were necessary improvements for respiratory efficiency (e.g., Brainerd et al. 1993). In organisms that were not adequately inventive, these requirements constituted limitations which in some cases stopped any further evolutionary progress. Retaining the buccal force pump and particularly the skin as a gas exchanger apparently consigned the amphibians to water or humidic habitats. The evolution of homologous structures in biology illustrates convergence in solutions to common problems (Gould 1966). In the reptilian lung, to increase the respiratory surface area, the subdivision of the lung was achieved through an inward growth of trabeculae towards the central air space, and in the mammalian lung, the process took place by outward projection of the alveolar septae from the bronchial system. In the latter, while an extensive respiratory surface was achieved, an efficient costodiaphragmatic ventilatory system was necessary to ventilate the more profusely compartmentalized lung.

2.3 Engineering Principles in the Design of the Gas Exchangers

Biological processes are intrinsically finite in magnitude and frequency. The boundaries within which operations occur are set by determinate physical constraints and regulated by evolved biological feedback mechanisms. For about 2 billion years, limitations set by diffusion firmly confined animal life to the protozoan domain. This grip was loosened only when O_2 rose above nascent levels and convective processes of transporting respiratory gases from the outside to the proximity of the gas exchangers onward to the tissue cells developed. A wide spectrum of respiratory plans, structures, and strategies based reasonably on common engineering plans has evolved in animals. With certain modifications, the sheet-flow (e.g., Fung and Sobin 1969; Tenney 1979; Farrell et al. 1980; Fung 1993) or tubular design (e.g., Guntheroth et al. 1982), depending on how one visualizes the thin blood conduits, occurs in practically all evolved gas exchangers, e.g., in fish (Figs. 11,49) and crustacean gills (Fig. 13) and in the reptilian

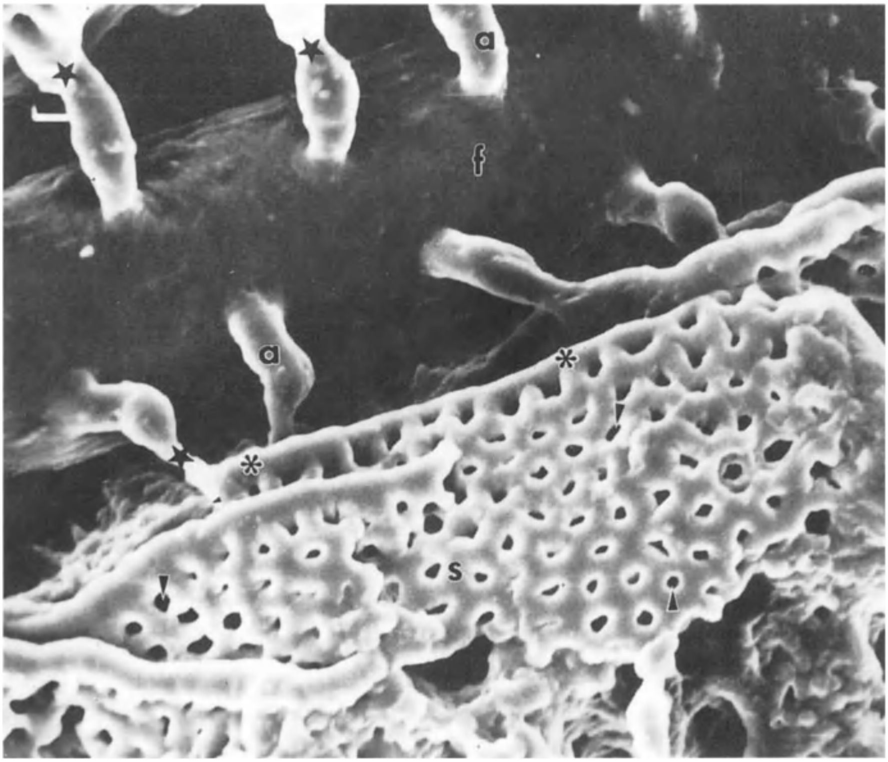


Fig. 11. Cast of the gills of a tilapiine fish, *Oreochromis alcalicus grahami*, showing a gill filament artery, *f*, giving rise to afferent lamellar arterioles, *a*, which supply blood to secondary lamellae, *s*. The constriction of the afferent lamellar arterioles, ★, are thought to be valves which regulate lamellar perfusion. ∗ marginal channel; ➤ pillar cells which subdivide the lamellar plate into spaces through which blood percolates. *Bar* 5 μm. (Maina 1994)

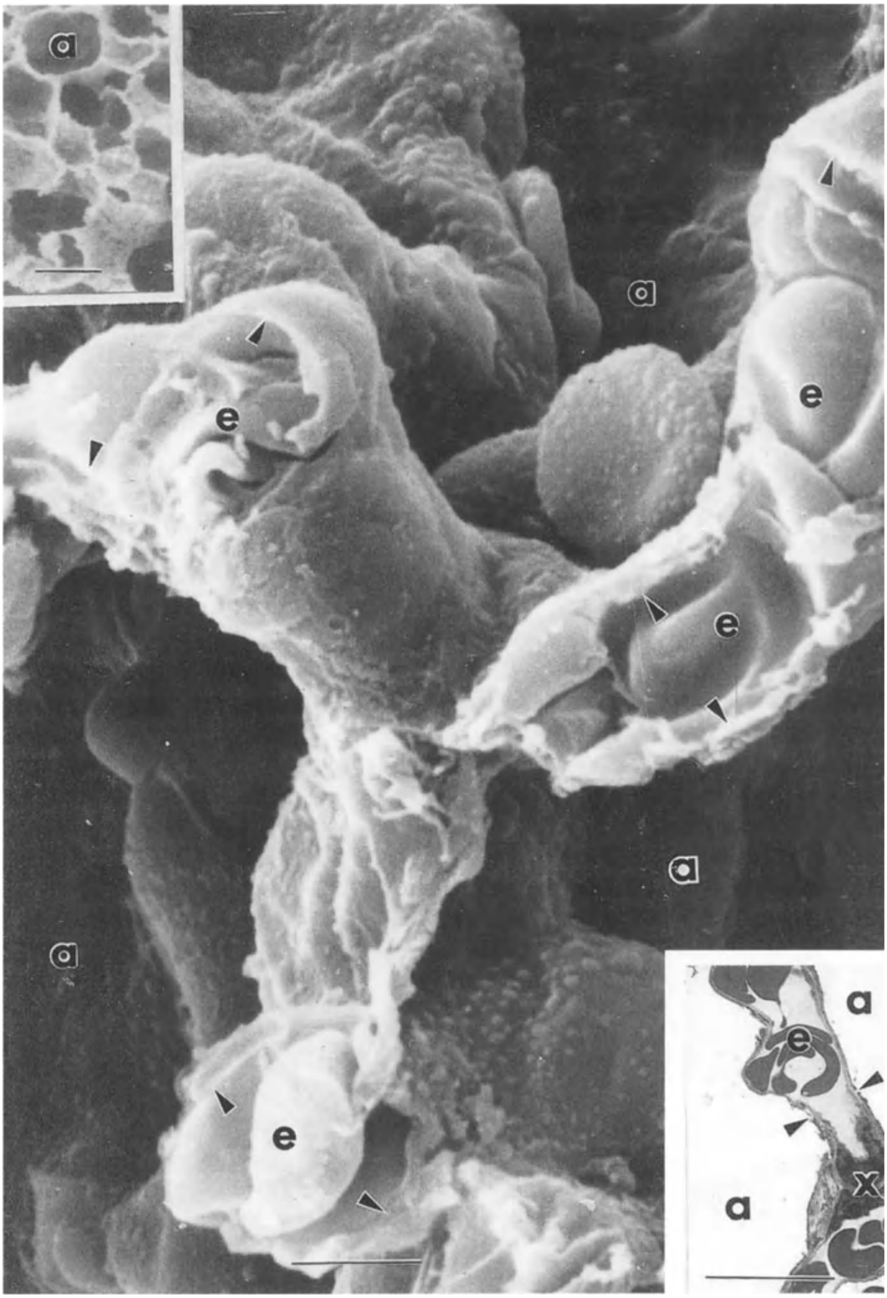


Fig. 12. Sheet blood flow pattern in a mammalian lung. *Top inset* The alveoli, *a*, separated in a honeycomb manner by interalveolar septa. *Main figure* Closeup of the interalveolar septum which is formed by two parallel epithelial cell layers, ➤, between which the blood capillaries are contained. *Bottom inset* Parallel epithelial cell layers, ➤; *e* erythrocytes; *a* alveolus; *x* endothelial cells. *Top inset bar* 21 μm; *main figure*, 3 μm; *bottom inset* 3 μm

Fig. 13. Sheet blood flow pattern in a gill lamellar of a crab showing epithelial cells, *, which line the blood space, *v*. The high energetic demands for ionic exchange are evinced by the abundance of mitochondria in the epithelial cells, *p*, and the highly amplified basal infoldings, □. →, cuticular lining; ➤, points where the epithelial cells closely approximate to regulate the rate of blood flow. *Bar* 3.5 μm. (Maina 1990b)

(Fig. 14), mammalian (Fig. 12), and avian (Fig. 29) lungs. The constructional plan comprises thin parallel epithelial cell layers which are joined by connective tissue or pillar-like cell struts. This architectural configuration produces fine channels through which blood flows, spreading out into an extremely thin film over an

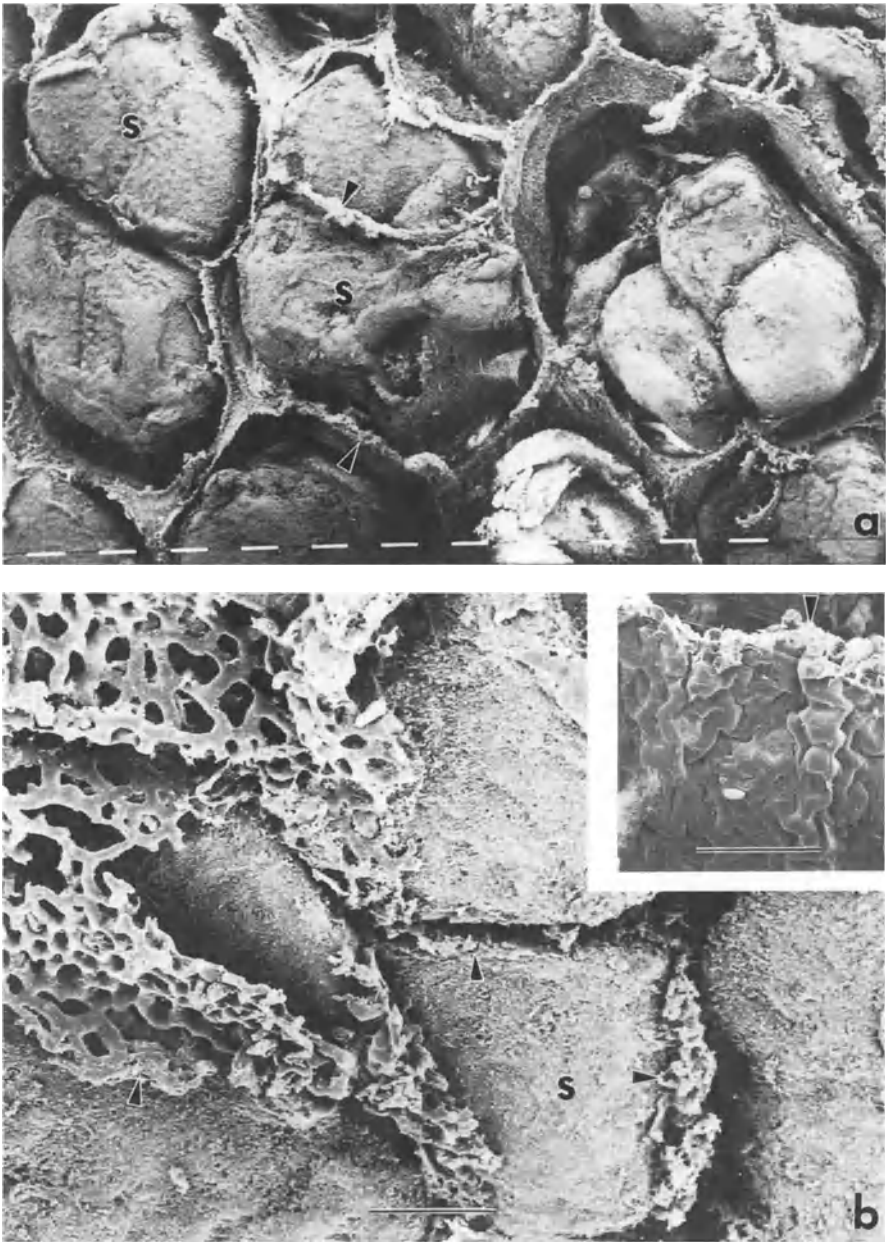


Fig. 14. **a** Semimacerated latex rubber cast of the gas exchange air spaces, *s*, of the lung of the snake, the black mamba (*Dendroapis polylepis*) showing the blood capillary bearing septae, ➤, **b** A completely macerated double latex cast of the gas exchange region of the snake lung showing the sheets of septal blood capillaries, ➤, which surround the air spaces, *s*. *Inset* Critical point dried material showing a septum, ➤, lining the air spaces. **a** *Bar* 100 μm; **b** 50 μm; *insert* 25 μm. (Maina 1989e)

extensive respiratory surface. This appears to be the only plan which adequately meets the structural requisites for efficient gas exchange. It provides optimal exposure of hemoglobin to the external milieu for maximal gas transfer. The external and internal gas exchange media are brought into as close proximity as possible, interfacing over an extensive surface area in a highly dynamic organ. In the human lung, about 213 cm^3 of the blood in the capillaries is spread over a respiratory surface area of 143 m^2 (Gehr et al. 1978; Weibel 1989), i.e., about 1.5 cm^3 of capillary blood per m^2, generating an extremely thin film (a sheet) of blood. While the mammalian fetal pulmonary circulation comprises less than 10% of the biventricular cardiac output, pulmonary vascular resistance is higher than the systemic and the PO_2 of blood is low. Soon before birth, the blood flow increases eight to ten times and a transition to low resistance circulation occurs (e.g., Dawes et al. 1953; Cassin et al. 1964; West 1974; Teitel et al. 1987). These changes appear to be influenced by the changes in the PO_2 in blood both in utero and after birth, the process being mediated by changes in the K^+ and Ca^{2+} channels in the smooth muscles of the pulmonary artery (e.g., Lewis et al. 1976; Sheldon et al. 1978; Accurso et al. 1986; Cornfield et al. 1994). Pulmonary vascular resistance is a product of pulmonary blood flow and the difference between the pulmonary artery pressure (average 2 kPa) and the left atrial pressure (about 0.7 kPa). Even at rest, all the capillaries of the lung are perfused with plasma within 2 min of blood leaving the heart (König et al. 1993). Failure in reduction of the pulmonary circulatory resistance after birth is a consequential clinical problem sometimes termed persistent pulmonary hypertension of the newborn and leads to various neonatal respiratory disturbances (Heymann and Hoffman 1984). In the fish gills, blood flow is slowed down as it percolates through the narrow vascular channels formed by the pillar cells (Fig. 15) improving O_2 uptake by the erythrocytes (e.g., Hughes and Wright 1970; Soivio and Hughes 1978; Farrell et al. 1980; Nilsson et al. 1995). While in transit, the erythrocytes are greatly compressed (Fig. 86) and exposed to the external respiratory medium on all sides across a thin tissue barrier. In the mammalian lung, it takes less than 1 s (West 1974; Lindstedt 1984; Swenson 1990) for the erythrocytes to pass through the alveolar blood capillaries, a period within which the erythrocytes are fully saturated with O_2 (Weibel 1984a). Because of the two-phase nature of blood, the erythrocytes and the plasma may take different paths through the capillary network (Okada et al. 1992; König et al. 1993) presumably depending on the resistances offered across different capillary segments (Okada et al. 1992) and the preponderance of leukocyte sequestration in the lumen of the blood capillaries (Perlo et al. 1975; Lien et al. 1987; Hogg et al. 1988; Yoder et al. 1990). In the skeletal muscle, 1 ml of mitochondria relates to about 14 km capillary length and 0.22 cm^3 of capillary blood (Conley et al. 1987). At term, the human placenta contains 45 cm^3 of capillary blood which is spread over an area of about 11 m^2 (Aherne and Dunnill 1966), generating a film of blood 0.41 μm thick. In the book lungs of arthropods (Fig. 15), air rather than blood flows through the thin external conduits.

The similarity in the design and construction of the gas exchangers could be attributed to the plausibility that gas exchangers arose from a common ancient

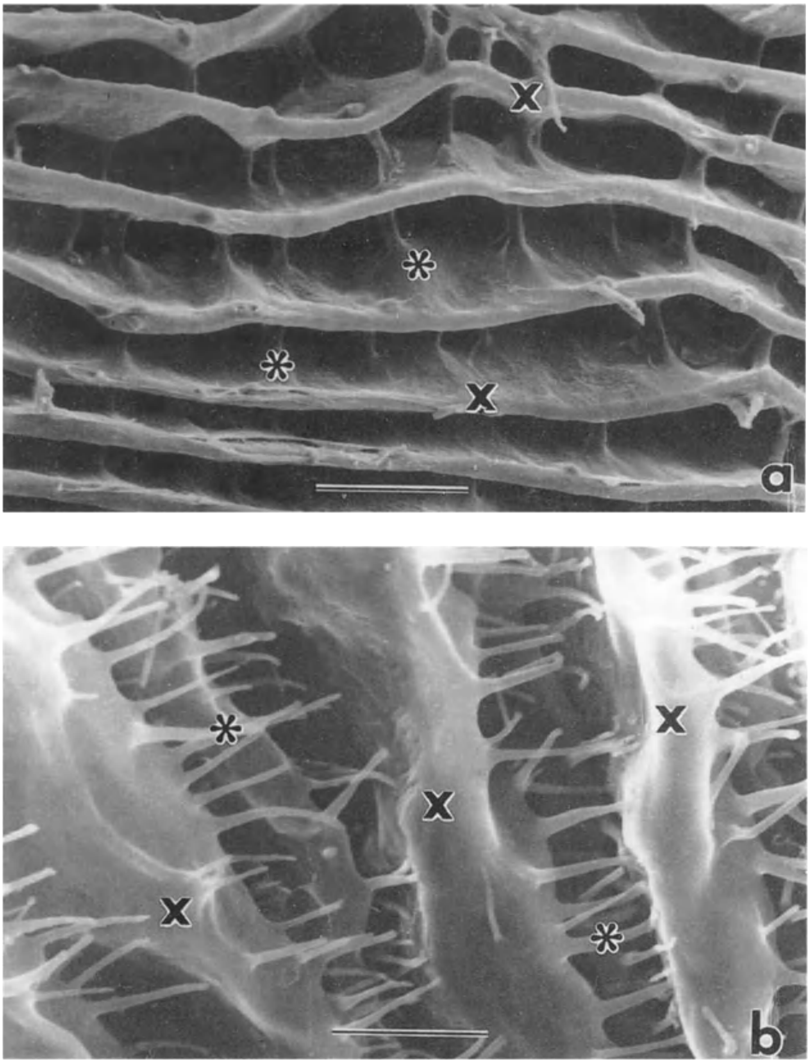


Fig. 15. **a** Book lungs of the desert scorpion, *Paruroctonus mesaensis*. The lamellae, *x*, are kept apart by vertical struts, *. **b** A higher view of the lamellae, *x*, and vertical struts, *. **a** *Bar* 40 μm; **b** *bar* 13 μm. (Farley 1990)

structure, whose basic plan has developmentally been highly conserved. Alternatively, as a process, gas exchange may enforced some basic, invariable structural attributes which all organs had to meet. Biological evolution does not occur by attrition but by parsimonious remodeling of common ancestral plans (Meyer 1988; Lauder and Liem 1989; Atchley and Hall 1991). In the ostariophysans (Order

Siluriformes), the accessory respiratory organs of the air-breathing fish developed directly from the branchial tissue in the immediate concavities above the gills (Hughes and Munshi 1968). In the African catfish, *Clarias mossambicus*, the suprabranchial chamber membrane is well vascularized (Fig. 66) and, where necessary, the labyrinthine organs developed as outgrowths from the gill arches (Maina and Maloiy 1986; Fig. 65c). Most bimodal-breathing fish have utilized default (already existing) organs like the stomach, intestines, and the anus. Only one siruriid, *Pangasius*, has evolved a gas bladder primarily for respiration (Browman and Kramer 1985). In principle, whether at molecular, cellular, or organismic level, when change must be made, existing structures are overhauled and improved. Rarely do totally new structures have to develop. For example, by evolving the appropriate enzymes, the evolution of aerobic respiration in the eukaryotes entailed addition of the citric acid (Krebs) cycle onto the original anaerobic (glycolytic) pathway of the anaerobic prokaryotes (Chapman and Schopf 1983). Homologous structures (similar constructional plans enforced by natural selection) illustrate the conservativeness of evolution. Investigating the basis of the different aerobic capacities of the athletic and nonathletic animals, Hoppeler et al. (1987) observed that in all species, the maximal average O_2 consumption of the mitochondria was the same (3.4 to 4.6 ml $O_2\,min^{-1}\,ml^{-1}$) independent of the aerobic capacity of the species: the greater oxidative capacity of the athletic species was brought about by "building more mitochondria of similar kind, rather than by modification of the metabolic rate of the mitochondria". It is, however, recognized that at a certain level of mitochondria-muscle fiber ratio, further increases in the mitochondrial volume density may not only be futile but may compromise muscle function (e.g., Pennycuick and Rezende 1984; Weibel 1985a; Hochachka 1987; Hochachka et al. 1988; Suarez 1992). Once established, morphologic characteristics appear to be retained for indefinite periods of time until there are imperatives for change. For example, mammalian orders have retained a basically similar body form for 50 to 60 million years (e.g., Eldredge and Gould 1972; Carroll 1988). Compared with the total longevity of a species, however, changes take a much shorter period to be effected (Carroll 1988). Only a very small proportion of the genome appears to be directed towards morphological restructuring. The amino acid sequence of 12 varied proteins differs by only 1% between humans and chimpanzees (King and Wilson 1975).

Though argued to the contrary (e.g., Rose and Bown 1984; MacFadden 1985; Chaline and Laurine 1986), evolutionary changes are not progressive nor are they necessarily gradual improvements on earlier designs (e.g., Carroll 1988; Gould 1994; Kardong 1995). The apparent disparity of form between the various gas exchangers has resulted from the singular fact that animals at different phylogenetic levels of development have had to respond to common selective pressures (e.g., Murdock and Currey 1978), in such circumstances, individual solutions being found using different strategies and resources. To a certain extent, phylogenetic plasticity will allow correspondent structures to develop, but in most cases, alternative solutions are pursued. For example, long lungs (which are difficult to ventilate) have evolved in the thin cylindrical animals such as the snakes and the caecilians (Renous and Gasc 1989). The ventilation of such lungs is greatly hindered by locomotion. In lizards, breathing has been uncoupled from locomotion

(Carrier 1984, 1991). On the other hand, in an energy-saving strategy, bats have adopted a 1:1 ratio between wing beat and breathing (Thomas 1987). Clearly, what may constitute a constraint in one animal may be beneficial in another. Amidst these shifts, some structures which may appear to be of no evident biological value to organisms may evolve (e.g., Bock and von Wahlert 1965; Kimura 1983; Pierce and Crawford 1997).

In biological systems, structure encompasses the qualitative and quantitative characteristics of the constitutive components and their geometric features and arrangements. By altering the proportions, positions, and configurations, new polarities and states are created and different functional states are established. The components of complex structures constitute an integrated pattern of up- and downregulation of diverse functional capacities. For example, the arrangement of the mineral crystals of $CaCO_3$ in the eggshell determines the porosity of the shell and hence its diffusing capacity for O_2, a feature which, in turn, ensures proper development of the embryo. The permeability of the fish's swim bladder to gases depends on the orientation of guanine crystals in the bladder wall (Lapennas and Schmidt-Nielsen 1977). Swim bladders of fish which operate at depths greater than 1000 m have a greater concentration of guanine per unit area of the wall (Denton et al. 1970). The principles of homology and analogy are fundamental to understanding the correlation between structure and function as modified by natural selection and effected by the process of adaptation. Those structures which undergo irreversible deconstruction become vestigial and eventually disappear while some may be commissioned to perform roles different from those for which they were initially configured. Such adaptive traits were called exaptations by Baum and Larson (1991). For example, the surfactant evolved in the ancestral piscine lungs (e.g., Todd 1980) mainly to protect the epithelial surface (Liem 1987a). However, with the development of the more complex lungs in the tetrapods (where the buccal force pump was no longer adequate to ventilate such lungs), compartmentalization of the gas exchanger was necessary to enhance respiratory efficiency. With this modification, the surfactant (Sect. 6.9), by increasing the lateral stability of the phospholipid layer (Cochrane and Revak 1991), assumed the important role of reducing surface tension (e.g., Wilson 1981; Golde et al. 1994). In the anaconda, *Eunectes murinus*, the surfactant lining occurs in the alveolated and the succular parts of the lung (Phleger et al. 1978). While in the protochordates the pharygeal region serves as a filter-feeding apparatus (Sect. 6.10.1), in the chordates, with the addition of a respiratory role, the trophic one was phased out. The complex relocation, erosion, and eventual disintegration of some of the aortic arch blood vessels (which serviced the gills) on the formation of the lungs, is another example of such drastic transformations. Among vertebrates, the pulmonary arteries make their first entry in the Dipnoi (lungfishes) as branches of the sixth pair of aortic arches. Early in the development, the blood vessels supplied the swim bladder which is thought to have given rise to the lungs (Sect. 6.2). Only the necessary early structures (e.g., some of the blood vessels of the branchial arches) were retained as the primal gill arch blood vessels were reconfigured. The degeneration of one lung in, e.g., snakes (Ophidia) and the caecilians (Gymnophiona), is thought to have been one of the sacrifices they had to make to develop thin, limbless, cylindrical bodies which are important for slithering through confined spaces.

Unlike human-made machines, which are configured to carry out specified functions, biological structures are dynamic, multifunctional, composite entities designed to continuously absorb and respond to the fluidity of the external pressures of natural selection. In what de Beers (1951) called mosaic evolution, the different parts of an animal are variably affected by natural selection. Needs, to a greater extent than phylogenetic level of development, dictate the direction, nature, and magnitude of adaptive change. For example, the similarity of the lung-air sac system of birds (Sect. 6.7.5) and the tracheal-air sac system of insects (Sect. 6.6.1), animals separated by over 200 million years of evolution, indicates a morphological convergence for flight. Furthermore, compared with the respiratory system of birds and that of insects, the lung of the human being at the acme of evolutionary development is not as efficient. In the benign evolution of the *Homo sapiens*, natural selection appears to have targeted the nervous and musculoskeletal systems, leading to development of complex mental capacity, bipedal locomotion, opposable thumb, articulated sound (speech), etc. In an adult human being, the brain utilizes 25% of the overall resting O_2 consumption. While it would be anticipated that these developments would impart particular specializations, especially with respect to the mechanisms and control of breathing, the pulmonary system appears to have been disregarded during these transformations as long as it was adequate to support the ongoing changes. Except for the Hering-Breuer reflex, which appears to be much less well developed, the human respiratory characteristics are similar to those of all other mammals (Dejours 1990).

2.4 Scopes and Limitations in the Design and Refinement of the Gas Exchangers

Animals are aphoristically said to be structurally and functionally well constructed to meet the adversities of life (e.g., Olson and Miller 1958; Frazzetta 1975). Though easily conceivable, dedicated biological engineering is not easy to experimentally test, empirically prove, and convincingly demonstrate. This is largely due to our anthropocentric approach and misconception that evolutionary change is determined and driven by the same rules (to serve the same purposes) as human technological innovations (e.g., Basalla 1989). Whereas for human insight advancement means improvement and improvement means more sophisticated products, in nature, changes are generally highly resisted. If they occur, they are strictly survival-oriented and are configured specifically around the existing structures and prevailing conditions to engage known loads. Paleontological studies do not support the popular belief that through the evolutionary continuum, organismal design and function have undergone appreciable refinement and complexity (e.g., Rudwick 1964; Hickman 1987; McShea 1991): the ancient organisms were no less exquisitely designed than the modern ones. Indeed, some ancient structures of now extinct animals seem to have dealt with complex problems that are unsolved in the present animals. Stipulation for originality in technical inventions is purely a property of human ambition and competitiveness: evolution advances without purpose or direction, resulting in unpredictable changes. Adaptation entails cumulative selection of innovations that build on top of primeval ones. Mosaic evolution, i.e., selective degeneration combined with progressive specialization, e.g., in the acoustic adaptations of the fossorial rodents (e.g., Nevo et al. 1982; Heth et al. 1985) is an occurrence which shows nature's conservativeness and yet quest for optimization. It has been suggested that human technological progress may be proceeding 10 million times faster than natural evolution (Arthur 1997). Experiments on guppies, *Poecilia reticulata* (Reznick et al. 1997), however, demonstrated that evolution can occur very rapidly: in a 4-year observation, the rate of change of certain features was some 10000 to 1 million times faster than the average rates estimated from fossil record. Thompson (1911) pointed out (but see counterviews by, e.g., Cody 1974 and Howell 1983) that "biology does not necessarily make progress toward perfection by mechanical analysis of changes that go on in living bodies". In nature, even where radical changes such as mutations occur, designs are altered through reconfiguring existing structures or enforcing new roles. Figuratively speaking, animals appear constantly to "reinvent the wheel" (though they have yet to evolve a real one!) as they look for the most relevant and least traumatic solutions to the demands prevailing in their ecological settings. Future developments are not anticipated. By combining the different assets they have gathered along the way, new "adaptive functional complexes" of high selective value are configured, conferring greater survival potential to an organism. S.A. Kauffman (cited in Ruthen 1993) asserts that "by selecting an appropriate strategy, organisms tune their coupling to their environment to whatever value fits them best". Comparative biology reveals the parameters in the "primitive" life forms which have been conserved during the evolvement of the complexity that characterizes the most "advanced" kinds (Fishman 1983), defining in broad terms the pathways followed and the strategies adopted in the quest for survival and self-perpetuation.

Establishment of optimum states calls for sound analysis of the alternative strategies, evaluation of the costs incurred, the benefits which accrue, and the difference between the level of operation with the theoretical maxima. In bats, for example, a typical mammalian lung has been structurally and functionally refined to supply the enormous amounts of O_2 needed for flight (Thomas 1987; Maina et al. 1991); (Sect. 6.7.4.1). Unequivocally, this shows that the lung-air sac system of birds and the tracheal-air sac system of insects, the gas exchangers which have evolved in the only other two volant taxa, are not prerequisite respiratory designs for flight. While the structural parameters are fixed, the functional ones are more flexible. Bats have shrewdly utilized combinations of these parameters and promoted the efficiency of a plainly inferior gas exchanger to rival and in a manner equal that of the distinctly superior bird lung (Maina 1998). After sojourn at high altitude (e.g., Bard et al. 1978; Heath et al. 1984; Durmowicz et al. 1993), factors such as ventilation, hematocrit, hemoglobin concentration, erythrocyte count, and blunted hypoxic pulmonary vasoconstrictor response change (some within a matter of hours or days) to avoid cellular hypoxia and to correct for adverse changes in the blood pH. The structural parameters, e.g., the thickness of the

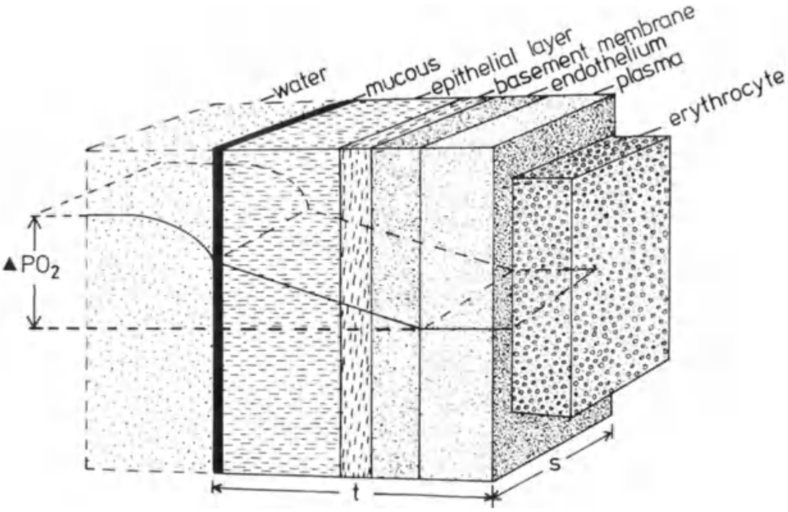


Fig. 16. Schematic drawing showing the resistance barriers across which O_2 diffuses in a water breather and the principal structural features, namely the barrier thickness, *t*, and the respiratory surface area, *s*, which influence the diffusion process. The partial pressure gradient of O_2 (ΔPO_2) decreases with the diffusion distance

blood-gas barrier and respiratory surface area, take months to change (e.g., Weibel 1984a). Whether in a water- or an air breather, O_2 procurement depends on parameters such as the diffusional distance, respiratory surface area, physical permeative properties of the respiratory barriers, and functional properties such as ventilation and perfusion states (Fig. 16).

For optimal energy production, in organisms, gas transfer is aligned with the metabolic needs. The correlation between an animal's environment and its respiratory needs is a very intimate one. Whereas O_2 need at rest is moderate, during exercise, e.g., flight, it increases tremendously (Weis-Fogh 1967; Tucker 1972; Thomas 1987). When exposed to a hypoxic environment, to support their normal metabolic activities, organisms still need to extract and transfer to the tissues the same quantity of O_2 as in a normoxic one. The respiratory system must be designed with adequate flexibility to accommodate the extreme demands which may occasionally be loaded on the organism (e.g., Maina 1998). Coordination of external factors (i.e., those involved in the procurement) and the internal ones (i.e., those involved in the uptake, transport, and distribution) ensures a satisfactory supply of O_2 to the tissues. In the event of hypoxia, it is the external factors rather than internal ones which become limiting. The high metabolic capacities, especially in the endothermic homeotherms, were achieved through evolution of more efficient means of O_2 procurement. This entailed development of features such as double circulation, greater blood pressure, higher tissue capillarity, higher mitochondrial volume density, and larger hemoglobin and myoglobin concentrations.

2.5 Optimal Designs in Biology and Gas Exchangers in Particular

2.5.1 Symmorphosis: the Debate

Form and function are inextricably interrelated. Indeed, it is axiomatic that animals should be constructed reasonably in order to be able to efficiently carry out the essential activities of life. The perception of a form-function correlation alludes to some advantages for the animals that possess the attribute (Gans 1988). Vogel and Wainright (1969) put it that "function without structure is a ghost; structure without function is a corpse" and Trivers (1985) bluntly stated that "organisms are designed to do something". The concept of optimal design of biological structures is based on the recognition that natural selection continuously regulates every aspect of structure and function. Though perceptively simple to conceive, the actual manner in which structure and function actuate each other is not that simple to read. This is particularly well known from the disappointing attempts to conceive form from phylogenetic reconstruction based on fossils (e.g., Cutler 1995). A correlation between structure and function can only be meaningfully made if both structure and function are simultaneously observed and quantified.

Based on their "firm belief that animals are built reasonably" and their confidence that "structural design is optimized for the role it plays", the rationale of structure-function interdependence for adept performance of the lung was formulated by Taylor and Weibel (1981) and Taylor et al. (1987b) and termed symmorphosis. Symmorphosis was defined as a state of structural design commensurate to functional needs resulting from regulated morphogenensis, whereby the formation of structural elements is regulated to satisfy but not exceed the requirements of the functional system. Direct morphological and physiological data on the mammalian lung and the skeletal muscle mitochondria, the primary O_2 sink, were adduced to show that the gas exchanger was reasonably well constructed to meet the metabolic needs. However, scaling the morphometric diffusing capacity (DLo_2m) and maximum O_2 consumption (VO_{2max}) with body mass indicated a paradox (Gehr et al. 1981; Weibel et al. 1983; Weibel 1989): VO_{2max} and DLo_2m scaled differently with body mass – VO_{2max} with a scaling factor (mass exponent b) of 0.8 and DLo_2m with that of unity. This suggested that large animals have a DLo_2m far in excess of their metabolic requirements and called in question the validity of what was initially conceived to be an encompassing concept (Taylor et al. 1987b; Weibel et al. 1991). Considering these observations, Taylor et al. (1987b) concluded that the principle of symmorphosis is only partially satisfied in the lung. This departure from the expected perhaps serves as a timely reminder of the intrinsic complexities of the biological systems. Such entities are multidimensionally regulated and when integrated, singular normally inconsequential events are greatly accentuated. Mathematical models with their intrinsic assumptions cannot possibly inclusively describe the arrangements and define the capacities of such complex matter. In complete departure from the Newtonian predictability in physical sciences, the cause and event interactions in complex systems are not necessarily linear and the output may not be anticipated. In fact, the predictive power in the physical sciences is only good for simple and single events operating under very narrow circumstances. Where multiple and possibly conflicting parameters interact and compromises and trade-offs permutate in space and time with unpredictable probability, except for within very broad limits, there may not be a single best solution to a problem. Maynard-Smith (1968) observed that "we rarely know enough about laws governing the components of biological systems to be able to write down the appropriate equation with any confidence". Wilkie (1977) pointed out that "biological systems are to some degree mixed regimes whose behavior is affected by physical quantities other than those assumed to be dominant". Compared with the physical structures, biological structures are complex and possess intrinsic hierarchical stratifications with certain resolutely restricting boundary conditions (Bartholomew 1982a; Brown 1994). Living entities are more difficult to conceive mentally while physical ones are generally simple enough to be adequately expressed in mathematical terms. Despite the limitations of applications in biology, mathematical reasoning is fundamental in defining the logical consequences of a situation at intellectual depths and expressing and understanding what is theoretically contemplated or observed.

Symmorphosis is not a totally new concept. Actually, the idea is as old as science itself: the great Greek philosopher Aristotle (3 B.C.) observed that 'nature does nothing to no purpose". The concept of symmorphosis corresponds with the theory of optimality (e.g., Rosen 1967; Maynard-Smith 1978; Alexander 1982b; 1996; Kramer 1987) and the principle of minimum work (e.g., Murry 1926; Mandelbrot 1983; Rossitti and Löfgren 1993a) which contend that, operating on finite resources, self-regulating systems strive to optimize their operations. Through cost-benefit trade-offs, some factors are subordinated while others are augmented as an optimal match between structural design and functional performance is established (e.g., Dullemeijer 1974; Wainright et al. 1976; Barel et al. 1989; Barel 1993). Remarking on the variability of the thermostability of proteins, an observation which may apply to all levels of biology, Wedler (1987) observed that "there is no single or universal mechanism (in nature) . . . it appears that nature has utilized every imaginable means, in different combinations, to achieve the same end". Evolution by natural selection is a continuous process of cultivating optimization: ways and means of enhancing fitness are aggressively pursued. Of all forms of life which have evolved during the about 4 billion years life has existed on Earth, about 99.99% are now extinct (e.g., Pough et al. 1989). Extant organisms represent a very narrow range of the designs which have developed during the long period of trial-and-error evolutionary experimentation and even less of the infinite theoretical possibilities. The history of life occurs in form of a complex, sporadic pattern of past evolutionary expansions and contractions as assemblages of organisms in a particular time frame respond to the prevailing conditions (Gans 1988): useful functions are intensified and improved while the less beneficial ones are relegated or even eliminated. For instance, the evolution of the complex, more efficient tetrapod lung entailed suppression and eventual elimination of the hydrostatic role of the ancestral piscine lung (Joss et al. 1991), creating a favorable situation for transition from aquatic to terrestrial life (Liem 1987a).

The structures which comprise the gas exchange pathway, namely the lung, heart, blood vessels, and mitochondria, have determinate functional capacities (Weibel 1984a, 1987). Pulmonary design is coadjusted with functional needs to supply O_2 at rates consonant with prevailing demands. Since animals have a definable capacity to bear natural loads (be they from within or without), overdesign and redundancy of biological systems is costly and untenable. An optimum structural design is one which requires the least metabolic (energetic) cost to work and sustain (e.g., Thompson 1959; Rosen 1967). Such a design may operate at an optimum level, though it may not necessarily be optimally adapted. While endeavoring to optimize their operations, biological systems appear never actually to attain an optimum condition (e.g., Gans 1983; Lindstedt and Jones 1988). Optimization is a process which appears to be continuously aspired for. There are, however, assertions that such states exist. For example, in their geometry, the cerebral arteries (Rossitti and Löfgren 1993b) and the medium pulmonary airways (Hammersley and Olson 1992) are thought to be optimized in respect to the ratio respectively between blood/air flow and blood vessel/airway radius minimizing resistance. Intuitively, a definitive optimal state should never be consummated. Considering the dynamical nature of environments and the plasticity of biological systems, optimum states cannot possibly be satisfied. As a matter of fact, it would be imprudent to achieve such a condition since an organism's capacity to respond to further changes would be undermined. Joyce (1997) asserts that "evolutionary search is a parellel process in which every individual in a population has an opportunity to give rise to novel variants with increased fitness": this is thought necessary in order to minimize the real possibility of the population "getting trapped in an evolutionary blind alley from which further improvements in the fitness are precluded". In constant pursuit of optimization, the best level of "workmanship" possible under certain constraints and opportunities is established, affording the best level of fitness. In this context, Gans (1983) and Lindstedt and Jones (1988) define optimization as "the best level of improvement possible under the evolutionary circumstances". Williston's law, which asserts that serially repeated structures are reduced to fewer sets of undifferentiated organs, illustrates an evolutionary process of optimization where through a rigorous process of trial and error superfluous features are pruned, leaving the bare essentials for life. The quest for optimization is a universal process which encompasses all self-organizing structures. Howell (1983) pointed out that "optimization does not belong exclusively to biologists, but to any discipline where the subject has some effect on fitness".

As a philosophical definition of the correlation between structure and function in the design of biological systems, the concept of symmorphosis is heuristically useful and as a working hypothesis implicitly valuable. It constitutes a useful tool for bridging the different disciplines of biology. The breakdown of the concept at some levels and in certain cases (e.g., Gehr et al. 1981; Weibel et al. 1983) is a clear manifestation of the vicissitudes of evolution. Paradigms of pulmonary structural-functional reciprocity occur in the nonmammalian gas exchangers but refinements to the extent envisaged in the dictum of symmorphosis cannot be proved owing to paucity of data. Birds, in particular, exhibit remarkable species-specific variations in the degrees of pulmonary structural refinements. The lungs of the nonflying species, e.g., the domestic fowl, *Gallus gallus* variant *domesticus* (Abdalla et al. 1982), emu *Dromaius novaehollandiae* (Maina and King 1989), and the penguin, *Spheniscus humboldti* (Maina and King 1987), have subordinate parameters compared with those of the more energetic ones, e.g., the passeriforms (Maina 1984) and the hummingbirds (Dubach 1981) (Sect. 6.7.5). Bats, the only volant mammals (Thewissen and Babcock 1992), have remarkably highly specialized lungs (Maina et al. 1982a; Maina et al. 1991) which enable them to provide the large amounts of O_2 needed for flight. Natural selection does not seek efficiency for its own sake but only in so far as it can improve fitness for survival and ensure self-perpetuation. Interestingly, in the construction of animal bodies, gravity has spared the very small. The structural integrity of a body which takes a jump from a height of 10 m is not threatened until the animal attains a size of a puppy or is larger (Went 1968). Interspecific deviations of the aspects which are envisaged to constitute safety factors, redundancies, or limitations exist: they may explain why different biological systems manifest different physiological threshold pressures.

2.5.2 The Operative Strategies for Optimization in the Gas Exchangers

The erythrocytes are packages which are said to provide an optimum environment for the function of the hemoglobin (Horvath and Borgia 1984). They present an excellent example of the "multiple tradeoffs" or "shared adaptive effort" as termed by Taylor et al. (1987b) of the morphohological, physiological, and biochemical processes involved in enhancing O_2 uptake and transfer (e.g., Edsall 1972). In vertebrates, the hemoglobin concentration of about 5 mM is close to the saturation mark (e.g., Riggs 1976). Acclimatization to hypoxia, e.g., at high altitude (Petchow et al. 1977; Wood and Lenfant 1979), and increase in aerobic capacity (Carpenter 1975; Balasch et al. 1976) are largely accompanied by an increase in the hemoglobin concentration so as to increase the O_2 carrying capacity of blood. In an exercising horse and steer, as O_2 consumption increases, circulating hemoglobin concentration rises, thereby enhancing the delivery of O_2 to the tissues through the circulatory system (Jones et al. 1989). While compared with the little auk, *Plautus alle*, the Arctic tern, *Stema paradisaea* has a lower hematocrit due to smaller red blood cells and hence a lower total repiratory surface area of the RBCs, the hemoglobin content per unit area of the RBCs in the two species is similar (Kostelecka-Mycha 1987). Upward regulation of the hematocrit (Hct) in particular serves a useful purpose only up to a certain point, when the returns start to diminish. The flow of blood is exponentially related to the blood viscosity, which in turn relates with the hematocrit. Change in the blood O_2 carrying capacity through increase in the Hct contracts extra cost of pumping work on the heart muscle. With a Hct of 65%, the blood viscosity of the elephant seals is three times that of the rabbit, which has a Hct of 35% (Hedrick and Duffield 1986). Birds with higher Hct such as the pigeon (Hct = 52%) adaptively have low plasma protein concentration in blood to maintain the viscosity of blood at a level similar to that of the birds with lower Hct, e.g., 32% in the domestic fowl (Viscor et al. 1984). There are diverse adaptations involved in optimizing gas exchange in blood. While the hemoglobin-hematocrit-blood viscosity intercourse appears to suggest an exhaustive process of refinement (e.g., Clarke and Nicol 1993), other evolved innovations continue to be discovered. For example, during hypoxia and/or hypercarbia, fish erythrocytes swell, resulting in intracytoplasmic dilution of the hemoglobin and nucleoside triphosphates, increasing the O_2 affinity (Lykkebone and Weber 1978). The rheology of the erythrocytes (Merrill 1969; Schmid-Schönbein 1975) and the hemodynamics of the blood flow in the blood capillaries can improve the delivery of O_2 to the tissues (Zander and Schmid-Schönbein 1973; Kon et al. 1983; Nilsson et al. 1995). This mainly occurs through diminution of the diffusion boundary layer of blood plasma around the erythrocytes and possible intracellular physical agitation of the hemoglobin molecules (Skalak and Branemark 1969; Secomb 1991; Maeda and Shiga 1994). The nucleated erythrocytes, e.g., those of birds, are more resistant to shear deformation than the nonnucleated mammalian ones (Gaehtgens et al. 1981; Nikinmaa and Huestis 1984; Nikinmaa 1990). The shear modulus of the membrane of the nucleated erythrocytes, which have a better-developed cytoskeletal system, is 5 to 15 times higher than that of the nonnucleated mammalian erythrocytes (Waugh and Evans 1976; Chien 1985). Decreased deformability causes the erythrocytes to be trapped in organs like the spleen, lung, and liver (Groom 1987; Simchon et al. 1987), reducing the microcirculatory blood flow in the tissues. Although experimentally more resistant to deformation than the nonnucleated erythrocytes, the nucleated erythrocytes are more deformed as they pass the blood capillaries (e.g., Chien et al. 1971; Akester 1974). Despite having a diameter 30% greater than the human erythrocytes, the fish erythrocytes are as deformable as the human ones (Hughes et al. 1982; Hughes and Kikuchi 1984). Deformation of the erythrocytes reduces the apparent viscosity of the blood (Chien 1970) and provokes convective mixing of blood (Bloch 1962). Contrary to anticipation, the size of the erythrocytes in mammals does not affect the lung diffusing capacity for O_2 (Betticher et al. 1991): small erythrocytes have a greater surface-to-volume ratio, thinner plasma boundary layer (Vandegriff and Olson 1984), and shorter intracellular diffusion distance (Yamaguchi et al. 1988), factors which would be expected to favor O_2 transfer. However, since a sphere is not deformable unless it is squeezed, the less spherical an erythrocyte, the more malleable it is without changing the surface area. Betticher et al. (1991), conceptualized that as the small erythrocytes are more spherical, the plasma around them is less well mixed than in larger cells, thus decreasing O_2 transfer into the cell. The elephant seals are thought to increase O_2 storage at the expense of aerobic scope which results from viscosity-limited perfusion efficiency (Hedrick and Duffield 1986). The normal hemoglobin concentration of 150 g/l of the mammalian blood is the value at which maximum amount of O_2 (210 cm^3), equivalent to the relative atmospheric concentration of the gas (Davenport 1974), is transported with least circulatory work (Schmidt-Nielsen 1984). Adaptive increase in the hemoglobin concentration at high altitude and in small animals such as shrews (Ulrich and Bartels 1963) and bats (Jürgens et al. 1981), values which may respectively be as high as 170 and 244 g of hemoglobin per l may set the operational limit to which hemoglobin and hematocrit levels may be usefully applied to improve respiratory efficiency. In the tracheolar system of insects (Sect. 6.6.1), the mean free path of O_2 molecules in air (i.e., the average distance a molecule travels in air before colliding with another) which is about 0.008 μm (Pickard 1974) sets the limit of the smallest tracheolar diameter. Due to the remarkable variability and functional lability of the respiratory pigment system (Sect. 2.8), among the evolved sections of the integrated gas exchange system, the respiratory pigments appear to be the most recent addition and hence the least conserved parts. As opined by Jones (1972), the more ancient factors such as the morphological features of the gas exchanger and the vascular system, which are less flexible, would to a greater extent constitute limiting factors in respiration.

Metabolically, animals operate at two extremes, a steady-state resting condition and under maximal stress. Contrived reserves enable them to harmonically perform under the two different sets of conditions. To ensure structural and functional integrity, the body systems must be designed to withstand the maximal stresses they are likely to be subjected to. Digressing a little from the gas exchangers, in all evolved biological structures, the spider's dragline perhaps best illustrates the process of optimization in biology. A spider's dragline, a tool which determines survival by providing means for procurement of food and escape from predators (a lifeline in the true sense of the word!) is a multiphase material which consists of double filaments (Vollrath 1992). Individually the filaments can support the weight of the animal (if one is accidentally cut). A single line will break at a stress equivalent to that generated by about six times the spider's weight (Osaki 1996). Activities such as movement, jumping, and rapid descent and ascent (when greater stress is exerted on the dragline) must be accommodated in the design. The elastic-limit of a dragline gives the maximum safety (a safety coefficient being the ratio between the mechanical strength of a dragline and a spider's weight) for supporting a spider's weight. The mechanical properties of the spiders' draglines have been refined over their 400 million years of evolution to this level of sophistication. Turning to the respiratory organs, in the rainbow trout and the lingcod, only about two thirds of the secondary lamellae are perfused at rest (Booth 1978; Farrell et al. 1979; Nilsson et al. 1995) but the fish can increase O_2 consumption during exercise eight to ten times (Jones and Randall 1978). Hypoxia, e.g., in warm, bottom, and standing waters and during low tide (in intertidal animals), e.g., in the blue crab, *Callinectes sapidus* is avoided by increased ventilation and perfusion of the gills (Tuurala et al. 1984; DeFur and Pease 1988), lamellar recruitment (Booth 1979; Farrell et al. 1980), shortening of the thickness of the water-blood barrier (Farrell et al. 1980; Soivio and Tuurala 1981), and effecting changes in the blood O_2 binding characteristics (Jensen and Weber 1985). In extreme circumstances, especially where hypoxia is accompanied by high temperatures, the metabolic rate may drop to conserve O_2 and/or the fish may relocate to less poorly oxygenated waters (Jones 1952; Whitmore et al. 1960). Cephalopods, e.g., *Loligo* and *Octopus*, can increase their O_2 consumption by a factor of 2 to 3 from rest (O'Dor 1982; Wells et al. 1983). Squids which live in cold, deep seawaters have a large gill surface area and a thin water-blood barrier compared with those which live in shallow waters (Roper 1969; Madan and Wells 1996). The large gill surface area in the pelagic cephalopods may enable them to cope with the hypoxia prevalent in their habitat and could give them a competitive edge over fish (Madan and Wells 1996). This view was, however, disputed by Seibel and Childress (1996) on the basis of the fact that many fish sympatrically coexist with the squids and in some cases may even displace them. The cephalopod heart mainly works aerobically, relying largely on amino acids as substrates for oxidative metabolism (Hoeger and Mommsen 1985). By retracting into the shell, the bivalve mollusk, *Pholas dactylus*, can effect a complete shutdown of the posterior parts of the gills and, at maximal extension, the gills may be three times as long as the shell itself (Knight and Knight 1986). Bats and birds increase their O_2 uptake from rest to flight by a factor of 10 to 20 times (e.g., Thomas 1987; Butler 1991b) and insects by as much as 120 to 400 times (Weis-Fogh 1967). In gills, ion pumping and gas transfer can be regulated by modulating gill ventilation (Randall et al. 1972; Wood and Randall 1973). The mammalian lung maintains a remarkable excess of diffusing capacity up to a factor of 2 (Weibel 1984a). Even under hypoxic conditions, goats attain maximum O_2 consumption and only the smallest mammals use all of their diffusing capacity under such conditions (Taylor et al. 1987a).

Those animals which have relatively greater O_2 demands during exercise, e.g., birds and insects, are in most respects endowed with more efficient respiratory designs than the human alveolar lung. In a radical departure from the norm, in some respects, it could be argued that, compared with the other organ systems, the respiratory processes have been less sensitive to phylogenetic changes. Adequacy for specific metabolic needs in a given habitat appears to be the primary factor which has determined the refinement and construction of the gas exchangers. Fluid designs have made animals at completely different levels of phylogenetic development coexist in the same general habitats by varying their metabolic demands to meet individual requirements. From the perspective of respiration, animals have had few choices. There are only two naturally occurring respirable fluids - water and air - and three livable spaces, namely the aerosphere, the hydrosphere, and the lithosphere, i.e., the livable superficial part of the Earth's crust generally called soil.

2.5.3 Symmorphosis and Optimization: are they Logical Outcomes of Evolution?

The concepts of optimization and symmorphosis may have been accepted by biologists basically for their instinctive appeal to simple intuitive logic. Recently, the concepts have been ardently debated in depth (see Diamond 1992; Weibel et al. 1998). Conceived as perfect matching between structure and function, symmorphosis has been questioned from phylogenetic and developmental considerations (e.g., Gould and Lewontin 1979; Lewontin 1979; Garland and Huey 1987; Gans 1988). Optimization for particular conditions and circumstances, though logically desirable, curtails the potential and the range of adjustments which organisms can mobilize to counter external assaults. As a practical rule, every adaptive refinement for a particular circumstance that an organism or organ system undergoes leads to exclusion of capacity to take on others.

Moreover, what may be an optimal solution for a particular situation at a particular time may be a limiting factor in another. Moore (1990a) asserts that "organisms cannot be complete specialists and complete generalists at the same time". Natural selection refines each and every lineage towards effective utilization of a specific quota of the available resources. Faunal structuring, partitioning of dietary and habitat resources, and the different morphological specializations acquired for procuring them minimize competition, providing optimal survival conditions. Animals which face similar ecological and developmental constraints evolve similar features, as demonstrated by the phenomena of convergent evolution (e.g., Lauder 1981; Lauder and Liem 1989; Wagner 1989). In the process of perfecting for a particular lifestyle in a given environment, each incremental increase in fitness is accompanied by progressively narrower scope of structural and functional adaptive flexibility. This predisposes a species to collapse and extinction through what has been termed overadaptive meltdown (e.g., Minkoff 1983; Stuart 1991). Borrowing from the comment made by Wells (1962) on the cephalopods, remarking on the extreme marine predatory capacity of the elasmobranchs, Tota and Hamlett (1989) observed that "in doing so (adapting) they have become specialized to the point where their own structure and physiology will preclude further adaptive radiation". Gans (1985) contends that "we should not be surprised to find that no structure is perfect and that few structures are optimized to any particular role". Through intense genetic breeding, a process termed directed evolution by (Joyce 1992), the horse and the domestic fowl, *Gallus gallus* variant *domesticus*, have respectively been exceedingly manipulated for speed and weight gain. While better feed and feeding regimen may contribute, in 1960 it took 70 days for a table bird to reach a live weight of 1.8kg and in 1985 it took only 40 days (Smith 1985). In the course of this enforced productivity, the functional integrity of some organ systems appears to have been severely compromised. Death due to aortic rupture (e.g., Carlson 1960) and vascular pathology (e.g., Julian et al. 1984) is a common problem in the turkey industry. A worldwide increase in occurrence of ascites has been reported in young broilers by Julian and Wilson (1986), Maxwell et al. (1986a,b) and Julian (1987). The syndrome was associated with right ventricular hypertrophy (Huchzermeyer and De Ruyk 1986; Julian and Wilson 1986). In an attempt to explain the pathogenesis of the condition, Huchzermeyer (1986) and Huchzermeyer et al. (1988) contended that hypoxia may cause pulmonary vasoconstriction with consequent pulmonary hypertension, resulting in a right ventricular hypertrophy. In the mammalian fetal lung, vasoconstriction due to hypoxia is thought to restrict blood flow to the developing lung in utero (Morin and Egan 1992). Environmental factors such as cold and altitude as well as nature of food have been associated with ascites in birds (Maxwell et al. 1986a,b; Julian 1987). Respiratory inadequacies in the domesticated birds may result from the poor pulmonary morphometric parameters which generally characterize the group (Abdalla and Maina 1981; Abdalla et al. 1982; Maina and King 1982a; Vidyadaran et al. 1987, 1988, 1990). The growth of the lung of a highly selected line of turkey did not match the increase in body mass (Timwood and Julian 1983; Timwood et al. 1987). The free-ranging village chickens are not susceptible to ascites (Pizarro et al. 1970). For similar reasons, i.e., intense selection for productivity in total disregard of the necessity for commensurate adaptation of the supporting organ systems, domestic fowls (particularly the males) are totally incapable of attaining VO_{2max} on treadmill exercise (Brackenbury and Avery 1980; Brackenbury et al. 1981; Brackenbury 1984). In the horse (an animal which has been fiercely genetically manipulated for speed performance), the pulmonary capillary blood pressure increases from 2.4kPa to about 6kPa during exercise (Sinha et al. 1996). Exercise-induced pulmonary hemorrhage has been reported to affect more than 40 to 80% of horses during high intensity exercise (Mason et al. 1983; Burrell 1985; West et al. 1991, 1993). Experimentally, the capillary transmural blood pressure which causes stress failure in the horse's pulmonary blood capillaries ranges between 10 and 13kPa (Birks et al. 1997). Even at maximum exercise, a safety margin appears to exist in the lung's capacity to tolerate transmural mechanical stress at the alveolar level.

Based on the fact that many complex designs and patterns can be generated by a few simple natural algorithms, an almost infinite number of different designs of gas exchangers should perchance have evolved in animals. Certain constraints, however, must have enforced convergence and adoption of similar designs, even in animals of remarkably different ancestry. Employing different strategies and resources, such animals have found similar solutions to common challenges. Like most organs and organ systems, the gas exchangers are known to carry out multiple functions which include feeding, sexual display (inflation of the lung, e.g., in frogs), osmoregulation, and secretion and metabolism of certain pharmacological factors (Sects. 6.10.1 and 6.10.2). Interspecific differences in the roles which similar structures play and the many roles carried out by the same structure in an individual animal occur (e.g., Gans 1985, 1988; Bennett 1988). The conflict between the roles may keep some parameters from optimizing. Moss (1962) called the aggregate number of roles an individual structure plays a functional matrix. For performance of multiple functions, such organs have integrated (compromised) designs. Over time, the individual structural components have been refined to carry out a particular role best. Uncoupling the roles that certain structures play eliminates the constraints placed on their improvement and hence imparts opportunity for greater diversity and refinement in form and function (Liem and Wake 1985). To illustrate this point, the emergence of suctional breathing from the buccal force pump dissociated the feeding from the breathing functions, leading to diversification and greater specialization of the two processes in reptiles. Biological structures evolve to satisfy the immediate needs. They do not have to be optimal to be conserved by natural selection. The difference between the cost of operation of an organ during unstressed state and under severe stress can be considered to be its adaptive phenotypic plasticity. Unless the maximal loads a system can bear are well known, the available scope of operation can be read as an overdesign, overconstruction, or even redundancy. It is envisaged that overdesign results from a genetic programming which is based on an unpredictable environment (Gans 1988). Though normally operating at a lower scope (e.g., Bennett 1988), organisms appear to preadapt for the worst-case scenario (Gans 1979). The apparent paradox in the scaling of the morphometric pulmonary diffusing capacity (DLo_2m) of mammalian lung and the Vo_{2max} with body mass (Gehr et al. 1981) suggested that, compared with the small animals, large ones have overconstructed lungs, with DLo_2m being 10 to 20 times that which they actually need. A number of explanations have been offered to explain this discordance. Federspiel (1989) suggested that erythrocyte redistribution in the pulmonary capillaries during exercise may bring the physiological diffusing capacity closer to the morphometric one. Heusner (1983) asserted that redundancy in the gas exchangers increases with body size. It is plausible that, compared with the small ones, the large animals may possess a greater capacity to generate multifarious solutions to different functional needs. Alternatively, rather than being a redundancy, this feature may be indicative of a safety margin of operation in the lungs of the large mammals in order to support their higher mass-specific expenditure of energy in locomotion (e.g., Hill 1950). Dejours (1990) contended that time-dependent events such as the duration of exercise performed to determine VO_{2max} are longer in the larger than in the small animals. If this were so, the larger animals would need greater gas exchange potential than the small animals to support aerobic metabolism over the longer duration. At sea level, Wagner (1993) concluded that the parameters which are involved in O_2 uptake and delivery to the tissues (e.g., ventilation, hemoglobin concentration, cardiac output, lung, etc.) have been optimized (i.e., there is very little reserve in them) such that further adjustments do not affect VO_{2max}: under such circumstances, the most important parameter which determines the VO_{2max} is the cardiac output – not the lung. Pennycuick (1992) suggested that the surface area fractal dimension of the mammalian lung, which may be as high as 2.5, differs between the lungs of the small and large animals, a feature that may impart a better gas exchange capacity in the lungs of the large mammals. The extinction episodes that have befallen multicellular animal life indicate that in cases of sudden catastrophic events, the existing safety reserves are easily overwhelmed. Animals have no inbuilt contingencies for such rare and sudden events of great magnitude. Raup and Sepkoski (1984) argued that major extinction events recur with a periodicity of 26 million years. Rather than pay the cost of supporting superfluous structures which may not be utilized for many generations, it would seem that animals have gambled away their survival and invested on features such as diversity and numerical density in hope that these would see them through such occurrences. It is possible that during the long periods of relative stability, new species with better fitness characteristics would have arisen from ill-prepared ancestral ones. Gould (1994) envisages that the reason that mammals survived the dinosaur demise of the end-Cretaceous (though the two groups had coexisted for over 100 million years) is not, as has been widely argued, that the mammals had evolved special adaptations – as animals cannot possibly anticipate and prepare for future events. Their relatively small size (size of a rat or smaller) enabled mammals to fit into less hostile ecological niches which were out of reach to the more robust reptiles. Janis (1993) appropriately calls the succession of mammals victory by default. Like mammals, birds appear to have endured the pressure very well: at least 20 mammalian groups and 22 avian lineages predate the Cretaceous-Tertiary catastrophe (Coope and Penny 1997).

The thickness of the blood-gas barrier and the diameter of the erythrocytes are two factors in the gas exchangers which have been pushed close to optimization if this has not already occurred. While mammals span the enormous range of body mass from the 2.5-g shrew to the about 150-t whale, a factorial difference of

60 million, the average thickness of the blood-gas barrier of the lung of the shrew (Gehr et al. 1980) of 0.334 μm is comparable to that of 0.350 μm of the lung of the whale, *Balaena mysticetus* (Henk and Haldman 1990). Although no estimations of stress failure of the pulmonary capillary blood vessels are available on these two animals, the alveolar wall in the lung of the rabbit, *Oryctolagus cuniculus*, fails above a transmural blood pressure of 3.3 kPa (Tsukimoto et al. 1991; Costello et al. 1992), a value which is astounding since the harmonic mean thickness of the blood-gas barrier is only 0.50 μm (Weibel 1973). The pulmonary capillary pressure in the rabbit (Maarek and Grimbert 1994), dog (Okada et al. 1992), and human being (Hellems et al. 1949; Comroe 1974), animals of notably different body sizes, is about 1.1 kPa, giving a safety factor of 3. In the dog, Okada et al. (1992) observed that the resistance in a segment of an alveolar blood capillary remains stable even after large changes in the transmural pressure. In the human being, pulmonary capillary blood pressure elevation has been associated with rupture of the alveolar blood-capillary barrier (Severinghaus 1971) and presence of erythrocytes on the alveolar surface in cases of high altitude pulmonary edema (Schoene et al. 1988; Heath and Williams 1989). The pulmonary blood flow is pulsatile (e.g., Wiener et al. 1966; Milnor 1982; Maarek and Chang 1991). It is envisaged that dampening of the pressure wave occurs in the capillary system (Wiener et al. 1966). The pulsatility of the pulmonary microvascular pressure may influence filtration of fluid across the capillary wall and gas exchange at the alveolar level (Maarek and Chang 1991). In mammals, the size of the erythrocytes presents a good example of structural optimization. The erythrocytes of the shrew, the smallest extant mammal, have a diameter of 7.5 μm and compare with those of the humpback whale of 8.2 μm (Altman and Dittmer 1961). Since the smallest blood capillaries should set the limit for the erythrocyte diameter (though the cells fold greatly as they traverse these narrow conduits), the diameters of the blood capillaries in the smallest and largest mammal appear to be comparable. This suggests an optimal setting of the capillary diameter for satisfactory supply of O_2 to the tissues.

The criteria of categorizing a biological structure as inconsequential, superfluous, excessive, subservient, nonfunctional, or constituting a controlling, regulatory, limiting, constraining, or even being a triggering factor is oftentimes highly subjective. In some cases, by acting differently, opposing selective pressures greatly alter the physiological profiles of the functional components, whereby some processes may be suppressed, some may synergize, while others may become totally obliterated or remain functionally neutral. The operational definition of what is optimal is oftentimes biased and misleading. The interpretations may depend on circumstances and even on anthropocentric perceptions and personal preference of what may be deemed beneficial. For example, while intrapulmonary air and lighter bones may be considered to be useful in increasing the buoyancy of a flying animal, in an aquatic one, both parameters are a vulnerability rather than a benefit. Though the lung is considered to be specifically designed in view of efficient uptake of O_2 and discharge of CO_2 (e.g., Weibel 1983a, 1985b), the organ plays important defensive, pharmacological, and endocrine functions (Sect. 6.10.2). To yet unknown extents, such roles must be accommodated in the overall design of the organ. The composite nature of biological tissues and the multiplicative effects between the various integral components may explain why the sum of the individual functional processes often exceeds the aggregate value expressed by the whole organism (Hoagland and Dodson 1995). For example, while the full energy budget of an organism in normoxia is totally aerobic, even the well-oxygenated mammalian cell cultures invariably manifest a partly anaerobic state (e.g., Gnaiger 1991).

2.6 Fractal Geometry: a Novel Approach for Discerning Biological Form

Geometry, as advanced by Euclid (300 B.C.) and Pythagoras (6 B.C.), uses straight lines and smooth and regular curves to make flat shapes and figures such as squares, triangles, and circles to model structures. When applied to natural things, however, it idealizes form in inherently chaotic structures (e.g., Olsen and Degn 1985; West 1990). The classical geometry defines space in terms of discrete dimensions, e.g., a point has no (zero) dimensions, a line has one dimension, a plane (area) has two, and a solid (volume) has three dimensions. These integer dimensions are unsatisfactory in describing the highly complex natural forms and the dynamical physiological processes that do not have specific scales of length and time. To adequately define the topological characteristics of dynamical structures and processes, fractional power dimensions (fractals) are necessary. The development of biological states and events are regulated by nonlinear, iterative algorithms which program morphologies and physiologies that lack absolute spatial and temporal boundaries (e.g., West 1985, 1987; Nonnenmacher 1987; Voss 1988; Nelson et al. 1990; Bassingthwaighte et al. 1994). The designs and operations present scale-invariant properties and self-similarity (Horsfield and Woldenberg 1986; Barnsley et al. 1987; Bassingthwaighte 1988; Giaver and Keese 1989; Goldberger et al. 1990). Discovered by Mandelbrot (1977, 1983), fractal geometry provides a powerful tool for rationally investigating form and function (e.g., Barnsley et al. 1987; Goldberger and West 1987; Tsonis and Tsonis 1987; West and Goldberger 1987; Glenny et al. 1991). Fractal characteristics have been reported in viruses (e.g., Briggs 1992) and tissue cells (e.g., Nonnenmacher 1988; Smith et al. 1989; Losa et al. 1992). They are integral to the functions of organs like the heart (Goldberger et al. 1985; van Beek et al. 1989; Goldberger 1991) and the gastrointestinal system (Pennycuick 1992). Structures such as the bronchial tree of the lung (e.g., Mandelbrot 1983; West et al. 1986; Nelson et al. 1990; Weibel 1991, 1994; Bates 1993, but see a dissenting view by Phillips et al. (1994) and the pulmonary arterial tree (Krenz et al. 1992) present fractal attributes. Blood flow in the lung (Glenny and Robertson 1990; Caruthers and Harris 1994), in the middle cerebral artery (Rossitti and Stephenson 1994), and in the myocardium of humans (Bassingthwaighte et al. 1989) has fractal properties.

Fractal geometry provides means for realistically analyzing dynamic forms and processes (e.g., Nelson and Manchester 1988) and studying physiological properties (Goldberger and West 1987). A corrugated structure in three-dimensional space is physically in transition between a smooth surface and a volume. Depending on the degree of amplification, such structures should have a fractal dimension between 2 and 3. A fractal dimension defines to what extent the topological details of an object fit between the Euclidean dimensions. The surface fractal value of the mammalian lung is about 2.5 (Weibel 1991). Mandelbrot (1977, 1983) observed that both the fractal dimension, D, and the diameter component, Δ, of the bronchial tree were about 3. Such high values indicate that the surface area of the lung has been sufficiently highly folded and the peripheral airways sufficiently regularly branched as to nearly fill a three-dimensional space. The two-dimensional surface area of the human vascular system is so highly folded that it has an effective fractal dimension of 3, with the arteries alone having a value of 2.7 (Briggs 1992). It has been argued by Goldberger et al. (1990), Nonnenmacher (1989), Weibel (1991, 1994), and Rossitti and Stephensen (1994) that fractal designs should permit biological systems to operate over a wide range of perturbations without failure. Fluidity in the configuration imparts greater error tolerance (i.e., safety margin) to a biological structure and may be decisive in the trial-and-error process of evolution (West 1987). The inbuilt fractal algorithm reduces the probability of error during morphogenesis since it is dependent on a well-tested self-similar, repeating (iterative) process. Functionally, a fractal attribute eliminates the need for drastic constructional overhauls in a system operating within reasonable boundaries and exposed to moderate assaults. Pennycuick (1992) envisages that the use of fractal structures can allow a particular plan to be scaled over a wide range of sizes without consequential allometric change. Functional plasticity should make adaptation and the more or less trial-and-error evolutionary process by genetic programming much easier to effect, against stochastic settings (e.g., Doebeli et al. 1997).

Unique to most organ systems, and perhaps an indication of the importance of respiration for survival, the gas exchangers have been configured by essentially molding together three characteristically fractal entities, namely the pulmonary arterial system (e.g., Lefevre 1983; Glenny and Robertson 1991a; Krenz et al. 1992), pulmonary venous system, and the bronchial-alveolar system (Weibel 1986). Though it may appear passive, the lung is intrinsically a highly dynamic organ. It is subjected to continuous cardiovascular hemodynamic changes as well as biomechanical ventilatory rhythms. It acts as an interface between blood and air, media which are physically remarkably different. The lung is the only organ in the body which transmits the entire volume of blood in the systemic circulation. The multifunctionality of the lung was pointed out by Bakhle (1975), who declared that "the lung should now be considered not merely as an apparatus for gas exchange or mechanical filtration of blood but also that of providing an essential control of the blood levels of many biologically active substances". The fractal characteristics of the surface of the lung allow the large internal surface area to be homogeneously ventilated and perfused at low energy cost (Weibel 1983a, 1991, 1996) and the circulatory system to be highly distensible (Caro and Saffman 1965; Yen 1989a,b; Bshouty and Younes 1990) to contend with the fluctuating hemodynamic blood pressures (Maloney et al. 1970; Zhuang et al. 1983; Al-Tinawi et al. 1991). Although only about 9% of the total blood volume is contained in the heart (Dock et al. 1961; Milner 1980), Hainsworth (1986) observed that the "distensibility of the pulmonary circulation is of particular importance as it permits transient imbalance between the outputs of the left and right hearts". Pulmonary blood flow is pulsatile from the entrance of the pulmonary circulation to its outlet in the left atrium (Morkin et al. 1965; Wasserman et al. 1966; Milnor 1982; Maarek and Chang 1991). The fractal dimensions of the diameter element of the arterial and the venous tree in the human lung are 2.71 and 2.64, respectively, while equivalent values for the length element are 2.97 and 2.86, respectively (Huang et al. 1996). In the dog lung, the fractal dimension of the blood flow is 1.22 (Barman et al. 1966). Pennycuick (1992) suggested that the morphological complexity of the avian pulmonary system (Sect. 6.7.5) may be due to a high fractal surface (with a dimension of about 2.5), enabling birds to achieve exercise capacities such as sustained flights at altitude without the need to vary the general plan of the respiratory system. The morphological features of the avian respiratory system bear this suggestion out: except for differences in the sizes and locations of the air sacs, pneumatization of the long bones, and development of the parabronchial systems (Sect. 6.7.5), the configuration of the lung-air sac system in birds is uncommonly uniform in such a numerically large and ecologically diverse group. A small fractal dimension in the design of the characteristically mammalian bat lung (Sect. 6.7.4.1) may have called for multiple extrapulmonary compensatory changes (Maina 1998) in order to provide the large volume of O_2 needed for flight. This line of reasoning is supported by a number of observations which include: (1) bats have enormous lungs which occupy much of the celomic cavity (e.g., Maina and King 1984), and (2) the mass of the heart and parameters such as the hematocrit and hemoglobin concentration are some of the highest values among mammals (Jürgens et al. 1981). The high demands imposed by flight on a gas exchanger of moderate efficiency may explain why the heaviest bats, the flying foxes (pteropodids), weigh only about 1.5 kg, a value which is an order of magnitude smaller than the weight of the heaviest flying bird (about 15 kg). For gas exchange, birds operate on what was termed a broad-based low-keyed strategy where many moderately refined parameters are variably utilized in combination, affording a large functional reserve (Maina 1998). The highly efficient tracheal system of insects (Sect. 6.6.1) is thought to have fractal surfaces of high dimension (Pennycuick 1992). The fractal dimension of 2 suggested for the fish gills by Pennycuick (1992) may be due to the assumption that the secondary lamellae of fish gills are smooth. Lamellar microridges (Fig. 50b) are characteristic of secondary lamellae of most fish gills, even those of the most ancient fish such as the coelacanth, *Latimeria chalumnae* (Hughes 1995), and the sturgeon, *Acipenser transmontanus* (Burggren et al. 1979). Microridges are, however, poorly developed in the gills of *Trachurus mediterraneus* (Hughes and Mondofino 1983) (a carangid fish) and appear to be lacking in the secondary lamellae of the hill-stream fish such as *Danio dangila* (Ojha and Singh 1986). It would seem that generally, like other gas exchangers, the gill surface is a fractal construction. Microridges increase the respiratory surface area of the gills, provide anchorage for the mucous lining, generate turbulence, and reduce drag forces at the water-gill interface (e.g., Sperry and Wassersug 1976; Hughes and Mondolfino 1983; Hughes 1979, 1984). Recently, applying fractal geometry to the allometric scaling of animal size, West et al. (1997) concluded that the enormous size disparity in the evolved animal life has been possible due to the intrinsic fractal nature of tissues and organ systems.

Cope's rule (see Cope 1896, generally considered a pervasive evolutionary pattern, but see dissenting views by Fenchel 1993 and Jablonski 1997), asserts that phylogenetically, animal lineages tend to evolve larger body size for reasons that they achieve greater mating success, better defense capacity, predatory ability, and resistance to environmental extremes (Bonner 1988). In biology, time-dependent events, e.g., ventilatory cycle, incubation and gestation periods, and duration of exercise needed to reach maximal O_2 consumption are longer in large than in small animals (Dejours 1990). The mass specific cost of transport is lower in larger animals than in smaller ones (Boulière 1975; Taylor 1977).

2.7 From Diffusion, Perfusion, and Ventilation to Respiratory Pigments

2.7.1 Diffusion

The evolution of respiration unfolds critical moments in the past when at certain times momentous developments occurred. Some of the most profound changes took place during the transformation of the anaerobiotic prokaryotes to the aerobiotic eukaryotes (the inquisition of molecular O_2 into respiration), accretion of cells into the Metazoa, shift from water- to air breathing, transition from water to land, and change from ectothermic-heterothermy to endothermic-homeothermy. At each of these stages, the metabolic needs of organisms would have exceeded those that could be serviced by the default gas exchanger. Changes which resulted in greater diversity and specializations of the gas exchangers were thereby instituted. In the theory of chaos (e.g., Stewart 1990) such phenomenal moments when conditions occur to create dynamical, self-driving structures by amplifying and locking the system's feedback together are called bifurcation points (Briggs 1992).

A distinct respiratory system cannot be clearly delineated below the level of mollusks and arthropods. The most primitive gas exchanger in such simple metazoans is an unspecialized epidermis. Gas transfer occurs by diffusion across the general body surface and in some cases through inbuilt modifications (e.g., Mangum 1994). Diffusion is a natural phenomenon which dictates spontaneous flow of molecules from places of high to low concentrations free of energy, just as water flows downhill. This must have been the earliest mode of gas transfer which was initiated by the increase of molecular O_2 in the primeval biosphere, resulting in the evolution of aerobic processes. When it is the only means of supplying O_2 to the cells, diffusion determines the shape and size of organisms (e.g., Burggren and Roberts 1991). A small and flat body form enhances gas exchange by diffusion (e.g., Jell 1978; Runnegar 1982). When O_2 needs are high, at 1 atm, diffusion can only be adequate in organisms up to about 1 mm in diameter and in animal tissues 2 to 5 mm thick (e.g., Comroe 1966; Schmidt-Nielsen 1990). Larger animal forms must possess a low rate of metabolism if they are to rely wholly on diffusion as the only means of securing O_2 and voiding CO_2. The evolution of complex energetic animals obliged the development of diverse specialized systems to deliver O_2 from the external environment to the tissue cells (Comroe

1966). As a spherical body provides the lowest surface to volume ratio, to overcome diffusional limitations, animals have deviated from this design by evolving long, highly attenuated bodies. Factors such as the habitat occupied and the mode of life determine the definitive shape and size of animals (Gould 1966) as well as the type of a gas exchanger needed to effectively service the total cytoplasmic mass. The innermost part of the developing embryos in an egg mass of the sand snail, *Polinices sordidus*, which weighs as much as 210 g (Shepherd and Thomas 1989) and has a radius of as much as 40 mm, experiences extreme hypoxia ($PO_2 < 1$ kPa) though the PO_2 in the outer layer of water may be moderately high at $PO_2 > 10$ kPa (Booth 1995). Water inside a spawn of *Rana temporaria* was found to be only 3 to 16% saturated while the saturation about 50 cm away from the egg cluster was 136% (Savage 1935). By adopting appropriate morphological designs and subsisting in a well-oxygenated medium, an organism can attain greater body size while relying on diffusion only. Through an assemblage of irregular shapes which increase the surface area, the diffusional distances can be reduced. In the sponges, where there is no internal perfusive mechanism, the body has flagellated cells (choanocytes) which move water (by the beating of cilia) through numerous incurrent pores or ostia into ramified water channels of about 1 mm diameter. This brings the tissue cells close to water enhancing gas exchange and nutrient uptake (Fig. 17). As much as 90% of O_2 is extracted from the water passing through the pores of sponges during maximal activity (Hazelhoff 1939). The largest known sponge is the barrel-shaped loggerhead sponge (*Spheciospongia vesparium*) which is found in the West Indies and in the waters off the coast of Florida: it stands at a height of 1.5 cm and is 9 cm in diameter. Sponges have been recovered from depths up to 5.6 km. In the coelenterates, a group which has a remarkably low metabolic rate, a steady water flow by ciliary movements across the gastrovascular canals is maintained. Pelagia,

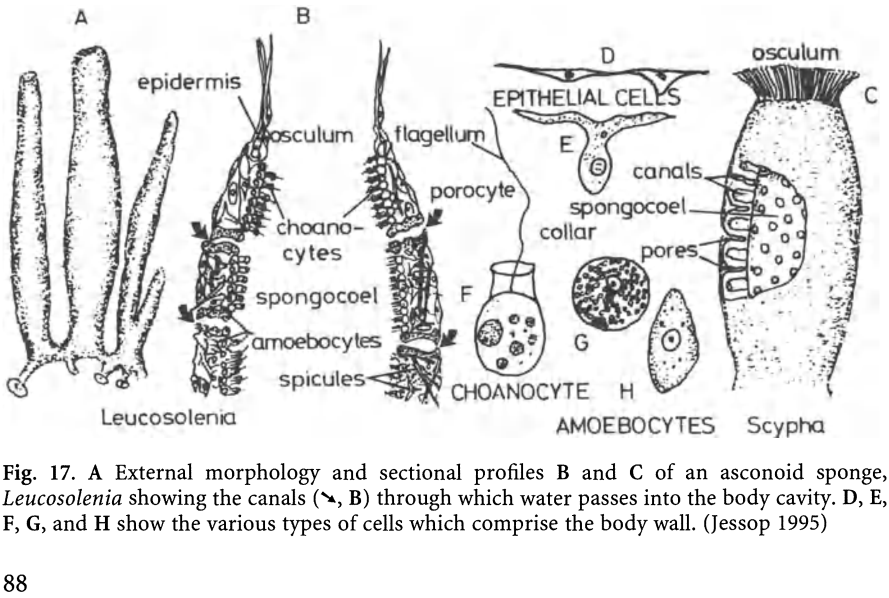


Fig. 17. **A** External morphology and sectional profiles **B** and **C** of an asconoid sponge, *Leucosolenia* showing the canals (↘, **B**) through which water passes into the body cavity. **D**, **E**, **F**, **G**, and **H** show the various types of cells which comprise the body wall. (Jessop 1995)

which can grow to a diameter of about 6 cm (Henze 1910), and the coelenterate *Cynea*, which can grow to a diameter of 2 cm, are said to rely sorely on diffusion for their O_2 needs (Krogh 1941). The tropical earthworms, animals which are as large as 1 kg in body mass, e.g., *Rhinodrilus fafner* and *Megascolides australis* have been recorded to attain lengths of 2.2 m (but have a diameter of about 24 mm), rely entirely on cutaneous diffusion for gas exchange (Stephenson 1930). In helminths, Fry and Jenkins (1984) estimated that to depend entirely on diffusion to maintain aerobic respiration, the critical thickness is 0.4 mm for the nematodes and 0.75 mm for the cestodes. The interstitial animals (animals which live in the water-filled spaces between the aquatic sediments) like the polychaete *Stygocapitella subterranea* and oligochaete *Marionina achaeta* do not have specialized respiratory surfaces. They acquire their O_2 needs entirely by diffusion through their great surface-to-volume ratio achieved from their thin, cylindrical body configurations. In an adult gastrotrich 500 μm long, Colacino and Kraus (1984) estimated that the O_2 transfer across the body surface was three times greater than its O_2 consumption when the PO_2 between the water and the mitochondria was only 0.13 kPa. Due to the much greater rate of O_2 diffusion in air than in water (Table 4) and the more constant level of O_2 in air, for the same concentration difference, the mass transfer attained over 1 μm in water can occur over a much longer distance of 1 cm in air. The PO_2 in the hemolymph of the gooseneck barnacle, *Pollicipes*, is elevated in air (e.g., Petersen et al. 1974). The air can support a spherical animal 100 times greater than water at the same rate of metabolism. However, such animals do not exist due to the parallel complications which would arise in air such as risk of desiccation and lack of mechanical support. In simple organisms, there exists a delicate compromise between the

Table 4. Some physicochemical properties of water and air[a]

Parameter	Unit	Water	Air	Water/air	Air/water
Density	$g\,ml^{-1}$	1.000	0.0012	833	–
Viscosity	Centipoises	1.00	0.02	50	–
O_2 Content	$ml\ 100\,ml^{-1}$	0.66	20.95	–	32
CO_2 Content	$ml\ 100\,ml^{-1}$	0.03	0.033	0.91	–
Thermal capacity	$Cal\,ml^{-1}\,°C$	1.00	0.0003	3333	–
Diffusion coefficients	$cm^2\,s^{-1}$				
O_2		0.000025	0.198	–	8000
CO_2		0.00008	0.155	–	2000
Capacitance coefficients	$nMol\,ml^{-1}\,mmHg^{-1}$				
O_2		1.82	54.74	–	30
CO_2		51.89	54.73	–	1
Krogh's constants	$nMol\,cm^{-1}\,s^{-1}\,mmHg^{-1}$				
O_2		0.000046	10.84	–	20000
CO_2		0.00093	8.46	–	9000

[a] Measurements made at 20 °C and at 1 atmosphere pressure.

need to have an extensive and thin respiratory barrier or a thick and less water-permeable one. By living in nondesiccating (cryptozoic = humidic) habitats, risk of desiccation is minimized and a thin barrier can prevail. In most organisms, exceeding a diameter of about 1 cm, a circulatory system becomes a necessity. From hypothetical mathematical computations (e.g., Harvey 1928; Rashevsky 1960), in a normobaric environment and at moderate O_2 consumption, the maximum radius of a spherical cell, where anoxic state would not occur except at the center (i.e., the farthest point from the surface), was estimated to be 0.5 mm. Krogh (1941) calculated that for a homogenous spherical organism of a radius of 1 cm, at an O_2 consumption of $100\,\mathrm{ml\,kg^{-1}\,h^{-1}}$ (about half of the O_2 consumption of resting man) an external PO_2 of 25 atm (2533 kPa) would be required for O_2 to diffuse to all parts of the organism. He calculated that an organism cannot have a radius of more than 0.5 mm if it were to rely on diffusion alone, even assuming that it lives in water almost fully saturated with air at 1 atm of pressure. Where the external medium is separated by a 50-μm barrier from an internal circulating medium, a PO_2 of one quarter of an atmosphere would be required for satisfactory diffusion. Relying entirely on diffusion, a paramecium (volume $0.0006\,\mathrm{cm^3}$, O_2 uptake 1.3 ml per g per h and diameter 0.11 cm) would need a PO_2 of 0.73 of an atmosphere (Prosser and Brown 1962). Clearly, such high PO_2 rarely occurs in natural environments. Denney (1993) estimated that at the normal metabolic rate of a typical protozoan of about $0.1\,\mathrm{mol\,m^{-3}\,s^{-1}}$, a cell would have to be almost 7.5 cm in radius to experience hypoxia. The disparities in the estimated theoretical maxima of organisms indicate likely flaws in the idealized models used to calculate the largest possible sizes that microorganisms can attain. Except probably for eggs, there are no organisms which are absolutely spherical. At the organismal level, scaling with size is nonisometric (Schmidt-Nielsen 1984). The largest protozoans that have ever lived were the now extinct nummulites which had a diameter of about 2.4 cm and the largest extant protozoan is *Pelomyxa palustris*, which can attain a length of up to 1.5 cm. This size difference may be accounted for by the emerging possibility that the PO_2 in the biosphere at certain time(s) in the evolutionary past was higher than the present level (e.g., Graham et al. 1995). One such case occurred in the late Paleozoic (between the Carboniferous and the Permian), when for about 120 million years, O_2 level was 1.7 times greater than in the present atmosphere (Berner and Canfield 1989; Landis and Snee 1991; Graham et al. 1995; Fig. 9). Extraordinarily, the endothermic plants, e.g., *Philodendron selloum*, which produce heat at a rate surpassing that of the insect flight muscles and can maintain a temperature gradient of 30 °C with the ambient (Seymour 1997; Koch et al. 1983) rely entirely on diffusion for supply of the O_2 needed for generation of energy. In a single floret of the inflorescence of *P. selloum*, O_2 diffuses across a distance of about 1.2 mm through about 170 stomates (Koch et al. 1984): the average diffusional length from the surface to the individual cells, which is less than 0.75 mm, compares with that of the trachea of most small diffusion-dependent insects (Sects. 6.5 and 6.6.1). This reveals nature's amazing congruent solutions to similar needs!

Diffusion over an undifferentiated surface is the method of respiration in the simple organisms, e.g., Protozoa, Rotatoria, Planaria, Nematoda, eggs and young embryos, copepods and ostracodes, while the more complex ones (which utilize this process) include Spongia, Cerripedia, Coelenterata, arthropods like Tardigrada and Pauropoda, eggs, and early developing embryos (e.g., McMahon and Wilkens 1983). Larvae of many insects rely on diffusion across the integument (Fraenkel and Herford 1938) with the flux of gases essentially being regulated by O_2 consumption and CO_2 production within the organism. The tracheal system of the *Cossus* larvae delivers adequate O_2 entirely by diffusion (Krogh 1920a). The occurrence of air in the tracheoles of the young adult which emerges after the larval gas-filled tracheoles have been shed (there having been no previous contact with air) is probably due to passive diffusion of O_2 (Keilin 1924; Buck and Keister 1955). Surface-to-volume ratio decreases with body size since volume increases as the cube while surface area increases as the square of the radius. Assuming that the metabolic rate remains constant, O_2 transfer by diffusion should decrease with size. Since some organisms (including the amphibian eggs) develop to sizes greater than those theoretically predictable and the PO_2 inside the cell exceeds that which would be expected from diffusion alone, it was conceived that another process must promote gas transfer (e.g., Longmuir and Bourke 1960; McDougal and McCobe 1967). In the protozoa, protoplasmic streaming, a normal circulation-like process in living cells, enhances intracellular gas transfer (Seifriz 1943; Andrews 1955). Mechanical vibrations appear to intensity permeability of tissues to gases (Longmuir and Bourke 1960). Dynamic organs such as the heart, lung, and diaphragm, as well as activities such as change in muscle tone and physical interaction between the erythrocytes and the endothelial wall of the blood vessels may to an unknown extent influence gas transfer at the tissue level.

2.7.2 Convective Flows

2.7.2.1 Perfusion

The inadequacy of diffusion as a means of gas exchange necessitated development of auxiliary respiratory processes as organisms became larger, more complex, and their O_2 needs increased. A progressive development of a circulatory system occurred, promoting the efficiency of the respiratory processes (Figs. 18,19,20). Mature animals having an elementary circulatory system close to the surface of the body, e.g., earthworms and echinoderms, where the blood is moved by a heart and not cilia, can grow to a body mass of a few grams and a length of 30 to 40 cm without calling for development of special respiratory organs as long as they subsist in water or in a humidic environment. In such animals, a directional flow of the lymph may not exist and hence a circulatory system strictly does not exist. Churning of the fluid underlying the respiratory surface through contraction of body muscles should enhance the flux of the respiratory gases. In organisms such as Chaetopoda, Synapta, and Pantopoda, there is no regular circulation but the coelomic fluid is kept in motion by cilia (Lindroth 1939). The blood of the earthworms has a high O_2 affinity (P_{50} = 0.3 to 1.1 kPa), is highly sensitive to temperature (Laverack 1963) and has a high O_2 carrying capacity of 8 to 12 vol % (Haughton et al. 1958). The blood of the giant earthworm

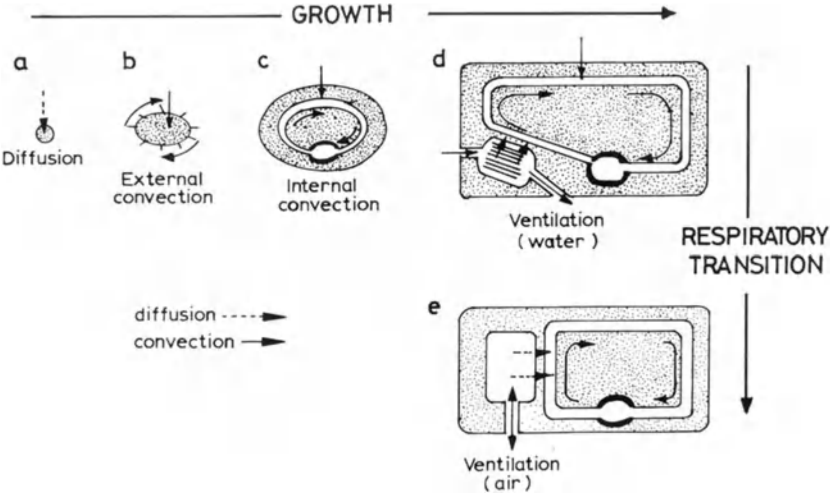


Fig. 18a–e. Development of the respiratory processes from unicellular to multicellular organisms. Diffusion (**a**) is the main process of gas exchange in simple animals with external (**b**) or internal convection (**c**). More complex animals combine perfusion and ventilation (**d** and **e**). While the gills are configured for continuous and unidirectional ventilation (**d**), the lungs and their derivatives are tidally ventilated (**e**). (Burggren and Pinder 1991)

(*Glossoscolex giganteus*), which can attain a body mass of 600 g, a length of 120 cm and a width of 2 to 3 cm, has a P_{50} of 0.9 kPa (at 20 °C and pH of 7.5) and a small Bohr shift (Johansen and Martin 1966). By regulating cutaneous perfusion (Burggren and Feder 1985) and surface area (Noble 1925), the hairy frog, *Astylosternus robustus*, can adjust gas exchange across the skin. In the higher vertebrates, the skin has been rendered virtually impermeable to O_2 and in the human being only 0.2% of the total O_2 need is acquired through it (Krogh 1941). The plethodontid salamanders (Collazo 1993; Ruben et al. 1993; Tilley and Bernado 1993; Wake and Marks 1993), which live in cold, well-oxygenated habitats and have adopted long and cylindrical body forms, rely entirely on the skin for gas exchange: this group, which is extremely successful (Pough et al. 1989), is presumed to have originated from torrential mountain streams (Beachy and Bruce 1992). In the freeze-tolerant frogs which can endure temperatures of between −3 and −7 °C, e.g., *Hyla versicolor, Rana sylvatica, Hyla cricifer*, and *Pesudacris triseriata macurata*, the heart does not beat in the frozen state (Lotshaw 1977; Storey and Storey 1988). In some species, intracellular glucose level increase and appear to serve both as a cryoprotectant and a metabolic fuel (Storey and Storey 1986). At natural wintering temperatures of 3 °C, freshwater turtles can remain submerged without O_2 for months (Carr 1952; Ultsch and Jackson 1982). Nemertines (ribbon worms) have only two main longitudinal blood vessels and in the species which have hemoglobin, reversal of blood flow is common (Hyman 1951). The bootlace worm, *Lineus longissimus*, which is found in the North Sea, can reach a length of 55 m. In some annelids, a closed circuit

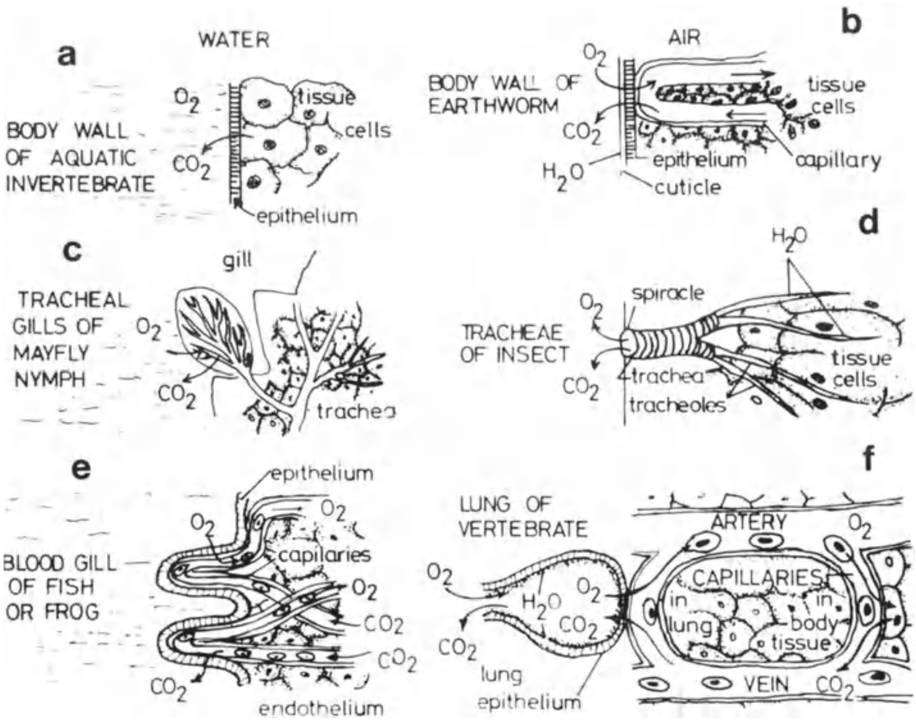


Fig. 19a–f. Mechanisms of gas exchange. The most basic gas exchange design is that which occurs across a cell membrane, e.g., in protozoa or across an unperfused skin (**a**). Perfusion of a respiratory site improves gas transfer by maintaining a concentration gradient (**b**). In the tracheal gills, e.g., of the mayfly, air rather than blood is contained in the gills (**c**). In the tracheal system of insects, air is delivered directly to the tissue cells by diffusion (**d**) and in the larger species by convection through abdominal pumping. In the conventional gills, e.g., of fish, the organs are well perfused with blood (**e**) and ventilated with water. The elaborate vertebrate gas exchangers combine tidal ventilation with perfusion (**f**). (Jessop 1995)

with well-developed blood vessels and pulsatile ancestral "hearts" exist in form of modifications along the blood vessels. In certain teleosts and elasmobranchs (sharks, skates, and stingrays), caudal hearts, which are located near the tail and powered by skeletal muscle, aid in venous return (e.g., Satchell 1992). Auxiliary hearts occur in the circulatory system of decapod crustaceans (Steinacker 1975) and locomotor movements generate large pressure differentials which promote the flow of the hemolymph (Belman 1975). The oscillations in the dorsal aortic blood pressure in the Atlantic hagfish, *Myxine glutinosa*, are associated with contractions of the gill musculature, a process which may be involved in propulsion of blood (Johansen 1960; Strathmann 1963). Such a process, however, does not seem to occur in the gills of the Pacific hagfish, *Eptatretus stoutii* (Chapman et al. 1963). At 10 °C, *M. glutinosa* has a heart rate of about 22 beats min^{-1}, a mean ventral aortic blood pressure of 1 kPa and a cardiac output of 9 ml per min per g

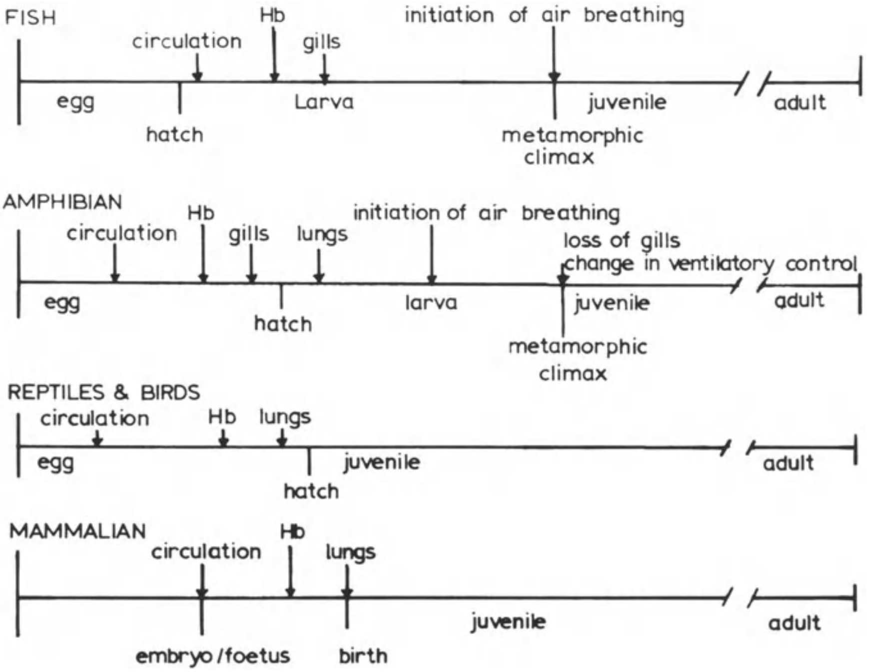


Fig. 20. Comparative schematic illustration of the stages at which cardiovascular and respiratory systems develop in relation to life histories of different vertebrate taxa. Some stages may fail to develop in some groups. For example, not all fish attain capacity for air breathing and not all amphibians develop lungs. Variably, the sequence in the increasing complexity and efficiency of the gas exchangers appears to progress from the simple membrane gas exchanger, a perfused one, a carrier-supported one, and finally to a ventilated one. Of note is the fact that hemoglobin (*Hb*) develops before respiration starts. (After Burggren and Pinder 1991, with the processes in birds and mammals added)

heart mass (Forster et al. 1988, 1991; Axelsson et al. 1990). While buried under the soft mud, *Myxine glutinosa* can remain without O_2 for at least 1 h (Strathmann 1963) and feed inside the body cavity of dead animals for a long period of time (Hardisty 1979): at 5 °C, the hagfish can survive in anoxic water for at least 20 h (Hansen and Sidell 1983). In most gastropods, to ensure forward blood flow, passive valves exist throughout the body (Jones 1983). In the open circulatory system, a large quantity of fluid is located in the intercellular space, providing mechanical support for locomotory activity and feeding movements (e.g., Jones 1983; Russell and Evans 1989). A fast circulatory return in a closed system with a smaller blood volume should be a more efficient design compared with a sluggish one with a large volume. Open circulations without hearts suffice where the respiratory demands are not high and where the diffusional distances are not great (Farrell 1991a). Heart rate in the terrestrial slug, *Deroceras reticulatum*, increases during feeding, a feature attributable to the need for substantial hemocoelic pressure required to protrude the odontophore (Duval 1983). Respiratory gas exchange across the body surface coupled with a simple circulatory system occurs in leeches, all oligochaetes, and some polychaete annelids. The organization is more complex in the more advanced animals (Fig. 19). In some fish embryos and larvae, circulation develops before the respiratory organs. Blood pressures as high as 2.5 kPa and fairly fast flow velocities have been recorded in some large earthworms (Johansen and Martin 1966). Ventricular pressure measurements in the black-lip abalone, *Haliotis ruber* (Russell and Evans 1989) ranges from 0.4 to 1.2 kPa and heart rate increases with water temperature, the maximum rate being reached at 22 °C. In teleosts and elasbobranchs, typical heart rates are 10 to 60 beats min^{-1}, cardiac outputs are 6 to 40 $\mathrm{ml\,min}^{-1}\,\mathrm{kg}^{-1}$ body mass and the mean ventral aortic pressure ranges between 3 and 6 kPa (Farrell 1984, 1991b; Lai et al. 1990; Axelsson et al. 1992).

The gastropod (Jones 1983; Andrews and Taylor 1988) and cephalopod mollusks (Wells 1983) were the first taxons to acquire a distinct circulatory system. The heart is well organized internally for directional blood propulsion and has regular beats. In the pneumonate gastropod mollusks, the systolic pressure is as high as 4 kPa (Jones 1983; McMahon and Wilkens 1983). In some terrestrial crabs, the systolic peak blood pressure can be as high as 6.7 kPa (Cameron and Mecklenburg 1973), gradually dissipating to zero after the gills which contribute 40% of the peripheral resistance (Bourne and Redmond 1977). The closed circulation in the cephalopods constitutes the threshold towards circulatory adaptation for more efficient gas transfer. With certain exceptions, the most common response to hypoxia in gastropods and bivalves (DeFur and Mangum 1979; Russell and Evans 1989) is bradycardia. In fish, a similar response occurs (Randall and Shelton 1963; Farrell 1982a; Gehrke and Fielder 1988; Fritsche 1990): the heart rate may drop by as much as 50%. Interestingly, hypoxic bradycardia is weak or does not occur in fish such as the sea raven, *Hemitripterus americanus* (Saunders and Sutterlin 1971), winter flounder, *Pseudopleuronectes americanus* (Cech et al. 1977), and the rockpool fish, *Gobius cobitis* (Berschick et al. 1987). While these differences may be genuine interspecific adaptive responses to hypoxia, it cannot be ruled out that the experimental approaches and the depth of hypoxia at which the tests are being carried out may contribute. Compared with other teleosts, e.g., the eels and the goldfish, which can withstand hypoxia for hours at elevated temperatures (e.g., Walker and Johansen 1977; Waarde et al. 1983), the salmonids have a particularly limited capacity of coping with hypoxia (Doudoroff and Shumway 1970). In aquatic amphibians where cutaneous respiration is particularly important (Johansen and Burggren 1980), a marked bradycardia, accompanied by decreased blood pressure and cardiac output, occurs with submergence (Shelton and Jones 1965). Cardiac output may be reduced to 5% of the predive levels and heart rate may drop to as low as 4 to 8 beats min^{-1} in turtles (White and Ross 1966; Penney 1977; Herbert and Jackson 1985). The mass specific volume of blood is greater in animals with an open circulatory system compared with those with closed ones (Prosser 1961). In the former, the peripheral resistance and blood pressures are generally low (Jones 1983). In crustaceans, blood volume constitutes about 30% of the body weight (Prosser 1973), in gastropod molluscs 25 to 30%, in the bivalves as much as 60%, and in the dog only 8.3%. The relative blood volume decreases with body size in mammals (Gregersen and Rawson 1959). In most insects (Sect. 6.6.1.), the circulatory system serves no consequen-

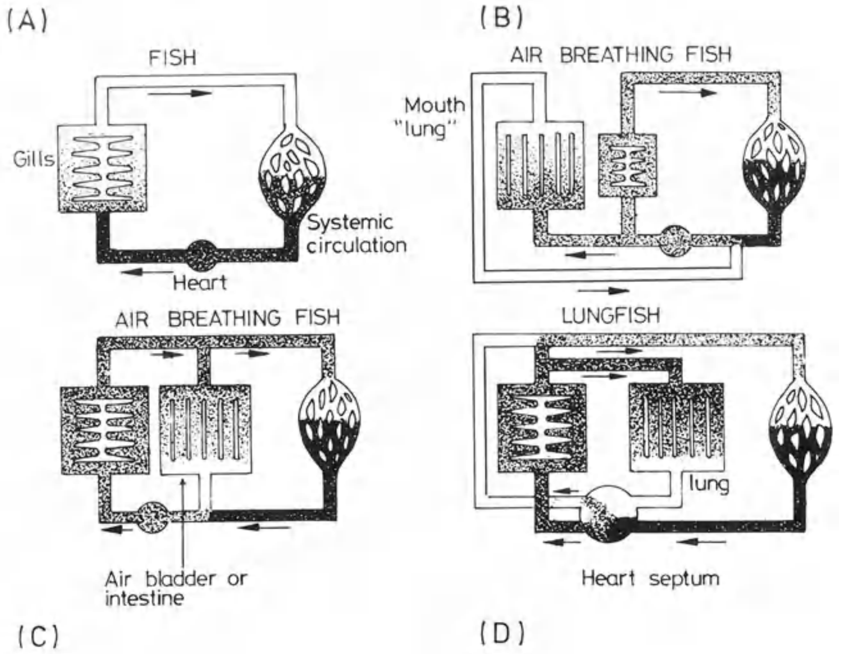


Fig. 21A–D. Arrangement of the vascular system relative to the accessory respiratory organs. In the single arch of a typical fish (**A**), the entire cardiac output is directed towards the gills. In various air-breathing fish, e.g., *Synbranchus* (**B**), *Hoplosternum* (**C**), and lungfish (**D**), to varying extents mixing occurs. The process is, however, minimal in the dipnoans (lungfish). (Johansen 1968)

tial role in gas exchange. In the lungless salamanders, respiration is entirely cutaneous. In the group, the left auricle is lacking. Invertebrates such as the crustaceans and mollusks have an open circulation where a capillary system between the arteries and veins is largely lacking and the blood returns to the heart more or less at random through a system of tissue spaces unbounded by endothelial cells (McMahon and Wilkens 1983; Burggren and McMahon 1988a).

The pinnacle of development of circulation, the double circulatory system took nearly 300 million years to configure from a single circulation. The lungfishes (Dipnoi), where a pulmonary vein and a partly divided heart are first encountered (Fig. 21), present a vital point in the evolution of the double circulation (Bugge 1960; Satchell 1976). All amphibians with a lung have a pulmonary vein and a complete or partial septum which separates the right and left atria. In air-breathing toads, at 22 °C, heart rate is 26 beats min^{-1} with an arterial pressure of 3 kPa and a systemic arch blood flow of 36 ml min^{-1} kg^{-1} body mass (Withers et al. 1988): the total cardiac output is about 30 ml per min per g heart mass (Driedzic and Gesser 1994). The crocodiles, a relatively remarkably advanced reptilian group (Densmore and Owen 1989; Norell 1989; Tarsitano et al. 1989), are the only ectothermic group which has virtually advanced to the stage of a four-chambered heart. In air-breathing turtles at 20 to 25 °C, the heart rate is 30 to 40 beats min^{-1}, cardiac output about 50 ml $min^{-1}g^{-1}$ heart mass and the aortic pressure about 3 kPa (Driedzic and Gesser 1994). At 35 °C, both the savanna monitors (*Varanus exanthematicus*) and the green iguana (*Iguana iguana*) have a resting heart rate of 40 beats min^{-1} with cardiac output of about 40 ml min^{-1} per g heart mass in *V. exanthematicus* and 70 ml min^{-1} per g heart mass in *I. iguana* (Gleeson et al. 1980). In a resting *V. exanthematicus*, the systemic blood pressure may approach 9 kPa (Burggren and Johansen 1982). It is only in the postembryonic endotherms, mammals and birds, where the heart is completely divided and the pulmonary and systemic circuits are anatomically distinct. The resting heart rate of a 500-g ectothermic vertebrate at 15 to 20 °C under normoxia is 20 to 60 beats min^{-1}, the arterial blood pressure ranges from 3 to 5 kPa and the cardiac output is in the order of 10 to 50 ml $min^{-1}kg^{-1}$ body mass (Driedzic and Gesser 1994): a mammal of similar size at 37 °C has a heart rate of 280 beats min^{-1}, a left ventricular output of 125 ml $min^{-1}g^{-1}$ and an aortic blood pressure of 13 kPa. The pulmonary circuit, which handles the entire systemic venous blood, is a low resistance circulation where the pressures on average are 1.7 kPa (Rushner 1965; West 1974). In the human lung, the resistance to blood flow across the blood capillaries of the lung (diameter 10 to 14 μm) which comprise a surface area of nearly 150 m^2 (Gehr et al. 1978) is so low that 5 to 10 l of blood can flow through the lung each minute with a pressure of less than 1.3 kPa (Comroe 1974). In fish, gill vascular resistance is one half to one third that of the systemic circuit (Cameron et al. 1977), with the difference being much greater (about ten times) in mammals and birds (Langille and Jones 1975). In the amphibious ghost crab, *Ocypode saratan*, the gills are perfused both in submerged and air-breathing crabs. The lungs are preferentially perfused in air but not during submergence (Al-Wassia et al. 1989).

2.7.2.2 Ventilation

The need to reduce cutaneous water loss, especially with advent of terrestrial habitation, necessitated development of an impermeable skin. This rendered much of the body surface nonrespiratory. Specialized respiratory sites, where soft and well-vascularized parts could be exposed to the ambient respiratory medium, formed. For such areas to be effective, convective movements of air or water through mechanical effort were necessary in order to create and sustain a satisfactory partial pressure to maintain O_2 influx. Ventilation entails mass renewal of the environmental medium in the immediate proximity of a respiratory surface. Except for the freshwater limpets, *Ancylus fluvialis* and *Acroloxus lacustris* (Berg 1951), invertebrates which subsist in running water (i.e., are passively ventilated) show a higher metabolic rate than those from stagnant water (Fox et al. 1935; Walshe 1948). The convective systems which have evolved differ remarkably and reflect heavily on the restrictions imposed by the physical characteristics of the respiratory media on the design of the exchangers (Fig. 18). In simple aquatic animals, e.g., the bivalve mollusks and amphioxus (e.g., Baskin and Detmers 1976), and ascidians, the movement of water across the gills is effected by cilia. The much more sophisticated branchial pumps move the water across the gills in the advanced fish. Tubiculous polychaetes rely on ciliary currents (e.g., *Nephtys*), peristalsis (e.g., *Arenicola*) or undulating movements of the body (e.g., *Chaetopterus*). In mollusks, where the gills are largely used both for feeding and respiration, water is moved across the gills by the beating of cilia which are located on the gills (Borradaille et al. 1963). The echinoderms respire through movable tubes (podia) which extend from basal dilatations (ampullae), structures which protrude through openings in the calcaneous outer covering of the body (Hyman 1955; Steen 1965). The hemolymph, which contains no respiratory pigments, is moved through ciliary action into the microcirculatory units. In the sea urchin, *Strongylocentrotus droebachiensis*, the podial respiratory surface area becomes limiting to O_2 consumption only at higher temperatures (Steen 1965): at 19 °C, O_2 consumption ($2\,\mathrm{ml\,h^{-1}}$, 70 g body mass) is directly proportional to the available respiratory area, while at 6 °C, only 20% of the available surface is utilized to transfer O_2. In *S. droebachiensis*, a 70-g specimen has some 100 podia which are about 20 mm long and 0.4 mm in diameter. The overall respiratory surface area is about $250\,\mathrm{cm^2}$ and the thickness of the diffusional pathway is about $15\,\mu\mathrm{m}$. The soft-bodied cucumbers (Holothuroidea) use an internal respiratory tree-like organ which they rhythmically ventilate through muscular contractions. *Holothuria tubulosa* renews the water of the respiratory tree every 1 to 4 min, with the expelled water having an O_2 content of about 50 to 80% of that of the surrounding water (Hazelhoff 1939). The marine annelid, *Chaetopterus variopedatus*, a burrow-dwelling filter feeder, has a high mass-specific ventilatory rate of the burrows of about $110\,\mathrm{ml\,g^{-1}\,h^{-1}}$ at 15 °C, a low O_2 extraction coefficient (the ratio of the amount of O_2 taken up to that available in the inspired medium) of about 30% and an O_2 consumption of $11\,\mu\mathrm{mol\,g^{-1}\,h^{-1}}$ in an actively ventilating organism of 4 g wet weight (Dales 1969). Fish embryos develop a rhythmic contraction of the tail muscles before the respiratory movements begin and show motor response to hypoxia (Polimanti 1912). To a slight extent, beating of cilia moves water currents into the molluskan mantle cavity. Some burrowing annelids, e.g., the marine echiuran worm, *Urechis caupo* (Wells 1949; Mangum 1985), generate a water current over their bodies and in the tubes by waving their bodies in water through peristaltic contractions of their muscular body wall. The mud shrimp, *Callianassa truncata*, a species which inhabits sand sediments in the Mediterranean Sea makes burrows which may be as much as 8 m deep (Ziebis et al. 1996): at a depth of 48 cm, the shrimp can maintain burrow O_2 concentration at 3 to 12% of air saturation by generating a water current of 10 m per second. Rhythmic movements of the external gills in the urodele, *Necturus*, renew the water on the surface of the gills. Increases in the PO_2 of the water in the burrows were recorded after a short period of irrigation (mean duration 21 s) produced by body undulations of the snake blenny, *Lumpenus lampretaeformis* (Atkinson et al. 1987): a flow rate of $40\,\mathrm{ml\,min^{-1}}$ in a burrow of a diameter of 2 cm was produced. Depending on the PO_2 in the water, the red band fish, *Cepola rubescens*, irrigates its burrow by body movements (Pullin et al. 1980) creating a water flow of $10\,\mathrm{ml\,min^{-1}}$ in a burrow of a diameter of 5 cm. In areas where the water flow is fast, the design of the burrows and the locations of the opening(s) relative to the direction of water flow may create pressure gradients which may passively suck water into the burrow (Vogel 1977). Passive ventilation is thought to occur in the burrows of the tile fish, *Lopholatilus chamaeleonticeps* (Grimes et al. 1986), and the mud-shrimp, *Callianassa truncata* (Ziebis et al. 1996). At a PO_2 of about 5 kPa, the lug worm, *Arenicola marina* stops ventilating the burrows (Toulmond 1991). Below the critical PO_2, it is clearly no longer cost-effective to expend energy ventilating the burrows. In the shelled *Nautilus* (a paleontological relic of more than 2000 extinct genera of nautiloids and ammonoids) where mantle movement is not possible, the ventilatory stream is generated by movements of fused collar and funnel folds, the "wings", which create small pressure gradients of the order of 0.1 kPa (Wells and Wells 1985). The ventilatory frequency, which is 35 times min^{-1} at 16 °C, increases with temperature and the stroke volume ranges from 5 to 22 ml for a 395-g animal. The volume of the mantle cavity in a fixed specimen of *Nautilus* (470 g) is 75 ml (Packard 1972). In *Octopus vulgaris*, the number of respiratory movements per minute decrease with increasing body mass (Polimanti 1913). Through a process called apneic oxygenation (Malan 1982; Szewczak and Jackson 1992), O_2 moves from the atmosphere down the trachea to the lung by diffusion or by bulk convection. If the respiratory quotient is greater than 1, in some hibernating animals with a low metabolic rate and long apneic periods, a significant amount of the resting O_2 needs can be met by diffusion down the respiratory tract through an open glottis during nonrespiratory periods. Ventilation by oscillatory movements of special appendages occurs in some polychaetes (e.g., *Chaetopterus*), amphipods (e.g., *Gammarus*), isopods (*Idotea*), and crustaceans, e.g., *Cancer pagurus* (Bradford and Taylor 1982). Such currents may deliver food, e.g., in *Chirocephalus, Artemia*, and *Daphnia*. In animals which live in torrential, air-saturated waters (rheophilic species) where the PO_2 of the water next to the gas exchanger is equal or almost equal to the atmospheric one, e.g., the hill-stream fish like *Danio dangila* which subsists in hyperoxic water with a concentration of O_2 of 9 mg $O_2 l^{-1}$ (Ojha and Singh 1986), the gills and skin are passively ventilated with water in an energy-saving process. In the oegopsid cranchid squids, which are known to store ammonia in the enlarged coelomes to regulate buoyancy (Denton et al. 1958), the mantle contractions do not participate in respiration. The flow of water over the gills is effected by movements of the coelom (Clarke 1962). The urodele salamanders (Plethodontidae), which lack lungs or gills, rely entirely on cutaneous respiration. Movements which stir the external respiratory medium and subcutaneous perfusion act as the only aids to the diffusive conductance across the skin (e.g., Gatz et al. 1974; Piiper et al. 1976).

The convection requirements are high in water breathers compared with air breathers. The requirements correlate inversely with the concentration of the molecular CO_2 of the medium. Due to the relatively low concentration of CO_2 in water, aquatic animals exhibit ventilatory rates 10 to 30 times those of the air breathers (White 1978). Increased ventilation in response to declining environmental O_2 has been observed in marine and freshwater bivalves (Zinkler 1966; McMahon 1988), crustaceans (Hughes et al. 1969a; Taylor 1982), polychaetes and oligochaetes (Mangum 1963), and holothurians (Newell and Courtney 1965). In cephalopods, hypoxia results in reduction of respiratory movements (Fredericq 1878) while activity (Ghiretti 1966) and hypercapnia (Winterstein 1925) elevate it. In some crustaceans, e.g., the crayfish, *Astacus leptodactylus* (Angersbach and Dekker 1978), and the crabs, e.g., *Cancer productus* (McMahon and Wilkens 1977)

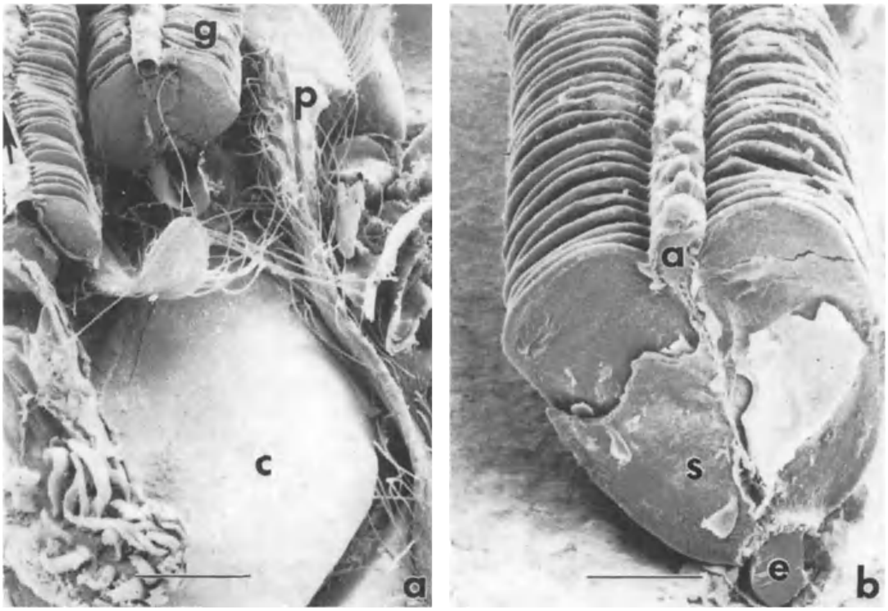


Fig. 22. (**a**) Gills of the freshwater crab, *Potamon niloticus* (*g*), showing a scaphognathite, *p*, the afferent gill artery, →, and the efferent artery, ➤; *c* skeletal mass. (**b**) A closeup of a gill arch showing gill lamellae, *s*, and afferent, *a*, and efferent, *e*, blood vessels. (**a**) *Bar* 500 μm; (**b**) 200 μm. (Maina 1990b)

and *Cancer pagurus* (Bradford and Taylor 1982), special mouth part appendages (the scaphognathites – flattened exopodities of the maxillae) ventilate the gills which are covered by lateral extensions of the carapace lined by a membrane, the branchiostegite (Lockwood 1968; Burggren et al. 1974; Fig. 22). The flow of the water through the branchial chamber is adequately effective to maintain a PO_2 of 15 to 20 kPa at the respiratory surface of the gills in normoxia (Butler et al. 1978; Wheatly and Taylor 1981). The PO_2 in the arterialized haemolymph is as high as 10 to 13 kPa (Butler et al. 1978; McMahon and Wilkens 1983). The direction of air flow can be reversed in some species of crabs, e.g., *Carcinus maenas* and *C. guanhumi* (Taylor and Butler 1978; Burggren et al. 1985a). It has been established that in some species of crabs (e.g., Yonge 1947; Hughes et al. 1969a), and the larvae of air-breathing fish (Liem 1981) the interaction between water flow and that of blood (in the gill lamellae) is countercurrent. In the species which burrow into the substratum, the direction of the ventilatory current is reversed when the animal is buried in the sediment (Arudpragasm and Naylor 1964a,b; Dyer and Uglow 1978). Except in *Holthuisana transversa* (Greenaway and Taylor 1976; Taylor and Whitley 1979), where tidal ventilation is achieved by movements of the membranous thoracic wall, the scaphognathites are effective in ventilation of the gills and the lungs of the land crabs while in air (Taylor and Butler 1978; Burggren et al. 1985a; Al-Wassia et al. 1989) especially during hypercapnia. Depending on ambient temperature (Taylor and Wheatly 1979), the shore crab, *Carcinus maenas*, occasionally partially emerges from water to bubble air through the branchial chamber, aerating the water it holds in it (Taylor and Butler 1973; Taylor et al. 1973; Taylor and Whitley 1979). The movements of the scaphognathites of *Coenobita clypeatus* in air create pressure wave forms corresponding to those generated by the scaphognathites of water breathers (McMahon and Burggren 1979). The ventilatory mechanism in *H. transversa* (Taylor and Greenaway 1979) is unique among land crabs. Its efficiency (of which the operational definition is mechanical work output per metabolic work input) approximates to that of vertebrate respiration of about 10%. In *Ocypode saratans*, the scaphognathites beat at a rate of 53 times min^{-1} in a submerged crab, 218 times min^{-1} when active in air, 43 times min^{-1} when inactive in air, and 235 times min^{-1} when exposed to hypercapnia (Al-Wassia et al. 1989). The intermittent beating of the scaphognathites is neurogenically synchronized with that of the heart (Young 1978; Young and Coyer 1979). By changing the dimensions of the gill lamellar blood vessels, scaphognathite movements which generate pressures of -0.53 to 0.93 kPa may play a significant role in the perfusion of the gills and the lung (Blatchford 1971). In the crab, *Carcinus maenas* (Taylor et al. 1973; Wheatly and Taylor 1979) and the crayfish, *Orconectes rusticus* (McMahon and Wilkes 1983), air is bubbled through water held in the branchial cavity by the scaphognathites beating in the reverse direction. In the amphibious ghost crab, *Ocypode saratan*, heart rate varies with ventilation (Al-Wassia et al. 1989): the lungs are not perfused while in water, but in air the lungs are perfused at four times the rate of the gills. The routine breathing frequencies in the juvenile and adult fish range from 30 to 70 times per minute (Roberts 1975) and ventilatory flows range from 100 to 300 $ml\,kg^{-1}\,min^{-1}$ (Wood et al. 1970; Johansen 1982). Functional coupling between respiration and locomotion occurs in some tetrapods. This may be a means of improving gas exchange efficiency or a saving on respiratory work. When a lizard runs, the left and right lungs are alternately compressed, pumping the air between the two lungs (Carrier 1987a,b). However, no significant movements of air from outside occur. In bats, during flight, synchronization between wing beat, respiratory rate, and heart rate has been reported (e.g., Thomas 1987) but in birds, this occurs in only a few species (Torre-Bueno 1985). In the horse and many mammals, breathing is closely coupled with locomotion (Bramble and Carrier 1983).

Gas exchangers have evolved in form of invaginations or evaginations from the body surface (Figs. 4,5). The former are generally categorized as gills and are largely used in aquatic respiration while the later are termed lungs and are used for aerial respiration. Gills are unidirectionally ventilated while tidal ventilation occurs in the lungs (Fig. 6,18). Compared with other vertebrates, fish exhibit diverse ventilatory mechanisms. These range from active and passive (ram) ventilation, continuous or intermittent unidirectional flow of water across the gills, to tidal process in the air-breathing organs of the bimodal breathers. In a four-phase serial pressure suctional buccal force pump, the gills are ventilated with a constant flow of water which is taken into the mouth and forced out through the opercular flap (Liem 1985; Brainerd 1994). Pressure differences of about 0.4 kPa fill the mouth and those of 0.7 to 1.3 kPa move the water across the gills (Ogden 1945; Hughes and Shelton 1958). Fish which swim strongly and much of the time such as the mackerel, the tuna, and some sharks move with their mouths open. Such fish have lost the capacity for mechanical gill ventilation and rely on ram effect (passive ventilation of water powered by swimming) for ventilating their gills. Because of the atrophy of the brachiomeric muscles, active ventilatory rate is very low in the group. Such fish cannot maintain an optimal level of oxygenation of the blood if they are held in restricted enclosures where forward movement is prohibited. The bimodal breathing fish use a slightly altered buccal force pump (analogous to that utilized on the gills) to ventilate their accessory respiratory organs. Air is forced into the organ(s) and exhalation is thought to be a passive process, especially in those air-breathing fish which have a fixed air space (e.g., a suprabranchial chamber) or through pulmonary elastic tissue recoil (DeLaney and Fishman 1977; Farrell and Randall 1978; Liem 1980). In some air-breathing fish, e.g., *Anabas testudineus* and probably in *Clarias mossambicus* (Maina and Maloiy 1986), where the inhalant and exhalant apertures are respectively contained in the pharyngeal and opercular cavities, the buccal and opercular pumps effect a unidirectional air flow across the labyrinthine organs which are found in the suprabranchial chamber (Peters 1978; Liem 1980). The cephalopods and mollusks have evolved a throughflow ventilatory mechanism which falls between the bidirectional one of the air breathers and the unidirectional one of fish: the inspired and expired streams flow through different openings over the gills, with some mixing probably occurring in the mantle cavity (e.g., Packard 1972; Gosline et al. 1983; Bone et al. 1994). With an O_2 extraction factor of 33 to 72%, e.g., in the scallops (van Dam 1954), and a possibility that the arterial PO_2 may in some cases be higher than that in the effluent water in the octopus (Johansen and Lenfant 1966), the throughflow ventilatory mechanism is exceptionally efficient. In *Nautilus*, there are two pairs of gills instead of one and the funnel is the main contractile structure (Ghiretti 1966). In the holothurians, e.g., sea cucumber and the cephalopods, the cloaca pumps water tidally across the ramified diverticula of the hind gut which forms the respiratory tree. In the sea cucumber, *Holothuria forksali*, 60% of the total O_2 needs is taken from O_2-saturated water across the cloaca, the remainder passing over the skin (Newell and Courtney 1965): O_2 consumption decreases with arrest of cloacal respiration. About ten successive cloacal contractions, each of which transfers 1 ml of water into the animal, are followed by body contractions which inject it out. Below an ambient PO_2 of 12 kPa, the organisms respond by respiratory inhibition and relocation to better oxygenated sites (Lutz 1930). Tidal breathing of water across the hind gut also occurs in annelids, e.g., *Urechis caupo* (Pritchard and White 1981; Menon and Arp 1992a), and in insects, e.g., dragon-fly nymph *Aeshna* (Fig. 23), via the branchial openings in lamprey eels (Johansen 1971) and through the mouth in some amphibians and reptiles, e.g., the soft-shelled turtle, *Amyda*. Such rather simple organs, of which the primary functions are olfactory and/or gustatory, are collectively called water-lungs (Sect. 4.6). Contrary to what one would expect from morphological evidence, a countercurrent exchange may occur in the lamprey during slow inspiratory phase (Johansen 1971). At normoxia, hind gut ventilation with seawater in *U. caupo* is about 0.7 ml per g body mass and at a PO_2 of 4 kPa rises to about 2 ml of seawater g^{-1} body mass (Julian and Arp 1992; Menon and Arp 1992a). The mucosa of the hind gut contains collagenous and

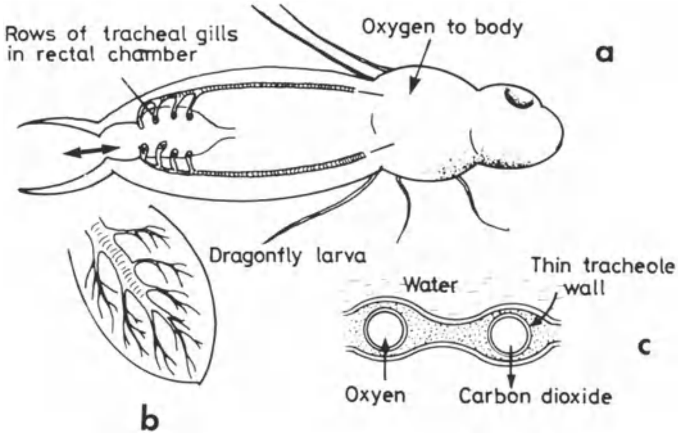


Fig. 23. **a** Rectal tracheal gills of the dragonfly. **b** Enlargement of a gas exchange site and **c** the gas exchange mechanism between water and air in the trachea. The rectum is tidally ventilated, ↔. (Hughes 1982)

Table 5. Distribution of the ventilatory mechanisms in vertebrates and the respiratory media in which they occur. (Randall et al. 1981)

Ventilatory process	Respiratory milieu	Vertebrate taxon	Environment
Buccal and opercular pumps with unidirectional flow of the medium	Water Air	Fish (gills) Some air-breathing fish (anabantids)	Aquatic Aquatic
Modified buccal force pump with tidal flow of medium	Air	Most air-breathing fish Dipnoi Amphibians	Aquatic
Aspiration pump with tidal flow of medium	Air	*Arapaima* Reptiles Birds Mammals	Aquatic Majority terrestrial, but some aquatic forms

elastic fibers which may allow greater stretching during filling under hypoxic conditions (Menon and Arp 1992a). A similar rectal-gill mechanism exists in the echiuran worm, *Arhynchite pugettensis* where extensive cloacal diverticula occur (Manwell 1960). In the diving turtle, *Stemothaerus minor*, 30% of the O_2 need is met by rhythmic gular movements which maintain movement of water in and out of the bucco-pharyngeal cavity (Belkin 1968).

In aquatic animals, buccal pumping is the ancestral mode of ventilation of the gills (e.g., Brainerd et al. 1993; Brainerd 1994). It may initially have been used to ventilate the accessory respiratory organs on attainment of utilization of atmospheric O_2 (Randall et al. 1981). Aspirational (suctional) breathing characterizes air breathers while buccal pumping occurs in both water and air breathers (Table 5). Buccal and aspirational breathing coexist in the obligate air breather *Arapiama gigas*, where the gas bladder is ventilated by aspiration and the gills by a characteristic teleostean buccal force pump (Farrell and Randall 1978; Randall et al. 1978a). During buccal pumping in the frog *Rana pipiens*, work is done by the floor of the mouth (against the elastic forces of the lung) at an average efficiency of about 8%. The O_2 cost of breathing constitutes about 5% of the total energy budget (West and Jones 1975). In *Rana*, the cost of respiration is about two times that in the human being but falls within the same range of fish.

2.8 Blood and the Respiratory Pigments

The increase in the complexity and efficiency of the gas exchangers has been a gradual process which has developed in response to specific needs that have called for greater and more efficient means of O_2 uptake and delivery to the tissues to support higher aerobic capacities. As in practically all transformations in biology, improvements were made on former simpler designs (e.g., Schaeffer 1965a,b; Riggs 1976). With the evolution of a circulatory system followed by a ventilatory mechanism, O_2 was initially carried in solution in the body fluids. In the ensuing period, demands must have exceeded supply, rendering the process inadequate. Respiratory pigments have evolved widely in the Animal Kingdom (e.g., Antonini 1967). They reversibly bind, store, and transport O_2 (and to an extent CO_2), increasing the O_2 carrying capacity of blood (Bauer 1974; Jensen 1991). The pigments are found dissolved in the plasma or in a two-phase system where the carrier is packaged in corpuscles, especially in those animals which require efficient internal fluid transport of O_2 to the body tissues (Lamy et al. 1985; Burggren et al. 1991). The primitive type of blood or hemolymph which contains no respiratory pigments has essentially the same respiratory capacity as salt water and can carry only about 0.2 ml O_2 per 100 ml water while vertebrate blood can carry 5 to 45 ml O_2 per 100 ml blood. In fish, the physically dissolved O_2 usually constitutes less than 5% of the total O_2 carried in blood (Boutilier et al. 1984). The development of hemoglobin increased the O_2 carrying capacity of blood by about 100 times. In the crustaceans, the presence of hemocyanin increases the O_2 carrying capacity of the hemolymph above the dissolved levels by a factor of 2 to 4 (Taylor 1982; Mangum 1980, 1983a,b; Shiga 1994). The arterial PO_2 (PaO_2) in resting crustaceans is reported to be generally low (1 to 3 kPa at 13 to 15 °C) independent of the blood pigment concentration (Forgue et al. 1992a,b). This baseline value corresponds with that of the mussel *Anodonta cygnea* which lacks blood pigment (Massabuau et al. 1991). Compared with the high values of PaO_2 (range from 2 to 13 kPa) that have been reported by Shelton et al. (1986) and McMahon and Wilkens (1983) in the water breathers, hemocyanin gives crustaceans a large functional reserve for uptake and transfer of O_2. Theoretically, in the human being, if O_2 was carried in physical solution in blood instead of by the hemoglobin, the circulatory rate would have to be 30 times more to meet the metabolic demands. Interestingly, the O_2 content of blood is equal to that of air, i.e., 20 ml O_2 per 100 ml (Davenport 1974; West 1974). This suggests a possible optimization of chemical binding and transfer of O_2 by the blood.

The development and refinement of the respiratory carriers added a significant factor to the gas exchange capabilities in animals, increasing the adaptability of the respiratory system to different environments. This entailed impressive molecular creativity directed at meeting the special needs of organisms (Perutz 1970, 1990a; Manning et al. 1990). For example, in the dimeric hemoglobin of the blood clam, *Sapharca inaequivalvis*, the hemes and the heme-linked helices E and F of adjacent subunits are in contact instead of facing outwards as is the case in the vertebrate hemoglobins (Royer et al. 1985). Certain invertebrate species have hemoglobins in which each polypeptide relates with multiple heme binding domains. Polymeric globin is thought to have occurred through fusion of multiple monomeric globin transcriptional units at the gene level in organisms ancestral to the invertebrate lineage some 200 to 500 million years ago (Manning et al. 1990). The tetrameric hemoglobin of the fat inn-keeper worm, *Urechis caupo*, shows neither cooperativity of O_2 binding nor a Bohr effect, while the hemoglobin of the brine shrimp, *Artemia*, the blood clam, *Sapharca*, and the earthworm, *Lumbricus*, displays both properties (see Perutz 1990a,b). Every vertebrate hemoglobin is an oligometric protein comprising four polypeptide subunits (protomers), each of which possesses an O_2 binding protoheme (Bauer 1974). While the fish hemoglobins are $\alpha_2\beta_2$ tetramers with a tertiary and quaternary structure similar to that of other vertebrate hemoglobins, among the teleosts, the amino acid sequences differ greatly between different groups (Kleinschmidt and Sgouros 1987). Many of the differences are functionally neutral (Perutz 1983).

Physiologically, the most important properties of hemoglobin are the cooperativity of O_2 binding and the effect of H^+, CO_2, and organic phosphate components on the affinity of hemoglobin for O_2. Cooperativity arises from the change of hemoglobin from low – to high-affinity forms with the binding of O_2 (e.g., Hewitt et al. 1972; Ten Eyck 1972; Perutz 1979). The limit to O_2 storage capacity in blood is set by the product of the respiratory pigment concentration and the blood volume (e.g., Davenport 1974). In general, diving animals have a larger blood volume than the nondivers (e.g., Bond and Gilbert 1958; Butler 1991a). They have a greater O_2 storage capacity of blood (Ridgway and Johnston 1966; Lenfant et al. 1969; Hedrick and Duffield 1986). During submersion, the concentration of the hemoglobin increases by a factor of 60 to 70% in the blood of the Weddell seal (Qvist et al. 1986). In the winter months, when the muskrat has to dive under water to look for food, its hemoglobin concentration in blood is at the high of 20 g per 100 ml of blood, while in summer, when the animal stops diving, the value drops to 14 g per 100 ml (Aleksiuk and Frohlinger 1971). In the aquatic pneumonate gastropod, *Planorbis corneus*, and several species of *Daphnia*, a low PO_2 initiates almost instantaneous synthesis and increase in the concentration of the hemoglobin (Fox 1955), a feature which has great survival value. Hemoglobin plays an important role in O_2 transport especially in hypoxic habitats (e.g., Johnson 1942; Cosgrove and Schwartz 1965). The lugworm, *Arenicola marina*, which has adapted to the anoxic intertidal sediment mainly because of its efficient anaerobic metabolic pathways, has a high O_2 affinity hemoglobin

(Toulmond 1985) and two kinds of body wall myoglobins of very high O_2 affinity (P_{50}, 0.1 and 0.2 kPa, at 20 °C) (Weber and Pauptit 1972). Presence of a hemoglobin with very high O_2 affinity (P_{50} about 0.13 kPa) was reported in specialized cells of gastrotrichs by Colacino and Kraus (1984). The alvinellids, polychaete annelids which live in the deep-sea hypoxic hydrothermal vents, have complex morphometrically well-adapted gills (Jouin and Toulmond 1989; Toulmond 1991). *Alvinella pompejana* has a closed vascular system (Toulmond 1991) and a high molecular mass extracellular hemoglobin (Terwilliger and Terwilliger 1984) with a high O_2 affinity (P_{50}: 0.02 to 0.3 kPa - measured at 20 °C, 1 atm pressure and pH 7.6 to 6.6; Toulmond 1991). Complex molecular mechanisms which included the effect of pH, CO_2, organic phosphates, and temperature developed to regulate O_2 uptake and transport by the hemoglobin (Nikinmaa 1990). Of the total proteins in the vertebrate erythrocytes, hemoglobin constitutes 95% (Antonini 1967).

The evolution of carrier pigments in blood (Fig. 24) constituted a significant improvement on the respiratory function and is probably one of the most recent innovations in the complex gas exchange adaptive strategies. The presence of blood pigments enhanced the rate of diffusion of O_2 even at low PO_2s (e.g., Hemmingsen 1963; Moll 1966). In the mammalian skeletal muscle (Wittenberg and Wittenberg 1989) and the heart muscle (Braulin et al. 1986), myoglobin facilitates diffusion of O_2 and in the fish cardiac muscle, it enables the hearts of some fish to extract O_2 at lower levels of ambient PO_2 than would otherwise be possible (Driedzic and Gesser 1994). Polar icefish (e.g., Douglas et al. 1985) and interestingly even nonpolar fish such as lumpfish (*Cyclopterus lumpus*), monkfish (*Lophius piscatorius*), and ocean pout (*Macrozoarces americanus*) have insignificant myoglobin content in their tissues (Driedzic and Stewart 1982; Sidell et al. 1987). On the other hand, some species of fish such as tuna (*Thunnus thynnus*), mackerel (*S. scombrus*), and the carp (*Cyprinus carpio*) have remarkably high levels of myoglobin in their hearts, respectively 580, 332, and 488 nmol per g wet heart mass (Giovane et al. 1980; Sidell et al. 1987). High myocardial myoblobin characterizes fish that have high swimming capacities and those tolerant to hypoxia (Giovane et al. 1980; Driedzic 1988; Driedzic and Gesser 1994). Presence of myoglobin enables the heart muscle to function at a lower level of extracellular PO_2 than would otherwise be possible (Braulin et al. 1986; Taylor et al. 1986).

Bohr and Root effects of the hemoglobin (decrease in O_2 affinity of blood) boost diffusion by increasing the blood-to-tissue O_2 gradient at the sites of CO_2 production. Blood hemoglobin concentration is increased in hypoxic mammals (Lenfant 1973). In fishes, both hypoxia and exercise highly elevate the blood hemoglobin level (Kiceniuk and Jones 1977; Weber and Jensen 1988). A high hemoglobin concentration in blood achieves a high blood O_2 capacitance coefficient, decreasing the pumping requirement of the heart (Jensen 1991). In the diving animals, myoglobin enhances the amount of O_2 which can be stored in muscle tissue. The concentrations increase with the increasing diving ability (Butler 1991a). In the physoclistic swim bladders, secretion of lactic acid from glucose metabolism at the gas-gland of the rete mirabile (Pelster and Scheid 1991, 1993) forces O_2 out of the hemoglobin (and N_2 out of solution) compressing them into the bladder (e.g., Pelster and Scheid 1992a,b). Through still unknown mechanisms, the Root effect (pH-dependent release of O_2 from the hemoglobin) is

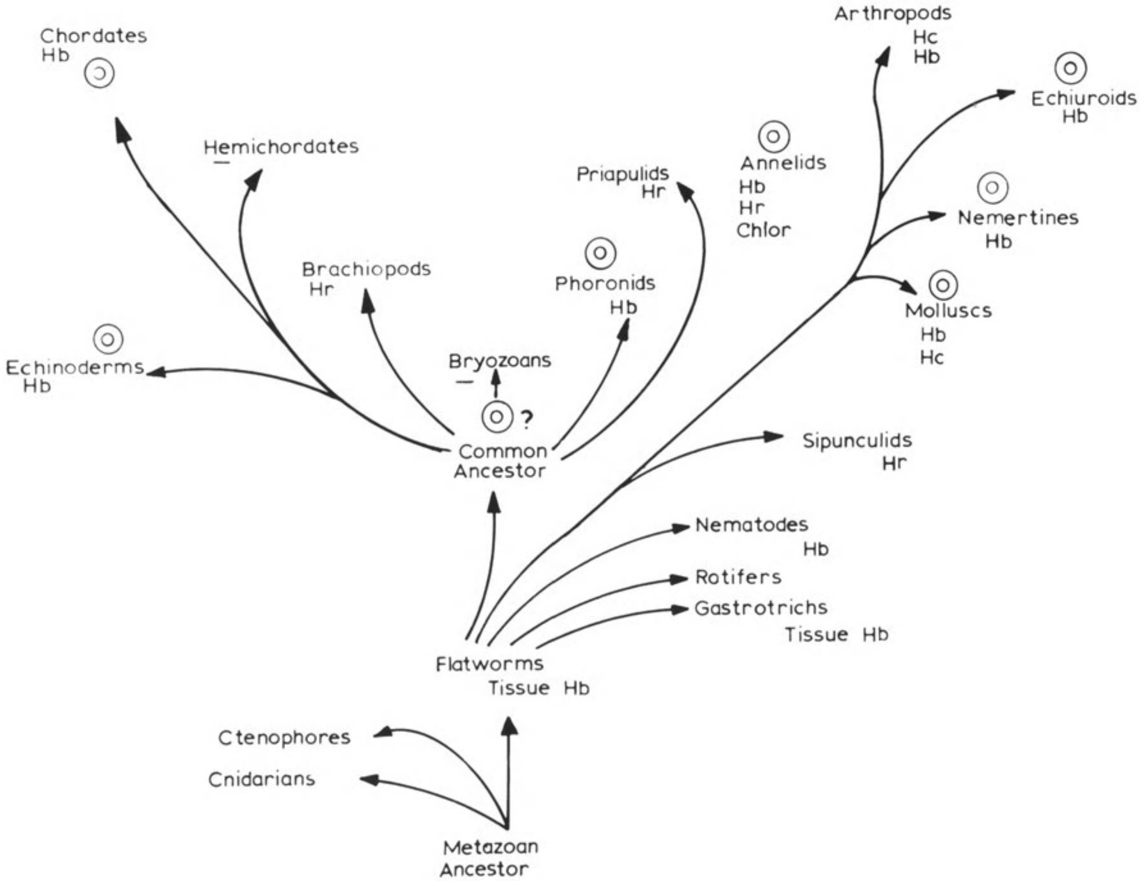


Fig. 24. Phylogenetic distribution of the blood respiratory pigments. The pigments found in a group are listed next to the particular names. A *circle logo* is appended to the animal groups with erythrocytes. *Hb* Hemoglobin; *Chlor* chlorocruorin; *Hr* hemerythrin; *Hc* hemocyanin. *Question mark* indicates a debatable point as to whether the common ancestor had erythrocytes. The hemichordates and bryozoans, –, have erythrocytes and the carrier (*Hb*) is intracellular. (Cameron 1989)

Table 6. Distribution of oxygen-carrying pigments in different groups of animals. (Cameron 1989)

Pigment	Environment	Occurrence	Comments
Hemoglobin	Intracellular (RBCs)	Nemertines, annelids, mollusks (bivalves), Phoronida, Echiurida, Echinoderms, Hemichordates, Chordates	Small: monomers to octamers
	Extracellular	Annelids, mollusks, arthropods	Highly variable
Chlorocruorin	Extracellular	Annelids	Formyl substitution on protoporphyrin
Hemerythrin	Intracellular (RBCs)	Brachiopods, annelids, sipunculids, priapulids	Nonporphyrin iron
Hemocyanin	Extracellular	Mollusks, arthropods	Probably of different origin in the two taxa

controlled by proton-induced allosteric conformational changes in fish hemoglobins (Howlett 1966). Hemoglobin may have evolved from the ubiquitous cytochrome molecule, a complex multicatalyst (Bernhardt 1995), with which it shares a common porphyrin nucleus and which has been implicated with facilitated diffusion of O_2 in some tissues (e.g., Scholander 1960; Burns and Gurtner 1973; Longmuir 1976). The incorporation of hemoglobin in the convective transport of blood in the vertebrates (Fig. 20) fully exploited the O_2 delivery role of the molecule. The large interspecific differences in the blood O_2 capacity, hemoglobin affinity, the extent of Bohr shift and erythrocyte morphometry and morphology (e.g., Riggs 1979; Dejours 1988), features which do not strictly correlate with phylogeny, environment, and mode of respiration (Fig. 24, Table 6) are strongly indicative of an ongoing intricate optimizing process. The carriers as well as other molecular factors are probably still being refined and integrated into the cardiovascular and respiratory systems for O_2 uptake and transfer. For example, as a means of ascertaining efficient O_2 delivery to the tissues by regulating peripheral blood pressure, while the erythrocytes are being oxygenated in the lung, the hemoglobin is S-nitrosylated to form S-nitrosohemoglobin (Jia et al. 1996; Perutz 1996). Subsequently, nitric oxide (NO), a recently recognized potent endothelium-derived relaxing factor (e.g., Palmer et al. 1987; Koshland 1992; Nathan 1992) is released during arterial-venous transit, causing vasodilation. The heme-bound NO [Hb(FeII)NO] is detectable in the venous blood when animals are subjected to oxidative stress (Kagan et al. 1996). Nitric oxide has, moreover, been reported to increase glucose transport in skeletal muscle (Balon and Nadler 1997). By increasing blood flow, nitric oxide ameliorates the effect of carbon dioxide on the brain (Meilin et al. 1996). Since the reaction between hemoglobin and O_2 is exothermic, increase in temperature results in a corresponding decrease in O_2 affinity, an adaptive feature especially in the homeotherms where high temperatures prevail in exercising tissues (e.g., skeletal muscle). A decrease in O_2 affinity promotes O_2 unloading. The hemoglobin in the tuna, *Thunnus*, a fish with exceptionally well-developed myogenic endothermia (e.g., Carey and Teal 1966) and high body temperature differentials, is insensitive to heat (Johansen and Lenfant 1972). Chum salmon have multiple hemoglobins, one group with a low Bohr effect and low temperature sensitivity and the other with normal proton and temperature sensitivity (Hashimoto et al. 1960). These forms are adaptively mobilized depending on the ambient temperature fluctuations. In facultative air breathers such as *Hypostomus* species and *Pterygoplichthys*, O_2 binding properties depend on the mode of breathing (Weber et al. 1979). While breathing air, the blood O_2 affinity increases and the Bohr effect decreases mainly owing to a drop in the erythrocytes organic phosphate concentration. Reptiles, a group which typically experience sudden body temperature changes especially as they bask in and withdraw from the sun, have a somewhat temperature-insensitive hemoglobin (Sullivan and Riggs 1967; Wood and Moberly 1970).

The effect of body size on the magnitude of Bohr effect and hemoglobin-O_2 affinity has been highly debated. Conflicting results ranging from a direct relationship (e.g., Schmidt-Nielsen and Larimer 1958), an inverse one (e.g., Clausen and Ersland 1968), and a weak or no correlation (e.g., Hilpert et al. 1963; Lahiri 1975) have been reported. The divergence may be characteristic of a nonoptimized state. The amphibians, a group which is highly instructive in the study of evolution of respiratory processes, show dramatic ontogenetic transformations in hemoglobin function (e.g., Gahlenbeck and Bartels 1970; Wood 1971). Changes in O_2 availability accompany the metamorphosis of a water-breathing tadpole to the adult air breather (Wood 1971; Broyles 1981). A notable decrease in O_2 affinity, increase in O_2 carrying capacity of blood, and metabolic rate occur with changes from larval to adult stages. With some exceptions, e.g., in the tuna and the lugworm, *Arenicola*, the concentration of the pigments is higher in the air breathers than in water breathers (Toulmond 1975; Dejours 1988). The O_2 affinity of the hemoglobin of the aquatic breathers which live in well-oxygenated water, e.g., the mackerel and salmon, are similar to those of air-breathing forms in the same habitat. This indicates that availability of O_2 rather than the nature of the respiratory medium influences O_2 affinity. Air breathers generally have a larger blood O_2 capacity, lower hemoglobin-O_2 affinity, and a larger Bohr shift than water breathers, at least in closely related species (Johansen and Lenfant 1966; Johansen et al. 1978; Fig. 63). Based on a wide cross section of species from the two taxa, a discordant view has, however, been expressed by Powers et al. (1979). Environmental PCO_2 and pH appear to determine the blood O_2 capacity of particular fish. At the physiological blood pH of 7.8 to 8.4, the Bohr effect is totally nonexistent in the blood of *Tilapia grahami*, which lives in the alkaline (pH 9.5 to 10.5) Lake Magadi of Kenya (e.g., Lykkeboe and Johansen 1975). In comparison with terrestrial mammals, the hemoglobin in diving animals has a low O_2 affinity, a high O_2 carrying capacity, and a large Bohr effect (Andersen 1966; Lenfant et al. 1970a; Wood and Johansen 1974). In the tench, *Tinca tinca*, hypoxia-hypercapnia causes an increase in hematocrit (due to an increase in the erythrocyte volume) associated with reduced intracellular concentration of the hemoglobin (Jensen and Weber 1985).

Increased capillarization of the tissues, a process which minimized the transcapillary-tissue diffusional distance and development of tissue-based high affinity O_2-storing noncirculating hemoglobin factor, myoglobin (found in some tissues) (e.g., Manwell 1963; Kreuzer 1970), were important innovations which enhanced delivery of O_2 to the cells. In the chiton, *Chryptochiton stelleri*, myoglobin has a lower P_{50} (0.4 kPa) than circulating hemocyanin, 2.7 kPa (Manwell 1958). In the buccal muscle of the mollusk, *Aplysia deplians*, the hemoglobin content is 6 mg% (Rossi-Fanelli and Antonini 1957) and in the human muscle tissue, myoglobin comprises about 2.5%. In his bucket-bridge model, Scholander (1960) envisaged that O_2 passes from one hemoglobin molecule to another. In this way, the O_2 flux can be increased eight times. It is, however, interesting that intracellular hemoglobin does not exist in the tissue barriers of the lung and fish gills. The role of hemoglobin in O_2-facilitated transfer has been questioned by Hemmingsen (1965) and remains an unsettled issue. The early proposition that the O_2 affinity of bird blood is lower than that of mammals (e.g., Jones 1972; Prosser 1973; but see dissenting views, e.g., Scheid and Kawashiro 1975 and Baumann and Baumann 1977) has been attributed to methodological error due to the time lapse between the collection of blood and analysis (Lutz et al. 1973, 1974; Holle et al. 1977). This may arise from the high metabolic rate of the nucleated avian erythrocytes. Though the erythrocytes in 90% of the vertebrate species are nucleated (e.g., Nikinmaa 1990), annucleation is thought to be the more evolved feature. Nucleated erythrocytes generate energy aerobically and their transmembrane pathways are more diverse than those of the nonnucleated mammalian cells. Nonnucleated erythrocytes have been described in some fish (Hansen and Wingstrand 1960). Compared with annucleate erythrocytes, nucleated erythrocytes have lower deformability, greater orientation instability, and show a greater propensity to interact with each other during steady capillary blood flow (Gaehtgens 1990). In these respects, nonnucleated erythrocytes which encounter less resistance due to low viscosity provide a distinct advantage in O_2 transfer.

Paradoxically, in some organisms, the contribution of the respiratory pigments in gas exchange is highly questionable. Some choronomid larvae and insects lack an O_2 carrier. Pigments appear to be of significance for life only during circumstances of high O_2 demand. Goldfish behave normally in water equilibrated with 80% carbon monoxide and 20% O_2 at temperatures below 20 °C (Anthony 1961). In the abalone, *Haliotes corrugata*, the concentration of the hemocyanin in different specimens was reported to differ by a factor of 900 times (Pilson 1965). In water equilibrated with air containing enough carbon monoxide to make hemoglobin totally inefficient as an O_2 carrier, the eel, the carp, and the pike will live for hours (Nicloux 1923). Extended exposure to reduced PO_2 results in manufacture of respiratory pigments in some animals but not in others (Fox 1955). In *Artemia*, hemoglobin synthesis is stimulated by high external salinity (Gilchrist 1954). The respiratory properties of the copper-containing hemocyanin are highly labile (Mangum 1980a) with the blood of the cephalopods being very sensitive to pH changes (i.e., having a marked Bohr shift), temperature, ionic, and osmotic composition of blood (Houlihan et al. 1982). By increasing hemocyanin-O_2 affinity, *Octopus vulgaris* can cope with hypoxia even if 30 to 50% of the gill surface area is surgically removed (Wells and Wells 1984). In *Sepia officinalis*, the P_{50} is 0.4 kPa at a pH of 7.97 but is 9.3 kPa at a pH of 7.24 (Wolvekamp et al. (1942). Although a notable degree of evolutionary refinement of the hemocyanin-O_2 transport has occurred in the cephalopods (Mangum 1980b, 1990), O_2 transport in blood is the major limiting factor for power output in the taxon (Brix et al. 1989; O'Dor and Webber 1991). The O_2 carrying capacity of the blood in *Loligo pealei* is only one-half that of the hemoglobin-based bloods of vertebrates (Mangum 1990). The O_2 affinity of the hemocyanins in the crabs, *Cancer magister* (Terwilliger and Brown 1993) and *Cancer productus* (Wache et al. 1988), and the lobster, *Momarus americanus* (Olson et al. 1988, 1990b), changes with the stage of development. Hemolymph inorganic ions particularly divalent cations change with development (Brown and Terwilliger 1992) and influence the O_2 affinity and cooperativity of decapod hemocyanins (van Holde and Miller 1982).

The evolutionary biology of the respiratory pigments is an unsettled subject (e.g., Wells 1990; Nikinmaa 1990; Mangum 1992; Weber 1992). Their inter-taxonomic distribution and functional diversity are intriguing (Jensen 1991). The best-known metalloprotein O_2 carriers are hemoglobin, hemocyanins, chlorocruorins, and hemerythrins (Fig. 24, Table 6). With some exceptions, chlorocruorins are found in some polychaetes, hemocyanins predominate in the mollusks but not bivalves (Ghiretti 1966; Mangum 1980b) and crustaceans (McMahon 1985; Lallier and Truchot 1989) while hemerythrins are restricted in distribution, occurring in unrelated taxa such as in the polchaete, *Magelona*, most sipunculids, some brachiopods, and some priapulids. Some mollusks have hemoglobin while some have both hemoglobin and hemocyanin. Polychaetes have either chlorocruorin or hemoglobin while yet others, e.g., *Serpula*, have both types of pigments (Jones 1972). Among the gastropods, in contrast to a large number of Prosobranchia and Pulmonata, Ophisthobranchia do not seem to have a respiratory pigment (Ghiretti 1966). Lack or presence of a particular pigment does not appear to correlate with either the type of respiratory medium a species utilizes or its phylogenetic level of development. It is conjectured that the evolution of the respiratory pigments is polyphyletic (Mangum 1985). Depending on species, hemoglobin is found in blood corpuscles or dissolved in plasma, chlorocruorin and hemocyanins are found only in solution, and hemerythrin is found in cells (Ghiretti 1966; Mangum 1980a; Cameron 1989). The occurrence of pigment carriers in cells, an ubiquitous feature in the higher vertebrates, has been interpreted to be an evolutionary innovation enabling more efficient O_2 uptake and transfer to support the higher aerobic states. The intracellular location of the carriers is thought to maintain an optimal colloidal osmotic pressure and viscosity of plasma for an equivalent amount of protein (e.g., Snyder 1977), provide a more efficient intracellular control of allosteric modulators of the pigment's O_2 affinity (Gillen and Riggs 1973), and avoid loss of the small hemoglobin molecule through renal filtration. Mangum (1985) asserted that the erythrocyte evolved several millions of years before it became associated with the roles used to explain its derivation. Some animal groups have even lost the erythrocyte in preference for dissolved extracellular pigments (Cameron 1989). As argued elsewhere in this account, from their remarkable plasticity (a feature characteristic of least conserved parameters), the carrier pigments and especially the erythrocytes appear to be the terminal parts of the respiratory evolutionary chain. In the trial-and-error process of refining O_2 uptake and transfer, the erythrocytes may have been suddenly mobilized to contribute to the respiratory process. This apparently was not without certain costs. Schmidt-Nielsen and Taylor (1968; but see contrary conclusions by Snyder 1973 and Gaehtgens 1990) observed that at equal O_2 carrying capacity, the viscosity of the red cell suspension is higher than that of the hemoglobin solutions. The diffusing capacity of the rabbit lung for O_2 is higher when the lung is perfused with a hemoglobin solution compared with when perfused with a washed human red cell suspension (Geiser and Betticher 1989). This is attributable to an extraerythrocytic diffusion resistance which arises from an unstirred plasma boundary layer (Coin and Olson 1979; Huxley and Kutchai 1983; Vandegriff and Olsen 1984; Yamaguchi et al. 1985). The resistance depends on the hydrodynamic conditions of the erythrocyte flow (Rice 1980) and the physical resistance offered by the lipid cell membrane and the hemoglobin (Fischkoff and Vanderkooi 1975; Kon et al. 1980). The stagnant plasma boundary layer of blood is as thick as 4.2 μm (Weingarden et al. 1982). In a trade-off process, in animals with particulate blood, i.e., where the hemoglobin is contained in cells, gas exchange efficiency may have been sacrificed for proper osmoregulation of the blood. Optimal O_2 uptake and transport in blood is established through compromises between factors such as hematocrit, hemoglobin concentration, body temperature, metabolic state, and erythrocyte morphology (Guard and Murrish 1975; Weathers 1976; Shepherd and Riedel 1982; Hedrick et al. 1986). The carriers which are found in cells have low molecular weights whereas the extracellular ones have high ones. The O_2 transporting function of respiratory pigments is dependent on interactions with organic and inorganic cofactors (e.g., Mangum and Lykkeboe 1979). The O_2 affinity of the vertebrate hemoglobins is decreased by the erythrocytes' organic phosphates (e.g., Weber and Jensen 1988). In the crustacean hemocyanin, L-lactate (Truchot 1980; Bridges and Morris 1986) and urate (Morris and Bridges 1986) increase O_2 affinity. In a self-regulating process, L-acetate and urate, products of anaerobiosis in decapod crustaceans (e.g., Bouchet and Truchot 1985; Czietrich et al. 1987), sustain O_2 transport in conditions of hypoxia or intense activity. Through resisting Bohr shift with pH change (Truchot 1987), the arterial blood remains highly oxygenated (Mangum 1983; Lallier and Truchot 1989): over some range of pH, especially in the marine gastropods, a similar phenomenon, i.e., a negative or reversed Bohr effect, occurs. During hypoxia, the Bohr effect improves O_2 loading and transport since hypoxia induces acidosis and hemocyanin-O_2 affinity increases with decrease in pH (e.g., Brix 1982).

When integrated with the circulatory system, the presence of blood pigments facilitates greater uptake, transport, and delivery of O_2 between the gas exchanger and the tissue cells, supporting high metabolic rates. A complex chain of respiratory adaptations was observed by Green et al. (1973) in the volcanic crater Lake Borambi Mbo in the Cameroon (West Africa), where one of the endemic species of cichlid fish, *Konia dikume*, which feeds on the larvae of *Chaoborus*, migrates to the anoxic layer to feed. A high mean concentration of the hemoglobin of 16 g per 100 ml was far above the range of the values of 5.4 to 8.7 g per 100 ml in the other ten sympatric cichlids. Fish from high latitudes generally have low concentrations of hemoglobin compared with tropical ones (e.g., Everson and Ralph 1968). Many fish possess multiple hemoglobins which in some cases (e.g., in the carp) are functionally similar (Tan et al. 1972; Weber and Lykkeboe 1978). The more energetic species, however, show functional differences in their O_2 binding capacities, allowing O_2 transport under different circumstances (Powers 1972; Brunori 1975; Weber et al. 1976). The hearts of some species of fish, e.g., the tuna, *Thunnus thynnus*, mackerel, *S. scombrus*, and carp, *Cyprinus carpio*, have high levels of myoglobin, respectively of about 580, 332, and 488 nmol per g tissue wet weight (Sidell et al. 1987). The maximum rates of O_2 consumption in active, free-swimming skipjack tuna (2.5 mg O_2 $g^{-1}h^{-1}$) is more than two times the values reported for other teleosts (Stevens and Carey 1981). Rainbow trout can survive and even swim up to 70% of their maximal capacity with the coronary vasculature ligated (Farrell 1993). The microaerophilic parasitic nematode, *Ascaris*, has a muscle myoglobin with high O_2 affinity and the perienteric fluid has an abundant hemoglobin that binds O_2 25 000 times more tightly than its mammalian homologue (Sherman et al. 1992).

2.8.1. Hemoglobinless Fish

Although hemoglobin is widely distributed in vertebrates, a few animals exist without it (Ruud 1954). The well-known group is that of the Antarctic icefish of the family Chaenichthyidae, e.g., *Chaenocephalus aceratus* and *Pseudochaenichthys georgianus* (Rudd 1965; Steen and Berg 1966; Jakubowski et al. 1969) which lack it. Furthermore, the fish generally lack myoglobin, except small amounts in the ventricles of the heart (e.g., Feller and Gerdy 1987; Sidell et al. 1997). The Perciform (suborder: Notothenioidei) which includes the icefish evolved around the Antarctica within the last 25 million years (Eastman 1993), a time during which the continent became separated on the opening of the Drake Passage and formation of circumpolar currents which produced rapid cooling of the Southern Ocean. In the icefish, O_2 is carried essentially physically dissolved in plasma: the O_2 capacity of blood in the icefish (0.7 vol%) is no higher than that of seawater (Ruud 1954) and is substantially lower (onetenth) that of about 8% by volume of the fish having hemoglobin (Holeton 1970). Icefish have evolved in well-oxygenated waters whose temperature fluctuates between +0.3 and −1.87 °C (Eastman 1991). To survive in such habitats, the fish have evolved manifold adaptive features. Special blood serum glycoproteins which lower their freezing temperature below that of the near or below zero sea temperature protect them from imminent death (DeVries 1971; Ahlgren et al. 1988). In *C. aceratus*, a relatively high arterial PO_2 of 16 kPa exists (Holeton 1970): since the water has a high concentration of O_2, less of it is passed over the gills in order to secure the required amount of O_2. This and the absence of erythrocytes, a feature which lowers the blood viscosity, reduces the cardiac work of pumping blood. The O_2 consumption of *C. aceratus* compares with that of other Antarctic fish (Ralph and Everson 1968; Holeton 1970).

Under similar conditions and circumstances, in absolute terms, the Antarctic icefish display higher rates of O_2 consumption than temperate ones by about two fold (Holeton 1974; Somero 1991). Delivery of O_2 is effected through immense cardiac outputs (per unit body mass) facilitated by particularly large hearts (0.3% body mass), and large blood volumes even though heart rate (14 times min^{-1}) is particularly low (Holeton 1970; Feller and Gerdy 1987; Harrison et al. 1991; Tota et al. 1991). In *C. aceratus*, at 1 °C, heart rate is about 16 beats min^{-1}, the mean ventral aortic pressure is about 2 kPa and the cardiac output is 20 to 40 ml min^{-1} per g heart mass (Holeton 1970; Hemmingsen et al. 1972). The large cardiac output may be a compensation for the relatively small gill surface area in the species (Hughes 1972a), a favorable feature which results in low resistance to branchial water flow. In order to enhance the flow of O_2 from the water to the tissues, the hemoglobinless Antarctic icefish have highly aerobic muscles (Johnston et al. 1983; Johnston and Harrison 1985; Harrison et al. 1991), remarkably profuse muscle blood capillary supply (Fitch et al. 1984), and the muscle mitochondrial volume density compares with that of the flight muscles of insects (e.g., Elder 1975; Ready 1983; Londraville and Sidell 1990). The activities of the mitochondrial enzymes that are essential for aerobic fatty acid catabolism are significantly greater in the Antarctic icefish compared with other ectotherms (Sidell et al. 1987). Although the percentage utilization of O_2 in water is relatively low, the efficiency of oxygenation of blood is very high in the icefish gills (Hughes 1972a) and the group survives very well in absence of hemoglobin (Andriashev 1962). The icefish, however, are not able to tolerate hypoxia as well as the red-blooded fish (Holeton 1970). *C. aceratus* succumbs when the PO_2 falls to below 6.7 kPa while the sympatric red-blooded species, e.g., *Notothenia neglecta*, and *N. gibberiforms* can extract O_2 down to a PO_2 of 2 kPa.

2.9 Energetic Cost and Efficiency of Respiration

In biology, O_2 is an essential resource which must be procured from outside at a cost. In bimodal breathers, the expense of procurement of O_2 from the surface can be gauged from the duration of stay at the surface, the distance traveled, and the intervals between surfacing. The proportion of O_2 acquired from aerial respiration decreases as the cost of traveling to the surface increases (e.g., Kramer 1988; Shannon and Kramer 1988). Bimodal breathers can regulate the cost of procuring O_2 to match the level of metabolism and the availability of O_2 from the environment (e.g., Anderson 1978). The respiratory patterns are determined by factors such as the efficiency of the water-breathing organ, the ambient temperature, and economical utilization of O_2 during submergence. Insects exhibit what has been termed cyclic CO_2 release (e.g., Buck 1962; Kanwisher 1966), a process which entails irregular discharge of CO_2. The frequency of spiracular opening corresponds with the energetic demands, with the bursts being more frequent during activity. Although no ventilatory movements accompany such events, as gas transfer takes place essentially by diffusion across the spiracles (at least in the small species), some degree of energy saving must be gained when the intervals of spiracular opening are widely spaced. At an ambient temperature of below 10 °C, when O_2 diffusion across the closed or fluttering spiracles is adequate to support the low rate of metabolism, in *Cecropia*, bursts stop altogether (Kanwisher 1966).

Respiratory efficiency is a measure of the performance of a gas exchanger and should express the ratio of gas procurement and transfer of O_2 against that of the energy expended in the process. The amount of O_2 consumed during respiration is required in two main areas: (1) to physically move the respiratory medium over the respiratory site(s) and (2) to power the contractions of the muscles which drive the process. Energy is needed for both ventilation and perfusion of the gas exchanger(s), complex processes of which the absolute costs remain largely unknown (e.g., Scheid 1987). In fish, the cost of breathing water (per O_2 uptake) has been reported to range from a mere 0.5 to 10% during routine ventilation to 70% of the overall O_2 consumption during exercise (e.g., Schumann and Piiper 1966; Alexander 1967; Edwards 1971; Jones and Schwarzfeld 1974; Jones and Randall 1978; Steffensen and Lomholt 1983; Milsom 1989; Rantin et al. 1992). The very high values in some species may be due to technical and experimental problems such as strenuous experimental conditions entailing physical restraint and effect of anethesia (e.g., Cameron and Cech 1970). Compared with those animals which breath air, e.g., in the healthy human being where the value is 1 to 2% (Dejours 1975), the high cost of breathing water is attributable to the greater density (about 800 times that of air), viscosity of water (50 times air) (Table 4) and the low solubility of O_2 in the medium: more work is needed for pumping water. Under normal circumstances, fish faced with hypoxia move from it (Dandy 1970) or reduce their O_2 consumption to conform with the availability (Hughes 1981). Positional changes of the gill filaments during water breathing and strict coupling of the buccal and opercular pumps, factors which improve the efficiency of the hydrodynamic flow of water, reduce ventilatory work (Ballintijn 1972). Faced with hypoxia, as an energy-saving strategy, most fish (e.g., Smith and Jones 1982; Fernandes and Rantin 1989; Rantin et al. 1992) increase gill ventilation by augmenting tidal volume and not ventilatory rate. A mechanical ventilator working at three times per minute was used to ventilate the human lung with hyperoxygenated saline (Kylstra and Schoenfisch 1972). It is probably due to the enormous cost of reversing water flow that tidal ventilation in aquatic respiration is a rare process in the evolved animals. It occurs naturally only in a few primitive organisms. In experimental liquid breathing, water has to be mechanically moved through the air passages (e.g., Kylstra et al. 1966; Sect. 6.11). The mean efficiency of the buccal force pump as it inflates the anuran lung is 8%, the O_2 consumption per 100 g of the respiratory muscle is 0.89 mlO_2 per min, and the O_2 cost of breathing at rest is about 5% of the total resting O_2 consumption (West and Jones 1975). The piston pump ventilatory mechanism of the lugworm, *Arenicola marina*, which occurs by means of peristaltic movements of its dorsal body wall musculature (Wells 1966) takes about 40% of the total O_2 uptake in animals ventilating normoxic or slightly hypoxic seawater (Toulmond 1975; Toulmond and Tchernigovtzeff 1984). At a hypoxia below 5.3 kPa, the worm is unable to pump water at an adequately high rate to overcome the reduced water O_2 content (Toulmond et al. 1984) and can withstand several days of experimental anoxia (Schöttler et al. 1984). During routine activity, in normoxic water, the gill convection requirement is 200 to 400 ml H_2O per ml O_2 (Johansen 1982). The cephalopod mollusk, *Nautilus*, which lives at depths of 100 to 300 m and regularly encounters areas of low O_2 concentrations, overcomes such episodic occurrences of hypoxia by remarkable suppression of aerobic metabolism to as low as 4 to 8% of that at the normoxic level (Boutilier et al. 1996), a value comparable to that of well-known facultative anaerobes (Hochachka and Guppy 1987). A hypometabolic-hypoxic animal conserves energy by decreasing the level of activity and by extending ventilatory and circulatory pauses. Water breathers have to irrigate their gills with a 40 times larger volume of water than the air breathers (with air) to extract an equivalent amount of O_2 (Block 1991a). Since water contains substantially less dissolved O_2 than air, to extract the same quantity of O_2, the ventilation-perfusion ratio in aquatic breathers is ten times or more that for air breathers. In mammals, the ratio is about 1. Deviations from unity result in dramatic impairment of O_2 diffusion (e.g., Escourrou et al. 1993). Ventilatory requirements for fish are four to eight times higher than those of terrestrial ectotherms with similar metabolic demands (Milsom 1989). In active species, ventilatory requirements can increase 10 to 15 times above resting while O_2 consumption rarely increases by a factor greater than 5 (Brett 1972). In juvenile to adult fish (body mass <100 g), ventilatory flow rates range from 100 to 300 ml per kg per minute (Johansen 1982). Indirect estimation of the cost of water breathing in fish as a factor of the drop in O_2 consumption when the fish changes from active to passive (ram) ventilation indicates that in the trout, O_2 consumption falls by more than 10% and in the sharksucker about 5% (Steffensen and Lomholt 1983). During emergence into air, the crayfish, *Austropotamobius pallipes*, ventilates its branchial chambers at very low rates (5 ml per kg per min; Taylor and Wheatly 1980).

To minimize the energy expended on ventilatory work, fish have adopted different strategies of optimizing gas exchange to fit particular circumstances as well as to relate the respiratory process to activities such as osmoregulation. In the flounder, *Platichthys fleus*, about 7 ml per kg per h of O_2 and in the rainbow trout, *Oncorhynchus mykiss*, $6\,\mathrm{ml\,kg^{-1}h^{-1}}$ of O_2 are utilized for osmoregulation, values which constitute 10 to 15% of their standard metabolism (Kirschner 1993). In absolutely resting fish, ventilation can be intermittent (Perry and McDonald 1993). Benthic fish such as the bullhead catfish, *Ictalurus nebulosus*, exhibit apneic periods which may last for as long as 1 min, whereas others show periods of very shallow breathing alternating with strong ones (Roberts and Rowell 1988). Ventilatory pauses may be as long as 30 min in some crabs (Taylor 1984). In the intermittent ventilatory pattern of the reptiles as well as during hibernation and sleep in endotherms, i.e., where the ventilatory periods alternate with breath-holding ones, the nonventilatory period may constitute an energy-saving strategy for minimizing ventilatory cost (e.g., Glass and Wood 1983; Milsom 1991; Wood and Glass 1991; West et al. 1992) and for reducing convective respiratory water loss (Innes et al. 1986). Pulmonary blood flow increases during the breathing phase (e.g., Shelton and Burggren 1976; Burggren 1977; Burggren et al. 1977).

The nonventilatory period in the crocodile, *Alligator sinensis*, may last from a few seconds to 20 to 30 min (Zhao-Xian et al. 1991): the pattern of "discontinuous" or "intermittent" ventilation has been reported in the air breathing brachyurans, e.g., *Cancer paguras* (Burnett and Bridges 1981), *Pseudothelphusa garhami garhami* (Innes et al. 1986), *Cardisoma* (Wood and Randall (1981) and *Holthuisana* (Greenaway et al. 1983), terrestrial insects (Schneiderman 1960), and air-exposed bivalves (Jokumsen and Fyhn 1982). In such animals, to optimize gas transfer during the ventilatory period, heart rate, cardiac output, and pulmonary perfusion are synchronized with ventilation (e.g., Shelton and Burggren 1976; White 1978; Zhao-Xiao et al. 1991). In a quiescent, unstressed state, the crab, *Cancer magister*, utilizes unilateral ventilation whereby only one scaphognathite beats (McDonald et al. 1977). During such a state, variable levels of oxygenation of the postbranchial blood are attained (McMahon 1985). In the active state, the combined ventilatory volume is 288 ml per kg per min and the PO_2 in the hemolymph is 10.8 kPa while in a quiescent one the values are 50% less and the O_2 consumption is reduced by 30% (McDonald et al. 1977). The displacement of the limb girdles into the rib cage and fusion of the skeletal parts into the protective armor prohibits turtles from utilizing abdominal or thoracic movements to ventilate the lungs. In the group, respiration entails rotation of the limb girdles and hence expiration and inspiration are active processes (Gans 1976). By estimating the O_2 consumption during artificial ventilation and normal ventilation, at 22 °C, the energetic cost of moving air in the lung of the turtle *Pseudemys floridana* was found to be 0.0047 ml O_2 ml^{-1} of gas ventilated (Kinney and White 1977).

In general, fish respond to hypoxia by increasing gill ventilation, reducing heart rate, and increasing the stroke volume. The cardiac output is held constant or is even elevated (Randall 1970). The two main costs of gill ventilation are energy loss due to the resistance offered by the gills to water flow and the loss of energy from cyclic acceleration and deceleration of water as it is pumped through the branchial chambers. Gill resistance to water flow occurs both during branchial and ram ventilation while loss of kinetic energy is abolished during ram ventilation. Frequently, ram ventilation occurs in the large pelagic predatory fishes, e.g., sharks, tuna, striped bass, and mackered which swim constantly (e.g., Roberts and Rowell 1988; Burggren and Bemis 1992). In very active fish, e.g., the mackered, the bucco-pharyngeal movements are not sufficient to provide the required volume of water for adequate O_2 to be extracted. The fish has to be continuously in motion to enhance ventilation. In the juvenile paddlefish, *Polyodon spathula*, as swimming speed increases, buccal ventilation becomes intermittent and continuous ram ventilation occurs above a speed of 0.6 to 0.8 body lengths s^{-1} (Burggren and Bemis 1992). In the torrential hillstreams, a fish need only physically place itself along a moving water current for the water to flow over the gills. In most fish, active buccal ventilation changes to ram ventilation at swimming speeds of 20 to 60 $cm\,s^{-1}$, with the actual transitional velocity depending on factors such as environmental PO_2 and temperature (e.g., Roberts and Rowell 1988). A transition speed between the two ventilatory processes is well marked in fishes such as bluefish (*Pomatomus saltatrix*), striped bass (*Morone saxatilis*), and rainbow trout (*Oncorhynchus mykiss*) (Freadman 1981; Steffensen and Lomholt 1983). During locomotory ram ventilation, the work of respiration is essentially transferred from the buccal and opercular muscles to the swimming muscles of the trunk (e.g., Burggren and Bemis 1992). In the bluefish and striped bass, the transition to ram ventilation is accompanied by as much as 50% increase in swimming speed without an increase in metabolic rate (Freadman 1981). Although constant swimming is energetically expensive, the energy conserved appears to justify adoption of ram ventilation. *Polyodon spathula* and fish such as anchovies and menhaden combine raw ventilation with filter feeding (James and Probyn 1989; Burggren and Bemis 1992), a process which results in energy saving on the cost of gill ventilation over the combined one which would be required for buccal pumping and foraging. Exercising fish increase their O_2 consumption five times and the ventilation of the gills about 15 times, raising the O_2 consumption of respiratory muscles to 15% of the total O_2 consumption (Hughes and Shelton 1958). The response to hypercapnia entails an increase in gill ventilation (Jansen and Randall 1975) but hyperoxia can alleviate or even abolish the ventilatory response (Randall and Jones 1973). In contrast to air breathers, which utilize a medium with high O_2 concentration, fish have lower heart rates than respiratory rates, a higher ventilatory requirement being necessary in a medium of low O_2 content. The ventilation-perfusion ratios in fish are greater than unity. In aquatic breathers, the ventilatory response is mainly directed to O_2 availability rather than to elimination of CO_2 (Randall and Cameron 1973). The bimodal breathers perceive and react to both hypoxia and hypercapnia in water and air to similar levels of sensitivity (Johansen 1970), with the degree of perfusion and ventilation depending on the actual role of a particular structure in CO_2 elimination or O_2 uptake. Some air-breathing fish, e.g., *Trichogaster*, however, seem to be incapable of distinguishing O_2 levels in the inspired air and water (Burggren 1979). In the continuous air breathers, where the lung is ventilated by a single medium (air) and the intrapulmonary CO_2 and O_2 levels are somewhat fixed, compared with the bimodal breathers, respiratory control is a rather simple and direct process. Peripheral as well as pulmonary afferent inputs are integrated in the brain to make the necessary cardiovascular and pulmonary adjustments in response to O_2 needs and CO_2 levels in the body. Fetal respiratory movements (e.g., Cooke and Berger 1990) are well known and their significance in lung developments has been suggested (e.g., Alcorn et al. 1980; Liggins et al. 1981). Fetal breathing is said to be energetically expensive, constituting as much as 30% of the overall fetal O_2 consumption (Rurak and Gruber 1983). This may explain the reduction in "respiratory" frequency towards term (Berger et al. 1986), the long periods of fetal apnea in utero, and the total apnea during labor when O_2 is conserved for utilization by the contracting uterine muscles of the mother.

In assessing and comparing the efficiencies of biological systems, it is important to estimate the extreme performances since biological systems have different inbuilt safety margins (e.g., Alexander 1981, 1996; Currey 1967; 1984; Wainright et al. 1976; Vogel 1988). In the case of gas exchangers, at the maximum O_2 consumption, all the reserve is exhausted as the functional and structural parameters are fully committed in procuring and delivering molecular O_2 to the tissue cells (e.g., Gehr et al. 1981; Weibel and Taylor 1986). The cost and efficiency of respiration will depend on the rate and nature of propulsion of the external respiratory medium to the respiratory site as well as the geometrical pattern of presentation of the internal and external gas exchange media. Using different means, the gas exchangers have been variably optimized. For example, the rectification of the air flow in the bird lung (whereby the highly efficacious unidirectional and continuous flow of air in the paleopulmonic parabronchi is generated) is passively achieved – there being no evident anatomical valves (Jones et al. 1981). The geometry of the secondary bronchi (especially the mediodorsal ones) relative to the primary bronchus and a recently described constriction of the primary bronchus (just before the origin of the first mediodorsal secondary bronchus) called segmentum accelerans (Banzett et al. 1991; Wang et al. 1992) are associated with the throughflow of air in the bird lung. Inspiratory aerodynamic valving has been shown to be dependent on factors such as gas density and the convective inertial forces generated by the air in motion (Banzett et al. 1987, 1991; Butler et al. 1988; Kuethe 1988; Wang et al. 1988).

It is now well recognized that in biological systems, geometric configuration and spatial disposition of the constitutive components can in some cases constitute limiting factors in function (e.g., West et al. 1986). Due to the great diversity in design of the gas exchangers, as well as the complexity of the respiratory process itself, the factors required to estimate the cost of respiratory work are presently uncertain and imprecise. Assumptions have to be made even on some fundamental aspects. Parameters such as O_2 extraction from the environment and the arterio-venous difference in O_2 content are used as approximate measures of

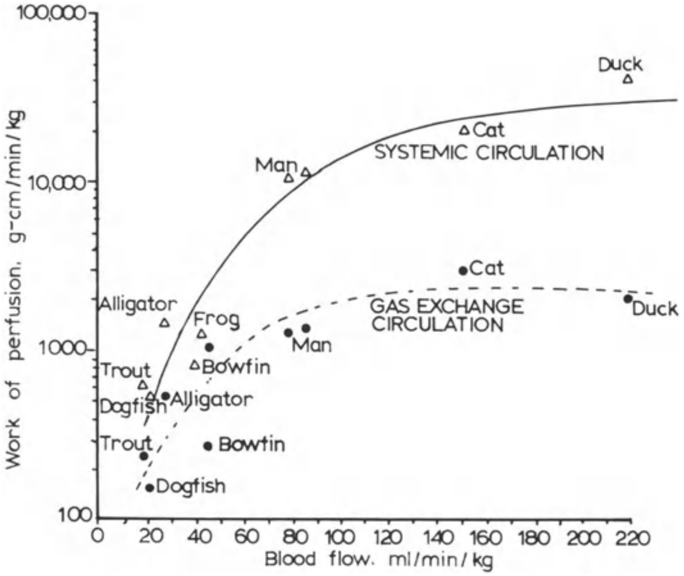


Fig. 25. Work of perfusing the systemic and gas exchange circulations in some vertebrate animals. The low work entailed in perfusing gas exchangers compared with the systemic circuit constitutes a substantial energy saving. (Johansen 1972)

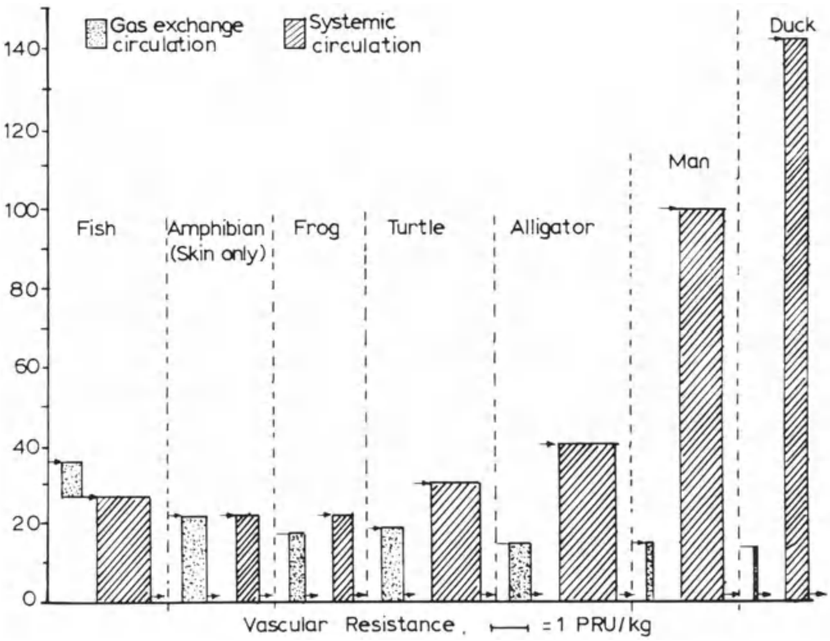


Fig. 26. Perfusion pressures and vascular resistance (VR) of the gas exchange and systemic circulations in some vertebrates. The *bar widths* show VR. Compared with water breathers, VR is very low in the circulatory system of the gas exchangers. This constitutes immense energy saving on respiratory work in the air breathers. *Arrows* show the scope of increased vascular resistance; *PRU* physiological resistance unit – a relative measure of resistance in the different animal groups. (Johansen 1972)

respiratory efficiency. In general, the greater specific gravity, viscosity, and lower O_2 content of water compared with air make the cost of aquatic respiration per unit volume of O_2 extracted greater than the aerial one (Johansen 1972). To optimize the gas transfer process, the vascular resistance of the gas exchangers is particularly low compared with the systemic one, especially in the air breathers (Figs. 25,26). In water, the ventilatory rate of aquatic crabs is three times that in air and the ventilatory cost is 30% that of O_2 consumption (Herreid and Full 1988). In the eel, a drop in the concentration of O_2 from saturation to $4\,\mathrm{ml\,l^{-1}}$ results in a 40% increase in O_2 uptake (=30% of the total metabolism) largely due to a five fold increase in ventilatory rate resulting from greater activity of the branchial muscles (Jones 1972). The energetic cost of aquatic ventilation in the crab, *Cancer*, may be as high as 76% (McMahon and Burggren 1979). The cost of breathing in the human being has been determined by increase in O_2 consumption due to isocapnic voluntary hyperventilation (e.g., Cournand et al. 1954) or by increased hyperventilation consequent to additional instrumental dead spaces, e.g., Milic-Emili (1991). At rest, the cost ranges from 1 to 2% of the total O_2 consumption but increases in hyperbaria because of increase in gas density and during exercise due to the work needed to overcome inertia and gas turbulence.

Deep sea divers need to substitute the lighter helium for nitrogen at depths in excess of 50 m in order to reduce respiratory work (Lanphier 1969). In fish, the respiratory cost, which ranges between 10 and 25%, is appreciably higher than in the human being (e.g., Hughes 1965; Dejours et al. 1970). The ratio of ventilatory requirement per unit O_2 consumption in the human being is ten times lower than in a goldfish (Dejours et al. 1970). In a hypocapnic turtle, *Pseudemys floridana*, the cost of breathing ranges from 10% (at 37 °C) to 40% (at 10 °C) of total O_2 consumption (Kinney and White 1977). The inverse relationship between the ventilatory cost and the body temperature (White 1978) indicates that respiration becomes more efficient with increasing metabolic capacity.

Air breathing has the salient advantage of energy saving on respiratory work and gives flexibility in the adjustment of respiratory rate without undue increase in energetic demands. The energy thus saved can be utilized for growth and development and to secure newer ecological opportunities. In air breathers, the cost of breathing is a fixed fraction of the total O_2 consumption and is in general about 5% or slightly less (Tenney 1979). The respiratory cost in the diving marine mammals, e.g., the cetaceans where the lungs are capable of emptying to 10 to 15% of total lung capacity (compared with only 20 to 40% in man) in as short a time as 0.3 s (1.5 to 2.0 s in man) have not been estimated (Olsen et al. 1969; Kooyman and Sinnett 1979; Kooyman and Cornell 1981). In fish, myocardial power output is a useful indicator of the O_2 cost of the cardiac pumping (Farrell 1993). Myocardial O_2 consumption is about $0.3\,\mathrm{ml\,s^{-1}}$ per $\mathrm{mW^{-1}}$ of cardiac pumping in various species of fish (Davie and Farrell 1991). The cost of cardiac pumping at rest constitutes 0.6 to 4.6% of resting O_2 consumption but in the hemoglobin-free Antarctic fish, *Chaenocephalus aceratus*, the cost may be as high as 23% (Farrell and Jones 1992).

2.9.1 The Requisites for Efficient Gas Exchange

The process of gas exchange is governed by various structural elements and functional events. These include: (1) the partial pressure gradient prevailing across the tissue barrier separating the blood and/or body fluids from the external milieu (Fig. 27), (2) the thickness of the blood-gas barrier, (3) the surface area available for gas transfer (Fig. 16), (4) the material properties (i.e., the intrinsic biophysical attributes) of the barrier tissue, properties which determine the permeability of the respiratory gases (Roughton and Forster 1957), (5) capillary transit times across the gas exchanger, (6) O_2-hemoglobin binding kinetics, (7) the physical properties of the external respiratory medium, e.g., air, water or artificial atmosphere or liquid, (8) an efficient neuroregulatory mechanism for coordination of ventilation and perfusion of the gas exchanger to establish optimal gas fluxes, and (9) dynamics and geometric pattern of presentation of the internal and external respiratory media. The limitations inherent in a particular respiratory medium and the nature of transfer of O_2 can be best assessed on the basis of the differences in the PO_2 and PCO_2 across a gas exchange surface. Oxygen and CO_2 molecules are convectively transported at equal rates whereas diffusion

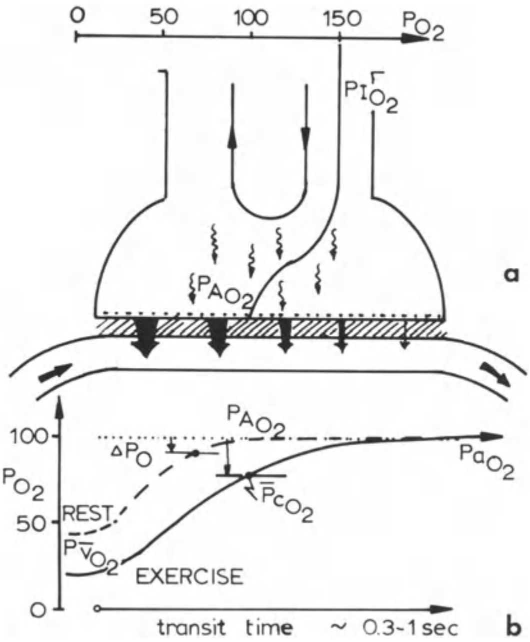


Fig. 27. **a** Schematic diagram showing the diffusion of O_2 in an alveolus across the blood-gas barrier, ↓, and the oxygenation profile of pulmonary capillary blood, ↗, in transit through the mammalian lung. The PO_2 in the alveolus, PAO_2, decreases as O_2 diffuses into the capillary blood, **b**. The pulmonary capillary transit time is longer during rest than during exercise when the capillary length is almost fully utilized. In normal cases, capillary transit times are adequate for complete arterialization of blood both during exercise and rest. PIO_2, partial pressure of O_2 in the inspired air; PaO_2, partial pressure of O_2 in the arterial blood; PcO_2, average capillary partial pressure of O_2; PvO_2, partial pressure of O_2 in the venous blood; ΔPO, partial pressure of O_2. (Weibel 1984a; reprinted by permission of Harvard University Press; copyright 1984 by the President and Fellows of Harvard College)

transport favors O_2 over the larger CO_2 molecule both in gaseous and aqueous media (e.g., Rahn et al. 1971). Since the ratio of the diffusion rate of CO_2 to O_2 is 0.78, for the same CO_2 tension, the O_2 gradient at a respiratory surface will always be higher (Wangensteen et al. 1971). This difference is particularly important in some organisms such as insects at various stages of development and avian, reptilian, and insect eggs, which depend wholly or partly on the diffusion of O_2 and CO_2 across the gas exchange surface. The extant amphibian eggs are restricted to a diameter of 9 mm (Carroll 1970) whereas in the much large eggs of reptiles and birds, where diffusion would not suffice in transfer of O_2, adaptations such as development of a well-vascularized chorioallantoic membrane which promotes uptake and transfer have evolved (e.g., Luckett 1976; Sect. 6.13). For historical interest now, at the beginning of this century, it was believed by physiologists as eminent as Christian Bohr and J.S. Haldane (see Haldane 1992), apparently from erroneous measurements which indicated a higher PO_2 in the pulmonary capillary arterial blood than in the alveolar air, that gas exchange in the vertebrate lung occurred by an active process. It was envisaged that the lung was able to "absorb" O_2 from the air spaces and "secrete" it into the blood. This was thought to occur particularly during exercise when the O_2 demand was high and during adaptation to hypoxia when there was deficiency of the same. The irreconcilable morphological observations of the day did not help to resolve the matter. Until the application of electron microscopy, debate ranged as to whether an epithelial lining covered the lung. Among others, Albert Policard (e.g., Policard 1929) championed the "naked alveolar capillaries" concept asserting that the respiratory surface of the lung was "like the flesh of an open wound" and that the inhaled air came into direct contact with blood. More accurate estimations of the PO_2 and PCO_2 in the alveolar and pulmonary capillary arterial blood (Krogh 1910) and better instrumentation and tissue processing when complete alveolar epithelium was discovered (Low 1953) dispelled these notions. In different animals, the alveolar PO_2 is consistently higher than the mean capillary blood PO_2 by an appreciable margin (e.g., Lindstedt 1984; Karas et al. 1987b; Constantinopol et al. 1989). In the lung of the Arctic fox, *Alopex lagopus* (Longworth et al. 1989), the pressure head (the pressure gradient = the driving force) for diffusion of O_2 (ΔPO_2) across the blood-gas barrier was estimated to be about 5 kPa, a value greater than that in the lungs of other highly aerobic animals, e.g., the pony (3.4 kPa) and the dog (4.6 kPa), the goat (1.9 kPa), and the calf (2.4 kPa) (Weibel and Taylor 1986; Karas et al. 1987b). In the horse, ΔPO_2 is 2.6 kPa and in the steer 2.1 kPa at VO_{2max} (Contantinopol et al. 1989). In muscles, during severe hypoxia, a condition when the ΔPO_2 between the blood capillaries and the mitochondria is drastically reduced, a diffusion limitation for O_2 occurs in animals with a normal hemoglobin O_2 affinity (Stein and Ellsworth 1993): left-shift of the oxyhemoglobin dissociation curve provides the means for the tissue to preserve its level of O_2 extraction within the blood capillary network. It has been shown that VO_{2max} can be increased by raised O_2 supply to the body through increased PO_2 in the inspired air (e.g., Welch 1987; Knight et al. 1992; Gonzalez et al. 1993). Hemoglobin concentration affects VO_{2max}, with changes as little as 1 to 2 g dl^{-1} being significant (Woodson 1984). Infusion of autologous frozen erythrocytes, a process which resulted in elevation of hemoglobin concentration from 15 to 16.3 g dl^{-1}, produced a 5% increase of VO_{2max} 24 h later and 4% 7 days later in the human being (Buick et al. 1984). In a similar procedure, Williams et al. (1981) reported an increased running capacity on a treadmill while Robertson et al. (1982) observed a 13% increased of VO_{2max} and 16% of endurance time in human subjects injected with 375 ml of frozen autologous erythrocytes on 2 successive days when hemoglobin concentration rose from 13.8 to 17.6 g dl^{-1} and the hematocrit from 43 to 55%. Carrier-mediated transfer of O_2 in the lung (Burns et al. 1975) and the placenta (Burns and Gurtner 1973) are known to occur, but play an insignificant role in the overall gas exchange process. Diffusion and convection are the only known processes involved in the transport of O_2 into the respiratory organs and within organisms. It is only in rare, specialized organs such as the swim bladder (e.g., Fänge 1966; Sect. 6.2) and the choroid rete of the eye of teleosts

(Wittenberg and Wittenberg 1962), where O_2 is known to be secreted against a concentration gradient. The respiratory roles of such organs, if any, is secondary. Since the solubility of CO_2 in water and tissues is much greater than that of O_2, its elimination and transportation in solution presents no problems to an aquatic organism and the need for its active secretion is even less necessary. The transfer of gases from the ambient milieu to the tissue cells takes place essentially by convection (the mass transfer of O_2 by the moving air in which O_2 is contained) and by diffusion, the molecular flux of O_2 through air or liquid in a manner essentially related to the continuous random Brownian motion. High rates of O_2 uptake and CO_2 elimination are germane to the high metabolic rate of the endothermic terrestrial vertebrate endotherms. These processes are only rivaled in rate and magnitude by the transfer of water vapor between an animal and its immediate environment. The efficiency and plasticity of the gas exchange processes is underscored by the fact that during exercise or exertion, the levels of flux of respiratory gases may increase more than ten times above the resting level.

Gas exchange is constrained by temporal limitations consequent to finite rates of convection, diffusion, and reaction kinetics of CO_2 and O_2 with the carrier pigments. Inert gases, i.e., those gases which dissolve in blood without undergoing any chemical reaction, equilibrate much faster than do CO_2 and O_2, which are chemically bound to the hemoglobin and other carriers. Such gases require a longer transit time at the respiratory site for full equilibration to occur. Respectively, O_2 and CO_2 require 430 and 210 ms to reach 99% equilibration while inert gases of equivalent molecular weights require only 15 to 20 ms (Wagner 1977). Capillary transit times depend on factors such as tissue, species, metabolic rate, temperature, blood flow rates, pressure, viscosity, and capillary architecture, i.e., density, number, length, and geometric configuration (Karas et al. 1987b; Fig. 27). At rest, capillary transit times (in s) scale disproportionately to body mass (kg) to a power of 0.20 in the mammalian lungs (Lindstedt 1984). In mammals, capillary transit times are shorter in small animals than in the larger ones (Swenson 1990; Table 7). Oxygen binding to hemoglobin may limit maximum O_2 consumption in the smallest mammals (Lindstedt 1984). Birds have capillary transit times always less than 1 s. Under experimental conditions, transit times as short as 0.3 s have been reported (Henry and Fedde 1970). Adversely short transit times are prevented by capillary recruitment (e.g., Malvin 1988) and opening of arterio-venous anastomoses. Since on average the transit times are longer than the saturation times and the pulmonary capillary distance necessary for exposure and full saturation of blood is more than adequate (Karas et al. 1987b), it is conceivable that the inert and the respiratory gases are fully equilibrated as the blood traverses the pulmonary capillaries, at least under resting normoxic state. The pulmonary capillary transit time of about 0.5 to 3.0 of a second in the fish gills (Perry and McDonald 1993) is the same order of magnitude as in mammals, i.e., 0.75 of a second (Roughton 1945; Constantinopol et al. 1989) but in birds (e.g., chicken) the average transit time appears to be much shorter (e.g., Burton and Smith 1967; Henry and Fedde 1970), a value as short as 0.31 of a second having been estimated by Henry and Fedde (1970) in the chicken. This may explain the lower arterial O_2 tensions in birds compared with mammals (Jones and Johansen 1972). Relative to

Table 7. Capillary transit times in various vertebrate species and organs. (After Swenson 1990)

Species	Organ	Condition	Average transit time (s)
Human	Lung	Rest	1.8
		Exercise	0.4
		Rest-hypoxia	0.3
Cow	Lung	Rest	4.6
		Exercise	0.9
Dog	Lung	Rest	1.8
		Exercise	0.3
	Muscle	Rest	0.9
		Exercise	0.13
	Heart	Exercise	0.6
Fox	Lung	Exercise	0.12
Mouse	Lung	Rest	0.6
		Exercise	0.12
Frog	Lung	Rest	1.3
	Skin	Rest	1.0
Fish	Gill	Rest	1.0
Bird	Lung	Rest	0.8
		Exercise	0.5

mammals, birds have relatively larger hearts (e.g., Hartman 1954, 1955; Tucker 1968) and faster heart rates and hence greater cardiac outputs and stroke volumes off (Lasiewski and Calder 1971; Grubb 1983). A flying budgerigar, *Mellopsitacus undulatus*, has a cardiac output of about $4 l kg^{-1} min^{-1}$, a value which is seven times greater than that of a mammal of equivalent body mass (Tucker 1968) and a heart rate as fast as 1020 beats min^{-1} has been reported in the giant hummingbird, *Patagona gigas* (Lasiewski et al. 1967). The cardiac blood pressure in birds is very high. Systolic pressures as high as 53kPa have been determined in the domestic turkey, *Melleagris gallopavo* (Speckman and Ringer 1963). In contrast, among the living vertebrate ectotherms (i.e., fish, amphibians, and reptiles), systolic blood pressure rarely exceeds 7kPa (Lindsay et al. 1971). Poikilothermic vertebrates store lipids primarily as tricylglycerols (Sheridan 1994). In birds, occasional deaths commonly attributed to fright are largely due to hemorrhage consequent to arterial rupture resulting from sudden excessive hypertension arising from such encounters (Walkinshaw 1945; Carlson 1960; Hamlin and Kondrich 1969). In *Nautilus*, during the hypometabolic state, i.e., after the PO_2 in the arterial blood has fallen to below 0.7kPa, a reversal of the normal arterial-venous blood PO_2 gradient occurs with the venous PO_2 exceeding that of the arterial blood (Boutilier et al. 1996). This is thought to be brought about by an extremely slow intermittent blood flow during severe hypoxia when the large vena cava which is located on the roof of the mantle cavity has time to equilibrate with the ambient PO_2. Most interestingly, during such episodes, the vena cava serves as a gas exchanger, transferring respiratory gases between the blood and the air in the mantle cavity!

Morphometric studies have shown that the erythrocytes offer the greatest resistance to O_2 diffusion in the gas exchangers (e.g., Hallam et al. 1989; Maina et al. 1989a). Due to lack of carbonic anhydrase in the capillary endothelial cells of the gills (e.g., Perry and Laurent 1990; Lessard et al. 1995), unlike in the mammalian lung, in fish, the erythrocytes appear to be the only site for HCO_3^- ion dehydration (Perry and McDonald 1993). The relatively long transit time of the blood in the gills, the high capacitance of water for CO_2, and the efficacious countercurrent system of the gills may account for the effectiveness of the gills in CO_2 elimination. The factors which may inhibit end capillary PO_2 equilibration include: (1) an overly high cardiac output, e.g., during exercise and disease conditions factors which cause loss of the functional capillary bed, resulting in shorter transit times (Wagner et al. 1986), (2) thicker tissue diffusional barriers, e.g., in pathological conditions such as edema (Staub et al. 1967; Staub 1974), (3) severe hypoxia (reduction in O_2 driving gradient), e.g., during high altitude exercise (Wagner et al. 1986), (4) large erythrocytes which are associated with greater unstirred layers, and (5) pathological conditions which are accompanied by reduction of the concentration of the hemoglobin or those characterized by reduced erythrocytes count, a factor which increases the thickness of the unstirred layer resulting in reduction of O_2 binding velocity (e.g., Nguyen-Phu et al. 1986). The erythrocytes of the bullfrog, which have a volume of 700 μm^3, take up O_2 at a rate five times slower than the smaller ones of 20 μm^3 of the goat (Holland and Forster 1966). Diffusional resistance during severe exercise may inhibit end capillary O_2 equilibration as the capillary transit times fall to as low as 200 ms (Groebe and Thews 1987). Owing to the shape of the haemoglobin-O_2 dissociation curve which causes large O_2 loading during the early part of intracapillary transit (see. e.g., Comroe 1974; Shiga 1994), even when the end capillary complete equilibration is not attained, the amount of O_2 taken up is adequate for the respiratory needs. The differences in the equilibration time courses in the inert gases and in the biochemically active gases such as CO_2 and O_2 can be attributed to the ratio of the solubility of the gas in the membrane barrier to that in blood. In inert gases, the ratio is unity while the value is several orders of magnitude less for CO_2 and O_2 (Piiper and Scheid 1980). The greater solubility of O_2 and CO_2 in blood relative to the membrane is due to the reversible chemical binding and reaction with hemoglobin and other proteins in the erythrocytes and plasma (Shiga 1994). The rate at which the partial pressure of a particular gas builds up is exclusively dependent on its solubility in blood. The more soluble a gas, the slower will be its rate of partial pressure change for a given quantity of gas transferred. The rate of equilibration of CO_2 in any solution is strongly dependent on the buffering capacity. The rate-limiting steps in O_2 transfer are ascribed both to diffusional resistances and chemical reactions in an inhomogeneous medium. Unlike in CO_2 exchange and in the Bohr-Haldane effects, these fast processes do not require enzymes or membrane transport carriers. Even during exercise, in mammals, O_2 transfer and equilibration with the capillary blood are usually complete by the end of the transit time (e.g., Karas et al. 1987b; Longworth et al. 1989; Fig. 27).

Ventilatory and perfusive processes are particularly important in gas transfer during episodes of extreme exertion, hypoxia, and respiratory acidosis. In the course of its passage from the external environment to the mitochondria, O_2 travels across several anatomical spaces which offer different degrees of resistance (Figs. 2,3). According to Fick's Law, the diffusing capacity of a gas through a barrier depends on surface area, the concentration gradient, the thickness of a barrier (the diffusional distance), and the diffusion (permeation) coefficient across the barrier (Figs. 16,28,29). Among air breathers, the thickness of the blood-gas barrier of the gas exchangers decreases from the amphibians, reptiles, mammals, to birds (e.g., Maina 1994). The water-blood barrier in the aquatic gas exchangers is in general thicker than the blood-gas barrier of the lung (e.g., Hughes and Morgan 1973). The diffusion rate in the mammalian lung is very efficient. Determinations by Wagner and West (1972) and Hill et al. (1973) showed that in the human alveolar-capillary barrier whose normal thickness is $0.62\,\mu m$ (Gehr et al. 1978), the thickness would have to be increased four to ten times before it becomes a limiting factor for end capillary PO_2 equilibration. From theoretical considerations (e.g., Scheid 1978) and experimental work by Powell and Wagner (1982a), in the avian lung the diffusion of O_2 in the gas phase of the air capillaries which radiate from the parabronchial lumen (Figs. 30,31) is not thought to constitute a limiting factor at rest (Powell 1982; Powell and Scheid 1989). Owing to the long diffusional distance (20 to $50\,\mu m$), cutaneous respiration is accompanied by limitations of diffusion (e.g., Malvin 1988) but movements of air over the skin may enhance the diffusional process. Increased perfusion may be utilized to enhance O_2 uptake particularly during hypoxic episodes (Malvin and Hlastala 1986). Movements by skin-breathing aquatic organisms may reduce

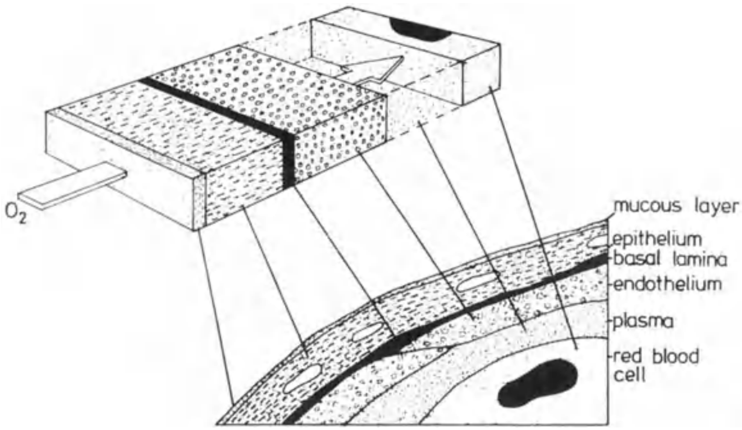


Fig. 28. Schematic view of the oxygen diffusional pathway in an aquatic breather. The diffusing capacity of the gas exchanger depends on the thickness and surface area of the respiratory barrier. In the water breathers, the unstirred layer of water over the gills may constitute a significant part of the resistance to O_2 diffusion and may need to be considered in modeling the diffusion capacity of the gills

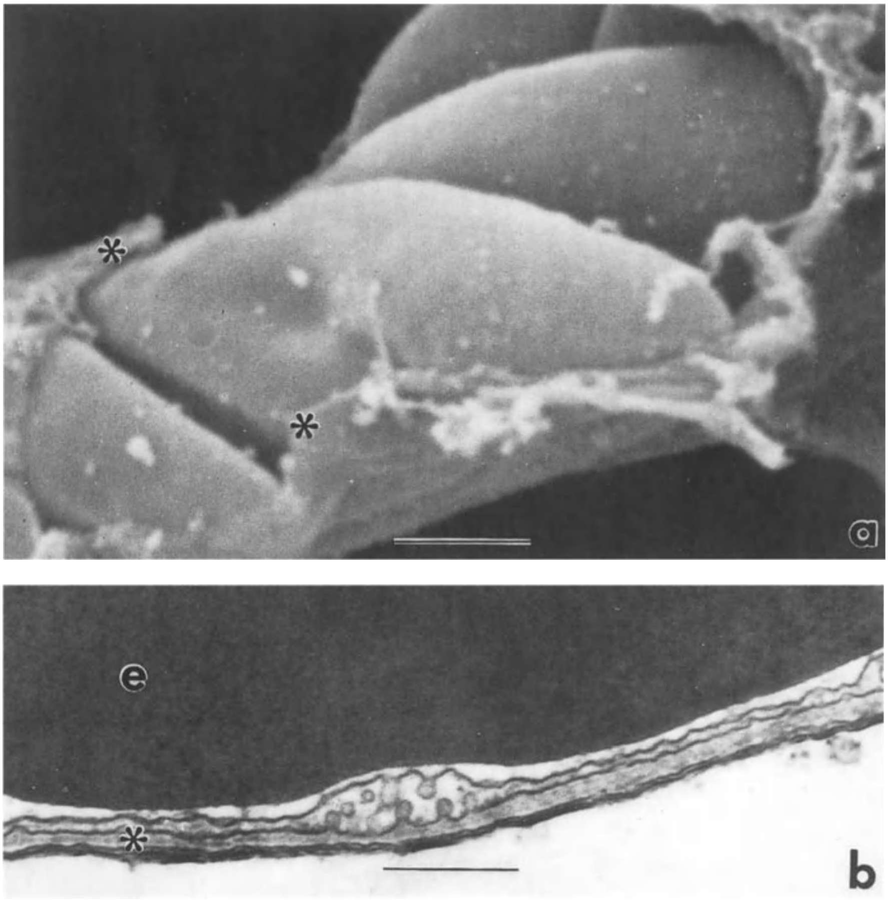


Fig. 29. **a** Blood capillary in the lung of the domestic fowl, *Gallus domesticus*, showing a file of erythrocytes in a blood capillary. *, blood-gas barrier. **b** The extremely thin blood-gas barrier, *, shows sporadic attenuations. *e* erythrocytes. **a** *Bar* 0.6 μm; **b** 0.6 μm. (Maina 1993)

diffusional limitations in the layer of water next to the skin (Feder and Burggren 1985a,b). In fish, factors such as low body temperature, thick water-blood barrier, and presence of an unstirred water layer over the secondary lamellae reduce O_2 transfer. They may cause significant diffusion limitations and curtail end-capillary equilibration particularly during resting normoxic conditions (Randall and Daxboeck 1984). At a simulated altitude of about 12 km, the resting bar-headed goose, *Anser indicus*, tolerated inspired PO_2 of about 3 kPa and no difference was observed between the PO_2 in inspired air and that in the arterial blood (Black and Tenney 1980): the arterial PCO_2 was as low as 1.1 kPa. Due to the large arteriovenous shunts which cause notable arterial O_2 desaturation in the amphibian and reptilian lungs (Glass and Wood 1983; Wood and Glass 1991), diffusional limitations are masked.

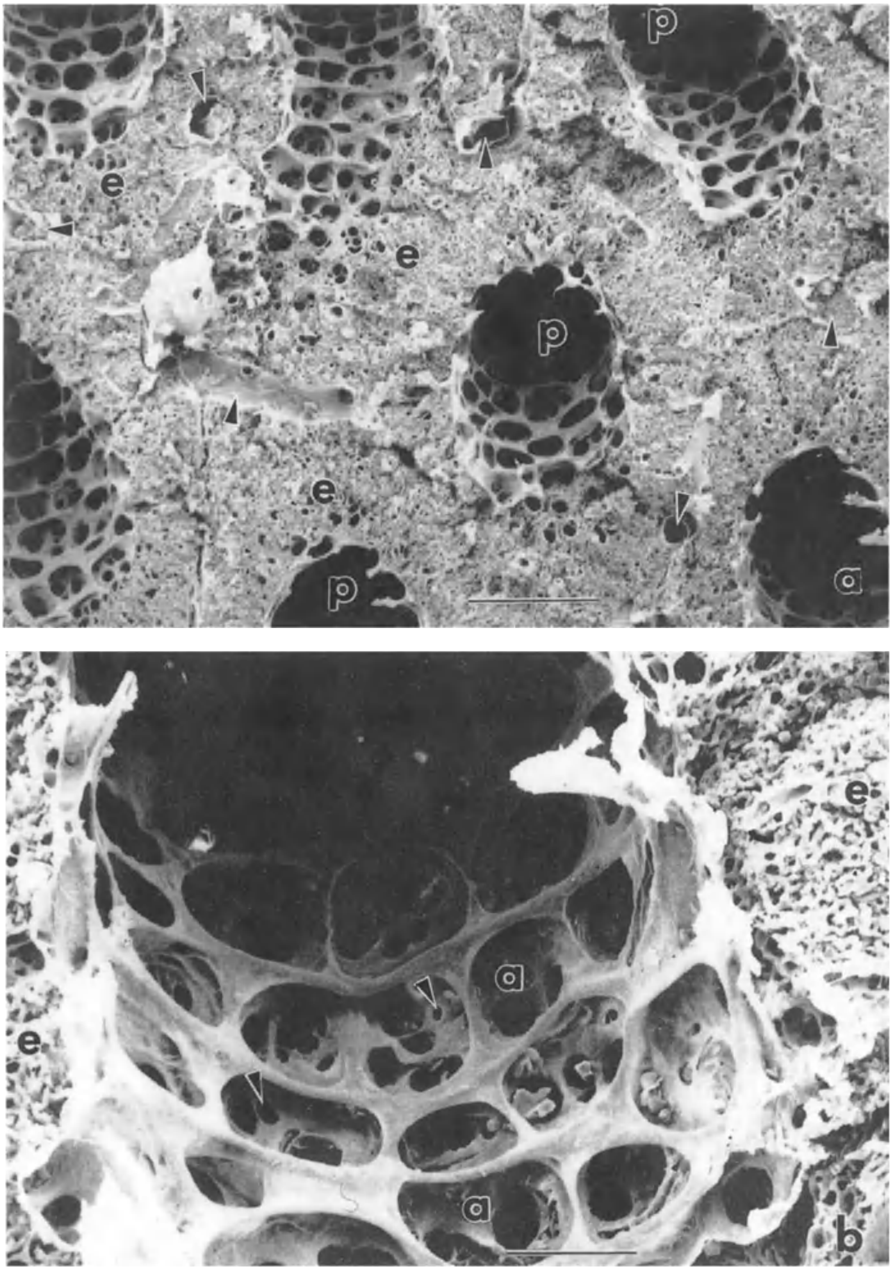


Fig. 30. **a** Lung of the domestic fowl, *Gallus domesticus* showing parabronchi, *p*, surrounded by gas exchange tissue, *e*, and blood vessels, ➤, located in the interparabronchial septa. **b** Closeup of a parabronchial lumen showing atria, *a*, and infundibulae, ➤, which channel air to the exchange tissue (*e*). **a** *Bar* 70 μm; **b** 20 μm

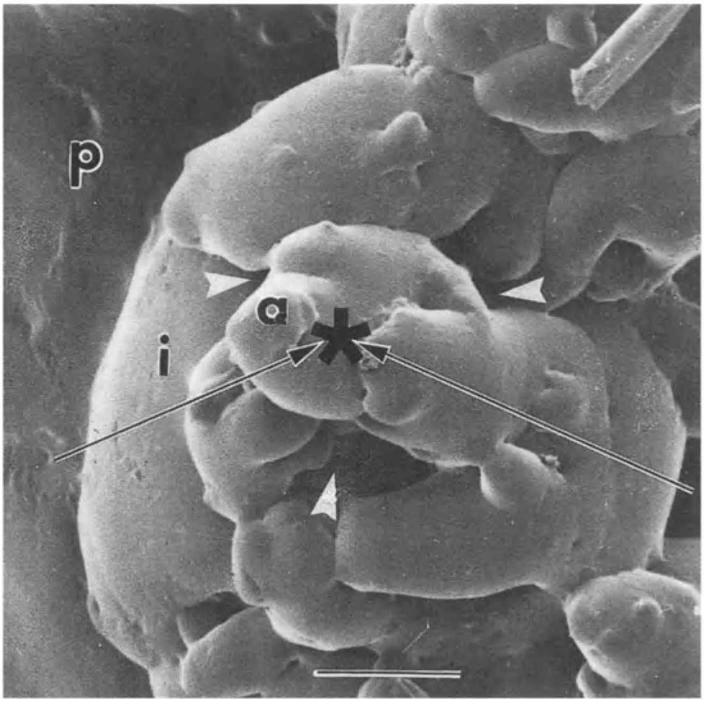


Fig. 31. Latex cast of the airways of a bird lung, *Gallus domesticus*. This closeup shows an atrium arising from a parabronchus, *p*, giving rise to an infundibulum, *i*, terminating in an air capillary, *a*. The perpendicular to the arrows, →, converging onto the star, *, illustrate the distance O_2 has to diffuse from the parabronchus to the air capillary. ➤, spaces occupied by blood capillaries. *Bar* 40 μm

2.9.2 Efficient vs. Inefficient – Primitive vs. Advanced Gas Exchangers: the Contention

From cladistic principles, the morphological, physiological, and biological character states of organisms are considered either to be primitive or derived. Commonly, these interpretations are subjective. For example, some organisms (e.g., bacteria) which are notably speciose and highly adapted to particular habitats where they thrive and even outcompete supposedly better-adapted forms are deemed primitive. Strictly, in a particular animal lineage, the primeval (plesiomorphic) features should be taken to be those which characterize the ancestral forms. The derived (apomorphic) features typify the more recent animal groups. A character which is unique to an animal (an autamorphic mark) indicates a unique adaptive state. The primitive features are assumed to be inefficient while the advanced (= derived) ones are taken to be adaptive (= more efficient). The fact that the so-called primitive features have been saved for millennia amidst intense selective pressures emphasizes either their neutral selective value or the exceptional advantage(s) they confer for survival in a particular habitat. Gould (1994) opines that "our impression that life evolves towards greater complexity is probably only a bias inspired by parochial focus on ourselves and consequent over attention to complexifying creatures while we ignore just as many lineages adapting equally well by becoming simpler in form". Along the same argument, Thompson (1959, p. 41) points out that "however important and advantageous the subdivision of the tissues into cells may be from the constructional, or from the dynamic, point of view, the phenomenon has less fundamental importance than was once, and is often still, assigned to it".

Primitive and derived features exquisitely allow different kinds of animals to subsist in the same habitat. The different resource procuring capacities enable the congeners to fill species-specific spatial and/or temporal ecological niches without undue competition. Special environments are characterized by low biodiversity though the numerical densities of the occupying species may be very high. Pough et al. (1989) assert that "the primitive character state is not inferior or necessarily less adaptive, it is simply older". These sentiments are echoed by Kardong (1995), who observes that "the notion of better does not apply to biological changes: primitive and advanced species represent different ways of surviving not better ways of surviving". From these sentiments, the terms primitive and derived should be used to define only the temporal appearance, i.e., the chronological advent of certain attributes in the phylogentic history of a particular animal lineage and not the polarity of a change. The primitive features are those that occur in the ancestral members of the group while the derived ones are found in the modern forms and differ in notable morphological and physiological ways from the primordial condition. Gas exchangers are designed to service given cytoplasmic masses operating within certain metabolic boundaries. Overdesign is costly and wasteful. In the context of functional capacities, strictly, primitive gas exchangers do not exist.

The simplest design and apparently the most efficient evolved gas exchanger has occurred in form of the insectan tracheal system (Sect. 6.6.1; Figs. 74,75). Few animals have successfully emulated it. Gas exchangers present certain properties which are fundamental in explaining the remarkable diversity of design. These are: (1) the transfer of gases from the external milieu to the body and vice versa occurs by the physical process of diffusion, (2) there is no ubiquitous structural plan: one or more pathways may be utilized simultaneously or in phase, (3) there is only a weak correlation between the constructional complexity, efficiency, and the phylogenetic level of development, and (4) the diffusion of gases across the tissue barriers occurs in solution. To enhance the diffusing capacity, efficient gas exchangers must have an extensive respiratory surface area, a thin blood-gas barrier, and must be well perfused with blood and ventilated with the ambient respiratory medium. Organs as diverse as the anus, stomach, mouth, and skin are used as gas exchangers. The advanced animals, e.g., mammals, do not necessarily have the most efficient gas exchangers. Invagination of the gas exchangers not only afforded a greater respiratory surface area but also provided better control and regulation of the physical characteristics of the inhaled air which must be cleansed and particularly moistened to curtail water loss from the alveolar surface.

2.10 Modeling: Utility in Study of Integrative Construction of the Gas Exchangers

Gas exchangers are complex, dynamic, high fidelity systems. Respiration entails intricate interplay between physiological features such as convection, diffusion, and chemical reactions (e.g., Piiper et al. 1971; Wagner 1977) and anatomical factors such as the architecture and geometry of the airways and the respiratory barriers. Morphological observations and quantification of the components of gas exchangers makes it possible to construct realistic models and also advance understanding of the evolutionary processes that have precipitated the diversity in form and function in the process of adaptation to environments and adoption of different lifestyles. Through selective pressure acting on the genotype, the gas exchangers have been honed to meet species-specific, design-oriented needs. The final constructional plans present rational, multifaceted, integrated engineering (Beament 1960; Dullemeijer 1974; Gutman 1977). An intractable number of variables (of which the individual functional capacities may not be sufficiently known) contribute to the ultimate fabrications of biological systems. Biology has long been mathematically emancipated and somewhat changed from how it was once perhaps legitimately described, as a descriptive (inexact) science (compared with physical science). In the gas exchangers, the pulmonary diffusing capacity, defined as the flow rate of O_2 from air to blood under partial pressure gradient between alveolar and mean O_2 tension in the alveolar capillary blood (Bohr 1909; Roughton and Forster 1957; Forster 1964; Weibel 1970/71) is the outcome of the integration of the functional and structural parameters. The functional anatomies of composite structures (e.g., the gas exchangers) can be adequately described through appropriate modeling, i.e., by integrating the relevant parameters central to an organ system, e.g., the respiratory (Singh et al. 1980; Federspiel and Popel 1986; Bozinovic 1993) and the cardiovascular systems (Zagzoule and Marc-Vergnes 1986; Wang et al. 1989; Melchior et al. 1992). Gutman and Bonik (1981) defines a model as “an abstraction of a real situation which describes only the essential aspects of the situation”. Implicit if not explicit assumptions underlying various parameters and properties are often made. A mathematical model aims to “dismember” a structure into the formidable number of individual components, isolates those components that are relevant in answering the question at hand, and then reassembles it. The model must endeavor to be accurately descriptive of the complex reality of nature, must be simple and easy to conceptualize, and must be theoretically and practically testable. By applying appropriate physical and physiological constants, a static structural model can mathematically be converted to an acceptably dynamic one. The net worth of a model can be judged from its predictive potential. In modeling highly dynamic systems, e.g., the wing beat kinematics of an insect in flight (Weis-Fogh 1973; Ellington 1981, 1984; Wilkin and Williams 1993) and atmospheric turbulence (e.g., Hollinger et al. 1994), a defined state (e.g., a steady- or a quasisteady state) has to be assumed. Complex systems are intrinsically chaotic and are hence unpredictable (Gleick 1987). Experimental manipulation of a functional model gives an insight into the cause-and-effect relations between the individual and the covariant factors that drive a system. Outcomes can be evaluated by altering one or more factors or conditions while holding others constant. Constraining, potentiating, and superfluous components can be identified and the relative performances determined. Based on structural-functional integrative studies, encompassing observations can be made on the gas exchangers. Depending perhaps on the approach adopted and the emphasis laid on the different parameters which are considered, in some cases the conclusions have turned out different. Assessing the factors which determine O_2 flow from the lung to the muscle tissue during exercise, Weibel et al. (1987a) and Karas et al. (1987a) concluded that "cardiac output is the most important variable controlling flow of O_2 through all steps of the respiratory system". However, evaluating the factors which limit the delivery of O_2 to the skeletal muscles in an exercising human being, Saltin (1985) resolved that "pulmonary diffusing capacity is the ultimate limiting factor" during extreme conditions. In a theoretical model, Wagner (1993) concluded that at sea level, cardiac output has the greatest effect on VO_{2max} while at altitude, muscle diffusing capacity is the most important parameter. Explaining the 2.5-fold higher maximum O_2 consumption in the athletic species (pony and dog) over that of the less athletic ones (calf and goat), Karas et al. (1987b) attributed one half of it to the higher PO_2 at the blood-gas barrier (1.7-fold greater in the athletic species) and the other half to the diffusing capacity which was 1.5-fold larger. It is most instructive to be able to accurately predict, infer the consequences of, or explain how one or a group of respiratory variables affects the others. Physiologic and morphometric estimations of diffusing capacities of different gas exchangers, e.g., fish gill (Scheid and Piiper 1976; Piiper et al. 1977, 1986; Hughes et al. 1986b), mammalian lung (Gehr et al. 1978; Weibel et al. 1983), and bird lung (Maina et al. 1989a; Vidyadaran et al. 1988; Burger et al. 1979) are now available. In all cases, the morphometric value exceeds the physiological one. This has been interpreted to indicate a safety margin of operation. In estimating the morphometric diffusing capacity, an ideal state is assumed, i.e., that O_2 flux occurs across the entire water-air /blood barrier under a ventilation-perfusion ratio of unity. This state is only approached at maximum O_2 consumption (e.g., Powell and Wagner 1982a,b). Gans (1985) holds that "animals cannot afford one-function/one-structure designs "and" each activity tends to involve multiple aspects of the phenotype and each aspect of the phenoytpe may be involved in multiple activities" (Gans 1988). Empirical prototypes in form of biological models provide useful insights (even though in theoretical way) into the underlying control mechanisms, the multidimensional utilization of the phylogenetic characteristics, and the effect altered parameters have on the entire system (Cameron 1989; Anker and Dullemeijer 1996). Simplification, abstraction, and generalization of biological processes and concepts have contributed greatly to the advancement of scientific thought (Homberger 1988; Vogel 1988).

Gas exchangers, like most organs, present a multilevel organizational character. The various parts of a structure are arranged in discrete functional units which are, in turn, intricately connected to ensure integrity in the overall performance. For optimal transfer of gases at the exchange site, the convective (ventilatory and perfusive) pumps must be coherently linked so that the gas delivered across the respiratory barrier is immediately removed to maintain a concentration gradient. Overperfusion relative to ventilation or vice versa incurs unnecessary metabolic cost. The actual quantity of respiratory gases transferred across the barrier in such episodes is lower than that prevailing during the optimal and less expensive conditions. The ideal ventilation-perfusion ratio in mammals is about 1 : 1 (West 1977a) and in the chelonian reptiles it is 2 : 1–5 : 1 (Burggren et al. 1977). In aquatic fish, the equivalent value is 9 : 1–35 : 1 (Randall 1970). By refining and multiplicatively integrating the structural and physiological parameters such as lung volume, cardiac output, hemoglobin concentration, muscle mass, and mitochondrial number, land vertebrates such as the pronghorn antelope, *Antilocapra americana* (Lindstedt et al. 1991), and the cheetah, *Acionyx jubatus* (Hildebrand 1959, 1961), can attain and sustain speeds of 75 to 100 km per h. Lindstedt et al. (1991) estimated that the pronghorn antelope can take up O_2 at a late of 3.2 to 5.1 ml O_2 $kg^{-1} s^{-1}$, a value 3.3 times greater than that predicted for a typical mammal (1.5 ml O_2 $kg^{-1} s^{-1}$) of a similar body mass of 32 kg. On the other hand, the naked mole rat, *Heterocephalus glaber*, a highly inbred (Reeve et al. 1990), eusocial (Burda 1993), heterothermic, low metabolism animal (McNab 1966) which lives in a stable environment (Cossins 1991) has neotenic lungs (Maina et al. 1992). The pulmonary morphometric diffusing capacity of the lung of the mole rat, *Spalax ehrenbergi* was found to be 40% greater than that of an equivalently sized surface-dwelling white rat (Widmer et al. 1997).

2.10.1 Evaluation of the Functional Efficiency of the Gas Exchangers

Analysis of the performance of a gas exchanger entails physiological measurements of O_2 tensions prevailing in the gas exchange media or that between the arterial and venous blood. This is done by taking cognizance of the inherent construction of the exchanger and the fluid flow dynamics within and without the gas exchanger. Respiratory efficiency can also be gauged from the quantity of O_2 transferred against the energy expended during the process (e.g., Piiper and Scheid 1992; Shelton 1992). By varying or holding certain factors constant while integrating or suppressing others, the contributions of the various variables to the overall function can be evaluated and the limiting or potentiating factors identified. The efficiencies of different or same gas exchanger(s) under different operating conditions can be compared. Though gross mathematical abstractions of a complex biological system which is regulated by an infinite number of variables, all of which are difficult to individually assess, manipulatable theoretical analogs are highly instructive in comparative experimental and analytical studies: they generate "artificial" didactic situations which afford a perception of a complex outlay. Physiological phenomena are cumulative effects of interactions between numerous minuscule, individually noneventful, nonlinear, but coupled local unit processes which interact at various levels with a potentiating or even a depreciative effect. Though with intrinsic limitations, functional and morphological models are extremely valuable in the understanding of the complex relations in multidimensional systems (e.g., Riggs 1963; Penry and Jumars 1987; Usry et al. 1991; Horn and Messer 1992). From the results of functional and structural analyses, a piecemeal synthesis of an organ system can be made. The efficiency of

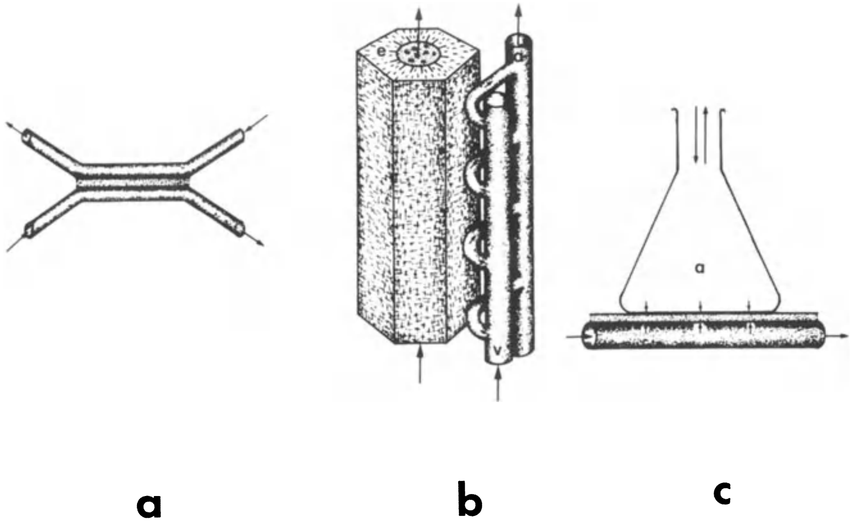


Fig. 32a–c. Schematic drawing showing the spatial relationship between air and blood flow, →, in the fish gills (**a**) and bird (**b**) and mammalian (**c**) lungs. In fish, air and blood flowing in a countercurrent manner. In birds, the flow between the parabronchial blood (*small arrows*) and the air flow in the parabronchial lumen is crosscurrent. In the mammalian lung, the flow is described as uniform pool. *e* Parabronchial gas exchange tissue and air flow in the lumen, ↑; *v* venous blood; *a* (in **b**) arterial blood; **c** *a* alveolar air; ↓, diffusion of O_2 across the blood-gas barrier: →, direction of alveolar capillary blood flow; ⇆, tidal ventilation of the mammalian lung. To a large extent, the efficiency of the gas exchangers depends on the presentations between the gas exchange media

a gas exchangers is largely determined by the nature of presentation of the respiratory media (Fig. 32) which is dependent on the intrinsic refinements and the geometric arrangements of the structural components (Figs. 29,33,34). Capillary geometry and tortuosity has a profound effect on the efficiency of O_2 transfer in muscles (e.g., Ellis et al. 1983; Groom et al. 1984a,b; Mathieu-Costello 1990; Mathieu-Costello et al. 1992). Biologists can appropriate the mathematical and conceptual contrivances of engineers to discern how animals function and why they have acquired certain morphologies.

2.10.2 Modeling the Gas Exchangers

In its most simplistic form, the respiratory system can be conceptualized as a set of compartments interposed between the body tissue cells and the environment. Across the cascade, which comprises the gas exchanger (ventilatory convection), water/air-blood barrier (diffusion), blood (circulatory convection), systemic capillary bend, interstitial fluid, and cells (diffusion), O_2 and CO_2 flux at intensities essentially determined by the metabolic states and environmental circumstances. It is mainly in the chordates where adequate structural and functional data have

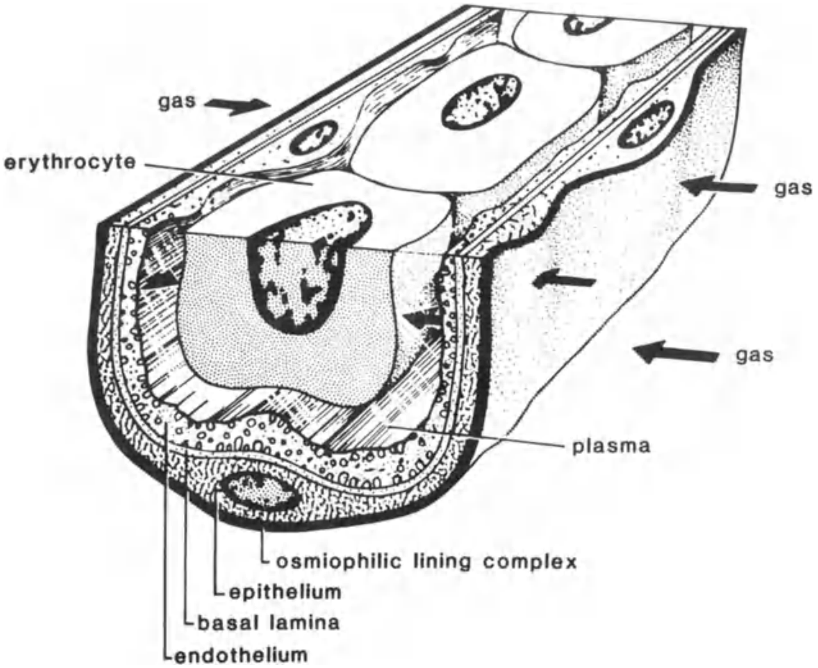


Fig. 33. Schematic view of a pulmonary blood capillary showing the in-series components of the air-hemoglobin pathway, namely the blood-gas (tissue) barrier (which comprises a surface lining, an epithelial cell, a basement membrane, and an endothelial cell), plasma layer, and the erythrocytes. O_2 uptake by the erythrocytes constitutes the greatest point of resistance to flow. (Maina 1994)

been gathered to warrant satisfactory modeling of the gas exchangers. The general model relating diffusion of gases across the blood-gas barriers and the water-blood barriers to ventilation and perfusion (e.g., Piiper and Scheid 1975) has been extensively used in different gas exchangers (e.g., White and Bickler 1987). Morphometric pulmonary modeling after Weibel (1970/71) has been carried out in many gas exchangers, e.g., fish gills (Hughes 1972b), reptilian (e.g., Perry 1983), avian (e.g., Maina 1989a), and mammalian lungs (e.g., Gehr et al. 1981).

When the gas exchange media, i.e., the external (the ventilatory) and the internal (the perfusive) media run parallel to each other and in the same direction, the design is termed concurrent. If the media run in opposite directions (e.g., water and blood in the fish gills), it is called countercurrent and when the media run at right angles to each other, e.g., the blood capillaries of the parabronchial exchange tissue relative to the flow of air in the parabronchial lumen of the bird lung), the arrangement is designated crosscurrent. When the external medium is held constant against a gas exchanger (e.g., skin) or is ventilated with a medium of which the gaseous partial pressures are fairly uniform (e.g., mammalian lung where the alveolar gas exerts a steady-state concentration)

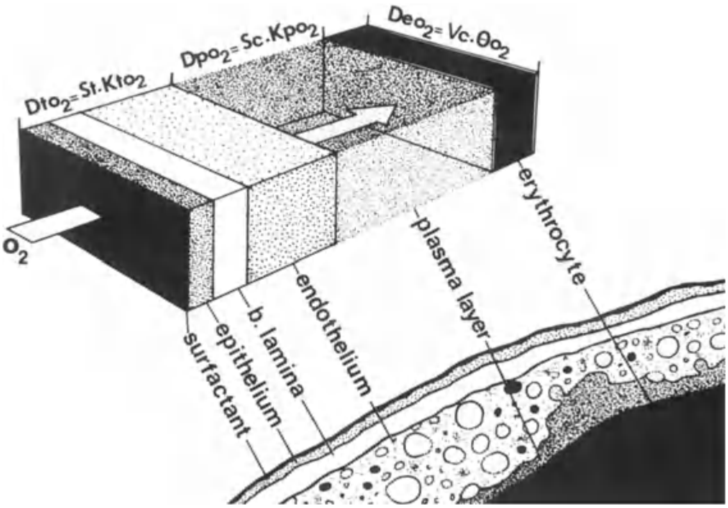


Fig. 34. Model for estimating pulmonary diffusing capacity or conductance of a lung for O_2 (DLo_2). The principal barriers which influence Do_2 are the tissue barrier [epithelium + basal lamina (interstitium in some cases) + endothelium], the plasma layer, and the erythrocytes. DLo_2 is directly proportional to the surface area and the permeation constant and inversely proportional to thickness. Respectively: Dto_2, Dpo_2 and Deo_2 diffusing capacities of the tissue barrier, plasma layer, and erythrocytes; *St* and *Sp* surface areas of the tissue barrier and plasma layer; *Vc* volume of the pulmonary capillary blood; Kto_2 and Kpo_2 Krogh's oxygen permeation coefficients of the tissue barrier and plasma layer; o_2 - O_2 uptake coefficient by the whole blood. The products of St and Kto_2 and Sc and Kpo_2 must be divided (not shown on the figure) by the harmonic mean thickness (τht) of the respective barriers. (Maina 1993 courtesy Pergamon Press). For a detailed account on the model as applied to the bird lung, see Maina et al. (1989a)

(Milhorn et al. 1965), respectively, the configurations are termed infinite pool and uniform pool (White 1978; Figs. 30,32,35,36). In the small insects, O_2 is conducted directly to the tissues by diffusion through trachea (Maina 1989b; Figs. 36,37) and by convection through the air sacs in the larger ones (Fig. 38). Delivery of O_2 directly to the tissue cells is a more efficient means of gas transfer (Sect. 6.6.1) compared with the conventional one where the molecule is convectively transported through a circulatory system (Levi 1967; Bromhall 1987).

By fitting or approximating a gas exchanger to any of the above main models, the efficiency and the limitations (be they developmental, structural, or functional) inherent in a particular gas exchanger under different circumstances can be gauged (Hills 1972; Piiper and Scheid 1972, 1975; Sikand et al. 1976). The relative efficiencies between different gas exchangers can be assessed. In a concurrent design, the gas tension in the internal medium leaving the exchanger cannot possibly exceed that of the external medium in normal and about equal fluid flows. However, under special conditions, e.g., when large quantities of water flow very fast over a small volume of slowly moving film of blood, a high degree of oxygenation with low utilization can be realized (Hughes 1963) but after

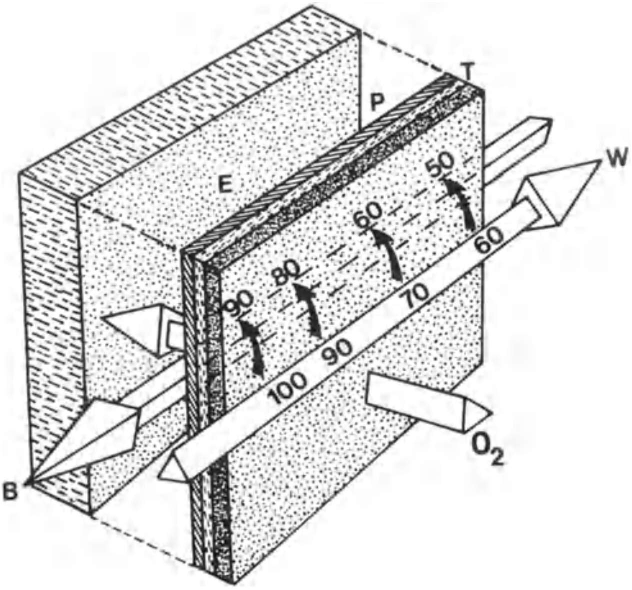


Fig. 35. Countercurrent system. The exchange media which contain O_2 at different concentrations flow in opposite directions. A diffusional gradient prevails over the duration and length of contact. A countercurrent arrangement occurs in the fish gills where O_2 extraction has been reported to be as high as 96%. *Numbers* Percentage concentrations of O_2 in the respiratory media; ↗ O_2 flows down a concentration gradient; *T* tissue barrier; *W* water; *E* erythrocytes; *P* plasma; *B* blood. (Maina 1994)

great energy expenditure on ventilatory work. In such cases, the gain in real terms is very small. In a countercurrent system, since the efferent blood has been exposed to the inhalant water, the PO_2 between the two media is high. Unlike in the mammalian lung, where theoretically ventilation-perfusion homogeneity may allow alveolar PO_2 to equilibrate with the arterial PO_2, in the fish gills arterial blood and inspired water never reach equilibrium (Randall 1970). This may be attributed to factors such as the thick water-blood barrier (e.g., Hughes and Morgan 1973), the large ventilation-perfusion inequalities (Booth 1978), and added diffusion limitations resulting from the boundary layer of water close to the surface of the secondary lamellae (Hills 1972). The ventilated uniform-pool design in most vertebrate lungs is more efficient than the nonventilated one (e.g., the skin and the buccal cavity). However, behavioral changes such as exposure to air currents and movement may initiate passive ventilation enhancing gas exchange. In the human lung, due to the tidal nature of air renewal, only about 12% of the intrapulmonary air volume is exchanged at the alveolar level per inspiratory cycle. Due to the low efficiency of the concurrent system, the design has only rarely been invoked in evolutionary biology. In contrast, the countercurrent system is widely encountered in biology (Scholander 1958) especially in form of heat exchangers, e.g., cephalic and ophthalmic rete (Jackson and Schmidt-Nielsen 1964; Kilgore et al. 1979; Baker 1982; Midtgärd 1983, 1984; Kamau et al. 1984;

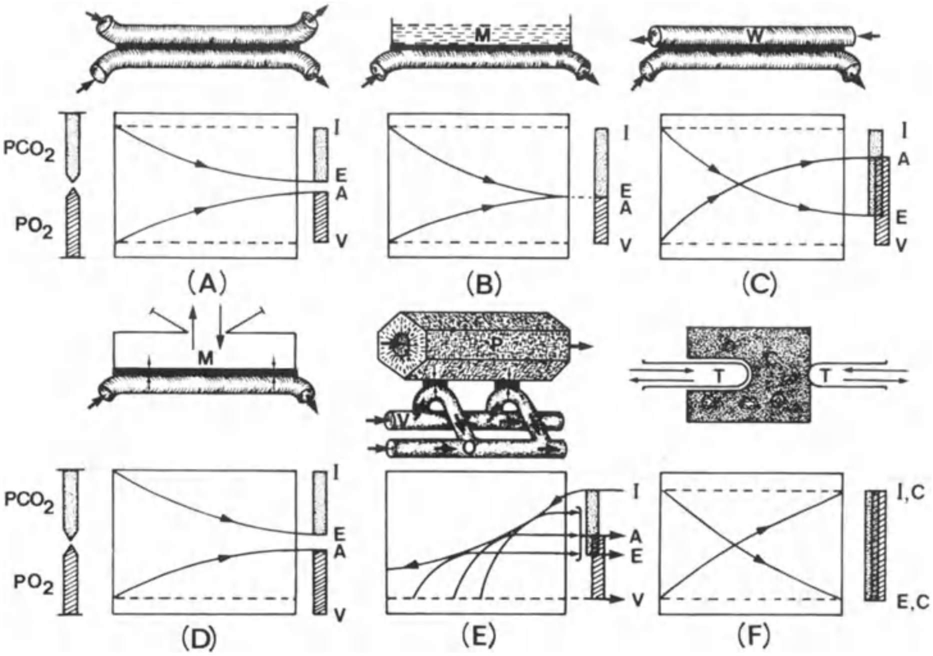


Fig. 36A–F. Schematic illustrations showing the geometric interactions between the respiratory media in different gas exchangers. The respiratory efficiencies are shown by the PO_2 and PCO_2 profiles in the inspired air, *I*, expired air, *E*, venous blood, *V*, and arterial blood, *A*. **A** Cocurrent system: gas exchange media flow in the same direction and O_2 flux is very low; **B** The skin: the gas exchanger is perfused but not ventilated. **C** Countercurrent arrangement: the PO_2 in the arterial blood exceeds that in the end expired air. **D** Uniform-pool: the influx of O_2 depends on ventilation and perfusion inequalities. **E** Crosscurrent system in the bird lung: through the multicapillary serial arterializational arrangement, the PO_2 in the arterial blood may exceed that in the expired air. **F** The insect tracheal system: O_2 is delivered directly to the tissue cells (by the tracheoles, *T*) with the PO_2 at the cell level being only slightly lower than that in the ambient. The PO_2 in the arterial blood may exceed that in the expired respiratory medium only in models **C**, **E**, and **F**. *m* Respiratory medium which depending on the type of animal could be air or water: *p* parabronchus; *c* cell; *v* blood (venous); *w* water. In the schematic drawings, the *single arrows* show the directions of flow of respiratory media and the diffusion of O_2; ⇆ *arrows* show the gas exchangers which are tidally ventilated. (Maina 1994)

Pinshaw et al. 1985; Block 1987), salt-concentrating systems such as kidneys and salt glands of birds (Kokko and Tisher 1976; Schmidt-Nielsen 1990), and in gas secretion organs, e.g., the choroid rete (Wittenberg and Wittenberg 1962) and the rete mirabile of the swim (air) bladder of fish (Fig. 39; e.g., Kuhn et al. 1963; Kobayashi et al. 1989a,b; Pelster and Scheid 1992a). Chemical (e.g., Coulson and Richardson 1965) and mechanical engineers (e.g., Carslaw and Jaeger 1959) exploit countercurrent systems to enhance concentration gradients in order to improve mass transfer. The functional efficiency of the countercurrent system depends on factors such as a thin and extensive surface area for interaction of the gas exchange media, optimum flow rates and physical states and characteristics.

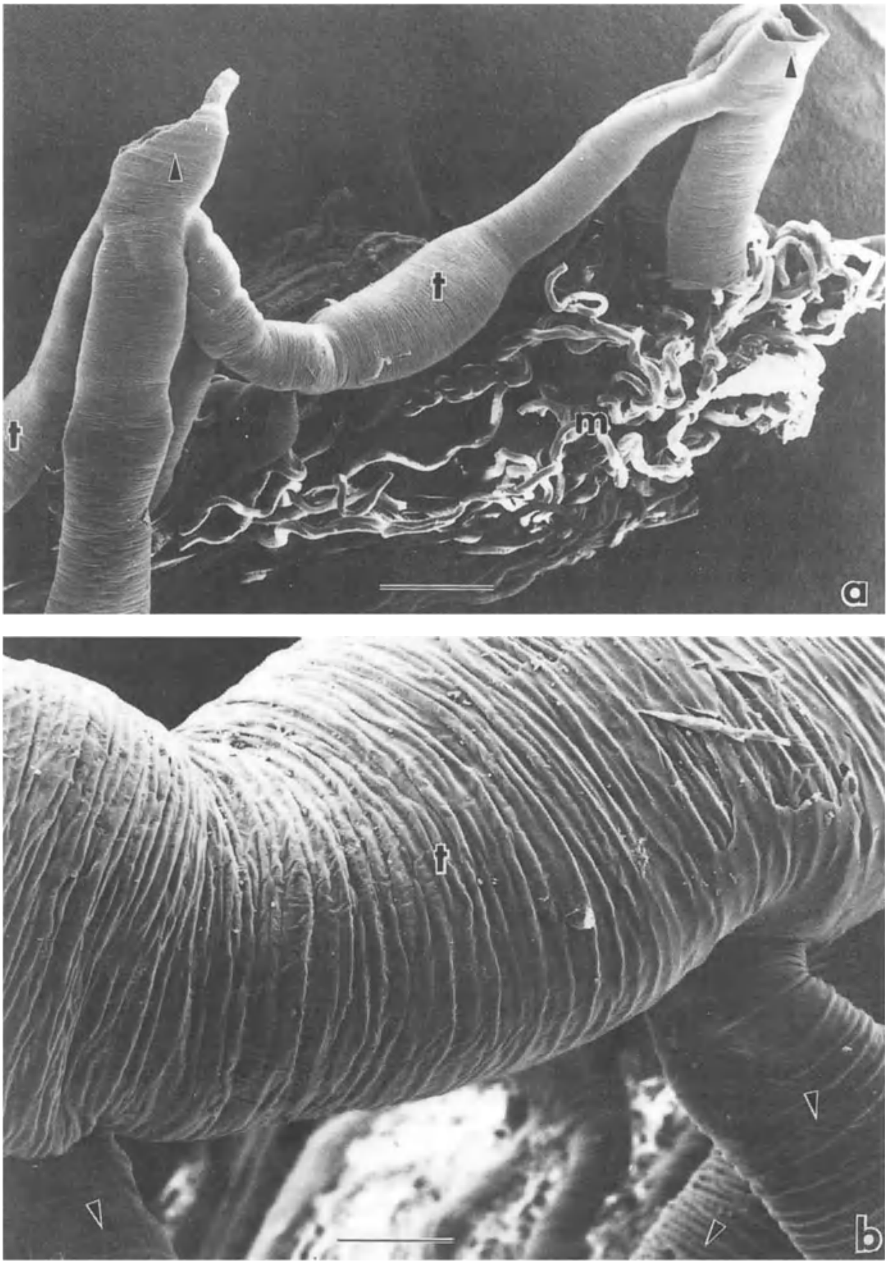


Fig. 37. **a** Tracheal system of a grasshopper, *Chrotogonus senegalensis*. The primary trachea which start near the spiracles, ➤, are connected through anastomotic chains, *t*. *m*, Malpighian tubules. **b** Closeup of a primary trachea, *t*, showing the spiral taenidia which maintain patency. ➤, secondary trachea. (Maina 1989b.) **a** *Bar* 700 μm. **b** 80 μm

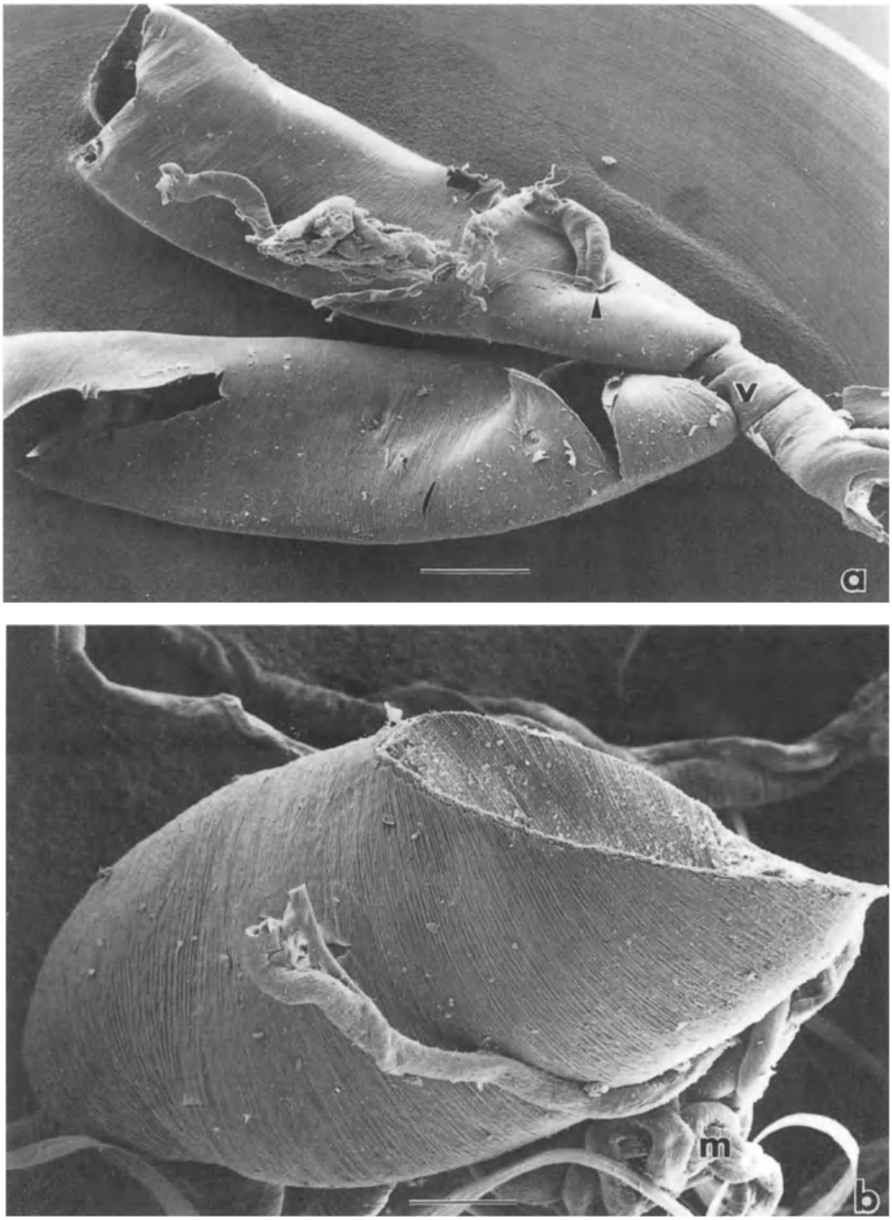


Fig. 38a,b. Air sacs of the grasshopper, *Chrotogonus senegalensis*. The air sacs occur in pairs (**a**), singly (**b**) or in clusters. They are characteristic of the large and the energetic insects which use abdominal pumping to enhance movement of air along the tracheal system. ➤, efferent trachea; *v*, possible location of a valvular apparatus which maintains a unidirectional flow of air in the tracheal system; *m*, Malpighian tubules. Like the trachea, the air sacs are made up of helical taenia, indicating that they are simply dilatations of the trachea. (Maina 1989b) **a** *Bar* 700 μm; **b** 220 μm

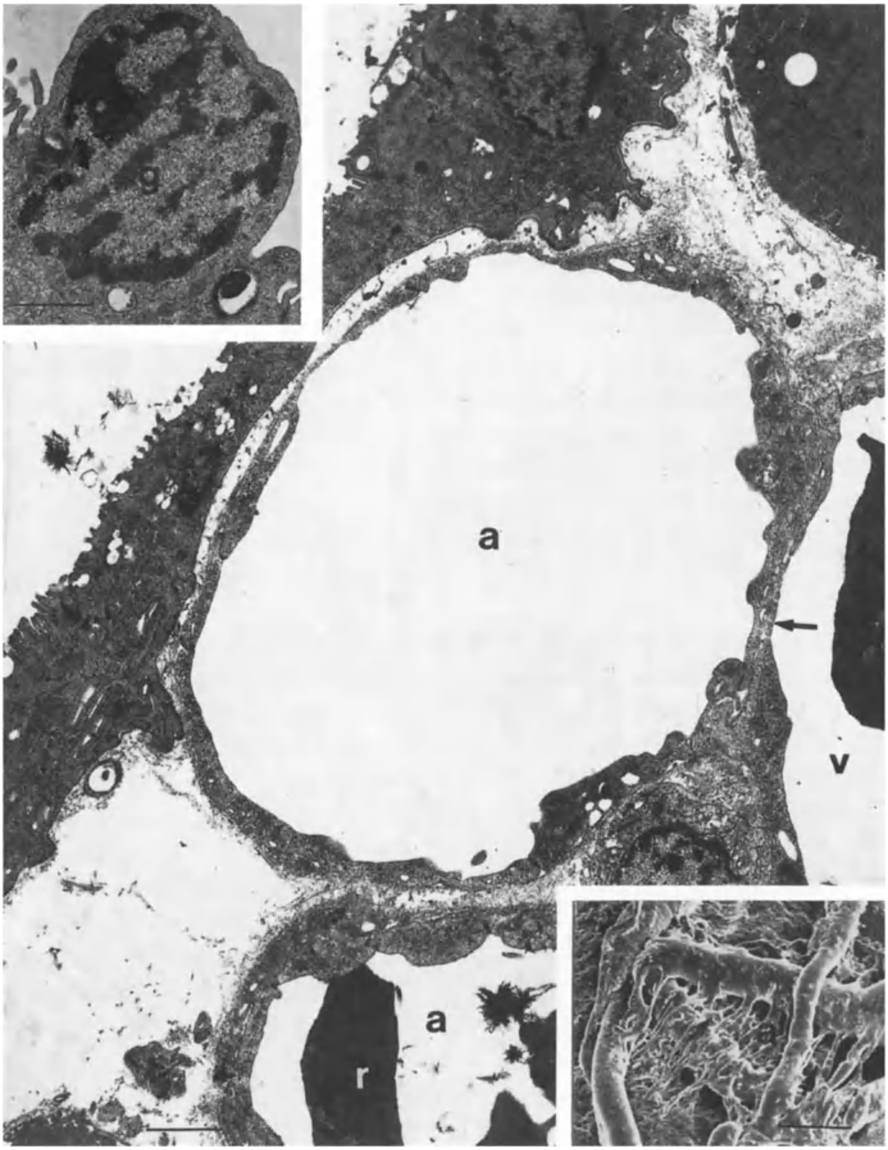


Fig. 39. The gas gland cell, *g* (*top inset*) and the rete mirabile of the swim bladder of a tilapiine fish, *Oreochromis alcalicus grahami* (*main figure* and *bottom inset*). The *bottom inset* is a latex cast SEM preparation of the arterial vasculature at the rete. The venules (*v* in the *main figure* and *arrow* in the *bottom inset*) and arterioles, *a* (*main figure*) run parallel to each other. Secretion of the acidic metabolites produced by the gas gland cells into the arterial blood and subsequent transfer into the venous blood causes release of blood gases into the bladder. ← (*main figure*) shows an extremely thin area of separation between a venule and an arteriole, sites which may promote the transfer of the acidic metabolites released by the gas gland cells. *r* Red blood cell. *Bars top inset*, 0.25 μm; *main figure* 0.8 μm; *bottom inset*, 16 μm. (Maina et al. 1996a)

In biology, however, countercurrent heat exchangers cannot simultaneously serve as efficient gas exchangers. To enhance heat transfer by bulk flow, the blood vessels of the heat exchanger have a diameter in excess of 1 mm. Gas exchange by diffusion can only efficiently occur at the capillary level where the walls are adequately thin. In fact, if O_2 were to diffuse equally well in the heat exchangers, very little, if any, O_2 would reach the peripheral tissue. Such arrangements (countercurrent heat exchangers) would have to be very sparingly used (if at all) in biology. The low O_2 tension found in the kidney tissue (e.g., Landes et al. (1964), an organ supplied with a large volume of blood, may be due to diffusion of O_2 between the blood capillaries supplying the renal papilla and those leaving it, i.e., the descending and ascending versa recta. In birds, interestingly, while the ophthalmic rete is considered a countercurrent exchanger (e.g., Kilgore et al. 1979; Midgärd 1983), it has been shown to supplement O_2 supply to the brain during high altitude flight (Bernstein 1989, 1990; Bernstein et al. 1984): the arterial blood passing through the rete en route to the brain exchanges O_2 with the venous blood, which has a higher PO_2 after draining the highly vascular eye, nasal cavity, and upper respiratory passages. Pigeons have been reported to increase cerebral blood flow during hypoxia (Pavlov et al. 1987). In mammals, direct estimations of the PO_2 in the arterial vessels of the carotid rete and systemic arterial blood indicate that a gas exchange process does not occur in the organ (Duling et al. 1979). The great efficiency of the countercurrent system of the fish gills (Fig. 36) may have been necessary for survival in a medium usually deficient in O_2 and where the levels may fluctuate dramatically spatially and temporarily. In birds, the interaction of the pulmonary capillary blood in the parabronchial gas exchange tissue (Maina et al. 1982b) occurs across a thin blood-gas barrier and an extensive surface area (Maina 1984, 1987a; Fig. 40). A continuous unidirectional air flow enhances the efficiency of the gas exchange process (Figs. 32,36). Through the multicapillary additive serial arterialization system which is built in the crosscurrent geometric arrangement between the parabronchial air flow (the air in the parabronchial lumen) and the pulmonary venous blood (Figs. 41,42), in some conditions (e.g., hypoxia and exercise), O_2 level in the arterial blood may exceed that in the end expired air (Scheid and Piiper 1972, 1989; Fig. 36). The avian lung-air sac system is more efficient in arterializing blood than all the other evolved air breathing organs of the vertebrates (Powell 1990). The arterial PCO_2 in birds may be as low as 0.93 kPa (equivalent value in mammals = 5.6 kPa) compared with that in the expired air of 5.3 kPa (Scheid and Piiper 1972; Scheid 1990). The O_2 extraction ratio in fish and cephalopods ranges between 50 and 80%, in polychaetes 30 and 70%, in crustacea 43 and 76%, sponges 6 and 40%, lamellibranchs 3 and 10%, and ascidians 4 and 7% (Benedict 1938; Hazelhoff 1939; Randall et al. 1967; Hanson and Johansen 1970). A remarkably high value of 92% has been reported in the triggerfish, *Balistes capriscus*, by Hughes (1967). In fish inhabiting well aerated water, the arterial PO_2 is generally high and usually exceeds the values needed to totally saturate the blood (Stevens and Randall 1967). Expectedly, the ventilation-perfusion ratios in fish are very high and range from 9 in the shark, *Scyliorhinus* (Baumgarten-Schumann and Piiper 1968), to as high as 70 in the trout (Randall et al. 1967): the markedly high value in the trout is due to a high ventilatory rate occurring with low O_2 extraction from water.

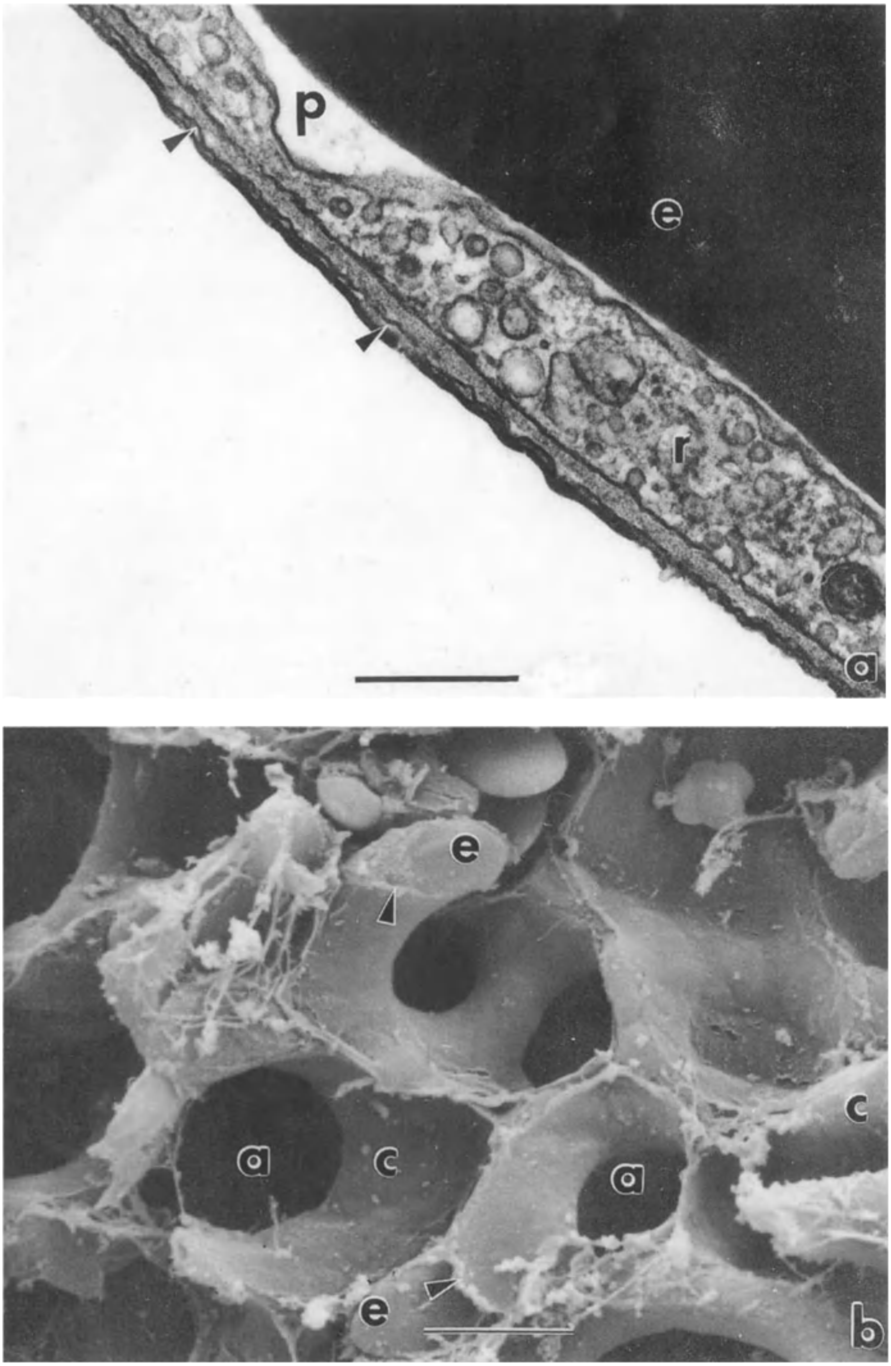


Fig. 40a,b

Oxygen extraction decreases with increasing ventilation-perfusion ratio in the dogfish, *Squalus suckleyi* (Hanson and Johansen 1970), and the water boundary layer provides about 80% of the overall resistance to O_2 exchange (Hills and Hughes 1970). The low O_2 extraction values in the gills with a trophic role (Table 8) may be due to the very high rate of flow of water necessary to procure food. In the human lung, where the concentration of O_2 in the inhaled air is 20.9% and in the expired air 16.4%, the O_2 extraction factor is about 22% while in birds (where the concentration of O_2 in expired air 14.5%), the value is 31% (Sturkie

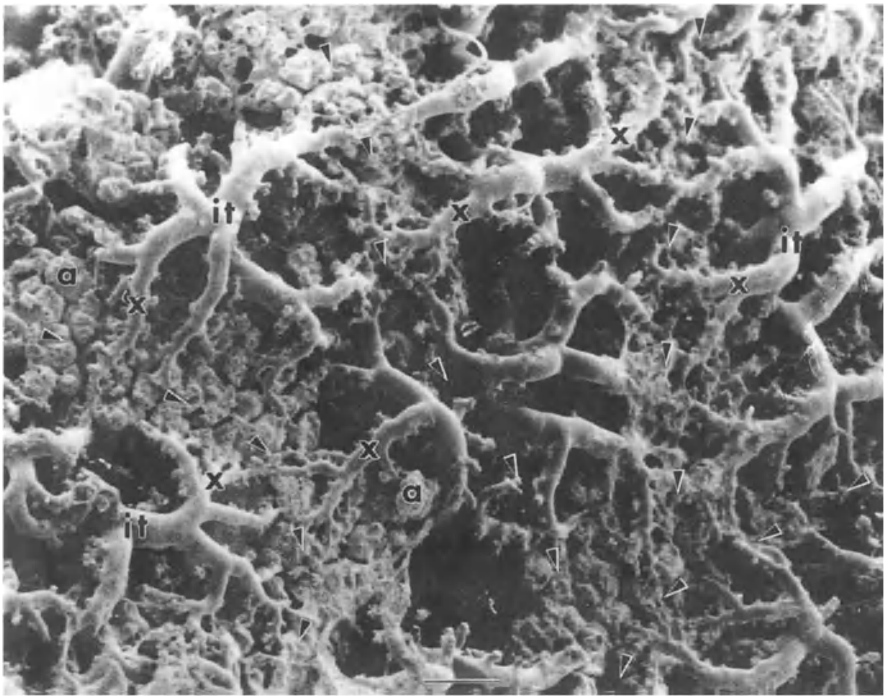


Fig. 41. Double latex cast preparation, i.e., simultaneous injection of cast material into the vasculature and into the airways of the lung of the domestic fowl, *Gallus domesticus* showing the crosscurrent relationship between the blood flow in the intraparabronchial arteries, *x*, and the airflow in the parabronchi of which the locations and the directions are shown by *arrow-heads*. Through this arrangement, gas exchange is effected along the parabronchial lengths, the concentration of O_2 in the pulmonary vein being an aggregate effect of that effected at many sites. The efficiency of the bird lung is largely attributable to this design. *it* Interparabronchial artery; *a* atria. *Bar* 100µm. (Maina 1988a)

Fig. 40. **a** Blood-gas barrier of the lung of a bird, the house sparrow (*Passer domesticus*) showing the extremely thin epithelial cells, ➤, and a much thicker endothelial one, *r*; *p* plasma layer; *e* erythrocyte. **b** View of the gas exchange region of the lung of the domestic fowl, *Gallus domesticus* showing the interdigitation of the blood, *c*, and air capillaries, *a*; *e*, erythrocytes; ➤, blood-gas barrier. **a** *Bar* 10.3µm; **d** 2µm. (**a** Maina and King 1982; **b** Maina 1982)

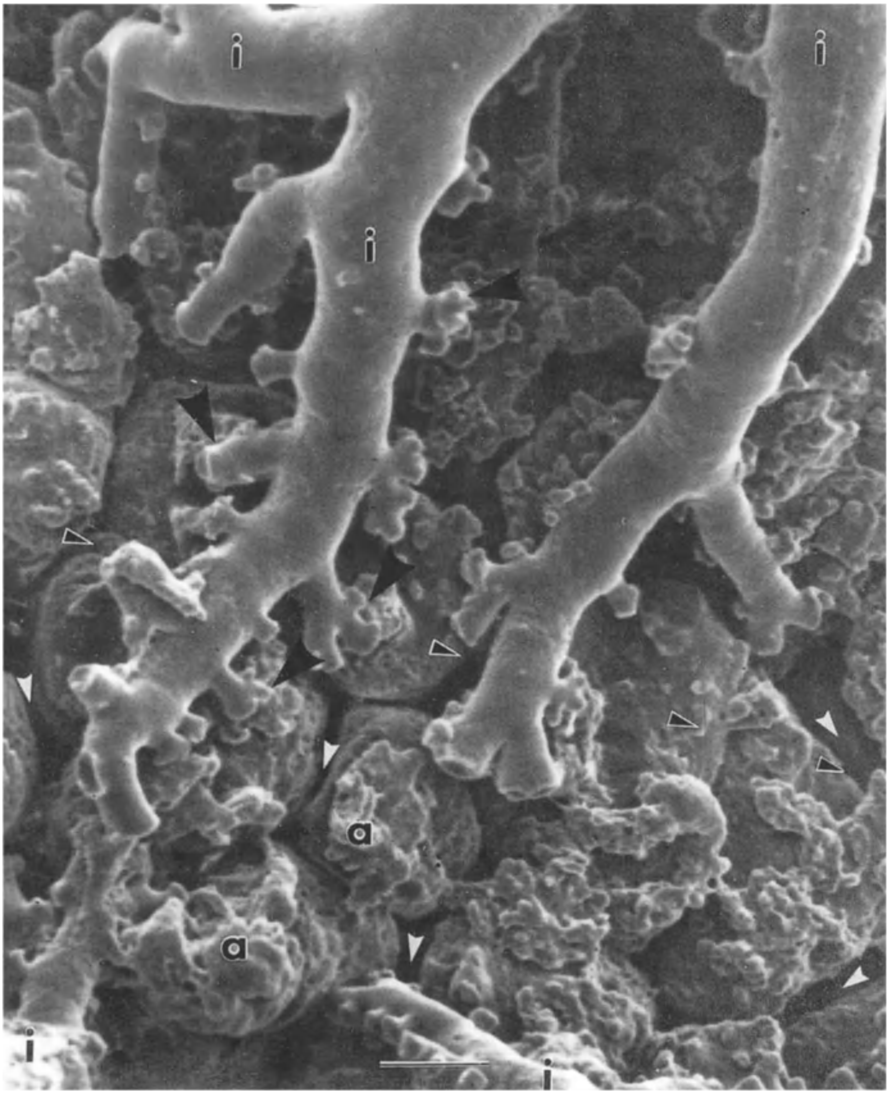


Fig. 42. Closeup view of a double latex cast preparation, i.e., injection of cast material into the vasculature and into the airways of the lung of the domestic fowl, *Gallus domesticus*, showing the crosscurrent relationship between the blood flow in the intraparabronchial arteries, *i*, and the air flow in a parabronchus (direction shown by *black arrowheads outlined in white*) which are studded by atria which terminate in air capillaries, *a*. The relationship between the intraparabronchial arteries with the parabronchi is crosscurrent, i.e., is perpendicular, while that at the gas exchange site (*large black arrowheads*, ➤) is countercurrent. The efficiency of the bird lung is largely attributable to the multicapillary serial arterialization system integral to the crosscurrent arrangement. *white arrowheads*, interatrial septae. *Bar* 20 μm. (Maina 1988a)

Table 8. Coefficient of oxygen extraction (FIO_2) from water in filter-feeding and non-filter-feeding animals. (Hazelhoff 1939)

Filter-feeding animals	FIO_2	Non-filter-feeding animals	FIO_2
Sponges	0.19 (0.06–0.57)[a]	Annelids	0.41 (0.30–0.66)
Lamellibranchs	0.07 (0.05–0.09)	Crustaceans	0.49 (0.29–0.76)
Ascidians	0.06 (0.04–0.07)	Gastropods	0.66 (0.38–0.70)
		Echinoderms	0.53 (0.49–0.55)
		Fish	0.62 (0.46–0.82)
Mean	0.11		0.55

[a] Values in parentheses show the range of the values.

1954). These values are on the lower side of the maximal ones of the water breathers given above. Although a countercurrent flow was established in the gills of the shore crab, *Carcinus maenas*, the O_2 extraction factor of 7 to 23% is relatively very low (Hughes et al. 1969a) compared with the values reported by Hazelhoff (1939) of 60 to 90% in *Caloppa granulata*. This is probably due to factors such as presence of a large branchial dead space, low permeability of the lamella cuticular lining, and inadequate lamellar perfusion in *Carcinus*. The importance of the countercurrent arrangement in the efficiency of gill function is evident from the fact that if the direction of flow of either of the respiratory media is reversed (i.e., to establish a concurrent system), the O_2 extraction ratio falls to below 10% (Hughes 1963). In the crosscurrent system, however, a similar procedure has no appreciable effect on the O_2 extraction ratio (Scheid and Piiper 1972). As expected from the geometric configuration of the parabrochial vasculature and blood flow to the exchange tissue relative to the air flow (Figs. 41,42), only the sequence of capillary arterialization is changed. The degree of arterialization remains the same.

Chapter 3

Gas Exchange Media, Respiratory States, and Environments

> *"The interaction between organisms and their environment is an old but very important problem to biologists. Organisms respond to environmental change in different ways according to the time during which the environmental change persists and according to the magnitude of the stress". Prosser (1958)*

3.1 Water and Air as Respiratory Media: General Considerations

Regarding the part of the biosphere they occupy, animal life is classified into aquatic, terrestrial, and aerial groups. Among vertebrates, fish are predominantly aquatic, amphibians are transitional, and reptiles, birds, and mammals are fundamentally terrestrial. Overlaps in occupation of various ecosystems occur. Among mammals, the cetaceans have reinvaded water while some amphibians live in highly desiccating deserts (McClanahan et al. 1994). The insects, the now extinct pterosaurs, the birds, and the bats, chronologically in that order, are the only groups which have evolved powered flight. The assortment of animals such as the flying squirrels, lemurs, snakes, lizards, and flying fish which can momentarily remain air-borne are essentially gliders. They use a part of their body to delay the fall and did not have to grapple with the aerodynamic and aerobic challenges which beset the active flyers.

The biophysical properties of water and air have profoundly influenced life patterns and body forms of animals (e.g., Alexander 1990; Giorgio 1990; Strathmann 1990). These features are fundamental to understanding the evolution of form, function, and the divergence between terrestrial and aquatic animals (e.g., Bliss 1979; Graham 1990; Table 9). In particular, the differences between water and air have so greatly influenced the respiratory processes that the mechanisms for obtaining O_2 and for eliminating CO_2 which are efficient in water often fail in air. Water has been abundantly and intricately incorporated in the composition of the living tissues and cells. It is required for life by practically all living things. This ubiquitous molecule makes up as much as 90% of the total protoplasmic mass. It is unequivocally the sine qua non of life. It has been worshipped (e.g., River Ganges in India), wars have been fought over it, and civilizations have risen from it or collapsed after losing or mismanaging it (e.g., Leopold and Davies 1968). While some very simple organisms can live without O_2, none can grow without it. The fluctuations in the levels of O_2 and CO_2 in water as well as in air have greatly determined the biomass and the species composition and distribution of animal communities (Davies 1975; Graham 1990).

Among animals, remarkable differences in the tolerance, response, and susceptibility to low O_2 and high concentrations of CO_2 exist. The primary factors which govern respiratory adaptation in both air and water include: (1) the

Table 9. Main differences between water and air and their physiological consequences. (Dejours 1988)

Parameter	Water	Air	Air/Water	Consequences
O_2 and CO_2 diffusivity	+	++++	≈8000	O_2 and CO_2 tensions; acid-base balance
O_2 capacitance	+	++	30	
CO_2 capacitance	++	++	1	
NH_3 capacitance	++++	++	1/700	N end products
Viscosity	++	+	1/60	Work of breathing
Density	+++	+	1/800	Circulation, skeleton, locomotion
Kinematic viscosity	+	++	13	Buoyancy, gravity
Water availability	+++	Very variable	–	Water turnover
Ionic environment	Very variable	–	–	Osmoregulation, ionoregulation
Sound velocity	++	+	1/4	Audition
Sound absorption	++	+	1/4	
Light refractive index	1.33	1	0.75	Vision
Light absorption	++	+	1/12	
Dielectric constant	+++	+	80	Electroreception
Solubility of molecules	Variable	–	–	Distance
Volatility of molecules	–	+		Chemoreception
Diffusivity of molecules	+	++++		
Heat capacity	++++	+	1/3500	Heat dissipation
Heat conductivity	++	+	1/24	Body temperature
Heat evaporation	$\approx 2450\,\mathrm{kJ\,l^{-1}}$			

molecular characteristics of the respiratory medium, (2) the solubility of the respiratory gases in a medium, and (3) the mode of transfer of the respiratory gases in a medium. Since other than subsistence in the different fluid media (water and air) there have been no physical barriers in the evolution of the possible gas exchangers, as envisaged by Perry (1989), water gills, air gills, water lungs, and air lungs should have evolved to the same extent. However, owing to the relatively low solubility of O_2 in water (0.031 mlO_2 per ml water), high viscosity of water, and low vapor pressure in air, water lungs and air gills have only rarely evolved. The difference in the physicochemical attributes of water and air prohibited direct conversion of the gills to lungs: a transitory gas exchanger which had to function equally well in both media was necessary. Air gills and water lungs occur (but rarely) in simple organisms, e.g., in the respiratory pleopods of the terrestrial isopods (e.g., Marsh and Branch 1979; Hoese 1983), in arachnids (Kaestner 1929), and in cases of retrogression from air- to water breathing, e.g., in the aquatic pneumonate gastropods. The gills nurtured the development of the air-breathing organs. In-series vascular connection followed. There was subsequently a gradual deemphasis of aquatic respiration, leading to subsidence of the gills. The gills were directly replaced by the air-breathing organs only where the skin served as a bridging organ.

3.2 Physical Characteristics of Water and Air

For utilization as respiratory media, only fluids are configured to offer the necessary convective transport of the respiratory gases. Water, a liquid over the biological range of temperature and pressure, and air, a gas under similar conditions, are the only two naturally occurring respirable fluids. The structural and functional consequences of the interactions between the respiratory media with the gas exchangers have depended on the magnitudes of the changes in the levels of the respiratory gases and the time scale over which the interfacing has occurred (Table 9). Water is an exacting environment to survive in. In saturated water, at 20 °C, 1 ml of O_2 is contained in 200 g of water while 1 ml of O_2 is present in 5 ml of air (weight, 7 g). The rate of diffusion of O_2 in water of $3.3 \times 10^{-5}\,cm^2\,s^{-1}$ (Grote 1967) is lower by a factor of 10^5 compared with that in air of $1.98 \times 10^{-1}\,cm^2\,s^{-1}$ (Reid and Sherwood 1966) while the capacitance coefficient, i.e., increment of concentration per increment in partial pressure of O_2, in water is only $1.82\,nmol\,min^{-1}$ per 0.133 kPa compared with the much higher one in air of $54.74\,nmol\,min^{-1}$ per 0.133 kPa (Dejours 1988; Table 4).

As a respiratory medium, the general properties of air are more obliging than those of water. Convection requirements are high in water breathers compared with the air breathers. An octopus ventilates 17 l of water for each mmol of O_2 consumed (Dejours et al. 1970). In air, all other factors held constant, diffusion facilitates supply of greater quantities of O_2. Less energy is expended in the convective transfer of the gas to the respiratory site. Aquatic organisms have evolved within the constraints of an O_2-deficient environment. Zaccone et al. (1995) contend that the lungs phylogenetically evolved as adaptations to the hypoxic conditions in the aquatic medium in which fish lived. Due to the high solubility of CO_2 in water, the molar concentration of the free gas is about equal to that in air while the concentration of O_2 in water is only about 5% of that in air. Diffusion rather than concentration reduces the rate of transfer of CO_2 in water. Both decreased diffusion and low concentration slow down the transfer of O_2 in water. Many accounts dealing with adaptations of organisms to dissolved gas levels in water address themselves to O_2 availability rather than the concentration of CO_2. Owing to the high $CO_2 : O_2$ solubility ratio, if originally normoxic water was to be rendered anoxic from aerobic metabolism alone, the PCO_2 would only increase by about 0.9 kPa (Rahn 1966). Owing to the high PO_2 in air, diffusion across the blood-gas barrier is highly efficient. The arterial partial pressures of O_2 reasonably approach those prevailing in the respiratory medium. While the O_2 extraction factor in the water breathers is high, e.g., 90% in sponges, 60 to 90% in the crab (*Caloppa granulata*), 33 to 70% in the octopus, 85% in the eel (van Dam 1938, 1954), and on average 85% in fishes (Steen and Kruysse 1964), in the air breathers, the O_2 extraction factor very rarely exceeds 25%.

3.3 The Distribution of Water and Air on Earth

There is ample evidence from geological records that water was available on Earth in abundant quantities as early as 3.8 to 3.5 billion years ago (Schopf and Walter 1983). The hydrosphere, which presently covers about 72% of the Earth, was much more extensive during the early times (e.g., Handerson 1913), reaching the greatest extent in the early Paleozoic (Bray 1985). The Earth has a geometrical surface area of about $5 \times 10^8 \mathrm{km}^2$ and the seas and oceans cover $3.6 \pm 10^8 \mathrm{km}^2$ of this area and contain $1.3 \times 10^9 \mathrm{km}^3$ of water. Practically all the Earth's water is contained in the oceans, with the water in the lakes and rivers constituting only 0.01% of that which is available to life. Freshwater constitutes about 2.5% of the total volume of the Earth's water, with nearly 75% of it locked in a frozen state in the polar ice caps and in glaciers while about 0.5% of it is held in aquifers as underground water (Gross 1990; Shiklomanov 1993). Rivers and lakes are complex, biologically highly productive habitats with short histories on geological time scale. For example, Death Valley in California, the hottest and driest place in the United States, was covered by a lake some 60 m deep only about 20 000 years ago (Leopold and Davies 1968). About one third of all bony fish have evolved and live in freshwater. While it is possible to accurately determine the limits of the aquasphere, the dimensions of the aerosphere are more difficult to define. The air gradually rarefies with altitude, approaching the total vacuum of the vast outer space at an altitude of between about 100 to 1000 km (e.g., Denney 1993). From the highest altitude at which aerial animals, especially birds, operate, which with some exceptions is about 10 km, the biologically utilizable fraction of the atmosphere is $5 \times 10^9 \mathrm{km}^3$ in volume. This is nearly four times the volume of the oceans. The physical characteristics of the ocean and seawater are fairly constant while those of the freshwater lakes and rivers are more variable (e.g., Clarke 1991). Mass movement of air by convection and diffusion equalizes the gas tensions within and between habitats. In the open seas, circadian variations in the respiratory gas tensions and concentrations are common in the superficial layers of the water (Riley and Skirrow 1975) but are much less than in ponds or rock pools.

By definition, a normoxic medium is one in which the PO_2 at sea level is about 20 to 21.3 kPa. For any PO_2, air contains more O_2 than water. The difference between O_2 production through photosynthesis and utilization in respiration determines the net levels and changes in the concentration of O_2 while CO_2 uptake by plants (during photosynthesis) and production during respiration by both plants and animals regulate its level (Fig. 10). Ensuing from the high diffusivity of CO_2 in air, increases in the PCO_2 to a level that would cause respiratory stress in the free atmosphere rarely occur except in certain microhabitats, e.g., in the waterlogged soils where local hyperbaria may occur. In free air, hyperoxia does not arise. However, in ponds or seawater pools, it may develop as a localized phenomenon. Peak levels as high as 80 kPa have been reported (Truchot and Jouve-Duhamel 1980; Heisler 1982a). In our presently stable aerial environment, hyperoxia is only studied as a means of understanding the respiratory control mechanisms and management of some clinical problems.

Although O_2 has been produced by photosynthetic organisms for the last 3.5 billion years (Chapman and Schopf 1983; Schopf et al. 1983; Fig. 8), anaerobic habitats have existed continuously during the entire Earth's history. The marine detrital sediments constitute the most extensive global continuum of an anaerobic niche. Oxygen penetrates the sediments to only a few millimeter (Revsbech et al. 1980a). The widespread distribution of black shales is a firm indicator of the anoxic conditions in the seas at particular depths in the early periods of the Earth's geomorphosis (Berry and Wilde 1978). Much of the CO_2 in the natural waters is derived from carbonates in solution and very little from the atmosphere. Acidity increases the PCO_2 in water while alkalinity, even in form of carbonates, lowers it. Even in carbonate-free water, the PCO_2 cannot be very much due to the high solubility of the gas in water, a factor which reduces its occurrence in a free molecular state to almost zero. It is presumably due to this singular fact that CO_2 does not constitute a regular respiratory stimulant in gill and other water breathers. In some habitats, putrefactive processes which entail bacterial anaerobic breakdown of organic matter may produce enormous quantities of CO_2, which may result in adverse tensions of it. In water which is free of or contains scarce aquatic plant life, dissolved O_2 is the most important respiratory factor. At a critical level, an organism may be unable to procure adequate amounts of O_2 for aerobic metabolism. In such cases, it has to evoke certain behavioral, physiological, morphological, and biochemical measures (essentially in that order) (e.g., Bartholomew 1988; Carroll 1988; Gans 1988). These may include relocation to more favorable habitats, increase in O_2 uptake from the inimical environment through physiological adjustments, and reduction in O_2 need by entering an ametabolic state. In long-standing cases of hypoxia, the animal is driven to evolve a capacity to procure O_2 directly from the atmosphere. In some organisms, extreme hypoxia results in reversible cessation of respiration especially in those animals like the lugworm, *Arenicola marina* (Toulmond and Tchernigovtzeff 1984), and the prawn, *Palaemon elegans* (Morris and Taylor 1985), which experience large diurnal fluctuations in O_2 levels in the rockpools. Hypoxia increases ventilation in all animals which have been studied and variably, hyperoxia results in hypoventilation inducing hypercapnia (Dejours 1988).

3.4 Water: a Respirable Medium and an Integral Molecule for Life

It is believed (e.g., Jervis 1995) that the quantity of water presently found on Earth already existed when the planet was formed some 5 billion years ago, but in the vapor form. With the gradual cooling of the planet to below 100 °C, liquid water was formed. In biological systems, the fundamental life processes like ionic and gas fluxes take place in aqueous solution. The suitability and fitness of the water molecule as the habitat in which life evolved on Earth was well affirmed by Handerson (1913). Over millions of years water has shaped and continues to shape the Earth. As a chemical compound, water (H_2O) is unique and paradoxical in many ways. It is a remarkably stable odorless, colorless and tasteless liquid with powerful solvent properties. Until 1783 (some 200 years ago) when Henry

Cavendish synthesized the water molecule by igniting hydrogen and oxygen, it was believed that water was an indestructible element rather than a chemical compound. The basis of the unique chemical and physical properties of water (e.g., powerful solvency power, high capillarity, expansion of liquid water between 0 and 4 °C, high thermal capacity) is the covalent bonding between O_2 and H_2 producing a dipolar molecule. Water boils at about 162 °C higher than its analog hydrogen sulfide. Its density at 4 °C is $1\,g\,cm^{-3}$. At 1 atm pressure, water melts at 0 °C and boils at 100 °C (the thermometric fixed points). It is a good ionizing solvent, a property connected with its high dielectric constant and its ability to donate and share electrons. Water acts as a catalyst, reactant as well as a solvent. For example, in some reactions dry ammonia will not react with hydrogen chloride and neither will dry carbon monoxide and dry O_2. Under geologic conditions of time, heat, and pressure, water has an important role in the conversion of plant and animal matter into organic fuels. At high temperatures, water carries out condensation, cleavage, and hydrolysis reactions (Siskin and Katritzky 1991). Ethers and esters, compounds which are not susceptible to heat alone, suffer facile cleavage and hydrolysis respectively in water at 250 and 350 °C. As the temperature of the water rises from 25 to 300 °C, some of its physical characteristics change dramatically: the density decreases from 0.997 to 0.731 g per ml, the dielectric constant decreases from 78.85 to 19.66, and the solubility parameter from 23.4 to $14.5\,cal\,ml^{-1}$. Between 250 and 350 °C, the water solvent properties approach those of polar organic solvents at room temperature.

Among the nine planets in our solar system, the Earth is endowed with large quantities of water naturally occurring in the three fundamental states of matter, i.e., liquid, solid, and vapor. It is debatable how liquid water was maintained on early Earth and Mars (e.g., Carr 1996; Sagan and Chyba 1997) despite the solar luminosity being 25 to 30% lower than at present (e.g., Newman and Rood 1977). It is popularly believed (e.g., Owens et al. 1979) that high levels of CO_2 produced by action of the carbonate-silicate cycle provided a greenhouse effect adequate to warm the early Earth. Though now cold and dry and having a thin atmosphere from constant loss of water and CO_2 into space, from study of the surface topography and the geometry of outflow channels, Mars appears to have experienced episodes of massive flooding (Baker et al. 1991). As recently as 300 million years ago, the conditions on Mars appear to have been amenable to life (Kargel and Strom 1996), at least as we know it. Compared with air, water is a more dynamic habitat. Aquatic animals may face wide extremes in O_2 availability due to factors such as ice cover, plant respiration, animals burrowing into the substratum for food or protection, and high environmental CO_2 and hence low pH, usually during nighttime plant metabolism.

Some of the unique physical features of water which are fundamental to animal and plant physiology include: (1) a high specific heat (0.9988 calories per g per °C) which affords a stable temperature, (2) relatively weak intermolecular forces which enable heat to be efficiently transferred by convection (thermal conductivity, $5.14\,cal\,h^{-1}\,cm^{-1}\,K^{-1}$ at 20 °C) within the medium, (3) high surface tension which at 72.8 dynes cm^{-1} is one of the highest among liquids, (4) high wetting property and capillarity, features which are crucial in protoplasmic-cell organelle interfacing, (5) neutral pH which promotes fast reaction kinetics in most biochemical processes, (6) great solvency power and high dielectric constant (80.1 in pure form) which enable it to accommodate different molecular and ionic factors, (7) maximum density (at 4 °C) which makes it possible for water to sink to the bottom while still in a liquid form. The top layer, which cools to below 0 °C, expands and floats to the top, providing a surface cover of ice which prevents the entire water mass from freezing and killing most of the organisms (which take refuge at the bottom), and (8) in vapor form, water has high diffusivity and is thus important for thermoregulatory processes. The presence of dissolved salts, e.g., in seawater, lowers the temperature at which the maximum density is attained. In brackish water (salinity 18 ppt), the maximum density occurs at 0 °C and in the ocean water (35 g of salt per kg of liquid), it occurs at −3.5 °C. Within ordinary conditions of life, water is incompressible. The intermolecular distance is about ten times less than the average value for most gases. Owing to the much weaker cohesive forces (van der Waal's forces), CO_2 and O_2 are gaseous at the physiological range of temperature while in water, where the forces are much stronger, the gas/liquid transition (when the cohesive forces are overcome by the kinetic energy of the molecules) takes place at the relatively high temperature of 100 °C (373 K) at 1 atm (101.3 kPa) pressure. It is only at extreme pressures, e.g., at great depths of the seas and oceans, that compression of water becomes significant in biology (Somero 1992). At a depth of 10 km, the PO_2 is 0.8 atm (Enns et al. 1965). Gases such as CH_4, H_2S, N_2, NH_3, SO_2, H_2, and CO_2 are found dissolved in some aquatic habitats. Many flatfishes burrow into the bottom mud, a process likely to reduce the flow of water across the gills impeding excretion of CO_2 and O_2 uptake (Lennard and Huddart 1989). A concentration of H_2S of 12 mg per l was reported in a lake in Cyrenaica by Smith (1952). Despite its abundance in the atmosphere, N_2, which constitutes about 78.08% by volume at normal pressures, plays no known respiratory role. At high pressures, it may be lethal by inducing narcosis.

3.4.1 Oxygen and CO_2 Content in Water: Effect on Respiration

In natural circumstances, O_2 and CO_2 are the only gases of biological interest in water. The concentrations of these gases have dramatically fluctuated during the past geological epochs (Graham et al. 1995; Fig. 9). While CO_2 tension decreased from a peak values of about 100 times of the Precambrian period to the present low level, O_2 has exhibited remarkable changes (e.g., Kasting et al. 1979). Mainly owing to the complex interrelationship between the total concentration of CO_2 and its partial pressure in water, particularly if water contains CO_2 fixing (buffering) factors such as carbonates, in many freshwaters and to a slight extent in marine water, it is difficult to accurately predict the amount of CO_2 in a given kind of water. The levels of CO_2 in waters (except in distilled water, which is devoid of any buffer system and hence CO_2 exists in a dissolved form) differ remarkably as opposed to its rather stable level in the atmosphere. Large quantities of CO_2 may exist at very low tensions due to formation of bicarbonates. Changes in CO_2 levels greatly affect its excretion and hence pH regulation in water breathers. In the ocean water, which has a high environmental buffering capacity, the PCO_2 does not vary much from the value of 0.03 kPa which is the equilibrium point with the atmosphere. When exposed to water, the atmospheric gases are taken up at the surface by diffusion and convection until an equilibrium ($PO_2 = 20$ to 21.3 kPa) is reached: the enrichment is effected mainly by the currents which are produced by the winds as well as by the variations in the temperatures which influence the specific gravity of the water. Over a distance of a few mm, diffusion is a very slow process. Krogh (1941) estimated that it would take as long as 42 years for an O_2 molecule to reach a depth of 250 m of water. In oceanic inlets, notable vertical stratifications in O_2 levels attributable to changes in temperature and salinity, horizontal variation associated with pockets of photosynthesis, and respiration and decay of organic materials occur (e.g., Platt and Irwin 1972): while the surface water is close to saturation, the bottom one is virtually anoxic, with the O_2 levels generally being below $1\,\mathrm{ml\,l^{-1}}$ at depths exceeding 100 m. In seas and oceans, as temperature and salinity increase, O_2, CO_2, and NH_3 content decrease (Gameson and Robertson 1955). In most cases, anoxia is accompanied by increased concentrations of CO_2 and H_2S (Powell et al. 1979). With increased temperature, O_2 content drops due to reduced solubility while the PO_2 drops only moderately owing to compensatory increase in the kinetic molecular diffusivity. The effect of temperature on the solubilities of CO_2 and NH_3 is rather complex owing to the chemical reactions with the water molecule. It is not as easily predictable as is the case for the relatively inert O_2.

Dependent on factors such as temperature, barometric pressure, photosynthetic activity of the plant matter, respiratory processes of the microorganisms, circulatory and mixing processes, and concentration of dissolved solids, at sea level, a liter of distilled and surface sea water contains only 6.34 and 5.11 $\mathrm{cm^3}$ of O_2 respectively. These values are equivalent to the O_2 content of the rarefied air at an altitude of over 20 km. At 15 °C, 1 l of pure water dissolves 1 l of CO_2 at 1 atm pressure. The great solubility of CO_2 in water compared with air suggests that the greatest challenge towards the evolution of air breathing was not that of acquisition of O_2 but rather that of elimination of CO_2 into the air (Sect. 1.18 and 5.4). The respiratory epithelia of the air breathing organs, e.g., gills in fish (Randall et al. 1981), skin and lungs of amphibians (Toews et al. 1978), and lungs of most higher vertebrates (e.g., Bidani and Crandall 1988) contain appreciable quantities of carbonic anhydrase which accelerates the dehydration of HCO_3^- ions in blood, enhancing CO_2 clearance across the gas exchanger (Burnett et al. 1981; Gros 1991). In torrential rivers and streams, as well as the surface waters of lakes, seas, and oceans, the PO_2 and PCO_2 are at or near equilibrium with the atmosphere due to turbulence and agitation, which enhances the solubility of air (Piiper et al. 1962). However, in a variety of closed or stagnant collections of water such as the Black Sea, (Sverdrup et al. 1949), the inner continental shelves like the Gulf of Mexico (Leming and Stuntz 1984), bottom or even surface waters of tropical marshes (Carter and Beadle 1931; Jones 1961), small ponds and intertidal pools (Sverdrup et al. 1949; Truchot and Jouve-Duhamel 1980), interstitial water held between sediments (Brafield 1964; Revsbech et al. 1980b; Reimers et al. 1986), and the hydrothermal vents of the midocean ridges (Johnston et al. 1986), the water is hypoxic and even virtually anoxic. In such waters, the depletion of O_2 usually correlates with elevated CO_2 concentration and low pH status especially at night

Table 10. Oxygen and carbon dioxide capacitances in distilled water, in seawater, and air at various temperatures. (Dejours 1981)

T		Distilled water		Seawater[a]		Air
	βWO_2	βWCO_2	$\beta WO_2/\beta WCO_2$	βWO_2	βWCO_2	βg
°C	$\mu mol\ l^{-1}\ mmHg$			$\mu mol\ l^{-1}\ mmHg$		
40	1.35	31.33	0.0431	1.10	29.40	51.23
37	1.40	33.52	0.0418	1.17	30.40	51.73
35	1.43	34.99	0.0409	1.21	31.30	52.06
30	1.53	39.30	0.0389	1.32	34.47	52.92
20	1.66	44.86	0.0370	1.43	39.01	53.81
15	2.01	60.23	0.0334	1.67	51.58	55.68
10	2.23	70.57	0.0316	1.83	60.00	56.66
5	2.52	84.17	0.0299	2.03	70.79	57.68
0	2.87	101.25	0.0283	2.28	85.00	58.74

[a] Data on seawater based on chlorinity of 19 ppt; in air, the capacitance of O_2 and CO_2 are identical.

when photosynthesis stops and respiration continues (Heisler et al. 1982; Truchot and Jouve-Duhamel 1980). Water PCO_2 values as high as 8 kPa (Heisler et al. 1982) and PO_2 values beyond 67 kPa (Dejours et al. 1977) have been recorded in natural waters. By suppressing gas ventilation and hence CO_2 elimination, hyperoxia may elevate PCO_2 in blood and precipitate acidosis. Respiratory gases are less soluble in salt solutions (Table 10). Whereas pure water at 0 °C contains 10.29 mlO_2 per l, at a salinity of 10 ppt, it contains 9.13 mlO_2 per l and at 20 ppt, 7.97 mlO_2 per l. At 30 °C, the quantities of dissolved O_2 are 5.57 mlO_2 per l (pure water), 5.01 mlO_2 per l (10 ppt salinity) and 4.46 mlO_2 per l (20 ppt salinity). Contingent on location, size of the water mass, and physical mixing, convective movements occur up to a particular depth, the thermocline. Below the critical level, the water is stagnant and is held at a relatively low temperature. In oceans, convective currents equilibrate the respiratory gas tensions to an appreciable depth but at 100 to 1000 m, O_2-poor areas exist (Harvey 1957). In physically isolated water masses such as the Black Sea and the Gulf of Panama, where conditions for circulation are restricted, hypoxia may exist at all levels. Due to the relatively slower rate of diffusion and convective movement of the respiratory gases, compared with air, aquatic environments are subject to greater spatial and temporal variations in O_2 and CO_2 levels resulting from biological activities of plant and animal life (Garey and Rahn 1970). In isolated water basins and fjords, convective mixing may be prohibited by flow and thermal differentials and/or salinity-induced layering of water leading to hypoxic and even anoxic conditions (e.g., Seliger et al. 1985). In some coastal estuarine areas, due to its lower density, the riverine water floats on top of the heavier seawater (as a result of its less salinity and higher temperature) causing differences in O_2 and CO_2 tensions between surface and deep waters (e.g., Gnaiger 1983; Officer et al. 1984). The diversity of benthic species decreases with depth and varies seasonally with the available O_2 (Hoss 1973).

Fluctuations in the levels O_2 and CO_2 are common in water. The frequency and amplitude are determined by factors such as depth and rate of water circulation, transparency and presence of dissolved and particulate substances, temperature, density of flora and fauna, eutrophication of organic matter, and presence of ice or plant cover (e.g., Carter 1955). The penetration of light through water is an important factor which determines productivity and hence availability of food to aquatic life. It depends on factors such as surface cover, turbidity from presence of suspended mineral particles, organic matter and microorganisms, and the wavelength of light. The blue-green light travels to a depth of 50 m and the red light is least penetrative (Harvey 1957). Solar light is entirely extinguished at a depth of 1000 m in the clearest of the oceans (Pough et al. 1989). In the turbid water of Lake Victoria, long wavelengths penetrate into the water layers more than the shorter ones (van Oijen et al. 1981; de Beer 1989): during the day, at a depth of 2.5 m, the light is about 5% of the intensity at the surface. During the day, owing to photosynthetic activity of algae and other simple plants, O_2 production may exceed the respiratory demands with the concentration increasing to very high levels, while during hours of darkness the water may be rendered totally anoxic from the ensuing respiration (Ultsch 1973; Kramer et al. 1978; Fig. 43). Compared with freshwaters, O_2 saturation levels are generally more stable in marine waters where, due to turbulent mixing with air, surface water is often at equilibrium with the atmospheric gases. In the sea, O_2 levels in the photic zone occasionally rise to 130% saturation or above owing to photosynthetic activities

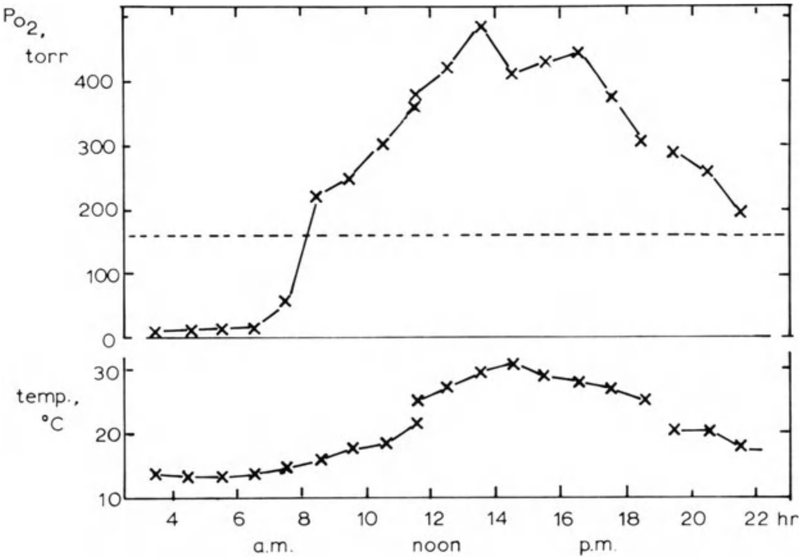


Fig. 43. Diurnal fluctuations of the partial pressure of O_2 and that of temperature in a pool of water containing aquatic plants. The water is saturated with O_2 at about midday and is virtually anoxic after midnight. *Dashed line* indicates the PO_2 in air. (After Dejours 1988)

(Fairbridge 1966). At the bottom, most water masses are asphyxic. In the brackish Japanese Lake Nakanoumi, at the surface, owing to algal photosynthetic activity, the water is 100% saturated with O_2 while at the bottom (depth 6.5 m), the concentration is almost zero due to the biodegradation of organic matter (Kimoto and Fujinaga 1990). In the marine intertidal rockpools, the PO_2 ranges from 0.27 kPa at night to more than 66.7 kPa during the day while the PCO_2 and the pH respectively range from 0.36 to 1.3×10^{-4} kPa and 7.3 to 10.2 (e.g., Truchot and Jouve-Duhamel 1980). Resulting from photosynthetic activity, over a 24-h period, in rockpools, the temperature reaches a high of 24 °C and a minimum of 14 °C. During the day, the concentration of O_2 is in excess of 20 mg per l (more than 300% saturation) dropping to less than 1 mg per l (about 3% saturation) during the night (Daniel and Boyden 1975): the concentration of CO_2 is reduced from 100 mg per l to about half of the value while the pH drops from a night time value of 7.5 to a daytime maximum of 9.5. In warm sunny days, the shallow ditches of the Dutch polder lands present a diurnal PO_2 peak level of 66.7 kPa dropping to 2.7 kPa at night (Jones 1961). Supersaturation with O_2 as high as 364.5% in the upper portion of a Wisconsin lake was attributed to the photosynthesis of the algal growth (Welch 1952). In Lake Waubesa (Wisconsin, USA), a concentration of O_2 as high as 30 mg per l which resulted in sudden fish mortalities was reported by Woodbury (1942). Similar observations were made by Wiebe (1933). Seasonal low levels of O_2 in freshwater masses can lead to massive deaths of fish (winter kills) which result from decay of organic materials especially where atmospheric O_2 recharge is prohibited by surface ice cover (Gnaiger and Forstner 1983). In such cases, aquatic hypoxia is exacerbated by reduced level of photosynthesis due to the decrease of the solar (shortwave) radiation available to the plant life. Atlantic lobster kills are sometimes attributed to low dissolved O_2 (Young 1973). Where light can get through, however, the bubbles which are released by underwater plants and accumulate under the ice may contain as much as 45% O_2 by concentration. The air may be utilized by aquatic organisms (Krogh 1941). In most air-breathing vertebrates, hypoxia is the main drive for respiration, but at sea level CO_2 and H^+ are the basic biochemical regulators. Such animals maintain CO_2 in a steady state leading to an average arterial PCO_2 of about 5.3 kPa. In the aquatic animals, PCO_2 levels are very low. The importance of CO_2 in the regulation of breathing increases with dependence on air breathing. Ventilatory activity in fish which breath water is driven by O_2 levels and is virtually insensitive to CO_2. Diving (e.g., Andersen 1966) and fossorial (e.g., Augee et al. 1970/71) air-breathing vertebrates (birds and mammals) have blunted sensitivity to CO_2.

3.4.2 Density and Viscosity of Water

Water is about 1000 times denser than air. The molecular diameter of water is about 2 Å while the intermolecular distance is about 3.1 Å. The average intermolecular distance in gases is about 33 Å while the molecular diameters of most gases ranges from 2 to 5 Å, i.e., about one tenth of their intermolecular spacing. Water, a medium with a high specific gravity and viscosity, provided the necessary support which promoted the development and evolution of the delicate invertebrate life to amazing sizes: a specimen of the Atlantic giant squid (*Architeuthis* sp.) weighing 2 t has been captured. However, the metabolic cost of convective transfer of water in the gas exchangers as well as the restrictive physical movement in it sets a limit to the exercise and metabolic capacities of aquatic organisms. The fastest fish, the tuna, can only briefly attain and sustain a maximal speed of about 20 m s^{-1} (for 10 to 20 s) while a bird, e.g., the swift will attain and sustain a speed of 40 m per s (Gray 1968). The cost of aquatic respiration is increased by the fact that although the PO_2 may be similar in water and air, water contains 30 times less O_2. To extract an equivalent quantity of O_2, a water breather has to expend much more energy than does an air breather (Sect. 2.9).

3.4.3 Thermal Capacity and Conductivity of Water

The heat transfer properties, caloric capacity, and conductivity of water is about 3 orders of magnitude greater than that of air (Tables 4,9). With exception of liquid ammonia, water has the highest specific heat (4200 J kg^{-1}) of any substance in liquid form at room temperature. The thermal conductivity and capacity of water are respectively 24 and 3000 times greater than that of air. These features present constraints for survival and respiration in water. In aquatic breathers, the metabolic heat carried by the blood to the gills is soon lost to the environment (Carey 1973; Carey and Lawson 1973). The temperature of the body tissues is within 1 °C of the ambient water temperature (Carey et al. 1971; Reynolds et al. 1976). The limitations precipitated by the water with respect to heat conservation and body temperature regulation obliged terrestrial location for evolution of endothermic-homeothermy to develop. For similar reasons, except for the endothermic fish, the extant members of the vertebrate classes Agnatha, Chondrichthyes, and Osteichthyes are obligatively poikilothermic (Hazel 1993).

For the period over which the multicellular organisms have been on Earth (Schopf et al. 1983; Fig. 8), the average temperature of the tropical surface waters has varied by only about 5 °C while that of air has changed by perhaps 15 °C (e.g., Cloud 1988). Surface temperatures may change dramatically within short intervals and distances. Annual temperature fluctuations of as much as 60 to 70 °C on land are occasionally recorded. The annual latitudinal fluctuations in temperatures throughout all temperate and subtropical seas range between 0 to 28 °C and at no place in the open sea is the annual range of temperature more than 10 °C (Nicol 1960). In the North Atlantic Ocean, the surface temperature varies by only 8 °C while at the equator, the mean yearly temperature variation is only 0.5 °C (Sverdrup et al. 1949): deeper waters exhibit less variations in temperature. The mean annual temperature of the ocean at the equator is about 27 °C, at 30°S latitude it is 20 °C, and at 30°N it is about 17.5 °C (Wüst et al. 1954). The narrow range of temperatures found in the ocean is attributable to constant convective circulation (F.G.W. Smith 1957) and the high specific heat of water (Dorsey 1940). Freshwater lakes exhibit greater stratification and fluctuation of temperature than oceans, the gradient depending on factors such as drainage, mass of water, latitudinal location, surrounding terrain, and depth (Beadle 1974; Hutchison 1975). The temperature characteristics of a lake particularly in the warmer parts of the year are more complicated than those in the seas and oceans (Beadle 1974): the temperature from the surface to a depth of about 6 m is fairly stable at about 20 °C, from 6 to 10 m it drops suddenly to about 5 °C (the thermocline) and stabilizes below that depth. Very small masses of water may show a range of temperature of 0 to 42 °C (Young and Zimmerman 1956). In the salt water pools in southeast England, Mardsen (1976) noted that in summer, diurnal temperature dropped from 24 to 14 °C over a 24-h period and in winter the temperature ranged from a minimum of −0.5 to 5 °C. Many aquatic animals are able to regulate their body temperatures within a very narrow range by ascending or descending in a water column or moving to shallower or deeper waters (e.g., Feder et al. 1982). As the O_2 content of water varies inversely with the water temperature, a compromise has to be established between the needs for O_2 and the preferred body temperature.

3.4.4 Derelict Waters: Respiratory Stress from Hypercapnia and Hypoxia

Derelict waters reproduce the inimical environmental conditions in which air breathing evolved. The adaptations by which animals are able to survive in hypoxic and hypercapnic waters are hence of relevant scientific interest. They demonstrate the factors which enforced and the strategies which animals adopted for transition from water- to air breathing. Current geoclimatic data suggest that the environment during the Devonian period, a time during which most of the bony fish first evolved lungs (Pough et al. 1989), was in all likelihood similar to a tropical swamp. It was characteristically anoxic, reducing, and CO_2 occurred at high concentrations (e.g., Valentine and Moores 1976). During the continental formative years, the drainage systems of most tropical swamps particularly the Central ones were not well formed (Bishop and Trendall 1967). Especially in the major land mass located at the equator, which is often called the Old Red Continent (e.g., Livermore et al. 1985), intense putrefaction of the plant matter resulted from the prevalent high temperatures. Pressure and the need to evolve potential for air breathing and even relocation to land was very intense for survival in such pernicious and noxious habitats. While the quantity and the PCO_2 in air is generally low, in some waters, a fairly large amount of CO_2 occurs at low tension but in a few cases it may be found in such a high tension as to suppress respiration (Table 11). Such conditions are common in the warm waters of the tropical regions of the world (Beadle 1974; Munshi and Hughes 1992). Apart from the ephemeral ones which exist only in wet seasons, there are few inland water masses which have not been radically changed in form and drainage pattern during the past million years. Such habitats are associated with abundant and distinct animal and plant communities. The presence of amphibious vertebrates in a swamp corresponds with a radical transformation of one ecosystem to another, a process which may be enhanced by natural and human factors such as drought, siltation, excessive infestation with aquatic flora, drainage, and land reclamation.

Table 11. Environmental features of some representative swamps of the tropical world. (Beadle 1932; Carter 1935; Rzoska 1974; Dehadrai and Tripathi 1976)

Swamp	Area	T	pH	cO_2	CO_2	Alkalinity	Conductivity
Nile swamps							
Swamp rivers	Bahr el Gabel	25	7.5	0.66–6.2	3–18	–	112–550
	Bahr el Ghazal	25	7.4	1.3–8.0	–	–	40–370
	Bahr el Sobat	25	7.3	3.4–6.2	–	15–50	110–280
	Bahr el Zeraf	25	7.8	2.2–5.9	–	92–116	245–370
Standing waters	Shambe Lagoon	25	7.5	2.4–6.0	–	32	–
	Lagoon RP 12	25	7.8	6.1–102	–	21–31	200–250
	Lake Ambandi	25	6.8	8.0	–	25	40–55
	Khar Perboi	25	–	1.8–7.2	–	–	–
	Khar Atar	25	8.3	6.9–12	–	29	–
Guiana swamps	Grass Swamp A	28	4.5	0.22–1.2	8–9	0	–
	Other Swamps	28	4.5	0.65	14	0	–
	Pool B	28	4.1	0.6–1.5	5.0	0	–
East African swamps	Lake Naivasha (Papyrus swamp)	25	7.8	2.5	–	–	–
	Kazinga Channel (papyrus swamp)	27	5.9	0	–	7.5	–
	Kitoma (papyrus swamp)	–	6.7	0	–	72	
Indian swamps	Polluted swamp	26	8.8	6.5–8.2	16–20	148 ppm	–
	Semi-senescent swamp	26	8.3	0.6–3.2	20	143 ppm	–
	Senescent swamp	31	8.0	1.5–2.7	12	94–162	–

Symbols and units: T – temperature (°C); cO_2 – dissolved $O_2\,mg\,l^{-1}$; CO_2 – free CO_2, $mg\,l^{-1}$; alkalinity – total alkalinity, 10^{-4}N; conductivity, μ mho cm^{-1} (20°C).

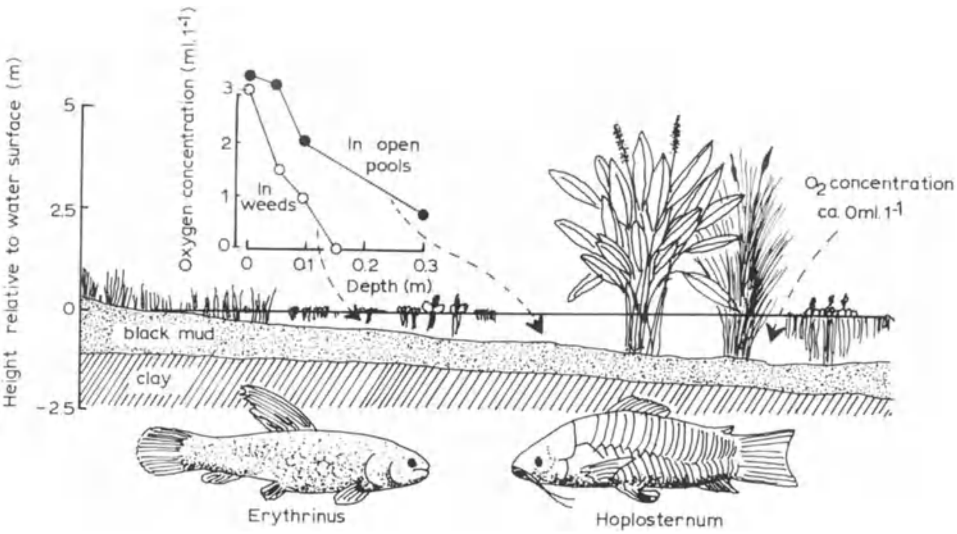


Fig. 44. Cross-section of the edge of a Paraguayan swamp showing the effect of aquatic plant growth on the O_2 levels in water. The O_2 tensions both in the open pools and the weeds decrease with depth but even close to the surface, the levels are very low. The commonest fish are *Hoplosternum litorale* and *Erythrinus unitaeniatus*. Both are air breathers. (Carter and Beadle 1931)

The tropical derelict masses of water which are shallow and stagnant or slow moving present adverse respiratory conditions. In standing waters, mixing of surface and deeper waters is inhibited by thermal stratification. The bottom water may be virtually anoxic while the top layer is saturated with O_2. In a Danish lake, Nielsen and Gargas (1984) observed that O_2 saturation was as low as 5% in the near-bottom water layers. In the tropical Paraguayan swamps, the Chaco, which are dominated by emergent macrophytes, *Thalia* and *Typha*, both of which grow to a height of 5 m and floating vegetation such as *Pistia*, *Azolla*, and *Aichhornia*, the surface O_2 levels are seldom above 50% saturation and the bottom ones are perpetually anoxic (Carter and Beadle 1931; Fig. 44). In some swamps, the dense plant canopy reduces the photosynthetic production of O_2 by algal activity and prohibits water stirring, factors which compounded by the intense utilization of O_2 in the putrefactive processes make the water anoxic within a fraction of a centimeter of the surface (Carter 1955; Beadle 1957). In the vegetation-covered Floridan swamps, the PO_2 is less than 0.67 kPa, $PCO_2 = 8.3$ kPa and the pH is 5.6 (Heisler et al. 1982). The waterlogged mat and the bottom peat are not only totally devoid of O_2 but are also highly reducing. Redox potentials (Eh) of −100 mV have been recorded within 30 cm of the water surface (Beadle 1957) and in most such cases, no measurable O_2 was detected within 2 cm of the surface. Due to the fact that the decomposing organic matter in the Lake Victoria basin swamps (largely covered by papyrus overgrowth) is mainly carbohydrate, the gaseous end product is mainly CH_4 (60%) with CO_2 consitituting only 30% and the remaining 10%

being made up of H_2, carbon monoxide, and ethylene (Visser 1963; Dehadrai and Tripathi 1976). In the extensive Sudd swamps of the Upper Nile (Rzoska 1974), a high concentration of H_2S has been reported (Talling 1957), a feature associated with the much greater reducing conditions where the O_2 levels deep inside the vegetation are only about 10% saturation (Rzoska 1974). The peculiar aspects of the swamps (scarcity of O_2, highly reducing environment and high CO_2 levels; Table 11) determine the variety, nature, and the biomass and productivity in such habitats (Carter and Beadle 1931). To complicate matters, toxic gases such as H_2S occur in high concentrations (Somero et al. 1989). In an ecosystem in which the conditions are highly adverse to life, adaptation for air breathing is intense. Such a change confers great selective advantage (Carter and Beadle 1931; Dehadrai and Tripathi 1976). In the Ugandan swamps, aquatic insects (Hemiptera, Coleoptera, mosquito larvae), pulmonate gastropods (e.g., *Biomphalaria sudanica*), oligochaete worms (e.g., *Alma emini*), and fishes (e.g., *Protopterus aethiopicus, Polypterus bichir, Clarias lazera, Ctenopoma muriei, Gymnarchus niloticus*), all of which are air breathers coexist (Beadle 1974; David et al. 1974). The swamps are characterized by a rapid growth of macrophyte cover and subsequent decomposition of the luxuriant organic matter leading to intense putrefaction and anaerobic decomposition of the overgrowth. These processes generally result in a hypoxic and hypercarbic habitat (Nassar and Munshi 1971; Dehadrai and Tripathi 1976; Ultsch 1976), except during episodes of peak photosynthesis.

The tropical swamps shrink during the hot spells or become muddy to the extent that the gills become unsuitable for gas exchange due to clogging by masses of floating and suspended detritus. Such waters are slightly acidic (with a pH of 6 to 6.5) mainly from the high levels of dissolved CO_2. The Guiana swamps have very low pH ranging from 4.3 to 4.4 (Carter 1935) while those in India are alkaline (pH 8 to 10; Dehadrai and Tripathi 1976; Munshi and Hughes 1992). Dissolved and bound CO_2 in the papyrus Ugandan swamps was found to be 148 mg per l at the end of a rainless season (Milburn and Beadle 1960). Up to 30 ppm free CO_2 was recorded in some Indonesian swamps by van Vass and Vaas (1960). During summer, in the water hyacinth-infested Floridan and Louisianian swamps, Lynch et al. (1947) measured a concentration of dissolved CO_2 as high as 80 ppm (about 213.3 kPa). A zero concentration of O_2 at a depth of about 30 cm, 0.6 ppm (about 1.2 kPa) at a depth of 5 cm and dissolved CO_2 level as high as 8 kPa were determined in a hyacinth infested pond in Gainesville, Florida (Ultsch 1976). In the tropical swamps, the CO_2 levels can rise to a level which would adversely affect the oxygenation of the hemoglobin and disrupt acid-base balance. In such desolate aggregations of water, in circumstances where the dissolved O_2 is low, that of CO_2 is usually high (Lynch et al. 1947). High concentration of O_2 alleviate the effects of high CO_2 levels: a 230-g salamander, *S. lacertina*, can tolerate a PCO_2 of 28 kPa for as long as 70 h when held in water in which the PO_2 ranges from 17.9 to 37.3 kPa (Ultsch 1976). Owing to their low metabolic rate (Whitford and Hutchison 1967) and capacity to tolerate high concentration of CO_2 (Ultsch 1976), the sirenids are well adapted to subsist in the hyacinth-infested waters where they constitute the dominant vertebrate fauna (Ultsch 1973). In the vegetation-covered lakes of the southeastern United States inhabited by two species of salamanders and the Congo eel, Heisler et al. (1982) reported a PO_2 of less than 0.67 kPa, a PCO_2 of

8.3 kPa, and a pH of 5.6. In a hyacinth (*Eichhomia crassipes*)-infested swamp, zero concentration of O_2 and a high one of CO_2 of 80 ppm were recorded (Lynch et al. 1947; Ultsch 1973). The temperate tidal pools examined by Truchot and Jouve-Duhamel (1980) had a temperature which ranged from 12 to 24 °C and the O_2 content amounted from virtual anoxia to hyperoxia within a 24-h cycle.

High concentration of CO_2 in water leads to certain physiological stesses on the aquatic animal life which call for specific adaptations for subsistence in such a habitats (e.g., Dubale 1959). These include: (1) low O_2 affinity of the blood (the Bohr effect), (2) decrease in O_2 capacity of blood (Root effect), (3) acid-base imbalance due to the decrease in pH of water consequent to an increase in PCO_2, and (4) reduced capacity to discharge CO_2 into the surrounding water owing to a reduction of the PCO_2 between the blood and the surrounding water. In *Anabas testudineus*, pH influences the pathway adopted for respiration (Hughes and Singh 1970s). Both aquatic and aerial respiration occur in neutral waters (pH 8 to 6.85) while aerial respiration predominates and aquatic respiration is depressed between pH 6.5 and 6.25. Gill ventilation completely stops (and is replaced by aerial respiration) in very highly acidic water ($pH < 6.25$). Similar behavior was observed in the yallow (*Erythrinus erythrinus*), an air-breathing fish, where gill ventilation virtually stopped and was replaced by aerial respiration in hypercarbic waters with a concentration of CO_2 above 39 ml per l (Willmer 1934). Such a response may be a safeguard against excessive transfer of CO_2 from water into blood across the gills, avoiding possible respiratory acidemia (Singh 1976). By switching to air breathing, the fish can tolerate high concentrations of CO_2 without adverse effects. Air-breathing fish, most of which subsist in hypoxic waters, are confronted with a real problem of losing O_2 through the gills into the surrounding hypoxic water (e.g., Smith and Gannon 1978). This is, however, minimized or avoided by vascular reflexes which lead to shunting of blood from the gills with a momentary elimination of branchial ventilation making the accessory respiratory organ(s) the only pathway(s) for transfer of O_2 to the body. Air-breathing fish, e.g., *Anabas* (Munshi 1968), *Channa* (Wu and Chang 1947; Hakim et al. 1978; Wu 1993), *Amphipnous* (Munshi and Singh 1968). and *Monopterus* (Liem 1961), have very poorly developed gills, perhaps to curtail O_2 loss through the gills during hypoxia. In the lungfish, *Protopterus*, the arteries of the embryonic 3rd and 4th branchial arches are devoid of gill filaments and form shunt vessels which correspond with the carotid and systematic arches of the Amniota (e.g., Wood and Lenfant 1976).

3.5 Terrestrial Habitation and Utilization of Atmospheric O_2

The degree of specialization and the survival strategies of most animals are determined by the efficiency with which they can in the first instance procure O_2 and secondly eliminate CO_2. In open aerial environments, production and utilization of CO_2 and O_2 are relatively small compared within the enormous volumes and high capacitances of the gases in the atmosphere (Dejours 1988). The constant level of O_2 and CO_2 in the atmosphere is of biological importance as major deviations from the tolerable range have harmful effects on unacclimatized animal life. With respect to composition and availability of respiratory gases, air is a much simpler medium to handle than water. Biological, physical, and chemical processes greatly influence the O_2 content of water. In stagnant waters and especially those covered by plant matter, there is reciprocity of environmental O_2 and CO_2 levels. As a result of organic respiratory processes, hypoxia will invariably be associated with some degree of hypercapnia. Except for fossorial habitats, terrestrial habitats are not normally liable to hypoxia or hypercapnia due to the great diffusivity of the gases in air.

3.6 Hydrogen Sulfide Habitats: Tolerance and Utilization

The energy-rich hydrogen sulfide (H_2S) is common in the hypoxic marine sediments and around hot springs at concentrations of 1 to 300 ppm (e.g., Berner 1963). Hydrogen sulfide is highly toxic even at very low molar concentrations. A concentration greater than 1 ppm is lethal to most organisms (Oseid and Smith 1974; Smith et al. 1976). The gas inhibits several heavy metal containing enzymes especially by binding to the heme of mitochondrial cytochrome c oxidase much as cyanide does. This prevents O_2 transport by the hemoglobin, arresting aerobic respiration (e.g., Somero et al. 1989). About 90% of cytochrome c oxidase is inhibited by a 5-molar sulfide solution (e.g., Julian and Arp 1992) and a sulfide concentration of 17 mol initiates maximal O_2 consumption (Eaton and Arp 1993). At moderately low concentrations (3.63 mol per l), specimens of *Rivulus marmoratus* were observed to leap from H_2S-contaminated water (Abel et al. 1987). Some animals, however, have acquired a capacity to tolerate H_2S and even utilize it for metabolic processes producing water and various sulfates (e.g., Felbeck et al. 1981). Others, e.g., in the Phylum Gnathostomulida (Farris 1976) and the turbellarian families Solenofilomorphidae (Crezee 1976) and Retronectidae (Sterrer and Rieger 1974), have adapted so well that they are virtually confined to the extreme anoxic H_2S-rich habitats (Fenchel and Riedl 1970). They survive by adopting different strategies which include: (1) physical exclusion of sulfide from the body, (2) possession of sulfide-insensitive cytochrome c oxidase, (3) direct detoxification whereby sulfide (H_2S, HS^- or S^{-2}) is chemically converted to less toxic products such as sulfate (SO_4^{-2}), sulfite (SO_3^{-2}), and thiosulfite ($S_2O_3^{-3}$) at the superficial tissue layers of the body or in certain specialized organs (Vetter et al. 1987; Menon and Arp 1992b), (4) strategic coexistence with chemoautotrophic endosymbiotic bacteria which break down H_2S, utilizing the energy thus acquired for production of ATP (e.g., Felbeck 1983; Fisher and Hand 1985; Powell and Somero 1985; Belkin et al. 1986; Firsher 1990), and (5) dependence on anaerobic metabolism. The marine echiuran worm, *Urechis caupo*, subsists in U-shaped burrows in intertidal mud flats where the concentration of H_2S may be as high as 66 μM and the concentration of O_2 as low as 3.3 kPa (Eaton and Arp 1993). Hydrogen sulfide passes through the body wall and the hind gut (Julian and Arp 1992), where hematin, which is contained in coelomic fluids and in the coelomocytes (Arp 1991), catalyzes its oxidation to nontoxic sulfur compounds as O_2 continues to be utilized for aerobic respiration (Powell and Arp 1989; Eaton and Arp 1993). A correlation between hematin concentration in the coelomic fluid and sulfide oxidizing activity was reported in *U. caupo* by Powell and Arp (1989). *U. caupo* has a very high tolerance for H_2S (Somero et al. 1989; Julian et al. 1991). The worm remains aerobic at concentrations above those which suppress the process in most aerobic organisms. In the intertidal lugworm, *Arenicola marina*, a specialized heme compound called brown pigment is thought to catalyze sulfide oxidation (Patel and Spencer 1963). The hemoglobins of the lugworm and the deep-sea hydrothermal vent-living polychaete, *Alvinella pompejana* (Desbruyères and Laubier 1986), are highly resistant to oxidation (Toulmond et al. 1988).

Extreme physiological conditions have been described in the submarine geothermal springs which have been discovered in the Galapagos Rift and East Pacific Rise fracture zones (e.g., Childress et al. 1989; Nisbet 1988). The water emerging from the fissures is as hot as 200 °C, is anoxic, and contains a high concentration of H_2S (Desbruyères et al. 1982; Johnston et al. 1988). The hot plume of water interfaces with the remarkably different sea-water at a temperature of about 2 °C, with a PO_2 6.7 kPa, pH about 7.5, and is totally devoid of H_2S (Johnston et al. 1986). This creates the greatest temperature gradient in any known environment occupied by animal life. Simple photosynthetic life is thought to have evolved in the submarine hydrothermal vents where chemotrophic organisms acquired the capacity to detect light (e.g., Russell et al. 1994; Nisbet et al. 1995). The interface between the hydrothermal plume and the bottom seawater constitutes a highly dynamic and complex ecosystem with fluctuating PO_2 (Johnston et al. 1986). A large number of different organisms such as sulfur oxidizing bacteria and animal species such as giant pogonophoran tube worms, crabs, shrimps, giant crams, fishes, and mussels flourish in complete darkness some 3 km below the suface (Grassle 1985; Fustec et al. 1987). Some of these species were unknown to science more than 20 years ago! The animals which stray from the vent risk starvation while those which get too close die of poisoning or heat. The hydrothermal plume crab, *Bythograea thermydron*, which has no bacterial symbionts, can tolerate high concentration of H_2S through having a particularly efficient sulfide oxidation capacity in the hepatocytes (Vetter et al. 1987) while *Riftia pachyptila* and *Solemya velum* possesses hemoglobins which hold and transport H_2S preventing toxicity (e.g., Doeller et al. 1988). In the deep sea hydrothermal vent cram, *Calyptogena pacifica*, which has symbiotic bacteria in the gills, O_2 consumption increases on exposure to concentrations of H_2S as high as 130 to 160 μM (Childress and Mickel 1982). The endosymbiotic bacteria in the gutless cram, *Solemya reidi*, which live in H_2S-rich sewage outflows, are able to maintain aerobic metabolism in the tissues through oxidation of H_2S to thiosulfate in presence of a concentration of H_2S of 100 μM (Anderson et al. 1990) and a much higher one of 500 μM in *Solemya velum* (Chen et al. 1987). The granules in the cytoplasm of the gill cells in *Solemya reidi* (Powell and Somero 1985; Powell and Arp 1989) and the osmiophillic electron dense organelles in the epithelial cells of the hind gut of *U. caupo* (Menon and Arp 1992b) are associated with H_2S detoxification. Similar granules have been observed in the epithelial cells of the "lung" groove (Fig. 45) of the oligochaete swamp worm, *Alma emini* (Maina et al. 1998)

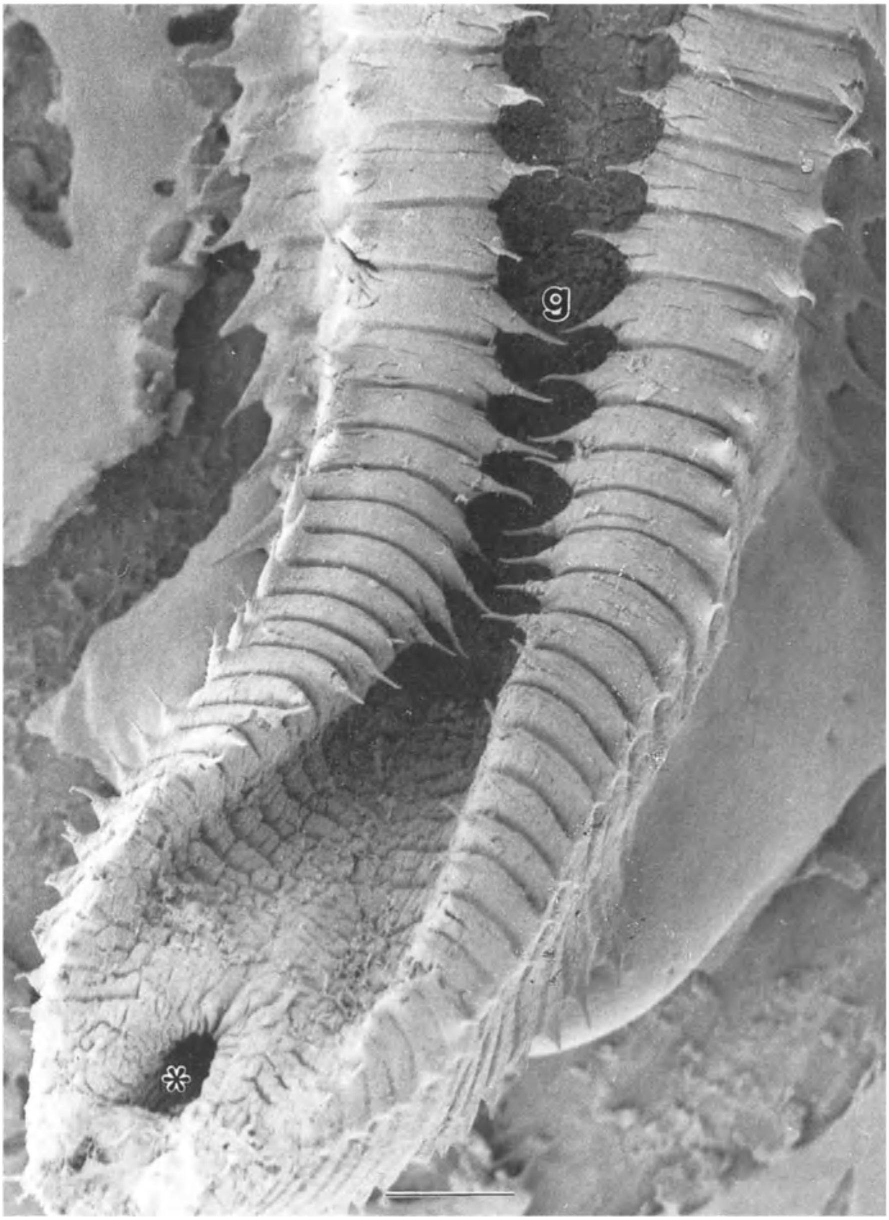


Fig. 45. Dorsal view of the temporary respiratory groove, *g*, of the oligochaete worm, *Alma emini*, which lives in putrefying plant matter of the East and Central African tropical swamps. The worm occasionally surfaces, forms a lung, and exchanges gases with the atmosphere. * cloaca. *Bar* 0.95mm. From Maina et al. (1998).

which lives in waterlogged soils where intense putrefaction of plant matter with possible release of H_2S occurs.

3.7 The Porosphere and Fossorial Respiration

In addition to the aerosphere and the hydrosphere, soil, the thin skin of the lithosphere, offers an important natural habitat to many animals. About 150 mammalian species temporarily or permanently live underground (e.g., Nevo 1970). The respiratory properties of the soil are very fluid. Its characteristics fluctuate between those of water (when the soil is wet or waterlogged) to those of air when it is dry. In three-dimensional space, the porosphere can be conceptualized as an intricate maze of fine air conduits between the soil particles. The air spaces open to the free atmosphere. Gas diffusivity in the soil may be up to one third that of free air (Ar 1987) but moist compact soil may offer a severe hindrance to gas diffusion (Currie 1984). Depending on the global temperature changes, soils offer an important source or sink of CO_2 (Susan et al. 1996). The principal factors which determine O_2 and CO_2 content of the porosphere are: (1) the intensity of respiration of the organic matter in the soil (Vannier 1983), (2) moisture content of the soil (e.g., Wilson and Kilgore 1978), and (3) the chemistry of the soil (Verdier 1975).

In general, the underground microenvironments are characterized by a high temperature, reduced light intensity, and in most cases perpetual darkness, low PO_2, high PCO_2, and frequently high humidity (e.g., Kennerly 1964; McNab 1966; Arieli 1979). These variables are translations of the surface (free atmospheric) factors except for CO_2, which is intrinsically produced by the soil fauna. The subsurface microclimates are more stable compared with the more variable and cyclic characteristics above. However, subterranean features such as O_2 and CO_2 levels and, in some cases, moisture content show greater range and oftentimes faster shifts than the corresponding surface ones. The stimulus of light as a physiological phenomenon, which to varying extents influences many of the surface-dwelling animals, is virtually eliminated under the soil. Since the gas requirements of an animal living in an underground burrow must in the first instance be derived from the free atmosphere by diffusion through the soil, many underground conditions, the physical features of the soil especially its porosity, are important in the distribution, abundance, and respiratory activity of fossorial animals (Kennerly 1964).

While many animals spend only part of their time underground in open burrows, only a few of them permanently live underground in closed burrows. In some habitats, subterranean (fossorial) animals constitute an important part of the total fauna. Burrows provide fossorial animals with protection against environmental extremes and predators and enable them to gain access to subterranean parts of plants particularly geophytes (roots, tubers, bulbs, and corms) and soil invertebrates. However, fossoriality imposes certain constraints on the animals which face huge energetic costs in subterranean excavation during foraging (Vleck 1979). Depending on soil hardness and burrow diameter, the cost of burrowing may be 360 to 3400 times greater than that of traveling the same distance on the surface (Vleck 1981). Pocket gophers can dig well over 200 m in 48 h (Hill 1944). The burrows of the naked mole rat (*Heterocephalus glaber*) may be as long as 3 km (Brett 1986). Wet soils constitute a limitation for thermoregulation in fossorial animals (Wierenga et al. 1969). As a consequence of their having had to adapt to a similar mode of life, remarkable convergence of form and function (e.g., Jarvis and Bennett 1990) has occurred in a remarkably phylogenetically diverse group.

The rate of diffusion of a gas or vapor through the soil is determined by the porosity, type of gas, and the prevailing concentration gradient between the air in the burrow and the free atmosphere (Penman (1940a,b). High concentration of CO_2 correlates with the soil moisture content (Kennerly 1964). When the content is high, water rather than air occupies the interstitial spaces between the soil particles thereby impeding the diffusion of gases. Respectively, moisture contents as high as 13 and 18% have been reported in fields occupied by the pocket gopher, *Geomys bursarius* (Kennerly 1964) and *Thomomys bottae* (Miller 1948). After heavy rain, 30 cm below the surface, Ege (1916) observed that the PCO_2 increased from 1.5 to 6.1 kPa and PO_2 dropped from 20.4 to 8.5 kPa. When the soil is waterlogged, gas diffusion may become a limiting factor, the soil becoming virtually anoxic (Currie 1962). Some animals living underground (e.g., the earthworms) may succumb to hypoxia or react to it by surfacing. The distribution of the pocket gopher, *Geomys pinetis*, correlated with that of the soils with a high water-holding capacity (McNab 1966). Acidic soils (podzols) are unable to chemically fix CO_2 while calcareous ones (e.g., clay soil) are able to buffer some CO_2. Due to the greater solubility and capacitance coefficient of CO_2 in water, O_2 rather than CO_2 diffusion should be the limiting factor in moist soils. Kennerly (1964), however, observed that in soils with different moisture contents, O_2 and CO_2 diffused through the soil at different rates, with O_2 reaching equilibrium much faster than CO_2. While CO_2 is organically produced within the soil, there is no subterranean source of O_2, which must be derived by diffusion from the surface. With the PO_2 falling to between 16 kPa in *Caretta* and 12 kPa in *Chelonia* and PCO_2, respectively, at 3.3 and 4 kPa in the nests, sea turtles hatch into a subterranean hypoxic and hypercapnic environment (Maloney et al. 1990): within 3 to 5 days, they must reach the surface or die of suffocation.

3.7.1 Gaseous Composition in Burrows

In addition to soil chemistry and porosity, the other factors which determine the composition of the air in the burrows include the size, length, location, and geometry of the burrow (Wilson and Kilgore 1978), and the numerical density of the burrow congeners. The burrows of the pocket gophers tend to be deeper in summer when the porosity and hence the diffusion capacity of the soil for O_2 is higher (Kennerly 1964). In most soils, the sum of the concentrations of O_2 and CO_2 remains almost constant and for soils with air porosities greater than 10% by volume, the rate of exchange of O_2 and CO_2 with the surface comes to equilibrium up to depths of 30 cm within a period of 1 h (Collins-George 1959). In the burrows of the pocket gopher, *Geomys bursarius*, burrows up to 30 cm in depth permit diffusion of O_2 from the surface at rates adequate for the respiratory needs of the gopher. Thermal equilibrium occurs up to a depth of 60 cm (Kennerly 1964). In a forest, 30 cm below the surface, Ege (1916) reported a CO_2 concentration of 0.2% (0.2 kPa) and one of O_2 of 20.6% (20.3 kPa). Aeration of the burrow must be most critical after rains when diffusion of O_2 and CO_2 between the burrow and the ground surface is greatly hindered. Under such circumstances, a net O_2 deficit in the burrow might occur. In the pocket gophers, *Thomomys* (Miller 1948) and *G. bursarius* (Kennerly 1964), burrows are opened in the early morning and late evening or night, a time when the cooler layer of air next to the warm ground enhances the diffusion of the air into the extensive burrow systems which range from 60 to 200 m in length. With an average diameter of 7.5 cm, a total burrow roof exposure area of about 60 to 200 m^2 is attained. This was considered by Kennerly (1964) to be more than adequate for the transfer of the respiratory gases while providing access to sufficient vegetation cover with subterranean plant parts, insects, and worms for food.

Concentrations of CO_2 as high 10% and O_2 levels as low as 10% have been reported in burrows (Boggs et al. 1984). The burrows of the pocket gopher (*Thomomys bottae*) had a concentration of O_2 as low as 6% and CO_2 as high as 3.8% (McNab 1966; Darden 1970; Chapman and Bennett 1975). Concentrations of O_2 as high as 20% and as low as 12.1% have been reported in the burrows of birds, with corresponding values for CO_2 ranging from 1.2 to 9% (e.g., Wickler and Marsh 1981). In ant hills, in summer, Portier and Duval (1929) found a PCO_2 of up to 1.9 kPa while Ege (1916) observed that while the PO_2 in the field was 20.4 kPa, in an ant hill it was 19.3 kPa and in a decaying beech trunk the value was 17.7 kPa. Concentrations of O_2 of 10 to 15% have been reported in some mammalian burrows by Kennerly (1964). In the burrows of five fossorial rodent species, the concentration O_2 ranged from 15 to 20% and CO_2 from 0.5 to 2.0% (McNab 1966). Concentrations of CO_2 as high as 2.3% and O_2 levels as low as 6% were estimated in the burrows of the pocket gopher, *Geomys bursarius* (Kennerly 1964), and in dens of hibernating mammals, concentrations of CO_2 as high as 13.5% and O_2 as low as 4% were reported by Williams and Rausch (1973). Soil flora (especially algae and bacteria) is thought to be the main source of CO_2 in the burrows (Kennerly 1964) though the intensity of activity, especially during mound building, must greatly elevate it. The gas concentrations in the burrows are remarkably different from those which can be tolerated by nonburrowing mammals. Extreme hypoxia as well as hypercapnia affect cardiac function in most mammals (e.g., Tucker et al. 1976), induce artificial hypothermia and in some cases torpor (Hyden and Lindberg 1970), have a general depressing effect on growth (Xu and Mortola 1989), and lower the ventilatory rate (Arieli and Ar 1979). The hypoxia that the mole rat, *Spalax ehrenbergi*, can withstand is comparable to an altitude of more than 9 km (Arieli et al. 1977). The respiratory physiology for subterranean subsistence is outlined by, e.g., Arieli and Ar (1979), Boggs et al. (1984), and Webb and Milsom (1994). Insensitivity of the pulmonary vasculature to hypoxia (Walker et al. 1982, 1984) may reduce resistance and ensure adequate pulmonary perfusion. Compared with those of the adult mammals, the lungs of the eusocial naked mole rat, *Heterocephalus glaber* show a remarkable degree of pedomorphy/neoteny (Maina et al. 1992). Perhaps what appears like a primitive (ancestral = plesiomorphic) state constitutes what has been called an evolutionary stable strategy by, e.g., Maynard-Smith (1996) and McNamara and Houston (1996) where the phenotype has been specially selected for the particular habitat the mole rat lives in. A highly refined resource use and niche occupation may reduce or even eliminate sympatric competition, decreasing fitness cost (e.g., Martin 1996).

3.7.2 Burrowing Aquatic Annelids, Crustaceans, and Fish

For reasons basically similar to those of the fossorial mammals, i.e., escape from predators and occupation of a more stable micromileu, a number of annelids (Mangum 1964; Myers 1972; Toulmond 1991), crustaceans (Little 1983; Atkinson and Taylor 1988), and fish (Pelster et al. 1988a,b; Taylor and Atkinson 1991) have adopted a subaquatic burrowing life-style. Among crustaceans, burrow construction is commonest in members of the infraorders Astacidea, Thalassinidea, and Brachyura. Fish such as the tile fish (Branchiostegidae) (Able et al. 1982) and the garden eels (Anguilliformes) construct mucus-lined tubular burrows (Taylor and Atkinson 1991). The marine polychaete, *Chaetopterus variopedatus*, lives in elaborate U-shaped tubes which are said to be impermeable to water and gases (Fauvel 1927; Dales 1969; Brown and McGee-Russel 1971) while the lugworm, *Arenicola marina*, an intertidal polychaete, lives in an L-shaped mucus-lined burrow system (Wells 1966). The mud shrimp, Mediterranean shrimp, *Callianassa truncata*, builds extensive burrows in the sediments to a depth of 48 cm (Ziebis et al. 1996): the shrimp can maintain burrow O_2 concentration at 3 to 12% of air saturation by generating water currents of a flow rate of $10\,\mathrm{m\,s^{-1}}$.

Like the surface-based fossorial mammals, the subaquatic burrowing animals face unique respiratory challenges that call for special adaptive strategies to overcome hypoxia and hypercapnia. High concentrations of H_2S are a common occurrence (Bridges 1987; Atkinson and Taylor 1988; Toulmond 1991). Burrowing fish such as *Periophthalmus cantonensis* may encounter extreme hypoxia (PO_2, 0.7 to 3 kPa) at a depth of 5 to 15 cm (Gordon et al. 1978) and may face total anoxia at a depth of about 1 m (Gordon et al. 1985). In the burrows of the snake blenny, *Lumpenus lampretaeformis*, the PCO_2 of the water in the burrow is above 0.2 kPa compared with that at the surface of the mud (Atkinson et al. 1987). To alleviate adverse respiratory stress, the crabs use their pleopods (e.g., Farley and Case 1968; Hill 1981) and to a small extent their scaphognathites (Taylor and Atkinson 1991) to intermittently ventilate their burrows and their gas exchangers with better oxygenated water. In most species, e.g., *Callianassa californiensis*, the beating of the pleopods increases with the level of hypoxia (e.g., Felder 1979).

Certain physiological adaptations have been reported in the aquatic burrowing crustaceans and fish. Greater O_2 affinity and high Bohr values, favorable parameters for O_2 uptake in hypoxia, have been reported (e.g., Innes 1985; Brigdes 1986; Pelster et al. 1988a,b). These features, however, do not appear to be specific to the burrowing mode of life but rather to the habitat they occupy (Taylor and Atkinson 1991). The greatest adaptive strategy that the burrowing crabs and fish possess is their overt capacity to tolerate hypoxia (e.g., Hagerman and Uglow 1985; Swain et al. 1987) and even withstand anoxia (Hill 1981; Mukai and Koike 1984). The red band fish, *Cepola rubescens*, and *Lumpenus lampretaeformis* can maintain their normal aerobic metabolism constant down to a PO_2 of 7 to 9 kPa (Pullin et al. 1980; Pelster et al. 1988a,b). Hypoxia causes increased opercular ventilation in the burrowing decapods and fish (Pelster 1985; Bridges 1987).

3.8 Living at High Altitude: Coping with Hypoxia and Hypobaria

With some exceptions, the majority of living organisms have evolved at or close to sea level. They have hence adapted to an O_2-enriched environment with an ambient atmospheric pressure of 1 atmosphere (101.3 kPa; Table 12). Including other factors such as cold, rarefied atmosphere, and harmful cosmic radiation, hypoxia is the most significant factor which limits survival at high altitude. Since the demands for O_2, whether at sea level or at altitude, are essentially the same, all other factors held constant, movement to a hypoxic environment imposes great metabolic demands on an animal and calls for definite physiological adaptations for procurement of the necessary amounts of O_2. Acute exposure to severe hypobaric-hypoxia equivalent to that at the top of Mt. Everest (altitude 8848 m, barometric pressure 33.7 kPa), where only 30% of the initial maximum aerobic capacity (maximum O_2 consumption) at sea level is lost, would be fatal to most unacclimatized human beings without an auxiliary source of O_2. With adequate adjustments, however, fit human subjects performing at the limits of their aerobic capacity have reached some of the highest peaks (Dejours 1982; West 1983; Houston et al. 1987). Animals living at sea level benefit from a considerable head

Table 12. Oxygen concentration in inspired air in animals of various body temperatures at different barometric pressures. (After Dejours 1981)

T (°C)	Alt. (m)	BP (mmHg[a])	K1	K2	FIO_2	CIO_2 ml STPD/ml BTPS	CIO_2 mmol/lBPTS
41	150	747	0.787	35.13	0.2095	0.165	7.37
15	150	747	0.915	40.83	0.2095	0.192	8.55
37	0(SL)	760	0.826	36.84	0.2095	0.173	7.72
37	3400	500	0.525	23.40	0.2095	0.110	4.91
37	7200	300	0.293	0.293	0.2095	0.061	2.74

T, body temperature; BP, barometric pressure; K1, reduction factor from values BTPS to volumes STPD; K2, reduction factor from 1 li of volume BTPS to the dry quality of substance in mMol; FIO_2, fractional concentration of O_2 in normal dry air; CIO_2, concentration of O_2 in inspired air; BTPS, body temperature, pressure, saturated with water; STPD, standard temperature, pressure, dry air (°C, 1 atmosphere pressure).

[a] To convert to kPa multiply by 0.133.

pressure of O_2 in the atmospheric air ($PO_2 = 21.2$ kPa). At the respiratory site, the pressure drives O_2 in adequate amounts past the tissue barriers into the blood and finally to the mitochondria where the prevailing PO_2 is between 0.1 to 0.3 kPa (Figs. 2,3). Diffusion of O_2 across the blood-gas barrier is the limiting factor for survival at high altitude (West and Wagner 1980; Piiper and Scheid 1981).

About 30% of the Earth's surface lies above 1 km altitude. There are many areas with an elevation in excess of 2.5 km (Webber 1979). Natural acclimation to moderate hypoxia is thus a common feature to many animals. Above an altitude of 3 km, most unacclimatized subjects will show overt signs of high altitude respiratory distress such as shortness of breath and increased pulse rate (e.g., Heath and Williams 1981). Physiological disturbances such as reduced aerobic capacity (Squires and Buskirk 1982) or night eversion (McFarland and Evans 1939) may start at the much lower altitudes of 1.2 to 1.5 km. At 11 km, an auxiliary source of O_2 will be needed while at about 19 km, without compensatory hyperventilation, little if any O_2 reaches the alveoli even when pure O_2 is breathed. This is because at that altitude the total barometric pressure of 11.6 kPa equals the sum of the partial pressure of the water vapor of 6.3 kPa (at 37 °C) and that of CO_2 of 5.3 kPa. Above this altitude, when the external vapor pressure falls below that of the body fluids at body temperature, in homeotherms, evaporation which may be accompanied by life-threatening formation of vapor bubbles (boiling) in the tissues, blood vessels, and body cavities occurs (e.g., Armstrong 1952). Just as the rarefaction of the atmosphere with altitude has a significant effect on the aerodynamics of flight, it has considerable influence on the tidal movement of air in the respiratory tract and the forces generated in the mechanical ventilation of the lung (e.g., Luft 1965). Since the resistance to turbulent flow scales with the square of the flow velocity, the effect of rarefaction of air with altitude is more predominant at high flow rates, e.g., during hyperpnea, which is one of the initial responses to high altitude hypoxia. The lungs and the chest, which function as pneumatic pumps, operate at a disadvantage at altitude while the driving force of the respiratory muscles is somewhat fixed (Johnson 1964). The overall respiratory work at altitude is, however, less than that at sea level mainly owing to the reduction of turbulent flow in favor of laminar one (Ulvedal et al. 1963). This may account for the fact that at 6.1 km, in acclimatized men, spontaneous pulmonary ventilation may exceed 200 l per minute during strenuous exercise (Pugh 1962). Though the fractional concentration of O_2 in the dry atmosphere stays constant at 20.93%, at least until an altitude up to 110 km, due to the compressible nature of gases, at sea level, the PO_2 is greater. With ascent to high elevations, the molar concentration of O_2 in air decreases in proportion to the decrease of PO_2. Long-term and immediate human physiological adjustments at high altitude are now well known. The subject has recently been reviewed by West (1991). High altitude hypoxia does not appear to restrict the distribution of reptiles and amphibians (Hock 1964). Eleven species of frogs live between a height of 3.7 and 5.2 km. The highest living known reptile, *Leiolopisma ladacense*, is found at an altitude of 5.5 km. *Telmatobius culeus*, a frog found in Lake Titicaca (altitude 3.8 km) is adapted to low aquatic PO_2 by combining behavioral, physiological, and morphological adaptations to the cool 10 °C O_2-saturated (13 kPa) water (Parker 1940; Monge and Monge 1968; Hutchison et al. 1976). Its skin is well vascularized and folded (to increase the surface area) and the blood has small, numerous erythrocytes (the highest count among amphibians), high hemoglobin concentration, and high hematocrit. These factors give rise to a high O_2 capacity. When swimming, the frog increases the convective movement of water over the skin through what has been described as bobbing behavior by Hutchison et al. (1976), a violent locomotory agitation of the water. Since the inhaled air in transit through the respiratory passages is warmed up to the body temperature and is maximally humidified, the PO_2 in the moisture saturated air is about 20% lower than that of the ambient dry air. The possible respiratory advantages of a lowered partial pressure of the water vapor in the ectotherms, where due to the lower body temperature the "alveolar" PO_2 should be higher compared with that in the endotherms, has not been fully investigated. The water vapor partial pressure is 6.2 kPa at the body temperature of 37 °C in mammals and is even higher in birds (7.3 to 8.3 kPa, Tb = 40 to 42 °C).

3.8.1 Tolerance of Arterial Hypocapnia in Birds

Migrating birds have been tracked at altitudes of over 6 km (e.g., Richardson 1976). The highest authenticated record of a flying bird is that of a Ruppell's griffon vulture, *Gyps rueppellii*, which was sucked into the engine of a jet craft at an altitude of 11.3 km over Abidjan (Côte d'Ivoire, West Africa; Laybourne 1974). At that altitude, the barometric pressure is about 24 kPa (i.e., 20% of that at sea level), the PO_2 in the expired air is less than 5.3 kPa (closer to 2.7 kPa if hyperventilation could bring the PCO_2 to about 0.67 kPa) and the ambient temperature is about −60 °F (Torre-Bueno 1985). The capacity of birds to survive, let alone exercise, under such circumstances is unmatched among animals. Flapping flight is energetically a very expensive mode of exercise (e.g., Tucker 1972). An actively flying animal consumes O_2 at two times the rate of a ground-dwelling one at maximum exercise (e.g., Thomas 1987). Hummingbirds hover with a muscle power output of nearly 100 to 120 $\mathrm{W\,kg^{-1}}$ at a 9 to 11% mechanical energy (Wells 1993a). In the housefly, a sure sign of approaching death is that of inability to fly (Sohal and Weindruch 1996). In a rarefied atmosphere, as occurs at high altitude, for a particular speed, the cost of flight is much greater than at sea level (Torre-Bueno 1985).

A fundamental respiratory physiological difference between birds and mammals is that birds can withstand greater hypocapnia where the arterial PCO_2 may drop to below 0.8 kPa (as the pH rises to 7.96) during panting (e.g., Faraci and Fedde 1986). Part of the respiratory efficiency and tolerance to hypoxia at altitude in birds must indirectly be related to this particular attribute which enables birds to hyperventilate and thus acquire sufficient amounts of O_2 without respiratory complications. A house sparrow at a simulated altitude of 6.1 km and ambient temperature of 5 °C has a respiratory frequency 38% above the sea level value and the ventilation of the parabronchi increases by 75% (Bernstein 1990). Birds can withstand the high level of arterial hypoxemia because brain blood flow is not affected by arterial hypocapnia (e.g., Faraci 1990). In fact, in species such as pigeons, the bar-headed geese, *Anser indicus*, and the duck, *Anas platyhynchos*, blood flow to the brain is not affected or actually starts to increase when the arterial blood PO_2 drops to below 10 kPa: the flow can increase sixfold (Grubb et al. 1978; Faraci and Fedde 1986; Pavlov et al. 1987). In the human being, lowering the arterial PCO_2 to 1.3 kPa results in hypocapnic cerebral vasoconstriction, causing a reduction of the flow of blood to the brain by about 50% (Wollman et al. 1968). In the bar-headed goose, *Anser indicus*, cerebral blood flow is not affected by reduction of the arterial PCO_2 to 0.9 kPa (Faraci and Fedde 1986). The remarkable efficiency of the bird lung particularly during hypoxia is brought about by a multiplicity of cardiovascular and pulmonary factors: the most significant advantage is imparted by the crosscurrent arrangement between the parabronchial air and blood flows (Fedde et al. 1985; Maina 1994, 1996, 1998). At altitude flight, birds can hyperventilate without the risk of experiencing respiratory alkalosis and cerebral vasoconstriction from the resultant hypocapnia. Using measurements and estimates of man at the altitude of Mt. Everest (Dejours 1982; West 1983), Scheid (1985) calculated that if the human alveolar lung were replaced by the avian parabronchial one, for the same arterial blood gases, the person would ascend 780 m higher in altitude.

3.8.2 Flying over Mt. Everest: the Bar-Headed Goose, *Anser indicus*

Perhaps the most astounding high altitude flight behavior in birds is that exhibited by the bar-headed goose (*Anser indicus*) during its annual trans-Himalayan migration from the wintering grounds of the Indian subcontinent to the breeding grounds around the large lakes in the south-central regions of Asia which are at elevations of about 5.5 km (Swan 1970). The birds take off from virtually sea level and cross the Himalayan mountains almost directly, reaching an altitude of about 10 km over the summits of Mt. Averest and Annapurna 1 (Swan 1961, 1970; Black et al. 1978; Black and Tenney 1980). The barometric pressure at these altitudes is about 31 kPa and the PO_2 in dry air is 6.5 kPa (West et al. 1983). Assuming that during these excursions the geese maintain a constant body temperature of 41 °C and the inhaled air is warmed to that of the body and is fully saturated with moisture, the PO_2 in the humid inhaled air which arrives at the gas exchange surface of the lung would barely exceed 4.9 kPa. Experimentally, the bar-headed goose withstands hypoxia at a simulated altitude of 11 km (Black and Tenney 1980) and up to an altitude of 6.1 km, it maintains normal O_2 consumption without need to hyperventilate. On ascending to 11 km, where the concentration of O_2 is only 1.4 $\mathrm{mmol\,l^{-1}}$, the bird takes in adequate O_2 to necessitate only a minimal increase in ventilation. At 39 °C and pH 7.4, the blood of the bar-headed goose has a much higher O_2 affinity ($P_{50} = 3.9$ kPa) than that of the greylag goose (*Anser anser*) ($P_{50} = 5.3$ kPa), a close relative which subsists at lower altitudes (Petschow et al. 1977; Black et al. 1978).

Extreme high altitude-adapted animals show a left shift of the O_2-hemoglobin curve (Perutz 1990b; Weber et al. 1993). In *A. indicus* (Weber et al. 1993) and the Andean goose, *Cleophaga melanoptera* (Hiebl et al. 1987), where unusually high blood O_2 affinity is crucial for survival, the amino acid residues α-119 and β-55, which form an $\alpha_1\beta_1$ contact in human hemoglobin, are respectively altered in these two birds. The loss of contact appears to increase O_2 affinity (Weber et al. 1993). In *A. indicus*, proline is replaced by shorter amino acid alanine (Weber et al. 1993) and in *Cleophaga*, leucine is replaced by short-chained serine, resulting in the loss of a single intramolecular contact (Hiebl et al. 1987). These observations suggest that adaptive changes in protein function evolved by substitution of one or a number of amino acids at specific sites, but a large proportion of such mutations are selectively neutral (Perutz 1983). The similarities in the strategies adopted by the bar-headed and the Andean geese, i.e., two single-point amino acid mutations that alter intramolecular contact enhancing hemoglobin-O_2 affinity in two geographically separated species (Weber et al. 1993) is a classic case of convergent evolution at the molecular level. In the bar-headed goose, cardiopulmonary parameters indicate that muscle blood supply and O_2 loading from the blood capillaries rather than ventilation or pulmonary gas transfer are the limiting steps in the supply of O_2 to the contracting flight muscles under hypoxia (Fedde et al. 1989). This conforms with the observation made by Black and Tenney (1980) that the PO_2 in the arterial blood at a simulated altitude of 11.6 km is only 0.13 kPa less than that in the exhaled air. Weinstein et al. (1985) observed that "the evolution of hypoxia tolerance in birds may have developed secondary to that of the effective gas exchange and transport features needed for flight".

3.9 Gravity: Effects on Respiratory Form and Function

Land animals evolved from aquatic forms which subsisted in virtual weightlessness. Within historical times, humans have experienced the almost constant gravity of about 9.81 $N\,kg^{-1}$ on the Earth's surface. Weightlessness or zero gravity (0-G) presents a completely new dimension in biology. Compared with the other three forces that govern matter in the Universe, i.e., electromagnetism and the weak and strong nuclear forces, gravity is unique in many ways: it only pulls but does not push and is a relatively very weak force that has an infinite range. Thompson (1959, p 32) observed that "gravity not only controls the actions but also influences the forms of all save the least of organisms" and humorously cites "sagging wrinkles", "hanging breasts" and "many other signs of old age" as part of gravity's slow, remorseless creations. Due to its assumed invariability since the formation of the Earth (but see different views from geological, e.g., Carey 1976 and paleontological, e.g., Holden 1993, studies that argue that the parameter has varied in the past) and lack of easy means and ways of manipulating it for purposes of testing, gravity has largely been considered to be of little consequence in biology. Experimentally, increase in gravitational field has been shown to increase the metabolic rate (Smith 1976, 1978; Economos 1979; Pace and Smith 1981). Like the other features which influence aspects such as body size, shape, and locomotion, and hence prescribe the metabolic scope of an animal, gravity must have greatly influenced the definitive designs, the allometric scaling, and the structural and functional parameters in all evolved life forms. The lung and chest, which on the ground have to be elastic to be able to carry out ventilatory activity, are easily deformed by their own weight just as the gills collapse out of water. Hypogravity greatly modifies the pleural pressure, shape, and regional distribution of air and blood in the respiratory system (e.g., Engel 1991). Both the structural and functional features of the pulmonary system such as alveolar and blood capillary size and volume (Glazier et al. 1967; Hogg and Nepszy 1969; Gehr and Erni 1980), ventilatory distribution (Michels and West 1978), and blood perfusion (West 1977a), factors which cause deformation of the parenchyma (e.g., West and Mathews 1978), are variably affected by gravity. The lungs of a variety of mammals and reptiles show remarkable vertical stratification of blood flow with the "highest" regions of the lung receiving substantially less blood than the dependent ones (e.g., West 1977b; Seymour et al. 1981). In the horse and the dog, there is a fourfold difference in the volume of alveoli from the apex to the base of the lung (Glazier et al. 1967; Hogg and Nepszy 1969; Gehr and Erni 1980). Recent studies, e.g., those by Glenny and Robertson (1991b) and Hlastala et al. (1996), however, indicate that the effect of gravity on the pattern of pulmonary perfusion is less important than was earlier thought. In the dog, topographical differences in pleural pressure exist (e.g., Proctor et al. 1968) and the intrapleural pressure is more negative on the dorsal than on the ventral aspect. The dependent regions of the lung have a small resting volume but a large increase in the inspiratory volume (Milic-Emili et al. 1966). The spatial characteristics of the pulmonary arterial tree play an important part in the perfusion of the lung (Glenny 1992). In the land crab, *Holthuisana transversa*, stratification of the hemolymph in the branchiostegal circulation occurs, with the ventral parts containing more hemolymph than the dorsal ones (Taylor and Greenaway 1984). Though the concentration of the vascular units in the apical and basal regions of the lung is the same (McGrath and Thomson 1959), hydrostatic differences lead to a decrease of blood flow from the gravity dependent parts of the lung to the apical parts (in an upright human lung), there being a nine times difference between the two regions of the lung (West et al. 1964). Ventilation decreases from the lower to the upper lobes of the lung though the decrease is not as much as that of the blood (e.g., West and Dollery 1965). The ventilation-perfusion ratio increases five times from the "bottom" to the "top" of the upright human lung, leading to regional differences in gas exchange efficiency (West and Jones 1965; Wilson and Beck 1992). Gravity-independent ventilatory inhomogeneities are as large as gravity-dependent ones (Verbanck et al. 1996). Such differences are to be expected in an organ that separates blood from air, fluids of very different densities, over a thin barrier.

Practically all the regional ventilation-perfusion inequalities which are observed at 1-G state are significantly reduced at 0-G (e.g., Michels and West 1978) or in a lung filled with and immersed in a fluid of which the specific gravity is the same as that of blood (West et al. 1965). At 0-G, increased redistribution of pulmonary perfusion to the upper parts of the lung occurs (e.g., Michels et al. 1979), increasing the diffusing capacity of the lung (Prisk et al. 1993; Vaïda et al. 1997). Acceleration (i.e., increased G), a process which is accompanied by compressive stresses, results in increased regional differences in lung expansion in the dog (Glazier et al. 1967) and in the human being (Crosfill and Widdicombe 1961).

Table 13. Effects of weightlessness during parabolic flight and of +2Gz on central venous pressure and heart rate in humans. (After Norsk et al. 1987)

Parameter	Ground			Inflight		
	Supine (+1 Gx)	Upright (+1 Gz)	Supine (1 Gz)	Upright sitting (+1 Gz)	0G	Upright
CVP, mmHg	7.7	1.9	5.0	2.6	68	2.8
HR, beats min^{-1}	–	–	65	70	79	80

CVP, central venous pressure; HR, heart rate; +Gz, headward acceleration with a head to foot direction of resultant inertial force; +Gx, forward acceleration with a chest to back direction of resultant inertial force.

Redistribution of the blood and extracellular fluid due to removal of the hydrostatic pressure gradient coupled with normal tissue elasticity and muscle tone in the lower limbs is an important response to acute weightlessness which induces a significant increase in the central venous pressure (CVP) in humans compared with that in the supine and upright sitting positions at 1-G (e.g., Pendergast et al. 1987; Engel 1991; Table 13). In the human being, the venous hydrostatic indifference point is located below the heart (Blomqvist and Stone 1983). The increase in the CVP leads to congestion of the intrathoracic circulation, including that of the respiratory system due to the negative intrathoracic pressure as the blood is removed from peripheral circulation and concentrated in the central systemic circulation. At 0-G, the CVP is 0.9 kPa compared with a value of 0.3 kPa on the ground (1-G, sitting position) and 0.35 kPa in flight (1-G, upright sitting position) (Norsk et al. 1987). The blood volume shift decreases the functional residual capacity while leading to an increase in the thoraco-abdominal volume (e.g., Kimball et al. 1976): the changes in blood volume cause reciprocal changes in lung volume and the chest wall. Increased intrathoracic pressure may lead to congestion and subsequent engorgement of the pulmonary vasculature, a feature which, all factors being normal or nearly so, would lead to increased pulmonary diffusing capacity of O_2 due to the greater capillary surface area. However, elevated pulmonary blood volume results in increased microvascular pressure which is likely to cause interstitial edema of the blood-gas barrier. This causes a reduction in the diffusing capacity of the lung especially during exercise, when pulmonary arterial and venous pressures rise in correspondence with the increase in pulmonary blood flow. Interstitial edema resulting from increased pulmonary capillary blood pressure due to redistribution of blood to the central circulation in microgravity leads to rapid shallow breathing as a result of stimulation of the J-receptors (Engel 1991) and may be life-threatening. Excesssive transmural pressure (TMP) may lead to stress failure of the blood-gas barrier, causing disruption of capillary endothelial cells, alveolar epithelial cells, or both (Tsukimoto et al. 1991; West et al. 1991; Costello et al. 1992). The blood-gas barrier is designed to withstand high intramural stress by having a thin layer of the strong collagen-IV in the extracellular matrix (Costello et al. 1992). Stress failure of the pulmonary capillaries leads to some pathophysiological conditions such as edema, exercise-induced pulmonary hemorrhage, and emphysema in horses (e.g., West et al. 1991). Above a TMP of 3.3 kPa, stress failure in the alveolar wall in the rabbit lung enhances exudation onto the alveolar surface (Costello et al. 1992). In the horse, the capillary transmural blood pressure which causes stress failure in the pulmonary capillaries ranges between 10 and 13 kPa (Birks et al. 1997).

Chapter 4

Water Breathing: the Inaugural Respiratory Process

> *"Of all the substances that are necessary to life as we know it on Earth, water is by far the most important, the most familiar, and the most wonderful; yet most people know very little about it." Thomson (1961)*

4.1 The Design of the Gills

By way of the hydrologic cycle, water on Earth is believed to have remained unchanged in amount and character for about 3000 million of years (Leopold and Davis 1968). From the current concepts of paleobiology, it is popularly considered that life started in water (e.g., Thompson 1980; Selden and Edwards 1989). Currently, as many as 21 000 species of fishes (e.g., Nelson 1976; Gilbert 1993), the largest extant vertebrate taxon, live in it. More than half of the living vertebrates have arisen from evolutionary lineages which still inhabit water (Pough et al. 1989). For the first 150 to 200 million years of life on Earth, owing to the harmful effects of the UV light, life was consigned to water. The earliest complete fish fossils, members of the long extinct group named ostracoderms, date to at least 425 million years ago (Repetski 1978). As an ecosystem, water presents greater microhabitat diversity than air and land. Some extreme aquatic habitats include the hot geothermal springs at the floor of the deep oceans 3 km from the surface (e.g., Childress et al. 1989) and the volcanic, hot, alkaline lakes, e.g., Lake Magadi of the Kenyan Rift Valley where the osmolarity of the water is $600\,\mathrm{mOsm\,l^{-1}}$, pH 9.6–10.5, O_2 level $2.2\,\mathrm{mg\,l^{-1}}$ and temperature about 43 °C (Reite et al. 1974; Johansen et al. 1975). During the millions of years that they have lived in water, fish have adapted very well. Presently, they have a cosmopolitan distribution, occupying diverse ecological niches.

Compared with air breathing, water breathing is the more ancient mode of respiration (e.g., Kämpfe 1980). Pharyngeal gills are a characteristic feature of the phylum Chordata (e.g., Gutman and Bonik 1981). Except for detailed morphology, for such a heterogenous taxon, the basic structure of the gills in the agnathan and gnathostomatous fishes is strikingly similar. The gills combine simplicity of design with functional complexity. Interestingly, some species such as *Hypopomus*, a tropical swamp fish from Paraguay, and *Gillichthys mirabilis* take in air bubbles and hold them over their conventional gills (Carter and Beadle 1930, 1931; Todd and Ebeling 1966; Gans 1971). This may have been the first but futile attempt to extract O_2 directly from air before respiratory concavities and pouches which subsequently evolved into lungs developed. The open aquatic environment contains respiratory gases in equilibrium with the aerosphere. Evaporative water loss as a factor in respiration does not arise. While the gills

Fig. 46. Gill filaments (*f*) of a tilapiine fish, *Oreochromis alcalicus grahami*, showing the bilaterally located secondary lamellae (*s*). The secondary lamellae are an efficient site of gas exchange where the blood and water flow in a countercurrent manner. *Bar* 80 μm

are highly efficient in O_2 uptake in water, except in a few specially adapted air-breathing fish, the lamellae, the numerous closely packed leaf-like plates which are arranged around the gill filaments (Fig. 46), after drying out in air, become impermeable to gases. Furthermore, out of water, the lamellae cohere due to surface tension and collapse under the force of gravity, in the manner of shore weeds at low tide. This reduces the respiratory surface area, creates large diffusional dead air spaces, and increases branchial vascular resistance, ultimately drastically lowering the gas exchange capacity of the gills (Burnett and McMahon 1987; Graham 1990). The animal becomes anoxic, hypercapnic, and eventually succumbs to asphyxia though exposed to a medium rich in O_2. Moreover, during exposure to air, CO_2 levels in blood increase, precipitating a hypercapnic and subsequently an acidotic state due to the inefficiency of the gills in discharging CO_2 into the air. The transfer of O_2 in the gills and lungs of the coconut crab, *Birgus latro*, decreases 30-fold if the chitin is allowed to dry up (Harms 1932). The decline of O_2 consumption of the intertidal limpet, *Patella granularis*, when held in air is due to a functional impairment of the external pallial gills which dry up after evaporative water loss (Marshall and McQuaid 1992). When out of water, the gas exchange capacity of the gills of aquatic crustaceans is severely reduced by a factor of 3 in *Callinectes sapidus* (e.g., O'Mahoney and Full 1984) and up to five times in *Cancer productus* (DeFur and McMahon 1978). After adaptations such as greater rigidity of the gills through increased sclerotization and wider spacing of the secondary lamellae, features which minimize adhesion and collapse, *Carcinus maenas* can use its gills in air (Taylor and Butler 1978) and may tolerate air exposure for several days (Truchot 1975). In the terrestrial crabs, e.g., *Geograpsus grayi, G. crinipes, Cardisoma hirtipes*, and *Gecarcoidea natalis*, and in fish like mudskippers, e.g., *Periophthalmus*, which live in shallow mudflats (Gordon et al. 1969, 1985; Mutsaddi and Bal 1969; Tytler and Vaughan 1983; Clayton and Vaughan 1986), the gills are diversely adapted through wider gill filament spacing, gill lamellae stiffening by thicker chitinous deposition and presence of nodules which physically keep the lamellae apart (e.g., Low et al. 1990; Farrelly and Greenaway 1992) enabling the gills to be used in air (Tamura and Moriyama 1976; Tamura et al. 1976). Terrestrial vertebrates which can permanently use gills in air have not evolved and probably never will since, in addition to the gas exchange role, the gills serve other important functions such as ionic regulation and ammonia excretion (e.g., Wendelaar-Bonga and Meis 1981; Laurent and Perry 1991) which can only be effectively carried out in water. Over 90% of the NH_3 excreted in aquatic fish takes place across the gills (Smith 1929). The development of accessory respiratory organs was utilized to circumvent this evolutionary dead end. Some fish which are well adapted to terrestriality, e.g., the mudskipper, *Periophthalmus* (Tytler and Vaughan 1983), can convert ammonia to the less toxic urea (Gregory 1977) and thus extend their survival out of water. Interestingly, insectan wings are thought to have evolved from ancestral gills which were used by aquatic insects for ventilation and swimming (Marden and Kramer 1994).

4.2 Adaptive Diversity and Heterogeneity of Gill Form

Developmentally, gills are gas permeable evaginated outgrowths from the body of aquatic animals (Figs. 4,5). They constitute an interface between two compartments filled with aqueous solutions, an external medium (water) and internal extracellular fluid (hemolymph or blood). Gills occur in different sizes, forms, and locations. They range in complexity from the simple tegmental evaginations like the tube feet and pupullae of some classes of echinoderms which provide only a minor supplement to gas transfer (much of which takes place across the skin), the external gills of the annelid polychaetes, some molluskan nudibranchs, larvae of teleosts (e.g., *Gymnarchus*), and the tadpoles to the more elaborate multifunctional internal ones contained in the branchial chambers, e.g., in crustaceans and teleosts or accommodated in a mantle cavity, e.g., in mollusks (e.g., Laurent 1982; Hughes 1984). The fragile and yet elegant structure of the gills (Ojha and Singh 1986; Olson 1996) has fascinated biologists for a long time. They constitute a paradigm of an efficient external (evaginated) aquatic gas exchanger and provide a fundamental model for the study of the manifold respiratory processes and mechanisms adopted by the higher vertebrates. Gills carry out diverse seemingly unrelated functions which include respiration, osmoregulation, acid-based balance, ammonia excretion, regulation of circulating hormones like catecholamines and angiotensin, and detoxification of plasma-borne harmful substances (e.g., Neckvasil and Olson 1986), locomotion (e.g., Septibranchs), and feeding. The definitive design of the gills must be a compromise between all the functional requirements (McDonald et al. 1991). The trophic (filter-feeding) role of the gills is exhibited by the simple chordates in the subphyla Tunicata and Cephalochordata, e.g., *Amphioxus* and *Petromyzon* (e.g., Baskin and Detmers 1976; Youlson and Freeman 1976) and actinopterygian fish, *Polypterus* (Hughes 1980), bivalve mollusks, in Ascidia, in ammocoete larva of lampreys (Youlson and Freeman 1976), and in embryos and larvae of amphibians (Billet and Courtenay 1973). Divergent views as to whether the gills initially evolved as trophic or respiratory organs persist (e.g., Willmer 1970; Gutman and Bonik 1981; Hickman 1984). In the lamellibranch mollusks, the gills have shifted from the primary respiratory function to filter feeding (Hazelhoff 1930; Jorgensen 1952). In those animals where the gills serve a dual function of respiration and filter feeding, ventilation is generated by cilia. Movement of the water in contact with the surface of the gills is an important part of the gas exchanging process and may occur in simple animals in form of ciliary action, e.g., on the branchial crown of sabellids, on the parapodial gills of polychaetes, e.g., *Nephtys*, and in the ctenidia of aquatic mollusks and ascidians. While enhancing procurement of food, the fast flow of water necessary for food uptake reduces the O_2 extraction capacity due to the short transbranchial transit time of the water (Table 8). Larval caecilians use gills for respiration in the egg but are lost soon after hatching (Welsch 1981). Some invertebrate organisms such as the terebellid worms (e.g., Weber 1978) present some localized areas of the body where the thickness is drastically reduced, gas exchange occurring to the same degree of efficiency as in the gills proper.

Vertebrate gills are categorized into external gills, i.e., those which dangle freely into the water, e.g., in the larval lungfishes and many amphibians and internal ones, i.e., those which are covered by various forms of cutaneous modifications, e.g., the opercular flap of the teleosts or are contained deep in the mesenchymal tissue mass, e.g., in sharks and the cyclostomes (e.g., Emery and Szczepanski 1986). Except for the cuticular gills of some insect larvae (Wigglesworth 1950), the external gills are highly susceptible to physical and chemical damage. Furthermore, they physically restrict locomotion in water. Typically, teleost fish have four pairs of gill arches. Gills have to be selectively permeable and well tuned to control and regulate transepithelial flux of ions and water between the internal and external milleu to curtail excessive loss or overload (Kirschner 1982). A conflict in the design of the gills is brought about by the need to optimize gas exchange by fully exposing extremely delicate organs to the elements. Any protective cover in form of a corneum cuticle or mucus would drastically limit the permeability and hence the transfer, especially of gases across the gills. In many animals with gills, however, the organs are housed in enclosures such as a mantle cavity, a shell (e.g., mollusks), outgrowths of the carapace (e.g. arthropods) and crustaceans, or are contained within a branchial cavity enclosed by the integument, e.g., in teleost fishes. While providing protection to the internal gills, this modification impedes water flow over the gills. This limitation was circumvented by evolution of an energetically expensive buccal force pump for moving a viscous O_2-deficient medium, through narrow spaces. In the larval amphibians, external and/or internal gills together with the general body surface play a major role in respiratory gas exchange. Except in two groups of animals, holothurians and cephalopods, aquatic respiratory ventilation is largely circulatory rather than tidal (Figs. 6,18). However, in sea cucumbers, the cloaca pumps water tidally whereas in the octopus and squid, the mantle serves as both a locomotory device and a respiratory one by pumping water into and from the mantle cavity. Tidal breathing of water across the anus occurs among annelids (e.g., *Urechis caupo*) and insects (e.g., dragon fly nymph, *Aeshna*; Fig. 23), via the branchial pores in lamprey eels and via the mouth in some amphibians and reptiles, e.g., the soft-shelled turtle, *Amyda* (McCutcheon 1954). The energetic cost of oscillatory ventilation in water explains why tidal ventilation rarely evolved in the active water breathers where throughflow designs predominate. Contraction of the gills, ciliary movements and mechanical ventilation (e.g., in the decapods and fish), placing the body in a moving current of water or active body movement maintain a PO_2 gradient across the respiratory surface. Fish which move constantly like the mackerel and the tunas ventilate their gills passively simply by keeping their mouths open. They have lost the power to mechanically pump water across the gills and hence must swim continuously. To avert physical damage during the fast forward movements, the gill filaments of such fish are fused to each other (Muir and Kendall 1968). By hitching a ride on a shark, the gills of *Remora remora* are passively ventilated but at rest, the fish utilizes active respiratory movements (Muir and Buckley 1967). In the siren, *Necturus maculosus*, the muscles associated with the gills are well developed and play an efficient respiratory role. Waving the external gills (in water) generates convective movement of the water. The process is stimulated both by increased water temperature and reduced O_2 content (Guimond and Hutchison 1972). The development of the external gills of larval amphibia depends on O_2 tensions in water (e.g., Foxon 1964). When placed in hypoxic water, the gills of *Rana temporaria* hypertrophy while in well-oxygenated water they atrophy. The external gills of the larvae of the salamanders which live in well-oxygenated waters are less well-developed, i.e., the respiratory surface area is small and the water-blood barrier is thicker than in those which live in O_2-poor waters (Dratisch 1925; Bond 1960). In fish living in water with a PO_2 of 10.7 kPa, the gills are much larger than in those at 100 kPa (Dratisch 1925). In *Xyelacyba myersi*, a fish which lives in the deep water of the Pacific Ocean (at depths of 1400 m), the gills are poorly developed (Hughes and lwai 1978). Unlike in some fish, amphibian gills are not specialized for exchange of gases in air. They never constitute the exclusive respiratory organs at any one stage of development. The contribution of the gills to the overall respiratory process in the amphibians differs from within and between species, depending on the habitat occupied and the level of development (e.g., Shield and Bently 1973a, b; Burggren et al. 1983; Malvin 1989). In the early stages of development, e.g., in the neotenic urodele larvae, the skin, lungs, and buccopharyngeal cavity function as adjunct respiratory organs. When exposed to low O_2 tensions ($2\,\mathrm{ml\,l^{-1}}$), ventilation in *Nereis virens* may become continuous and at very low values (0.6 ml per l) stop altogether (Lindroth 1938a). In the octopus, *Octopus vulgaris*, the O_2 extraction factor may be as high as 80% (Winterstein 1925), with the ventilatory rate of the gills increasing ten times above normal during hypoxia.

4.3 The Functional Innovations of the Gills for Aquatic Respiration

In all evolved gas exchangers, the structural adaptations which favor O_2 transfer are a thin barrier between the respiratory media and extensive surface area. In many aquatic animals, these features engender new problems of maintaining ionic and osmotic steady states in the body fluids. Opercular breathing movements in fish have been reported to occur before hatching. They appear to assist in the hatching process itself (S. Smith 1957). Except for the external gills of the neotenic urodeles, the amphibian gills (Fig. 47) can be considered to be transient or disposable gas exchange organs. Vascular shunt (anastomotic) vessels between the afferent (dorsal segment of the aortic arch) and efferent (ventral segment of

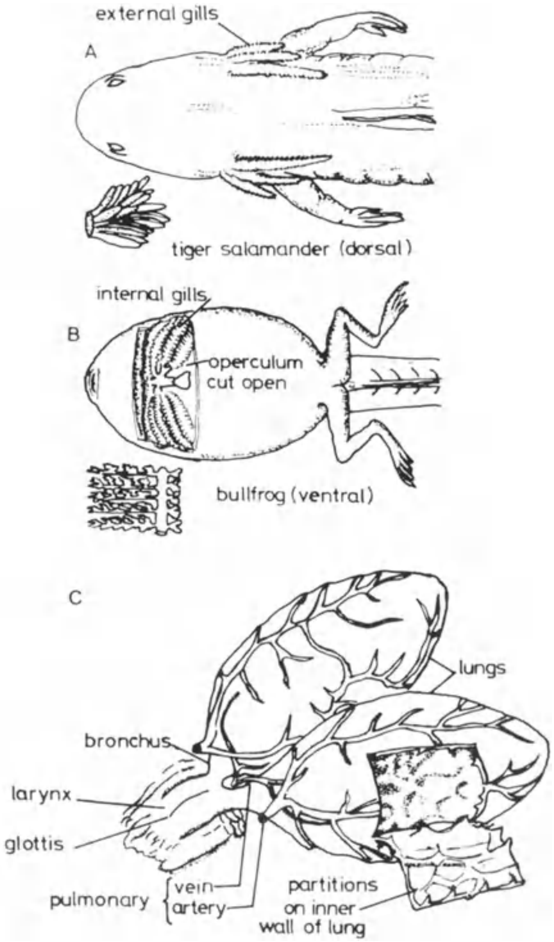


Fig. 47A–C. Respiratory organs of amphibians at different stages of development. A External gills of the larvae enlarged in the inset. B Internal gills of a bullfrog tadpole. C Lungs of an adult frog showing the large peripherally located air cells. (Jessop 1995) the aortic arch) gill arteries which bypass the external gills occur in both *Rana temporaria* and *Bufo bufo* (De Saint-Aubain and Wingstrand 1981) and in the gills of the urodele amphibians, e.g., *Amblystoma tigranum* (Baker 1949). The shunts are presumed to sustain circulation after metamorphosis when the external gills atrophy on changeover to pulmonary respiration.

Although aquatic animals procure O_2 through the gills, the majority of them take up a substantial fraction across the skin and lose a significant amount of CO_2 through it. In normoxic diving, the soft-shelled turtles, *Trionyx spiniferus asperus*, and musk turtles, *Stemotherus odoratus*, can remain submerged under water for 100 days and maintain normal acid-base status (Belkin 1968). Although the skin of fish has been considered to be impermeable to gases, measurements made on the eel, trout, and tench indicate that substantial uptake of O_2 occurs transcutaneously (Kirsch and Nonnotte 1977). Much of the O_2 is, however, used by the skin itself. The partial pressure of CO_2 in the blood of the lungfish, *Protopterus* declines after vasodilation of the cutaneous vasculature owing to enhanced loss of CO_2 (DeLaney et al. 1974). Nonpulmonary CO_2 elimination is substantial in many aquatic reptiles but only a small fraction of the total O_2 need is acquired in that way. Of the total CO_2 output in the aquatic turtle, *Trionyx mucita* (Jackson et al. 1976), 65% and as much as 94% in the sea snake, *Pelamis platurus* (Graham 1974), is lost cutaneously. In the aquatic snake, *Acrochordus javanicus*, 8% of the total O_2 uptake and as much as 33% of CO_2 excretion occurs through the skin (Standaert and Johansen 1974). Invertebrates such as the oligochaetes, platyhelminthes, mollusks such as Scaphoda, some Aplacophora, and some Gastropoda which have no distinct respiratory organs rely entirely on the skin for O_2 uptake. Such animals have a large surface-to-volume ratio which allows enough O_2 to be taken up by diffusion. Blood capillaries arranged in form of loops are present in the outer (circular) muscle layers in the gill-less maldanids (Pilgrim 1966), terebellid worms (e.g., Weber 1978), and on the parapodia of the annelid sandworm, *Nereis succinea* (Mangum 1982a). In such areas, the diffusional distance is thin enough to facilitate satisfactory transcutaneous movement of the respiratory gases. In *N. succinea*, the diffusional distance from the medium to the blood ranges from only 1.5 to 2.3 μm (Mangum 1982a). The naked gastropods of the genera *Lymnea* and *Helicostoma* can stay under water for a long period acquiring O_2 through the skin (Cheatum 1934). In the limpet, *Siphonaria zelandica*, 25% of gaseous exchange occurs across the side of the foot (Innes et al. 1984). Some salamanders such as *Desmognathus quadramaculatus* (Gatz et al. 1974) rely entirely on the skin for gas exchange. Oxygenation of the tissues which lie beyond the limiting diffusional distance must be effected by the coelomic fluid though in most species the fluid has a very low O_2 carrying capacity. In *Arenicola cristata*, at the microenvironmental PO_2, the PO_2 in the coelomic fluid is less than 6.7 kPa (Mangum 1982a). The metabolic rates of the deeply located and poorly vascularized tissues is relatively low and is finely tuned to O_2 availability. Respiration in *Arenicola* is intermittent with pauses of about 20 min. During the activity periods which last for about 10 min (at 20 °C), about 90 ml of water is passed across the body with an O_2 extraction factor of 50% (van Dam 1935, 1938). In amphibians, those species with smooth, poorly vascularized internal surface have a thinner epidermis and a much denser capillary network on the skin than those with well-developed lungs (Foxon 1964; Czopek 1965). The relative length of the cutaneous capillaries expressed as percentage of the total length of respiratory surface-associated capillaries is about 50 to 80% (Czopek 1965).

4.4 The Simple Gills

4.4.1 Morphological Characteristics

The general features of both the simple and the complex gills have been described by Kennedy (1979). Not all gills or gill modifications play a significant role in gas transfer (e.g., Fox 1921; Thorpe 1930). Certain hair-like or plate-like external outgrowths from the body which have been called gills play no determinate respiratory role. Such forms are found externally in echinoderms, mollusks (e.g., Nudibranchia), arthropods (e.g., Brachiopoda) (Kikuchi 1992), fishes (e.g., adult lungfish, *Lepidosiren*), blood gills of *Chironomous*, and in some amphibians (e.g., adult salamanders). In the larval stages, such gills may function as appendages and/or filter feeders with respiration being a secondary process. The freshwater brachiopod, *Branchinella kugenumaensis*, has ten pairs of gills (metepipodite segments of thoracic legs) and the neck organ (located on the cephalothorax) is an important respiratory organ (Kikuchi 1992). The anal gills of Diptera larvae are largely salt-absorbing organs (Koch 1938). Among the Cirripedia, the extensions attached to the cirri in the four genera of Lepadidae, though described as gills by Darwin (1851), appear to play no role in respiration. This was, however, refuted by Kaestner (1970) and Burnett (1972): a large number of species in the group flourish without them. On the other hand, some structures generally considered to be feeding organs such as the tentacles of the sea anemones may play a notable role as gas exchangers (Sassaman and Mangum 1973; Mangum 1994). The so-called ventral gills or blood gills of the aquatic Chironomid larvae take up a smaller quantity of O_2 from the water than the skin (Harnisch 1937). The annelids are among the simplest animals which have an organ morphologically recognizable as a gill. In the ancestral members of this taxon, the gill is a simple, smooth tubular evagination of the body wall (e.g., Nakao 1974; Mangum 1976a) where, e.g., in *Glycera* and in *Nereis succinea* the water outside and in the coelomic fluid is kept in motion by cilia, a closed circulatory system lacking. In others such as the oligochaete, *Alma nilotica*, the comparably simple gills (Gresson 1927; Khalaf EI Duweini 1957) are perfused through a closed circulatory system (Stephenson 1930). The parapodia in many polychaetes, e.g., *Nereis*, *Arenicola*, and *Dasybranchus*, are well vascularized and serve as gills (Nicoll 1954). Relatively simple gills which are located inside the branchial skeleton rather than outside (Randall 1972), as is the case in the gnathostomatous fishes, are found in the lower animal forms, e.g., the Cyclostomata, i.e., the hagfish (Jensen 1966; Bardack 1991) and the lampreys (Youlson and Freeman 1976; Lewis and Potter 1982; Mallatt and Paulsen 1986). The larval forms of the viviparous aquatic caecilian, *Typhlonectes*, exchanges gases by apposition of the fetal gills to the highly vascularized wall of the oviduct (Wake 1977): the gills are absorbed before birth.

4.4.2 Ventilation and Functional Capacities

The advantage of having respiratory organs on locomotory parts of an aquatic animal, e.g., in some crabs (Fig. 48) is great (Maitland 1986). Mechanical displacements of the appendages confer a ventilatory advantage. This may be of particular importance especially in standing hypoxic water. The development of gill modifications on the locomotor parapodia in polychaetes (e.g., *Arenicola* and *Dasybranchus*) guarantees efficient ventilation. The primary role of respiratory pumping in the marine snail, *Aplysia californica*, has been presumed to be that of enhancing O_2 uptake into the hemolymph through the gill epithelium (Kanz and Quast 1992). A negative correlation between respiratory pumping and O_2 consumption under hypoxic conditions has, however, been reported by Levy et al. (1989) in related species, i.e., *A. depilans* and *A. fasciata*. Gills without any specific ventilatory adjuncts are encountered in echinoderms where cilia produce fluid movement, e.g., in mollusks (Nudibranchia), arthropods (Brachiopoda and insect larvae), fishes (e.g., adult lungfish *Lepidosiren* – in the male during breeding and in larvae of teleosts and elasmobranchs), and amphibians (e.g., mud puppy, *Necturus*, and a number of other salamander adults and in numerous larval and tadpole stages of frogs). In *Necturus maculosus*, when the animal is stationary,

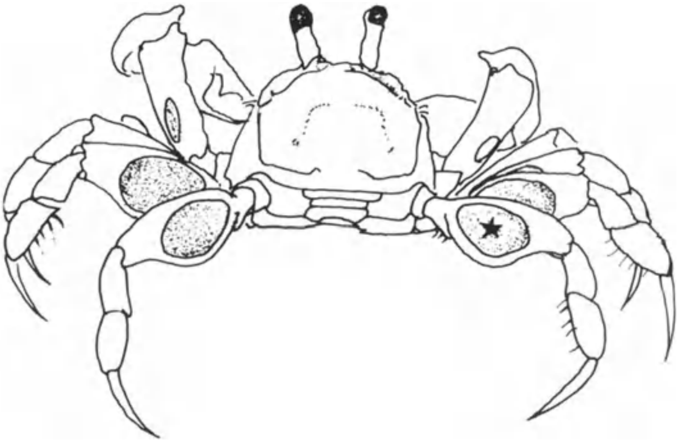


Fig. 48. Sand-bubbler crab, *Scopimera inflata*, has pairs of membranous disks (gas windows) in each leg meral segment, ★, which are utilized for gas exchange during low tide. The gas windows are mechanically ventilated during locomotion, enhancing the gas exchange process. (Maitland 1986; reprinted by permission from *Nature*, vol. 319, pp. 493–495; copyright 1986; Macmillan Magazines Ltd.)

muscles at the base move the gills especially when the animal is at rest (Guimond and Hutchison 1972) but many other urodeles, though possessing similar gills, are not known to execute such maneuvers. The gills hang out in water, where they are passively ventilated by the physical movement of the animal in water or when the gills are placed in a water current. Agitation of the immediate (boundary) water layer over the gills or the skin renews the water, thereupon increasing the PO_2 (Feder and Burggren 1985a, b; Feder and Pinder 1988). Consequently, diffusion of O_2 across the tissue barrier is enhanced. Some species, e.g., *Dasybranchus*, exhibit sporadic gill contractions presumably effected by movements of the coelomic fluid (Mangum et al. 1975). Ventilatory activities can be effected by ciliary movements (e.g., in nudibranchs), by physical movement (e.g., in Phyllopoda), muscular contractions of the branchial outgrowths (e.g., in Amphibia and Ephemend larvae) and in others, e.g., crustaceans, by the beating of special appendages (e.g., pleopods) which maintain a water current across the gills. The high shore littoral crustacean, *Ligia*, obtains about 50% of its O_2 needs through the pleopods and the rest through the ventral surface of the abdomen (Edney and Spencer 1955). Terrestrial woodlice breath through the pleopods, with *Porcellio scaber* obtaining as much as 70% of their O_2 needs through them. The book gills of the chelicerate arthropod, *Limulus polyphemus*, are borne on five pairs of modified appendages which are located on the ventral surface of the opisthosoma (Mangum 1982a). Each modified appendage consists of about 150 rounded lamellae which in a 1-kg specimen are 3 to 4 cm wide. The thickness of the water-blood barrier is on average 5.6 μm thick. When *Limulus* is in hypoxic water, the frequency of the ventilatory movements of the opisthosomal appendages increases. On exposure to extremely hypoxic or hypercarbic water, the totally aquatic and solely cutaneous breathing amphibians, *Cryptobranchus alleganiensis* and *Telmatobius culeus*, rock or sway their bodies back and forth in water (Hutchison et al. 1976; Boutilier and Toews 1981), passively ventilating their skin, In *Necturus*, at 25 °C, through agitation of the gills in water, 60% of the O_2 needs can be transferred across the gills (Guimond and Hutchison 1976) while at the same temperature, in the inactive gills of *Siren lacertina*, the gills meet less than 5% of the O_2 needs (Guimond and Hutchison 1973a, 1976). *Necturus* is found in diverse habitats which range from clear waters of lakes, streams, weed-choked canals, and drainage ditches (Bishop 1943). Adaptive features such as physical movement of gills, capacity to undergo long periods of anaerobiosis, and lowering metabolic rate some 30 to 40% below normal are some of the adaptive features which enable animals to withstand hypoxia.

4.4.3 Gas Exchange Pathways and Mechanisms

Amphibians possess gills during their larval stages of development. Caudata and caecilians (Gymnophiona = Apoda), have external gills, while in Silentia they are internal. In the neotenic forms, e.g., *Necturus* and *Ambystoma*, the gills persist throughout life. Many aquatic salamanders utilize a trimodal gas exchange strategy in which pulmonary, branchial, and cutaneous surfaces variably contribute to gas exchange. In the *Siren*, of the total amount of O_2 taken up by the animal (at 25 °C), the gills account for only 2.5% while they eliminate 12% of the total CO_2 (Guimond and Hutchison 1972). A 42% reduction in the total gas exchange capacity occurs on ligation of the gills of *Necturus* at 22 °C (Shield and Bentley 1973a,b). The external gills contribute as much as 54% of the total O_2 need and void 61% of the total CO_2 at 5 °C, with the O_2 consumption through the gills increasing to 60% at 25 °C (Guimond and Hutchison 1972). *Necturus* quickly lowers the aquatic PO_2 from 20 to 5.3 kPa (Guimond and Hutchison 1972). An arterial PO_2 of about 4.7 kPa was reported by Lenfant and Johansen (1967) in the blood of *Necturus*, a value indicative of a high efficiency of the gills in O_2 extraction at very low ambient PO_2. Fanelli and Goldstein (1964), however, observed that the gills of *Necturus* are of no consequence in respiration. This may, nevertheless, only be true in an inactive animal at low ambient temperatures in O_2 saturated water. In cool (5 to 15 °C) aerated water (PO_2 = 17 to 20 kPa), in undisturbed animals, the gills do not move and are retracted and held to the side of the head. However, as temperature increases, the animal becomes restless and the gills oscillate (Guimond and Hutchison 1976). When removed from water, at 20 °C, the gills of *Necturus* collapse (Lenfant and Johansen 1967). This is followed by a dramatic rise in the arterial PCO_2 and a marked reduction in arterial PO_2 in spite of evident pulmonary ventilatory and gulping movements. The gills of *Siren* are less involved in respiration than those of *Necturus* and are notwithstanding more efficient in CO_2 elimination than O_2 uptake (Shield and Bentley 1973a,b; Bentley and Shield 1973). Features such as a thick branchial epithelium (e.g., Cope 1885), abundant arterial venous shunts which bypass the gill filaments (e.g., Darnell 1949), small size, structural simplicity, and immobility of the gills (Guimond and Hutchison 1976) explain the respiratory inefficiency of the gills of the *Siren*. The branchial beating frequency in *Necturus* depends on factors such as metabolic rate and environmental hypoxia or hypercapnia. The rate increases from about 10 times per min to more than 50 times per min (with temperature increasing from 10 to 25 °C (Guimond and Hutchison 1972, 1973a). In insect and amphibian larvae, extended hypoxia induces gill growth and cutaneous vascularization (Bond 1960). The role of the external gills of the larval anuran amphibians in gas exchange is not known (Boutilier 1990) but the internal ones of the lungless tadpoles of *Rana catesbeiana* and *R. berlandieri* account for as much as 40% of the total O_2 and CO_2 exchange at 20 °C (e.g., West and Burggren 1982). In some anuran species, ventilatory rates as high as 90 times per min at 20 °C have been reported by Burggren and West (1982) and in some, ventilatory frequency appears to be synchronized with the heart rate (Wasserzug et al. 1981).

In the different amphibian species, the levels of development of the external gills correspond with the availability of O_2 in the environment in which they subsist and the functional needs (Noble 1931). During the development of the lungs, the unidirectional ventilation of the internal gills with water through bucco-pharyngeal muscular activity decreases by as much as 50% as the skin assumes a prominent respiratory role (Burggren and West 1982). *Siren*, which is endowed with capacity for efficient cutaneous and pulmonary respiration, has moderately developed gills while *Necturus*, which relies on pulmonary exchange, has more elaborate gills to supplement cutaneous gas exchange (Guimond and Hutchison 1976). Gills of *Necturus* kept in cool well-oxygenated water atrophy compared with those kept in warmer nonaerated water (Guimond and Hutchison 1976). After being forcefully held under water for over 2 weeks, the gills of *Necturus* enlarge. The lugworm, *Arenicola cristata* which lives in burrows, a fairly anoxic habitat, has 11 pairs of gills which are located in the midregion of the body. The main trunks of the gills branch four times, the terminal branches which account for much of the respiratory surface being 0.6 mm long and 0.07 to 0.10 mm in diameter while the diffusional distance is 2 to 4 μm thick (Mangum 1982a). Features such as high hemoglobin-O_2 affinity and great cooperativity of O_2 binding (Mangum 1976b) may enable such species to subsist in a hypoxic environment. In the polychaete families (e.g., Wells et al. 1980) and in the filamentous gills of other taxa such as crustaceans (McLaughlin 1983), the gills are organized in the same general pattern as in *Arenicola*. The gills of the members of the family Sabellidae, which inhabit vertical tubes either within soft sediment or, as in the case of *Eudistylia vancouver*, attached to firm substratum, are considered to be more advanced (in some respects) than those of the lugworms (Mangum 1982a). The gill, a pinnate structure known as a branchial crown, is not metamerically arranged but is confined to the anterior end where the respiratory gases can be easily exchanged with water: the gill serves as a filter-feeding organ while the organism is still confined to the tube. In *E. vancouveri*, the gill consists of two principal trunks or branchioles which divide at the first level to give rise to numerous long ciliated pinnae giving rise to a double row of filaments called pinnules at the second level of branching (Vogel 1980). A single branchial crown consists of about 54 000 pinnules which provide a surface area accounting for more than 70% of the surface area of the body. This translates into a mass-specific surface area of $30\,\mathrm{cm}^2\,\mathrm{l}^{-1}$ (wet wt.). Individual branchioles are associated with a single blood vessel which divides in the same bifurcating plan, terminating blindly at the pinnules. Owing mainly to the absence of the afferent and efferent blood vessels, the blood flow pattern in the branchioles is believed to be tidal in nature (Fox 1938; Ewer 1941). In the cephalochordates and tunicates, the blood flow in the gills is irregular. In the tunicates, the flow reverses in direction (Remane et al. 1980). In both groups, hemoglobin is lacking but the tunicates have a vanadium-based pigment which may carry O_2. The respiratory differences between the sabellids and the lugworms include: (1) the ventilatory rate in the sabellids is three times greater than in arenicolids (Dales 1961; Mangum 1976b), (2) the O_2 extraction factor from water is only 6 to 10% in sabellids and 30 to 60% in arenicolids (Dales 1961; Mangum 1976b), and (3) the affinity of the sabellid respiratory pigment (chlorocruorin) is generally low, ranging from 5.9 kPa in *Myxicola* (Wells and Dales 1975) to 6.9 kPa in *Spirographis* (Antonini et al. 1962) at a pH of 7.4 and a temperature of 15 °C. Of all respiratory organs which have been studied, in *E. vancouveri*, blood may pass in and out of the gill a number of times before reaching the ventral blood vessel which distributes it to the body tissues (Ewer 1941). The sebellid gills present a unique model of a microcirculatory configuration in the animal kingdom in which multiple cycling of the blood occurs (within a gas exchanger) to maximize O_2 uptake by the blood.

In modern tadpole larvae of Anura, internal gills (Fig. 47) from rows of branched lamellae supported by gill bars which are separated by four gill slits (e.g., Uchiyama et al. 1990). With the onset of pulmonary respiration, the gill slits close up except in some Urodela which have readapted to aquatic life where some slits remain open throughout life. External gills are rare in adult fish but play an important respiratory role in amphibian larval forms of the tadpoles and neotenic larvae (e.g., in *Amblyostoma* – Axolotl), in *Discoglossus*, and in water-breathing adults (e.g., *Necturus maculatus*). In the larval forms of elasmobranchs and some larvae of Chondrostei and Teleosti, external gills form as long filaments floating in the albuminous fluid within the egg case. True external gills occur in the larval forms of fishes, e.g., Polypteridae and Dipnoi, and in amphibians in form of threads or fine feathers (Dunel-Erb and Laurent 1980b). In the less advanced invertebrate gill-breathing life forms, the circulatory system is not very well connected to the branchial respiration: the gills are located on the venous side of the heart which receives arterial blood. In most Gastropoda, Cephalopoda, advanced Crustacea, and fishes, the venous blood is collected and passed to the gills and then distributed to the rest of the body. The amphibian external gills differ remarkably from those of fish in that macroscopically they form arborescent organs and are not arranged in a refined hierarchical order.

In many lower forms of animals, the regulation of branchial respiration is absent or very poorly developed. In *Ligia oceanica*, the beating of the pleopods, which produce water currents across the gills, does not change with O_2 tension in water except at very high or low concentrations. In *Gammarus locusta*, the pleopods stop beating at a concentration of O_2 above 5.6 ml per l while a drop causes rapid beating (Fox 1921). In the aquatic insect larvae, *Cryptochaetum iceryae* (Diptera, Agromyzidae) and *Icerya purchasi* (Coccidae, Monophlebini), Thorpe (1932) observed that CO_2 efflux occurred at specific areas of the body. In the fish larvae, before the gills develop, the body surface serves as the only gas exchange pathway. To maintain a high PO_2 in the layer of water next to the skin, the larvae cause convective movement of the surrounding water either by positioning themselves in moving water currents or by executing physical movements (Liem 1981). The external gills of newly hatched larvae of *Protopterus* have cilia which move water across the gills before the ventilatory muscles develop (Whiting and Bone 1980). During the postlarval development, in *Protopterus ampibius*, the fraction of the total O_2 which is acquired through the external gills and the skin declines with the development of the lung (Johansen et al. 1976). In the bimodally breathing teleost *Monopterus*, the large muscular fins generate a posteriorly directed water current which interacts with a well-vascularized region below the epithelial surface of the fins and the yolk, creating a highly efficient countercurrent gas exchange system (Liem 1981). This adaptive property may enable the fish to subsist in hypoxic water. The tuft-like structure on the pelvic fins of the male *Lepidosiren paradoxa* which is highly vascularized has been considered to be important in the parental rearing of the eggs and larval forms in burrows constructed for that purpose (Kerr 1898; Agar 1908): the gill-like organ has been assumed to be involved in O_2 uptake from water. This prospect may be supported by the fact that during the husbandry period, the fish does not surface as frequently as it normally does to exchange gases in air. It is thought that the pelvic fin respiratory elaboration may be utilized for transferring O_2 from the blood of the male fish to the immediate vicinity of the eggs and the developing larvae in the frequently hypoxic tropical swamps in which the fish lives (Kerr 1898; Cunningham and Reid 1932). On hatching, the young larvae of *Lepidosiren* respire through the external gills which start to atrophy after 45 days of life (Carter and Beadle 1930; Krogh 1941). At about the same time, the pelvic gills of the male lungfish begin to regress as the larvae surface to breath air (Agar 1908).

4.5 The Complex Gills

4.5.1 Structure and Architectural Plans

The structure and arrangement of the internal gills varies remarkably. The most complex ones are found in the bony fish (class: Pisces) which typically have four pairs of gill arches. In fish, a single ventricle receives venous blood that is subsequently pumped to the gills for the uptake of O_2. The gills of the elasmobranchs lack a skeletal support. In adult cyclostomes, the design of the gills fundamentally differs from that of fish: the main skeletal mass lies external to the gill epithelium (Jarvik 1968; Youlson and Freeman 1976; Lewis 1980; Lewis and Potter 1982). In the hagfish, coronary arteries are lacking: the heart, which is thin-walled, receives nourishment from the venous blood it pumps. Gills are generally poorly developed in air-breathing teleosts (e.g., Munshi 1976), mudskippers (e.g., Low et al. 1988, 1990), and the lungfishes, Dipnoi (Laurent 1982). The bimodal breathing fish face the singular problem of losing O_2 (acquired during air breathing) to the surrounding hypoxic water as the blood traverses the gills. Shunting of the blood away from the gills (Fig. 21) and reduction in the gill respiratory surface area avert such losses. In the most terrestrial of these fish, the gills are retained mainly for elimination of CO_2 which is more readily discharged into the water. The gills of the lungfishes are remarkably different from those of other classes of fish (Laurent 1982, 1996). They do not form regular arrays of primary and secondary lamellae but look like the external arborescent gills of a tadpole rather than the gills of Teleosti and Chondrichthyes (Laurent et al. 1978). Moreover, pillar cells (Fig. 49) are lacking in the dipnoan gills (Laurent et al. 1978; Laurent 1982). The gills of the hemoglobinless Antarctic ice fish, *Chaenocephalus aceratus* and *Chamsocecephalus esox* (Steen and Berg 1966), and *Chaenichthys rugosus* (Jakubowski et al. 1969), much as they are structurally similar to those of other fish which have hemoglobin, have fewer secondary lamellae and the skin is very well vascularized. Fast-swimming fish, e.g., the tuna, show certain modifications of the gills which include presence of calcified flattened gill rays which offer the filaments better physical support (Iwai and Nakamura 1964) and fusion of the gill filaments to the lamellae, preventing lamellar deformation during high speed cruising especially during passive or ram ventilation (Muir and Kendall 1968). The bowfin, *Amia calva*, a freshwater fish which differs remarkably in habit and habitat from the marine fish, has independently arrived at lamelar fusion (Bevelander 1934). It has been speculated that the attribute supports gas exchange

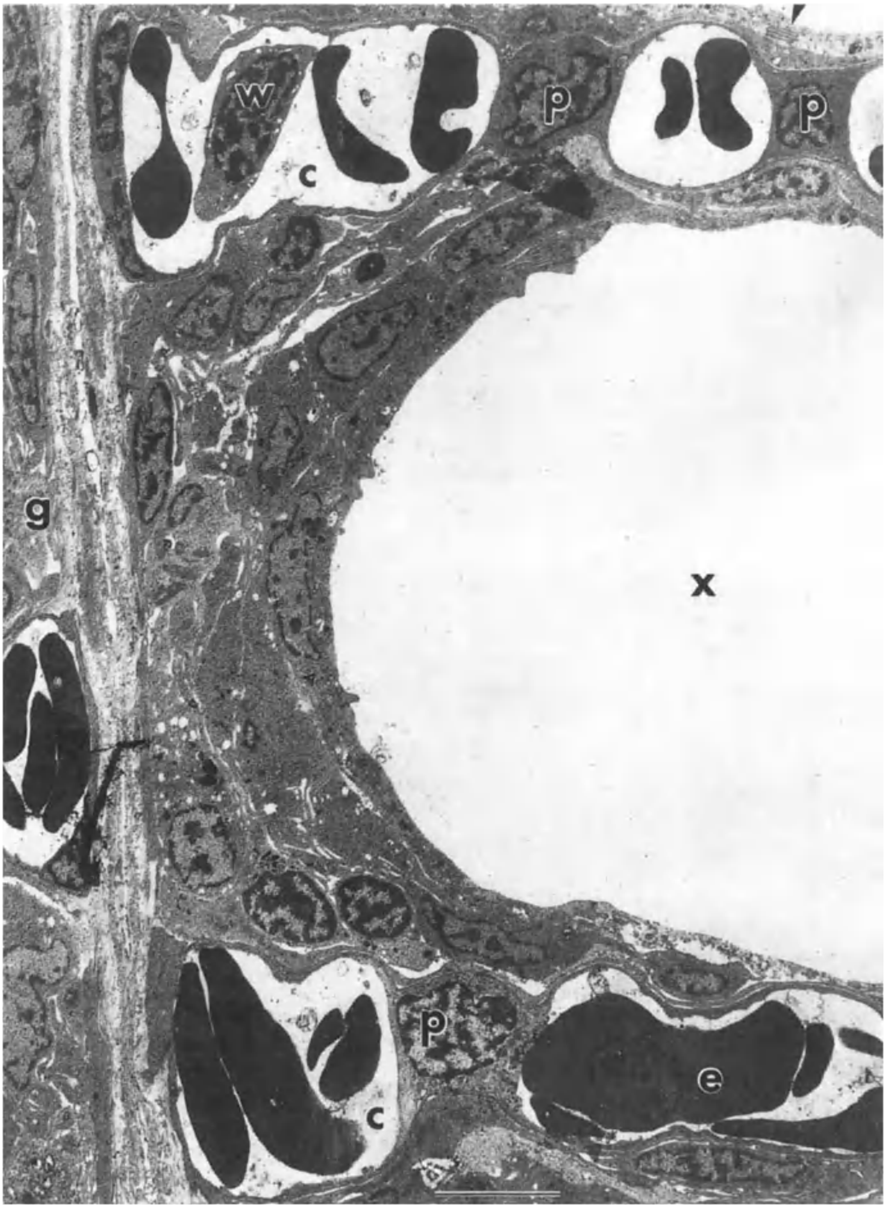


Fig. 49. Gills of a tilapiine fish, *Oreochromis alcalicus grahami* showing a gill filament, *g*, and secondary lamellae separated by an interlamellar space, *x*; *p* pillar cells; *c* vascular channels; *e* erythrocytes; *w* white blood cell; ➤ intercellular junction of epithelial cells. Note the extremely thin water-blood barrier over the vascular channels. *Bar* 17 μm. (Maina 1990)

in the O_2-deficient turbid water and prevents gill collapse during air breathing. Cutaneous gas exchange contributes about 40% of the total O_2 uptake in these fish (Hemmingsen and Douglas 1970). The high efficiency of the skin in O_2 transfer compared with that of the gills may be a means of economizing on respiratory work through conserving the activities of the bucco-pharyngeal pump. In the cold polar water where O_2 levels are normally high, to increase gas exchange, a fish only needs to physically move to sufficiently "ventilate" the skin. The resting O_2 consumption of the ice fish is one half to one third that of hemoglobin-carrying fish of similar size found in the same habitat (Hemmingsen and Douglas 1970). Further compensations for the low O_2 capacity of the ice fish include a high blood volume (7.5% of the body weight) compared with 2 to 3% in normal fish and a reduced viscosity of blood due to absence of erythrocytes, factors which enhance O_2 transport by blood. In fish, during growth, the number of gill filaments increases more rapidly than that of the secondary lamellae (Hughes 1982).

The filament is the functional unit of a branchial arch system (e.g., Olson 1996). Gas exchange, however, occurs across the secondary lamellae which are thin semicircular flaps which are bilaterally set on the filament perpendicular to its longitudinal axis (Figs. 11,46). An elaborate epithelium (the primary epithelium) covers the gill filament while a less complex one, the secondary epithelium, lies over the secondary lamellae (Laurent and Dunel-Erb 1980; Laurent 1984; Maina 1990a, 1991). Three types of cells, the pavement cells, the chloride (= mitochondria-rich = ionocytes) cells, and the mucous cells are most prevalent on both types of epithelia. The different functions of the gills, i.e., osmoregulation (e.g., Leatherland et al. 1974; Eddy et al. 1981), acid-base balance (e.g., Heisler 1984), elimination of products of nitrogen metabolism (Goldstein 1982; Randall et al. 1989), and respiration appear to occur at specific sites of this highly well-organized and differentiated epithelium. The first two processes take place in the composite primary epithelium while the last two occur in the thin, less elaborate secondary epithelium. Like the vertebrate lung (Sect. 6.10.2), the gills perform certain metabolic functions whereby they modify the plasma hormones in the arterial blood before they pass to the systemic circuit (Neckvasil and Olson 1986; Olson et al. 1986a). The pavement cells are simple squamous broad cells which are characterized by surface microridges (e.g., Olson and Fromm 1973; Kendall and Dale 1979; Hughes 1979; Hughes and Umezawa 1983; Hossler et al. 1986): the patterns of the microridges differ between species. Lamellar epithelia of pelagic fish such as bluefish, *Pomatomus saltatrix*, Atlantic mackerel, *Scomber scombrus*, and Atlantic bonito, *Sarda sarda* (Olson 1996) and the hill stream fish, *Danio dangila* (Ojha and Singh 1986), are virtually devoid of microridges. The microridges decrease in size and frequency from the gill arch, the gill filament to the secondary lamellae (Dunel-Erb and Laurent 1980a; Karlsson 1983), and have been associated with diverse roles which include trapping and holding mucus, providing structural integrity to the gill epithelium, and increasing the surface area at the water-epithelial surface interface (Sperry and Wassersug 1976). Olson (1996) contemplated that microridges generate an unstirred boundary layer of water over the gill epithelium hindering gas transfer. The presence of a mucous cover, which streamlines the gill surface by evening out the crypts between the microridges, should reduce the resistance of the flow of water across the gills (Daniel 1981; Hughes and Mondolfino 1983). The presence of microridges on the nonrespiratory surfaces of the accessory respiratory organs (AROs) in fish such as the climbing perch, *Anabas testudineus* (Munshi and Hughes 1991; Wu 1993), and the snake-head fish, *Channa striata* (Hughes and Munshi 1986), supports the suggestion that developmentally, the AROs arise from in situ modifications of the gills. Microridges have been said to enable the pavement cells to greatly distend without engendering mechanical disruption (Knutton et al. 1976). This may be crucial for the integrity of cells which are exposed to a medium whose ionic composition and osmotic pressures may change over short distances. The size and shape of microridges are thought to be influenced by electrolytes, salinity, hormones, and hydrodynamic flow of the water over the gills (Hughes 1979; Schwerdtfeger 1979; Wendelaar-Bonga and Meiss 1981). The mucus covering of the gills has been associated with numerous functions which include protection from mechanical damage and invasion by pathogens, absorption and expropriation of toxic heavy metal ions (e.g., Varansi et al. 1975; Varansi and Markey 1978), and regulation of O_2 (Ultsch and Gros 1979), and electrolyte (Handy 1989) transfer across the epithelial lining of the gills. From morphological characteristics and location within the epithelium, factors which may depend on the stage of cell maturity, two types of chloride cells have been described in fish gills (e.g., Laurent 1984; Maina 1991). An accessory chloride cell has been described in the gills of the saltwater fish (Dunel-Erb and Laurent 1980a; Laurent et al. 1995). The epithelial cells of the gills, especially the chloride cells, are highly sensitive to changes in ambient conditions. Movement of euryhaline fish from freshwater and seawater generates reversible changes in chloride cell morphology, location, and numerical density (e.g., Hossler 1980; Laurent and Hebibi 1989; Laurent and Perry 1991). Hyperoxic-effected hypercapnic acidosis causes an increase in the apical surface area of the chloride cells (Laurent and Perry 1991) while ambient hypercapnia increases the chloride cell number in the catfish, *Ictalurus punctatus* (Cameron and Iwama 1987). In what was construed to be an adaptive process, injections with cortisol for 10 days increased the number of chloride cells by a factor of 3 (Laurent and Perry 1990). The organization of the gill microcirculatory pathways in fish gills is far from settled (e.g., Steen and Kruysse 1964; Boland and Olson 1979; Dunel-Erb and Laurent 1980b; Olson 1996). The lamellae are divided into vascular channels which are lined by polygonal endothelial pillar cells (Figs. 11, 49). In the gills of some land crabs like *Carcinus maenas* (e.g., Farrelly and Greenaway 1992) and some teleosts, e.g., *Oreochromis alcalicus grahami* (Fig. 11), the pillar cells which contain the contractile microfilamental actomyosin elements and collagen (Bettex-Galland and Hughes 1973; Youlson and Freeman 1976) may play an important role in regulating translamellar blood flow. No shunts that bypass the secondary lamellae en route from the ventral to the dorsal aorta occur in the common water breathing teleosts (Olson 1996). In the gills of the European eel, *Anguilla anguilla*, the principal sites of gill vascular resistance are at the level of the afferent lamellar arterioles and the secondary lamellae (Bennett 1988).

The epithelial cell layer, basement membranes, interstitial space and endothelial cell (Fig. 49) constitute the water-blood barrier. Though typically thick in most fish (Hughes and Morgan 1973), the barrier may be as thin as 0.2 μm in some regions of the secondary lamellae of some species (Maina 1990a, 1991; Laurent et al. 1995). The morphometric features of the gills, especially the respiratory surface area, correlate with the metabolic demands of fish as well as the environment in which they live (e.g., Hughes and Morgan 1973; Maina et al. 1996a). The pillar cells are arranged as struts which span the width of the space between the two parallel epithelial sheets. They maintain the structural integrity of the secondary lamellae and the blood spaces by preventing overdistension under undue intramural blood pressures which may be as high as 12 kPa (Bettex-Galland and Hughes 1973; Hughes 1976). Fish can regulate the surface area of their gills as well as the exposure of the chloride cells to water (Fig. 50). In that way, gas exchange and ionic regulation can be optimized to suit the prevailing needs and circumstances (e.g., Randall 1982; Butler and Metcalfe 1983). The position of the gill filaments can be varied by contraction of smooth muscles which are enervated by adrenergic nerves (e.g., Nilsson 1985). In a single gill filament, the blood flow across the lamellae at the tip is less than in those at the base (Hughes 1980) and can be regulated by certain pharmocological agents, e.g., serotonin, adrenaline, and noradrenaline (Östlund and Fänge 1962; Nilsson 1986; Fritsche et al. 1993; Sundin et al. 1995). In an individual secondary lamella, by contraction or relaxation of the pillar cells, the blood/hemolyphatic flow may be shifted to and from the larger marginal channels (Fig. 11). In the gills of the mudskipper, *Boleophthalmus boddarti*, a species which lives on the surface of the mudflats of the Arabian Gulf where it makes U-shaped burrows which may be as deep as 1 m (Clayton and Vaughan 1986), the water-blood barrier is thinner around the marginal channels (Hughes and Al-Kadhomiy 1996). Blood remains in contact with water for about 0.5 s, a duration considered to be adequate for complete oxygenation of the erythrocytes (Hughes et al. 1981).

4.6 The Water Lungs

Gas transfer from water by ventilated lung-like (invaginated) structures is utilized by only a small group of animals. It presents a very simple mode of respiration. In the relatively more advanced organisms, it illustrates a retrogressive use of an earlier air breathing organ. In the marine snail, *Aplysia califormica*, respiratory pumping (e.g., Kandel 1979) or interneuron II response as it was called by, e.g., Eberly et al. (1981), is an activity which entails synchronized contraction of the gills, parapodia, and siphon. The seawater is taken in and injected from the mantle cavity. A more complex respiratory pattern which is depressed by long-term (24 h) exposure to hypoxia (about 2 mlO_2 per l of water) occurs in *A. califomica* (Kanz and Quast 1990). Hypercapnia (Croll 1985), hypoxia, or anoxia (Levy et al. 1989) increase the respiratory frequency in *A. californica*. Aquatic animals like the sea cucumber (holothurians) have water lungs which occur in form of branched thin-walled tree-like perivisceral tubes that stretch from the

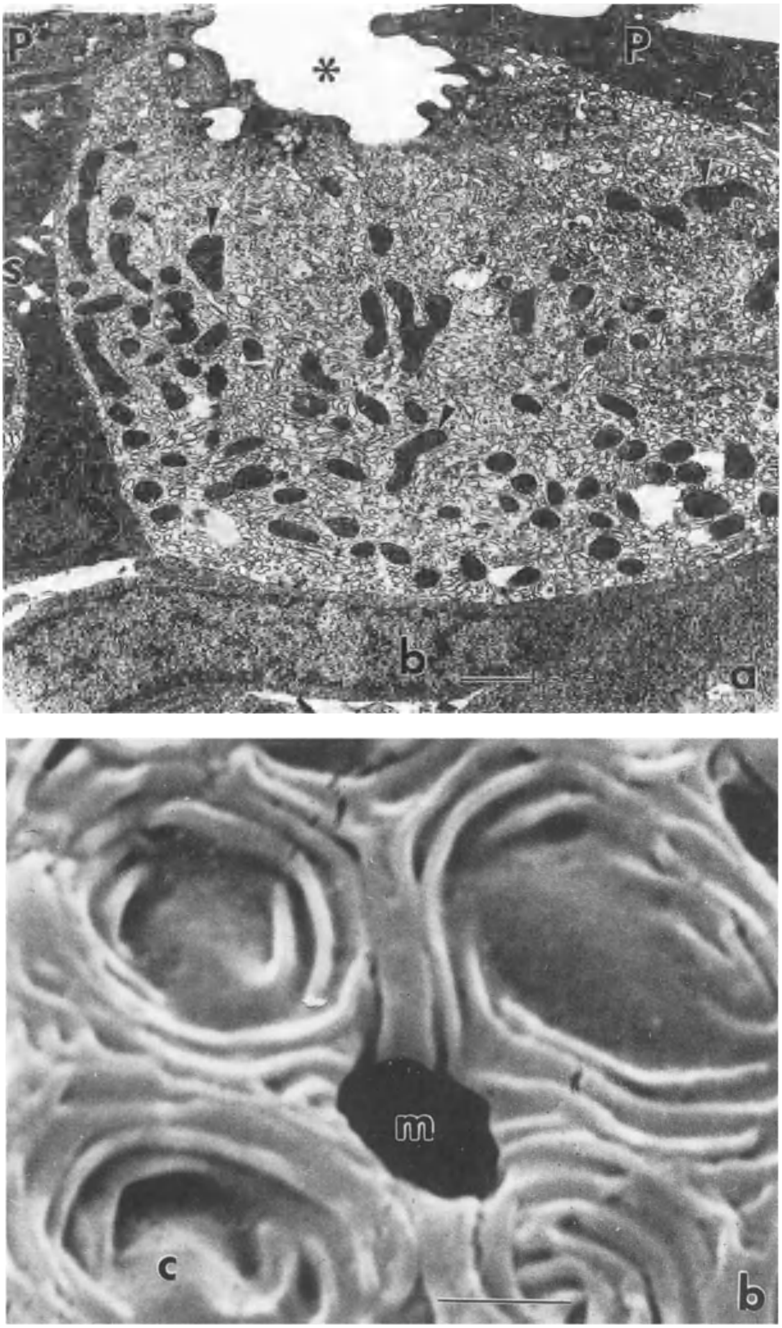


Fig. 50. **a** Chloride cell on the gills of a tilapiine fish, *Oreochromis alcalicus grahami*. The cells are involved in ionic exchange between the blood and water. ➤ mitochondria; *s* supporting cells; *p* pavement cells; * pore; *b* basement cell. **b** A surface view showing closed chloride cells (*c*) and an open mucus cell (*m*). **a** *Bar* 1 μm; **b** 6 μm. (**a** Maina 1990a)

cloaca, running through the whole length of the body. Expulsion of the seawater is produced by irregular contractions and relaxations of the body wall muscles and inspiration by the pumping action of the cloaca (Newell and Courtney 1965): gas exchange takes place between the inspired sea water and the hemoglobin containing coelomic fluid, a process enhanced by the stirring action of the peristaltic waves. In *Holothuria forksali*, cloacal O_2 uptake contributes about 60% of the total need. Gas exchange is reduced by 50% when cloacal ventilation is arrested. Although circulation of the body fluids in the Holothuria has been described (e.g., Kawamoto 1927), it appears to occur to a very small extent. The ventilatory activity of the lung is a more significant factor in effecting movement and mixing of body fluids. In a number of annelids, respiration through the walls of the gut has been suspected though the actual mechanism is not known (Krogh 1941). In a large number of Oligochaetes and polychaetes, antiperistaltic and ciliary movements in the anus are considered to be respiratory (Stephenson 1930). With the exception of *Owenia*, however, Lindroth (1938b) refuted that any significant per rectal movement of water occurs in the polychaetes to warrant the gastrointestinal system being considered to be of any functional consequence in respiration. Stephenson (1930) described a water-swallowing process and expulsion through the anus in the large worm, *Aphrodite aculeata*. In the small threadlike freshwater tubiform worms, e.g., *Tubifex* and *Limnodrilus*, antiperistatic movements of the hind gut occur (Alsterberg 1922). The worm, *Limnodrilus*, builds tubes in the very soft organic mud (which is virtually free of O_2) and stretches its hind parts further into the surrounding water and makes strong undulating movements. When the O_2 tension drops to below 0.08 ml per l, the worms become immobile. In well-aerated water, *Tubifex tubifex* completely retracts into its burrow and, in a hypoxic condition, the worm waves its tail freely in the water (Alsterberg 1922; Palmer 1968). High O_2 concentration is said to be toxic to *T. tubifex* (Fox and Taylor 1954; Walker 1970). The worm has been shown to be highly tolerant to H_2S toxicity (Degan and Kristensen 1981). The tracheal gills on the abdomen of nymphal Plecoptera and Ephemeroptera and larval Trichoptera consist of a panoply of tracheae which are ventilated by rhythmic movements in water while in some larval Odonata (e.g., *Aeschna*), similar structures are found in the hind gut where they are ventilated by contractions of the muscles of the body wall (Fig. 23).

The freshwater pulmonate gastropods of the Order Basommatophora after evolving air breathing have readapted remarkably well to aquatic life (Macchin 1974). This is demonstrated by the fact that the group lacks ctenidia and the mantle cavity has been totally converted to a water lung (Hunter 1953). In *Planorbis corneus*, the mantle is regularly extended into the water to serve as an accessory gill while in *Lymnaea pereger*, air is taken in as the animal dives. This presents a gas-gill function. In specimens living at considerable depths, the mantle cavity functions as a water lung (Ghiretti and Ghiretti 1975). In most pulmonate gastropods, a substantial quantity of O_2 is normally absorbed through the skin. The lung can remain closed for a long period of time and some of the aquatic species, e.g., *Limnea* and *Helicosoma* can remain indefinitely submerged at considerable depths at low temperatures (Cheatum 1934). If the O_2 drops below a critical level, the animal surfaces to breath. When exposed to a hypoxic environment or as the tide recedes, the bivalve *Pholas dactylus* collects water in the aperture on the inhalant siphon from which it draws 47% of its O_2 needs (Knight 1984; Knight and Knight 1986). The lungs of aquatic pulmonate gastropods, *Lymnaea pereger* and *Physa fontinalis*, which live away from water, may be filled with water throughout life (Hunter 1953). *Arhynchite pugettensis* has extensive cloacal diverticula (Manwell 1960) which may serve a similar role. The gephyrean worm, *Urechis caupo*, lives in U-shaped burrows in the intertidal flats along the Pacific coast of America. The levels of H_2S may be as high as 25 to 30 μl and the water becomes hypoxic during low tide, with O_2 levels dropping to 46% of the air saturation. Through muscular contraction of the body wall, the worm ventilates its hind gut (which serves as the primary site for gas exchange) with seawater (e.g., Julian and Arp 1992): the maximum inflation of the hind gut is 2 ml of water per g body weight. At normoxia, the mean hind gut ventilatory volume is 0.70 ml of water per gram body mass and increases to 1.4 ml g^{-1} at 4 kPa, the critical PO_2 at which O_2 uptake ceases (e.g., Eaton and Arp 1990). At maximal inflation, the mucoserosal thickness at the respiratory hind gut decreases from its resting size of 283 to 21 μm (Menon and Arp 1992a), a change which reduces the diffusional resistance to O_2, enhancing gas transfer but adversely increasing the permeability of H_2S into the tissues (Julian and Arp 1992). A similar rectal gill mechanism exists in the echiuran worm, *Arhynchite pugettensis*, which has an extensive cloacal diverticulum (Manwell 1960). The skin of the echiuroid worm is remarkably thick to reduce O_2 loss to the ambient hypoxic water. To compensate for this, the hind gut is thin-walled and extends along the whole length of the body (e.g., Redfield and Florkin 1931). In a 60-g animal, the total ventilation of the burrow is 29 ml per min when the animal is feeding, and when it is not, it is 13 ml per min (Hall 1931): one half of the water is taken into the hind gut where one third of O_2 is utilized. Over and above causing mixing of water in the hind gut and hence ensuring more efficient delivery of O_2 into the tissues, the peristaltic waves also lead to movement of the coelomic fluid (which contains a large number of corpuscles which have hemoglobin), further promoting O_2 transfer to the tissue cells. The soft-shelled river turtles of the family Trionychidae, namely *Amyda mutica* and *Aspidonotus spirifer*, ventilate their mouths and pharynx with water at a rate of 16 times min^{-1} when submerged and absorb O_2 through villus-like highly vascularized processes which cover the mucous membrane of the pharynx (Simons and Sussana 1886). The well-vascularized mouth of the cuchia eel, *Amphinous cuchia*, is utilized for gas exchange in both air and water (Singh et al. 1984). Through rhythmic ventilation of the cloacal bursae of the Amazon turtle, *Podocnemys*, 90% of the O_2 needs are met (Steen 1971). Due to the very small quantities of water taken up by the peristaltic processes, doubts have been expressed on the effectiveness of the rectal and intestinal gas exchange process particularly in hypoxic water (Krogh 1941). In such organisms, the skin is utilized for respiration to a greater extent.

A number of air-breathing aquatic snails successfully subsist in the tropical African swamps. The best-known one is the large amphibious *Pila ovata* (Ampullariidae), of which the mantle cavity is divided into water- and air-breathing chambers, and *Biomphalaria sudanica* (Planorbidae), an entirely aerial pulmonate gastropod. The European snails, *Planorbis* (*Biomphalaria*) *corneus*

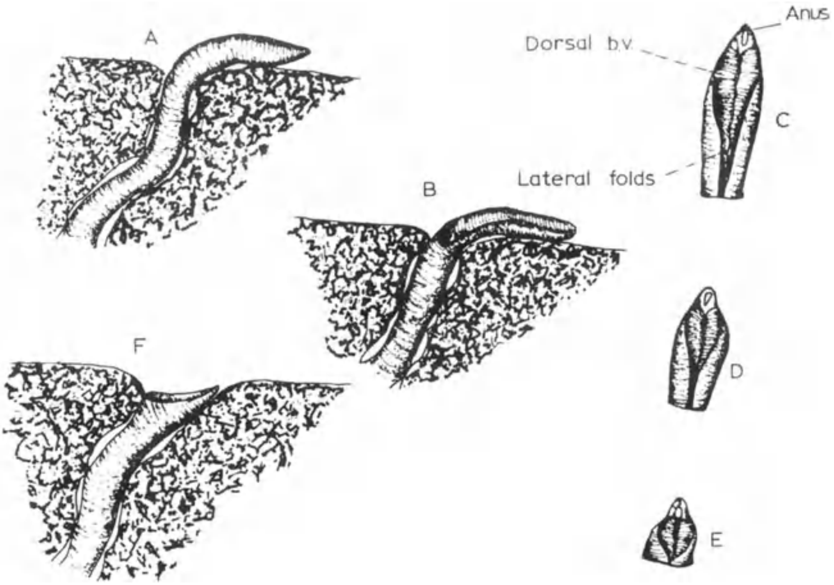


Fig. 51A–F. Respiratory mechanisms and structure of the "lung" of the swampworm, *Alma emini*. **A** Surfacing from the soil. **B** Formation of a respiratory groove. **C, D, E** Closing up the respiratory groove. **F** Retracting into the mud. (Beadle 1957)

and *P. ovata* (Jones 1964), are, however, only marginally adapted for survival in a hypoxic environment by having a slightly higher blood O_2 affinity. Compared with the well-established fish, the tenuous hold of the snails and the insects on the anoxic tropical swamps is a reflection of their much recent reinvasion of this habitat, conceivably after earlier perfection for life on dry land. The swamp worm, *Alma emini*, presents a particularly fascinating adaptation for respiration in the tropical African swamps. Its ecological success in the habitat is reflected in its numerical abundance in the floating mats of papyrus swamps (Stephenson 1930; Beadle 1974). Like most African species of the genus *Alma*, the worm can lead a successful amphibious existence (Beadle 1957; Wasawo and Visser 1959). It can extract O_2 from both air and water: in water, the respiratory groove functions as a water lung. *Alma* subsists in a habitat which is both anoxic and highly reducing. The worm can survive for at least 2 days in total absence of O_2 (Beadle 1957). The dorsal surface which is highly vascularized is spread out on emerging from the soil (Fig. 51) to form a temporary tubular "lung" (Figs. 45,52) through which gas exchange occurs (Maina et al. 1998). Air bubbles are thought to be trapped in the lung and drawn down into the soil for use during the subterranean sojoum. Mangum et al. (1975), however, noted that much of the air captured by the lung at the surface is lost during descent but some bubbles may be held by the hydrophobic cuticle, leaving a volume of about 0.2 μl in an average specimen. The rate of O_2 uptake by the lung is 50 to 60% of that which occurs across the total

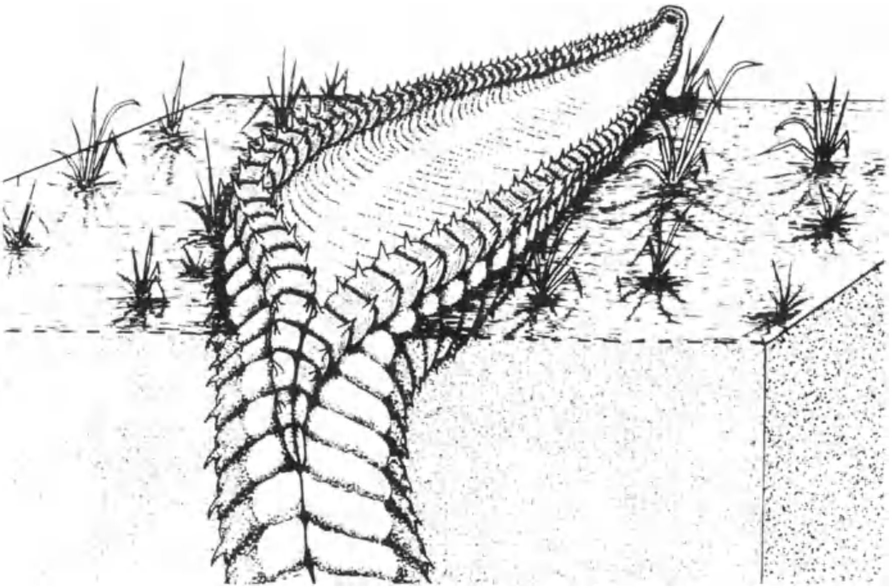


Fig. 52. Schematic view of the respiratory groove of the swampworm, *Alma emini*, which subsists in waterlogged hypoxic soil with abundant putrefying plant matter. The capacity to form a temporary lung for exchange of gases with air enables the worm to live in a hypoxic and hypercarbic habitat

body surface while in water or in air though the lung constitutes only 1.5% of the surface area of the body (Mangum et al. 1975): a 0.75-g worm was reported to have a respiratory surface of 11.4 mm^2. Greater values (lung volume 67 cm^3) and respiratory surface area 245 mm^2) were estimated by Maina et al. (1998). The blood of *Alma* contains an extracellular high molecular weight hemoglobin with a remarkably high O_2 affinity (Mangum et al. 1975). The hemoglobin is fully oxygenated at a PO_2 of 0.3 kPa in absence of CO_2 and at less than 1.3 kPa at very high PCO_2 (27 kPa) (Beadle 1957). The high mortality rate when the worms are prohibited from gaining access to air (Beadle 1957) indicates that O_2 uptake occurs exclusively through the "lung". Metabolism in *Alma* may be mainly anaerobic with aerobic gas exchange serving only to neutralize the toxic end products of glycolysis. The biochemistry of aerobic metabolism in *Alma* is essentially similar to that of other multicellular animals (Beadle 1957; Coles 1970). Coles (1970) estimated that O_2 consumption in air is only 10.8 $\mu l\, g^{-1} h^{-1}$ at 23 °C but much higher values were reported in both water (123 $\mu l\, g^{-1} h^{-1}$) and air (230 $\mu l\, g^{-1} h^{-1}$) by Mangum et al. (1975). These observations correspond with those made by Laverack (1963) on related aquatic tubificid worms. In the juvenile stages, the suprabranchial chamber membranes of the climbing perch, *Anabas testudineus*, are used for aquatic respiration, i.e., as water lungs (Munshi and Hughes 1986), a process which persists in adult anabantoids (e.g., Peters 1978).

4.7 The Placenta: an Ephemeral Liquid to Liquid Gas Exchanger

Though ubiquitous among the metatherian and eutherian mammals, in lineages where viviparity is ancient and appears to have evolved only once from a common inceptive ancestor and was from then conserved (e.g., Guillette and Hotton 1986; Packard et al. 1989), the placenta has developed in practically all vertebrate groups except in the agnathan and avian species. In some vertebrate classes, viviparity has evolved repeatedly (Hamlett 1986, 1989; Wourms and Callard 1992). For example, among reptiles, in the squamates, e.g., the lizards *Sphenomorphorus quoyii* (Grigg and Harlow 1981) and *Niveoscincus metallicus* (Stewart and Thompson 1994), and the snakes, e.g., the adder, *Vipera berus* (Bellairs et al. 1995), and the garter snake, *Thamnophis sirtalis* (Hoffman 1970), the process has evolved many times (Weekes 1935; Blackburn 1993). In the sphenodontids, crocodilians, and turtles, however, it does not appear to have ever evolved (e.g., Blackburn 1982; Shine 1985). The lizard, *Sceloporus aeneus*, which lives at high altitudes in Mexico, exhibits a bimodal mode of reproduction, i.e., both viviparity and oviparity can occur (Guillette 1982; Guillette and Jones 1985). Among amphibians, a few anurans, 15% of the urodeles, and 50% of the caecilians (e.g., *Typhlonectes compressicauda*; Garlick et al. 1979) exhibit viviparity (Wake 1989, 1993). Fish like the teleost, *Zoarces viviparous* (Weber and Hartvig 1984; Hartvig and Weber 1984), sharks, e.g., *Scyliohinus settaris* (Wourms et al. 1988; Hamlett 1989; Wourms 1993), and insects (e.g., the tse-tse fly) have functional placentae. Viviparity affords protection of the embryo from adverse environmental conditions and predation (Blackburn 1982; Shine 1983; Shine and Guillette 1988). Extended internal fetal nutrition supports development to a more advanced state (e.g., Lillegraven et al. 1987; Shine 1989; Guillette 1993), improving chances of survival. Oviparity is thought to be ancestral to viviparity (Hamlett 1989). It is envisaged that reduction of the thickness of the eggshell, e.g., in the lizard, *Sphenomorphus fragilis* (Greer and Parker 1979) where the thickness of the shell is only 10 μm, the egg membrane in sharks (Hamlett 1987, 1989) and reduction of the number of eggshell glands, and increase of oviductal vascularity, e.g., in the shark, *Squalus acanthias* (Jollie and Jollie 1967) may be the initial morphological preparations that preceded the evolution of viviparity (Guillette 1989, 1991). Decrease in the eggshell thickness brings the embryonic and maternal circulations closer, predisposing implantation, egg retention, and formation of the placenta, an organ that serves both nutritive and respiratory roles. The transition from oviparity to viviparity is a gradual process which entails both morphological and endocrine changes (Guillette 1991; Hamlett 1989).

Like the gills, the placenta is a liquid-to-liquid gas exchanger. Unique to practically all evolved gas exchangers, the placenta is a secondary gas exchanger, in that it relies entirely on another organ (gill or lung) for gas transfer. While the placenta performs other important roles which include synthesis of hormones, transfer of ions and metabolites (e.g., Faber 1993), and protection of the fetus from adverse ambient pertubations (Laburn et al. 1994), its primary function is unequivocally that of gas exchange (Mayhew 1992). As in other multifunctional organs, the ultimate design of the placenta must accommodate all the constitutive roles. Faber et al. (1992) observed that, despite the purpose of the placenta in all species that have evolved it being essentially the same, "there is no other mammalian organ whose structure and functions are so species-diverse". The respiratory challenges faced by the mammalian fetus are to an extent similar to and in some ways different from those of the bird embryo (Sect. 6.13): both operate within a limited and fixed space. Compared with the eggshell, however, the placenta is a dynamic organ which grows and changes with gestation to meet the increasing fetal demands for O_2. The placental function is determined by the growth and development of the terminal villi, the sites where materno-fetal exchange of respiratory gases and metabolites occurs (e.g., Teasdale 1980; Fox 1986; Mayhew et al. 1986; Stoz et al. 1988; Jackson et al. 1992). The human placenta has been conceived as a spongy medium whose porosity is set by the spatial interdigitation and configuration of the maternal and fetal villous systems (Schmid-Schönbein 1988), giving a villous surface area of about 11 m^2 contained in an average volume of about 500 cm^3 (Aherne and Dunnill 1966). The geometry of the maternal and fetal vasculature determines the perfusive (hemodynamic) characteristics and the diffusive capacities of the placenta to the respiratory gases (e.g., Lee and Mayhew 1995). With a few falling in between, dependent on factors such as molecular weight, electrical charge, vascular geometry, and concentration gradient, the transfer of substances across the placenta is either entirely flow-limited or diffusion-limited (Faber et al. 1992). During normal human placental development, villous maturation is characterized by increased tissue and blood volume. The cross-sectional surface area of the terminal villi increases gradually stabilizing at 2000 μm^2 between the 28th and 36th week of gestation (Ruckhäberle et al. 1977; Teasdale 1980; Stoz et al. 1988; Karsdorp et al. 1996). As in all gas exchangers, a short diffusional distance and an extensive surface area are the structural features for efficient gas exchange (Figs. 53,54). In the placenta, the distance between the two blood streams, i.e., the materno-fetal placental barrier, ranges between 2 to 6 μm in man, 6 to 8 μm in the cat, and 1.5 to 3 μm in rodents and

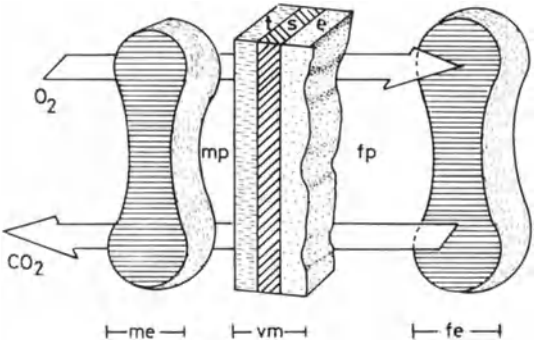


Fig. 53. Schematic drawing of the maternal-fetal gas exchange pathway. The maternal placental circulation is separated from the fetal one by a tissue barrier, *vm*, composed mainly of trophoblast, *t*, syncytiotrophoblast, *s*, and endothelial cells, *e*. The placental barrier is highly attenuated to enhance gas exchange; *mp* maternal plasma; *fp* fetal plasma; *me* maternal erythrocytes; *fe* fetal erythrocytes

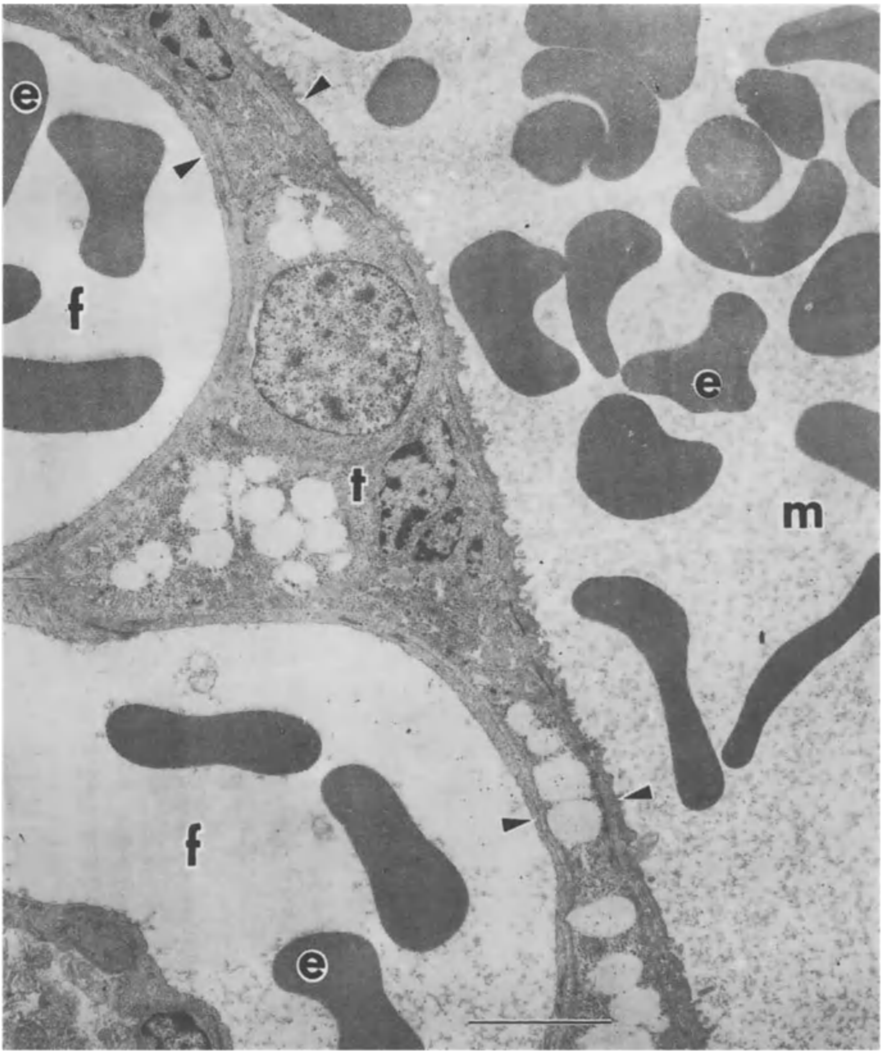


Fig. 54. Maternal-fetal barrier, ➤, of the placenta of the spotted hyena, *Crocuta crocuta*, showing the fetal capillaries, *f*, and the maternal blood spaces, *m*; *e* erythrocytes; *t* trophoblast. The *white spaces* in the barrier are lipid aggregations which have been removed after tissue processing. *Bar* 3 μm. (Courtesy Prof. D.O. Okello, Department of Veterinary Anatomy, University of Nairobi, Kenya)

Leporidae (Bartels 1970). The transplacental O_2 transfer is effected by diffusion driven by prevalent partial pressure gradient between the maternal and fetal blood streams. A human placenta with a surface area of 15 m^2 and a thickness of 5 μm will transfer 0.113 ml $O_2 s^{-1} mbar^{-1}$ (Bartels 1970). The microsomal membrane carrier, cytochrome P_{450} which reversibly binds with O_2 has been implicated in promoting O_2 transfer across the placenta (e.g., Burns and Gurtner 1973). The importance of P_{450} in the flux of O_2 across the materno-fetal placental barrier, however, appears to be very small. No increase in the concentration of P_{450} occurs during hypoxia (Gilbert et al. 1979). In dog and sheep lungs (Burns et al. 1975, 1976), in the liver (Rosen and Stier 1973), and in body tissues in general (Longmuir and Sun 1970), P_{450} has also been incriminated with O_2 transfer. There is presently no hard evidence to support occurrence of active transport of O_2 in any evolved gas exchanger (Dawes 1965). Present experimental evidence strongly indicates that the process occurs entirely by simple physical diffusion.

The placental diffusional pathway is complicated, even in the much simpler hemochorial human placenta. The maternal-fetal placental barrier is neither uniform in thickness nor is it homogenous in composition (e.g., Jackson et al. 1985). Oversimplified physiological models fail to take into account factors such as tissue inhomogeneity (e.g., Laga et al. 1974), maternal-fetal placental perfusion inhomogeneities (Bøe 1954), and placental O_2 consumption and vascular shunts (Barcroft and Barron 1946). About 40% of the human placenta consists of maternal blood (hematocrit, 36%) which is three to five times greater in volume than that of the fetal blood (Ht, 50%) (Mayhew et al. 1984): the mean harmonic mean diffusional distances of the maternal blood plasma, the villous membrane, and the fetal plasma are respectively 0.92, 4.08, and 1.88 μm, giving an overall placental thickness of 6.8 μm. Aherne and Dunnill (1966) reported a thinner maternal-fetal barrier of 3.5 μm. The villous membrane exhibits remarkable sporadic attenuation (Aherne and Dunnill 1966; Jackson et al. 1985), a property similar to that presented by the blood-gas barrier of the mammalian (Gehr et al. 1981) and avian lungs (Maina and King 1982a; Figs. 29b,49a), where it is said to enhance O_2 transfer by generating an overall thin boundary without compromising the mechanical integrity of the gas exchanger. In the human placenta, the maternal-fetal barrier, which constitutes as much as $58\,cm^3$ of the trophoblast (Aherne and Dunnill 1966), may constitute a significant sink for O_2.

The fundamental structural features of any gas exchanger include an extensive surface area and a thin barrier between the respiratory media. These features are achieved in the placenta through different processes which include: (1) plasmodial activity which results in nuclear aggregation of the trophoblastic cell masses at syncytial knots leading to attenuation in some regions, especially those overlying the blood capillaries - such sites from the extremely thin vasculosyncytial membranes which promote gas and nutrient transfer (Bender 1974; Jones and Fox 1977; Heijden 1981), (2) through a mechanistic process which causes distension and margination of fetal capillaries and their relocation to the overlying trophoblast (Amaladoss and Burton 1985; Jackson et al. 1988a,b; Mayhew and Wadrop 1994), and (3) enlargement of the surface area through increase in the number of microvilli (Firth and Farr 1977; Heijden 1981). Attenuation of the trophoblast occurs in the guineapig placenta (Bacon et al. 1984) and in the human cultured one after long-term maternal exposure to hypoxia (Burton et al. 1989). Some parts of the placenta may be concerned with gas exchange while others are involved in processes which require greater tissue density such as hormonal synthesis and nutrient transfer (e.g., Bartels and Metcalfe 1965) as well as mechanical support. Interestingly, a similar engineering process appears to occur in the bird lung where the cell bodies of the pneumocytes are largely confined to the penultimate gas exchange sites, the atria and infundibulae: the extremely thin blood-gas barrier is virtually lined by the attenuated cytoplasmic extensions (Maina and King 1982a). In the mammalian lung, thin and thick sides of the interalveolar septae occur (Fig. 86). The thin parts are utilized for gas transfer while the thick ones render mechanical support and provide pathways for lymphatic drainage (Fishman 1972).

It is widely assumed that the structural complexity of a placenta, i.e, the number of tissue layers comprising it, determines the thickness of the materno-fetal placental barrier and hence the diffusing capacity of the organ for O_2. The less elaborate hemochorial placentae are hence thought to be more efficient than the more elaborate epitheliochorial ones. There are, however, no reliable data to indicate that the simple placentae are in a way more efficient in gas exchange and in promoting fetal growth and development (e.g., Dempsey 1960). Furthermore, it is known that in certain epitheliochorial placentae, the overall barrier thickness is smaller than in some hemochorial ones, which specific areas of the barrier being only about 1 μm thick (Ludwig 1965). The maternal-fetal placental barrier thickness varies greatly in different species and even in the same species during different stages of gestation. Moreover, it has been shown that placental forms may be mixed, i.e., epitheliochorial and hemochorial parts may coexist in the same placenta (e.g., Starck 1959). The diffusing capacity of the placenta depends not only on the path length of the barrier and permeability but also on factors such as the mean diffusion gradient and the placental surface area, features which can be altered according to needs. The transplacental O_2 gradient in the Ilama (about 2 kPa) is remarkably low, a state perhaps compensated for by the extensive placental gas exchange surface (Barron et al. 1964). The mean diffusional gradient of O_2 in the hemochorial placenta of the rabbit at 27 to 30 days gestation (term about 31 days) ranges from 1.2 to 1.9 kPa and in the syndesmochorial placenta of sheep between 126 and 137 days of gestation (term about 147 days) ranges between 4.3 and 6.4 kPa (Barron and Meschia 1954). From estimates of O_2 consumption of the pregnant human uterus and PO_2 in the maternal and fetal blood streams, Metcalfe et al. (1967) calculated that the physiological diffusing capacity of the human placenta ranges from 0.014 to 0.018 ml $O_2\,s^{-1}mbar^{-1}$. Calculations based on the diffusing capacity of CO_2 in pregnant women (Forster 1973) gave higher value of 0.025 ml $O_2\,s^{-1}\,mbar^{-1}$. On average, data indicate that the physiological diffusing capacity of the human placenta lies between 0.013 and 0.038 ml $O_2\,s^{-1}\,mbar^{-1}$ and is appreciably lower than the morphometric one, which ranges from 0.055 to 0.072 ml $O_2\,s^{-1}\,mbar^{-1}$ (Mayhew et al. 1984). The placental membrane of the physiologist (= villous membrane + serial blood plasmas) accounts for 86 to 94% of the total placental resistance with only minor contributions made by the O_2-hemoglobin interactions with the erythrocytes (Mayhew et al. 1984, 1986). In the human lung (Gehr et al. 1978), the physiological and the morphometric diffusing capacities of the lung differ by a factor of 2. This is taken to constitute a functional reserve (Weibel 1984a). The value of the physiological diffusing capacity approaches the morphometric one at the maximum O_2 consumption (Vo_{2max}). The difference between the morphometric and the physiological diffusing capacity of the placenta may functionally be accounted for by vascular shunts, placental O_2 consumption, and regional inequalities of perfusion (Metcalfe et al. 1967; Mayhew et al. 1984, 1990), as well as the lack of uniformity of the thickness of the villous membrane. The latter feature may lead to local inhomogeneities of diffusion resistances across the sporadically attenuated barrier (Mayhew et al. 1984; Jackson et al. 1985). In the vertebrate lung, anatomical and functional shunts and regional inhomogeneities in gaseous diffusion and vascular perfusion contribute to the discordance between the physiological and morphometric diffusing capacities (e.g., Crapo and Crapo 1983). Aherne and Dunnill (1966) envisaged that the mass of the placenta and hence the development of the chorionic villous area (transfer area) correlate directly with the total fetal metabolism.

While the lung is subjected to sudden increases in functional demands from rest to maximal O_2 consumption during exercise, the needs of a fetus tend to be fairly stable and gradually increase with gestation. In the human being, during the 3rd month of fetal life, the O_2 capacity is 12 ml O_2 per 100 ml blood, increasing to 20 to 22 ml O_2 per•100 ml blood during the next 5 months: the maximum O_2 capacity is reached at 6 to 8 weeks (e.g., Betke 1958). From the evident progressive degenerative changes such as infarcts, fibrinoid deposition, thickening of the trophoblastic basement membrane, partial obliteration of decidual arteries, and endothelial cell proliferation and calcification (Mayhew et al. 1984), the morphometric diffusing capacity of the placenta would be expected to remarkably increase towards term. This deterioration is, however, counteracted by a gradual decrease in the thickness of the villous membrane which occurs with gestation when the remarkably attenuated vasculosyncytial regions become more pronounced (Fox 1964a; Jackson et al. 1988b). The arithmetic mean thickness of the trophoblast in the human placenta decreases from about 11 μm at 12 weeks to 5 μm at 38 weeks (Jackson et al. 1988b), a change brought about by displacement of the trophoblastic cell masses, leading to better exposure of the fetal capillaries to maternal blood (Teasdale 1978; Jackson et al. 1988a,b).

4.7.1 The Functional Reserves of the Placentae

The placenta is widely taken to be a progressively aging organ of which the functional capacity declines gradually towards term (Winick et al. 1967). This process is oddly accompanied by increased fetal demands which occur with growth and development. Towards term, fetal requirements come close to totally eroding the functional reserves of the placenta, in some cases leading to intrauterine growth retardation (Hellman et al. 1970; Garrow and Hawes 1971). Winick et al. (1967) found that no further increase in placental DNA content occurred once the fetus reached a body mass of 2.4 kg or the placenta reached a weight of 300 g. According to Rolschau (1978; but see a contrary observation by Sands and Dobbing 1985), growth of the human placenta levels up at 35 weeks of gestation. At altitudes above 3 km above sea level, due to hypobaric hypoxia (Mayhew 1991), human fetal growth is retarded (e.g., Haas 1976). Increased fetal erythropoiesis expressed as high hematocrit, hemoglobin concentration, and proportion of hemoglobin-F suggest that the fetus experiences hypoxia during the last stages of pregnancy (Ballew and Haas 1986). Maternal adjustments, among others hyperventilation and elevated hematocrit, during high altitude pregnancy (Moore et al. 1982), appear to fall short of providing the necessary driving pressure of O_2 across the placenta. Mayhew (1991) observed that with altitude, while adaptive diffusive changes occur on the maternal side of the placenta, fetal conductances especially of the erythrocytes and plasma do not adjust to the same degree, leading to low fetal birth weights at altitude (Mayhew et al. 1990). The difference between the maternal and fetal adjustments for high altitude hypoxia is greatest at birth weights greater than 3 to 3.3 kg, which is about the average birth weight at altitude (Mayhew 1991).

The O_2 transferred by the placenta and made available to the fetus must initially be procured by the maternal lung. The fetus is essentially a temporary addition to the maternal gas transfer cascade (Figs. 2,3). On this account, it is plausible that at some critical point, the fetus would be indirectly affected by extreme states and circumstances which may occasion inadequacy in maternal pulmonary gas flux and cardiovascular transfer. These may result from exposure to hypoxia, i.e., reduction of the driving pressure of gases across the lung and the placenta or may be due to pathological conditions at either or both sites. An increase in the fetal O_2 saturation is generated on maternal exposure to high PO_2 (e.g., Dawes and Mott 1962; Cassin et al. 1964; Assali et al. 1968). Overdesign and/or plasticity to respond to circumstances when the functional capacity of the maternal gas exchanger may become insufficient is necessary (e.g., Becker 1963; Bender 1974). Such instances include maternal exposure to acute life-threatening hypoxia and pathological conditions such as edema, atelectasis, and pulmonary infarction (e.g., Staub et al. 1967; Staub 1974; Heijden 1981), changes which constrain gas exchange. Perfectly normal reproduction can occur when the maternal blood PO_2 is subnormal, e.g., in women with congenital heart disease (Bartels 1970): in most cases, the consequences largely affect the mother more than the fetus (Burwell and Metcalfe 1958). The Korean Ama (sea women) who voluntarily dive to harvest food at the bottom of the ocean (at depths as much as 30 m) work up to the last day of pregnancy and after giving birth nurse the babies between shifts (Hong and Rahn 1967). Maternal diabetes mellitus does not appear to affect placental development (Teasdale and Jean-Jacques 1986). Oxygen tension in the umbilical vessels was found to be similar in sheep fetuses at sea level and those of ewes living at high altitude (3.5 to 4.0 km) (Metcalfe et al. 1962), indicating that the mother offers efficient protection against changes in blood PO_2. During the birth process, the fetus is protected from hyperthermia: in sheep, during parturition, the maternal body temperature rose at $0.70\,^{\circ}\mathrm{C\,h^{-1}}$ in the final stages of labor but the fetal one rose at a significantly lower rate of $0.45\,^{\circ}\mathrm{C\,h^{-1}}$ (Laburn et al. 1994). In normally developing human pregnancies, a drop in the peripheral vascular resistance in the placenta occurs after a gestational age of 16 weeks. This results in positive end diastolic flow velocity waveform in the umbilical artery (van Zalen et al. 1994). In pregnancies complicated by hypertension and/or intrauterine growth retardation, however, placental flow resistance is elevated. This may lead to absent or even reversed (negative) end diastolic flow velocities in the umbilical arteries during the second and third trimester of pregnancy. Such a condition may result in preterm delivery, neonatal death, and lower birth and placental weights (e.g., Aherne and Dunnill 1966; Trudinger et al. 1991; Pattinson et al. 1993; Karsdorp et al. 1994, 1996).

Like the avian and mammalian lungs, the placentae possess a substantial functional reserve. Large fetal lambs (a few days to term) can maintain an O_2 consumption of 5 to 6 $ml\,kg^{-1}\,min^{-1}$ (values within the normal range) even when the umbilical venous and arterial saturations are respectively reduced to 54 and 35% at an umbilical flow rate of 180 $ml\,kg^{-1}\,min^{-1}$ (Dawes et al. 1953). Perhaps it is as a part of an inbuilt safety margin of operation that the morphometric diffusing capcity of the human lung (2.47 $ml\ O_2\,s^{-1}\,mbar^{-1}$; Gehr et al. 1978) is about 33 times greater than that of the placenta of 0.075 $ml\ O_2\,s^{-1}\,mbar^{-1}$ (Mayhew et al. 1984). Structurally, the placenta is a highly adaptable organ with a considerable functional reserve capacity (e.g., Karsdorp et al. 1996). Perfusion of the fresh human placenta with varying concentrations of O_2 causes obvious thinning of the trophoblast from 0.44 to 3.3 μm in a matter of 6 h and when the O_2 levels are brought back to normal, the dimensions are reversed (Tominage and Page 1966). The proliferation of the cytotrophoblast appears to be sensitive to the prevailing O_2 levels (Fox 1964b; Kaufmann 1972): cytotrophoblast decreases when oxygenation is good and increases in conditions associated with intrauterine hypoxia (Fox 1964b, 1970; Kaufmann et al. 1977). Chronic maternal exposure to hypoxia in guinea pigs leads to thinning of the trophoblast (Bacon et al. 1984). The rate of flow of the placental blood at term, which is 500 to 600 $ml\,min^{-1}$, is in excess of that of 300 to 400 ml required to supply 16 ml of O_2 to the human fetus per minute (Gahlenbeck et al. 1968). A maternal-fetal PO_2 of 0.3 to 0.4 kPa is adequate to supply the required amount of O_2 to the fetal tissues (Bartels 1970) but a much higher gradient of 2 to 4 kPa has been determined in the larger blood vessels (Metcalfe et al. 1967). Infections, underlying pathological conditions, and exposure to severe conditions such as extreme hypoxia appear to accelerate placental development (Jackson et al. 1995; Lee and Mayhew 1995; Karsdorp et al. 1996). Terminal villi of placentae, of which the pregnancy is accompanied by absent or reversed end diastolic blood flow in the umbilical artery, show a more homogeneous pattern of small villi (Karsdorp et al. 1996). Hitschold et al. (1992) suggested that the accelerated development of the terminal villi may be a compensatory mechanism but the potential advantages gained from it may be curtailed by the concomitant reduction in the blood flow rate in the umbilical artery (Erskine and Ritchie 1985; Karsdorp et al. 1996). The harmonic mean thickness of the placentae of women living at high altitude (average thickness 4.5 μm) was 8 to 19% thinner than that of those living in the lowlands (average thickness 5.2 μm) and the morphometric diffusing capacity of O_2 in the former was higher than in the later (Mayhew et al. 1984; Table 14). Elevated fetal hematocrit, high hemoglobin concentration, low O_2 affinity, and high O_2 carrying capacity of blood (e.g., Ballew and Haas 1986; Tables 15,16) are vital physiological adjustments in highland pregnancy and increase the diffusive conductance of the placenta in a hypobaric and hypoxic circumstance. The most critical point of the development of the human placenta when there is substantial increase in volume,

Table 14. Diffusive conductances in low and high altitude placentae. (After Mayhew et al. 1990)

Variable	Low altitude	High altitude
Dme	1050	1700
Dmp	620	1190
Dtr	28.6	28.7
Dst	49.8	70.8
Dfp	726	666
Dfc	290	237
Overall Dp	15.7	17.5
Specific Dp	4.7	5.79

Units: $\mathrm{ml\,O_2\,min^{-1}kPa^{-1}}$); specific value, $\mathrm{ml\,O_2\,min^{-1}\,kPa^{-1}\,kg^{-1}}$).
Symbols: me, maternal erythrocytes; mp, maternal plasma; tr, trophoblast; st, stroma; fp, foetal plasma; fe, foetal erythrocytes; Dp, diffusing capacity of the placenta.

Table 15. Oxygen affinity (P_{50}) and oxygen carrying capacity of maternal and fetal blood of various species (After Novy and Parer 1969)

Species	P_{50} at pH 7.40 (mmHg)		O_2 capacity $\mathrm{mlO_2\ 100\,ml^{-1}}$	
	Maternal[a]	Fetal[a]	Maternal	Fetal
Man	26	22	15	22
Rhesus monkey	32	19	15	18
Rabbit	31	27	15	14
Sheep	34	17	15	17
Goat	30	19	13	12
Pig	33	22	13	13
Elephant	24	21	20	17
Camel	20	17	15	17
Llama	21	18	14	19
Cat	36	36	12	16

[a] To convert to kPa multiply by 0.133.

surface area, length of villi, and overall thinning of the trophoblast lies between 17 to 21 and 22 to 26 weeks of gestation (Jackson et al. 1992; Simpson et al. 1992; Mayhew and Simpson 1994).

The performance of the placenta falls between that of the lung, which on average operates well below its maximal capacity but can respond to sudden demands placed on it, and the eggshell, in which the structural parameters are firmly incorporated. There are fundamental limitations intrinsic to the placenta as a gas exchanger: the O_2 consumption of the human hemochorial placenta (2 to 10 ml $O_2\,kg^{-1}$ wet mass min^{-1}) at term indicates that placental tissue utilizes as much O_2 as the fetus itself (e.g., Nyberg and West 1957). The placental O_2 con-

Table 16. Maternal and fetal oxygen capacities of a number of spacies. (After Bartels 1970)

Species	O_2 Capacity ml O_2 100 ml $blood^{-1}$		Half saturation pressure (mmHg)	
	Maternal	Fetal	Maternal[a]	Fetal[a]
Man	15	22	26	22
M. mulatta	15	18	–	–
Rabbit	15	14	31	27
Sheep	15	17	34	17
Goat	13	12	30	19
Guineapig	16	16	30	19
Elephant	20	17	23	17
Camel	15	17	21	16
Llama	14	19	21	18
Cow	15	12	21	22
Chicken	14	12	49	34
Seal	32	28	29	21

[a] To convert to kPa multiply by 0.133.

sumption in the more complex placentae like the epitheliochorial ones which have a greater tissue density would be expected to have an even greater O_2 consumption. In sheep, the placenta and fetal membranes consume as much as one third of the fetal O_2 uptake (e.g., Longo et al. 1973). This suggests that in cases of anoxia, the fetus may be critically deprived of its normal O_2 needs. In the cow, the physiological diffusing capacity between the 5th and 9th month of gestation is 0.0016 ml $O_2\,s^{-1}\,mbar^{-1}\,kg^{-1}$ (Gahlenbeck et al. 1968) but the placenta increases in mass three to ten times during the same period. Experimental Swiss mice at a simulated altitude of 4.3 to 6.1 km show normal mating behavior, fertility, and reproduction, but early embryo resorption occurs at a greater frequency than in the control (sea level) group (Baird and Cook 1962). The resorption takes place at an embryo size of about 7 mm crown rump length, presumably due to deprivation of O_2 (by the placenta) at a critical stage of development. In an attempt to overcome these limitations, the epitheliochorial placentae of sheep and goat and the hemochorial ones of rabbit and guinea pig have developed the efficient countercurrent arrangement between fetal and maternal blood flows (e.g., Kaufmann and Davidoff 1977; Faber et al. 1992). In the rabbit and the guinea pig, the PO_2 in the umbilical vein exceeds that in the uterine vein. The placentae of the rabbit and the guinea pig are categorized among the efficient group of exchangers with the hemochorial placentae of the rhesus monkey and human being including the epitheliochorial placentae of goat and sheep being placed in the inefficient category (Faber et al. 1992; Table 17). From studies of compensatory mechanisms of the injured guinea pig placenta, Heijden (1981) observed that the organ has a very small functional reserve capacity and its potential to respond to reduced capacity is very poor. The countercurrent system of the placenta in sheep and goat is notably inefficient as evinced by the lower physiological diffusing capacity of the organ in the two species (Metcalfe et al. 1967). Having an efficient placenta has its

Table 17. Placental type, vascular geometry, foetal oxygen consumption (Vo_2), oxygen pressure gradient between maternal and fetal blood (PO_2) and diffusion capacity (Dpo_2) of placentas of several species. (After Bartels 1970)

Species	Placental type	Vascular geometry	Vo_2	PO_2 (mmHg)[a]	Dpo_2[b]
Human	Hemochorial	Multivillous	7.4	23	0.32
M. mulatta	Hemochorial	Multivillous	10.0	33	0.30
Cow	Epitheliochorial	Countercurrent	9	38	0.24
Sheep	Epitheliochorial	Countercurrent	9	40	0.22
Goat	Epitheliochorial	Countercurrent	12	40	0.30
Rabbit	Hemochorial	Countercurrent	7.7	10	0.70
Guineapig	Hemochorial	Countercurrent	7.0	10	0.70

[a] To convert to kPa multiply by 0.133.

[b] Dpo_2 calculated using the carbon monoxide method of Longo et al. (1967).

Units: Vo_2, ml O_2 min^{-1} kg $fetus^{-1}$; PO_2, mmHg; Dpo_2, ml O_2 min^{-1} $mmHg^{-1}$ kg^{-1} fetus.

Table 18. Oxygen partial pressure in maternal arterial and uterine vein blood as well as in venous and arterial fetal blood for a number of species. (After Bartels 1970)

Species	PO_2[a]				Placenta type	Flow pattern
	Maternal		Fetal			
	Art.	Ven. Ut.	Ven. Umb.	Art. Umb.		
Cow	70	34	21	12	Epitheliochorial	Countercurrent
Sheep	86	52	29	18	Epitheliochorial	Countercurrent
Goat	84	46	33	14	Epitheliochorial	Countercurrent
Man	100	33	29	17	Hemochorial	Multivillous
M. mulatta	88	30	16	12	Hemochorial	Multivillous
Rabbit	80	25	46	17	Hemochorial	Countercurrent
Guinea pig	92	20	30	8	Hemochorial	Countercurrent

[a] Units: mmHg – to convert to kPa multiply by 0.133.

Art., arterial; Ven., venous; Ut., uterine; Umb., umbilical.

price and risk. The rate of flow-limited transfer diminishes much more steeply in the countercurrent exchanger than in the concurrent one when the flow rate of one of the blood streams decreases (Faber et al. 1992). After a flow reduction of 50%, gas exchange in the countercurrent system falls by as much as one half but in the concurrent system this drops by only one third. In this respect, the rabbit and guinea pig placentae possess a lower safety margin or operation, as has been noted by workers who have observed the remarkable fragility of the rabbit and guinea pig placentae, compared with the more resilient ones of the sheep. Despite the intrinsic structural differences, the mature hemochorial placentae show notable similarity in diffusional permeabilities regardless of whether they belong to the hemomonochorial (guinea pig and human), hemodichorial (rabbit), or hemotrichorial (rat) groups (e.g., Metcalfe et al. 1967; Štulc 1989; Tables 17,18).

Dawes (1965) observes that "there is a rugged quality about the way these machines (placentae) are put together which appears to give a wider safety margin than is usually supposed". Placental morphology very poorly reflects the phylogenetic and systematic affinities, especially in mammals (Mossiman 1987; Luckett 1993). The morphological disparity of the placenta defies simple logic. It is a showpiece of the remarkable intrinsic plasticity of biological entities for solving different challenges. Different animal groups have achieved viviparity through manifold strategies and with it design-specific placentae. In a transient organ on which enormous resources are invested to ensure proper growth and development of the fetus, perhaps need to evolve a common architectural plan, a process which would be limiting to some animals, has not arisen. As for the evolution of the blood pigment carriers (Sect. 2.8), those aspects of biology which show great diversity of form and function may be symptomatic of conditions and processes which are far from attaining optimal designs and states. In such cases, encompassing solutions are untenable due to immutable phylogenetic constraints.

Chapter 5

Bimodal Breathing: Compromise Respiration

> *"For animal lines moving from water to land, the changes in physical and chemical characteristics of the environment are immense. These changes affect all possible life processes, from respiration and excretion to methods of movement, the functioning of the sense organs and reproductive mechanisms. The transition must therefore have been made very gradually, and some of the transition stages are repeated by present day groups." Little (1990)*

5.1 The Water-Air Interface: an Abstract Respiratory Rubicon

The division of the Animal Kingdom into aquatic and terrestrial life is ancient: it is still relevant to contemporary life. This distinction is ascribed to the different structural and functional attributes which have been imposed by the physical characteristics of the two different fluid media. While looking at this broad picture, it is too often forgotten than a rich assortment of animals regularly commutes between water and air. While some largely subsist in water and extract their O_2 needs from the air above, some start their development in water and end up on land at maturity. The mutual assemblage and the distribution of the animals that share this complex lifestyle demonstrates the highly pragmatic strategies which animals have adopted to overcome the ceaseless selective pressures that have beset them (Fig. 55). While hypoxic conditions are a rare occurrence in terrestrial environments except at high altitude and in deep, compact wet soil, many marine and freshwater habitats are characteristically hypoxic and/or hyperbaric (Carter and Beadle 1931; Carter 1935, 1955; Hora 1935; Saxena 1963; Rhoads and Morse 1971). Depending on nature and rate of organic putrefaction of plant and animal matter, such habitats may contain noxious gases such as H_2S, a potent inhibitor of cytochrome c oxidase systems, and ammonia (e.g., Theede et al. 1969).

One of the pivotal developments which promoted the adaptive radiation in the Animal Kingdom was that of realization of capacity to procure molecular O_2 directly from air in the Paleozoic fish (e.g., Romer 1967; Johansen 1968; Packard 1974; Dejours 1994; Smatresk 1994). Once having attained air breathing, the aquatic animals seized the opportunity for terrestrial habitation. In evolutionary terms, such milestone events have been called evolutionary novelties (e.g., Miller 1949; Mayr 1960; Riedl 1978), key innovations (Lauder and Liem 1989), or broad adaptations (e.g., Schaeffer 1965a). Baum and Larson (1991) defined such monumental events as "derived traits instrumental in acquiring entry into a novel adaptive zone featuring novel selective regimes". Those innovative animals that underwent the transition to air breathing and life on land are by inference thought to have formed the stem reptiles and are all now certainly extinct. The ones caught at the water-air interface include the extant air-breathing amphibi-

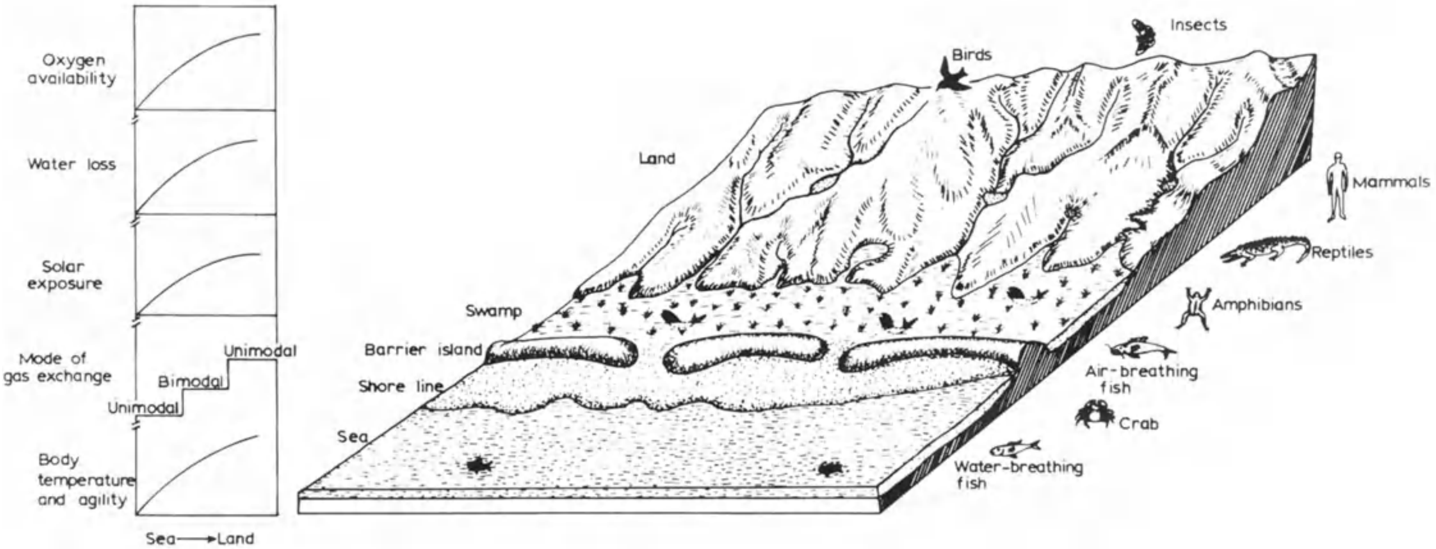


Fig. 55. Schematic view showing the evolution of air breathing and transition from sea to land. Also shown are some of the benefits gained and challenges faced. Representative taxa at various levels of respiratory development are given. Air breathing evolved in hypoxic stagnant waters which were claimed by plants to form swamps. The amphibians still rely on water for many of their physiological processes such as respiration and reproduction while reptiles, mammals, birds, and insects, after developing a waterproof cover, rely entirely on internalized gas exchangers for O_2 procurement. Hypoxia was the main driving pressure which prompted sojourn on land

ous forms and the aquatic air breathers (Rahn and Howell 1976). The contemporary transitional (= amphibious = intermediate = bimodal = dual) breathers, animals which are able to exchange gases in both air and water (using the same or multiple organs), however, do not constitute the direct progenitors, i.e., the bridging animals, between the gill breathers and animals with a modern lung (Rahn and Howell 1976). The early stem forms of animals with a derived (modern) lung would have been the Devonian amphibians (Romer 1972). They had a simple lung capable of taking up ample amounts of O_2 and eliminating a substantial measure of metabolic CO_2, as the gills gradually regressed. The surviving bimodal breathers constitute a contemporary paradigm of the processes and pathways through which air breathing and terrestriality evolved: they occupy a central position in the ecology and physiology of the evolved animal life. There is no physiological or paleontological evidence to indicate that direct passage from water to land has ever occurred (Dejours 1994). The contemporary transitional vertebrate breathers, in particular the lungfishes, comprise a provocative group that occupies a pivotal point in the evolution of the terrestrial tetrapods (Joss et al. 1991; Meyer and Dolven 1992). The adaptive diversities and the extents to which animals went to attain air breathing suggest that the selective pressures that launched the change were extremely severe and pervasive (Carter 1957, 1967). The great flexibility required to adapt to the transitional habitats may explain the dearth of intermediate breathers in many taxa. On exposure to a new habitat, adaptive measures are instituted in the order of behavioral, physiological, and structural shifts, transformations, and modifications. The intensity and the frequency of the changes in the environment and the capacity to adapt to the variations may determine the difference between survival and extinction.

The subject of the evolution of air breathing is of particular interest to both physiologists and morphologists. It presents a model for understanding some fundamental changes in the structure and function of one of the central organ systems in an animal's body. Air breathing was a monumental event in the sequence of different preadaptations for terrestrial habitation, a process which culminated in the emancipation of animals from water (Das 1940; Dejours 1989; Moore 1990b). The archaic fish, e.g., lungfishes (Dipnoi) and the bichirs and three quarters of the modern amphibious fish that inhabit the tropical and subtropical regions (Table 19) breath air (Burggren et al. 1985a; Munshi and Hughes 1992). This suggests that the factors which inspired air breathing may have been most severe in such regions. Fish in the Amazonian basin, the largest freshwater equatorial basin, have been widely studied (e.g., Carter and Beadle 1931; Junqueira et al. 1967; Johansen 1968; Kramer et al. 1978; Stevens and Holeton 1978a; Cala 1987): the majority of them have evolved air breathing. The induction of air breathing in the aquatic breathers is widely ascribed to intrinsic changes in the aquatic environment, especially hypoxia and, by extension, ambient temperature (e.g., Townsend and Earnest 1940; Davis et al. 1963; Tulkki 1965; Moshiri et al. 1979; Kutty and Saunders 1973). High metabolic demands for O_2 and intense putrefactive processes precipitated a hypoxic crisis which was exacerbated by hypercapnia (Johansen 1968; Table 11). This combination of events appears to have constituted a decisive force which prompted search for an alternative source

Table 19. Systematic position, habitat, and types of accessory respiratory organs (AROs) of air-breathing teleosts. (After Dehadrai and Tripathi 1976)

Species	AROs[a]	Family	Habitat
Electrophorus electricus	BPA	Electrophoridae	Rivers and swamps – S. America
Opicephalus (=Channa) punctatus, marulius, striatus, gachua	PL	Ophicephalidae	Tropical ponds and rivers – Asia and Africa
Amphipnous cuchia	PL	Ophicephalidae	Tropical ponds and rivers – Asia & Africa
Hypopomus brevicostris	OC	Sternarchidae	Swamps – S. America
Symbranchus marmoratus	OP	Symbranchidae	Swamps – S. America
Monopterus javanensis	OP	Symbranchidae	Freshwaters – Southern Asia
Pseudapocryptes lanceolatus	OP	Gobiidae	Pools and swamps – S. Asia
Heteropneustes (=Saccobranchus) fossilis	OL	Saccobranchidae	Ponds and swamps – Sri Lanka, India, Burma, Laos, Thailand, and Vietnam
Clarias (C. lazera, C. magur and C. mossambicus)	OL	Clariidae	Ponds and swamps – Africa, S. and W. Asia
Macropodus cupanus	OL	Anabantidae	Tropical ponds – Asia
Colisa fasciata	OL	Anabantidae	Freshwater – S. Asia
Betta	OL	Anabantidae	Freshwater – S. Asia
Osphronemus gorami	OL	Anabantidae	Freshwater – S. Asia
Anabas testudineus	OL	Anabantidae	S. Asia, IndoMalaysian Archipelago, Tropical and S. Africa
Ancistrus (A. anisitsi, A. chagresi)	SM	–	Swamps – S. America
Plecostomus plecostomus	SM	Loricariidae	Swamps – S. America
Misgurnus fossilis	I	Cobitidae	Rivers and pools – Europe and Asia
Lepidocephalichthys guntea	I	Cobitidae	Freshwaters – Asia
Doras	I	Doradidae	Rivers and swamps – S. America
Hoplosternum litorale	I	–	Swamps – S. America
Arapaima gigas	SB	Arapaimidae	Swamps and R. Amazon – S. America
Gymnarchus	SB	Gymnarchidae	Swamps and rivers – S. Africa
Erythrinus unitaeniatus	SB	Characinidae	Swamps – S. America
Umbra	SB	Umbridae	Stagnant waters – Europe and N. America
Notopterus (N. notopterus, N. chitala)	SB	Notopteridae	Freshwater – Asia
Phractolaemus ansorgii	SB	Phractolaemidae	Tropical – W. Africa
Anguilla (A. anguilla, A. bengalensis, A. japonicus)	SK	Anguillidae	Rivers – Europe, Asia, Africa, and N. America

[a] BPA, buccopharyngeal apparatus; PL, pharyngeal lung; OC, opercular chamber; OL, opercular lung; SC, stomach; I, intestine; SB, swimbladder; SK, skin.

of molecular O_2 (e.g., Das 1927, 1940; Saxena 1960; Johansen 1968; Kramer et al. 1978; Kramer 1980; Randall et al. 1981; Davenport 1985). Dramatic spatial and temporal variations in aquatic hypoxia in local inland water masses, especially those formed after flooding, have been a common feature of the Earth's surface since the Cambrian period (e.g., Barrell 1916; Fish 1956; Street and Grove 1976; Jenkyns 1980; Bray 1985; Little 1990). At various geological times, increases in environmental temperatures resulted in low solubility of O_2 especially in the tropical freshwater ponds, prompting the quest for an alternative source of molecular O_2 (e.g., Graham 1949; Grigg 1969; Graham et al. 1978a,b). Drying up of the shallow and extensive continental shelves not only aggravated the respiratory conditions but caused overcrowding and competition for finite resources. Physicochemical changes such as increase in salinity and turbidity must have acted as additional stimuli for abandoning water for land (Sayer and Davenport 1991). Evidently, severe respiratory episodes have occurred frequently in the past. In the Silurian-Devonian periods (e.g., Inger 1957; Berkner and Marshall 1965; Thompson 1971), O_2 levels are thought to have dropped to about 10% compared with the present-day levels (Fig. 9): arising from microbial as well as animal respiratory processes, a reciprocality of environmental O_2 and CO_2 levels occured. Invariably, environmental hypoxia is associated with some degree of hypercapnia especially in standing, plant-infested waters. Hypoxia, especially when accompanied by hypercapnia, constitutes a powerful force which induces air breathing. In the tench, *Tinca tinca*, hypoxia-hypercapnia reduces routine O_2 consumption and causes a swelling of the erythrocytes (Soivio and Nikinmaa 1981; Jensen and Weber 1985). Though morphologically similar (Godoy 1975), the respiratory physiology of the two ecologically distinct erythrinid fish, *Hoplias malabaricus* and *H. lacerdae*, which occur in the South American tropical and subtropical shallow waters and streams, is remarkably different (Rantin et al. 1992, 1993): compared with *H. lacerdae* which lives in well-aerated streams, *H. malabaricus*, which inhabits stagnant O_2-deficient environments, is characterized by low metabolism, higher O_2 extraction, tolerance to low O_2 tensions, low gill ventilation (Rantin and Johansen 1984; Rantin et al. 1992), and large respiratory surface area (Fernandes et al. 1984; Fernandes and Rantin 1985) and high aerobic capacity (Driedzic et al. 1978; Hochachka et al. 1978). The critical O_2 tensions for *H. malabaricus* is 2.7 kPa and for *H. lacerdae* 4.7 kPa (Rantin et al. 1992). Around the Gulf of Mexico, during the summer months when the eastwards winds push the surface waters offshore and make the hypoxic deeper water flow inshore (May 1973), the marine crab, *Callinectes sapidus*, emerges into the air (Loesch 1960). An El Niño effect, a major oceanographic change related to shift in global weather patterns that originated from the eastern Pacific during the winter of 1982–1983 and the spring and summer of 1983, caused massive extensive upwelling of apparently hypoxic warm tropical equatorial water along the shores of South and North America (Cane 1983; Philander 1983) resulting in massive mortality of the Oregon's coho (*Oncorhynchus kisutch*) and chinook (*O. tshawytscha*) salmon (Johnson 1988): El Niños have been associated with larval dispersal of and southward displacement of tropical species (DeVries et al. 1997). When exposed to hypoxic water (4 to 5.3 kPa), the freshwater crayfishes, *Austropotamobius pallipes* (Taylor and Wheatly 1980) and *Orconectes rusticus* (McMahon and Wilkes 1983), surface to ventilate their (branchial chambers) "lungs". The air-breathing fish *Erpetoichthys calabaricus* senses and deliberately avoids hypoxic areas of the water in which it lives (Beitinger and Pettit 1984). No examples of air breathing have evolved in animals which subsist in well-aerated waters such as fast-flowing streams where the O_2 levels are perpetually at or near saturation. Krogh (1941) considered the transition to air breathing to have been stimulated by "emergency respiration" resulting from withdrawal of water (from which animals extracted O_2) from the intertidal animals. From the morphological similarity and close topographical relationships between the gills and the accessory respiratory organs (both are located around or open in the pharynx), the evolution of air breathing appears to have been a carefully crafted slow process. It did not involve an ovehaul of the gills but a gradual phasing out. In the mud-eel *Amphipnous cuchia*, for example, the air sac which develops from the gill arches 2 to 5 and the ectoderm cells (derived from the integument bordering the pharyngeal openings) receives venous blood through the afferent branchial vessels of the second and third gill arches and the vascular papillae which develop in the buccal cavity and in the air sacs exchange gases with air (Singh et al. 1984).

The exigency to procure O_2 directly from air has evolved many times in response to different environmental pressures (e.g., Randall et al. 1981; Graham 1994). In *Polpterus bichir*, the gas bladder functions as an accessory respiratory organ only when the O_2 content of the water is low (Budgett 1900). A few air-breathing fish, however, show anomalous air-breathing behavior. About 40 marine species in 6 families regularly breath air in a habitat which is not characterized by hypoxia or hypercarbia (Graham 1976). In some species of aquatic bimodal breathers, e.g., young tarpons, *Megalops atlantica*, air breathing is socially regulated (Böhlke and Chapline 1968; Kramer and Graham 1976). Interestingly, not all the present-day bimodal air breathers are phylogenetically ancient forms which have survived. This indicates that the quest for air breathing is an ongoing covert process which is being aggressively pursued by some of the contemporary aquatic animals especially those which experience hypoxia or sudden fluctuations of O_2 in their habitats. Oxygen is both an important factor for aerobic metabolism and a necessary resource in growth and development. Bader (1937) demonstrated that normal development of the accessory respiratory organs of *Macropodus* (Belontiidae) was hindered if the fish was refused access to air. It has been interestingly postulated that by reducing the risk of desiccation through respiratory water loss, atmospheric hyperoxia, as occurred during the mid-Devonian and Carboniferous periods (Fig. 9), may have enhanced terrestrial habitation: breathing hyperoxic air reduces respiratory frequency and hence lowers respiratory water loss (Withers 1992). The evolution of air breathing, however, did not have a direct causal relationship with terrestrial colonization (e.g., Carter and Beadle 1931). Occupation of land happened to offer one of the many solutions to the prevalent respiratory stress in water. This is evinced by, among others, the air-breathing fish which even after acquiring a significant preadaptation for terrestriality (i.e., capacity to breathe air) permanently live in water. In water, a highly dynamic habitat, animals are behaviorally and physiologically adapted to cope with sudden changes in O_2 availability, temperature, and salinity (Horn and Gibson 1989): at high tide they take O_2 from the water and during low tide from air. The dragon-fly larva surfaces to breath when the PO_2 in water falls below 7.3 kPa (Wallengren 1914). Similar behavior occurs in the fish, *Leuciscus erythrophthalamus*, when the PO_2 falls to below 2 kPa (Winterstein 1908). Behavioral, functional, structural, biochemical, and molecular changes, plausibly in that order, were utilized to accommodate aquatic hypoxia as animals switched from water to air breathing (Hiebl et al. 1987; Weber et al. 1993) and then gravitated towards land. The gills, the archetype aquatic gas exchangers honed for respiration in water proved deficient in air, a physically remarkably different medium (Tables 4,9). The gills were gradually phased out as extraction of O_2 from water was deemphasized and air breathing consolidated. In terrestrial crabs (Sect. 5.6.2), a great deal of this change entailed expansion of the branchial cavity, modification of the branchial epithelium, and mechanical ventilation of the same. In the pneumonate gastropods (Sect. 5.6.1), the ctenidia in the mantle cavity was replaced by a lung.

5.2 Strategies and Adaptive Convergence for Air Breathing

The intermediate breathers use the accessory respiratory organs or lungs to procure about two-thirds of their O_2 needs and eliminate only about one quarter of the metabolic CO_2. The nonpulmonary gas exchanger(s) void roughly three fourths of the metabolic CO_2 irrespective of whether the animal lives in water or air (Rahn and Howell 1976). Some of the primary attributes of an accessory respiratory organ are that: (1) it must possess regular or irregular means for renewal of air, (2) the gas voided from the organ must contain less O_2 and more CO_2 compared with the inspired (atmospheric) air, and (3) the epithelial surface must (in most cases) present conspicuous morphological modifications such as good vascularization and/or surface amplifications. An inverse correlation occurs between the level of commitment of an accessory respiratory organ to air breathing and the degree of regression of the alternative respiratory sites such as the skin, buccal cavity, and gills. The capacity of air breathing in many animal groups and the remarkable uniformity of the morphological, physiological, and biochemical features inaugurated in so phylogenetically different taxa is a model case of convergent evolution. Those features which are common to a wide cross-section of animals contributed the foundations to the comprehensive gas exchange process and those traits unique to a particular group present a solution to a specific problem. By identifying the pressures to which the animals were subjected, by analogy, reconstruction of the events which initiated and sustained the momentous change can be made. There is now ample evidence indicating that the need to breath air evolved essentially because the O_2 levels in water were unstable and largely low (e.g., Carter and Beadle 1931; Schmalhausen 1968; Randall et al. 1981). Due to the remarkable differences in the physiochemical properties water and air (Sect. 3.2), the shift drastically affected the form and function of practically all the biological processes (e.g., Edney 1960; Young 1972; Mangum 1982b; Greenaway et al. 1983; Bridges 1988; Val et al. 1990; Morris 1991; Morris and Bridges 1994). These included locomotion, respiration, reproduction, excretion, and sensory perception of external stimuli. The impact was, however, greatly minimized since need for direct switch from water (a fairly stable environment) to air (land), a highly fluid one, rarely arose. The aquatic and terrestrial habitats intergraded extensively especially during the formative years of the continental land masses when massive uplifting, subsidence, and displacement of the plates caused dramatic shifts in the sea level and flooding of land (Takeuchi et al. 1970; Ben-Avraham 1981; Fig. 55). The intermediate zone had adequate water vapor pressure stability to sustain the development of the accessory respiratory organs without the risk of desiccation in predominantly aquatic animals. In such humidic habitats, the animals adapted to hypoxia tolerance in water and instituted measures for air breathing and terrestrial existence. Among the erythrinids (Order: Cypriniformes) which inhabit shallow O_2-poor freshwaters of the tropical and subtropical regions of South America (Dickson and Graham 1986), *Hoplias malabaricus*, which lives in stagnant hypoxic water, is more tolerant to hypoxia (threshold PO_2 for onset of bradycardia = 2.6 kPa) than *H. lacerdae*, which inhabits well-oxygenated rivers (threshold PO_2 for onset of bradycardia = 4.7 kPa; Rantin et al. 1993). Factors such as the larger respiratory surface area (320 mm^2 per g; Fernandes et al. 1984) and high O_2 affinity of blood (Wood and Lenfant 1979) in *Hoplias malabaricus* compared with *H. lacerdae* may explain the differences in hypoxia tolerance in the two species. Some erythrinid fish, e.g., *Hoplererythrinus unitaeniatus* and *Erythrinus erythrinus* (Randall et al. 1981), have adopted air breathing. Surface skimming for air and/or well-oxygenated top water layer is a common strategy of overcoming hypoxia in the tropical freshwaters (Kramer and McClure 1982). Gulping air at the surface elevates O_2 transport during aquatic hypoxia in the goldfish, *Carassius auratus* (Burggren 1982a). Of the 20 000 or so species of fish, only a relatively small number has evolved the capacity for air breathing (e.g., Dehadrai and Tripathi 1976; Sayer and Davenport 1991; Graham 1994; Table 19). An even much smaller number has adopted terrestrialness. Clearly, air breathing and subsequently shift to land were attempted at the extremes of circumstances, e.g., at the threshold of failure of normal O_2 transfer and/or when there were particular benefits to be derived from the shift. The least drastic and most economical solution to air breathing in the Devonian fish would have been to utilize the gills, the highly engineered aquatic gas exchangers, for procuring O_2. The probable sequence of events utilized for adaptation to hypoxia should have entailed: (1) physical avoidance of it by relocating to more hospitable areas (Whitmore et al. 1960; Cook and Boyd 1965; Costa 1967; Gamble 1971), and (2) skimming the top 1 to 2 mm surface of water which is richer in O_2 (Burggren 1982a; Kramer and McClure 1982; Barton and Elkins 1988; Horn and Gibson 1989), gulping in air, e.g., in the gobies (Gee 1976; Graham 1976; Gee and Gee 1995) and holding it in vascularized buccal and/or pharyngeal cavities (Coutant 1987; Kramer 1987). In the interim, long-term physiological tolerance to hypoxia would have become established. In the bivalve mollusk, *Pholas dactylus*, air gaping occurs in the laboratory after a drop in PO_2 in the surrounding water and in nature during low tide (Knight 1984). The Amazonian freshwater ray (*Paratrygon* sp.) surfaces when the PO_2 drops to below 2 kPa and utilizes the O_2-rich surface water (Steen 1971). Increased CO_2 in water depresses branchial respiration and stimulates air breathing. Like the fossorial mammals and birds (Sect. 3.7), fish which live in derelict waters are less sensitive to CO_2 than those from well-aerated ones (Hughes 1963). It has been argued that it was not lack of molecular O_2 per se but factors such as availability of new food sources, reproductive needs, escape from predators (Little 1990; Sayer and Davenport 1991), and the enormous energetic advantages derived from the switch (Bennett 1978; Fig. 56) which led to the development of air breathing, especially in the shore tidal areas. The gastropod mollusk, particularly those of the family Ampullariidae, provide excellent examples of the extents to which animals went to attain and maintain an air-breathing capacity. Some, e.g., the amphibious prosobranch, *Pomacea depressa*, which lives in the Everglades swamps in Florida, a rather extensive stagnant mass of warm water where intense organic putrefaction of the massive vegetational growth occurs, have evolved a divided mantle cavity with a gill in one half, the other half acting as a lung (McClary 1964; Little 1990). Such animals are able to breathe air and water simultaneously or switch from one medium to another depending on needs and circumstances.

Water characteristically constitutes an environment where O_2 is scarce (Table 4). In some habitats, survival is compounded by the presence of a high concentration of CO_2 and other gases such as H_2S and NH_3. Owing to the effect of CO_2 on the central control, O_2 consumption falls drastically with rising PCO_2 particularly when the PO_2 is low (Saxena 1962; Tenney 1979). When exposed to hypoxic water, *Gillichthys* gulps air as its oxidative metabolism decreases (Todd 1971). In *Pseudapocryptes* (Das 1934), hypoxia induces air breathing and in *Tomicodon* (Eger 1971), stagnation of water elicits air breathing. When held in hypoxic water, *Clarias* and *Heteropneustes* show metabolic rates which are 60% below normal (Hughes and Singh 1970b; Singh and Hughes 1973). Depending on the ambient temperature and level of activity, the bowfin, *Amia calva*, an ancestral halecomorph North American actinopterygean fish which is an active swimmer and subsists in an environment which is cold and covered with ice in winter and warm in summer, relies on the gills and a vascularized gas bladder for gas exchange (Johansen et al. 1970a; Liem 1987a; Hedrick and Jones 1993): at temperatures between 10 and 30 °C, O_2 consumption is shared equally between the gills and the air bladder, at above 30 °C the air bladder accounts for more than two thirds of the O_2 consumption while at 10 °C and below, the gills meet all the O_2 needs. Breath holding can last from 5 to 55 min depending on temperature, amount of light, and the O_2 concentration in the water (Liem 1987a). Ambient temperature (Burggren et al. 1983) and PO_2 (Burggren and Mwalukoma 1983; Burggren and West 1982) influences the pathway utilized for procuring O_2 in the larval *Rana berlandieri* and *R. catesbeiana*.

The development of the amphibians from eggs through tadpoles to air-breathing adult forms is accompanied by dramatic changes in the respiratory strategies (Fig. 47) and offers a highly instructive model in understanding the change from water to air breathing and transition from water to land. The amphibian eggs acquire O_2 entirely by diffusion across the surface, the tadpoles initially have external gills which are followed by internal ones, and later in life the adults develop fully functional lungs. Metamorphosis starts in water, a medium from which O_2 is less available, with the animal proceeding to the much better oxygenated aerial habitat. The access to a more O_2-rich medium is accompanied by a

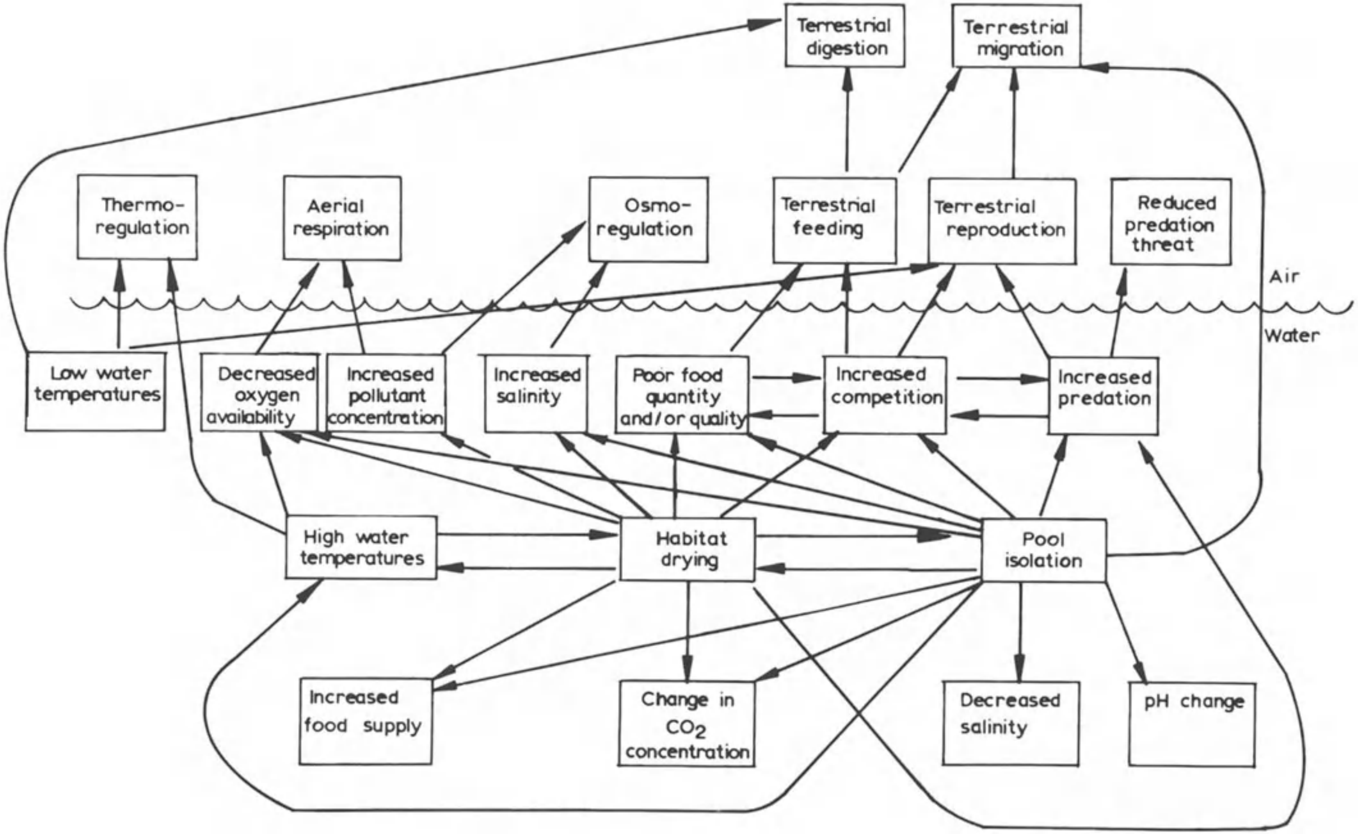


Fig. 56. Principal biotic and abiotic factors which elicited emergence behavior from water by amphibious fish in closed systems (e.g., freshwater and intertidal pools). While the prompting factors differed from habitat to habitat, the pervasive features which prompted air breathing and shift to land included decreasing O_2 and food availability in isolated, shrinking aquatic habitats. In this complex and highly dynamic process, other factors included increasing temperatures, CO_2, and pH. While definite rewards were reaped such as access to abundant O_2 and newer resources, certain costs such as adaptations for reproduction independent of water, more efficient capacity for osmoregulation, and excretion of products of nitrogen metabolism, e.g., urea and uric acid, were called for. (Sayer and Davenport 1991)

decrease in the O_2 affinity on metamorphosis from a tadpole to an adult amphibian (Broyles 1981; Burggren and Wood 1981). The P_{50} of the blood of the tadpole of a bullfrog, *Rana catesbeiana*, is 0.7 kPa (McCutcheon 1936), a PO_2 at which in the adult frog the blood is only 5% saturated. After giving rise to the successful amniotes, the amphibians have literally lingered on with one foot in water and the other on land. Though the first animals to conquer terra firma, owing to their reliance on water for crucial physiological processes such as reproduction, excretion of waste products, osmoregulation, and gas exchange, in general, the amphibians, a group recalcitrant to change, are a defeated group. They constitute an inconspicuous taxon among the extant tetrapods. The contemporary amphibians can be looked on as a relic of an evolutionary stage between air-breathing fish on one hand and reptiles, the first animals with a true lung, on the other.

5.3 Risks, Costs, and Benefits in the Change to Air Breathing

In changing residence from water to land, animals faced fundamentally different environmental and physiological challenges (Fig. 7). They had to procure O_2 from air and void CO_2 into the same, avoid desiccation, store or excrete different toxic products of nitrogen metabolism, somewhat regulate body temperature, and avoid or confront completely new predators. Whereas aquatic habitats offer rather stable and predictable "climatic" features, terrestrial ecosystems show greater spatial and temporal diversity. The terrestrial macrophytes, particularly gymnosperms and angiosperms, generate remarkably different microclimates over short distances (e.g., Geiger 1965). In order to derive the best of two worlds, the aquatic (water-residing) air breathers have chosen to physically remain in water and periodically surface to extract O_2 from the air. Such animals lack specializations like means for aerial vision, terrestrial locomotion, adaptations to curtail cutaneous water loss, and specific means for elimination of products of nitrogen metabolism in form of urea and uric acid, as occurs in amphibious fish (e.g., Gordon et al. 1978; Table 9). Although most aquatic animals will cope with hypoxia by appropriate microhabitat selection, this strategy is not very effective in dealing with long-term (i.e., diurnal and seasonal) fluctuations in O_2 levels. In such cases, permanent solutions are obligatory. Aquatic animals, especially those which live in highly dynamic microhabitats such as tidal pools, thermoclines, or shallow coastal waters display different mechanisms for coping with the extremes of hypoxia. Though indirect, the effect of temperature on respiration is far-reaching. Elevated temperature leads to reduced solubility of O_2 in water and increased metabolic rate. In a hypoxic condition, raised temperature makes life highly precarious, and access to the atmosphere, where O_2 is available in large quantities, becomes a necessity (Serfaty and Gueutal 1943). In the freshwater fish, temperature preference increases with exposure to hypoxia (Bryan et al. 1984; Schurmann et al. 1991). By selecting a lower temperature, the animal takes advantage of reduced metabolism and increased blood O_2 affinity (Schurmann and Steffensen 1992). Similar strategies have been adopted by the reptiles (Hicks and Wood 1985) and salamanders and crayfish (Dupré and Wood 1988). Owing to the more stable PO_2 in air, habitat relocation in a heterothermal environment with changing O_2 saturations is particularly important in aquatic ectotherms, especially in coastal and standing waters. When the circulation of water is limited or respiratory demands of aquatic organisms are high, anaerobiosis may result. In the bowfin, *Amia calva*, air-breathing frequency increases with aquatic hypoxia (Johansen et al. 1970a). This also occurs in most other air-breathing fish (e.g., Shelton et al. 1986). Due to factors such as different capacities to tolerate hypoxia and the variability in the levels of hypoxia in different habitats, the physiological traits acquired during evolution of air breathing appear to have followed different and independent pathways which were dictated entirely by need. The designs of the contemporary gas exchangers and the existing respiratory adaptations cannot be accurately used to discern the systematic affinities between taxa.

The transition to air breathing and, subsequently, terrestrialness called for profound changes in the respiratory strategies. Animals aggressively mobilized resources and changed their habits and habitats with the specific goal of acquiring O_2 from "above". Switching from one respiratory medium to another and from one gas exchange pathway to another enabled the transitional breathers to utilize the most convenient and efficient method(s) for extracting O_2 from the alternative respiratory media. This provided the necessary flexibility to optimally meet the changing conditions. Plainly, the evolution of air breathing was not ipso facto the attainment of terrestriality. Procurement of molecular O_2 directly from air, a medium eloquent of the gas, was simply the immediate, most convenient, and permanent solution for surmounting the critical problem of hypoxia prevailing in the aquatic biotope. Residence on terra firma, a venture first attempted by the now extinct rhipidistian crossopterygians some 350 million years ago (in the Upper Devon) (Pough et al. 1989), was a costly, risky process which was approached parsimoniously using different strategies (Figs. 57,58). It had to await decisive preadaptions which included: (1) redesigning of the existing gas exchangers, (2) development of an impermeable surface cover, (3) solution of problems of acid-base and osmotic balance, and (4) development of more appropriate ways and means of eliminating products of nitrogen metabolism (e.g., Little 1990). Furthermore, animals had to cope with factors such as thermal instability, exposure to new predators, and locomotory problems resulting from the greater gravitational effect on the body. Air breathing and subsequently relocation to land arose when and only if there was absolute need for it or where tangible advantages and rewards, e.g., acquisition of more livable space and greater ecological opportunities, were to be reaped to offset the enormous risk and cost. Due to the abundance of O_2 in the free air, when expressed in terms of ventilatory requirement per unit of O_2 consumption, an air breather expends much less energy to extract an equivalent volume of O_2 compared with an aquatic one (Dejours et al. 1970; Sect. 2.9). When subjected to intra- or interspecific competition, amphibious fish, e.g., the climbing perch, *Anabas testudineus* and *Monopterus albus*, will embark on overland excursions (Liem 1987b). The highly aerial behavior of the pearl blenny, *Entomacrodus nigricans*, is thought to have arisen as a result of competition amongst the intertidal fish (Graham et al. 1978a). Air breathing and subsequent transfer to land opened new ecological opportunities which resulted in remarkable adaptive radiation. Among the marine teleost fish, the family Gobiidae, which has extensively evolved air breathing (Lewis 1970), contains the largest number of the present-day species in this taxon. Generally, the obligate air-breathing fish, which, due to greater access to O_2, are apparently more agile and can hence acquire more nutriments, are larger (25 to 30 cm) than the facultative ones (at 7 to 15 cm) (Munshi and Srivastava 1988).

The extant bimodal breathers provide modern analogs of the transitional animal forms in evolution of air breathing. In the lungfish, contact with air is a more powerful stimulus than a tactile or painful stimulus (Johansen and Lenfant 1968). The intertidal clingfish, *Sicyases sanguineus*, increases the number of exposures to air as the dissolved concentration of O_2 decreases (Ebeling et al. 1970). As the PO_2 in water drops, *Mnierpes macrocephalus* spends 92% of the time out of water, returning briefly at regular intervals (Graham 1970). The shanny, *Blennius pholis*, totally avoids water at low partial pressures of O_2 (Davenport and Woolmington 1981). The catfish, *Eremophilus mutisii*, uses its accessory respiratory organ (the stomach) in both normoxic and hypoxic water (Cala 1987) by periodically dashing to the surface to swallow air. In fish which surface more often in normoxic than hypoxic water, air breathing may be utilized for buoyancy control rather than gas exchange (e.g., Gee 1976; Gee and Graham 1978). Since the water breathers have evolved definite mechanisms for regulating hydrogen ions in face of high

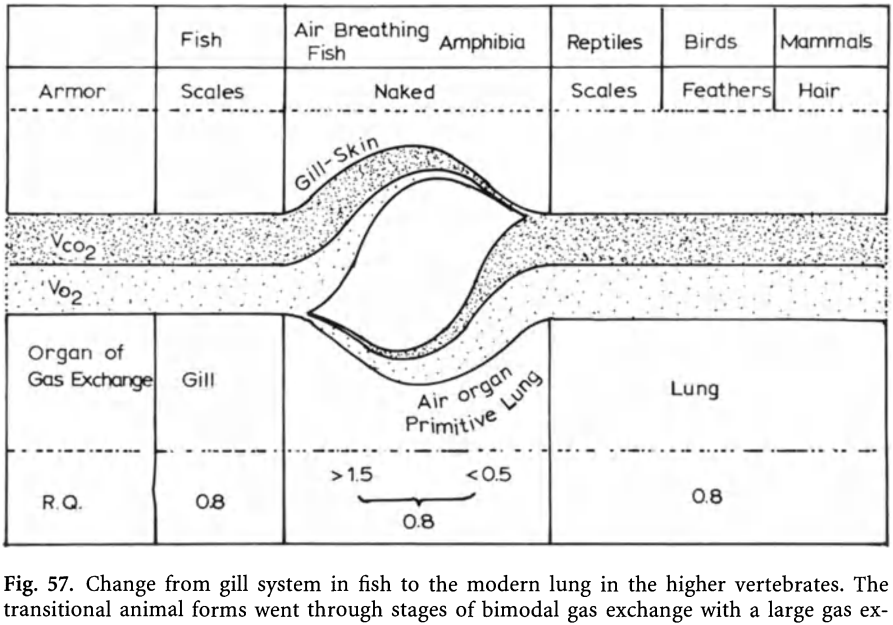


Fig. 57. Change from gill system in fish to the modern lung in the higher vertebrates. The transitional animal forms went through stages of bimodal gas exchange with a large gas exchange ratio initially in the gill-skin system and a low ratio initially in the primitive lung (air organ). During this stage, the skin was naked and acted as a "bridging" respiratory organ. Such animals were highly susceptible to dehydration on land. The development of surface covers like scales, feathers, and hair had to await the development of the modern lung. In essence, the switch over from water to air breathing was made very slowly and cautiously. *R.Q.* Respiratory quotient. (Rahn and Howell 1976)

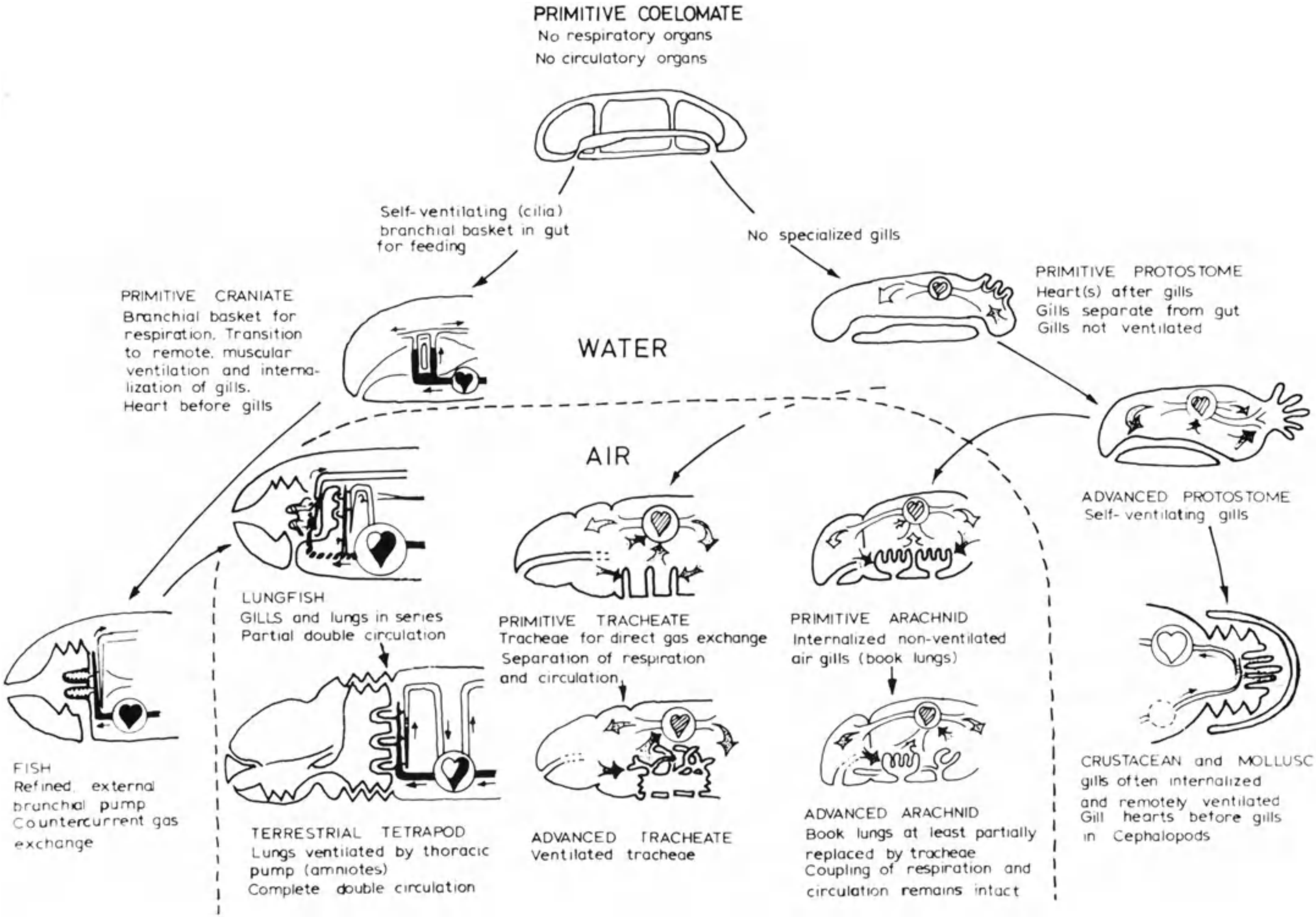


Fig. 58. Suggested pathways for evolution of air breathing, the increasing organizational complexities of organisms, and the corresponding sophistications of the gas exchangers. Endothermy, as evolved in birds and mammals, could only be supported by ventilated and perfused aerial gas exchangers. (Perry 1989)

ambient concentration of CO_2, deficiency of O_2 rather than elevation of CO_2 appears to have been the most important stressor in the evolution of air breathing. Changing pH levels and/or raising CO_2 levels do not elicit emergence from water in *Boleophthalmus pholis* (Davenport and Woolmington 1981). Low ambient PO_2 does not cause *Monopterus albus* and *Anabas testudineus* (Liem 1987b) or the mangrove forest fish, *Rivulus marmoratus* (Abel et al. 1987), to immerse their bodies into water. In the bimodally breathing fish, the accessory respiratory organs are located away from contact with water. In this way, such organs can be utilized simultaneously with the gills. The bimodal breathers avoid desiccation and CO_2 accumulation by subsisting in water while exploiting air as a source of O_2: they hence enjoy the benefits which accrue from the two habitats. While movement to land may be induced by a definite need to feed or may simply be behavioral and purposeless (e.g., Gordon et al. 1978; Sacca and Burggren 1982), abiotic factors such as high CO_2 and NH_3 levels and biotic ones such as predation and interspecific aggression may, to varying extents, prompt migrations to land (Fig. 8). Compared with the many complex integrated processes which were essential for terrestrial habitation (Little 1990), though an important initial step, the attainment of air breathing was a rather simple and direct affair.

5.4 CO_2 Elimination: Impediment to Evolution of Air Breathing and Terrestriality

Oxygenation is the primary purpose of respiration and in case of conflict, CO_2 clearance is unequivocally subordinate (e.g., Dejours 1988). Adaptations favoring O_2 uptake are automatically adopted in preference to those aiding CO_2 elimination. In this sense, O_2 plays a more central role in the process of gas exchange. In the bimodal breathers, while the accessory respiratory organs supply O_2 to the body, they are unable to eliminate CO_2 as efficiently (e.g., Randall et al. 1978a). Indeed, this particular limitation appears to have been a fundamental obstacle in the transition from water- to air breathing as the modern lung evolved (e.g., Gans 1970, 1971; Withers 1992; Olson 1994; Fig. 57). Even after some bimodal breathers could secure as much as 96% of their O_2 needs from the air, the skin and/or the gills continued to be the major organ(s) for CO_2 elimination (Tables 20,21). This restricted such species to water. In the totally land-based solely air-breathing crustaceans, appropriation of the enzyme carbonic anhydrase into the membrane fraction of the branchiostegites may have been one of the vital molecular events which enabled pulmonary CO_2 elimination into the air (Morris and Greenaway 1990; Henry 1994). During activity, in the highly terrestrial coconut crab, *Birgus latro*, CO_2 accumulates in the hemolymph if the gills are surgically removed (Smatresk 1979). Since CO_2 is not a highly toxic molecule, at least not as much as O_2 (Sect. 1.18), and concentrations can moderately rise without causing irreparable physical damage, regulation of the concentration of CO_2 in the body is utilized strictly to adjust body pH and not CO_2 levels. Unlike the charged molecules such as HCO_3^- and H^+ ions, which are transferred through ionic exchange for Cl^- and Na^+ ions, respectively, the uncharged molecular CO_2 easily moves

Table 20. Partitioning of gas exchange between the lung and the skin system in terrestrial amphibia. (After Rahn and Howell 1976)

Taxon	Species	T (°C)	Lung (%)		Skin (%)	
			VCO_2	VO_2	VCO_2	VO_2
Urodela	*Ambystoma maculatum*	25	29	69	71	31
	Taricha granulosa	25	32	68	68	32
Anura	*Rana clamitans*	25	24	74	76	26
	Rana pipiens	25	43	68	57	32
	Hyla gratiosa	25	19	68	81	32
	Hyla versicolor	25	16	67	84	33
	Bufo americanus	25	17	66	83	34
	Bufo boreas	25	31	69	69	31
	Bufo cognatus	25	30	44	70	56
	Bufo marinus	25	24	50	76	50
	Bufo terrestris	25	25	78	75	22
Mean			26	65	74	35

Table 21. Gas exchange partitioning between water-breathing organs (gill, G and skin, S) and air-breathing organs of some air-breathing fish. (After Singh 1976)

T (°C)	Species	VO_2 (%)			VCO_2 (%)		
		From water	Organ	From air	Into water	Organ	Into air
20	*Amia calva*	63	G	37	75	G	25
25	*Heteropneustes fossilis*	59	G,S	41	94	G,S	6
25	*Anabas testudineus*	46	G	54	91	G	9
25	*Clarias batrachus*	42	G,S	58	94	G,S	6
22	*Lepisosteus osseus*	27	G	73	92	G	8
23	*Monopterus albus*	25	G,S	75	–	–	–
26	*Electrophorus electricus*	22	S	78	81	S	19
25	*Cobitis fossilis*	20	–	80	34	–	66
20	*Protopterus aethiopicus*	11	G	89	70	G	30
24	*Protopterus aethiopicus*	10	G	90	68	G	32
20	*Lepidosiren* (Juvenile)	64	G,S	36	76	G,S	24
20	*Lepidosiren* (Adult)	4	G,S	96	41	G,S	59

across the cell membranes. During the transition from water to land, the skin, though often considered evolutionarily a dead end or a failed experiment, functionally acted as an important respiratory/acid-base bridging organ during the development of air breathing and subsequently terrestrial habitation (Fig. 57).

With the gradual involution of the gills, ionic exchange and CO_2 clearance were translocated to the skin (Rahn 1967; Randall et al. 1981). In amphibians, blood flow to the mid-dorsal skin is 1.8 times that to the ventral thoracic skin (Moalli et al. 1980). This indicates that the former site may be more important in CO_2 excretion than the latter (Talbot and Feder 1992). In the contemporary bimodal breathers, the gill-skin system removes about 76% and the lung 24% of CO_2 while O_2 uptake varies with the species, the gas exchanger utilized, and habitat occupied (Emilio et al. 1970; Rahn and Howell 1976). In aquatic amphibian species, *Siren lacertina* and *Amphiuma means*, the lung takes up 65% of the O_2 needs but the gills and/or skin eliminate nearly 75% of the CO_2 (Guimond and Hutchison 1973a, 1976). The utilization of the skin for gas exchange in many animals in different habitats attests to its great importance of having served as a bridging organ during the development of the aerial gas exchanges. To compensate for its inherent limitations as a gas exchanger, cutaneous respiration is much less energetically expensive (Feder and Burggren 1985a,b). Interestingly, though the marine air-breathing fish do not have very well-developed accessory respiratory organs, they appear to have developed the capacity to release CO_2 into the air so efficiently that most of them will maintain the same level of metabolism when exposed to air (Graham 1976).

Relatively, the absolute values of PCO_2 and HCO_3^- in blood and tissues are lower in the water breathers than in the air breathers. Weighted against the air breathers, generally, challenges for acid-base balance are less severe in water breathers (e.g., Driedzic and Gesser 1994). In the plasma of fishes, PCO_2 ranges between 0.1 to 0.5 kPa and HCO_3^- from <5 to 15 mM (Heisler 1984). Fish gills contain a high concentration of carbonic anhydrase which catalyzes breakdown of plasma HCO_3^- ions to CO_2 (e.g., Haswell and Randall 1978) with a small amount being voided across the kidneys (e.g., Wood and Cadwell 1978). About 90% of the total CO_2 in *Anabas*, *Clarias*, and *Heteropneustes* is voided through the gills (Hughes and Singh 1970a,b, 1971): the ratio of aquatic to aerial CO_2 removal is 10 : 1. Characteristically, the drop in pH induced by hypercapnia is corrected by elevation of HCO_3^-. Exposure of *Conger conger* and *Scyliorhinus stellaris* to an environmental PCO_2 of 1 kPa lowers plasma pH by about 0.4 units as plasma PCO_2 rises from about 0.25 to about 1.3 kPa (Heisler 1982b): over a period of 5 to 10 h, the pH was partially corrected by an elevation of HCO_3^- from <10 to about 20 mM. In exercising *S. stellaris,* H^+ released from skeletal muscle caused the arterial pH to drop from 7.8 to 7.2, the PCO_2 to rise from about 0.25 to 0.67 kPa, and the HCO_3^- to drop from 7 to 3 mM (Holeton and Heisler 1983). In the facultative air-breathing fish, *Symbranchus marmoratus*, change from water to air breathing alters PCO_2 from about 0.75 to 3.5 kPa with an accompanying drop in pH of about 0.6 units and a fourfold increase in intracellular HCO_3^- (Heisler 1982b). Vertebrate air breathers excrete much of their CO_2 in molecular form across the lung although a little of it is removed as HCO_3^- ions through the kidneys (Boutilier et al. 1979a,b). In fish, the processes of CO_2 elimination in pH regulation are different from those of mammals: HCO_3^- ions regulation, rather than molecular CO_2, is the more important factor in the process (e.g., Cameron 1978). Unlike in mammals, in fish, ventilation affects the CO_2 concentration of blood and hence pH only in the extremes of circumstances, e.g., during hyperoxia when ventilation is suppressed (Randall and Jones 1973) or during extreme hypoxia (Dejours 1973). Fish have evolved in a demanding habitat naturally deficient in O_2. Ventilation has been configured solely for delivery of O_2 to the gills, rendering CO_2 clearance somewhat of secondary importance.

The transition to air breathing and residence on land presented a challenge towards acid-base balance. It necessitated an increase in blood PCO_2 and a corresponding increase in plasma HCO_3^- ions for maintenance of normal pH (e.g., Rahn 1966; Hughes 1966; Howell et al. 1970; Lenfant and Johansen 1972; Tables 2,22). Plasma PCO_2 tends to increase as an animal shifts from water- to air breathing (Driedzic and Gesser 1994) though there is no clear correlation between the mode of breathing and the total CO_2 (Toews and Boutilier 1986). The high capacitance coefficient of CO_2 in water compared with O_2 curtails the ability of aquatic animals to regulate internal acid-base status by ventilatory adjustments of blood PCO_2 (e.g., Cameron 1979). In aquatic breathers, pH control is largely effected by exchange of acidic or basic equivalents between the extracellular fluid and the environment. This leads to changes in plasma HCO_3^- ion levels. In transitional breathers, ventilation does not correspond with CO_2 levels in blood as in the air breathers. The significance of ventilation in pH regulation is of little importance as the gills and the skin are the main pathways for CO_2 excretion. Fish appear to possess a mechanism for enzymatically curtailing CO_2 and H^+ ion loss across the gill epithelium (e.g., Haswell and Randall 1978) with the respiratory rate being mainly responsive to the PO_2 in the arterial blood (e.g., Randall et al. 1981). On the other hand, in the air breathers, CO_2 has to be voided before it accumulates to the level where the lowered pH interferes with the O_2 binding properties of the hemoglobin. Elimination of CO_2 across the vertebrate lung and hence the significance of ventilation in pH regulation was enforced onto the lung with the decrease in the CO_2 diffusing capacity of the gills. This resulted in high levels of CO_2 in blood (Randall et al. 1981). The increase in the permeability of the erythrocytes to HCO_3^- ions comprised a further means of enhancement of CO_2 clearance through the lungs.

Table 22. Some respiratory variables in some water and air breathers. (After Dejours 1988, from where individual sources of data should be consulted)

Taxon	T (°C)	PIO_2 (mmHg)[a]	PEO_2 (mmHg)[a]	PbO_2 (mmHg)[a]	$PbCO_2$ (mmHg)[a]	pHb	(HCO_3^{-1})b (meq l^{-1})
Water breathers							
Lugworm *Arenicola marina*	19	160	35	–	1.7	7.3	1.6
Octopus dofleini	11	127	94	78	3.1	7.1	–
Crab *Carcinus maenas*	10	156	–	–	2.3	7.8	7.2
Cancer magister	8	141	97	75	1.7	7.9	–
Dogfish *Scyliorhinus stellaris*	16	149	56	49	2.0	7.8	–

Table 22. *Continued*

Taxon	T (°C)	PIO_2 (mmHg)[a]	PEO_2 (mmHg)[a]	PbO_2 (mmHg)[a]	$PbCO_2$ (mmHg)[a]	pHb	(HCO_3^{-1})b (meq l^{-1})
Transitional breathers							
Frog							
Rana catesbeiana							
Tadpole	23	150	–	–	4.3	7.8	6.8
Adult	23	150	–	–	17.2	7.8	29
Salamanders							
Cryptobranchus alleganiensis	25	154	–	27	6.2	7.8	–
Desmognathus fuscus	19	150	–	40	7.9	7.4	9.2
Lungfish							
Neoceratodus forsteri	18	131	–	40	4.7	7.6	5.3
Protopterus aethiopicus	25	130	–	27	26	–	–
Gar-fish							
Lepisosteus osseus	25	155	–	–	13	7.4	10.2
Electric eel							
Electrophorus electricus	27	150	–	12	27	7.6	30
Amphipnous cuchia	25	155	–	–	12	7.5	–
Air breathers							
Snail							
Otala lactea	15	154	144	144	8.6	8.1	–
Crab							
Gecarcinus lateralis	21	155	–	–	8.9	7.5	11.4
Uca pugilator	20	155	–	–	10.6	7.7	21.2
Birgus latro	29	150	–	27	9	7.7	12.7
Turtle							
Pseudemys scripta	25	155	–	–	27.4	7.6	33.0
Pekin duck	41	144	10.8	91	33	7.5	23
Toad (Adult)							
Bufo marinus	25	155	–	80	11.1	7.8	21.4
Human being	22	149	119	93	20.4	7.7	–

Symbols: PIO_2 and PEO_2 partial pressure of O_2 in the inspired and expired air/water; PbO_2 and $PbCO_2$, partial pressures of O_2 and CO_2 in the arterial blood; pHb, acidity of blood; (HCO_3^{-1}) bicarbonate concentration in blood.

[a] To convert ot kPa multiply by 0.133.

In order to disengage the primary functions of the gills (respiration, ionic exchange, and pH regulation), a transitional respiratory stage was necessary (Fig. 57). The accessory respiratory organ was charged with O_2 uptake and the gills or any other respiratory surface, e.g., the skin and the buccal cavity with CO_2 removal and hence pH regulation and ionic homeostasis. A relocation of CO_2 excretion to the accessory respiratory organs had to await development of adequately efficient gas exchangers and ventilatory mechanisms. Osmoregulation and excretion of nitrogenous waste products was consigned to the kidneys (Schwartz 1976), the urinary bladder (Sachs 1977), and to a lesser extent to the skin (Ehrenfeld and Garcia-Romeu 1977). In the higher vertebrates, the lungs play an important part in acid-base regulation by tuning PCO_2 levels in blood with ventilation and, to a smaller extent, through elimination of plasma HCO_3^- ions by the kidneys (Davenport 1974; Burg and Green 1977). Such animals can dissociate themselves from water for ion and pH regulation. The highly terrestrial Trinidad mountain crab, *Pseudothelphusa garhami*, which has evolved very efficient lungs (Innes and Taylor 1986a,b), has very a low PCO_2 in the hemolymph. The passive buffering capacity of blood with respect to both HCO_3^- and non- HCO_3^- ions is five to six times smaller in water breathers than in mammals and birds, with the buffer value of the skeletal muscle tissue being only 50 to 70% that of mammals (e.g., Heisler 1984). The arterial PCO_2 in the rainbow trout (*Oncorhynchus mykiss*) is about 0.3 kPa, in the facultative air-breathing jeju (*Hoplerythrinus unitaeniatus*) it is 1.6 kPa, and in the obligate air breather piracucu, *Arapaima gigas*, it is 3.7 kPa (Randall et al. 1978a,b). The absolute values of PCO_2 and HCO_3^- ions in blood and tissues are lower in water breathers than in air breathers (Tables 2,22). The PCO_2 characteristically ranges between 0.1 and 0.5 kPa and HCO_3^- ions from 5 to 15 mM in the plasma of fishes (Heisler 1984): a drop in pH induced by hypercapnia is counteracted by elevation of HCO_3^- ions. Exposure of the eel, *Conger conger*, to an environmental PCO_2 of 1 kPa lowered plasma pH by about 0.4 units as plasma PCO_2 rose from 0.25 to 1.3 kPa (Heisler 1982b): over a duration of 5 to 10 h, the concentration of HCO_3^- ions increased from under 10 to about 20 mM, partly adjusting the pH. In the facultative air breather, *Synbranchus marmoratus*, movement from water to air changes plasma PCO_2 from about 0.75 to 3.5 kPa: pH falls by about 0.6 units and the intracellular concentration of HCO_3^- ions rises by a factor of 4 (Heisler 1982b).

The changes in the blood PCO_2 which occurred in animals moving from water to air are well demonstrated by the contemporary amphibians which start their life (larval stage) in water where they are obligate water breathers and metamorphose to become perfect air breathers. In *Rana catesbeiana*, at the tadpole stage, where the gills and the skin are the main gas exchangers, the blood PCO_2 is about 0.3 kPa while during and after metamorphosis, when the gills disappear and the lung assumes a prominent respiratory role, the blood PCO_2 increases notably (Erasmus et al. 1970/1971; Just et al. 1973; Burggren and Wood 1981; Tables 2,22). In the garfish, *Lepisosteus osseus*, the blood PCO_2 fluctuates with the ambient concentration of O_2 and the use of the gills or lungs for respiration (Rahn et al. 1971). During the summer months when the concentration of O_2 decreases due to the elevated temperature and its demands are high owing to increased metabolism, the blood PCO_2 increases. In winter (when the dissolved concentration of O_2

is high and metabolic rate lower) the gills are largely utilized and the blood PCO_2 drops. At such times, the fish rarely comes to the surface to breath and the diving durations are longer (e.g., Kruhoffer et al. 1987). In the bimodal air breathers, long respiratory intervals are possible because the greatest porportion of CO_2 is eliminated through the skin. The lungfish, e.g., *Protopterus amphibius*, and the bowfin, *Amia calva* (Dence 1933), regularly estivate during unpropitious circumstances, with the former staying in this state for as long as 5 years. When in water, the fish loses CO_2 and NH_3 through the gills and on land (during estivation), CO_2 accumulates internally and NH_3 is converted to urea and stored. This strategy allows the fish to survive during a time when water breathing is impossible.

5.5 Control and Coordination of the Bimodal Gas Exchange Process

In both air- and water breathers, ventilation is generally a constant and rhythmic process. Endogenous respiratory rhythm in mammals might emanate from specialized pacemaker cells located in the respiratory neural system (e.g., Onimaru and Homma 1987; Smatresk 1990; Smith et al. 1991). Response to hypoxia in fish and mammals is mediated by peripheral chemoreceptors (Sinclair 1987; Burleson and Milsom 1990; Smatresk 1994). In the air breathers, the central ventilatory control is more responsive to PCO_2 and/or pH while in the water breathers there does not appear to be a direct correlation between PCO_2 and ventilation (e.g., Batterton and Cameron 1978; Hedrick et al. 1991). Only after successfully switching the major CO_2 clearance role to the lung could a bimodal breather dispense with the need to use the skin for respiration and develop an impermeable surface cover to avoid dehydration on land. Such a change, however, had to await development of a more efficient lung and respiratory ventilatory mechanism to clear CO_2. Aspiratory breathing (a costal suction pump effected by action of the ribs and the intercostal muscles) first evolved in reptiles (Hughes 1963). The modern lung (first encountered in reptiles) has adopted the dual role of O_2 and CO_2 exchange and acid-base regulation. The cost and risk in air breathing was that of increased pulmonary water loss, a process accentuated by the fact that the air breathers relied exclusively on respiratory ventilation for O_2 acquisition and CO_2 clearance. Furthermore, except in reptiles, respiration in mammals and birds is regular and continuous. Exposure of the eel, *Anguilla*, to air causes the blood CO_2 level to rise and the arterial PO_2 and the O_2 consumption to decrease (Berg and Steen 1965). In *Synbranchus*, aerial respiration inhibits CO_2 elimination leading to increase in the blood PCO_2 (Johansen 1966). The inability to lose CO_2 into the air through either the gills or simple lungs is one of the main factors which constrained emergence from water (Hughes 1966; Thompson 1969). This explains why some modern air breathers with lungs and/or special respiratory organs inhabit water for the singular purpose of ease of CO_2 elimination. The air-breathing crabs which cannot eliminate CO_2 across the hard carapace have retained the gills (Innes and Taylor 1986a,b). This, while enabling them to maintain a low arterial PCO_2, confines them to habitats where water is easily accessible. In the robber crab, *Birgus latro*, much of the CO_2 is eliminated across the gills during rest, but during activity about one half of it is voided via the lungs (Greenaway et al. 1988).

On adopting air breathing, the bimodal breathers were not only faced with the problem of detecting respiratory stimuli from both internal and external milieus but also that of controlling physiologically distinct modes of respiration (e.g., West and Burggren 1983; Shelton and Croghan 1988; Smatresk 1988; Boutilier 1990). The respiratory control changed from a centrally modulated process to a diffusely coordinated one: the central control on the branchial ventilation was attenuated and the aquatic and air breathing integrated. The complexity of the plan depended on the relative importance of each mode of breathing to the overall respiratory needs and on factors such as the degree of adaptation to aquatic or terrestrial subsistence, the level of activity, and external factors such as hypoxia, temperature, and humidity. Fast, multiple respiratory responses are essential for animals subsisting in highly dynamic habitats characterized by precipitate fluctuations in O_2 and CO_2 levels. In the unimodal air breathers, e.g., birds and mammals, the control of ventilation is mediated centrally with the peripheral inputs simply modulating centrally produced impulses. However, in the intermittent air breathers, the ventilatory effort and pulmonary blood flow appear to be mainly regulated and synchronized through chemical and/or mechanical information initiated by the prevailing needs for O_2 (e.g., Johansen et al. 1997; Milsom 1990; West et al. 1992). Mechanoreceptors, which detect the gradual decrease in lung inflation (as O_2 is used up to some baseline value) have been described in the lungs of the bowfin (*Amia calva*) (Milsom and Jones 1985) and in the lungfish (*Protopterus aethiopicus*) (DeLaney et al. 1983). In *Amia*, aquatic hypercapnia at a concentration of CO_2 of up to 3% increases branchial ventilation (Johansen 1970). The absence of ventilatory or cardiovascular responses after intracranial perfusions of hypercapnic and low pH solutions shows that a central chemoreceptor involvement of O_2 or CO_2/pH in ventilatory regulation is lacking in *A. calva* (Hedrick et al. 1991). In terrestrial vertebrates, central chemoreceptive loci sensitive to CO_2 levels and/or pH changes are known to include the ventral region of the medulla oblongata (e.g., Hitzig and Jackson 1978). Internal O_2 chemoreceptors which stimulate air breathing have been described in the "lung" of the gar-fish (Smatresk et al. 1986) and in *P. aethiopicus* (Lahiri et al. 1970). The characteristic response of bimodal breathers to hypoxia is a notable increase in the ventilation of the accessory respiratory organs and a reduction in gill ventilation (Willmer 1934; Johansen et al. 1970b): in the gar-fish, a ten-times increase in ventilatory volume occurs consequent to increases in the ventilatory frequency and tidal volume (Smatresk et al. 1986). In *Protopterus*, respiratory responses appear to be highly sensitive to arterial gas tensions or pH (Lenfant and Johansen 1968; Johansen and Lenfant 1968). In *Neoceratodus forsteri*, the Australian lungfish, branchial ventilation increases remarkably as the PO_2 in the "inhaled" water falls below 10 kPa while aerial respiration is induced at a water PO_2 level of 11.3 kPa (Johansen et al. 1967): the chemoreceptors responsible for these respiratory responses are apparently external (branchial) as injection of urea into the lung does not elicit any compensatory response. In adult *Protopterus aethiopicus*, water PO_2 does not affect branchial or aerial breathing (Johansen and Lenfant

1968) but reduced lung PO_2 and systemic PO_2 stimulate the frequency of air breathing (Johansen and Lenfant 1968; Lahiri et al. 1970). Sectioning the nerves to the branchial arches reduces the responsiveness of *P. aethiopicus* to hypoxia (Lahiri et al. 1970), suggesting that chemoreceptive area(s) may exist in the branchial arches of the species. Such site(s) have, however, not been morphologically identified (Fishman et al. 1989). Using chemical probes such as sodium cyanide for O_2-sensitive elements (Lahiri et al. 1970) or nicotine (Johansen 1970), the existence of intravascular chemoreceptors in *Protopterus* has been demonstrated. Juvenile *Protopterus* rely more on aquatic respiration and respond to low water PO_2 (8% O_2 by volume) with a 50% increase in branchial and 300% increase in aerial breathing.

In the air-breathing fish, the ambient and internal CO_2 tensions are important regulatory factors of aquatic and aerial respiration. There are indications that water facing chemoreceptors occur in the gills of the air-breathing fish, e.g., *P. aethiopicus* (Johansen and Lenfant 1968) and the gar-fish, *Lepisosteus* (Smatresk et al. 1986; Smatresk and Azizi 1987). In *Protopterus*, the CO_2 receptors are located in the branchial region (or arterial side of the branchial circulation) (Johansen and Lenfant 1968), a feature which shows that increased gill PCO_2 inhibits branchial breathing before the arterial PCO_2 increases (Jesse et al. 1967). Externally situated O_2 receptors are important in monitoring the ambient PO_2 while the internal ones monitor the O_2 levels in blood. Switching to the most economical mode of gas exchange, i.e., from aquatic to aerial modes and vice versa, optimizes O_2 consumption to suit different metabolic needs and circumstances. Air-breathing fish are particularly sensitive to CO_2. In *Neoceratodus*, increased gill concentration of CO_2 reflexively inhibits branchial respiration while stimulating air breathing (Johansen 1966). A biphasic response to CO_2 similar to that in the terrestrial vertebrates was observed in *Protopterus* by Johansen and Lenfant (1968) and Jesse et al. (1967): at physiological levels of water concentration of CO_2 of 0.5% by volume or lower, both gill and lung ventilation were stimulated and at higher levels of CO_2 (1 to 5%), gill ventilation declined steadily. In both air and water breathers, the main response to hyperoxia is reduction of ventilation in correspondence to increased PO_2 in blood. The ventilatory inhibition in air breathers leads to accumulation of CO_2, resulting in respiratory acidosis which stimulates ventilation to correct the acid-base status. In many surviving air-breathing fish, maximal heart rates occur soon after the ventilation of the aerial gas exchanger (Singh and Hughes 1973). This optimizes transfer and utilization of the inhaled air. Due to the apparent ventilatory insensitivity of the water breathers to PCO_2, a persistent hypercapnic acidosis develops (Heisler 1982b). Mechanical inflation of the accessory respiratory organ in many air-breathing fish and amphibians often causes depression of the air-breathing activity (Lenfant et al. 1970b; Pack et al. 1984, 1992). In *Amphiuma*, inflation of the lung with pure nitrogen delays the onset of breathing, suggesting that mechanical distension may be an important factor in regulating O_2 ventilatory patterns (Toews 1971). Following an interbreath period of 4 to 5 min, in *Protopterus* (Lenfant and Johansen 1968), soon after inhalation, cardiac output is increased four times over the apneic level and almost three quarters of the injected blood is directed to the lungs (Johansen et al. 1968a). In the frogs, *Xenopus laevis* (Shelton 1970) and

Rana pipiens (Jones and Shelton 1972), the relative flow of blood to the gas exchangers depends on the breathing pattern. As in lungfishes and other air-breathing fish, apneustic breathing in amphibians determines the blood flow through the different circuits. During sustained breathing, the pulmocutaneous blood flow exceeds the systemic one, a condition reversed during apnea (Shelton 1976).

In *Bufo marinus* (e.g., West and Burggren 1984) and the lungfish, *P. aethiopicus* (DeLaney et al. 1983), mechanoreceptor elements are an integral factor in regulating and effecting ventilation-perfusion equality through regulated vasodilatation and constriction of the pulmonary vasculature. During air breathing, in lungfishes, vasomotor activity maintains a lower pulmonary than systemic vascular resistance, enhancing lung perfusion. In the most aquatic of all lungfishes, the Australian *Neoceratodus forsteri*, branchial vascular resistance is highest in the taxon and compares with that in the elasmobranchs and teleosts (Johansen et al. 1968a). Branchial vascular resistance in *Protopterus* as well as in *Lepidosiren* is very low due to the presence of low resistance vascular shunts which allow much of the cardiac output to bypass the branchial arches which have virtually lost all the gill filaments (Johansen and Reite 1968; Laurent et al. 1978). The same regulatory mechanism prevails in the clawed toad, *Xenopus laevis*, where pulmocutaneous blood flow increases two to four times over the prebreath level compared with the systemic flow which almost remains constant (Shelton 1970). In the snakehead fish, *Channa argus*, aerial hypoxia (a rather rare occurrence) results in a five-times increase in "lung" ventilation as the PO_2 decreases from 20.7 to 5.3 kPa, but hypercapnia produces little change in lung ventilation (Glass et al. 1986). In intermittently breathing animals, e.g., *Xenopus* (Emilio and Shelton 1974), the diving turtles, *Pelomedusa subflava* (Glass and Wood 1983), *Chrysemys* (=*Pseudemsy*) *scripta* and *Testudo graeca* (Burggren and Shelton 1979), *Chelonia mydas* (West et al. 1992), and the garter snake, *Thamnophis* (Burggren 1977), O_2 exchange is greatest soon after inspiration when the blood flow is highest. In some air-breathing fish, e.g., the gourami, *Trichogaster* (Burggren 1979), aquatic hypercapnia results in increase in ventilation but in the spotted gar-fish no such a significant response seems to occur (Smatresk and Cameron 1982a,b). While in air, *Trichogaster* can efficiently eliminate CO_2 across the accessory respiratory organ (the labyrinthine organ) because the epithelial lining which is derived from gill tissue contains a high concentration of carbonic anhydrase (Randall et al. 1981).

5.5.1 Ventilatory Modalities of the Gas Exchangers in the Bimodal Breathers

During transition to air breathing, the general pattern of breathing changed from regular transfer of water across the gills to the episodic breathing pattern which typifies a large number of air-breathing fish, amphibians, and reptiles. A determinate breathing pattern (of air) was thereafter reverted to (under resting conditions) in mammals and birds (Table 5). In the Dipnoi (McMahon 1969; Burggren and Johansen 1986) and the amphibians (Burggren and Doyle 1986), the air-breathing mechanism was derived from the aquatic mechanism with inspiration occurring by a buccal force pump and expiration by elastic recoil of the lung. In the bimodally breathing teleosts, air ventilation is less well understood (Peters 1978; Kramer 1978; Liem 1980; Hellin and Chardon 1981; Ishmatsu and Itazawa 1981. In *Channa*, air breathing is complex and differs remarkably from water breathing (Liem 1984). In what was described as a cough mechanism, convergently, phylogenetically different air-breathing teleosts, the Channidae (Liem 1984), Anabantoidae (Peters 1978), and Clariidae (Hellin and Chardon 1981) have adopted a primeval aquatic process used to clear debris from the gills to ventilate the air-breathing organ(s). Since coughing is a water-dependent mechanism, fish utilizing the process only to ventilate their accessory respiratory organs are restricted in the period during which they can stay out of water (Liem 1984). The pressures which induced selection for interrupted ventilation and hence a lower respiratory frequency in bimodally breathing fish include: (1) need to reduce the number of vertical migrations to breath at the air-water interface, providing a substantial energy saving (e.g., Kramer and McClure 1981; Kramer 1983), and (2) avoidance of risks of predation during travels to the surface. When breathing air, *Gillichthys* becomes positively buoyant and has to hold onto substrate with its sucker-like pelvic fin (Todd and Ebeling 1966) while *Pseudapocryptes* is reported to float on the surface of the water with the opercular chambers inflated (Das 1934). During a dive, turtles, e.g., *Chrysemys* can breath-hold for as long as 1 to 2 h even when they have access to air: active breathing takes only 2 to 15% of the total activity when undisturbed (Belkin 1964; Burggren 1975). Intermittent breathing occurs in the bimodal breathers due to the large O_2 stores in their body and the fact that during the breath-holds, gas exchange can be effected through secondary respiratory site(s) (e.g., Farrell and Randall 1978). Animals which do not have these features, e.g., fish and vertebrates like birds and mammals, though with large O_2 stores, have a high O_2 consumption and must continuously ventilate their gas exchangers. Those animals whose O_2 needs are low, e.g., amphibians, reptiles, and air-breathing fish, can: (1) acquire supplemental O_2 through multiple pathways, (2) reduce their O_2 consumption by adopting anaerobic metabolism, or (3) reduce their overall energy needs, e.g., by estivating or displaying rhythmic breathing. Since they contain O_2-rich air, the accessory respiratory organs of the bimodal breathers increase body O_2 stores by an order of magnitude. This lowers the ratio of O_2 consumption to O_2 store in the body. Episodic respiration in bimodal breathers rarely influences CO_2 and pH levels in the body as CO_2 is eliminated through pathways such as the skin and the gills. However, the intermittent air breathers have higher body CO_2 stores than the continuously breathing aquatic animals. Most bimodal breathers increase the ventilation of the accessory respiratory organ when the arterial or mixed venous blood PO_2 falls. This occurs, e.g., after exposure to hypoxia, when the ambient temperature increases beyond a critical point or when the activity level is raised. In the larva of the dragonfly (*Aeschna*), when the O_2 content is reduced to 2.5 ml per liter ($PO_2 = 7.3\,kPa$), the organisms move to the surface of the water. Such a reflex is not initiated in the fish, *Leuciscus erythrophthalmus*, until the concentration of O_2 drops to a low of $0.6\,ml\,l^{-1}$ (Winterstein 1908). In *Protopterus*, exposure to 8% O_2 increases lung ventilation three times but gill ventilation is raised by a factor of only one half. This suggests that different receptors are involved in the control and coupling of respiration in the air breather (Jesse et al. 1967). The buccal force pump used to ventilate the gills of the water breathers has been carried over to the air-breathing fish and the amphibians to ventilate the accessory respiratory organs. The pump in *Rana catesbeiana* is particularly efficient since remarkably high arterial PO_2 levels (values as high as 12.7 kPa) are attained (Lenfant and Johansen 1967). In fish, it is only in the Amazonian osteoglossid, *Arapaima gigas* (Farrell and Randall 1978), and the lungfish, *Protopterus amphibius*, during estivation (Lomholt et al. 1975) that aspirational breathing has been alleged. Suctional breathing may have evolved in water but is clearly a design characteristic of air breathers (e.g., Brainerd 1994). The respiratory frequency in air-breathing fish can vary from 1 breath min^{-1} to less than 1 breath h^{-1} (Johansen et al. 1971a; Smatresk and Cameron 1982a,b). It has been suggested that the buccal force pump in modern amphibians may have evolved secondarily after loss of ribs (Foxon 1964).

5.5.2 The Circulatory Patterns in the Gas Exchangers of the Bimodal Breathers

The transition from water to air breathing entailed drastic reorganization of the cardiovascular system. An elaborate mechanism of regulating the perfusion of the aerial gas exchanger(s), especially where they were arranged in parallel with the systemic circuit, was formed (e.g., Olson 1994). The occurrence of anatomical gill shunts is unique to the bimodal breathers (Laurent 1985). They have not been reported in the exclusively water-breathing fish (Laurent 1984). A number of attendant physiological problems arose from the superimposition of the accessory respiratory organ(s) on the branchial and systemic vascular circuits. These changes are most evident and better understood in the vertebrate transitional breathers. In the single arc circulatory pattern of the ancestral water-breathing fish, the entire cardiac output is directed to and perfuses the gills. The oxygenated blood passes to the dorsal aorta for distribution to the rest of the body. Attainment of air breathing necessitated integration of a separate circulatory network onto the original single circuit (Fig. 21). After the relocation of the ionic and gas exchange from the gills to the kidneys and the lungs, respectively, the aquatic vertebrates (which by now had developed into the terrestrial tetrapods) reverted to the original plan where all the cardiac output was driven through the only gas exchanger, the lung. The parallel arrangement in the bimodal breathers was converted into two circuits, pulmonary and systemic circuits.

The attendant gas exchange complications which arose with the evolution of bimodal breathing included: (1) undersaturation of arterial blood resulting from mixing of deoxygenated systemic blood with the efferent (oxygenated) blood from the accessory respiratory organ, (2) an apparent drop in respiratory efficiency consequent to perfusion of a gas exchanger with blood which had already passed through the gills, (3) shunting of the efferent oxygenated blood from the accessory respiratory organ(s) resulting in admixture with the systemic venous blood, (4) risk of transbranchial efflux of O_2 from the oxygenated blood if the gills were ventilated with hypoxic ambient water, and (5) undue tissue blood pressure arising from the addition of extravascular resistance pathways. These limitations were overcome or minimized by: (1) a drastic modification of the vascular layout, (2) axial blood flow separation, and (3) development of vascular shunts. In the lungfishes (Dipnoi), which have gills and lungs, the blood pumped from the ventricle is separated into two streams. One stream perfuses the anterior gill arches which are devoid of gill filaments (Parker 1892) and the other passes through the posterior gills and then onto the pulmonary artery (Johansen and Lenfant 1967; Burggren and Johansen 1987; Fig. 21). The latter pathway is accentuated when the ambient PO_2 is low (Johansen et al. 1968a). Laurent et al. (1978) described a vascular shunt in the posterior gill arches (IV and VI) of *P. aethiopicus* which bypassed the secondary lamellae. The arrangement corresponds with that of the external gills of the amphibians (e.g., Fige 1936) and *Lepidosiren paradoxa* (Robertson 1913). As the blood returns to the heart, mixing of the pulmonary arterial blood with the systemic deoxygenated blood is avoided by the presence of a spiral valve in the conus arteriosus. By establishing and maintaining laminar flow, the valve effectively separates the two blood streams in the heart. The oxygenated blood passes through the gill arches to the body while the deoxygenated blood passes to the lungs (Johansen and Hol 1968; Satchell 1976) for oxygenation. In the lungfishes, the degree of intracardiac separation of the arterial and venous blood depends on the degree of reliance on air for O_2, with the process being least effective in the obligate water breather, *Neoceratodus*, and best developed in the obligate air breathers, *Lepidosiren* and *Protopterus* (Johansen and Lenfant 1967; Johansen and Hanson 1968; Lenfant and Johansen 1968). The partial separation between the pulmonary and systemic circuits similarly occurs in amphibians although no distinct intracardiac anatomical modifications are evident (DeJong 1962; Johansen and Hanson 1968). Unlike in fish, in amphibians, the cutaneous circulation is arranged in parallel with the systemic and the pulmonary circuits and can be greatly varied without affecting the other two pathways (Johansen 1979). In the air-breathing teleosts such as *Channa* (Ishmatsu et al. 1979; Munshi et al. 1994; Olson et al. 1994), *Anabas testudineus* (Munshi et al. 1986a; Olson et al. 1986b), *Monopterus cuchia* (Munshi et al. 1989, 1990), *Heteropneustes fossilis* (Munshi et al. 1986b; Olson et al. 1990a; Hughes et al. 1992), and the lungfishes (Fishman et al. 1989), cardiovascular remodeling occurs as a part of a gross reorganization of the vascular connections between the gills, the accessory respiratory organs, and the systemic circuit. To a less conspicuous but significant extent, modifications in the form of vascular shunts (preferential perfusion channels), changes in microcirculation, and vascular endothelium (Hughes and Munshi 1979) develop.

Hemodynamic considerations and physiological functions are the main factors which initiated, regulated, and determined the changes in the circulatory patterns in bimodal breathers (Olson et al. 1994). In *Channa*, the vascular organization allows partial separation of blood flow to the gills, accessory respiratory organs, and systemic tissues (Munshi et al. 1994) resulting in basically two functional circuits: (1) heart → gills (1st and 2nd arches) → the accessory respiratory organ(s) → heart, and (2) heart → gills (3rd and 4th arches) → systemic tissue → heart. The accessory respiratory organs are essentially in series with the branchial vasculature and in parallel with the systemic circuit. The total cardiac output must hence first pass through the gills before perfusing the accessory respiratory organ or systemic tissues and both the deoxygenated systemic venous blood and oxygenated blood from the accessory respiratory organs returns to the heart. The first pathway (at the gill level) performs functions like osmoregulation, acid-base balance, CO_2 clearance, and metabolic N_2 excretion: Oxygen is subsequently taken up at the level of the accessory respiratory organ. The second pathway serves the role of shunting blood past the gills and delivering oxygenated blood directly to the systemic tissues: this curtails O_2 loss to a hypoxic aquatic medium. In the holostean, *Amia calva*, to minimize O_2 efflux from the gill blood, the blood flow in the gills is altered so that much of it is shunted to the nonrespiratory parts of the gills (Johansen et al. 1970a). In having elaborate gill filaments and secondary lamellae with an adequate number of chloride cells (ionocytes), the 1st and 2nd pairs of gill arches of the bimodal breathers retain features characteristic of those of the water-breathing teleosts and the well-developed gills in air-breathing species. The 3rd and 4th arches are less elaborate (e.g., Munshi et al. 1990; Olson et al. 1990a; Olson 1991). In most species, e.g., in the cuchia eel *Amphipnous cuchia* (Lomholt and Johansen 1976), and the electric eel, *Electrophorus electricus* (Johansen et al. 1968b), the 3rd and 4th gill arches are used as a bypass of the vestigial gills to avoid loss of O_2. Vascular and intracardiac modifications close to the heart and gills reduce the mixing of the arterial and venous streams of blood. The deoxygenated systemic venous blood and the oxygenated blood from the accessory respiratory organ returns to the heart, facilitating delivery of the deoxygenated fraction to the accessory respiratory organs. The systemic tissues are perfused with the oxygenated fraction (Ishmatsu et al. 1979; Ishmatsu and Itazawa 1983; Munshi et al. 1994).

The intracardiac physical separation of the venous and arterial streams of blood was unequivocally demonstrated by Ishmatus and Itazawa (1983): in *Channa argus*, it was found that the PO_2 in the anterior ventral aortic blood is lower than that in the posterior ventral aortic blood. The overall efficiency of the gas exchange process is to a great extent dependent on the effectiveness of minimization of the mixing of these two blood streams in the heart. In air-breathing fish, the perfusion of the accessory respiratory organ is well matched to the O_2 available for aerial gas exchange. In the cuchia eel, *Amphipnous cuchia* (Lomholt and Johansen 1976), and electric eel, *Electrophorus electricus* (Johansen et al. 1968b), when breathing air, 75% of the cardiac output, respectively 80 and $70\,\mathrm{ml\,kg^{-1}\,min^{-1}}$, is directed to the accessory respiratory organ: during apnea, the perfusion of the organ drops to 20%. This marks an incipient stage in the evolution of synchronization of ventilation and perfusion and functional separation of pulmonary and systemic perfusion. The process is better refined in the lungfishes, where a partial separation has been attained (Johansen at al. 1968a; Fig. 21). Total separation is reached in the higher vertebrates, birds and mammals. The low pressure pulmonary circuit (Figs. 25,26) which appears to have evolved very early, e.g., in the Dipnoi (Johansen et al. 1968a) enables extreme refinements of the structural parameters of the gas exchangers accommodating the development of a very thin blood-gas barrier in a highly dynamic organ.

5.6 Taxa with Notable Propensity for Bimodal Breathing

5.6.1 Mollusks

The Phylum Mollusca, with about 100 000 species, is one of the largest and most successful in the Animal Kingdom (e.g., Jones 1983; Seed 1983). It is exceeded in specific diversity and numerical density only by Arthropoda and perhaps by Protozoa and Nematoda. Ecologically, the mollusks have penetrated a wider range of habitats than any other animal group (Ghiretti 1966). The gastropods, which constitute about 80% of all living mollusks, are the only group in the taxon which has colonized land. After the arthropods, the slugs are probably the most successful land invertebrates (Jones 1983). The success of the pulmonate gastropods is largely attributable to the development of certain physiological and behavioral adaptations which have enabled them to cope with problems of water balance, temperature, osmotic and ionic regulation, and gas exchange (Riddle 1983). Mollusks, which have a respiratory pigment with low O_2 unloading tension, can subsist in hypoxic environments and to a certain point may show metabolic independence to external O_2 levels (Borden 1931; Chaetum 1934).

Air breathing in pulmonate gastropods probably arose in O_2-deficient waters such as estuaries, swamps, and muddy rivers (Seed 1983). In the prosobranches. e.g., *Littorina rudis*, there is a tendency towards formation of a lung on exposure to air. In the intertidal pulmonate limpets constituting the Siphonariidae, on return to the sea, secondary gills may appear within the former lung (Yonge 1952). The related *Trimusculus (Gadinia)* continues to breath air while residing in water (Yonge 1958). In the pulmonate gastropods, the mantle cavity has been converted into a highly vascularized lung (Maina 1989c; Figs. 59,60) where a large volume of "blood" is brought into close proximity to a respiratory medium for gas exchange in air or secondarily in water. Pulmonate gastropods are structurally the most conservative gastropods and their evolutionary advances have been committed essentially to face the challenges of terrestrial colonization. In a notable deviation from the normal pattern, some pulmonates, e.g., the siphonarid limpets, possess secondary gills which are housed in a dorsal mantle cavity (e.g., McMahon 1983; DeVilliers and Hodgson 1987). The gills of the pulmonate, *Siphonaria capensis*, bear ciliary tufts (about 400 cilia per mm^2). The surface is covered by a single layer of epithelial cells with interspersed mucus-secreting cells (DeVilliers and Hodgson 1987). From the ciliated gills and other anatomical features, *Siphonaria* is believed to be one of the least developed pulmonates (Marcus and Marcus 1960; Hyman 1967). While Marcus and Marcus (1960) contend that the secondary gills have always been a feature of siphonariids, it has been suggested by, e.g., Yonge (1952) and Morton (1979) that the gills were initially lost as the taxon evolved terrestriality but redeveloped when it reverted to water. In the freshwater pulmonate gastropods, *Lymnaea stagnalis* and *Planorbis corneus*, which have secondarily taken to water after the extirpation of the gill-like ctenidia, the mantle cavity was converted into a well-vascularized water lung which is rhythmically filled with water (Precht 1939; Hunter 1953). As the ambient PO_2 drops below a critical level, the snail comes to the surface to breath air

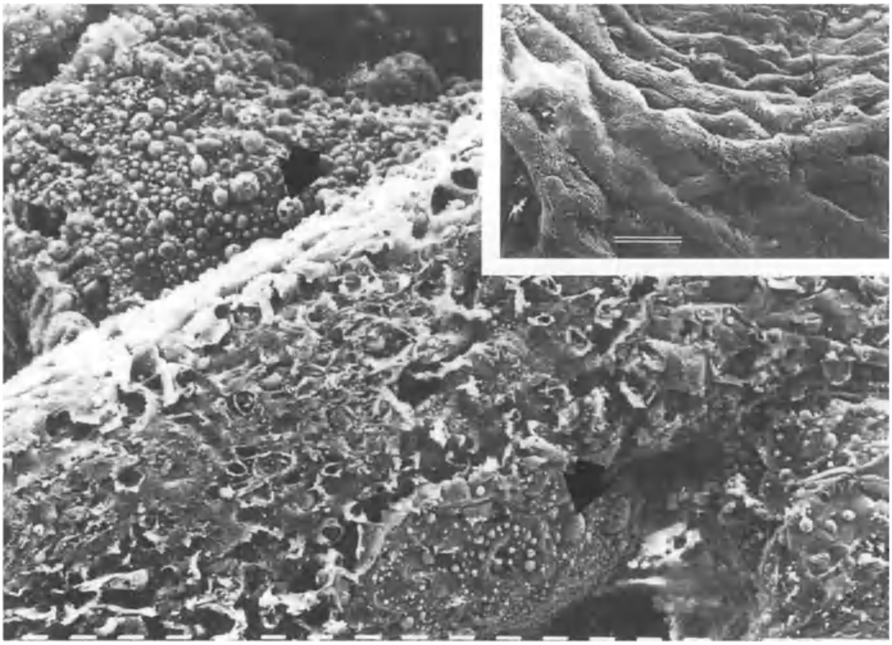


Fig. 59. Surface of the lung of a pneumonate gastropod, *Trichotoxon copleyi*, showing the vascular network of blood capillaries (*inset*). The *main figure* shows one of the blood capillaries and clusters of mucus cell, ➧, which lie on the epithelial surface. *Bar* 10 µm; *inset* 90 µm. (Maina 1989c)

(Cheatum 1934). When access to air is prohibited, *Lymnaea* responds by elevating the concentration of hemocyanin in blood to enhance extraction of O_2 from the lung (Jones 1972). The opening of the pneumostome is regulated to optimize gas exchange while limiting water loss. Low ambient concentration of O_2 stimulates the opening of the pneumostome, which may remain permanently open at concentrations below 10% (Ghiretti 1966). The opening of the pneumostome in the terrestrial gastropods *Limax*, *Arion*, and *Helix* is influenced by the level of CO_2. It remains permanently open at a concentration of CO_2 of 3 to 5% (Dahr 1927; Prosser 1961). In *Helix pomatia*, at 20% O_2, the pneumostome remains closed and only opens when O_2 drops to 10% or less (Ghiretti 1966). Other factors which regulate pneumostomal size include temperature and humidity (Ysseling 1930; Wit 1932; Mass 1939). In the inactive slug, *Limax maximus*, the lung contributes 20% of the O_2 consumption, the value rising to 50% during activity (Prior et al. 1983). In all mollusks, even where specific respiratory organs exist, gas exchange through the body surface occurs to varying extents. Transcutaneous gas exchange may be of critical importance under certain circumstances. In the land snail, *Otala lactea*, a significant amount of CO_2 is eliminated across the skin (Barnhart 1986a). In the aquatic air-breathing snails, *P. corneus* and *L. stagnalis*, where CO_2 is soon lost into the water through the skin, CO_2 does not act as a respiratory

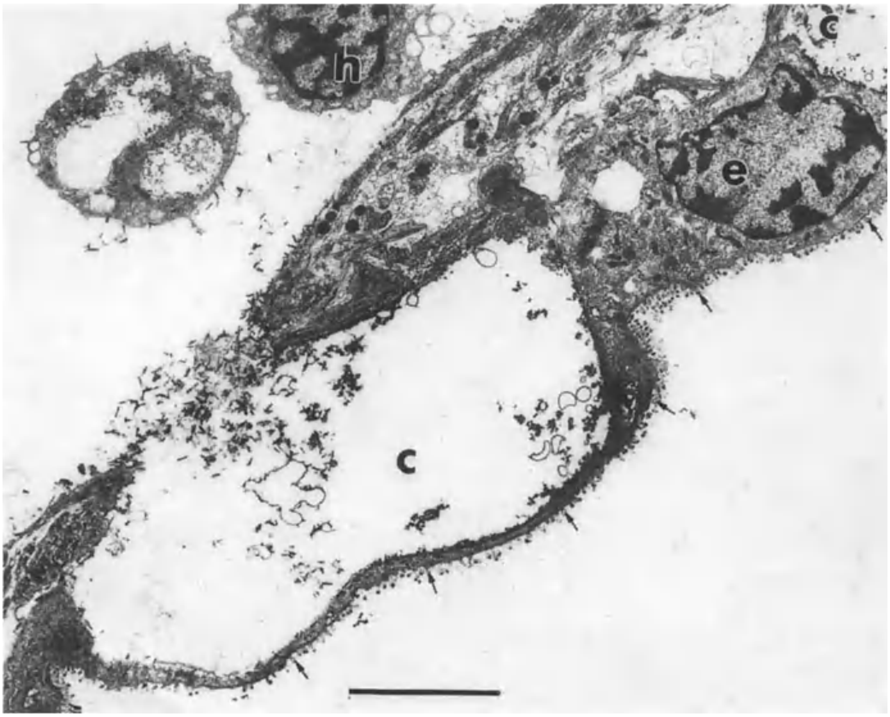


Fig. 60. Blood capillaries, *c*, on the surface of the lung of a pneumonate gastropod *Trichotoxon copleyi*; *e* epithelial cell; *h* hemocyte; → microvilli on the epithelial cell surface. *Bar* 2 μm. (Maina 1989c)

stimulus. Factors such as PO_2 and loss of buoyancy regulate respiration (Jones 1961). In the Athoracophoridae, the lung is small. Many fine tubules lead from it to the roof of a blood sinus in a manner resembling the trachea of insects (Runham and Hunter 1970). Accordingly, the taxon has been termed the Tracheopulmonata.

The respiratory surface area of the lung in pulmonate gastropods ranges from 7 to $13.5\,cm^2\,g^{-1}$ (wet body mass) (Yonge 1947). The dimensions compare and exceed those of some vertebrate air breathers, e.g., the lizard, *Tupinambis nigropunctus* $3.2\,cm^2$ per g (Perry 1983) and the domestic fowl, *Gallus domesticus*, $10\,cm^2\,g^{-1}$ (Abdalla et al. 1982). Perhaps due to the large respiratory surface area of the lung and the thin blood-gas barrier (Maina 1989a), diffusion is adequate for gas exchange even at the very low PO_2 of 0.3 kPa characteristic of the habitats in which the slugs live (Ghiretti 1966). Depending on temperature, slugs can increase their O_2 consumption by as much as 400 to 500% (Mackay and Gelperin 1972; Prior et al. 1983). In *O. cygnea*, in the process of repaying the O_2 debt after activity, maximum O_2 consumption is reached after 1 h (Hers 1943). In active snails, PO_2 and PCO_2 in the lung of the land snail, *Otala lactea*, differed by less than 2 kPa from air, the arterial PCO_2 was similar to that in the gas in the lung but the arterial PO_2 was 8kPa lower than that in the lung (Barnhart 1986b). This bespeaks a strong diffusional limitation of O_2 transfer across the blood-gas barrier. Only about 10% of the hemocyanin-O_2 carrying capacity is utilized at 5 °C but rises above 70% at 25 °C in the active land snail *O. lactea* (Barnhart 1986c). In *H. pomatia*, O_2 affinity is 1.5 to 2kPa at 20 °C and pH 7.6 to 8.2 (e.g., Konings et al. 1969), in *Arion ater* it is 2.2kPa at 20 °C, pH 7.94 (Wells and Weber 1982) and in *O. lactea* 5.3kPa at 25 °C, pH 7.9 (Barnhart 1986b). In *Trichotoxon copleyi* (Maina 1989c) and *H. pomatia* (Pohunkova 1967), the lung has developed in the form of a modified mantle cavity. The roof, which is highly vascularized, is lined by a respiratory epithelium which is made up of squamous cells bearing stubby microvilli. The blood vessels protrude into the air space (Figs. 59,60). Scattered among the squamous cells are goblet mucus cells (Fig. 59). Contrary to the observations made by Pohunkova (1967) on *H. pomatia*, the air-blood pathway lacks a continuous endothelial lining (Maina 1989c). In the pneumonate gastropods in general, the thin blood-gas barrier ranges in thickness from 6 to 10μm (Runham and Hunter 1970). In *Trichotoxon* (Maina 1989c), some parts of the barrier are as thin as 0.2μm. The diffusion potential for O_2 in the lung of *Agriolimax agrestis* is six times greater than the animal's total O_2 requirement (Runham and Hunter 1970). As in the lung-breathing exothermic vertebrates (e.g., Jackson 1978), in the arterial blood of *O. lactea*, PCO_2 increases and pH and PO_2 decrease with temperature, presumably due to a hypoventilatory response (Barnhart 1986b).

5.6.2 Crustaceans

The crustaceans have exploited habitats ranging from totally terrestrial ones to the deep sea (Bliss 1979; Hartnoll 1988; Henry 1994). The decapod crustaceans present remarkable respiratory diversity with evident progressive sophistication occurring from aquatic through to air breathing and terrestrial species (e.g., Bliss 1979; Cameron 1981; McMahon and Wilkens 1983; Innes and Taylor 1986a,b; Burggren and McMahon 1988b; Henry 1994). Land crabs are members of the Anomura and Brachyura which can to varying extents survive on land. The majority belong to the families Coenobitidae, Gecarcinidae, Grapsidae, Potamoidea, and Ocypodidae (Hartnoll 1988). Among the terrestrial species, respiratory efficiencies correlate with the O_2 demands which are imposed by factors such as habitat and level of activity (Johnson and Rees 1988). Most of the non-malacostracan crustaceans have no specialized respiratory organs: gas exchange occurs across the integumentary surfaces (Wolvekamp and Waterman 1960; McLaughlin 1983). In brachiopods and phyllopods, it occurs through appendages and their modifications such as the gills which come in remarkably different forms (Eriksen and Brown 1980a,b; McLaughlin 1983). The internal surfaces of the carapace are well adapted for gas exchange in the Brachyura (Cameron 1981; McLaughlin 1983).

Crustaceans developed in the sea and have evolved air breathing and invaded land severally (e.g., Bliss and Mantel 1968; Bliss 1979; Cameron 1981). The notably terrestrial species come from the groups Amphipoda, Isopoda, and Decapoda (Bliss and Mantel 1968; Powers and Bliss 1983). Land crabs are of particular interest in comparative respiratory physiology as they display relevant adaptations associated with transition from water- to air breathing and terrestrial colonization (Innes and Taylor 1986a,b; Taylor and Innes 1988). Air-breathing crabs have complex lungs which are contained in the branchial chambers formed from branchiostegal and sometimes thoracic walls (e.g., Farrelly and Greenaway 1987, 1992; Maitland 1987; Fig. 61). In crustaceans, terrestrialness and air-breathing efficiency correlate with the elaboration of the lung (e.g., Diaz and Rodriguez 1977). Though restricted to burrows and demonstrating nocturnal activity, isopods inhabit some of the most xerix habitats such as the Sahara desert (Cloudsley-Thompson 1977). The notably terrestrial species of crabs such as *Birgus latro, Holthuisana (=Austrothelphusa) transversa, Pseudothelphusa garhami*, and *Ocypode saratan* have evolved an elaborate well-perfused, highly amplified epibranchial chamber lining which constitutes for all practical purposes a lung (e.g., Farrelly and Greenaway 1987, 1992; Maitland 1987; Al-Wassia et al. 1989; Fig. 62). Such species can stay away from water for a long time. The anomuran coconut crab, *Birgus latro*, can survive in air with its gills removed (Harms 1932; Smatresk 1979) and, like *Ocypode*, will drown if forcefully submerged in water. The respiratory physiology of *Birgus* differs from that of aquatic crabs in certain ways (Cameron and Mecklenburg 1973). As in the vertebrate lung breathers, the acid-base balance of its hemolymph is effected by respiratory exchange rather than by ionic transfer mechanisms. The blood pressure in most terrestrial crabs is two to four times greater (up to 6.6 kPa) than aquatic crabs and ventilation of the branchial cavity is efficient and continuous, a mechanism which, though the O_2 extraction factor of the lung is only 2 to 8%, promotes gas exchange rate greatly (McMahon and Burggren 1988; Fig. 63). The PCO_2 of the venous blood of *Birgus latro*, which is as low as 1.2 kPa (Burggren and McMahon 1981), may be explained by high ventilatory rates (Dejours and Truchot 1988). During severe hypoxia or hypercapnia, continuous scaphognathite beating (at a

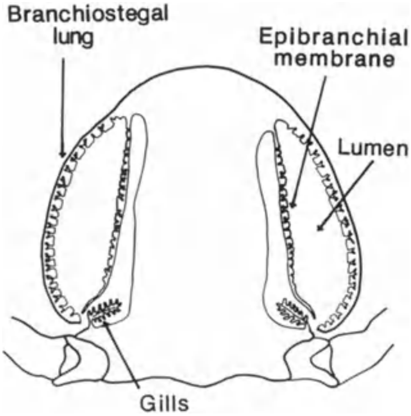


Fig. 61. Transverse section of the body of a soldier crab, *Mictyris longicarpus*, through the branchial chambers which are divided into an inner gill space and an outer space which has been converted into a lung. (Farrelly and Greenaway 1987)

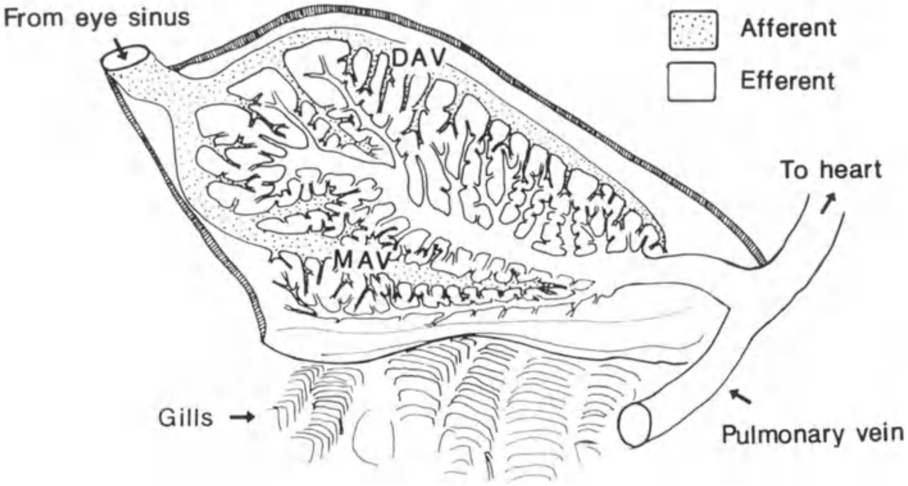


Fig. 62. Schematic diagram of the vascularization of the epibranchial membrane of the lungs of the soldier crab, *Mictyris longicarpus*. The lung is very elaborate, providing a very highly efficient gas exchange capacity and hence ability to subsist over long periods on land. *DAV* Dorsal arterial vessel; *MAV* middle arterial vessel. (Farrelly and Greenaway 1987)

rate of 50 to 300 beats min^{-1}) produces a ventilatory volume of $100\,\mathrm{cm}^3\,\mathrm{min}^{-1}$ in a 1- to 2-kg specimen of *Birgus iatro*. In such circumstances, O_2 extraction factor may increase to 20% (Maitland 1990a). The gills provide $29\,\mu l\ O_2\,g^{-1}\,h^{-1}$ while the balance of about 60 to $110\,\mu l\ O_2\,g^{-1}\,h^{-1}$ in a routinely active land crab (at 25 °C) is transferred across the lungs.

As in the air-breathing fish (Hughes and Morgan 1973; Pelzenberger and Pohla 1992), in crabs, the evolution of alternative air-breathing sites is associated with reduction in the gill surface area (Table 23). While the active aquatic crabs have a respiratory surface area of about 900 to $1400\,\mathrm{mm}^2\,g^{-1}$ (Gray 1954, 1957; Veerannan 1974, Hawkins and Jones 1982; Johnson and Rees 1988; Henry et al. 1990), that in the intertidal ones ranges from 500 to $900\,\mathrm{mm}^2\,g^{-1}$ (Hawkins and Jones 1982; Rabalais and Cameron 1985; Santos et al. 1987) and in the fully terrestrial species the values range from 12 to $500\,\mathrm{mm}^2\,g^{-1}$ (Cameron 1981; Farrelly and Greenaway 1992). The branchial chambers of the bimodal breathing crabs are larger than those of the aquatic ones (Henry 1994). Internal modifications in form of intense foldings and invaginations (e.g., Innes and Taylor 1986a; Farrelly and Greenaway 1987; Maitland 1987; Fig. 62) provide a large respiratory surface area (Greenaway and Taylor 1976; Diaz and Rodriquez 1977). Combined with a remarkably thin blood-gas barrier of 0.2 to 0.4 μm (Farrelly and Greenaway 1992; Table 23), a high diffusing capacity of the lung for O_2 is generated in the terrestrial crabs. Air channels in *P. garhami* run from the lung to the air sacs beneath the carapace and are actively ventilated in a throughflow manner (Diaz and Rodriguez 1977; El Haj et al. 1986) giving a high arterial PO_2 (16 to 18.7 kPa)

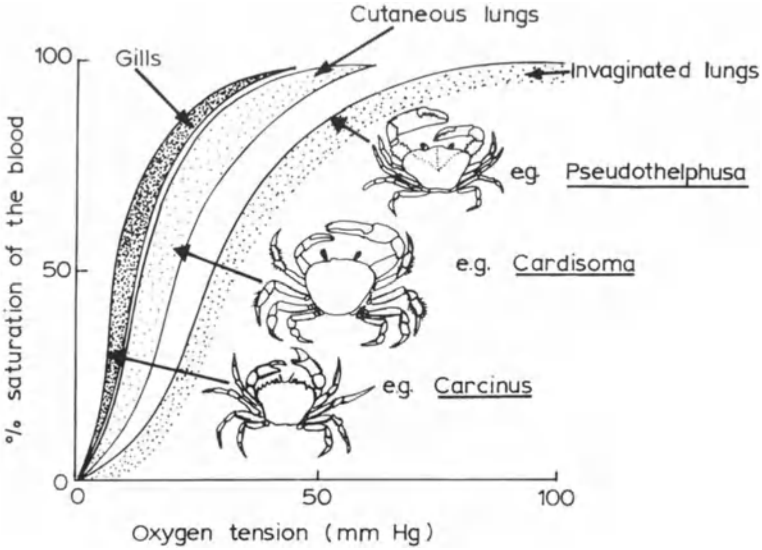


Fig. 63. Correlation between O_2 affinity of blood of air-breathing crabs and mode of gas exchange. In an aquatic breather, e.g., *Carcinus*, O_2 uptake through the gills is aided by the high affinity of the hemocyanin to O_2 (i.e., values of P_{50} – the PO_2 at which 50% of the Hc is saturated – are low). In terrestrial crabs with well-vascularized gill chambers, e.g., *Cardisoma* and species such as *Pseudothelphusa* which can efficiently ventilate their lungs, a high arterial O_2 tension can be attained. In such species, P_{50} is much greater. (Innes and Taylor 1986a)

and a low PCO_2: gas exchange does not seem to be diffusion-limited (Innes and Taylor 1986a,b). The arterial PO_2 in the soldier crab, *Mictyris longicarpus*, is 12.8 kPa (Farrelly and Greenaway 1987) and in the shore crab, *Carcinus maenas*, is 14.2 kPa (Lallier and Truchot 1989). Many semaphore and grapsid intertidal and supratidal crabs carry some water on the lower parts of the branchial chambers (e.g., Burnett and McMahon 1987; Maitland 1990b). On average, crabs carry 0.35 to 0.5 ml of water per 7-g live body mass. The pumping action of the scaphognathites (aided by setae) circulates 0.2 ml of it (per 3-g body mass) around the body across the branchial chambers while on excursion on land (e.g., Hawkins and Jones 1982; Felgenhauer and Abele 1983). The water keeps the gills moist (avoiding desiccation and enabling aquatic respiration in air), functions as a sink for the excreted CO_2 (Burnett and McMahon 1987), and moistens the food during eating (Fielder 1970; Maitland 1990b). In some species, air is bubbled through the water in the branchial cavity to oxygenate it (McMahon and Burggren 1988). In the fully terrestrial land crabs, e.g., *Birgus latro*, CO_2 is excreted through the gills (Greenaway et al. 1988).

Although the factors which have limited the terrestrial radiation of the land crabs are not well known (e.g., Hartnoll 1988), compared with the most successful arthropod groups, e.g., Arachnida, Chilopoda, Diplopoda, Insecta, and terrestrial vertebrates like birds and mammals, as a group, the crustaceans display relatively weak adaptation for air breathing and terrestrialness. They manifest an extremely

Table 23. Gas diffusional distances and respiratory parameters in some terrestrial and aquatic crabs

Crab	Diffusion distance		VO_2 ($\mu mol\,g^{-1}h^{-1}$)	PaO_2 ($mmol\,l^{-1}$)	PVO_2 ($mmol\,l^{-1}$)
	Gills (μm)	Lung (μm)			
Terrestrial					
Holothuisana transversa	5–8	0.2–0.3	0.80	–	–
Birgus latro	–	0.5–1.2	1.41	27	13
Pseudothelphusa garhami	5	0.4–1.0	1.51	124–140	–
Mictyris longicarpus	3.5–7.0	1.2–3.6	–	79–95	20–27
Ocypode ceratophthalmus	2.9–3.5	0.25–0.3	–	–	–
Cardisoma hirtipes	5–12	2.5–4.5	2.29	–	–
Aquatic					
Procambarus clarkii	3.15–8.7	–	–	–	–
Astacus pallipes	1.4–5.7	–	–	–	–

Respiratory parameters from McMahon and Burggren (1988) and thicknesses from Burggren and McMahon (1988b).

tenuous hold on land. In contemporary biology, the crustaceans are a living model for studying the prerequisites for air breathing, terrestrial colonization, and occupation of new habitats. It is not surprising that in the taxon, potential respiratory organs/sites are still being discovered and debated (e.g., Mangum 1994).

5.6.3 Fish

The common expression "like a fish out of water" conveys the general inability of most fish and other aquatic life forms to survive and effectively exchange gases in air. Phylogenetically, the lungs are thought to have evolved as adaptations in hypoxic or anoxic conditions in the aquatic medium in which the ancestors of the modern fish lived. A small number of the contemporary descendants of the ancient fish, especially those which continued to subsist in derelict hypoxic warm tropical freshwaters, have retained air breathing (Burggren et al. 1985b). In the entire ichthyoid fauna, only the Holostei and the tropical freshwater teleosts can efficiently breathe air (e.g., Munshi and Hughes 1992). The process of air breathing has become so perfected in some fish that they succumb on extended forced submersion. Fish, the most successful vertebrate taxon with 20000 or so species, have lived in water for over 350 million years (Gilbert 1993). Only a handful, the majority of which are teleosts, have evolved air breathing (Bertin 1958; Fänge 1976). As many as 60 (Sayer and Davenport 1991) and, according to Graham (1994), as many as 370 species of fish are known to breath air to varying extents (Table 19). More than any other animal group, fish present the broadest perspective of the evolution of air breathing (Graham 1994) and, to an extent, terrestriality.

The extant teleosts are far from being ancestral to the terrestrial air-breathing vertebrates as they only arose from the holosteans during the late Triassic period (e.g., Jarman 1970). They are thus far removed from the mainstream progenitors of the land vertebrates. The air-breathing teleostean fishes present remarkable morphological, physiological, biochemical, and behavioral respiratory diversity. However, considering their very different systematic backgrounds, the similarity in the preadaptations and the strategies adopted to achieve air breathing are astonishing and overwhelm the differences. In general, larval and juvenile bimodal breathing fish, e.g., *Clarias*, *Colisa*, and *Anabas*, derive much of their O_2 needs from water utilizing the gill/skin system. Their dependence on water for O_2 decreases with age (Hughes et al. 1973; Prasad 1988). These fishes acquire the air-breathing capacity at about 8 to 20 days after hatching (Bruton 1979; Singh and Mishra 1980; Singh et al. 1982). In *Anabas*, the labyrinthine organs start developing at the 5th day of hatching but air breathing does not occur until the 13th to 14th day (Hughes et al. 1986a). Obligate air breathers, e.g., adult piracucu, *A. gigas*, die if refused access to the atmospheric air even when kept in well-oxygenated water (Stevens and Holeton 1978b). The gar-fish, *Lepisosteus*, is a facultative air breather at low temperatures but an obligate one at higher ones (Rahn et al. 1971). At high PO_2, in water, *Piabucina* derives 10% of its O_2 need from air but at a lower water PO_2 of 4.7 kPa, it acquires 70% from air (Graham et al. 1977, 1987). In the snake-headed fish, *Channa punctatus*, and the climbing perch, *Anabas testudineus*, the accessory respiratory organs develop during larval and juvenile stages. They leave water only when the development is complete (Singh et al. 1982; Hughes et al. 1986). Many air-breathing fish possess reduced scales and have a well-vascularized skin through which substantial gas exchange occurs (Lenfant and Johansen 1972; Romer 1972). At a temperature of 7 °C, buccal and cutaneous breathing in the common eel, *Anguilla vulgaris*, supports the metabolic needs (Faber and Rahn 1970). The buccal cavity of the eel is both profusely diverticulated and highly vascularized. It is ventilated every 2 to 5 min with air (Johansen et al. 1968b). At 26 °C, the O_2 uptake rate of 30 ml per kg per h, which constitutes 80% of the overall needs, is procured from the air across the buccal cavity and the rest across the skin. The highly atrophied gills contribute an insignificant amount of O_2. The gills are, however, responsible for elimination of as much as 94% of CO_2 (Table 21). The accessory respiratory organs in fish are diverse and are variably ventilated. They include the skin (e.g., *Amphipnous cuchia*), bucco-pharyngeal membrane (e.g., *Electrophorus electricus*), suprabranchial chamber membranes, and labyrinthine organs (e.g., *Clarias mossambicus*), gastrointestinal system (e.g., *Ancistrus anisitsi* and *Plecostomus plecostomus*), and the air bladders (e.g., *Arapima gigas* and *Amphipnous cuchia*). In *Plecostomus* and *Ancistrus* (both tropical Siluroidae), the stomach is a respiratory organ into which air is swallowed and regurgitated (Carter and Beadle 1931; Carter 1935). In the pond loach, *Cobitis* (=*Misgurnus*), the middle and distal parts of the gastrointestinal system (GIT) are respiratory (McMahon and Burggren 1987) and the residual air is passed out through the anus (Krogh 1941; Jeuken 1957). The blood-gas barrier in the respiratory sites of the GIT is remarkably thin (Jasinski 1973). Respiration using the gastrointestinal system may have been a forerunner to the development of the lung by evagination of the foregut. Morphometrically, the air sac of *Heteropneustes fossilis* is superior to that of *Aphipnous cuchia*, similar to that of *Lepidosiren*, but less than that of *Protopterus* (Hughes et al. 1992): the respiratory surface area of a 40-g specimen was reported to be 24 cm^2, the harmonic mean thickness of the blood-gas barrier 0.342 μm, and the morphometric diffusing capacity 3.2×10^{-5} ml O_2 s^{-1} $mbar^{-1}$. In those air-breathing fish which use isolatable diverticula such as the stomach, intestine, and gas bladder, the gills can simultaneously be ventilated to supplement O_2 uptake and carry out processes such CO_2 elimination, ionic transfer, and clearance of nitrogenous waste products. This cannot occur in those fish, e.g., the electric eel (*Electrophorus electricus*) and the knifefish (*Hypopomus*) which use the buccal cavity as an accessory respiratory organ, a time when aquatic respiration is impeded and hence bimodal respiration momentarily eliminated (e.g., Graham et al. 1987). Reckoning from the spatial and temporal diversity of the evolved accessory respiratory organs, air breathing is an independently evolved attribute. Different lineages endeavored to look for solution to common selective pressures, especially hypoxia. Bimodal breathing is estimated to have evolved at least 67 separate times (Graham 1994). Regression of the accessory respiratory organs has occurred in many fish which have radiated into habitats where need for bimodal breathing is not intense. This has occurred in fish which live in stable, well-oxygenated waters, e.g., in the swift mountain streams, expansive freshwater lakes, or at great depths (Greenwood 1961; Graham 1994). Together with the ancestral crossopterygians which gave rise to the primitive amphibians, the dipnoans are the closest extant relatives of the modern tetrapods (e.g., Rosen et al. 1981; Duellman and Traub 1986; Panchen and Smithson 1988; Pough et al. 1989; Joss et al. 1991; Meyer and Dolven 1992). For this reason, the group continues to arouse substantial interest in biology. Respiratory modifications for air breathing were extensively found in most or all of the late Paleozoic fishes (Romer 1972) when the O_2 content of the water, e.g, in the Silurian period, was only 1.9 kPa. The earliest functional lungs are presently found in only the three genera (and six living Southern Hemisphere freshwater species) of lungfishes (Dipnoi), namely *Lepidosiren, Protopterus*, and *Neoceratodus*, in the chondrosteans (*Polypterus* and *Calamoichthys*), and the holosteans (*Amia* and *Lepisosteus*) (e.g., Burggren et al. 1985b; Sacca and Burggren 1982). Developmentally, these fish have been extremely conservative. They have changed very little since they attained the capacity for breathing air and hence serve as living examples for understanding the adaptive strategies and the backgrounds against which air breathing evolved. The South American *Lepidosiren* and the African *Protopterus*, genera which evolved in separate continents after the splitting of the Gondwana Land in the early Mezozoic but continued to live in similar habitats (respectively in the poorly oxygenated waters of the Amazonian basin and the derelict inland freshwater masses of the continental Africa) have paired, symmetrical internally sudivided lungs (Fig. 64; Klika and Lelek 1967; Hughes 1973; Hughes and Weibel 1976; Maina and Maloiy 1985; Kimura et al. 1987; Maina 1987a) and vestigial gills (Laurent et al. 1978; Laurent 1996). Both are obligate air breathers (Table 25) and have a better CO_2 buffering capacity of blood than the Western Australian *Neoceratodus forsteri*, a facultative air breather. *Protopterus aethiopicus* acquires 89% of its O_2 needs and eliminates 40% of CO_2 through the lungs (Johansen and Lenfant 1968; Lenfant and Johansen 1968; Table 24). *Neoceratodus* has a single, unpaired, thin-walled but internally subdivided lung (Grigg 1965) and possesses fully functional gills (Johansen and Lenfant 1967). The diameter of the pulmonary blood capillaries of *Neoceratodus* is 20 μm, a value which corresponds with the large (40 × 30 μm) oval erythrocytes (Gannon et al. 1983). In *Protopterus*, the posterior branchial arches carry a notable number of lamellae while the anterior ones, which provide shunt pathways for systemic circulation, are vestigial (Laurent 1996). To support CO_2 clearance, the functional branchial arches are continuously perfused (Lenfant and Johansen 1968; Laurent et al. 1978) even though pulmonary ventilation is intermittent. Encased in a cocoon of hard soil as the water dries up, *Protopterus amphibius* has been reported to survive in a semianimated (estivated) state for months to years as it episodically breathes air through a "snorkel" which connects the cocoon with the surface (DeLaney et al. 1974). The harmonic mean thickness of the blood-gas barrier in *Neoceratodus* ranges from 1.5 (Hughes 1973) to 2.5 μm (Gannon et al 1983), that of *Lepidosiren* is 0.85 μm (Hughes and Weibel 1976), *Protopterus* 0.37 (Maina and Maloiy 1985) and 0.85 μm (Hughes and Weibel 1976), and in *Polypterus* 1.22 μm (Zaccone et al. 1995).

To varying extents, the air-breathing fish rely on air or water for their O_2 needs (Table 25). The more terrestrial species are obligate air breathers. Among the actinopterygian fishes (Lauder and Liem 1983), only the polypterids have devel-

Table 24. Gas exchange in the fish lungs. (After Wood and Lenfant 1976)

Species/T (°C)	Total VO_2 ($ml\,min^{-1}kg^{-1}$)	Lung VO_2 (% of total)	Lung VCO_2 (% of total)	Tidal vol. (% of lung vol.)
Neoceratodus				
(18–20)	0.25	0	0	40–60
Protopterus				
(20)	0.3	89	40	60–80
Lepidosiren				
(18–20)	0.37	96	60	≤100
(25–28)	-	-	-	-
Lepisosteus				
(22)	0.65	73	40	40
(10)	0.30	0	-	-
Amia				
(10)	0.30	0	0	-
(20)	1.5	35	25	≤100
(30)	2.0	75	40	-

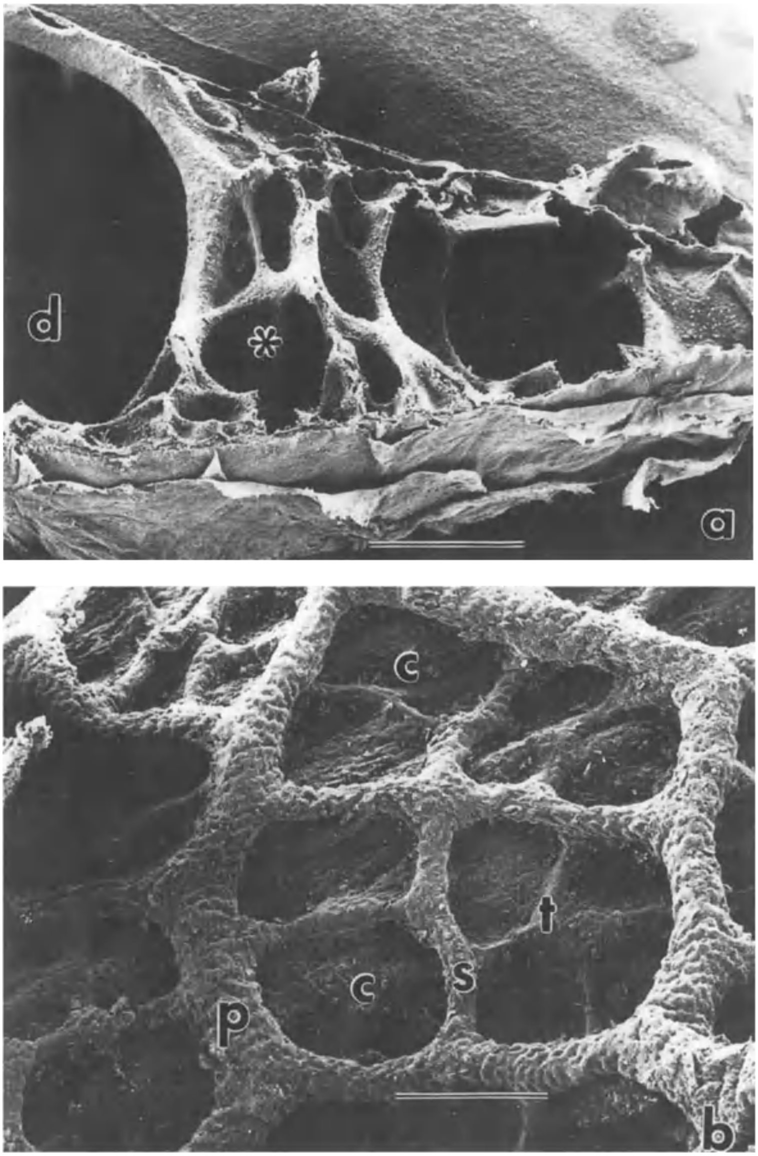


Fig. 64. **a** Cross section of the lung of the African lungfish, *Protopterus aethiopicus*, showing the eccentrically located air duct, *d*, and the gas exchange cells, *. **b** Closeup of the gas exchange air cells, *c*, of the lung of *Protopterus* which are formed by hierarchically arranged septa, i.e., the primary septa, *p*, secondary septa, *s*, and tertiary septa, *t*. The septa support the blood capillaries and contain the contractile and supporting tissue elements like collagen, elastic tissue, and smooth muscles. **a** *Bar* 0.67 mm; **b** 0.28 mm. (Maina 1987a)

Table 25. Oxygen uptake in some air-breathing fishes. The proportion of Vo_2 from water and air and the quotient between aquatic and aerial Vo_2 are also given. Numbers in parentheses are % proportions. (After Singh 1976)

T (°C)	Species	O_2 uptake (ml kg^{-1} h^{-1}) Aquatic	Aerial	Total	Aquatic/aerial
25	*Anabas testudineus*	52.62 (46.40)	60.80 (53.60)	113.42	0.865
25	*Clarias batrachus*	38.85 (41.60)	54.54 (58.40)	93.39	0.712
25	*Heteropneustes (=Saccobranchus) fossilis*	50.10 (59.25)	34.45 (40.75)	84.55	1.454
26	*Electrophorus electricus*	6.92 (23.07)	23.08 (76.93)	30.00	0.300
20	*Amia calva*	66.00 (68.75)	30.00 (31.25)	96.00	2.20
30	*A. calva*	30.00 (26.32)	84.00 (73.68)	114.00	0.357
22	*Lepisosteus osseus*	14.40 (24.66)	39.00 (75.34)	58.40	0.369
25	*Cobitis fossilis*	14.40 (19.51)	59.40 (80.49)	73.80	0.242
20	*Protopterus aethiopicus*	1.26 (11.05)	10.14 (88.95)	11.40	0.123
24	*P. aethiopicus*	5.80 (9.28)	56.70 (90.72)	62.50	0.102
18	*Lepidosiren* (Juvenile 150 g)	54.00 (63.83)	30.60 (36.17)	84.60	1.764
20	*Lepidosiren* (adult)	1.4 (4.36)	30.70 (95.64)	32.10	0.045

oped conspicuous lungs. The lungs are, however, relatively more primitive than those of the Dipnoi. The lungs of *Polypterus* are slender and lack discernible internal compartmentation (Klika and Lelek 1967; Hughes and Pohunkova 1980) with the right lung being better developed than the left. *Hoplostemum thoracatum* from the Paraguayan swamps, which travels overland across the grass from one pool to another (as they dry), swallows air continuously: O_2 is absorbed from the posterior part of the intestine which is profusely supplied with blood (Carter and Beadle 1931; Huebner and Chee 1978). The Indian catfish, *Clarias batrachus*, which subsists in shallow derelict waters at night emerges from the water to feed on earthworms (Dehadrai and Tripathi 1976). During such a time, it uses the suprabranchial chamber membranes and the labyrinthine organs for respiration. The organs are similar to those of *Clarias mossambicus*, an African catfish (Figs. 65,66; Maina and Maloiy 1986). Other Indian species such as the climbing perch, *Anabas testudineus*, and the Cuchia eel, *Amphipnous cuchia*, are highly terrestrial, spending much of their time out of water (Munshi and Hughes 1992). *Anabas* (weighing 29 to 51 g) acquires about 53.6% of its O_2 need from air (Hughes and Singh 1970b). Due to the lower metabolic rate and the relatively greater

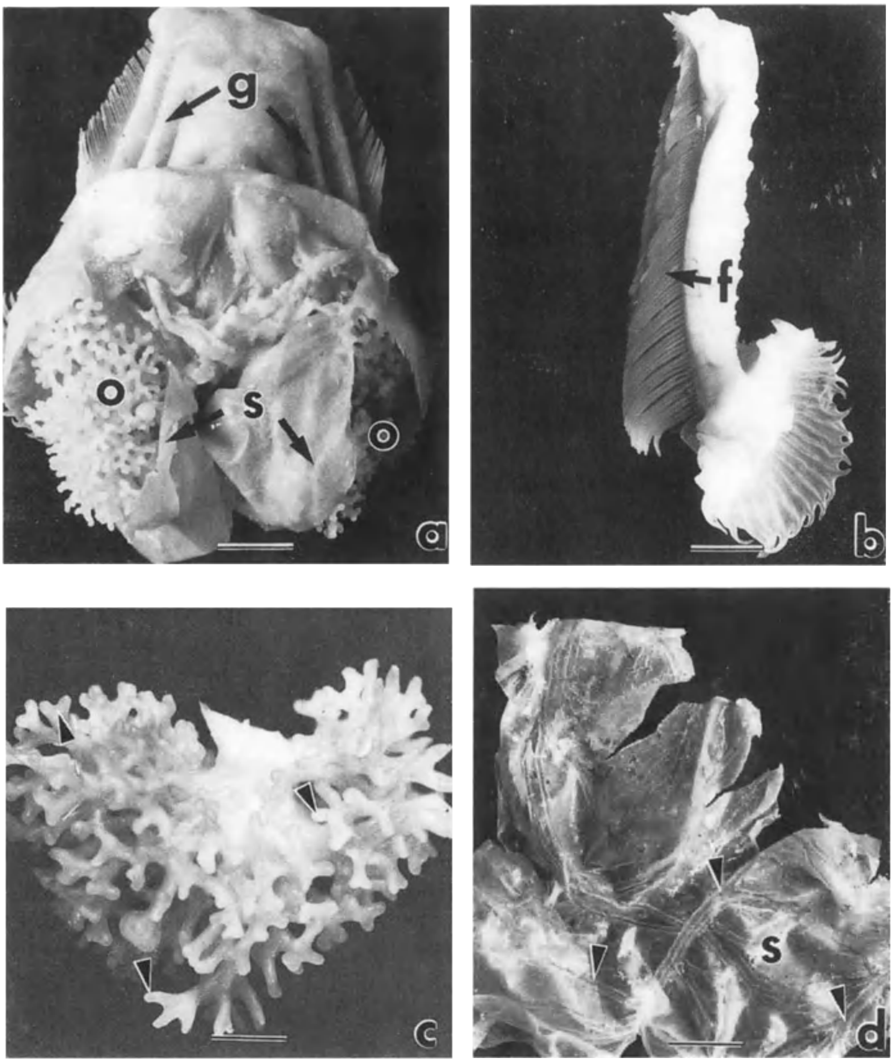


Fig. 65. **a** Respiratory organs of the catfish, *Clarias mossambicus*, showing the gills, *g*, labyrinthine organ (*o*) and suprabranchial chamber membrane, *s*. **b** A gill arch showing gill filaments, *f*. **c** Tree-like labyrinthine organ which terminates in rounded knobs, ➤. **d** Suprabranchial chamber membrane which has many blood vessels, ➤. **a** *Bar* 0.2 mm; **b** 0.1 mm; **c** 0.15 mm; **d** 0.15 mm. (Maina and Maloiy 1986)

amount of dissolved O_2, at lower temperatures (17 to 20 °C), specimens of *Anabas* weighing up to 30 g survive well for a few months without air breathing but at higher temperatures (30 to 31 °C) even smaller fish (10 to 15 g) succumb within 24 h (Dube 1972). *Amphipnous* has a particularly high O_2 capacity exceeding 20 vol% and high hemoglobin-O_2 affinity (Lomholt and Johansen 1976): after 30 min

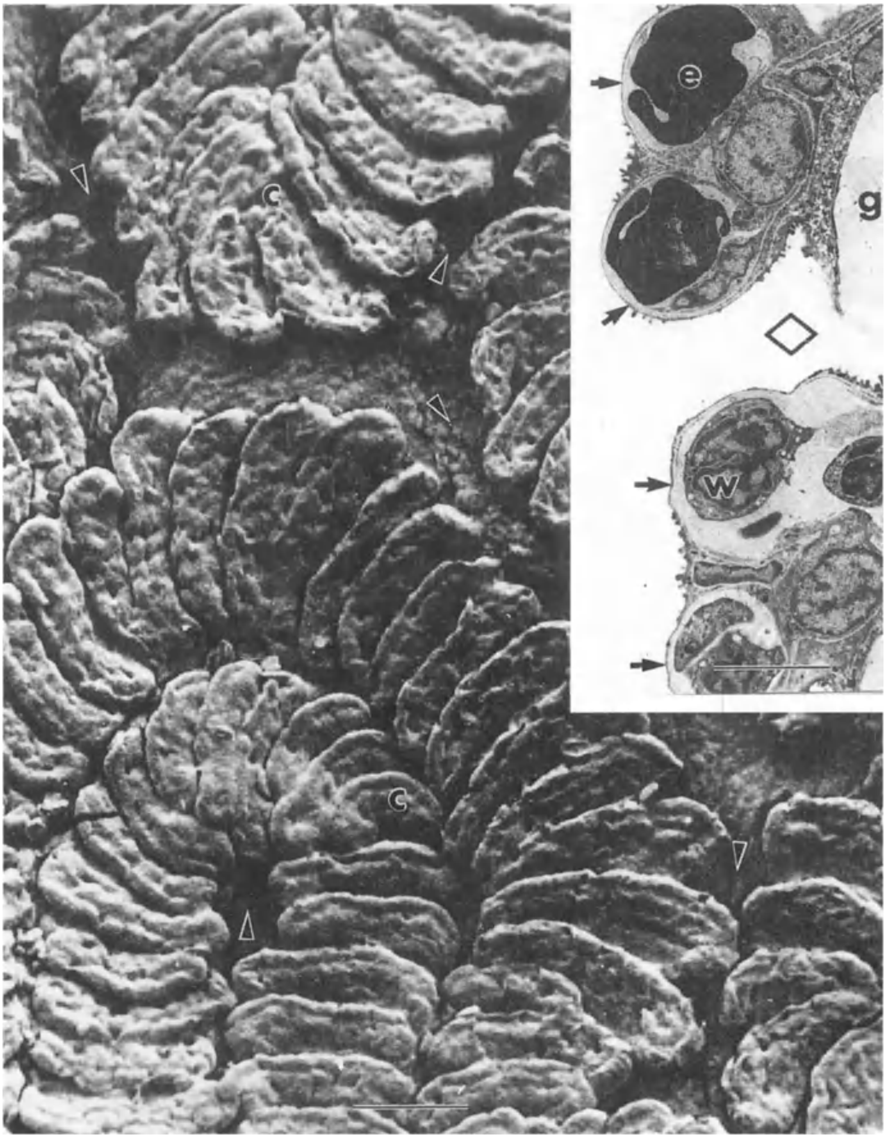


Fig. 66. Views of the surface of the labyrinthine organ of the African catfish, *Clarias mossambicus*, showing the intense vascularization in form of surface transverse capillaries (*c*) which are separated by bare tracts, ➤, and ◇ (*inset*), areas that contain mucus cells, *g* (*inset*). ➜ (*inset*), transverse capillaries, *e*, erythrocytes contained in the transverse capillaries; *w*, white blood cell. *Bar* 13 μm; *inset* 10 μm

of apnea, only a modest drop in arterial saturation (90 to 60%) occurs in the fish. The secondary reduction of the suprabranchial chambers and the increase in the gill respiratory surface area in some species of *Dinotopterus* (Clariidae) in the deep Lake Malawi and that in *Sandelia capensis*, an anabantoid fish in the South

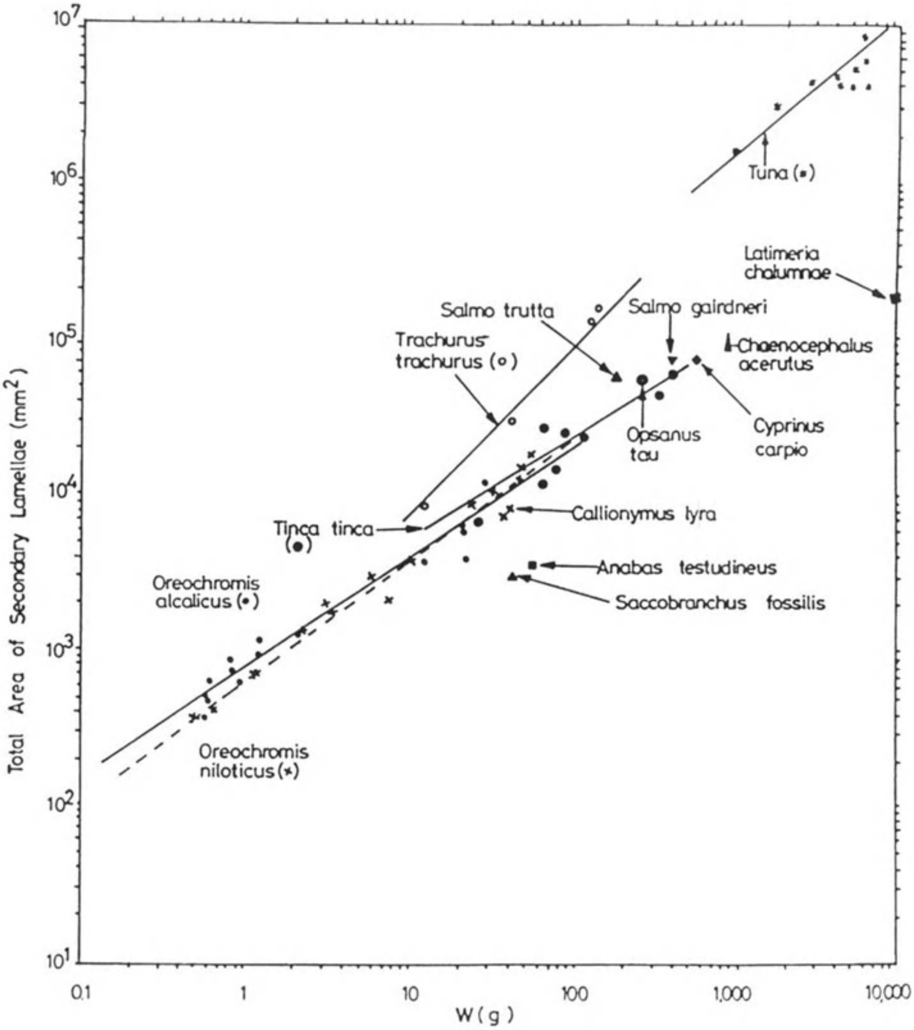


Fig. 67. Plot between total respiratory surface area and body mass in different species of fish. Energetics, habitat, and mode of respiration determine the development of the gas exchangers. The tuna, a highly energetic fish, has remarkably extensive gill surface area while in the air-breathing fish, gill development is generally inhibited. In the air-breathing fish, e.g., *Anabas testudineus* and *Saccobranchus fossilis*, the accessory respiratory organs have a high diffusing capacity of O_2. This compensates for the reduction in the development of the gills. Data on *Oreochromis* from Maina et al. (1996a) and those of the other species from Hughes and Morgan (1973) and other publications

African Cape region (Barnard 1943), may be viewed as a reversion to totally aquatic respiration in fish formerly adapted to aerial breathing. A greater spacing of secondary lamellae, an adaptation which prevents gill filament adherence and collapse in air, characterizes most air-breathing fish (e.g., Todd and Ebeling 1966; Hughes and Morgan 1973). In marine air-breathing fish, this situation occurs in *Sicyases* (Ebeling et al. 1970) and in the mudskipper, *Periophthalmus vulganris* (Singh and Munshi 1968). In *Periophthalmus schlosseri* (Schöttle 1932), the first gill arch is replaced by a well-vascularized epithelium and the fish has only three pairs of functional gill arches. In *Gillichthys* (Todd and Ebeling 1966), the gills are short and the total respiratory surface area is less than in those species which do not breathe air. The more amphibious fish, e.g., *Mnierpes* (Graham 1973), have stronger gills (with a smaller surface area) which are less susceptible to collapsing out of water than in aquatic ones, e.g., *Blennius pholis* (Milton 1971). A smaller gill surface area reduces the rate of loss of O_2 through the gills into the hypoxic external medium. Shunting of blood within the gill system reduces the energetic cost of branchial perfusion (Satchell 1976; Randall et al. 1981; Smatresk and Cameron 1982a,b). The bimodal breathers in general have smaller respiratory surface area than the entirely water-breathing types (Figs. 67,68, Table 26). The extremely thin blood-gas barriers of the accessory respiratory organs provide a greater diffusing capacity than the gills (Table 26; Maina and Maloiy 1986). The

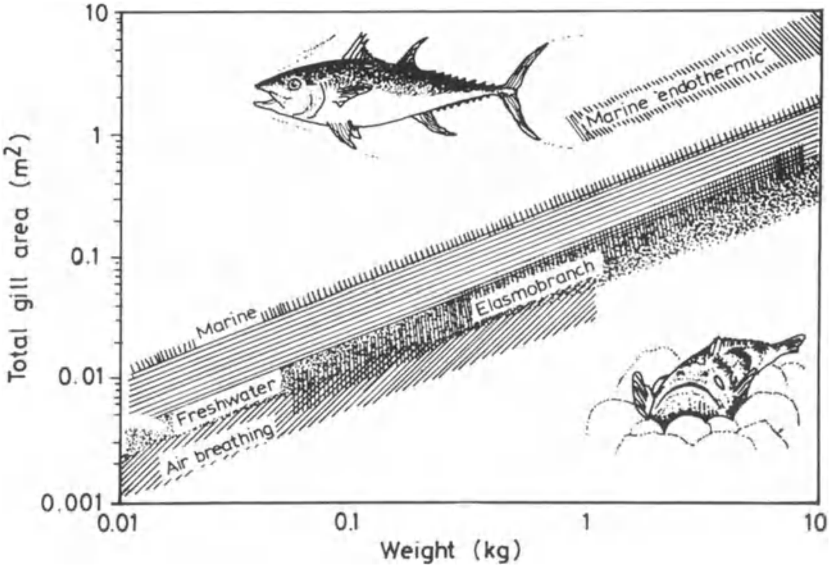


Fig. 68. Correlation between total gill surface area and body mass in fish living in different waters and exhibiting different modes of respiration. Marine endothermic fish which include the tuna have relatively high values while air breathers, especially the obligate ones, have low values. (Pelzenberger and Pohla 1992)

Table 26. Morphometric pulmonary diffusing capacity of the tissue barrier (Dt) and measurements for respiratory surfaces of the gills and air-breathing organs of some air-breathing fish. Data on some water-breathing fish and invertebrates are included for comparison

Species/organ	Body wt. (g)	Thickness of tissue barrier (μ)	Surface area ($mm^2 g^{-1}$)	Dt ($ml\,O_2\,min^{-1}\,mmHg\,kg^{-1}$)
Air-breathing fish				
Anabas testudineus	100			
All gills		10.00	47.2	0.0071
Labyrinthine organ		0.21	32.0	0.2286
Heteropneustes fossilis	100			
All gills		3.58	57.7	0.0242
Air sac		1.60	30.7	0.0288
Skin		98.00	200.0	0.0031
Clarias mossambicus	458			
All gills		1.97	19.30	0.0213
Suprabranchial chamber		0.313	7.79	0.050
Labyrinthine organ		0.287	4.65	0.070
Channa punctatus	–			
All gills		2.033	71.88	0.0530
Suprabranchial chamber		0.780	39.17	0.0753
Labyrinthine organ		–	–	–
Amphipnous cuchia	–			
Air sac		0.435	4.84	0.0165
Skin		0.44	227.5	–
Channa striatus				
Suprabranchial chamber	–	1.359	–	–
Clarias batrachus	–			
Labyrinthine organs		0.55	–	–
Water-breathing fish				
Tinca tinca	141	2.47	228.0	0.1493
Salmo gairdneri	35	4.30	260.0	0.1180
Tuna	100	0.50	2000.0	6.000
Opsanus tau	100	5.00	210.0	0.0630
Latimeria chalumnae	10 000	5.00	18.9	0.0057
Invertebrates				
Carcinus maena	100	5.00	744.0	0.0540
Nautilus macromphalus	135	10.00	930.0	0.1395

Sources of data: *Anabas*, Hughes et al. (1973); *Heteropneustes*, Hughes et al. (1974); *Clarias mossambicus*, Maina and Maloiy (1986); *Carcinus*, Scammell and Hughes (1981); *Nautilus*, Perseneer (1935); rest Hughes and Morgan (1973).

fact that the gills have been widely retained in virtually all transitional breathing fish shows their importance for CO_2 clearance in water. In amphibians, the change to terrestriality and air breathing is accompanied by greater dependence on the lungs for gas exchange (Lenfant and Johansen 1967).

Chapter 6

Air Breathing: the Elite Respiration

> *"The external gas exchangers that have evolved in higher organisms – fish gills, bird lungs, and alveolar lungs of amphibia, reptiles, and mammals have some basic features in common, irrespective of the different principles that determine their functioning in detail."* Weibel (1984a)

6.1 Is the Surface of the Lung Dry, Moist, or Wet? Do Real Air Breathers Exist?

Water forms an important structural and functional constituent of the intercellular and intracelular lung tissue (e.g., Bastacky et al. 1987). Furthermore, a hydrated layer lines the air spaces of the lung (e.g., Fishman et al. 1957; Cantin et al. 1987; Chinard 1992). In the larger air spaces, the aqueous layer is comprised mostly of mucus, a glycoprotein-containing phase which is about 98% water (e.g., Sturgess 1979). The mucus forms an important source of moisture which humidifies the inhaled air, traps solid particles, and protects the ciliated epithelium. At the alveolar level, the hydrated layer occurs in form of an aqueous subphase in which proteins, carbohydrates, ions, and surfactant are dissolved. In the vertebrate lungs, where detailed investigations have been carried out, gas exchange occurs across an extracellular alveolar fluid film which lines the surface. The lining has been lucidly demonstrated by Finley et al. (1968), Weibel and Gil (1968), Kikkawa (1970), Bastacky et al. (1987, 1993), and Hook et al. (1987). In the airways, the thickness of the surface liquid lining is 20 to 150 μm (Widdicombe 1997) while on the alveolar surface, the thickness ranges from 0.1 to 0.24 μm (Weibel and Gil 1968; Bastacky et al. 1993, 1995; Stephens et al. 1996). In the human lung, it has been estimated physiologically (e.g., Rennard et al. 1986) that the epithelial lining fluid (ELF) makes up 20 to 40 ml while through morphometric techniques (e.g., Untersee et al. 1971; Gorin and Steward 1979), the ELF was estimated to range from 15 to 70 ml. The alveolar fluid layer contributes significantly to the gas exchange function of the lung. During strenuous exercise, accumulation of extracellular fluid on the surface of the lung is thought to cause a transient decrease in the membrane-diffusing capacity of the lung (Manier et al. 1991). In a delicate process which includes regulation of hydrostatic and colloidal osmotic forces across the capillary wall, the pulmonary surface is kept moist but not flooded (Levine et al. 1965; Fishman 1972). In the mammalian lung, 1 to 4% of the blood fluids lost to the surrounding tissue is efficiently carried away by the lymphatic vessels (Comroe 1974). When introduced into the alveoli, water quickly passes into the pulmonary blood capillaries (Effos and Mason 1983; Jones et al. 1983; Effros et al. 1992; Grimme et al. 1997). This is because the pulmonary blood capillary (microvascular hydrostatic) pressure of about 1.1 to 1.2 kPa (which is inclined to filter blood into the alveoli) is always well below the colloidal (osmotic) pressure of the plasma proteins of about 3.3 to 4 kPa which draws fluid from the alveoli into the blood (Comroe 1974). Normally, the lung would be expected to be dry and to absorb but not filter fluid in its circulation.

Water is not a foreign factor in the lungs of the air-breathing vertebrates. Due to their extensive surface area, during prenatal development, the lungs play an important role in the production of the amniotic fluid (Setnikar et al. 1959). During fetal life, the lung is filled with liquid that flows into the developing air spaces in response to Cl^- secretion across the epithelium of the respiratory tract (Olver and Strang 1974). In sheep, the rate of production may be as high as about $2\,ml\,kg^{-1}h^{-1}$ (Normand et al. 1971) and at birth the total pulmonary fluid is estimated to be as much as $30\,ml\,kg^{-1}$ (Normand et al. 1971). Experimental or congenital obstruction of the trachea or the bronchi leads to intrapulmonary accumulation of fluid and overdistension of the lung (Potter and Bohlender 1941). In some animals, e.g., the turtles, which have relatively high arterial pulmonary blood pressures and low osmotic pressure of the plasma proteins (White and Ross 1965; Shelton Burggren 1976), water may constitute a significant portion of the O_2 diffusional pathway. In *Pseudemys scripta*, at a blood flow rate of 12 to $14\,ml\,kg^{-1}min^{-1}$, during ventilation, 20 to 40% of the fluid may be left behind in the nonvascular part of the lung tissue (Burggren 1982b): the net loss of plasma into the tissues in the ventilated reptile lung is 10 to 20 times greater than in the mammalian lung. Well-developed intercellular junctions in the air-blood barrier were demonstrated in the lung of the turtle, *Pseudemys* by Bartels and Welsch (1983) by freeze fracture electron microscopy: they may account for the remarkable "leakiness" of the pulmonary capillaries of the turtle's lung. It is interesting to note that in insects, the terminal tracheoles contain fluid which is osmotically absorbed into the surrounding cells or released in the air tubules depending on the metabolic state of the tissues (Wigglesworth 1953). In mammals, about 2 to 3 days before birth (Kitterman et al. 1979; Dickson et al. 1986) or during labor (Bland et al. 1982; Brown et al. 1983), pulmonary filtration stops and absorption of the intrapulmonary fluid starts. Both processes are influenced by the level of circulating epinephrine or isoproterenol (e.g., Walters and Olver 1978), adrenaline (Brown et al. 1983), or Na^+ flux out of the lung lumen (Cotton et al. 1983; Bland 1990; Chapman et al. 1994). In the newborn calf, the mean pulmonary arterial pressure drops from 8.7 to 4 kPa in the first 6 h of birth (Reeves and Leathers 1964). The intrapulmonary fluid is physically expelled through: (1) the upper respiratory airways due to pressure exerted on the fetal thorax during transit through the pelvic canal (Borell and Fernstrom 1962; Karlberg et al. 1962); (2) absorption into the lymphatics (Humpreys et al. 1967; Strang 1967; Gonzalez-Crussi and Boston 1972); and (3) transfer by the pulmonary capillaries (Egan et al. 1975; Hutchison et al. 1985). The fluid remaining in the lung after delivery is cleared from the lung within a couple of hours (Humpreys et al. 1967; Fletcher et al. 1970; Adams et al. 1971; Bland et al. 1980).

The general perception of the surfaces of the internalized gas exchangers of the terrestrial air breathers as dry organs needs to be reconsidered. It is more realistic to consider them as moistened but not flooded. Oxygen does not diffuse efficiently across dry tissue barriers. In the toad (Dupre et al. 1991), dehydration reduces cutaneous gas diffusion capacity. Owing to a dependence on water for efficient respiration across the lungs, it could be argued that air breathing has not yet strictly evolved. However, since terrestrial animals seek and take up O_2 from air and discharge CO_2 into the same, according to the general definition, such animals are recognized as air breathers. This also includes those insects which have secondarily invaded water and extract O_2 from air bubbles regularly ferried from the surface (Sect. 6.12). It is only if an air breather was to "aspirate" water into its lungs, a rather rare retrogressive move which has, nevertheless, developed in some simple animals, e.g., aquatic pulmonate gastropods (Sect. 5.6.1) after the ctenidia (gills) were lost and the mantle cavity converted into a "water lung", that an animal is categorized a water breather.

About 1 week before hatching, in the loggerhead turtle, *Caretta caretta* (Perry et al. 1989a), and during stage one of development of *Salamandra salamandra* (Goniakowska-Witalinska 1982) the lungs are filled with water. The intrapulmonary fluid is removed soon after hatching (Gatzy 1975) and in sheep soon after birth (Strang 1977; Bland 1990). It has been postulated that the flooding of the lungs with fluid provides biomechanical support necessary for proper development of the air passages and spaces (Alcorn et al. 1977; Maloney 1984). It is envisaged that after the contraction of the smooth muscles, the pressure in the fluid-filled lung increases, leading to an outward formation of the air cells (e.g., Marcus 1937). In deviation from the moist surface requirement, some animals such as the minute aerial arthropods are known to exchange respiratory gases through a dry cuticle (Krogh 1941). The same process probably occurs in the book lungs of some spiders (Zoond 1931; Herreid et al. 1981; Strazny and Perry 1984). The low O_2 demands in such animals may account for the adequacy of O_2 transfer across a dry surface.

6.2 Lung and Swim Bladder – Which Developed Earlier and for What Purpose?

Swim bladders and lungs are said to be homologous (Fänge 1983). Lungs are envisaged to have evolved in the Paleozoic freshwater vertebrates as a means for adaptation to hypoxic stress (e.g., Romer 1972; Graham et al. 1978a,b). All bony fish (Osteichthyes) have a swim (air) bladder at least at one stage of their development (e.g., Marshall 1960). In most contemporary fish, the swim bladders are hydrostatic with no discernible respiratory role while some teleosts breath air by a lung or a swim bladder (Fänge 1983; Alexander 1993). The bladder is historically interesting for the following reasons: (1) in some fish, the organ serves as an auxiliary respiratory organ and hence its biology may shed some light on the evolution of the respiratory organs and processes, (2) its role as a hydrodynamic organ helps to explain some of the adaptive processes which were essential for subsistence in water (a medium of relatively higher viscosity) and the necessary subsequent postural and locomotory biomechanical adjustments for living on land, and (3) the capacity of the organ to passively secrete and concentrate gases to several hundred atmospheres of pressure far in excess of those in blood and in the external environment (e.g., Scholander 1954; Marshall 1960; Fänge 1976; Kobayashi et al. 1989a,b) is a most intriguing and unique biophysical phenomenon. Recent works and reviews on this aspect include those of Gerth and Hemmingsen (1982), Fänge (1983), Kobayashi et al. (1989a,b), and Pelster and Scheid (1992a,b). It is now generally thought that a multiplicative salting-out effect in the countercurrent system of the rete mirabile (e.g., Pelster et al. 1988c); (Fig. 39) explains the passive secretion of gases into the swim bladder. The lactate acid which is produced by glucose metabolism in the gas-gland epithelium (Pelster and Scheid 1991, 1993; Figs. 39,70) is secreted into the blood (D'Aoust 1970; Kobayashi et al. 1989a,b; Pelster et al. 1989), where it acidifies the blood, increasing the blood PO_2 by Bohr and Root effects, PCO_2 by conversion of HCO_3^- into CO_2, and the inert gases by reducing their physical solubility (= salting-out effect) (Pelster et al. 1988c). Back diffusion of CO_2 in the rete mirabile increases the blood pH, enhancing the secretion of O_2 into the swim bladder (Kobayashi et al. 1990). Oxygen constitutes the greater proportion up to 95% of the gas mixture secreted into the swim bladder (Wittenberg 1965) with N_2, CO_2, and rare gases like argon constituting lesser proportions (Tait 1956). The PO_2 in the swim bladders of fish which live in great depths may exceed 150 atm (Scholander and van Dam 1953). In such cases, the PO_2 in the swim bladder may be as much as 10 000 times that in the surrounding water (Kanwisher and Ebeling 1957). Considering that all the gases must in the first instance be derived from water, to generate such a pressure differential calls for a remarkably efficient concentrating process. In the European eel, *Anguilla anguilla*, under hypoxic conditions, gas deposition and blood flow through the rete mirabile were significantly reduced (Pelster and Scheid 1992c). Fish which live at depth may required a substantial amount of work to secrete air into a swim bladder against partial pressure gradients (Alexander 1982). In fish such as the swordfish, *Xiphius*, which have been recorded to surface from a depth of 100 m in less than 5 min (Carey and Robinson 1981) and the lantern fishes which are recorded to commute between 300 and 50 m at rates in order of 160 $\mathrm{km\,h^{-1}}$ (Barham 1966), the process must be remarkably efficient.

The chronology of the evolvement of the lung and the swim bladder and whether the two organs are homologous is an ongoing debate (e.g., Romer 1972; Fänge 1976; Liem 1987a). While the early evolution in potentially O_2-deficient waters may be a pointer to an essential initial respiratory role (e.g., Liem 1991), on the contrary, subsistence in the pelagic marine well-oxygenated waters emphasizes a predominant hydrostatic function (Liem 1987a). It is conceivable that swim bladders may have been necessary to offset the increase in weight with the development of the bony skeleton in fish (Alexander 1993). However, the hydrodynamic and respiratory roles of the swim bladder are by no means mutually exclusive and neither can the possibility that the two organs evolved independently of each other be discounted based on the presently available data (e.g., Liem 1989; Hedrick and Jones 1993; Alexander 1993). It is plausible that an initial simple saccular air-containing organ may have served both roles, as evident in some of the Central American catfishes (e.g., Gee 1976, 1981) and the subsequent functional and structural differences may have arisen to meet specific environmental demands. In *Hoploerythrinus unitaeniatus*, a small tropical fish, during the periods between the respiratory cycles, the concentration of O_2 in the swim bladder is reduced to 8%, indicating a very high degree of extraction of molecular

O_2 from the organ (Carter and Beadle 1931). The absorption rate of O_2 from the swim bladder of the mudminnow, *Umbra limi*, is very high (Safford-Black 1944). Some teleosts in which the swim bladder functions as a lung include *Arapaima* (Osteoglossidae), *Gymnarchus* (Mormyridae), *Erythrinus* (Characinidae), *Umbra* (Esocidae), *Notopterus* (Notopteridae), and *Lepisosteus* (Potter 1927; Dehadrai 1962; Fänge 1976). *Gillichthys* consumes O_2 from its physoclistous (closed) bladder to support metabolism during the short transitional period (average 17 min) from aquatic to aerial respiration (Todd and Ebeling 1966). Through a buccal force pump mechanism, physostomatous fish (i.e., those with open bladders) which live close to the surface of the water inflate their bladders with air gulped from the surface of the water (Fänge 1976). Some physoclistic fish are known to use a pneumatic duct during their larval stage for the first filling of their bladders (e.g., Jacobs 1938). In *Erythrinus unitaeniatus*, the middle region of the physostomatous bladder is well vascularized and is used for gas exchange (Carter and Beadle 1931). The tarpon, *Megalops*, regularly ventilates its physostomatous swim bladder even in normoxic water (Böhlke and Chaplin 1968). The tarpon's swim bladder has been described as being lung-like since it has alveolar-like tissue (Shlaifer and Breder 1940): the swim bladder facilitates aerial respiration, a process which augments the tarpon's aquatic respiration and enhances the fish's metabolic scope of activity (Johansen 1970). In the holostean air-breathing fish, *Amia calva*, and the teleost, *Arapaima gigas*, gas exchange is effected through a physostomatous swim bladder which is supplied with blood from the dorsal aorta, coeliac, or mesenteric arteries. While not directly involved in gas exchange, the physoclistous swim bladder of *Dormitator* in hypoxic water generates positive buoyancy, which enables the fish to expose its vascularized frontal skin to air (Todd 1973). The swim bladder of the teleost, *Oreochromis alcalicus grahami*, a small cichlid fish which lives in the alkaline lagoons of the volcanic Lake Magadi of Kenya (Wood et al. 1994; Maina et al. 1996b), has a well-vascularized swim bladder (Figs. 69,70); (Maina et al. 1996b). The bladder is probably used for gas exchange during the night when the water is virtually anoxic (Narahara et al. 1996): on exertion, e.g., after being chased with a net, the fish are observed to skim the surface of the water, probably taking air into the bladder or ventilating the gills with the better oxygenated top layer of water. In the physostomatous bladders, the neuromuscular mechanisms involved in the intake and expulsion of air are not well known. Inspiration may be effected by the buccal force pump while expiration may be brought about by the activity of the smooth muscles of the pneumatic duct of the bladder. In *Hoploerythrinus*, the pneumatic duct is notably wide and muscular (Lüling 1964) and in the eel, *Anguilla anguilla*, the duct is adapted for gas exchange by diffusion and has a distinct circulatory system (Fänge 1953). In most physostomatous fish, e.g., in the salmonids (Fahlén 1971), cyprinids (Plattner 1941), the electric eel (Evans 1929), and notopterids (Müller 1950), the entrance of the pneumatic duct to the esophagus is guarded by smooth and striated muscle sphincters. Dependent on species, gas is released through the pneumostome by deflation. This occurs by a reflex action, the so-called gas spitting reflex, which is initiated by a reduction of the external pressure and/or by nervous excitation (Fänge 1976). The elasticity of the bladder wall due to contraction of the well-developed smooth muscles (Maina et al. 1996b) and contraction

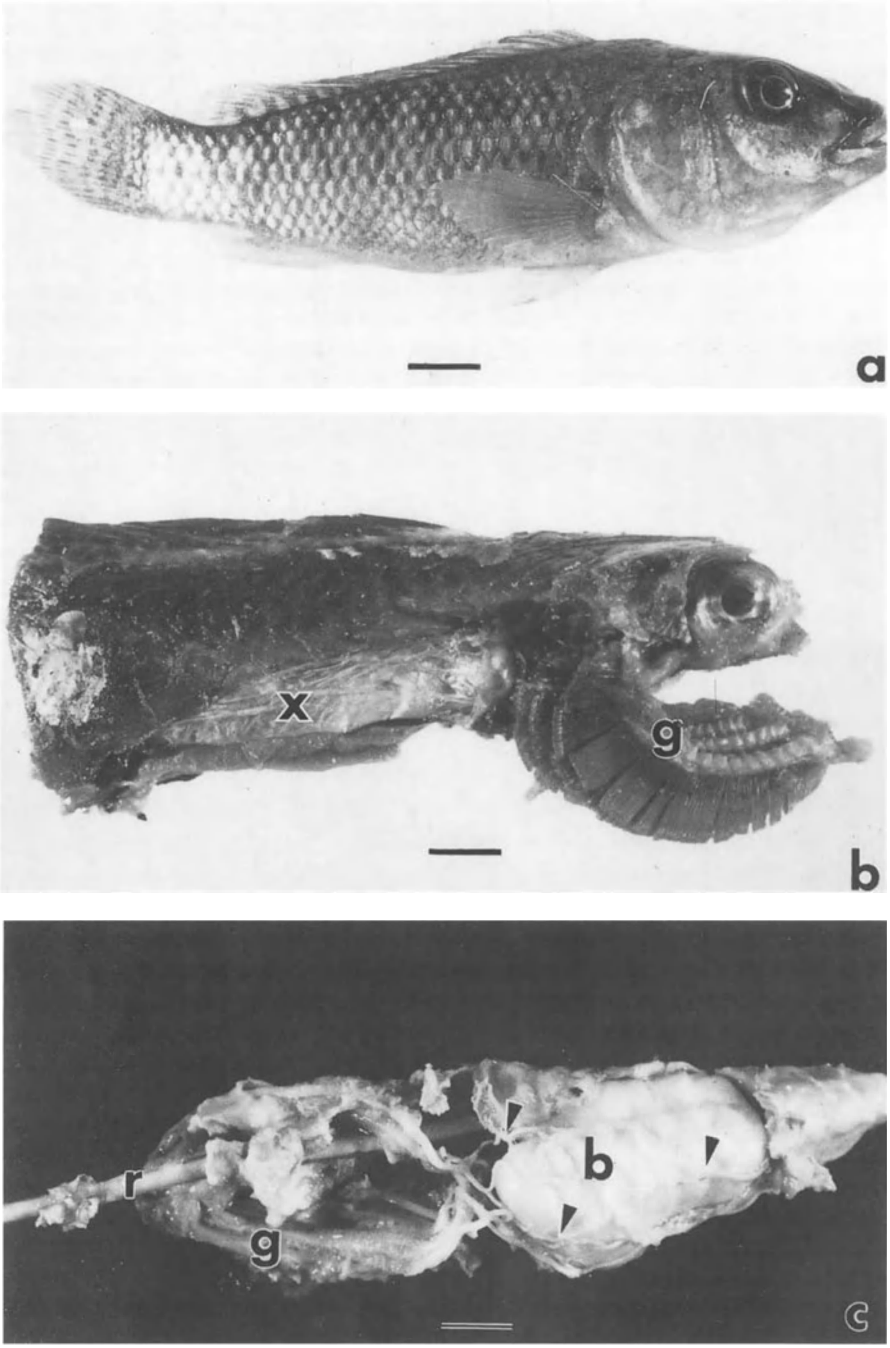


Fig. 69a–c

of body wall muscles (Evans and Damant 1928) may help in the release of gases. In an aquatic animal, the use of a gas exchanger for hydrostatic control is inefficient since when O_2 is removed and little if any CO_2 is secreted back, the animal becomes less buoyant and sinks (Gee 1976; Gee and Graham 1978). The animal then has to surface to refill the lung. Oxygen consumption (i.e., removal of O_2 from the lung) has to be synchronized both with hydrostatic requirements and respiratory frequency. During hypoxic episodes, the cephalopod mollusk, *Nautilus* (often referred to as a living fossil due to its multichambered shell which resembles that of extinct animal forms from the early Paleozoic) draws O_2 from the buoyancy chambers of the shell (Boutilier et al. 1996): in a 459-g (fresh weight) *Nautilus* at 18 °C, the shell volume is $100\,cm^3$, the O_2 store in the shell is $6.9\,cm^3$ and a partial pressure gradient of O_2 of 7.3 kPa exists. In a hypometabolic state, it is estimated that the O_2 stores in the shell should support metabolic rate for as long as 6 h. In the European eel, *Anguilla anguilla*, 83% of O_2 removed from the blood was secreted into the swim bladder and only 17% was used for metabolic purposes (Pelster and Scheid 1992c).

The swim bladder of the teleosts may have evolved independently from the gas chambers of *Polypterus* and the lungfishes (Dipnoi), a respiratory organ having been more urgent for gas exchange in the early hypoxic aquatic medium. On the other hand, it has been surmised that the swim bladder may have evolved entirely for buoyancy control and in some cases, e.g., in the Dipnoi, secondarily acquired a respiratory role. The lungs of the Dipnoi and the ancestral actinopterygian fish such as *Amia, Polypterus*, and *Lepisosteus* are considered to be homologous with the swim bladders of fish (Packard 1974). In teleosts, Dipnoi and Polypteridae, the swim bladder and the lungs originate as outgrowths from the wall of the foregut, the primodial air-sac/lung becoming evident very early in development (Packard 1974). Both organs are enervated by branches of the vagus and sympathetic nerves. However, this is as far as the similarity between the two organs goes. The swim bladder: (1) arises from the dorsal or lateral walls of the foregut (e.g., Goodrich 1930) and the lungs from the floor (ventral aspect) of the pharynx, (2) the lungs receive left and right pulmonary arteries which originate symmetrically from the last pair of epibranchial arteries but the swim bladder is supplied with arterial blood from the aorta (Goodrich 1930), (3) the lungs remain connected to the pharynx while physoclistic swim bladders totally lose connection with it, and (4) the lungs are generally lined by a surface active factor, a complex mixture of phospholipids, neutral lipids, and proteins. Due to their ventral location and the inherent problems of balance which would accompany such an organ, the lungs may have all along been respiratory while the dorsally located swim bladder could combine hydrostatic and respiratory roles. In teleosts, the swim bladder is mainly

◄

Fig. 69. **a** *Oreochromis alcalicus grahami*, a small tilapiine cichlid fish which lives in the highly alkaline Lake Magadi of Kenya where there are dramatic diurnal fluctuations of levels of O_2 in water. **b** The swim bladder, *x*, and the gills, *g*, are very well developed. **c** Latex rubber cast of the gills, *g*, and the swim bladder, *b*, showing the air way, marked by a cannula, *r*, and vascular connections, ➤, between the two organs. **a** Bar 7 mm; **b** 5 mm; **c** 3 mm. (Maina et al. 1996b)

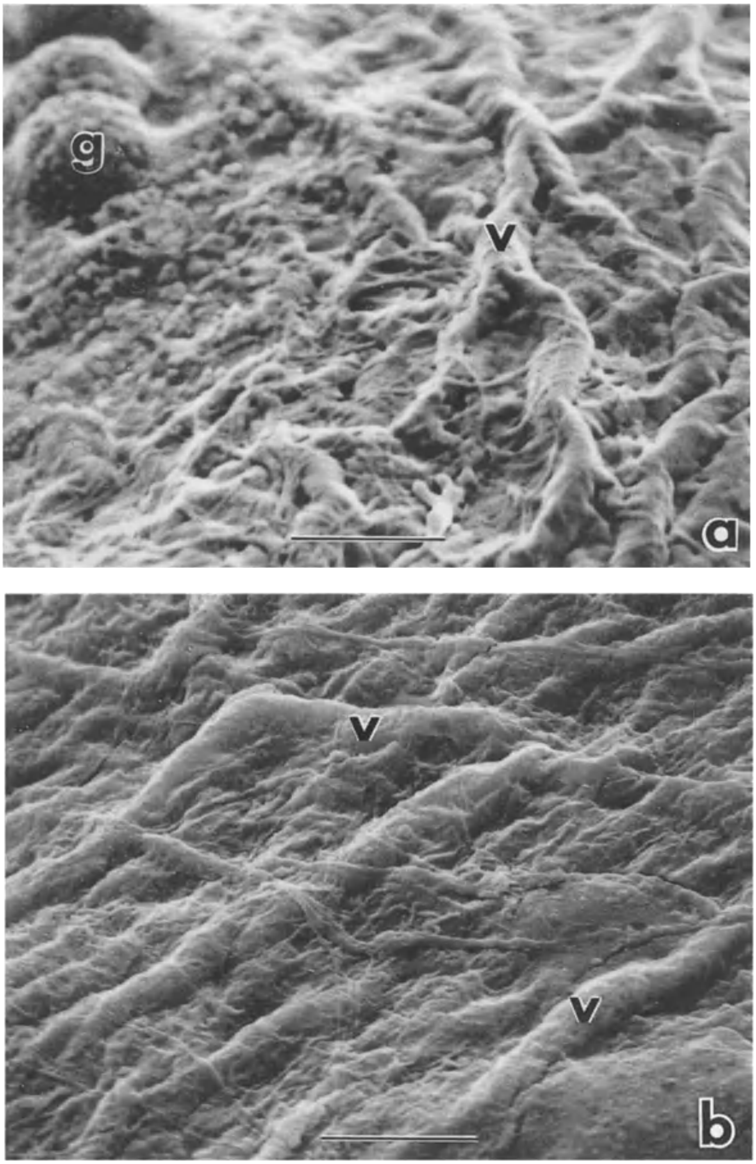


Fig. 70a,b. Views of the surface of the swim bladder of *Oreochromis alcalicus grahami*, showing the profuse vascularization, *v*; *g* gas-gland cells. It is probable that the physostomatous swim bladder in this species may be utilized for gas exchange during extreme hypoxia **a** Bar 20 μm; **b** 17 μm. (Maina et al. 1996b) a hydrostatic organ and is thus structurally much less complex than the Dipnoan (Fig. 64) and Polypteridae lungs which are essentially respiratory (Klika and Lelek 1967). The nonseptate saccular lungs of the urodele amphibians, the salamanders, e.g., *Cryptobranchus* and *Necturus*, appear to be largely hydrostatic (Noble 1931; Guimond and Hutchison 1973b). However, the well-developed finely subdivided lungs of some aquatic frogs, e.g., *Xenopus laevis* and *Pipa pipa* (Czopek 1962a; Goniakowska-Witalinska 1995), which inhabit hypoxic waters and the salamanders, *Amphiuma tridactylum* (Stark-Vancs et al. 1984) and *Salamandra salamandra* (Goniakowska-Witalinska 1978; Meban 1979), which have an extensive surface area, are predominantly respiratory.

6.3 Evolution of Air Breathing and Terrestriality: the Limitations

In virtually all terrestrial habitats, the atmospheric air is never 100% saturated with moisture. On this account, terrestrial habitation is accompanied by an enduring conflict between the need to procure O_2 and the necessity to preserve water. Extended emergence from water was impossible until the two processes could be harmonized. Conservation of water entailed development of an impermeable surface cover and invagination of the respiratory organs (e.g., Hadley 1980; Loveridge 1980; Quinlan and Hadley 1993). Terrestrial air breathers are in constant danger of desiccation especially through respiratory water loss. No other internal organ is in more intimate contact with the external environment as the lung. Everyday, about 12000 l of air are filtered by the human lung and 6000 l of blood perfuse it (Burri 1985). The interaction occurs over a surface area of nearly $150\,m^2$ across a blood-gas barrier $0.6\,\mu m$ thick (Gehr et al. 1978). In most respects, air breathing is a less complicated process than water breathing. Whereas in air breathing only O_2 and CO_2 are exchanged, in water, superimposed on the gas exchange process is ionic exchange and elimination of end products of nitrogen metabolism (e.g., Goldstein 1982; Zadunaisky 1984). Even if all other factors were held constant, gill respiration should energetically be more demanding than air breathing owing to the fact that except for the animals which are iso-osmotic to seawater, energy has to be expended to selectively regulate ionic flux. A large number of mitochondria rich cells (= ionocytes = chloride cells), occur, e.g., in fish (Fig. 50; Maina 1990a, 1991) and the crab gills (Maina 1990b; Figs. 13,71). Aquatic animals are exposed to a medium which has the same heat capacity as blood compared with the air breathers where the heat capacity of air is 3000 times lower than that of blood (Table 9). Since for equivalent volumes water contains about one thirtieth of the volume of O_2 in air, to extract an equal amount of O_2, aquatic breathers expose their blood to a heat sink which has a heat transfer capacity 9×10^4 times greater than air (Steen 1971). This may explain why only some degree of endothermy has evolved in a few aquatic animals and in most cases only in specific tissues. In fish, endothermy occurs in a few fish, e.g., the swimming muscles of the tuna and some sharks (e.g., Carey and Teal 1966, 1969; Block 1991b). Endothermic-homeothermy, an evolutionary step which delinks an animal's physiological processes from the environmental thermogenic

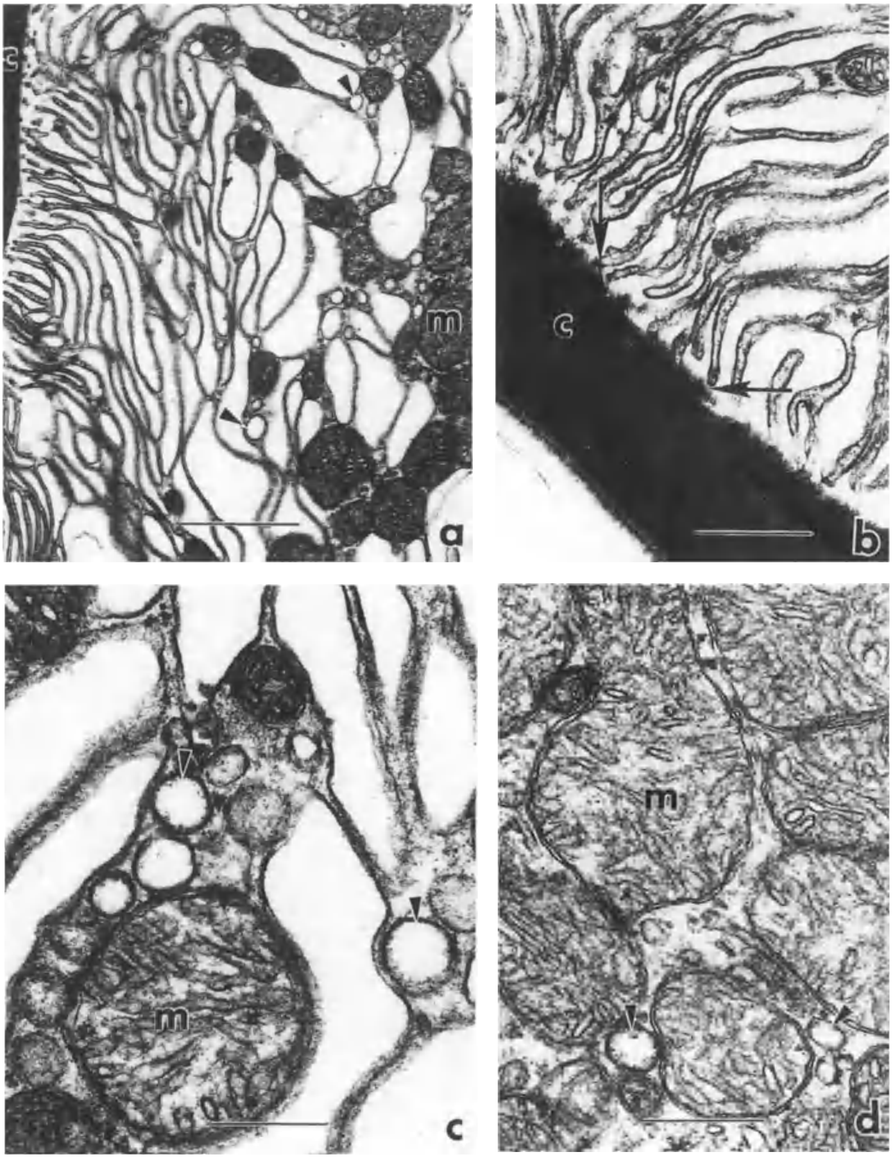


Fig. 71a–d. Gills of the freshwater crab, *Potamon niloticus*, showing: **a** the basal aspect of the epithelial cells with numerous membrane infoldings which attach onto the surface cuticle (*c*); mitochondria, *m*, and a micropinocytotic vesicles, ➤. **b** A closeup of the basal aspect of an epithelial cell showing the attachment of the basal infoldings, ➔, to the cuticle, *c*. **c** A view of the mitochondria, *m*, in close proximity to the micropinocytotic vesicles, ➤. **d** The numerous mitochondria, *m*, with profuse cristae in close proximity to micropinocytotic vesicles, ➤. The general structural features of the gills of the crab illustrate a compromise design between a thin water-blood (hemolymph) barrier and osmoregulatory exchange. **a** *Bar* 0.75 μm; **b** 0.5 μm; **c** 0.3 μm; **d** 0.3 μm. (Maina 1990b)

fluctuations, has been exclusive to the elite air-breathing animals, namely mammals and birds (Romer 1967; Crompton et al. 1978; Bennett and Ruben 1979; Hochachka 1979). At the extreme small body sizes, e.g., in the about 2-g Cuban bee hummingbird, the Etruscan shrew, and the Thai bumblebee bat, endothermic homeothermy is extremely expensive to maintain. Hummingbirds hover more than 100 times a day as they feed on nectar (Krebs and Harvey 1986), each bout lasts about a minute, and 20% of the daylight hours are spent feeding (Diamond et al. 1986). At night, some but not all hummingbirds undergo torpor to conserve energy (Lasiewski 1963b; Bucher and Chappell 1989). Though energetically expensive (Else and Hubert 1981, 1985), regulation of body temperature at a higher level imparts certain biological advantages. The biochemical reactions are faster, the rate of information processing is rapid (through quicker nervous coordination and response to environmental changes), and because diffusion is a physical process, gas transfer across the respiratory organs is faster. It is envisaged (e.g., Randall et al. 1981) that endothermy in terrestrial vertebrates evolved in temperate regions where the low ambient temperature may have called for dissociation of the body temperature from the ambient. In whichever way it evolved, the origin of endothermy had to await development of more efficient respiratory organs and processes to provide the large amounts of O_2 necessary to support a high metabolic rate (Wood and Lenfant 1979; Duncker 1991). Amazingly, for somewhat different purposes, some plants, e.g., aroid plants such as *Philodendron selloum* and *Arum maculatum* (Nagy et al. 1972; Seymour 1997) and the lotus plant (Seymour and Schultze-Motel 1996) have evolved endothermy. Heat production in the two aroid plants rivals the high levels generated by the flight muscles of bees (Seymour 1997)! In *P. selloum*, a 125-g spadix produces about 9 W of heat to maintain a temperature of 40 °C against an ambient one of 10 °C (Koch et al. 1983, 1984; Seymour 1991), surpassing heat output in some thermoregulating animals (Seymour 1997).

In abandoning liquid breathing and adjusting to air breathing, the chances of survival of animals on land depended on the level of structural development and functional adequacy of the gas exchangers as well as that of the necessary homeostatic changes, especially those relating to acid-base balance (e.g., Robin et al. 1969; Rahn 1974; Reeves 1977). Among the different animal lines, air breathing has evolved independently many times, following different pathways (e.g., Truchot 1990; Graham 1994). The possession of lung-like structures by non-teleostean groups of ray-finned fish is paleontologically well documented (e.g., Romer 1972; Jarvik 1980). Primeval lungs which developed from the floor of the junction of the esophagus and the pharynx are recognized in the ancestral armored fossil placoderm fish, *Bothriolepis* (Denison 1941), and among some of the oldest fishes, e.g., the bichirs, *Polypterus* (Lauder and Liem 1983; Burggren et al. 1985a). The elaborate dipnoan lungs (Fig. 64) are acclaimed to be the possible precursors of those of the tetrapods (e.g., Inger 1957; Romer 1967; Løvtrup 1977; Gardner 1980). The earliest definite lungs in the chordates occurred in the ancestral fishes. Lungs are present in all extant holosteans, dipnoans, and predominate in the chondrosteans. The evolution of the lungs enabled animals to fully emerge from water and enjoy the physical advantages of occupying an O_2-potent environment and an almost limitless habitat. So perfected has the process of air breathing become that most of such animals soon succumb on submersion in water irrespective of the concentration of O_2. Inundation of the pulmonary airway tree prohibits gas exchange in the lung, producing obstructive asphyxia. Physiologically, this is characterized by hypoxia, hypercapnia, and acidosis. Depending on the nature of the aspirated liquid, ionic imbalance also occurs (Moritz 1944) leading to complications such as hydremia, hemoconcentration, hemolysis of the erythrocytes, ventricular fibrillation, cardiac arrest, and death.

The colonization of land by the tetrapods at about the Early Devonian and that of the higher plants in the Upper Silurian or a little earlier (e.g., Romer 1967; Gray 1985a,b) formed important steps in the evolution of the major ecosystems on Earth. The problems and challenges which accompanied air breathing and transition to land included: (1) postural problems as a result of increased effect of gravity on the body as animals lost the buoyancy provided by the water; (2) potentially large ecological variability of water vapor pressure and hence risk of desiccation; (3) thermal instability due to the low thermal capacity of air; and (4) problems of reproduction and fertilization (in water the gametes could simply be released into the water). Evidence of a causal relationship between hypoxia and evolution of air breathing is overwhelming (Sects. 5.1 and 6.3). Air breathing in general and terrestrial habitation in particular entailed a conflict between O_2 uptake, water conservation, and acid-base balance. To effect the change, certain trade-offs and compromises were necessary. It is probably in an attempt to maximize on the advantages while giving up very little that a substantial number of animals after having evolved the capacity for aerial respiration, a major preadaptive step towards land habitation, opted to subsist in water. Indeed, it is only in arthropods and vertebrates where extensive evolutionary adaptation to air breathing has occurred. The main problem which faced the pioneering colonizers of the aerial biotope was elimination of CO_2. The challenges in acid-base balance are apparently less in water than in air due to the high solubility of CO_2 in water. The absolute values of PCO_2 and HCO_3^- ions in blood and tissues are lower in water breathers than in air breathers (Tables 2,22). In reptiles, the first exclusively lung breathers (except for the aquatic species which significantly use the skin), the PCO_2 and the concentration of HCO_3^- ions vary remarkably depending on ecological adaptations, morphological design, and lifestyle (Jackson 1986). In Squamata and Crocodilia, the mean concentration of HCO_3^- ions is $15\,mM\,l^{-1}$ at a PCO_2 of 2 kPa and in Chelonia, the concentration of HCO_3^- ions is $39\,mM\,l^{-1}$ and the PCO_2 4.5 kPa (Howell 1969). The PCO_2 ranges between 0.1 and 0.5 kPa and the concentration of HCO_3^- ions from 5 to $15\,mM\,l^{-1}$ in the plasma of fishes (Heisler 1984). Owing to the greater amount of O_2 in air, to maintain a PO_2 of 13.3 kPa in the alveolar air (at a respiratory quotient of 1), an air breather need only move 17 ml air min^{-1} ml^{-1} O_2 compared with an aquatic animal which must move 480 ml water min^{-1} ml^{-1} O_2 to maintain an equivalent PO_2 in the gill water (Rahn 1967; Howell 1969, 1970): the alveolar PCO_2 in the air breather would be 6.7 kPa while in a water breather the PCO_2 in the gill effluent would be only 0.24 kPa. The ventilatory rate of an aquatic animal at 20 °C is 28 times (at that temperature the solubility of CO_2 is about 28 times greater than the solubility of O_2 in water!) that of an air breather: the PCO_2 of the blood of a fish is one-twenty eighth that of an air breather. Thus, animals which endeavored and succeeded in attaining air breathing could drastically reduce ventilatory rate but would be faced with a profound increase in arterial PCO_2 which in terms of acid-base balance results in a respiratory acidosis. The alternative strategies which were used to surmount these obstacles included: (1) renal mechanisms which resulted in increased blood concentration of HCO_3^- ions thus maintaining a constant OH^-/H^+ ratio and/or, (2) evolution of an alternative pathway other than the lung, e.g., the skin and the buccal cavity, for CO_2 clearance during the traumatic switchover of respiration from the gills to the modern lung (Fig. 57). Conceivably, the transition was interfaced by a relatively simple precursor of the modern lung which must have been, from perspectives of design and mechanical ventilation, relatively inefficient. The forfeiture of the skin, after the integument was covered with scales or armor to reduce water loss, in reptiles (Mertens 1960) was the initial step in the transfer of gill to lung respiration (Hughes 1963). During this time, the lung and respiratory mechanics developed to a level where the air-breathing organ could eliminate the entire load of CO_2 produced in the body. The role of acid-base balance was wholly shifted to the modern lung and, to a smaller extent, the kidney. At 20 °C, only about 3% of the CO_2 output is cutaneous in the tortoise, *Testudo dendriculata* (Jackson et al. 1976) and in the desert lizard, the chuckawalla (*Sauromalus obesus*) about 4% of CO_2 output and less than 2% of O_2 uptake occurs through the skin at 25 °C (Crawford and Schultetus 1970). In the land-dwelling box turtle, *Terrapene ornata*, a large proportion of CO_2 is voided through the skin at the low hibernating temperatures (Glass et al. 1976). Gans (1970) observed that cutaneous respiration is an acquired mode of respiration unique to the modern amphibians without any relationship to the Devonian ancestral lineage of the extant tetrapods. Romer (1972) and Colbert and Morales (1991) have espoused the theory that the Carboniferous amphibians were completely heavily armored. If this is correct, the highly gas- and water-permeable skin characteristic of the extant amphibian species is an adaptive secondary condition. Clearly, in amphibious animals the skin was not as efficient as the gills in CO_2 elimination, as demonstrated by the fact that, despite the role the integumentary system played in gas exchange, it was still necessary for the level of the plasma HCO_3^- ions to be elevated in the air breathers. The increase in the arterial PCO_2 and the concentration of the HCO_3^- ions occurred as animals became more dependent on air for their O_2 needs, starting from the water-breathing fish through the various forms of bimodal breathers to the air breathers. Despite the differences in the PCO_2 and the concentration of the HCO_3^- ions in the arterial blood of the water- and air breathers (e.g., in the carp and the bullfrog), the pH (about 7.9) of these animals at the same temperature (20 °C) is essentially the same (Howell et al. 1970; Table 2). The pH of the water-breathing tadpole at 20 °C is the same as that of the air-breathing frog at the same temperature despite the fact that the arterial PCO_2 and the concentration of the HCO_3^- ions of the bullfrog are about five times greater than that of the tadpole (Erasmus et al. (1970/71). Conceivably, since the bimodal breathing occurred in O_2-deficient waters, the O_2 affinity of blood of such animal forms should be lower, i.e., P_{50} should be higher, the more aerial-breathing an animal is. The P_{50} of the blood of the air-breathing fish ranges from 2 to 2.7 kPa at 20 °C, values which are higher than those of water breathers in similar habitats. In the amphibians, the most aquatic species have a P_{50} about one half that of the completely aquatic aerial species (Lenfant and Johansen 1967). The differences are accounted by the fact that air is a respiratory medium much richer in O_2.

6.4 Aerial Gas Exchangers: Structural and Functional Diversity

The air-breathing organs are thought to have evolved as special adaptations to the prevalent hypoxic conditions, presumably those which prevailed in the warm tropical waters of the late Devonian (e.g., Zaccone et al. 1995). Confinement of gas exchange to specific site(s) of the body where the process could be well regulated, water loss restricted, the inhaled air "cleaned" and physically modified, and better protection from toxicants and trauma afforded were prerequisites for efficient aerial respiration and successful terrestrial habitation. If the human lungs were like the external gills of fish, i.e., were evaginated and exposed to air, even in a moderately desiccating environment, the water loss would be about 500 l day^{-1}. This value is about 1000 times greater than the normal loss (McCutcheon 1964). In arthropods, removing the cuticle (by scratching) increases cuticular water loss much more than it affects gas exchange (Ito 1953; Richards 1957). The reduction of the respiratory rate in the air breathers (owing to accessibility to a greater O_2 concentration) constituted an important step in the reduction of respiratory water loss. Most animals die if water loss exceeds 20 to 50% of their body mass (Adolph 1943). The majority of terrestrial vertebrates cannot tolerate a body temperature of 45 °C or more but, when provided with adequate water for evaporative cooling, they will withstand even higher temperatures (Calder and King 1974). The development of internalized gas exchangers (Figs. 4,5), however, was accompanied by certain functional limitations. While the gills, e.g., in crustaceans, mollusks, agnathans, and fish by virtue of their external location can be ventilated unidirectionally and continuously, the "dead-ended" lungs of the vertebrate air breathers can only be ventilated periodically and bidirectionally (i.e., tidally) through narrow opening(s) (Figs. 6,18). This constituted a major trade-off in the design of the aerial gas exchangers. While in the gills the configuration was compatible with the highly efficacious countercurrent system, as a consequence of their invagination, only the relatively inefficient uniform pool arrangement was tenable in the aerial gas exchangers (Figs. 6,35,36; Sects. 6.2 and 6.4). The internalized gas exchangers fail to maximally exploit the high ambient PO_2: the inspired air is greatly diluted by the residual air, reducing the head pressure from 21 kPa to about 13 kPa, a loss of about one third of the potential partial pressure gradient. The arterial PO_2 in *Amia calva*, *Synbranchus*, and *Neoceratodus* (an obligate water-breathing lungfish) are below 1.3 kPa in water but are higher when held in air (Lenfant et al. 1966; Johansen et al. 1970a). In a resting human being, where the dead space is about 140 cm^3, about 28% of the 500 cm^3 of the inhaled air does not reach the gas exchange region. Compensatory advantages such as low cost of ventilation in air, greater O_2 loading and transport due to presence of hemoglobin, and better ventilation-perfusion controls help overcome the apparent limitations intrinsic to the design. On the plus side, tidal ventilation makes it possible for a much more stable and well-controlled local respiratory condition to be established. The alveolar PO_2 is lower and the PCO_2 higher than in the ambient air, the elevated alveolar PCO_2 in the vertebrate lung being used in the HCO_3^- ion buffer system for pH regulation. Such microenvironments are impossible to create in those gas exchangers which are unidirectionally ventilated or directly exposed to the external respiratory medium. Mechanical ventilation is necessary for mass renewal of the air in contact with the respiratory surface(s) to maintain the partial pressure gradient essential for O_2 influx. The most elaborate of the respiratory processes are restricted to the large and phylogenetically more advanced animals. A highly developed nervous system and proper nervous integration were necessary to operate these complex organs and functions. Shrewdly, by isolating the lung from the air sacs, birds have developed a unidirectional continuous air flow in the parabronchial system of the lung within an invaginated, tidally ventilated organ! The tracheal system of insects has attained a remarkable state of efficiency through synchronization of spiracular opening with the ventilation of the air sacs (Weis-Fogh 1967). Intermittent breathing in reptiles (e.g., Glass and Wood 1983; Wood and Glass 1991), amphibians (De Jong and Gans 1969), and lungfishes (Lenfant and Johansen 1968) is possible because of their low O_2 needs and the great O_2 stores in their lungs. Episodic respiratory pattern constitutes an energy-saving strategy compared with the continuous mode of breathing in birds and mammals (Milsom and Jones 1979). Although incidental breathing is a common feature of the ectothermic vertebrates (Milsom 1988; Shelton and Croghan 1988), it occurs in hibernating nondiving mammals such as hedgehog, dormouse, and the little brown bat (e.g., D.W. Thomas et al. 1990) and in the ground squirrel, *Spermophilus lateralis*, during deep hypothermia (e.g., Garland and Milsom 1994). When in such a state, large fluctuations in lung and blood PO_2 and PCO_2 occur (e.g., Musacchia and Volkert 1971). Functionally, gas exchangers in terrestrial air breathers fall into three general categories. In the diffusive type which, e.g., occur in most small insects, pneumonate gastropods, and some terrestrial crabs, no ventilatory movements occur: diffusion is adequate to supply O_2 and remove CO_2. In the mixed type, as found in the large insects and terrestrial crustaceans, mechanical pumping aids convective movement of air at least in the principal respiratory pathways. Mass transport of air to the pulmonary surface is necessary to produce efficient transfer of respiratory gases in the convective (ventilatory) type gas exchangers. These are found in the air-breathing fish, amphibians, reptiles, mammals, and birds.

6.5 The Diffusive Type Gas Exchangers

As a means of delivering O_2 to a respiratory site, diffusion is only efficient over short distances. The process can hence only effectively service the extremely small, low-metabolism animals. Diffusion lungs occur in most pulmonate gastropods (Ghiretti 1966). A diffusive tracheal system has evolved in the terrestrial arthropods – in the uniramians (e.g., insects, centipedes, and millipedes), in chelicerates (e.g., scorpions and spiders), in isopods particularly the Porcellionidae (e.g., sow bugs) (Paul et al. 1987; Fincke and Paul 1989), and even in plants (Walsby 1972). The simplest lungs are found in snails and slugs where the mantle cavity has been converted into well-vascularized internal respiratory spaces (Fig. 59). Through muscular contractions when the pneumostome is closed, the intrapulmonary pressure increases to about 0.2 to 0.3 kPa. The periodic compression of the air inside the lung is thought to enhance the diffusion of O_2 into the blood (Ghiretti 1966). According to Dahr (1924, 1927), a very small PO_2 of 0.3 kPa is adequate to provide the animal with sufficient O_2. In *Arion* and *Helix*, at a PO_2 of 2 kPa, the pneumostome opens 15 to 30 times in 30 min, remaining open for 7 min (Dahr 1924). The opening of the pneumostome in the gastropods is determined by factors such as levels of CO_2, O_2, humidity, and temperature (Mass 1939). The arachnids are among the earliest animals to occupy land and acquire the capacity to breathe air (Paul 1992). Their respiratory organs, the book lungs, have literally been frozen in time. In having changed very little since the Devonian, they are highly instructive in the understanding of the design of the gas exchangers in the original air breathers. The book lungs of the spiders and the scorpions (Figs. 15,72) consist of stacks of parallel blood-filled lamellae or plates contained in invagination(s) of the abdominal wall (Pohunkova 1969; Moore 1976; Vyas and Laliwala 1976; Herreid et al. 1981; Strazny and Perry 1987). The spiracular muscles, which respond to CO_2 (or low pH) and PO_2 (Fincke and Paul 1989) regulate the size of the opening into the atrium, expelling CO_2, letting in O_2, and regulating water loss and pH (Angersbach 1978; Fincke and Paul 1989). Gas

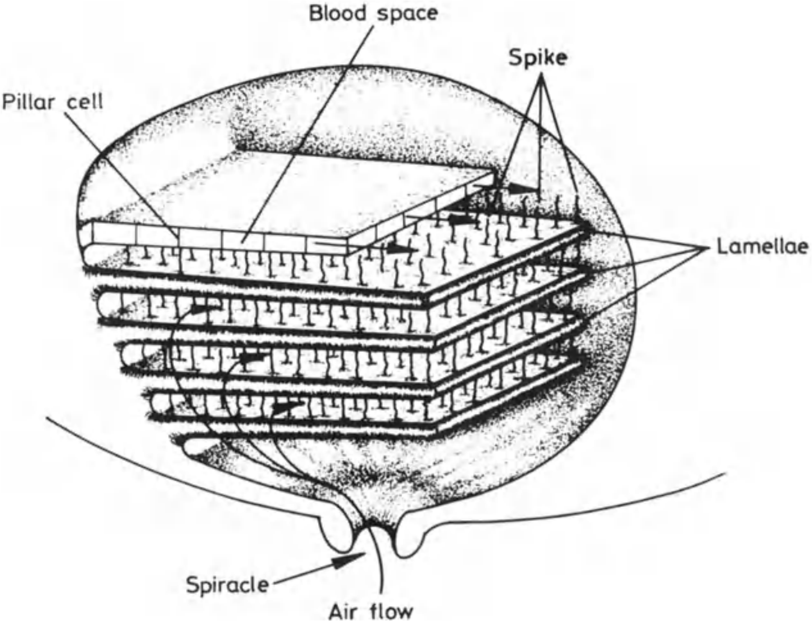


Fig. 72. Schematic view of the diffusive, sheet flow book lungs of a spider showing stacks of lamellae through which hemolymph flows, →, and spikes which keep the lamellae apart

exchange is effected with the hemolymph, which is pumped across the hollow chitinous lamellae (Anderson and Prestwich 1982; Fincke and Paul 1989; Farley 1990; Fig. 72): in *Eurypelma*, when the spiracles are open, arterial PO_2 rapidly rises from 3.7 to 9.9 kPa and hemocyanin is fully saturated (Angersbach 1978). The absence of ventilatory activity and control of the spiracle entrance area in the diffusion lungs minimizes water loss. It is compatible with low aerobic metabolic rate reflected in the low O_2 uptake especially in arachnids (Anderson 1970). Peristaltic movements in the book lung lamellae of some spiders have been reported (Moore 1976). The actual significance of these movements in respiration is, however, not well known (Paul et al. 1987). Anaerobic metabolism plays an important part in the activities of arachnids (Prestwich 1983). Their locomotory muscles lack mitochondria (Linzen and Gallowitz 1975). Only the heart, CNS, Malpighian tubules, and midgut glands work aerobically (Paul et al. 1987). The largest known spider is the bird-eating spider, *Theraphosa blondi*, of northern South America, which attains a body mass of about 55 g (Dresco-Derouet 1974).

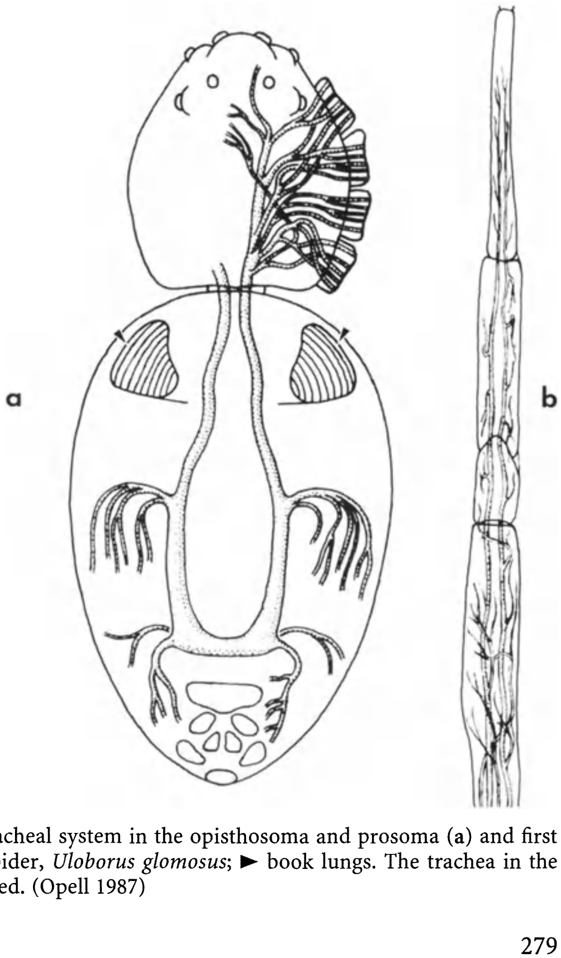


Fig. 73a,b. The well-developed tracheal system in the opisthosoma and prosoma (**a**) and first legs (**b**) of the web monitoring spider, *Uloborus glomosus*; ► book lungs. The trachea in the highly active legs are well developed. (Opell 1987)

Variably, spiders possess two kinds of respiratory organs, the book lungs and the trachea. The so-called pulmotracheates possess both organs (Fig. 73). The more metabolically active spiders and scorpions have book lungs and a tracheal system, while the ancestral ones (e.g., the orthognaths) have book lungs only (Paul et al. 1987; Strazny and Perry 1987). In some families of spiders, e.g., Caponiidae and Symphytognathidae, only the trachea exist (Paul 1992) but unlike in insects, the trachea do not directly contact the tissue cells. Hemocyanin is used to carry O_2 over the remaining distance (Foelix 1982). Some pulmonate snails of the family Athoracophoridae (e.g., tropical snails, Janellidae) and some other unrelated animals, e.g., the sow bug (an isopod) *Porcellio*, the house centipede (chilopods), and *Scutigera* (Krogh 1941) present a fairly complicated respiratory system which combines the features of gastropod lungs with the tracheal system in insects: the pneumostome/spiracles open into a common vestibulum from which an array of fine diverticula radiate into a blood sinus providing a large respiratory surface area. A pneumotracheal organization provides a more efficient gas exchange capacity compared with simple smooth respiratory invaginations. In analogy, the design is closer to the mammalian tracheobronchial lung than to the tracheal system of insects. The largest diffusive lungs are probably those of the African pulmonate snails, *Achatina* and *Bulimus*, which attain a volume of up to 500 ml (Krogh 1941). In the freshwater pulmonates, *Planorbis corneus* and *Lymnea stagnalis*, despite lack of ventilatory activity, the PO_2 rises to 18 kPa before the closure of the pneumostome (a value higher than the alveolar level of the mammalian lung of about 13 kPa. The PO_2 may drop to as low as 2.7 kPa before the pneumostome reopens (Precht 1939; Jones 1961). There is no respiratory system in the vertebrates which is adapted to diffusive respiration alone. In states such as hibernation (e.g., in the lungfish) and conditions such as exposure to high humidity (e.g., in the bullfrog), the skin may meet most, if not all, the O_2 requirements. Dogs have been experimentally kept alive for an hour on diffusive respiration alone. This, however, occurs only under conditions of minimal O_2 demands such as in states of anesthesia and while the animal is breathing pure O_2 (Lambertsen 1961).

6.6 The Mixed Type Gas Exchangers

6.6.1 The Insectan Tracheal System

Among the air-breathing animals, the insectan tracheal respiration is unique. In many ways, it is astonishing both for its intuitive architectural simplicity and functional efficiency. In a degree of refinement almost past belief, the insects have disengaged the circulatory and respiratory systems, totally relegating the former from any meaningful role in gas exchange. This is a radical deviation from the prevalent plan in the vertebrate and the invertebrate (nontracheate) air and water breathers where a circulatory system is intercalated between the gas exchanger and the body tissues (Figs. 1,2,3). In insects, O_2 is delivered by the trachea directly to the body tissues (Figs. 75,76). The trachea, the portals of entry of air to the body

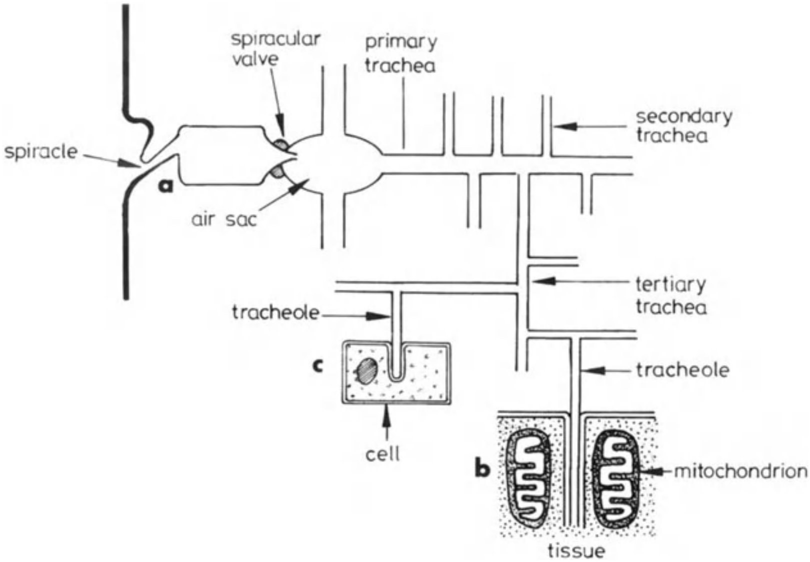


Fig. 74a–c. Schematic diagram of the air flow pathway in the tracheal system of insects. The vulvular spiracles (**a**) open to the outside while the tracheoles terminate deep in the animal's body (**b**) in some cases indenting some tissue cells (**c**)

(Figs. 37,74), form as ectodermal invaginations. With minimal drop in PO_2 along the way, virtually every individual cell in the body is served by a tracheole(s), structures which are analogous to the vertebrate blood capillaries (Fig. 77). The PO_2 between the tracheoles and the metabolizing tissue cells in insects is about 5.3 kPa (Weis-Fogh 1964a, 1967) compared with that of less than 0.3 kPa in the mammalian tissues. In adult *Aphelocheirus*, between the spiracles and the tracheoles, the PO_2 drops by only 0.3 kPa (Thorpe and Crisp 1941). Generally, the concentration of O_2 drops by only 1% from the spiracle to the tissues (Buck 1962). The tracheal system can supply ten times more O_2 g^{-1} tissue than the blood capillary system (Steen 1971). With the spiracular valve serving as a carburetor, in mechanical terms, the trachea operate simultaneously both as a compressor and an exhaust pipe, presenting the epitome in the design of the gas exchangers. Contrary to the cases in the branching tubular structures like the bronchial system of the mammalian lung (e.g., Horsfield 1981), where between the principal and the terminal bronchi the flow velocity decreases by a factor of 700 due to increase in the cross-sectional area (Horsfield and Thurlbeck 1981; Horsfield and Woldenberg 1986), the insect trachea are the only system of air conduits known where the cumulative cross-sectional area and hence the flow velocity remain constant with length (Krogh 1941). In the endothemic insects (Heinrich 1992), thermoregulation of the thorax during flight enables them to attain some of the highest known muscle power outputs in the Animal Kingdom (Harrison et al. 1996). The aerobic rates of the flight muscles are some of the highest reported for any tissue (Kammer and Heinrich 1978), values which approach those of pure microbial cultures (e.g., Hughes and Wimpenny 1969). Insect flight muscles do

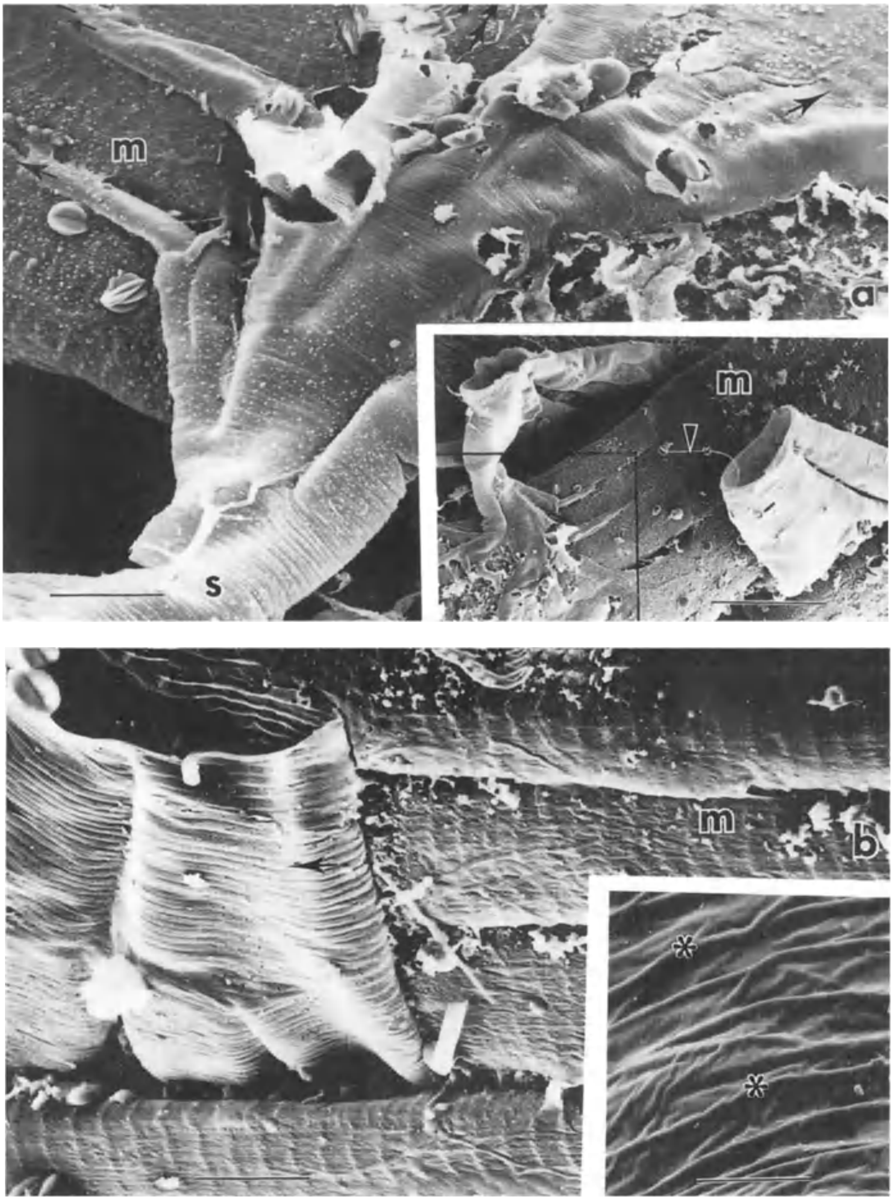


Fig. 75a,b. Air supply to the flight muscles of a grasshopper, *Chrotogonus senegalensis* showing: **a** secondary trachea, *s*, approaching the flight muscle, *m*, and tertiary trachea, ➜, indenting the muscle. The trachea are supported by the spiral taenidia (➤ *inset*) which keep them open. The main figure is an enlargement of the enclosed region in the inset. **b** Closeup of a tertiary trachea with distinct taenidia, ➜, about to indent the flight muscle, *m*. *Inset* ∗, taenidia. **a** *Bar* 20 µm; *inset* 80 µm; **b** 45 µm; *inset* 30 µm. (Maina 1989b)

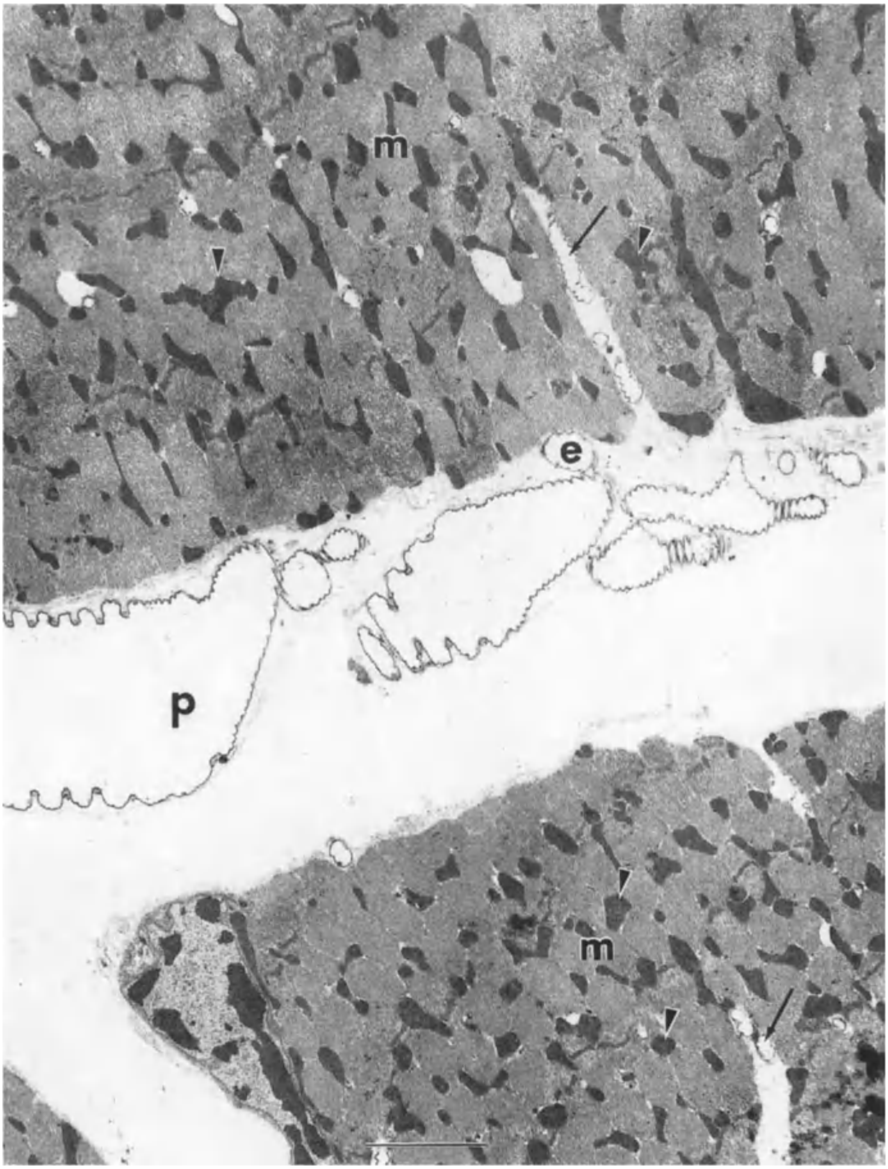


Fig. 76. Flight muscles, *m*, of the desert locust, *Locusta migratoria migratoria* showing secondary trachea, *p*, on the surface of the muscle and tertiary trachea, *e*, indenting the muscle. The terminal tracheal, →, lie in very close proximity to the muscle fibers and the mitochondria, ➤. *Bar* 3 μm

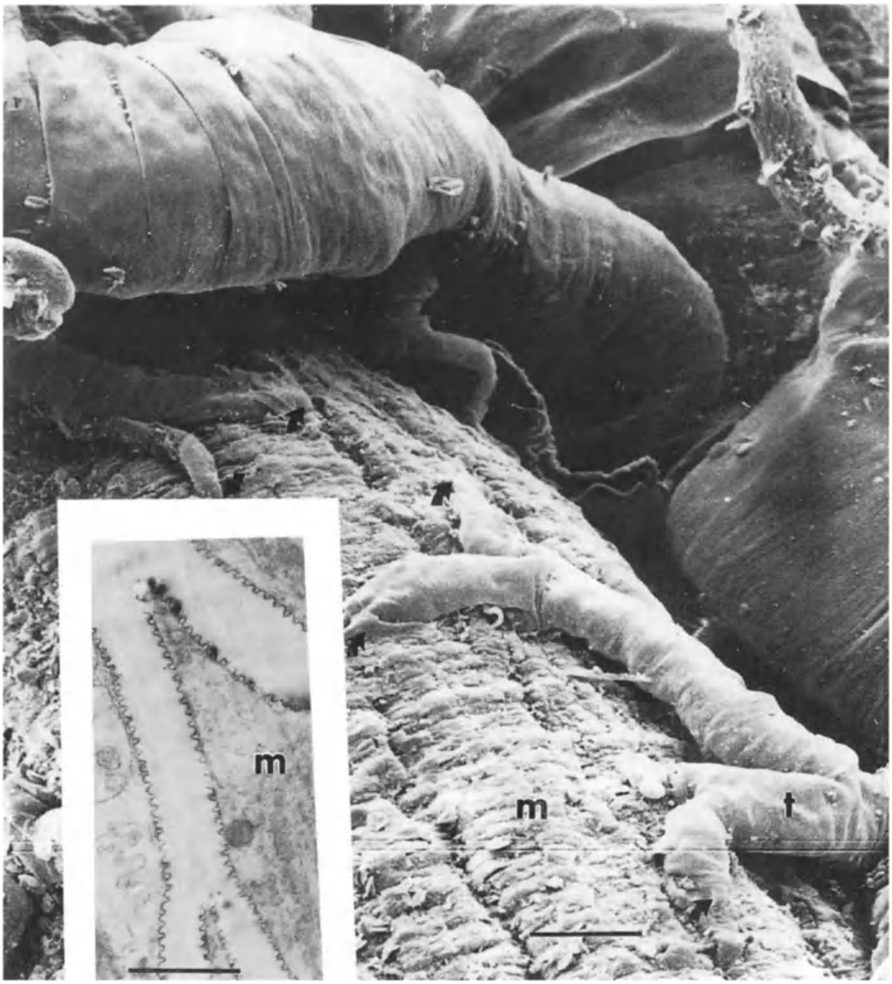


Fig. 77. Secondary trachea, *t*, giving rise to tertiary trachea, ➘, indenting the abdominal muscles of the grasshopper, *Chrotogonus senegalensis*. *Inset* View of a tertiary trachea in the flight muscle, *m*. *Bar* 185 μm; *inset* 0.6 μm. (Maina 1989b)

not contain myoglobin (Elder 1975). In some small insects the flight muscles may attain a wing contraction frequency of up to 1000 Hz (Sotavalta 1947), a process amazingly powered entirely by aerobic metabolic pathways. Such high metabolic rates are possible because of the direct delivery of O_2 to the tissues and the remarkably high volume density of the mitochondria (Weis-Fogh 1964a; Elder 1975; Ready 1983). In the process of attaining an optimal respiratory design, by exposing their body tissues to the ambient environment through a myriad of air conduits, the tracheates, and in particular insects, have had to pay a great price. They are particularly vulnerable to invasion by pathogens (e.g., Engelhard et al. 1994) and aerosol-based toxicants which pass the spiracles. It is common knowledge that some of the insecticides which are commercially advertised as to knock - down - insects - dead do exactly that! While vertebrate muscles can continue contracting by anaerobic metabolism for a period of time after O_2 supply stops, since insect muscles lack lactic dehydrogenase, to function, they have to have a continuous supply of O_2 (Pringle 1983).

Although best studied in insects, tracheal respiration has evolved in animal groups such as Onychophora (Peripatus), Solifugae, Phalangidae, some Acarina, Myriapoda, and Chilopoda. The bodies of the tracheates are pervaded by fine air-filled tubes, the trachea, which are simple noncollapsible hollow airways strengthened by endocuticular spiral or annular chitinous thickenings, the taenidia (Figs. 37,78). In some of the most metabolically active tissues, the finest branches of the trachea (the tracheoles) as they approach the tissue cells may be as narrow as 0.2 μm in diameter and may indent the cells in the manner of a finger poked into a balloon (Steen 1971; Fig. 74). In the case of the flight muscles, in some insects, the very narrow unventilated tracheoles, which are about 1 mm long, must supply O_2 at a tremendous rate of 6.5 mol per m^3 of tissue per s (Weis-Fogh 1964a). In the highly metabolically active tissue such as the flight muscles, the terminal tracheoles are never more than 0.2 to 0.5 μm from a mitochondrion (Fig. 76) and in some tissues they may be as close as 0.005 μm (Wigglesworth and Lee 1982; Maina 1989b). The mitochondria cluster around the terminal tracheoles forming what has been termed mitochondrial continuum (Edwards et al. 1958). In the flight

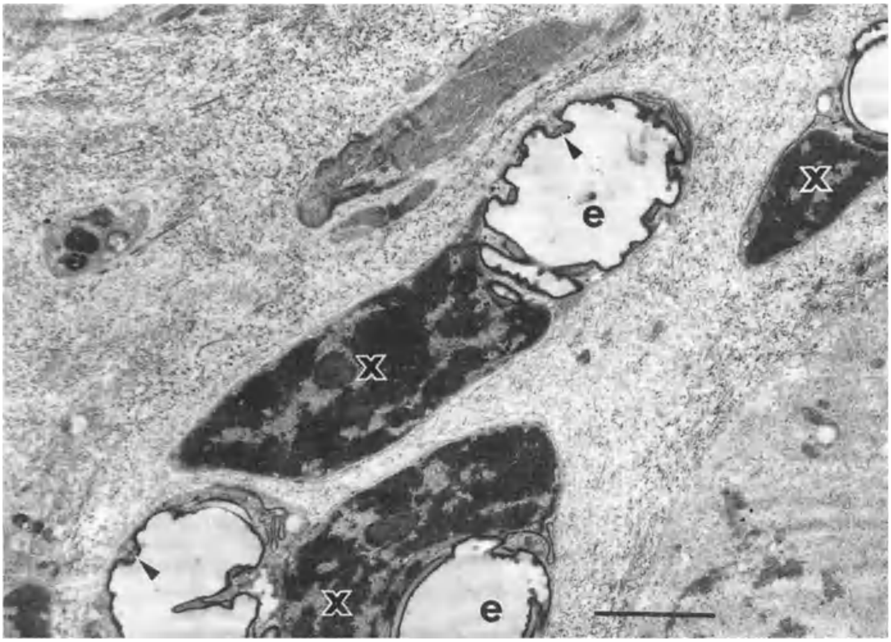


Fig. 78. Trachea, *e*, in the abdominal muscles of the desert locust, *Locusta migratoria migratoria*, surrounded by tracheoblasts, *x*, cells that are thought to be involved in laying down trachea. ➤, taenidia. *Bar* 0.3 μm

muscle, the tracheoles may invest single muscle fibrils (Krogh 1941). The tracheoles terminate blindly (Richards and Korda 1950) though possible anastomoses have been reported (Buck 1948). Estimations made on the tracheal system of the giant lepidopteran, *Cossus cossus*, larva (mass 3.4 g, length 60 mm) gave a total cross-sectional surface area of all trachea supplying the tissues of 6.7 mm^2 with an average length of 6 mm: O_2 diffuses at a rate of 0.3 $mm^3 s^{-1}$ at a pressure head of 1.5 kPa, a value which is more than adequate even during muscular exertion (Krogh 1920b). Depending on factors such as age and stage of development, the tracheal system constitutes 5 to 50% of the volume of an insect. In the silkworm, *Bombyx mori*, the tracheoles are 1.5 m long (Buck 1962) and the volume which for a 5.7-g worm is 49 $\mu l g^{-1}$ makes about 5% of the body volume (Bridges et al. 1980). In the adult cockchafer, *Melolotha*, the trachea constitute a volume of 585 $\mu l g^{-1}$ (Demoll 1927). The tracheal volume of a 5-g *Cecropia* pupae is about 250 mm^3 (Kanwisher 1966).

The terminal tracheoles are filled with fluid, the degree of filling depending on the level of activity (e.g., Wigglesworth and Lee 1982). The endotracheal fluid is removed osmotically by the increased concentration of the end products of metabolism in the interstitial cell spaces during times of increased metabolic demands and exposure to hypoxia. The air/fluid interface is brought closer to the tissue cells as the interstitial fluid is drawn upstream of the peripheral tracheoles and into the cytoplasm of the surrounding cells (Wigglesworth 1953, 1965). The process shortens the diffusional pathway of the respiratory gases. When the acidic metabolites are eliminated and better aerobic conditions preponderate, the action is reversed. Such a sequence of events is not unique to insects as it is utilized by many other animals to open up capillary beds in specific body tissues during conditions of high O_2 demand. Evidently, the diffusion-based insectan tracheal system evolved entirely for aerial respiration. Because the diffusion of O_2 in water is 10^3 lower than in air, the tracheoles would need to be as small as 12 μm to adequately supply O_2 to tissues respiring at the same rate as the insect flight muscle (Denney 1993). Theoretically, aquatic insects relying on delivery of O_2 entirely by diffusion would need to greatly increase tracheolar density, lower their metabolic rate, and drastically reduce the distance between the body tissue cells and the surrounding water. This would call for extremely thin, minuscule, intensely tracheated bodies. Such requirements may not be compatible with the essential insectan morphology. Those insects which have reverted to living in water have retained air-filled trachea (the gas gills) which essentially act as internal plastrons (Sects. 6.6.1 and 6.12): the O_2 taken up from the surrounding water is transferred along a gas phase within the tracheal system in much the same way as in a surface-dwelling insect.

The insectan tracheal system provides a unique and perhaps the most cost-effective design for supplying body tissue cells with O_2. However, the limitation of diffusion and the large mechanical ventilatory forces which have to be generated to move air at extremely high rates in the countless fine conduits have consigned the insects to small body sizes. This may explain why such an efficient scheme was never adopted in the larger animals. The heaviest living insects are the Goliath beetles (family: Scarbaeidae) of the Equatorial Africa: *Goliathus goliathus* weighs between 70 and 100 g. The hairly-winged beetles of the family Ptiliidae (=

Trichopterygidae) and the battledore-wing fairly flies (parasitic wasps) of the family Myrmaridae which measure only 0.2 mm in length are the smallest insects: the smallest insects are smaller than some of the largest protozoa! The average tracheolar length for optimal diffusion appears to be 5 to 10 mm and the minimum diameter 0.2 μm (Krogh 1920a,b; Weis-Fogh 1964a). The tracheates which utilize diffusion as the main mode of gas exchange include the Onychophora (Peripatus), the tracheate Arachnoidea, Myriapoda, and Chilopoda, almost all terrestrial insect larvae, all pupae, and most of the small imagines. This is made possible by the relatively fast diffusion of O_2 in air compared with that in water. The largest ever known insect was the dragonfly-like *Meganeura* of the Carboniferous, which reached a length of 60 cm and was 3 cm in width (Krogh 1941). It is well known that the levels of atmospheric O_2 have greatly fluctuated over geological times (Sect. 1.11). A greater PO_2 in air as occurred in the Carboniferous period (Graham et al. 1995; Fig. 9) may have allowed the development of the giant insects. Presently, the largest extant insects are the tropical beetles which reach a length of 15 cm. Flying insects range in body mass from 1 μg to 20 g (Norberg 1990). The stick insects best demonstrate the compromises between size and shape which have occurred in insects, features which have been modulated for optimal tracheolar ventilation and diffusion. Some of the longest insects in the world are the tropical stick insect, *Phamacia serratipes*, and the Central and South American dragonfly, *Megaloprepes caeruleata*, which have very narrow bodies which are respectively 33 and 12 cm long. While a housefly, which weighs about 15 to 20 mg, does not need to ventilate the tracheal system, a bee, which is more energetic and weighs about 100 mg, does so regularly. In insects such as locusts, dragonflies, and cockroaches, at rest, well-synchronized abdominal and, to a smaller extent, thoracic ventilation occurs (Brocher 1931). Although during rest no ventilatory movements take place in the cockroaches, *Peripaneta* and *Blatella*, during flight when O_2 consumption increases 10 to 100 times, wing beats compress the thorax ventilating the trachea and the air sacs (Brocher 1920; Portier 1933). Ventilation in flight may be aided by direct inflow of ambient air at the ventral surface and the slightly reduced pressure over the abdominal spiracles due to a Bernoulli-Venturi effect. During steady flight in the desert locust, about $320\,l\,kg^{-1}\,h^{-1}$ of air with an average tidal volume of $167\,cm^3$ and frequencies of 30 to 60 times min^{-1} is ventilated into the tracheal system by abdominal and thoracic pumping. The intratracheal pressure increases to 0.9 to 3.3 kPa at the peak of an abdominal contraction (Miller 1960; Weis-Fogh 1967). The giant beetle, *Petrognatha gigas*, has a ventilatory rate of about $2000\,l\,kg^{-1}\,h^{-1}$ (Miller 1966).

Through synchronized action of the spiracles, the trachea are ventilated continuously and unidirectionally, particularly among the Orthoptera (e.g., Fraenkel 1932; Weis-Fogh 1964a, 1967). In the honeybee, the flow is unidirectional during flight (Bailey 1954) and in *Sphodromantis*, 95% of the inhaled air passes unidirectionally while only 5% passes tidally (Miller 1974). Among the cockroaches, *Periplaneta* and *Blatella*, tidal ventilation only occurs during stress while in other roaches, *Byrsotria*, *Blaberus*, and *Nyctobra*, anteroposterior ventilation occurs during rest (Buck 1962). The unidirectional and continuous ventilation, as occurs in the parabronchial bird lung (e.g., Scheid 1979), minimizes or abolishes dead space air, ascertaining that the gas exchange site is supplied with air at the highest possible PO_2. Abdominal pumping is inadequate in supplying O_2 to the long muscles of the legs in some large insects. In the grasshopper, the concentration of O_2 in the tibial tracheae is fairly high (16%) in the resting state but drops to 5% during physical exertion (Krogh 1913). Special spiracles have developed on the legs of the harvestmen (Opiliones) apparently to overcome the diffusive and convective limitations (Hansen 1893). The smallest tracheoles in insects which measure about 0.2 μm are close to the mean free path (MFP) of O_2 molecules in air (the average distance a molecule travels in air before colliding with another) which is about 0.008 μm (Pickard 1974). Below the MFP, the effective diffusion coefficient is reduced, lowering the rate at which O_2 is delivered to the tissues. The minimum tracheolar diameter in insects appears to have been set by the MFP of molecules in air. In the most energetic species, this parameter seems to have been optimized in the most highly metabolically active tissues such as the flight muscles.

The development of the tracheal system appears to be partly determined by certain intrinsic factors in the target tissues (Locke 1958a,b,c) while the actual distribution to specific organs is determined by the local aerobic conditions (Edwards et al. 1958). In much the same way as occurs between the capillarization of the tissues and metabolic activity in vertebrates, in insects, tracheolar density is dependent on the metabolic activities and PO_2 levels in particular organs and parts of the body (Edwards et al. 1958; Wigglesworth 1965; Steen 1971). The trachea are particularly well developed in the legs, which are actively used for web-monitoring activity in the spiders of the family Uloboridae (Opell 1987). In larval meal-worms, *Tenebrio molitor*, hypoxia influences tracheal growth. Development at an ambient PO_2 of about 10 kPa leads to wider trachea (London 1989). In the wing muscle of the locust, between 10^{-1} and 10^{-3} (volume of the trachea per volume of muscle) is taken up by the tracheal system (Weis-Fogh 1967). The entire respiratory system in insects may form as much as 50% of the entire body volume (Steen 1971). In the small and relatively inactive insects and arachnids, the tracheal system may be simple but in larger and more energetic species (e.g., wasps and bees), it may be complex with the system comprising an intricate maze of longitudinal and transverse branches (Fig. 37) connected to air sacs (Fig. 38). The air sacs increase the tidal volume by as much as 70% of the total air capacity affordable by the trachea alone (Bursell 1970) and reduce the longitudinal diffusion gradient for O_2 along the gas exchange pathway. They are well developed in Diptera and Hymenoptera but are absent in the subclass Apterygota. In cicada, *Fidicina monnifera*, the air sacs together with the tracheal system constitute 45% of the body volume (Bartholomew and Barnhart 1984).

6.7 The Convective Type Gas Exchangers

6.7.1 Ventilatory Mechanisms and Organization of the Gas Exchangers

The ventilatory lungs have evolved only in the vertebrates. They were a major factor which provided the means for realization of large and complex body sizes and forms as well as high metabolic lifestyles. Different ventilatory processes have evolved in the air-breathing vertebrates. The bucco-pharyngeal pump, where air is literally swallowed, occurs in the amphibians and the dipnoans (Brainerd et al. 1993). The mechanism appears to have arisen as a compromise between respiration and feeding. The energy which operates the force pump arises from contraction of the muscles of the mouth (De Jong and Gans 1969; West and Jones 1975; Liem 1987a). The amount of air which can be transferred during a single breath is a function of the pressure differential between the lung and the buccal cavity and the potential change in the volume of the buccal cavity (Liem 1987a). In the aquatic habitat, during feeding, pressure changes far exceed those recorded during air ventilation (Lauder 1980; Bemis and Lauder 1986). The buccal force pump operates below its maximum potential during air breathing and is hence an overdesign for the role it plays in the medium. The tidal volume acquired by the buccal force pump is limited. The buccal force pump is ineffective for filling long narrow lungs like those of snakes (Gans 1971; Guimond and Hutchison 1976) and is a rather inefficient method which cannot support high levels of metabolism. The ventilatory inefficiency of the buccal force pump in the terrestrial settings is thought to have constituted a major obstacle in the evolutionary progression of the amphibians (Gans 1970; Liem 1987a). Suctional (aspirational) breathing occurs in most reptiles and all mammals and birds (Bainerd 1994), animals which operate at a higher level of metabolism and have long complex lungs which cannot be effectively serviced by a buccal force pump. The evolution of suctional breathing dissociated the feeding apparatus from the breathing one. It comprised a milestone in the development of more complex, efficiently ventilated gas exchangers which were necessary on transition to land and the resultant higher metabolic requirements. While suctional breathing occurs in various reptiles, positive-pressure inflation through the buccal force pump preponderates in the taxon (Gans and Hughes 1967; Gans 1971): breathing is exclusively effected by movement of the rib cage and complex changes in the volume of the visceral cavity, as a diaphragm is lacking (e.g., Perry and Duncker 1980; Gaunt and Gans 1969; Gans and Clark 1976, 1978). Modem amphibians have vestigial ribs. It is, however conjectured that the larger now extinct forms had functional ribs which they utilized to draw air into their lungs. In amphibians and reptiles, postural changes and presumably contraction of the pulmonary smooth muscles (Figs. 79,80; Stark-Vancs et al. 1984; Maina 1989b) and elastic tissue (Fig. 80) as well as hydrostatic forces (when the animal is immersed in water) may aid in expiration or air. The smooth muscles which line the central cavity of the lung of the tegu lizard, *Tupinambis nigropunctus* (Hlastala et al. 1985), as well as snake lungs (Maina 1989e; Fig. 80) have been associated with changing the shape of the lung and assisting in the convective mixing of the intrapulmonary air. In birds, the ventilation of the lung is unique among vertebrates. The virtually rigid lungs are ventilated by a synchronized activity of the air sacs which are interspersed in the abdominal cavity, pneumatizing some of the adjacent bones. The pressure changes in the air sacs are generated by contraction of muscles which attach to the thoracic wall adjusting the thoracoabdominal space. A partition between the thorax and the abdomen is lacking: the liver and not the lung (as is the case in mammals) surrounds the heart. The oblique and the horizontal septa (see King

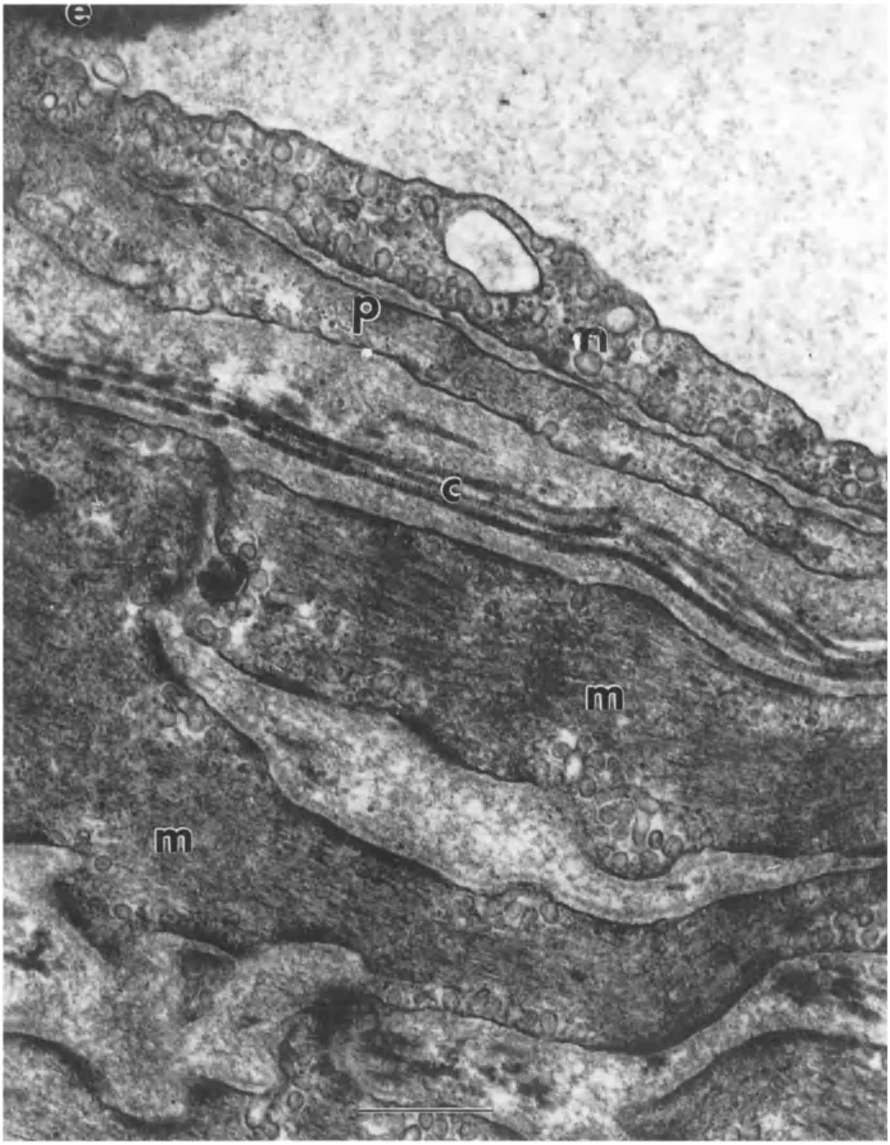


Fig. 79. Smooth muscles, *m*, and collagen, *c*, in the lung of the tree frog, *Chiromantis petersi*. *p* pericyte; *n* capillary endothelial cell; *e* erythrocyte. Contraction of the smooth muscle may assist in the expiration. *Bar* 1 μm. (Maina 1989d)

and McLelland 1975) are thought to be homologous to the mammalian diaphragm but fall far too short of anatomically dividing the coelomic cavity. The mammalian lung can be divided in two zones: the nonparenchyma (the conducting zone) of branching air conduits (the bronchi) and the parenchyma (the respiratory zone), made up of millions of alveoli. Together with the intercostal

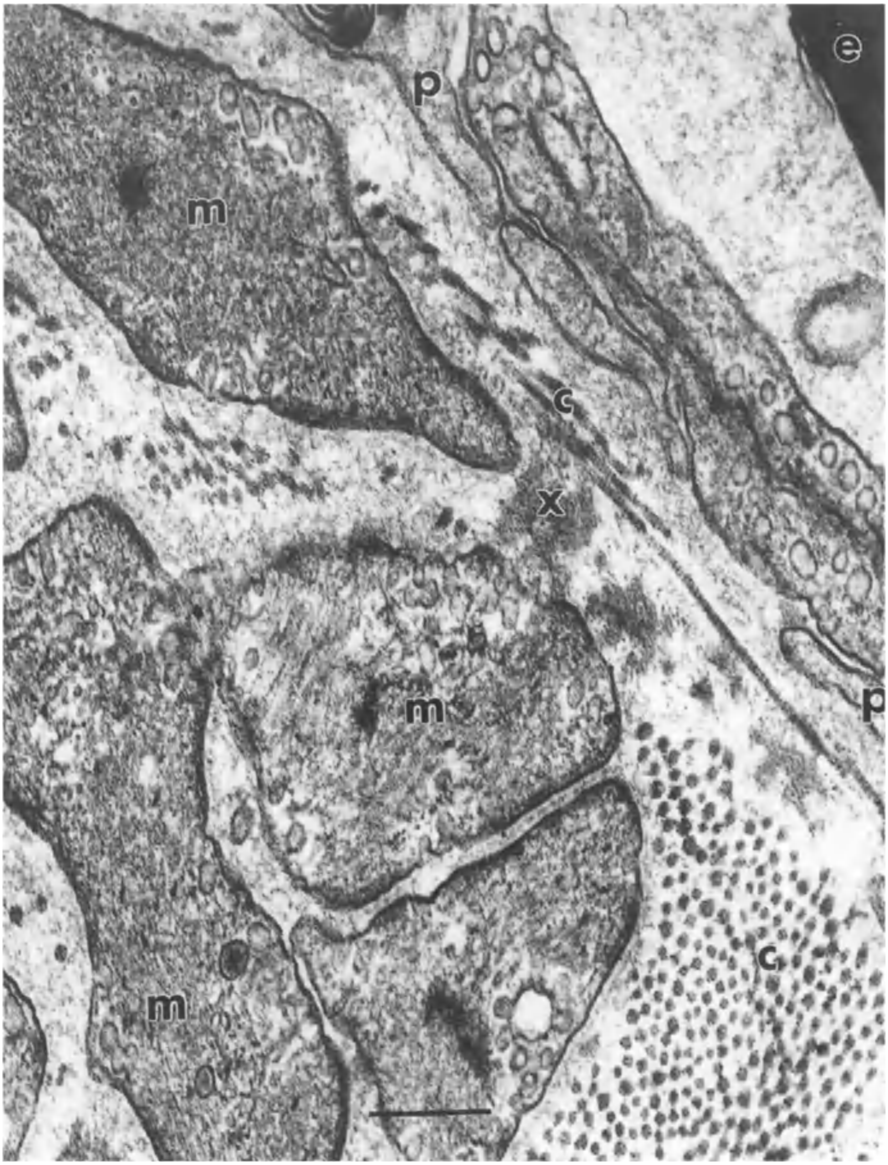


Fig. 80. Smooth muscles, *m*, in the lung of the black mamba, *Dendroapis polylepis*. *x* Elastic tissue; *c* collagen; *p* pericyte; *e* erythrocyte in a blood capillary. The smooth muscles may assist in intrapulmonary movement of air. *Bar* 1 μm. (Maina 1989e)

muscles, the diaphragm is an important respiratory muscle. By changing the volume of the thoracic cavity, air is moved into and out of the lung. The complete separation of the coelomic cavity into the thoracic and the abdominal cavities by the diaphragm was a key evolutionary development for efficient respiration in mammals. The evolved ventilatory mechanisms show varied levels of refinement which correspond with the phylogenetic levels of progression. The lungs in amphibians are filled with air under pressure from the bucco-pharyngeal cavity. In some reptiles (e.g., *Chamaeleo*), this process has been conserved and is used only in emergency cases to inflate the lungs. The various forms of suctional breathing which have developed in both terrestrial and aquatic animals allow greater flexibility in the tidal volume and have facilitated the development of the respiratory organs independent of the ventilatory mechanisms. Gas exchange has been totally disengaged from feeding. In general, those vertebrates which are adapted to respiration in xeric environments have the more specialized lungs (Fig. 81) and are capable of the highest sustained rate of gas exchange. This supports a high level of metabolic activity, enabling a greater degree of organizational and ecological progress. Such animals are found in only a few taxa which include insects,

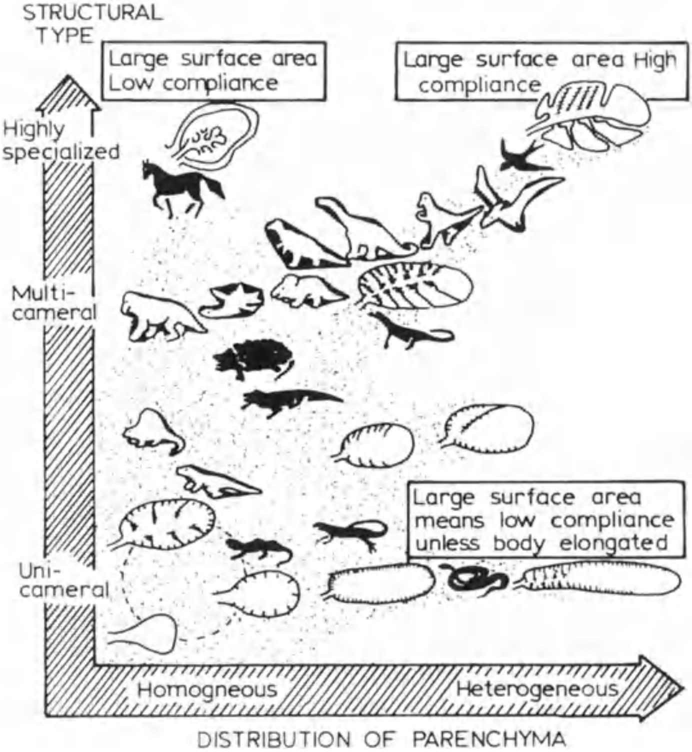


Fig. 81. Scheme of the structural complexities of the vertebrate lungs showing that a parameter such as an extensive respiratory surface area can be attained both in homogenous and heterogenous lungs through different modifications. For example, birds have isolated the ventilatory and the gas exchange parts of the lung and through intense subdivision of the lung achieved an extensive respiratory surface area in a relatively small lung. Pulmonary design corresponds with the metabolic needs and phylogenetic statuses of individual animal groups. Animals shown *on a black background* are now extinct. (Perry 1989)

reptiles, birds, and mammals. In these animals the integument is almost totally impermeable to water, O_2, and CO_2. Among vertebrates, the simplest forms of lungs are the smooth-walled saccular types, e.g., in *Proteus* (Hughes 1970), which are poorly vascularized. Though such lungs develop at the early larval stages, they play very little, if any, role in respiration until the midlarval stage (Goniakowska-Witalinska 1995). In the aquatic or amphibious groups, the lungs play diverse roles such as hydrostatic (Milsom and Johansen 1975; Pohunkova and Hughes 1985a), sexual display, and sensory perception (Duykers and Percy 1978; Schmidt 1982; Ehret et al. 1990). Internal subdivision of the lung imparts a greater respiratory surface area (Maina et al. 1989b; Fig. 82), increases the volume of blood in the lung, provides better exposure of blood to air (Hughes 1978), and ensures mechanical integrity of the organ. In most lungs, the exposure of the pulmonary capillary blood to air is promoted by a construction which entails not only increase in vascularity but also distension of the blood vessels over the epithelial surface, e.g., in the pneumonate gastropods (Maina 1989c; Figs. 59,60) and the mammalian lung (Fig. 87). In the double capillary system of the amphibians (Maina 1989d; Fig. 84) and most reptilian lungs (Maina 1989e; Figs. 83,85), a parallel row of blood capillaries which are exposed to air on only one side occur. A single capillary plan, where a sheet of blood capillaries which are supported by

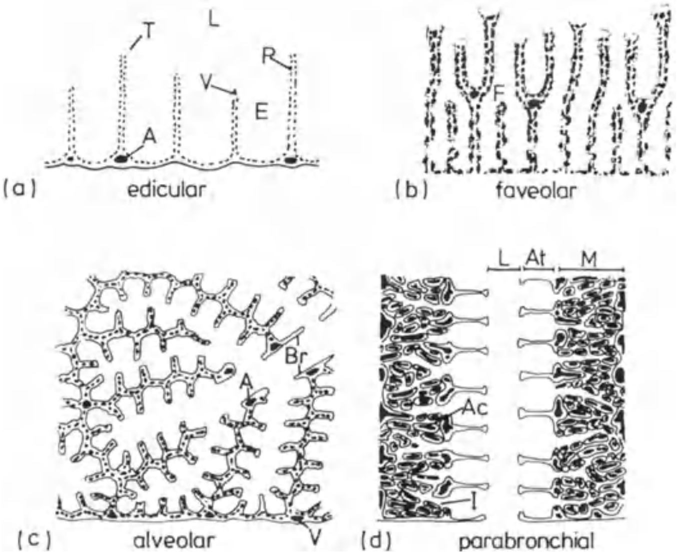


Fig. 82a–d. Subdivisions of the parenchyma of the vertebrate lungs. The simple unicameral lungs (**a**) have large air spaces, the ediculae; the faveolar lungs have layered air spaces (**b**), the faveoli; the highly specialized mammalian (**c**) and avian lungs (**d**), respectively, have alveoli and air capillaries as the terminal gas exchange components. Evidently, a basic design appears to have given rise to all forms of lungs, the particular design and complexity depending on the level of development and the metabolic needs of different animals. *T* Trabeculae; *A* artery; *V* vein; *E* ediculae; *L* lumen; *P* pneumocytes; *F* faveolus; *A* alveolus; *Br* bronchus; *At* atrium; *M* exchange tissue; *Ac* air capillary; *I* infundibulum. (Perry 1989)

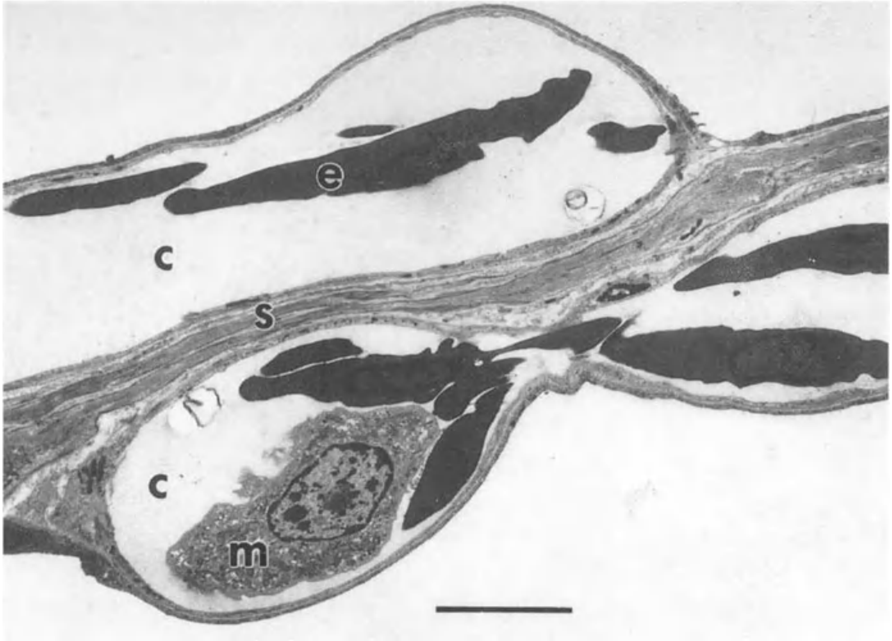


Fig. 83. Double capillary arrangement in the snake lung, *Dendroapis polylepis*. This design is limiting in that only one side of the blood capillary can be used for gas exchange. An attempt is made to increase the available surface area by the blood capillaries protruding over the surface of the lung. *c* Blood capillary; *e* erythrocytes; *s* interfaveolar septum; *m* white blood cell. *Bar* 5 μm. (Maina 1989e)

a thin septum, exists in the highly refined mammalian lungs (e.g., Alcorn et al. 1980; Burri 1984a; Figs. 86,87). In such cases, the capillary blood is essentially suspended in a three-dimensional space. The arrangement provides better exposure of blood to air compared with the double capillary one where the capillary loading, the ratio between the blood volume and the surface area available for gas exchange, is very high (Perry 1983). A notable exception to the general plan in the mammalian lung is that found in the rather placid herbivorous marine mammals, the sirenians, i.e., manatees and dugongs. Abundant connective tissue in the interalveolar septa, large alveoli (Tenney and Remmers 1963), and a well-developed double capillary system (e.g., Belanger 1940; Wislocki and Belanger 1940) occur. The pattern is similar to that found during the embryonic stage of development of the mammalian lung (e.g., Pinkerton et al. 1982). The preponderance of collagen and other supporting tissue elements in the lung (Laurent 1986) may provide the biomechanical support necessary to overcome the hydrostatic forces during deep dives. The exposure of the pulmonary capillary blood to air in the lungs of birds occurs in form of a diffuse arrangement between the air and blood capillaries (Maina 1982a, 1988a; Figs. 88,89) which intimately interdigitate with each other maximizing the respiratory surface area (Dubach 1981; Maina et

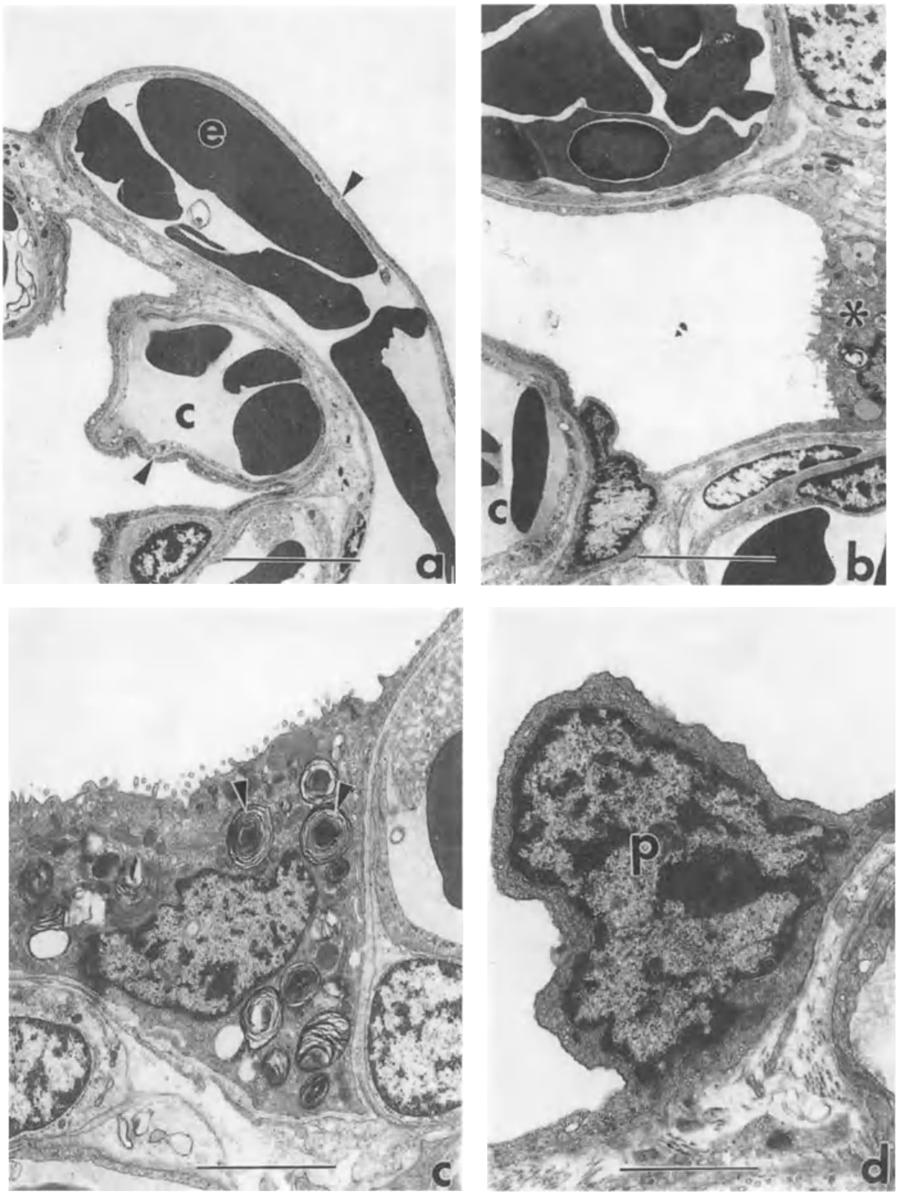


Fig. 84a–d. Structrue of the lung of the tree frog, *Chiromantis petersi*. **a** Blood capillaries, *c*, which contain erythrocytes, *e*, exposed to air across a thin blood-gas barrier, ➤. **b** Blood capillaries, *c*, bulging into an air space; ∗, granular pneumocyte. **c** Granular pneumocyte containing lamellated osmiophilic bodies, ➤. **d** *p*, nucleus of a Type I pneumocyte overlying a blood capillary. **a** *Bar 8* μm; **b** 4 μm; **c** 3 μm; **d** 0.2 μm. (Maina 1989d)

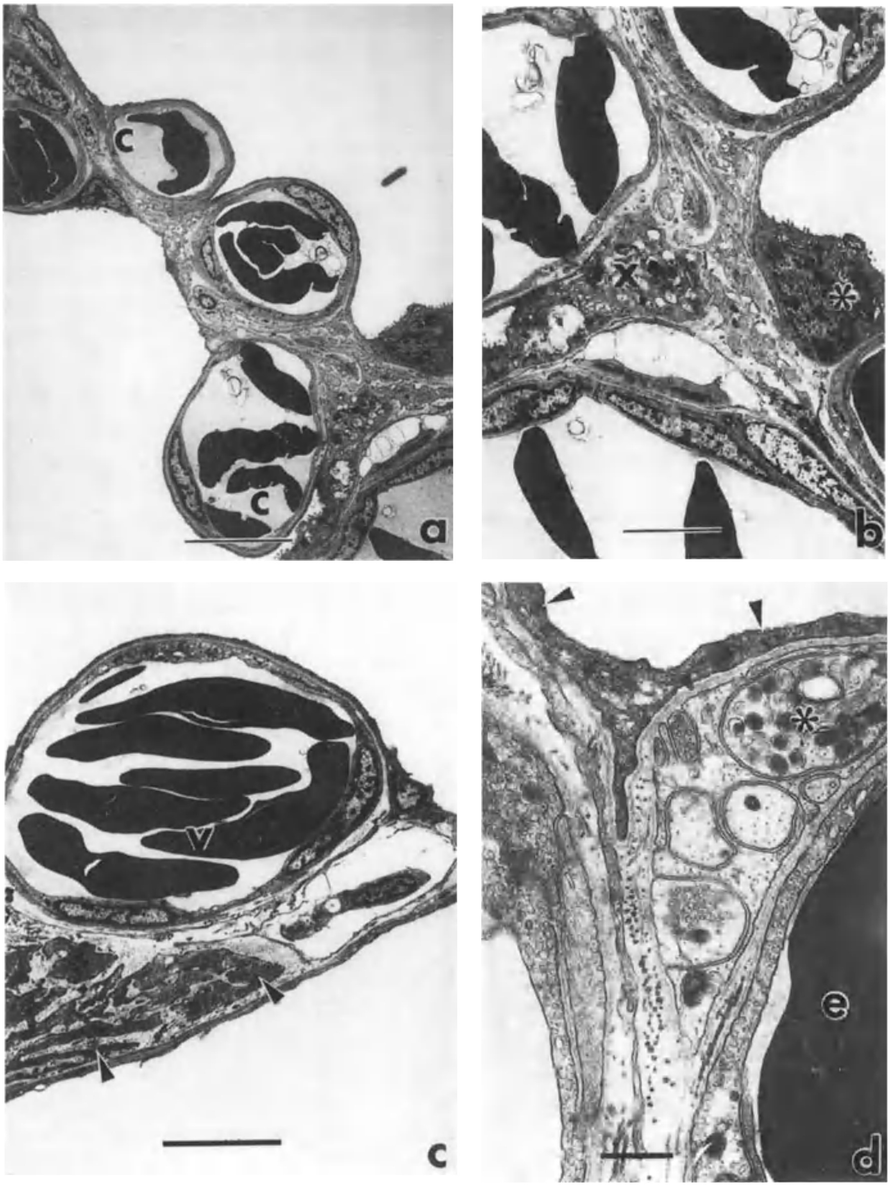


Fig. 85a–d. Structure of the lung of the black mamba, *Dendroapis polylepis*, showing blood capillaries bulging into the air spaces. Reptilian lungs generally manifest a better exposure of blood to air than the amphibian ones. **a** *c* blood capillaries. **b** * granular pneumocyte (type II cell) located between blood capillaries; *x* interstitial macrophange. **c** *v* a blood capillary bulging into an air space; ➤ smooth muscle. **d** * nonmyelinated axons in the lung; ➤ squamous type I cell; *e* erythrocytes. **a Bar** 10 μm; **b** 5 μm; **c** 5 μm; **d** 1 μm. (Maina 1989e)

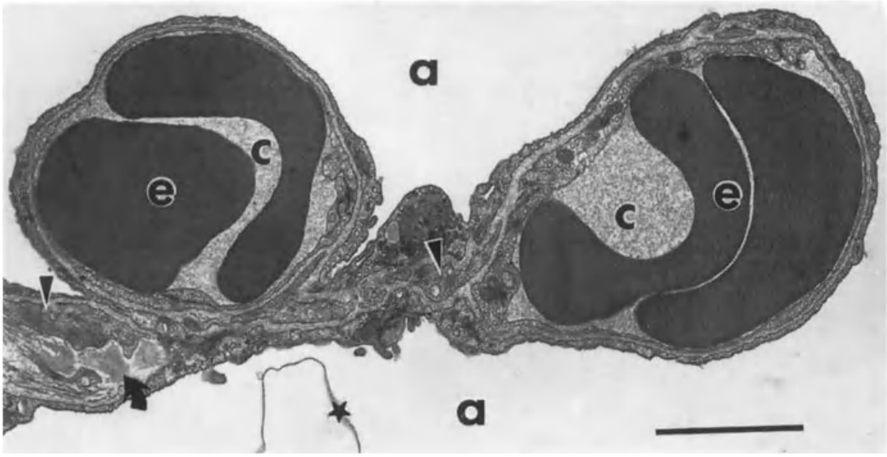


Fig. 86. Lung of a bat, *Epomophorus wahlbergi*, showing alveoli, *a*, and blood capillaries, *c*, containing erythrocytes, *e*. The interalveolar septum contains smooth muscle, ➤, and elastic tissue elements, ↘. The pulmonary capillary blood in the mammalian lung is better exposed to air than in amphibian (cf. Fig. 84) and reptilian (Fig. 85) lungs but thick and thin parts of the blood-gas barrier are evident. ★, detached surfactant lining. *Bar* 1.8 µm. (Maina et al. 1982a)

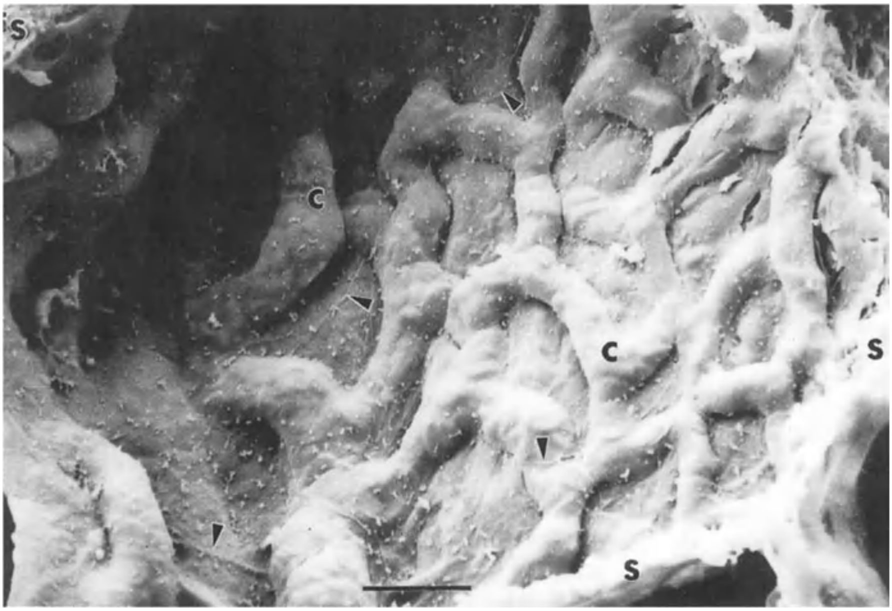


Fig. 87. An alveolus of the lung of the lesser bushbaby, *Galago senegalenis*, showing the blood capillaries, *c*, bulging into the air space. ➤ junctions of type I cells; *s* interalveolar septum. *Bar* 120 µm. (Maina 1990c)

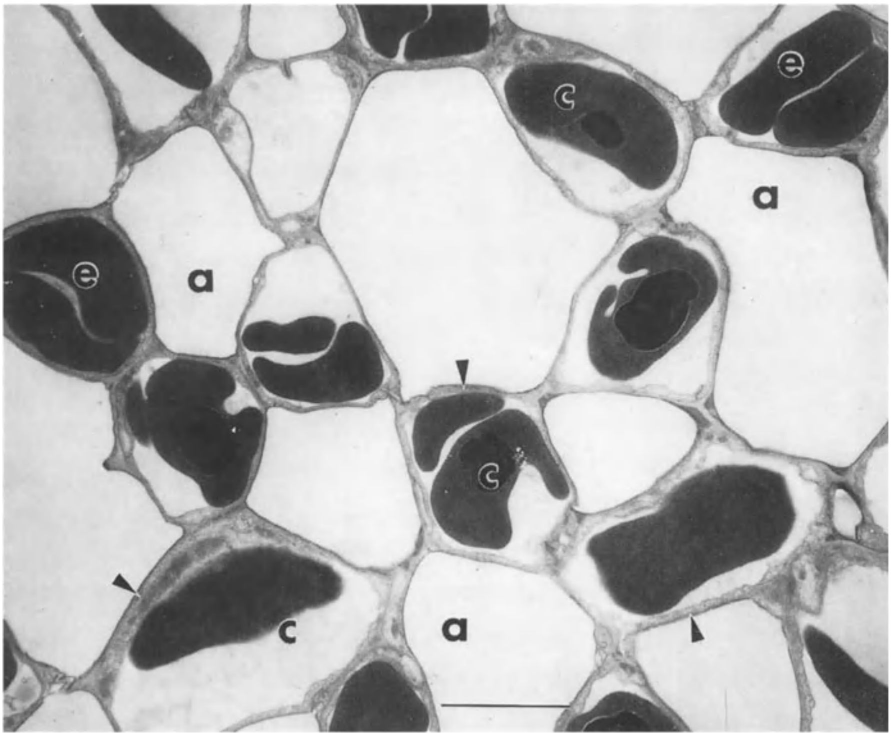


Fig. 88. Exchange tissue of the lung of the house sparrow, *Passer domesticus*, showing the air capillaries, *a*, and blood capillaries, *c*, which interdigitate very profusely. The blood capillaries are exposed to air on all sides giving rise to an extensive respiratory surface area per unit volume of the exchange tissue. ➤ blood-gas barrier; *e* erythrocytes. Bar 3 μm

al. 1989a) and providing an extremely thin blood-gas barrier (Figs. 40a,90). These features generate a remarkably high pulmonary diffusing capacity for O_2 (Maina 1989a, 1993; Maina et al. 1989a). In the lungfish, *Lepidosiren paradoxa*, the pulmonary capillary blood volume constitutes 3.5% of the total lung volume, in the rat lung the value is 14%, and in the bird lung 25% (Maina et al. 1989a).

6.7.2 The Amphibian Lung

The actual evolutionary origin of the amphibians is not well known (e.g., Szarski 1962; Schaeffer 1965b; Løvtrup 1977; Milner 1988). The osteolepiform fish (which are thought to have evolved a primal lung) or the lungfishes (Dipnoi) are conjectured to have given rise to the tetrapods (Romer 1946, 1967, 1972; Pough et al. 1989; Meyer and Dolven 1992). The transition to land by the vertebrates was inaugurated by the amphibians in the Devonian and concluded by the reptiles in

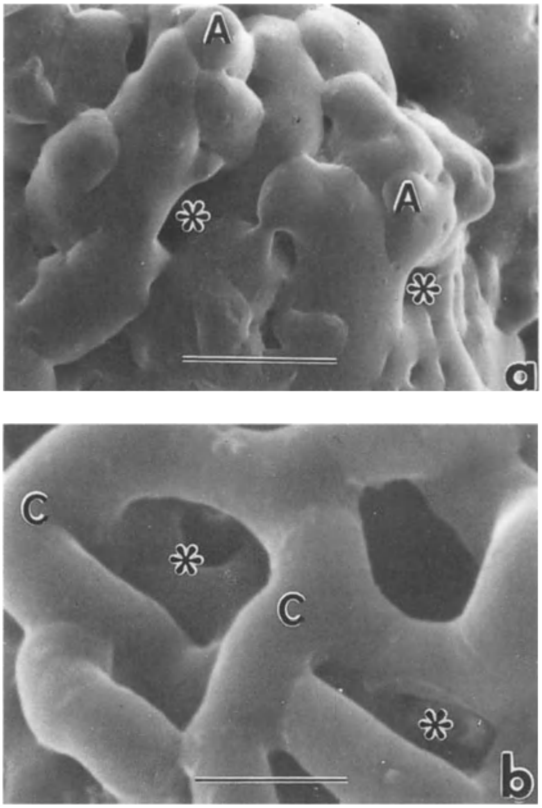


Fig. 89. **a** Cast preparations of the air capillaries, *A*, and **b** blood capillaries, *C*, of the lung of the domestic fowl, *Gallus domesticus*. **a** * spaces occupied by blood vessels. **b** * spaces occupied by the air capillaries. The two gas exchange units intertwine intimately increasing the surface area available for gas exchange. **a** *Bar* 10 μm; **b** 3 μm. (Maina 1982)

the Paleozoic era. For a good part of their evolution (about 70 million years), the early amphibians were strictly aquatic bimodal breathers (Thompson 1991). The contemporary amphibians occupy a focal point in the study of some fundamental biological processes such as the realization of air breathing and terrestrial colonization (Szarslo 1977; Smits and Flanagin 1994). Dual subsistence in water and land has obligated development of unique physiological and morphological respiratory adaptations in the taxon (Lenfant and Johansen 1967; Duellman and Trueb 1986; Jackson 1987; Burggren 1989). The unique nature of development (metamorphosis from aquatic to air breathing), the diversity of the habitats the taxon occupies, and the multifunctional nature of the lungs (respiration, vocalization, buoyancy control, and defense) explain both the heterogeneity of the lung morphology and the multiple pathways utilized for gas exchange (Guimond and Hutchison 1972, 1973a,b; Rahn and Howell 1976; Burggren and Wood 1981). Amphibians largely live in water and humidic habitats but a few species have adapted to the highly desiccating deserts (e.g., McClanahan et al. 1994). Terrestrial anurans such as *Chiromantis xerampelina*, which have developed an impermeable skin (Stinner and Shoemaker 1987) and ureotelism (Shoemaker et al. 1972), have acquired remarkable tolerance to desiccation. The two species can withstand a water loss in excess of 60% of their body mass (Loveridge 1970). The highly xeric African tree frog, *Chiromantis petersi*, leads a characteristically unamphibian lifestyle: it prefers direct solar insolation and temperatures of 40 to 42 °C (Loveridge 1970, 1976). The need to balance water conservation with gas exchange may explain why there are no large existing amphibians.

During the larval stages, amphibians have transient external and internal gills. Subsequently, the lungs and the bucco-pharngeal cavity become highly vascularized and assume an important respiratory role in air. The skin is a dual respiratory organ, exchanging gases in both water and air. The neotenic amphibians retain the gills throughout life. In the egg, larval caecilians use gills for respiration. The gill are lost soon after hatching (Welsch 1981). Using gills, the larvae of the viviparous caecilian, *Typhlonectes*, exchange gases and nutrients with the lining of the oviduct (Wake 1977): the gills are lost before birth. The neotenic larva of *Amblyostoma* (Axolotl) has perennial external gills. The flow of blood to the various respiratory organs is controlled mainly by ventilatory rate and the levels of ambient O_2 (Wood and Glass 1991). Hypoxia affects the flow of blood to the gills, skin, and the lungs (Shelton et al. 1986; Malvin and Heisler 1988). A drop in the PO_2 in the lung increases the perfusion of the skin (Boutilier et al. 1986) and vice versa. In aerated water, the skin receives 20% of the pulmocutaneous blood flow, the amount decreasing to an insignificant amount when the water is hypoxic (Wood and Glass 1991). In the lungless salamanders (Plethodontidae), gas exchange which occurs entirely across the skin and the buccal cavity (Gatz et al. 1974; Gratz et al. 1974) is diffusion-limited (Piiper et al. 1976). Such animals have acquired long, cylindrical bodies to secure a greater surface-to-volume ratio, a feature which promotes gas exchange across the skin. The lungless salamanders normally live in cold, well-aerated waters. In the aquatic amphibians, locomotion generates passive ventilation of the skin, a process which can increase O_2 uptake markedly (Feder 1985; Full 1985).

Living amphibians exist in three orders, namely the Gymnophiona (= Apoda = caecilians), Salentia (= Anura), and Caudata (= Urodela). Biologically, the caecilians are the least known group (Stiffler et al. 1990; Smit and Flanagin 1994). They are an elusive, vermiform tropical aquatic, semiterrestrial, or subterranean group (Nieden 1913; Taylor 1968; Renous and Gasc 1989). Evolutionarily, the caecilians are a monophyletic distant group (Milner 1988): they have been isolated from the other living amphibian orders for at least 70 million years. As characteristic of other similar animals with thin cylindrical bodies, e.g., the snakes (Ophidia) (e.g., George and Shah 1956), the caecilians possess long, tubular lungs (Fig. 99; Wake 1974; Maina and Maloiy 1988; Renous and Gasc 1989). In some species, the left lung is remarkably reduced or totally missing (e.g., Wiedersheim 1879; Pattle et al. 1977; Maina and Maloiy 1988; Burggren 1989; Fig. 98). In the aquatic *Typhlonectes compressicauda* (Sawaya 1947), however, as many as three lungs occurs (Toews and Maclntyre 1978): the anterior (tracheal) lung is located between the buccal cavity and the heart, while the other two run from the buccal cavity to the cloaca (Fuhrmann 1914; Toews and Maclntyre 1978). The lungs of the caecilians are internally subdivided to form air spaces by a single row of septa which are mechanically reinforced by two diametrically opposite trabeculae (Wiedersheim 1879; Wake 1974; Welsch 1981; Maina and Maloiy 1988; Fig. 99). Marcus (1928, 1937) observed that the structure of the caecilian lung is particularly primitive. The organization of the lung compares with that of the almost limbless, large aquatic salamanders like *Amphiuma* and *Siren* (Bell and Stark-Vancs 1983; Martin and Hutchison 1979). A relatively elaborate lung as in *Boulengerula* (Maina and Maloiy 1988) and *Geotrypetes* (Bennett and Wake 1974) may enable the caecilians to procure adequate amounts of O_2 from the hypoxic fossorial environment in which they live. Adaptively, the hematocrit and the hemoglobin concentration respectively, of the aquatic *Typhlonectes compressicauda* (38% and 11.3 gHb per 100 cm^3 blood; Toews and Maclntyre 1977, 1978) and the terrestrial *Boulengerula taitanus* (Wood et al. 1975; 40% and 10.3 gHb per 100 cm^3 blood) are some of the highest values reported in amphibians. The large blood volume (24 to 26% of the body mass; Toews and Maclntyre 1978) and low P_{50} of the blood hemoglobin, e.g., in *Typhlonectes* 3 kPa (Toews and Maclntyre 1978) and 3.7 kPa in *Boulengerula* (Wood et al. 1975), provide an efficient mechanism for uptake and storage of O_2 in the blood. While the caecilians have a lower resting rate of metabolism than the anurans and the urodeles, the aerobic capacity during exercise exceeds that of the two other groups (Smits and Flanagin 1994). The elongated nature of the lung of the caecilians may introduce ventilatory limitations during locomotion as a result of compression of the lung by the trunk muscles. A temporal dissociation between breathing and locomotion has been reported in the running lizard (Carrier 1991), an animal with a similarly long lung and general body form. In many ways, the development of the gas exchangers in the amphibians identifies with that of the lungfishes (Dipnoi) (Wassnetzov 1932; see Fig. 64a,b). Physiological adaptations such as high hemoglobin concentration, small numerous erythrocytes, and large blood volume have been reported in the caecilians which live in hypoxic environments (Wood et al. 1975; Toews and Maclntyre 1978). At 25 °C, O_2 uptake in the fossorial caecilian, *Boulengerula taitanus*, which lives in hypoxic-hypercarbic habitats, is equal to that of other amphibians (Hutchison 1968; Wood et al. 1975). The Caudata, which are mostly aquatic, e.g., the newts, have poorly vascularized lungs with a smooth internal surface (Hightower et al. 1975; Meban 1977; Goniakowska-Witalinska 1980a,b). Such animals mainly use the skin for gas exchange (Noble 1925,1929). The characteristically low metabolic rate newt, *Triturus alpestris*, has smooth-surfaced lungs (e.g., Claussen and Hue 1987) with 569 capillary meshes cm^{-2} while the metabolically more active tree frog, *Hyla arborea* (Goniakowska-Witalinska 1986), has more elaborate lungs with 652 capillary meshes per cm^2 (Czopek 1965). Plethodontidae constitute the largest family among the Caudata (Feder 1976; Ruben et al. 1993; Wake and Marks 1993). They acquire all their O_2 needs from the cold, well-oxygenated water in which they live across their highly vascularized skin. The length of the skin capillaries constitutes 90% of all blood vessels associated with the respiratory surfaces, with the other 10% being in the buccal cavity (Czopek 1965). The epithelial lining of the buccal cavity is very thin (Noble 1931; Czopek 1965). In caudates such as *Salamandra*, *Amphiuma*, *Megalobatrachus*, and *Siren*, species which predominantly utilize the lung for gas exchange, the internal surface of the lung is well subdivided (e.g., Goniakowska-Witalinska 1978; Meban 1979; Hashimoto et al. 1983; Matsumura and Setoguti 1984). The skin is poorly vascularized, with the epidermis being very thick (47 to 110 μm) (Czopek 1965). The lungs of most amphibian species such as *Amphiuma* and the toad, *Bufo marinus*, have a preponderance of smooth muscle tissue (Czopek 1962b; Smith and Rapson 1977; Martin and Hutchison 1979; Goldie et al. 1983; Stark-Vancs et al. 1984; Maina and Maloiy 1988; Maina 1989d), which may account for the great compliance of the lungs (Hughes and Vergara 1978). In *Amphiuma*, during expiration, the lung virtually collapses, producing an almost 100% turnover of air (Stark-Vancs et al. 1984). The amphibian lungs are best developed in the Salentia where septa intensely subdivide the lung, converting the large central air space into small stratified air cells (e.g., Okada et al. 1962; Smith and Rapson 1977; Goniakowska-Witalinska 1986). The internal morphology of these relatively elaborate lungs is similar to that of the lungs of the lungfishes (Dipnoi) (e.g., de Groodt et al. 1960; Klika and Lelek 1967; Gannon et al. 1983; Maina 1987a; Fig. 64). The lungs of *Pipa pipa* (Marcus 1937) and *Xenopus laevis* (Goniakowska-Witalinska 1995) are reinforced with septal cartilages to ensure patency of the air passages. In Salentia, the skin contributes very little towards gas exchange. The length of the skin capillaries constitutes only 30% of the total length of the blood capillaries located in the respiratory surfaces (Czopek 1965). However, in two species of Salentia which live in well-oxygenated high mountain lakes, e.g., *Telmatobius* and *Batrachophrynus*, the lungs are very small, the body very well vascularized, and the epidermis very thin (Muratori et al. 1976; Czopek and Szarski 1989). Well-differentiated pneumocytes (Fig. 103) as well as dust cells (free phagoctes; Fig. 102) have occasionally been observed on the surface of the amphibian lung (Welsch 1983; Maina 1989d).

The morphological heterogeneity of the amphibian gas exchangers and the lungs in particular correspond with the remarkable diversity of the environments they occupy, the mode of life they lead, and their property of interrupted development. Though amphibians have multiple options for gas exchange, only one pathway is best developed for optimal performance in a particular environment (Guimond and Hutchison 1976). Pulmonary vascularization correlates with the degree of terrestriality, behavior, and tolerance to dehydration. The skin is the main pathway for gas transfer in the predominantly aquatic species, while in the more terrestrial ones it has been relegated or rendered totally redundant as the lung has assumed a central position in gas exchange. *Necturus* experimentally held in cool, well-aerated water has better-developed gills than those of animals kept in warmer, poorly aerated water (Guimond and Hutchison 1976). Despite its strong reliance on water, the lung of the anuran clawed toad, *Xenopus laevis*, is very well developed for aerial respiration (Smith and Rapson 1977; Pohunkova and Hughes 1985a): 80% of its O_2 needs are transferred across the skin (Emilio and Shelton 1974). The perfusion of the skin is regulated by dilation and constriction of the cutaneous vasculature (Poczopko 1959). In *Bufo marinus* and *Rana catesbeiana* (Hillman 1987a,b), dehydration leads to increased vascular resistance due to a hemoconcentration effect on the blood viscosity. Dehydration in the terrestrial frog, *Eleutherodactylus coqui* (Pough et al. 1983), and the aquatic

Xenopus laevis (Hillman 1987a,b) lowers the capacity to utilize aerobic metabolism during activity. Systemic O_2 transport may be the limiting factor to aerobic capacity in the air-breathing amphibians (Hillman et al. 1985). In the xerophilous anuran, *Phyllomedusa sauvagei* and *Chiromantis xerampelina*, at the resting evaporative water loss (EWL), cutaneous respiration is insignificant, but with increased water loss, fractional cutaneous gas exchange correlates with the cutaneous EWL (Stinner and Shoemaker 1987). Adaptively, the blood of the highly xeric *Chiromantis petersi* has a low O_2 affinity and a temperature-insensitive O_2-hemoglobin binding capacity (Johansen et al. 1980).

Compared with the other air-breathing vertebrates, the amphibians have some of the simplest lungs, generally with low diffusing capacities for O_2 (Glass et al. 1981a). The lungs of *Necturus* and *Cryptobranchus* are thin-walled, transparent, poorly vascularized, and nonsepted (Guimond and Hutchison 1976): hydrostatic control may have the more significant role in such simple lungs. Regarding morphological and morphometric characteristics, generally, the lungs of the anurans and the apodans are more advanced than those of the urodeles (Meban 1980): on average, the arithmetic mean thickness of the blood-gas barrier in the urodeles is 2.59 μm, 2.35 μm in the Apoda, and 1.89 μm in the Anura. Some areas of the blood-gas barrier of the lung of the caecilians *Chthonerpoton indistinctum* and *Ichthyophis paucesulcus* (Welsch 1981) may be only 1 μm thick, while in the tree frog, *Hyla arborea*, the barrier may be as thin as 0.6μm (Goniakowska-Witaliniska 1986): *H. arborea* has a relatively high metabolic rate (Goniakowska-Witaliniska 1973) and the skin is richly vascularized (Czopek 1965). The lungs of the terrestrial species, e.g., the toad, *Bufo marinus* (Smith and Rapson 1977), the tree frogs, *Hyra arborea* (Goniakowska-Witalinska 1986) and *Chiromantis petersi* (Maina 1989d; Fig. 84), are eminently elaborate, having a series of hierarchical septa which delineate the air cells, which range in diameter from 1.45 mm in *Rana pipiens* to 2.3 mm in *Bufo marinus* and *Rana catesbeiana* (Tenney and Tenney 1970). The respiratory surface area in the lungs of the more terrestrial species is higher than that in the lungs of the aquatic ones (Tenney and Tenney 1970). Elementary lungs are adequate in amphibians, a group which characteristically has low aerobic metabolism (Whitford and Hutchison 1967; Goniakowska 1973; Goniakowska-Witalinska 1974; Feder 1976; Guimond and Hutchison 1976). Together with the Dipnoi, the amphibians have the largest tissue cells among vertebrates (Wintrobe 1934; Misiek and Szarski 1978; Szarski 1983). *Amphiuma* and *Necturus* exhibit great tolerance to anaerobiosis, withstanding 6 h of total anoxia (Rose and Zambernard 1966). When exposed to hypoxia and hypercapnia, the amphibians utilize behavioral hypothermia to reduce their O_2 need (Glass et al. 1983; Riedel and Wood 1988; Wood and Glass 1991).

Though the first vertebrates to invade land some 300 million years ago, by erecting a strong dependence on water for essential processes like aquatic oviparous reproduction, in regard to specific and numerical abundance and ecological distribution, modern amphibians constitute only a rather obscure vertebrate taxon. Their geographical distribution corresponds with freshwater, wet, high humidity, and high rainfall areas, feature which reflect strongly on their physiology. Cutaneous respiration (CR) presents very few possibilities for innovative designs and is generally considered an evolutionary dead end. Gans (1970), however, argued that CR may be a secondary condition in amphibians. This observation was supported by the suggestion by Romer (1972) that the Carboniferous amphibians may have been well scaled and thus had a water-impermeable skin cover. For all it is worth, the water-permeable skin of modern amphibians may represent a specialized secondary condition!

6.7.3 The Reptilian Lung

The reptiles were the first vertebrates to be adequately adapted for terrestrial habitation and pulmonary respiration. By evolving a cleidoic egg and an impermeable surface cover, parameters above those achievable by amphibians from which they evolved (e.g., Olmo 1991), they were able to delink their physiology from water. The Mesozoic era, which lasted for nearly 200 million years, is often called the age of the reptiles, as the taxon dominated the Earth. Reptiles are exclusively lung breathers. Like the amphibians, reptiles display remarkable pulmonary structural diversity which to an extent can be correlated with the diverse habitats occupied and lifestyles led. There is no single model for the reptilian lungs. Based largely on the nature of internal organization (e.g., Milani 1894; Marcus 1937; Baudrimont 1955; Duncker 1978a, 1979; Perry 1983, 1992a; Hlastala et al. 1985), different morphological classifications of the lungs have been attempted. The lungs range in complexity from the profusely compartmentarized (multicameral) ones of the turtles, monitor lizard, crocodiles, and snakes (Perry 1978, 1988; Perry and Duncker 1978, 1980; Maina et al. 1989b; Maina 1989e; see Figs. 92,97) through the less elaborate (paucicameral) ones of the chameleons (Fig. 96) and the iguanids to the simple, saccular, smooth-walled, transparent, (unicameral) ones of, e.g., the teju lizard, *Tupinambis nigropunctatus* (Klemm et al. 1979; Perry 1983). This classification is overly simplistic as transitional forms and gradations occur. The simplest lungs, which correspond in development to the amphibian lung, occur in the Sphenodontia. Such lungs have a central air duct and peripherally situated, shallow air cells, which give a low surface-to-volume ratio.

The brochoalverolar lung of mammals and parabronchial lung of birds are thought to have evolved from transformation of a multicameral lung (e.g., George and Shah 1956, 1965; Duncker 1978a; Klaver 1981; Perry 1983, 1989; Becker et al. 1989). With an elaborate anterior space in which much of the gas exchange occurs, and a simple posterior one analogous to the air sacs of the bird lung, the design of the avian lung-air sac system is more closely related to the reptilian lungs (Brackenbury 1987). While the reptilian lungs fill up from the peripheral walls into the axial air space (centripetal = centralizing = compacting growth), the air conduits constituting the unfilled gaps, the mammalian and avian lungs fill from inside (centrifugal = radiative = diffusive growth), i.e., from outward bifurcation of the central airways. These developmental differences may account for the fact that the volume density of the parenchyma in the reptilian lung is only 25.2% in the tegu lizard, *Tupinambis nigropunctus*, 32.1% in the monitor lizard, *Varanus exanthematicus* (Perry 1981), and 25% in the Nile crocodile, *Crocodylus* *niloticus* (Perry 1988). In the avian lung the average value is 50% (e.g., Maina et al. 1989a) and in mammals the value is as high as 90% (e.g., Gehr et al. 1981; Maina and King 1984). The faveolar air spaces in the parenchyma constitute 40% of the intrapulmonary air in the crocodile lung (Perry 1988), a value lower than that in the mammalian lung (about 56%; Maina and King 1984) and 53% in the bird lung (Maina et al. 1989a). In the more advanced snakes, e.g., Colubridae, Viperidae, and Elapidae, the left lung is greatly reduced or is totally lacking. In the primitive species, e.g., the boas and the pythons (Cope 1894; Verde 1951; Luchtel and Kardong 1981; Pohunkova and Hughes 1985b; Maina 1989e; Pastor 1995), the left lung occurs. The right lung is atrophied in the Amphisbenia (Gibe 1970). In the order Squamata, single-chambered lungs predominate especially in the families Teiidae (Klemm et al. 1979), Scindae (Gibe 1970), Lacertidae (Meban 1978a), and Gekkonidae (Perry et al. 1989b). Similarly, simple lungs occur in the family Angioidea (Meban 1978b). The land-based chelonians have paucicameral lungs, i.e., lungs with two or three peripheral compartments, which open into a central air space and lack an intrapulmonary bronchus. The marine species have multichambered bronchiolated lungs (Solomon and Purton 1984; Pastor et al. 1989). The elongated lungs of the ophidia and the amphisbaenids are divided into two functional zones, an anterior respiratory region which is well vascularized and a posterior one which is saccular and avascular (Kardong 1972; Klemm et al. 1979; Stinner 1982; Maina 1989e; Pastor 1995). In the crocodile lung, most of the parenchyma is located in the anterior two thirds of the lung where the blood makes 38 to 50% of the total volume (Perry 1988). The posterior part of the lung is thought to store air (e.g., Heatwole 1981), serve a hydrostatic role (Graham et al. 1975), and mechanically ventilate the anteriorly located exchange tissue in the manner of air sacs in birds: the arrangement may enhance the efficiency of gas exchange (Gratz et al. 1981; Stinner 1987; Vitalis et al. 1988). In heterogenous lungs, the design should convey a distinct functional advantage since the lungs of the more primitive reptiles are more homogenous (e.g., Luchtel and Kardong 1981). The varanids present the greatest level of pulmonary complexity in the suborder Sauria. *Varanus exanthematicus* and the pancake tortoise, *Malacochersus tornieri*, have multichambered lungs with a bifurcated intrapulmonary bronchi and profuse internal subdivision (Perry and Duncker 1978; Maina et al. 1989b; Fig. 93). The single-chambered lungs with an edicular parenchyma are thought to require low energy for convective ventilation: they occur in animals with low metabolic rates (Pastor 1995). The reptilian lung constitutes 5% of the body weight (Tenney and Tenney 1970). In animals of similar body mass, a reptile has a lung volume which is seven times greater than that of a mammal (Crawford et al. 1976; Glass and Johansen 1981) but the diffusing capacity for O_2 is relatively low (Crawford et al. 1976). The aerobic capacity of reptiles is remarkably lower than that of mammals. At a temperature of 37 °C, a 1-kg lizard consumes 122 ml O_2 h^{-1}, a value which constitutes 18% of the O_2 consumption of an equivalent-sized mammal (Bennett and Dawson 1976). The muscle capillary surface per unit muscle mass of a reptile is about 20% the value of a mammal of similar size (Pough 1980). At maximal exercise, anaerobic metabolism provides 86% of the total energy consumption in the water snake, *Natrix rhombifera* (Gratz and Hutchison 1977). At a body temperature of 20 to 23 °C, the physiological diffusing capacity of the reptilian lung (DLo_2p) is an order of magnitude smaller than that of a mammal of the same size (Crawford et al. 1976; Glass and Johansen 1981). The DLo_2p of the lung is similar in reptiles and amphibians (Glass et al. 1981a,b; Gatz et al. 1987; Lutcavage et al. 1987). Compared with mammals (e.g., Baldwin and Winder 1977; Scheuer and Tipton 1977; Dudley et al. 1982), where endurance exercise precipitates changes such as increases in tissue oxidative capacities and O_2 consumption, the adaptive response of lizards, *Amphibolurus nuchalis*, to endurance exercise is different (Gleeson 1979; Garland et al. 1987): trained lizards exhibit decreased heart and muscle masses but increases in liver mass, hematocrit, liver pyruvate kinase, and heart citrate synthetase activities. Interestingly, physical training enhances the swimming performance of the African clawed frog, *Xenopus laevis* (Miller and Camilliere 1981).

The epithelial cells lining the respiratory surface of the reptilian lung, are completely differentiated into types I and II cells (e.g., Okada et al. 1962; Nagaishi et al. 1964; Luchtel and Kardong 1981; Daniels et al. 1990; Maina 1989d,e; Perry et al. 1989b) and type III cells – the brush cells (Gomi 1982). A rare mitochondria-rich cell has been described in the lung of the turtle, *Pseudemys scripta* (Bartels and Welsch 1984). The type I cells are squamous and have remarkably thin, long cytoplasmic extensions. The much smaller, rather cuboidal surfactant-secreting type II cells are scattered between the type I cells (Figs. 84,85,87,90). In general, the pneumocytes in the lungs of the amphibians (Goniakowska-Witalinska 1995) and the lungfishes (Hughes and Weibel 1976; Maina 1987a) are undifferentiated while those in the reptilian, mammalian, and avian ones are. The differentiation of the pneumocytes in the higher vertebrates may be an adaptive strategy for greater functional efficiency (Maina 1994): reducing the numerical density of the more metabolically active surfactant-producing type II cells to a minimum and the type I cells adopting an extremely thin form lowered the overall O_2 consumption by the tissues of the gas exchanger. Furthermore, the design generated a thin blood-gas barrier, an important structural feature which enhanced the diffusing capacity of the gas exchanger for O_2 (Liem 1987a; Maina 1987a). Sporadic attenuation of the endothelium (Figs. 40,90), where extremely thin areas of the blood-gas barrier are generated without jeopardizing the mechanical integrity of the lung (Figs. 29b,40a,90) is a common scheme evoked to maximize gas transfer in the lungs of the higher vertebrates (e.g., Weibel 1973; Maina and King 1982a). Dust cells (macrophages) have been described in some reptilian lungs, e.g. in the turtle, *Testudo graeca* (Pastor et al. 1989). Unlike in the mammalian (Fig. 86) and bird lungs (Figs. 88,90), where owing to a single capillary system arrangement the exposure of the pulmonary capillary blood to air is very efficient, in the reptilian lung, depending on the species and the particular areas of the lung, a double capillary system (Fig. 85) commonly occurs. Reptilian lungs have a prevalence of smooth muscle tissue (Fig. 80). In the tegu and the monitor lizards, respectively, smooth muscle tissue constitutes 7.4 and 1.3% of the nontrabecular tissue (Perry 1981; Perry et al. 1989b,c). The smooth muscle tissue has been associated with intrapulmonary convective movement of air (Klemm et al. 1979; Tenney et al. 1984; Carrier 1988). The compliance of the lung of the garter snake, *Thamnophis sirtalis* of 0.042 ml per cm H_2O per g (Bartlett et al. 1986) is 50 times that of the lung of a mouse, a mammal of about the same body mass (Bennett and Tenney

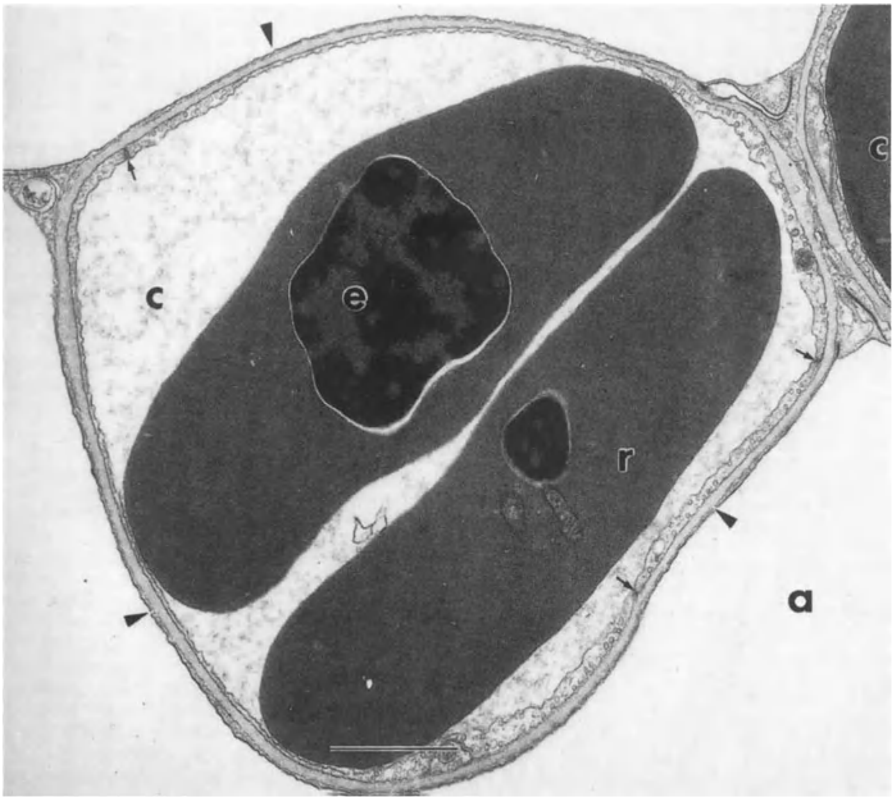


Fig. 90. High power view of the pulmonary blood capillaries, *c*, of the lung of the domestic fowl, *Gallus domesticus*, showing the blood-gas barrier, ➤, which is characterized by sporadic attenuations especially of the endothelial cell. →, endothelial cell junctions; *r* red blood cells; *e* nucleus of the red blood cell; *a* air capillary. *Bar* 0.5 μm

1982). At the peak of an expiratory phase, the residual volume of air (18 ml kg^{-1}) in the crocodile lung is only 13% of the maximal lung volume (Perry 1988). The compliance of the lung of the crocodile (0.7 ml cm^{-1} H_2O g^{-1}) is over four times that of the body wall (Perry 1988). The overall compliance of the reptilian lung is determined by the contractile elements of the lung, i.e., smooth muscle and elastic tissue, the saccular nature of the lung (Craig 1975), and the very effective pulmonary surfactant (Perry and Duncker 1978). Coupled with the irregular pattern of breathing, the properties may provide an energy-saving system on the respiratory work (Milsom 1984). The volume-specific lung compliance of the multicameral lung of the crocodile is similar to that of the much simpler lung of the gecko (Perry 1988; Perry et al. 1989b), suggesting that lung compliance in the reptilian lung may be an attribute of the parenchymal structure and not of lung type. The reptilian lungs may serve as air stores during apnea and in the aquatic species may support extended dives (Ackerman and White 1979). In the alligator, the pulmonary O_2 store constitutes 85% of the total lung volume (Andersen 1961).

Turtles can withstand complete anoxia for days or months, in the process accumulating lactic acid levels up to 200 $\mathrm{mmol\,l^{-1}}$, surviving a decrease in brain pH to 6.4 (Glass and Wood 1983). During the episodic apneic periods, which may last for a few minutes to hours (Glass and Wood 1983), the perfusion of the gas exchanger is reduced through a decrease in heart rate, stroke volume, and/or by the blood being shunted away from the lung. Ventilation-perfusion matching is necessary for efficient gas exchange (Burggren et al. 1977; Wood et al. 1978). In the Chelonia, the difference between the PO_2 in air spaces and that in the arterial blood (a factor determined by central cardiovascular admixture of the systemic venous blood into the systemic arteries and shunting of the blood within the pulmonary circulation; Seymour 1978) may be as high as 6 to 6.7 kPa (Burggren and Shelton 1979), in sea snakes it may exceed 8 kPa (Seymour and Webster 1975), and in resting lizards it ranges from 2.7 to 13 kPa (Mitchell et al. 1981). The respiratory parameters such as ventilation-perfusion ratio, respiratory frequency, and tidal volume are difficult to characterize in the periodic breathers (Glass et al. 1979). It has been hypothesized that structural limitations in the design of the reptilian lungs prevented the reptiles from attaining endothermic-homeothermy (Perry 1992a), relegating their aerobic capacities behind birds and mammals. In the green turtle, *Chelonia mydas*, during swimming, intermittent breathing gives way to a continuous breathing pattern (Butler et al. 1984). Uncharacteristic of reptiles, green turtles can endure sustained exercise: they make long migrations between their feeding grounds and breeding beaches, covering distances of as much as 4800 km, most of the time continuously swimming in the open sea at speeds of 2 $\mathrm{m\,s^{-1}}$ (Carr and Goodman 1970; Carr et al. 1974). They can increase their O_2 consumption by a factor of 3 (Prange 1976; Butler et al. 1984) without resulting in a significant level of anaerobic metabolism as most reptiles do during long bouts of activity (e.g., Bennet 1982). Hypoxia (10% O_2) caused continuous ventilation in resting green turtles and pulmonary blood flow was elevated and sustained (West et al. 1992): during swimming, increased heart rate was accompanied by a sevenfold increase in the ventilatory rate. Interestingly, physiological conditions of periodic ventilatory flow pattern do constitute a significant impairment in the parabronchial gas exchange efficiency in the avian lung (Scheid et al. 1977). This may indicate the remarkable functional reserves inherent in the bird lung (Sect. 6.7.5) where adjustments can be made to overcome certain limitations.

6.7.4 The Mammalian Lung

The beginning of the Tertiary saw the mammals take over and eclipse the reptiles as the dominant terrestrial vertebrate group (Romer 1967). The appearance of the placental mammals (subclass: Eutheria) formed the pinnacle in the development of the taxon. Among vertebrates, the mammalian lung, especially the human one, has been best studied both structurally and functionally. Recent excellent integrative reviews on these aspects include those by Weibel (1984a,b, 1986) and Burri (1984a,b). Owing to the abundance of literature in the area and need for brevity here, in-depth discussion of the mammalian lung (except for that of bats, which are less well known) will not be made. Suffice it to say now that the blind-ending, tidally ventilated mammalian lung falls far short of the level of efficiency attained by other gas exchangers, e.g., the insectan tracheal system and the avian lung-air sac system. With respect to O_2 consumption in standard conditions as well as maximal activity, Dejours (1990) observed that "compared with other mammals, the human exhibits no species-specific characteristics". Among the air-breathing vertebrates, the heterogeneity of the design of the lung decreases from the ectotherms – the Dipnoi (lungfishes), amphibians, and reptiles to the endotherms – mammals and birds. Morphological homogeneity appears to be an essential attribute for optimal design in gas exchangers. Structurally, the lungs of mammals are similar except for fine differences like bronchiolar bifurcation, lobulation, and topographic relationships between the airways and the vasculature. The need to optimize respiratory function must have become critical with changes to lifestyles which called for increased metabolic demands for O_2. Over and above the phylogenetic level of development, the organization complexity of the gas exchangers and respiratory stratagems adopted by an animal are greatly determined by the needs placed on them and the habitat occupied. For example, in the lungs of the nonhuman primates, e.g., the baboon, *Papio anubis* (Maina 1987b), and the vervet monkey, *Cercopithecus aethiops* (Maina 1988b), the lungs of the small, supposedly primitive prosimians, e.g., the lesser bushbaby, *Galago senegalensis* (Maina 1990c), are better from a morphometric perspective. The naked mole rat, *Heterocephalus glaber*, a small, eusocial poikilothermic fossorial bathyergid rodent which lives in thermostable burrows, has remarkably neotenic lungs (Maina et al. 1992). The diffusing capacity of the lung of the Japanese waltzing mouse, *Mus wagneri*, a pathologically hyperactive animal, is 55% greater than that of a normal one (Geelhaar and Weibel 1971). Lungs of high altitude-raised rats have smaller alveoli and a greater respiratory surface area than sea level dwellers (Pearson and Pearson 1976). Experimental lobectomy results in a compensatory overgrowth (Rannels and Rannels 1988), the remaining lobes in young rats attaining the same diffusing capacity as the control animals (Burri and Sehovic 1979).

6.7.4.1 Lungs of Bats

Bats (order: Chiroptera) are unique among mammals by their ability to fly (e.g., Thewissen and Babcock 1992). Flight has enabled remarkable adaptive radiation to occur in bats. Of all known mammalian species, one in five is a bat. About 800 species of bats have been recognized, the number falling between that of Rodentia (1600) and Insectivora (400). After the human being, *Myotis* (family: Vespertilionidae) is reputed to be the most widely spread naturally occurring mammalian genus on Earth (Yalden and Morris 1975). Despite the abundance and the wide geographical distribution, perhaps due to their elusive nocturnal lifestyle to which they were relegated by the birds, the only other older apparently well-established volant vertebrate, bats remain animals of curiosity, myth, and prejudice. The phylogenetic affinity between bats and the mainstream mammals is not clear (e.g., Novacek 1980, 1982; Scholey 1986). The groups which have evolutionary been closely associated with bats include Scandentia (Tupaiidae or tree shrews), primates, and the Dermoptera (e.g., van Valen 1979; Padian 1982; Pettigrew et al. 1989). Bats comprise the Suborders Megachiroptera and Microchiroptera and are considered by some investigators, e.g. van Valen (1979) and Novacek (1982), to be monophyletic, while others, e.g., Jepsen (1970), Smith (1977), Scholey (1986) and Pettigrew et al. (1989), consider them diphyletic. The earliest reliably known fossil record of a bat is that of *Icaronycteris index* of the Eocene (50 million years ago) which morphologically resembles the modern Microchiroptera (Jepsen 1970): the protobats may have been tree-dwelling omnivores which started to glide between trees while foraging (Norberg 1981, 1986). The general anatomy of bats is mammalian (Yalden and Morris 1975).

Powered flight is defined as capacity to produce lift, accelerate, and maneuver at various speeds (e.g., Pennycuick 1975; Norberg 1976a,b; Rayner 1986). The large number of animals which are said to fly, for example the freshwater butterfly fish, *Pantodon buchholzii* of the West African rivers, the parachuting frog of Borneo, *Rhacophorus dulitensis*, the flying snakes of the jungles of Borneo, *Chrysopelea* sp., the flying squirrel of North America, *Glaucomys volans*, the flying lemur, *Cyanocephalus volans*, and the East Indian gliding lizard, *Draco volans*, are essentially acrobatic passive gliders or parachutists which use part of their body to slow down a fall by using drag and lift (see Scholey 1986; Davenport 1994). Energetically, powered flight is a highly demanding mode of locomotion which has evolved in only a few elite animals (Tucker 1972; Berger and Hart 1974; Carpenter 1975; Thomas 1975), the insects, pterosaurs, birds, and bats - chronologically in that order. The mass-specific aerobic capacities of flying bats are essentially the same as those of forward-flapping birds but are 2.5 to 3 time those of running mammals of the same size (Thomas and Suthers 1972; Carpenter 1975; Thomas 1987). Bats can increase their O_2 consumption during sustained flight by a factor of 20 to 30 times (Bartholomew et al. 1964; Thomas and Suthers 1972). At an ambient temperature of 20 °C, a 12-g bat, *Myotis velifer*, is reported to increase its O_2 consumption by an astounding factor of 130 (Riedesel and Williams 1976). By avian standards, bats are excellent fliers in terms of speed, distance, and maneuverability (Vaughan 1966; Griffin 1970; Norberg 1976a,b; Fenton et al. 1985; Norberg and Rayner 1987). Speeds of $16\,\mathrm{km\,h^{-1}}$ in *Pipistrellus pipistrellus* (Jones and Rayner 1989), 30 to $50\,\mathrm{km\,h^{-1}}$ in *Myotis* (Hayward and Davis 1964) and $64\,\mathrm{km\,h^{-1}}$ in *Eptesicus fuscus* (Petterson and Hardin 1969) have been estimated. Migratory distances of about 1000 km have been reported in *Lasiurus borealis*, *L. cinereus*, *Lasionycteris noctivagans*, *Nyctalus noctula*, and *Tadarida brasiliensis* (Baker 1978; Thomas 1983). As they forage, *Epomophorus wahlbergi* and *Scotophilus viridis* are known to cover distances of about 500 km in a night (Fenton et al. 1985). Flight style and optimum speed in bats depend on, among other factors, choice of food, foraging behavior, and habitat selection (Norberg 1981). The small bats show a greater scope for flight with respect to agility and are even able to momentarily hover (Norberg 1976a,b). However, unlike birds, which commonly use energy-saving modes of flight like gliding and soaring (Rayner 1985), bats only rarely do so. *Pipistrellus pipistrellus* adopts gliding flight for only

13.4% of its flight time and the glides last for only 0.1 to 0.3 s (A.L.R. Thomas et al. 1990).

Despite the basic limitations intrinsic to the design of their characteristically mammalian lungs (Yalden and Morris 1975; Maina 1985), bat lungs have been structurally highly refined (e.g., Maina and Nicholson 1982; Maina et al. 1982a, 1991; Maina and King 1984; Maina 1986). These features have been functionally closely integrated with other anatomical and physiological aspects, enhancing the uptake and transport of the necessary large amounts of O_2 for flight. The strategies necessary to afford flight in bats evolved within the constraints presented by an inferior lung. This is a classic case of the innate plasticity of biological systems. In bats, a typical mammalian lung was exquisitely modified to exchange respiratory gases during flight at rates equal to those of the seemingly better-designed bird lungs. The most important parameters in this portfolio included (1) development of relatively large hearts with a huge cardiac output (Hartman 1963; Snyder 1976; Jürgens et al 1981), (2) high hematocrit, hemoglobin concentration, and O_2 carrying capacity of blood (e.g., Riedesel 1977; Wolk and Bodgdanowicz 1987), and exceptional pulmonary structural parameters (Maina et al. 1982a, 1991; Lechner 1984; Jürgens et al. 1981; Maina and King 1984). *Phyllostomus hastatus* can maintain the same high lung O_2 extraction factor of 20%, a value comparable to that of bird during the metabolic stress of flight (Thomas 1981; Thomas et al. 1984) or when at rest during exposure to a severe hypoxic stress (Farabaugh et al. 1985). The mean resting O_2 extraction factor at thermoneutral range in *Noctilio albiventris* of 18.3% lies between that of a bird (20.8%) and a nonflying mammal (16.6%) of the same body mass (Chappell and Roverud 1990). It increases from 35 to 40% at low ambient temperature. These values surpass those of most birds under similar conditions (Bucher 1985). One of the highest venous hematocrits in the vertebrates (75%) has been reported in a specimen of a 13-g bat, *Tadarida mexicanobrasiliensis* (Black and Wiederhielm 1976). In the five species of bats examined by Jürgens et al. (1981), venous hematocrits ranged from 51 to 63% and hemoglobin concentration and erythrocytes numbers were respectively 24.4 g dl^{-1} and 26.2 million l^{-1}. While high hematocrit may enhance O_2 uptake, the advantages conferred are soon compromised by the increased viscosity of blood (Stone et al. 1968; Hedrick et al. 1986; Hedrick and Duffield 1991). On account of the different effects of hematocrit on blood O_2 capacity and viscosity, where O_2 capacity increases linearly with the hematocrit while viscosity increases exponentially, an optimal O_2 transport level is established (Crosswell and Smith 1967; Shepherd and Riedel 1982; Kiel and Shepherd 1989). Increase in the hematocrit beyond optimal level causes a reduction in cardiac output, maximum O_2 consumption, and aerobic scope (Hillman et al. 1985; Tipton 1986).

In all bats which have been studied, a 1:1 synchronization between wing beat and breathing cycles has been observed (Suthers et al. 1972; Thomas 1981, 1987; Carpenter 1985, 1986): in birds, this occurs in only a few species (e.g., Tomlinson 1963; Berger et al. 1970; Berger and Hart 1974; Butler and Woakes 1980). It has been suggested (e.g., Bramble and Carrier 1983) that locomotory activity provides mechanical assistance to respiratory muscles. In birds, though flight muscles attach on the sternum, there appears to be very little effect on the actual pulmonary respiratory air flow and volume. Bernstein (1987), however, suggests that the disparity between the wing beat to breathing rates may be caused by the complex nature of the air flow in the avian parabronchial lung. In the European starling, *Sternus vulgaris*, the ventilatory volume change associated with wing beat ranges from 3 to 11% at most (Banzett et al. 1992). To a yet undetermined degree, the synchronization of wing beat with breathing cycles must enable bats to ventilate their lungs at a lower cost and probably more efficiently. In the bats *Antrozous pallidus* (Basset and Wiederhielm 1984) and *Myotis daubentoni* (Krátký 1981; Lundberg et al. 1983), the maturation of the O_2 transport system (i.e., blood O_2 capacity) to the adult status closely coincides with the start of flight behavior. Bats have exceptionally large lungs which occupy a large proportion of the coelomic cavity (e.g. Maina and King 1984; Maina et al. 1991). The gastrointestinal system is small and morphologically poorly differentiated (Makanya and Maina 1994; Makanya et al. 1995). Compared with nonflying mammals, bats have relatively large respiratory surface areas. The mass-specific respiratory surface area of $138\,cm^2 g^{-1}$ reported by Maina et al. (1982a) in the epauletted fruit bat, *Epomophorus wahlbergi*, is the highest value so far reported in a vertebrate. Compared with nonflying mammals, bats have relatively thin blood-gas barriers. The thinnest blood-gas barrier so far reported among mammals is that of $0.1204\,\mu m$ in *Phyllostomus hastatus* (Maina et al. 1991), a bat in which the O_2 extraction factor equals that of an energetic bird of comparable size (Thomas 1987) and which has a venous hematocrit of 60% (Jürgens et al. 1981). Pulmonary respiratory surface area can be increased by an overall enlargement of the lung, as occurred in bats, and/or increased subdivision of the gas exchange tissue, as in birds. In the compliant mammalian lung, increased subdivision of the parenchyma, however, generates smaller alveoli which are not only highly susceptible to collapse (due to large surface tensional forces at the air-tissue interface) but obligate greater amount of energy to inflate.

Unlike birds, which have dispersed widely and penetrated the remote cold regions of the world such as Antarctica, bats are largely tropical and neotropical in distribution (Wimsatt 1970; Yalden and Morris 1975; Carpenter 1985). This may probably be due to the need for reliable food sources in order to procure adequate metabolic substrates for production of the large amounts of energy for flight. Furthermore, due to the relatively poor insulation of the bat wings and presence of skeletal muscles on the wings (compared with the feathered bird wings which do not have muscles on the wing surface), excessive convective heat loss to the cold air at extremely low temperatures may occur in bats. The wing muscles may be cooled to a critical temperature where the proper coordination which is necessary for efficient flight is curtailed. On isolated forearm muscles from a number of species of temperate zone bats, Nelson et al. (1977) observed that the duration of contraction of forearm muscles at temperatures below 8 °C were five to ten times longer than those at 32 °C. However, some bats have been reported to fly in ambient temperatures as low as −5 °C (O'Farrell and Bradely 1977). Temperate-zone bats are known to hibernate or migrate to warmer regions of the world during winter (Kulzer 1965; A.L.R. Thomas et al. 1990). In hibernating *Myotis lucifugus*, O_2 consumption is 1.5% of their respective normothermic resting rates at or about thermoneutrality (Hock 1951): at 5 °C, breathing is arrhythmic in character, and apneic phases last for as long as 48 min.

6.7.4.2 The Respiratory Stratagems for Flight in Bats and Birds

In principal, animals use different strategies to attain optimal states (Howell 1983). Due to their remarkably different evolutionary backgrounds, different genetic resources, designs, and strategies were utilized by bats and birds to independently meet the aerodynamic and energetic requirements of flight. In pursuit of optimization of respiration, bats and birds evoked remarkably different paradigms: structural and functional parameters were variably integrated to promote gas exchange efficiency (Maina 1998). From modeling anatomical and physiological data, it appears that in bats, the process occurred through synergism of performances of relatively fewer, highly refined parameters which operate at or close to their maximum capacity. We have called this the narrow-based – high-keyed scheme (NB-HKS). Birds, on the other hand, have incorporated a wide spectrum of parameters in their gas exchange arsenal (and conspicuously conserved some) in what has been termed the broad-based – low-keyed scheme (BB-LKS): similar to this scheme, Heinrich (1983) has described a program of integrated suboptimal parts for a better whole in foraging bumblebees. Inevitably, consequent to the different respiratory contrivances in birds and bats, different functional reserves have evolved. In bats, the NB-HKS leaves a very limited margin of operation while the BB-LKS of birds affords an enormous reserve. This model-based inference (Maina 1998) is supported by the observation made by Chappell and Roverud (1990) that whereas with changing ambient temperature birds and nonflying mammals adjust respiratory frequency and tidal volume to meet changing O_2 demands, O_2 extraction remains fairly constant and in some species actually decreases (Casey et al. 1979; Withers et al. 1979; Bucher 1985; Chappell 1985; Kaiser and Bucher 1985; Chappell and Souza 1988; Bucher et al. 1990), bats (at least the lesser bulldog bat, *Noctilio albiventris*, on which data are available) accommodate varying thermogenetic O_2 consumption by simultaneously changing all three factors, namely respiratory frequency, tidal volume, and O_2 extraction, which may increase by a factor of as much as 2. The margin of operation in bats depends on factors such as the magnitude, nature, and duration of exposure to stress. Some degree of respiratory functional reserve must, however, exist in bats since they are able to absorb changes which call for moderate increases in O_2 demand such as flight during pregnancy, flight after the premigratory weight gain, and thermogenetic heat production associated with low ambient temperatures. For example, a female red bat, *Lasiurus borealis*, reported to weigh 12.9 g and presumed to have a wing loading of $0.09\,\mathrm{g\,cm^{-2}}$ is reported to have carried four young ones whose total mass was 23.4 g, i.e., 181% of her body mass (Staines 1965). In experimental tests to assess weight-lifting capacities, Davies and Cockrum (1964) observed that a female long-eared bat, *Plecotus townsendii*, with a body mass of 10.1 g, could lift 73.3% of her own mass, but *Tadarida brasiliensis* could manage only 9.3%. No bat is truly herbivorous as rodents are. Fermentative microbial digestion of cellulose calls for a voluminous gastrointestinal system (GIT) (e.g., Chivers and Hladik 1980; Warner 1981) and a long transit time for the ingesta (e.g., Balch and Campling 1965). Such an increase in mass for low energy yield per unit weight of the ingesta perhaps would be untenable for flight: bats have simple GITs contained in restrictive abdominal cavities (Forman 1972; Makanya and Maina 1994; Makanya et al. 1995) and the transit times of the ingesta must be relatively short. Bats of the temperate regions are exclusively insectivorous but tropical regions support both fruit-eating and insectivorous bats (Wilson 1973; Yalden and Morris 1975). While there are numerous herbivorous birds, e.g., the hoatzin, *Opisthocomus hoazin* (Dominguez-Bello et al. 1993), such birds are fairly large and have poor, if any, flight capacity.

From differentiation and integration the factors involved in gas exchange (Maina 1998), birds appear to have refined the structural parameters in preference to the physiological ones in contrast to bats, which favored the physiological ones: about 60% of the gas exchange capacity in birds can be attributed to the structural parameters and 40% to functional ones while in bats, 61% of the capacity can be attributed to physiological factors and 39% to the structural ones. Being generally small in size, the heaviest bat, *Pteropus edulis*, being about 1.5 kg (Yalden and Morris 1975; Carpenter 1985; Pough et al. 1989), leading a particularly energetic lifestyle, and operating from a level of a rather inferior lung, bats appear to have had very few choices but to fully refine and maximally exploit practically all the resources available to them. An "optimized" species is threatened with extinction if and when it is faced with increased demands to which it cannot respond (e.g., Minkoff 1983). Appropriate behavior and niche selection help minimize ambient pressures. In bats, we may unconsciously be witnessing a taxon living within very narrow tolerance limits of the environmental factors. The nocturnal lifestyle led by the bats may be explained by their more recent evolution of flight long after the birds had firmly occupied the diurnal niche for about 100 million years. The rather mundane respiratory physiological specializations for flight apparent in bats ruled out any possibility of successfully competing with birds.

6.7.5 The Avian Lung

It has been speculated by, e.g., Duncker (1978b) and Perry and Duncker (1980), that the avian lung-air sac system had its origin in the multicameral reptilian lungs like those found in the monitor lizards. Such lungs have a large ventilatable surface area (Maina et al. 1989a). The close phylogenetic affinity between reptiles and birds (e.g., de Beers 1954; Ostrom 1975; Jones et al. 1993) accounts for the anatomical similarities which abound between the two taxa. The chameleons possesses extensions from the lung similar to the air sacs of birds (Grassé 1970; Patt and Patt 1969; Klaver 1973, 1981; Fig. 96). Having arisen from reptiles much later than mammals, birds are phylogenetically more primitive than mammals (Romer 1967). From the arguments that some degree of endothermy may have developed in the Mesozoic and even Paleozoic reptiles (e.g., Romer 1967; Bakker 1975) and from the presence of a robust pectoral girdle, extensively ossified sternum, and expansive deltopectoral crest of the humerus (Romer 1966) (features which indicate well-developed flight muscles, excellent capacity to fly, and hence a high aerobic capacity), it has been conjectured that the direct progenitors of birds, the pterosaurs (order: Archosauria) of the Jurassic and Cretaceous, e.g., the 250-kg *Quetzalcoatlus northropi* (Langston 1981; Paul 1990, 1991) and *Pteranodon* (Bramwell 1971; Padian 1983) had developed complex, multichambered lungs. We shall, however, never know for certain about the structure and function of the lungs in these interesting now extinct reptiles. Fundamental differences in the design of the lungs with respect to respiratory gas flow pattern and overall efficiency occur between reptiles, birds, and mammals (Scheid and Piiper 1987).

Unique to the other vertebrate air-breathing groups, in birds, the lung has been uncoupled from the compliant bellows-like ventilatory air sacs (e.g., Fedde 1980; Maina 1983, 1996): the avian lungs are compact and virtually nonexpansile (Fig. 91). They are continuously ventilated by a synchronized action of the totally avascular air sacs (Lucas and Denington 1961; Marin-Girón et al. 1975) which play no role in gas exchange (Magnussen et al. 1976). During respiration, the volume of the lungs changes by a mere 1.4% (Jones et al. 1985). Experimental compression of the lung does not result in a substantial collapse of the air capillaries (Macklem et al. 1979). Although birds have smaller lungs per unit body mass than mammals (Maina et al. 1982b, 1983, 1989a; Maina 1989a; Maina and Settle 1982), the virtual rigidity of the avian lung has resulted in a substantial increase in the surface area per unit volume of the lung. The respiratory surface exceeds that of mammals of similar body mass (Maina et al. 1989a). The "insertion" of the bird

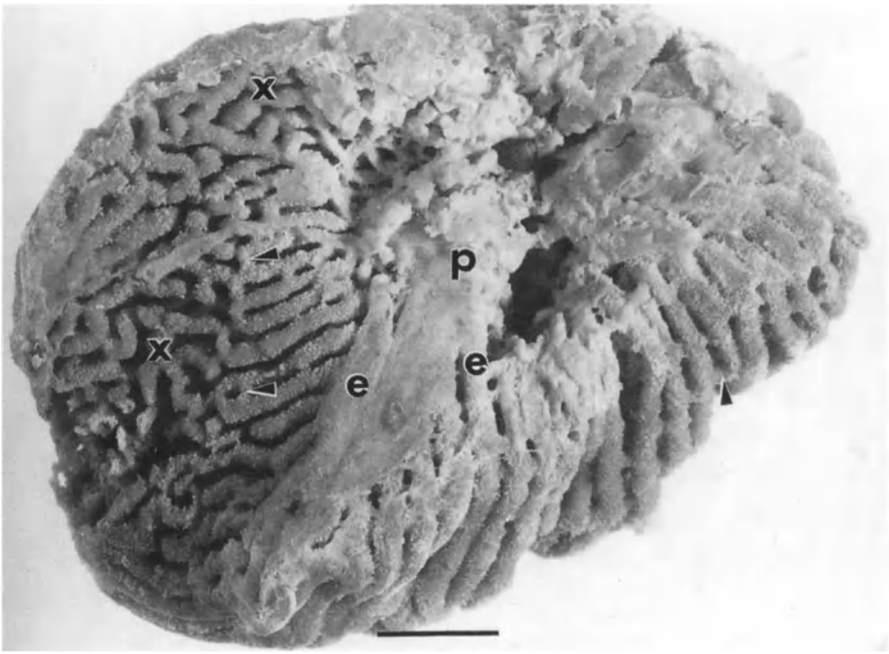


Fig. 91. Cast of the lung of the domestic fowl, *Gallus domesticus*, showing compact nature. The air conduits include the primary bronchus, *p*, the secondary bronchi, *e*, and the parabronchi, *x*. The ➤ show the anastomoses of the parabronchial system. *Bar* 8 mm

lung to the ribs followed by the relegation of the ventilatory compliance to the air sacs meant that surface tension was no longer a restricting factor in the extent of internal subdivision of the parenchyma. This resulted in extremely narrow terminal gas exchange components, the air capillaries, which gave rise to an extensive respiratory surface area and a thin blood-gas barrier (Maina 1981a; Maina and King 1982a). Considering the large number of species of birds (about 9000 species; e.g., Morony et al. 1975; Gruson 1976) and the remarkably diverse habitats they live in, the bird lung is morphologically remarkably homogenous. Subtle differences such as the degree of development of the parabrochi, spatial arrangement of the secondary bronchi, and size and location of air sacs, however, occur. The congruency in the morphological configuration of the bird lung may perhaps arise from the fact that all birds evolved from a common volant lineage (e.g., Cracraft 1986) and hence at one stage, they had to grapple with the demands for flight which some groups abandoned late. A fascinating difference in the morphologies of the bird lung is, however, that of the spatial arrangement, the degree of development, and the location of the tertiary bronchi (parabronchi). Two sets of parabrochial systems, the paleopulmo and neopulmo have been described (e.g., King 1966; Duncker 1974). The main differences between the papeopulmonic and the neopulmonic zones of the lung are: (1) the paleopulmonary parabronchi are located on the dorsocranial region of the lung and constitute about two thirds of the lung volume, while the neopulmonic set is located ventrocaudally and comprises about one third of the lung volume; (2) the paleopulmonic parabronchi are arranged in parallel stacks while the neopulmonic ones are irregularly arranged and anastomose profusely (e.g., López 1995); (3) while the air flow in the paleopulmo is continuous and unidirectional, that in the neopulmo changes with the phase of respiration (e.g., Fedde 1976); and (4) both sets of parabronchi start to develop at different embryonic stages (Romanoff 1960). The lungs of the primitive birds such as the kiwi and the penguin only have the paleopulmonic parabronchi while the neopulmo is variably well developed in the less conserved species, reaching maximal development in the relatively highly evolved passerines (King 1966; Duncker 1974). The substantive functional implication of the presence and absence of the development of the paleo- and neopulmo is still unclear. There are no morphometric differences in the structure of the gas exchange components in the two regions of the lung (Maina 1982b; Maina et al. 1982c). It is plausible that the bidirectionally ventilated neopulmonic parabrochi may provide a site for CO_2 cycling to alleviate occurrence of respiratory alkalosis due to excessive washout of CO_2 across the undirectionally ventilated paleopulmonic parabrochi especially during panting in thermal stressed birds (e.g., Jones 1982). The ostrich can pant continuously for as long as 8 h without experiencing acid-base imbalance (Schmidt-Nielsen et al. 1969). The avian lung is satisfactorily described by the crosscurrent model which considers that blood and parabronchial air interact at right angles (Fig. 32). Unlike in the mammalian alveolar system, under most conditions, the PCO_2 in the arterial blood ($PaCO_2$) and the PCO_2 in the end-expired air ($PECO_2$) are different, with the $PaCO_2$ being as much as 0.8 kPa less than $PECO_2$ (Scheid and Piiper 1970; Meyer et al. 1976; Hastings and Powell 1986). High-frequency respiration reduces the respiratory efficiency of the avian lung (Hastings and Powell 1987).

6.7.5.1 The Energetic Demands for Endurance and High Altitude Flight in Birds

Flight is the most energetically demanding form of locomotion that has evolved in animals. It places substantial metabolic demands on an animal. Skeletal muscle accounts for 96% of a flying animal's total energy consumption during flight, as it does in a human being at maximum exercise (e.g., Folkow and Neil 1971). In practically all active vertebrate groups, locomotion exerts the greatest demands on the respiratory system (Banzett et al. 1992). A significant metabolic barrier differentiates volant vertebrates from nonvolant ones. The fact that birds and bats are the only extant vertebrates capable of powered flight attests to the extreme selective pressure these taxa have endured during the course of evolution of this mode of locomotion. Wind tunnel experiments show that the energetic demands of flight are beyond those attainable by nonflying vertebrates (e.g., Tucker 1968; Carpenter 1975; Thomas 1975). In turbulent air or when ascending, a bird can increase O_2 consumption for brief periods by about 20 to 30 times whereas even a good human athlete can attain such an increase for only a few minutes (Tucker 1970). The O_2 consumption in the pigeon while running was estimated to be 27.4 ml per min and while flying at 19 m per s was 77.8 ml per min, a factorial difference of 2.8 (Butler et al. 1977; Grubb 1982). Although expensive in its absolute demands for energy, active flight is a highly efficient form of locomotion, as at fast speeds the distance covered per unit of energy expended is less than in most other forms of locomotion (Tucker 1970; Thomas 1975; Rayner 1981). In the bats, *Phyllostomus hastatus* and *Pteropus gouldii*, the energy required to cover a given distance is only one sixth and one fourth, respectively, of that needed by the same-sized nonflying mammal (Thomas 1975). At their optimal speeds, the minimum cost of flying for a 380-g bird is about 30% of the energetic cost of a 380-g mammalian runner (Hainsworth 1981). After evolving independently from reptiles, birds and small mammals acquired aerobic metabolic scopes between resting and maximal rates of exercise or cold-induced thermogenesis which are 4 to 15 times greater than those of their progenitors at the same body temperature (Bennett and Dawson 1976; Bartholomew 1982b; Dawson and Dawson 1982).

Whereas most birds fly at moderate speeds with the smaller and more agile passerines attaining speeds of 15 to 40 kph, the swifts (Apodidae), the loons (Gaviidae), and the pigeons (Columbidae) have been reported to reach speeds of between 90 and 150 kph, while the peregrine falcon (*Falco peregrinus*) has been reported to dive on its prey at a speed in excess of 180 kph (Welty 1964): a yet unsubstantiated speed of 360 kph has been reported in a diving male falcon. When the avian flight speeds, which may appear mediocre by general standards, are normalized with body lengths covered, they turn out to be remarkably fast. The small passeriform birds, e.g., swifts, starlings, and chaffinches, flying at a moderate speed of 40 kph, cover about 100 body lengths per s (Alerstam 1982; Kuethe 1975) compared with only 5 in a highly athletic human being and only 18 body lengths per s in the cheetah, one of the fastest land mammal (Hildebrand 1959, 1961). In its annual migration, the Arctic tern (*Sterna paradisea*) flies from pole to pole, a distance of 35 000 km between breeding seasons (Berger 1961; Salomonsen 1967) while the American golden plover (*Pluvialis dominica*) flies

3300 km nonstop from Aleutian Islands to Hawaii in only 35 h (Johnston and McFarlane 1967). Collision between a vulture with a jet craft at an altitude of 11 km was reported by Laybourne (1974) and a flock of swans (probably whooper, *Cygnus cygnus*) was observed by radar at an altitude of 8.5 km (Stewart 1978; Elkins 1983). Amazingly, the 3-g ruby-throated hummingbird (*Archilochus colubris*) flies nonstop for nearly 1000 km across the Gulf of Mexico from the Eastern United States, a distance which may require about 20 h to cover (Lasiewski 1962, 1963a,b). A 3- to 4-g rufous hummingbird (*Selasphorus rufus*) has about 1 g of flight muscles which consume O_2 at a rate of 82 μmol per minute (Suarez et al. 1990). Many passerine species are known to fly continuously for 50 to 60 h on the Europe to Africa trans-Saharan route (Berger 1961). The swifts (Apodidae) are said to fly continuously, day and night, sleeping, eating, drinking, and mating on the wing (Lockely 1970): they only come to land when nesting or drop down when they die! The same has been said of the wandering albatross (Jameson 1958). The alpine chough (*Pyrrhocorax graculus*), which is reported to nest above 6.5 km (Swan 1961), not only faces hypoxia ($PO_2 = 9$ kPa) but also low temperatures (-27 °C) and a desiccating atmosphere. In premigrating hummingbirds, body mass may increase by up to 60% with fat stores (Odum and Connell 1956; Norris et al. 1957). Carpenter et al. (1983) and Carpenter and Hixon (1988) observed that during the period before migration, the rofous hummingbirds gain weight at an average rate of 0.23 to 0.30 g per day (about 8–10% of lean body mass). Brain hypoxia at altitude inhibits the central nervous stimulus for shivering thermogenesis and may set the limit for high altitude residence (Bernstein 1990). Due to the lower density and viscosity of air at altitude, though the aerodynamic drag is reduced, a bird has to do more work to generate the required thrust for level flight (Tucker 1974).

6.7.5.2 Functional and Structural Respiratory Adaptations for Flight in Birds

The efficiency of the lung-air sac system of birds is remarkable. Its capacity to provide the large amounts of O_2 needed for flight at high speeds, across huge distances, and at high altitude is exceptional by mammalian standards. Unequivocally, the main adaptive feature which enables birds to fly in hypobaric hypoxia is their unrivaled tolerance to hypocapnia (Bouverot et al. 1976; Black et al. 1978; Black and Tenney 1980). The increased ventilatory rate under strenuous activity of flight is not accompanied by an increase in the tidal volume and excessive CO_2 washout (Bernstein 1987). By reducing the PO_2 gradient between the arterial blood and that in the inhaled air (Shams and Scheid 1987) and by evoking a Bohr effect which raises the O_2 content of blood (Grubb et al. 1979), the hyperventilatory response during high altitude hypoxia enhances O_2 uptake. The champion high altitude flyer, the bar-headed goose, *Anser indicus* (Sect. 3.8.2) exhibits unique adaptations for coping with hypoxia. Experimentally, the goose is able to withstand hypoxia to a simulated altitude of 11 km (Black and Tenney 1980) and cerebral O_2 flow is not limiting (Faraci et al. 1984): up to an altitude of 6.1 km, the bird maintains normal gas exchange without hyperventilating, and at about 11 km, when the O_2 concentration is only 1.4 mmol l^{-1}, it extracts adequate amounts of it to necessitate only a minimal increase in ventilation (Black and Tenney 1980). Fedde et al. (1989) observed that muscle blood supply and O_2 loading from the muscle capillaries rather than ventilation or pulmonary gas transfer are the limiting steps in the contraction of the flight muscles of the bar-headed goose under hypoxia. Black and Tenney (1980) observed that the PO_2 in the arterial blood at a simulated altitude of 11.6 km is only 0.13 kPa less than that in the inhaled air, indicating a very high O_2 extraction efficiency of the lung.

The remarkable functional efficiency of the avian lung is a product of a synergism of various structural and functional parameters and processes. The principal ones are: (1) the crosscurrent arrangement between the parabronchial air and the pulmonary venous blood (Figs. 36,41,42); (2) to a yet undetermined extent the countercurrent disposition between the air capillaries and the blood capillaries (Maina 1988a; Fig. 42); (3) a large tidal volume; (4) a large cardiac output; (5) a continuous and highly efficacious unidirectional ventilation of the parabronchial gas exchange tissue (Colacino et al. 1977; Scheid 1979); (6) a short but adequate pulmonary circulatory time (Burton and Smith 1967); and (7) superior morphometric parameters which provide a high diffusing capacity of the lung (Maina 1989a; Maina et al. 1989a). The total volume of the pulmonary system in birds (i.e., the volume of the lungs, air sacs, and pneumatic spaces) on average constitutes about 20% of the total body volume, with the value being as high as 34% in the mute swan, *Cygnus olor* (Duncker and Guntert 1985a,b). The volume of the entire avian respiratory system (lung + air sacs) is three to five times larger than in mammals and two times larger than in reptiles. The total volume of blood in the bird lung comprises as much as 36% of the lung volume, with 58 to 80% of it being held in the capillaries (Duncker and Guntert 1985a,b; Maina et al. 1989a). The pulmonary capillary blood volume in birds is 2.5 to 3 times greater than in the mammalian lung, where only 20% of it is found in the alveolar capillaries (Weibel 1963). The gas exchange tissue (the parenchyma) of the bird lung on average constitutes only about 46% of the lung volume (Maina et al. 1982b) while in the mammalian lung the parameter constitutes a greater proportion (about 90%) of the lung volume (Gehr et al. 1981; Maina and King 1984; Maina et al. 1991). The large surface area per unit volume of the parenchyma in the avian lung (Maina 1989a; Maina et al. 1989a) is achieved through intense subdivision of the parenchyma into the remarkably small terminal gas exchange components, the air capillaries. The air capillaries generally range in diameter from 5 to 10 μm (Maina et al. 1981; Maina 1982a,b; Duncker 1974). In comparison, the smallest alveoli in the mammalian lung are the 30-μm diameter ones of the lung of the shrew (Tenney and Remmers 1963), the smallest extant mammal with the highest mass-specific metabolic rate (Fons and Sicart 1976). The surface density of the blood-gas barrier (the surface area per unit volume of parenchyma) in birds ranges from $172\,mm^2\,mm^{-3}$ in the domestic fowl (*Gallus domesticus*) Abdalla et al. 1982) to $389\,mm^2\,mm^{-3}$ in the hummingbird, *Colibri coruscans* (Dubach 1981; Duncker and Guntert 1985a,b): in the mammalian lung, the values are about one tenth those of birds (Gehr et al. 1981). It should be empasized that the intense internal subdivision of the gas exchange tissue in the bird lung occurs within the confines of a proportionately much smaller lung which has a smaller parenchymal volume proportion (Maina 1989a; Maina et al. 1989a). This division is so intense that the epithelial surface area of the air capillaries is essentially equal to that of the capillary endothelium. In the process of optimizing the gas transfer surface area, the terminal gas exchange components interdigitate closely with each other, nearly constituting mirror images. The capillary loading, i.e., the ratio of the pulmonary capillary blood volume to the respiratory surface area, a parameter which indicates the degree of exposure of the capillary blood to air, is near unity (Maina 1989a; Maina et al. 1989a). The rigidity of the avian lung (Macklem et al. 1979), of which the change in volume has been estimated not to exceed 1.4% during inspiration (Jones et al. 1985), has facilitated the intense subdivision of the bird lung, providing an extensive and thin blood-gas barrier with a high diffusing capacity for O_2 (Maina and King 1982a; Maina et al. 1989a). While in the mammals the compliance of the respiratory system (excepting the thoracic walls) is determined by the terminal parts of the respiratory tree (mainly the alveolar spaces), in the avian system, compliance is confined to the air sacs (Piiper and Scheid 1989). In the domestic fowl, the maximum compliance of the respiratory system was reported to be $9.6\,\mathrm{ml\,cm^{-1}}$ H_2O (Scheid and Piiper 1969), in the duck $30\,\mathrm{ml\,cm^{-1}}$ H_2O (Gillespie et al. 1982) and in the anesthetized pigeon $2.8\,\mathrm{ml\,cm^{-1}}$ H_2O (Kampe and Crawford 1973).

6.7.5.3 *Functional Reserves of the Avian Respiratory System*

The lungs of birds maintain a large functional reserve. In the pigeon, *Columba livia*, Bech et al. (1985) and Koteja (1986) observed that cold exposure did not result in any perceivable respiratory distress, and Brackenbury et al. (1989) and Brackenbury and Amaku (1990) noted that experimental isolation of the thoracic and abdominal air sacs, a surgical procedure which renders about 70% of the total air capacity nonfunctional, had no detrimental effect on the gas exchange efficiency of the respiratory system of the domestic fowl: the birds could still run at three times the preexercise metabolic rate. From these experiments, Brackenburry (1991) observed that "there is considerable redundancy within the lung-air sac system in terms of its ability to adapt to removal of functional capacity, both at rest and during exercise". Investigations by other researchers corroborate this conclusion. The lung O_2 extraction was the same in exercising Pekin ducks in both normoxic and hypoxic conditions (Kiley et al. 1985). During flight, at ambient temperatures between 12 and 22 °C, lung O_2 extraction remains unchanged in the crows (Bernstein and Schmidt-Nielsen 1976) and starlings (Torre-Bueno 1978). The mute swan, *Cygnus olor* (Bech and Johansen 1980), has a lung O_2 extraction factor of 33% and the ventilation-perfusion ratio is near unity (Hastings and Powell 1986). Lung O_2 extraction values as high as 60 to 70% have been reported in some species of birds (Brent et al. 1984; Stahel and Nicol 1988). They exceed those of 40 to 45% reported in bats by Chappell and Roverud (1990). In the bar-headed goose, *A. indicus*, neither ventilation nor pulmonary gas transfer were limiting in a bird experimentally exercising in a hypoxic environment (7% oxygen) (Fedde et al. 1989). Hummingbirds, e.g., *Selasphorus platycerus*, can tolerate additional loading up to a maximum of 29.4% (Wells 1993b): a 10% increase in load called for a 5.7% increase in mass-specific O_2 consumption. The rufous-tailed hummingbird, *Amazilia tzacatl* has been reported to lift a mass about 80% of its body mass (Marden 1987). With high operational reserves, figuratively speaking, birds have not found it necessary to refine and/or utilize some of the structural and functional parameters commonly used by other animals. For example, the respiratory rate in birds is generally lower than in mammals (Calder 1968; Lasiewski and Calder 1971; Schmidt-Nielsen 1975) and the hemoglobin concentration and O_2 affinity of blood on average are essentially similar in the two groups (Lutz et al. 1973, 1974; Palomeque et al. 1980). In the mute swan, *Cygnus olor*, the respiratory rate is as low as three times per minute (Bech and Johansen 1980). Shams and Scheid (1989) and Scheid (1990) have suggested that the great endurance of birds to hypoxia is not due to the higher efficiency of the parabronchial lung compared with the broncho-alveolar one but rather in their ability to withstand lower arterial PCO_2 levels than mammals. In the resting domestic fowl, the arterial PCO_2 was estimated to be 4.4 kPa (Kawashiro and Scheid 1975) and in the exercising emu, *Dromaius novaehollandiae*, a value of 4 kPa, which is much lower than the average one of 5.3 kPa in the mammalian lung, was measured (Jones et al. 1983). In the mute swan, a pronounced positive PCO_2 difference between end-tidal gas (5.6 kPa) and mixed venous blood (4.3 kPa) averaging 1.3 kPa was reported by Bech and Johansen (1980). Experimentally, birds have been shown to tolerate arterial PCO_2 below 0.9 kPa (Shams and Scheid 1987; Faraci and Fedde 1986; Scheid 1990). Even after an increase of ventilatory rate by about 78% at a simulated altitude of 6.1 km, house sparrows, *Passer domesticus*, do not incur respiratory alkalosis (Tucker 1968; Lutz and Schmidt-Nielsen 1977). Unlike mammals, birds can withstand the high level of arterial hypoxemia because through a yet unknown mechanism, brain blood flow is not affected by arterial hypocapnia (Grubb et al. 1977; Wolfenson et al. 1982; Faraci and Fedde 1986). Paradoxically, in some species such as pigeons and bar-headed geese, the flow increases during such circumstances (Grubb et al. 1978; Faraci et al. 1984; Pavlov et al. 1987). Grubb et al. (1979) observed that by evoking a Bohr effect, hypocapnic birds reduced arterial PCO_2, raising blood O_2 content for any particular PO_2. This illustrates that in hypoxia, a hypocapnic bird enjoys better cerebral O_2 delivery than a normoxic one! In the human being, a reduction of the arterial PCO_2 to 1.3 kPa results in cerebral vasoconstriction, leading to a reduction of the flow of blood to the brain by about 50% (Wollman et al. 1968). In an apparent reassessment of their earlier view which recognized the superior design of the avian lung as a contributive factor in its exceptional efficiency (e.g., Scheid and Piiper 1987, pp. 123–124), based on small differences of the arterial PO_2 during gas exchange between birds and mammals, Scheid (1979, 1990) and Shams and Scheid (1989) cast doubt on the importance of the structure of the parabronchial lung (compared with the broncho-alveolar one of mammals) during exposure to extreme hypoxia. In Scheid (1990, p. 6), he expresses his sentiments as follows: “we have then to admit that we cannot decide whether the lung structure of birds has evolved out of functional needs or simply out of structural constraints with no significance for the higher efficiency”. These sentiments warrant further debate. It is highly unlikely that the evolution of such an intricate and efficient system as the avian-lung air sac system could have been coincidental.

6.7.5.4 Structure-Function Interdependence in the Design of the Avian Lung

The lungs of the small and the metabolically active species of birds show distinct morphometric specializations (Maina 1993; Duncker and Guntert 1985a,b). The generally small passerine species which have a higher metabolic rate and operate at a higher body temperature (see King and Farner 1969) have lungs superior to those of the nonpasserine ones (Maina 1981b, 1982c,d, 1984). The small highly energetic violet-eared hummingbird, *Colibri coruscans* (Dubach 1981), has remarkably highly refined lungs while the gliding and soaring birds which expend less energy for flight, e.g., gulls (see Norberg 1985), have relatively inferior lungs (Maina and King 1982b; Maina 1987c). Among birds, hummingbirds have the highest hemoglobin content, O_2 carrying capacity, erythrocyte counts, and large hearts (e.g., Carpenter 1975; Johansen et al. 1987). By developing a very small body size, the hummingbirds have occupied an ecological niche used earlier only by the insects (Suarez 1992). Hummingbirds have a heart rate as high as 1300 times min^{-1} during hovering flight (Lasiewski 1964), a wing beat frequency of up to 80 times s^{-1} (Greenewalt 1960), a heart size about twice that of a mammal of equivalent body mass (Schmidt-Nielsen 1984), and whole body circulatory time of about 1 s (Johansen 1987). During hovering, the O_2 consumption is 40 ml $O_2\ g^{-1}$ per h (Lasiewski 1963a,b; Epting 1980; Bartholomew and Lighton 1986; Suarez et al. 1990). To support hovering, the most energetical mode of flight when lift is generated both at up- and downstrokes to overcome gravity (Weis-Fogh 1972; Epting 1980), the flight muscles (Pectoralis and supracoracoideus) constitute about 30% of the body mass (Hartman 1961; Suarez et al. 1990). The mitochondrial volume density (the fraction of the muscle fiber volume occupied by the mitochondria) in the flight muscles of hummingbirds is about 35% (Suarez et al. 1991). The highest mass-specific respiratory surface area of about $90\,cm^2 g^{-1}$ has been reported in the small and highly energetic violet-eared hummingbird (Dubach 1981) and the African rock martin, *Hirundo fuligula* (Maina 1984). The value is substantially greater than that of $43\,cm^2 g^{-1}$ in the shrews, *Crocidura flavescens* and *Sorex* sp. (Gehr et al. 1980). The very high value of the repiratory surface area of $800\,cm^2 g^{-1}$ reported in a hummingbird by Stanislaus (1937) must be treated with caution. An extremely thin blood-gas barrier (harmonic mean thickness) of $0.090\,\mu m$ has been reported in the rock martin (Maina 1984) and the violet-eared humming bird (Dubach 1981): the thickness of the blood-gas barrier in the shrew is $0.334\,\mu m$ (Gehr et al. 1981). The indolent galliform species, e.g. the domestic fowl, *Gallus gallus* variant *domesticus* (Abdalla et al. 1982), a bird which has been domesticated for over 5000 years (West and Zhou 1988) and the guinea fowl, *Numida meleagris* (Abdalla and Maina 1981), have low pulmonary diffusing capacities. Among birds, the lowest pulmonary morphometric values have been reported in the emu, *Dromaius novaehollandiae* (Maina and King 1989), a huge bird which in nature is exposed to few predators. The Humboldt penguin, *Spheniscus humboldti*, a good diver (Butler and Woakes 1984), has a remarkably thick blood-gas barrier (Maina and King 1987), a feature presumed to enable the lung to resist collapse under hydrostatic pressure (Welsch and Aschauer 1986).

The resemblance between the structure (presence of air sacs and air conduits) and function (unidirectional and continuous air flow) between the avian and insectan respiratory sytems (Sects. 6.7.5 and 6.6.1) is an astonishing example of morphological convergence (Weis-Fogh 1964b; Maina 1989b). The insects evolved at the middle of the Paleozoic era some 400 million years ago (Callahan 1972) and the birds about 150 million years ago (de Beers 1954). The congruent morphology in such evolutionary distant animals presents a historic masterpiece of convergence which occurred as the two groups of animals grappled with the challenges involved in acquiring the large amounts of O_2 needed for volancy. This entailed radical transformations of their ancient gas exchangers. While bats retained but highly refined the structure of the mammalian lung, the insects honed the book lungs into the exceptionally efficient tracheal system, pterodactyls (of which the design of the respiratory system is unknown), and birds modified the ancestral multicameral reptilian lung. Clearly, there is no immutable design of a gas exchanger which is a prerequisite for flight. Subject to other features like aerodynamic configuration of the body (e.g., development of wings) being met, theoretically, at a cost, the mammalian lung can be refined for flight. Except in insects with the highly efficient tracheolar system (Sect. 6.6.1), endothermy appears to be a fundamental requirement for flight. Interestingly, momentary (preflight) endothermy has evolved in many insects (e.g., Heinrich 1992). The different strategies adopted by distant animals to solve common problems of uptake and delivery of O_2 to the tissues during strenuous activities such as flight depend on the different resources available to them to make the necessary adjustments. Those animals which accomplished flight reaped substantial benefits which included occupation of the almost limitless aerial biotope, adoption of a more economical mode of foraging, escape from ground predators, and dispersal to diverse habitats. Such taxa have undergone remarkable adaptive radiation. In the Animal Kingdom, the insects are the most populous taxon with about 750 000 species (Wigglesworth 1972). Among the terrestrial vertebrates, birds constitute the most speciose group with about 9000 species (e.g., Morony et al. 1975; Gruson 1976) compared with 4200 in mammals. Among mammals, the bats, of which there are about 1000 species (Wimsatt 1970; Yalden and Morris 1975), constitute 25% of all mammalian species. The now extinct flying reptiles which included *Pteranodon*, the largest flying animal that ever evolved, displayed exceptional diversity of body form (Norberg 1990).

6.8 The Internal Subdivision of the Lung: the Functional Implications

In the higher vertebrates, an extensive respiratory surface area per unit volume is achieved by internal partitioning of a finite volume of parenchyma, e.g., in reptiles (Figs. 92,93), mammals (Fig. 94), and in birds (Fig. 95). Among the air breathers, except for the avian lung and the insectan tracheal system where the terminal gas exchange components, i.e., the air capillaries and the tracheoles are

Fig. 92. Cast of the lung of the monitor lizard, *Varanus exanthmaticus*, showing the remarkable differences in the sizes of the air spaces in different regions of the lung, ➤. Unlike the lung of birds (Fig. 91), this lung presents some degree of lobulation, *x*; *t* trachea; *b* principal bronchi. *Bar* 13 mm

tubular structures, the amphibian, reptilian, and mammalian lungs are made up of numerous foam-like air bubbles surrounded by a moist surfactant-lined epithelium. Dilatation of these spaces requires energy. According to Laplace's Law, the pressure required to inflate a sphere is proportional to the surface tension and inversely proportional to the radius of a bubble. In practical terms, it requires more energy to inflate a lung with small alveoli than that with larger ones. It hence follows that while an intensely subdivided lung provides a more extensive respiratory surface area, more energy is needed to ventilate it. There must be an intrinsic compromise between the endeavor to establish an optimal pulmonary design and the cost of operating it. The low metabolism ectotherms have evolved lungs with large air spaces, mammals have developed small alveoli and an efficient ventilatory mechanism, while birds have evolved a rigid, noncompliant lung with remarkably small terminal gas exchange components. Initially, the surfactant developed in the archaic piscine lungs mainly to provide a protective continuous barrier over the epithelium (Liem 1987a). With the increasing internal complexity of the lung, the surfactant was commissioned to serve as a surface tension-reducing agent in order to prevent the collapse of the small terminal gas exchange components (Wilson and Bachofen 1982). In snakes (Ophidia), there is a tendency for a single lung to occur and in chameleons, extrapulmonary saccular extensions are characteristic of the lung (Fig. 96). The general pulmonary design in such reptiles approximates that of birds, where the gas exchange tissue (the

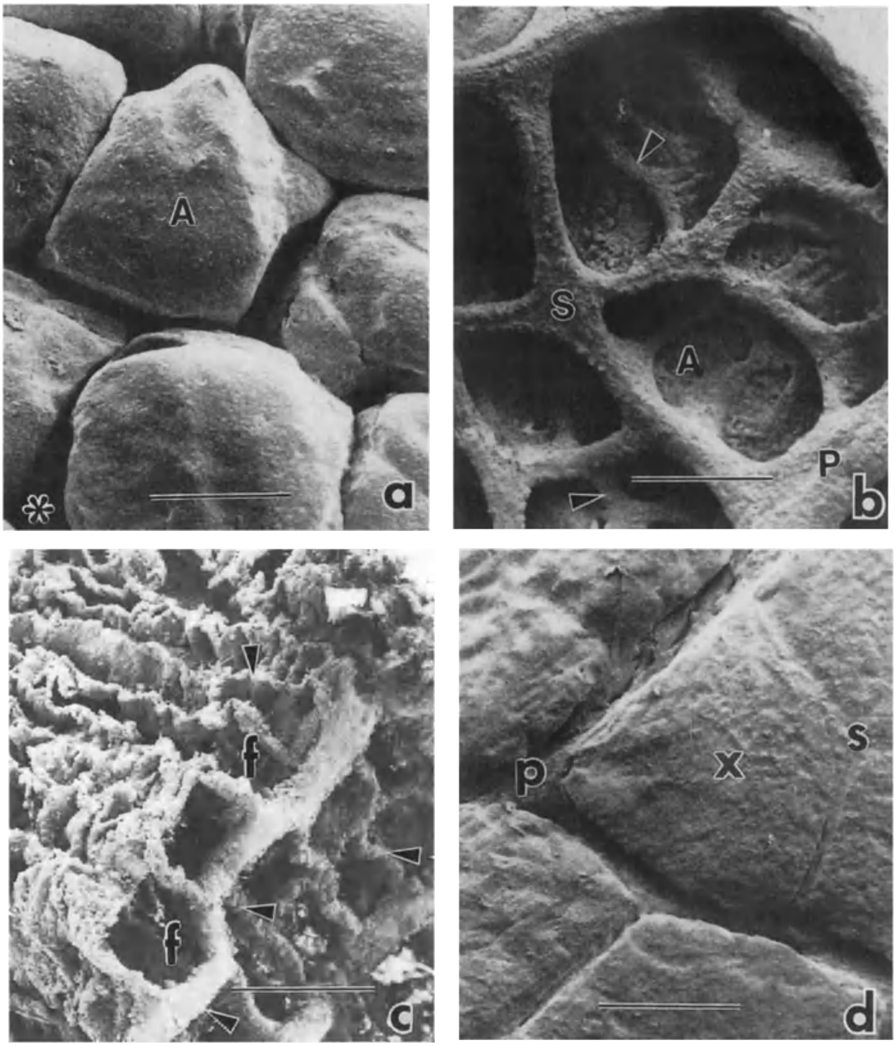


Fig. 93a–d. The respiratory surface area of the lung is increased by internal subdivisions. This process is shown in the reptilian lung. **a** Cast and **b** critical point dried preparation showing spaces, *A*, of the lung of the pancake tortoise, *Malacochersus tornieri*, formed by septation of the lung, ✻. **c** Lung of a snake, *Dendropis polylepi*, showing air spaces, *f*, separated by septae, ➤. **d** Cast preparation of the lung of the monitor lizard, *Varanus exanthematicus*, showing the various levels of septations; *p* primary septum; *s* secondary septum; ➤ tertiary septa; *x* terminal air spaces-definition of symbols also apply to fig. b. **a** *Bar* 300 μm; **b** 400 μm; **c** 500 μm; **d** 360 μm. (**a**, **b**, **d** Maina et al. 1989b; **c** Maina 1989e)

respiratory zone) is separated from the avascular (mechanical) region. Gas exchange tissue is located at the cranial part of the lung (Fig. 97) with the caudal saccular part ventilating it. The air passes twice through the gas exchange tissue, i.e., during inspiration and expiration, possibly enhancing O_2 extraction. A

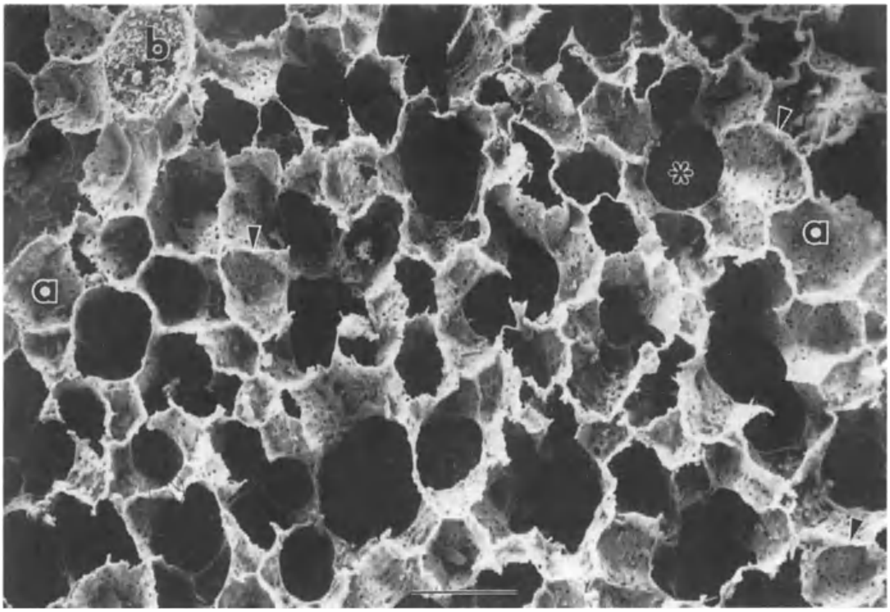


Fig. 94. Lung of the lesser bushbaby, *Galago senegalensis*, showing alveoli, *a*, the terminal gas exchange components. ➤ interalveolar septa; ∗ alveolar duct; *b* blood vessel. *Bar* 133 μm. (Maina 1990c)

Fig. 95. Exchange region of the lung of the emu, *Dromaius novaehollandiae*, showing an intraparabronchial arteriole, *x*, giving rise to blood capillaries, *c*, which interdigitate with air capillaries, *a*; *e* erythrocytes. *Bar* 2.5 μm. (Maina 1994)

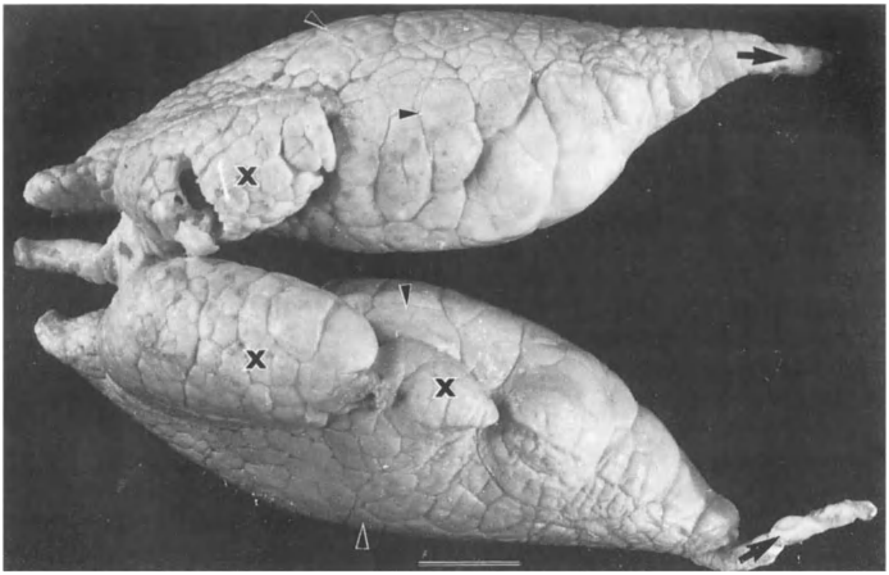


Fig. 96. Cast preparation of the lung of the chameleon, *Chamaeleo chameleo*, showing the notably large terminal gas exchange spaces and the size differences between the dorsal and ventral aspects of the lung, ➤. *Arrows* show the posterior saccular extensions similar to the air sacs of the lungs of birds. Some degree of lobulation of the lung, *x*, is evident. *Bar* 6 mm

similar organizational plan occurs in the lungs of the serpentine caecilians (Apoda), e.g., *Bourengerula taitanus* (Maina and Maloiy 1988). The left lung is very small and the tubular right lung is well subdivided in the cranial region with the caudal part being smooth (Figs. 98,99). Stratified septa provide mechanical support, which is necessary to avoid lung collapse. The smooth muscle and elastic tissue (Stark-Vancs et al. 1984; Goniakowska-Witalinska 1986) impart the tractability essential for pulmonary ventilation in air (Smith and Campbell 1976; Toews and Maclntyre 1978). In two genera of Salentia (Pipidae), the lung is internally supported by cartilaginous plates which are located in the 1st order of the septal walls in *Pipa pipa* (Marcus 1937) while in two Gymnophiona species, *Chthonerpeton indistinctum* and *Ichthyophis paucisulcus*, tiny aggregates of cartilage cells occur in the proximal part of the lung (Welsch 1981).

Internal partitioning of the lung increases its respiratory surface area. The intensity of the internal partitioning positively correlates with factors such as the metabolic rate, the lifestyle, and the environment in which an animal lives. While a sphere of a volume of 1 cm^3 has a surface area of 4.8 cm^2, 1 cm^3 of the lung of the shrew, *Sorex minutus*, has an alveolar surface area of 2100 cm^2 (Gehr et al. 1980). In the human lung, there are about 300 million alveoli of an average diameter of 250 μm (Weibel 1963), giving an overall surface area of nearly 150 m^2 and a thickness of the blood-gas barrier of 0.65 μm (Gehr et al. 1978). The respiratory surface area is about 100 times the total surface area of the body (Comroe 1974). Such an extensive surface area over which the respiratory media, air and

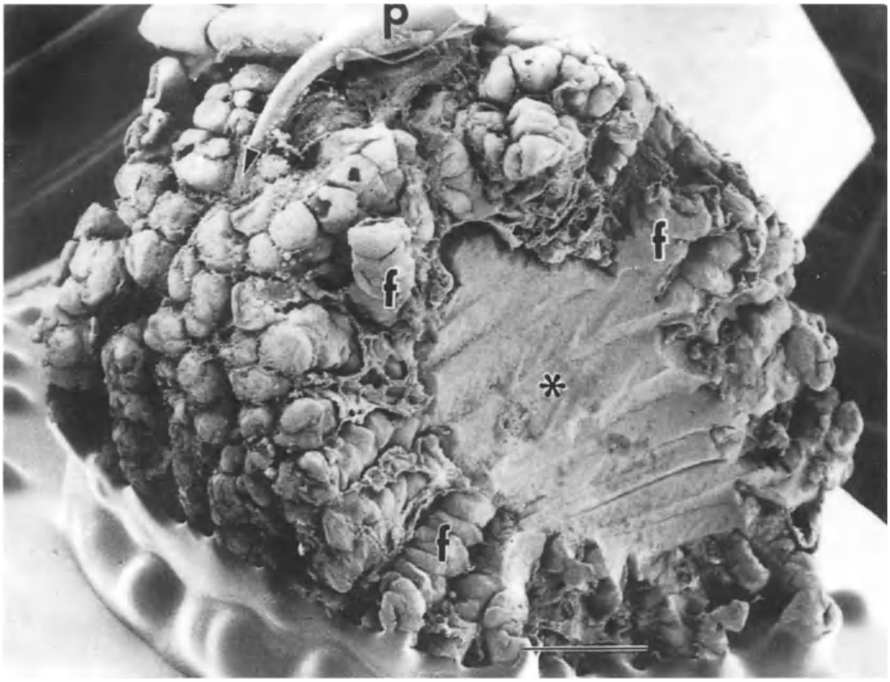


Fig. 97. Semimacerated double cast of the gas exchange region of the lung of the black mamba, *Dendroapis polylepis*, showing the air spaces, *f*, which radiate from the central air duct, *; *p* dorsal aorta; ➤ pulmonary artery. *Bar* 2 mm

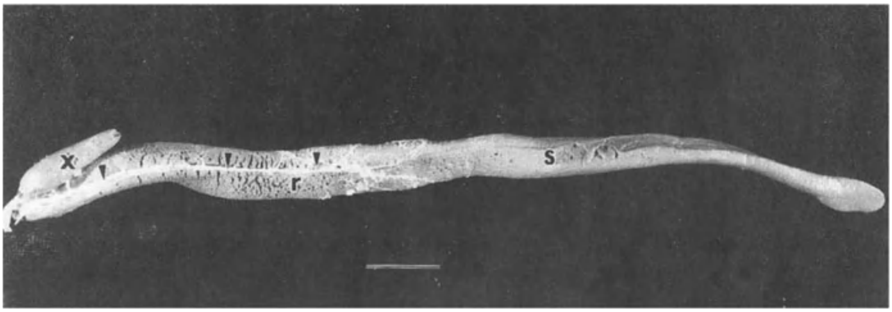


Fig. 98. Cast of a lung of a caecilian, *Boulengerula (Afrocaecicilia) taitanus*, showing the vestigial left lung, *x*, and the pulmonary artery, ➤, which runs three quarters of the length of the right lung. The posterior part of the lung, *s*, is smooth and saccular while the gas exchange region, *r*, is found in the anterior part of the lung. *Bar* 5 mm

blood, are separated by a thin barrier has called for development of various lines of defense to avoid damage by toxic substances and infection by pathogens. These include presence of mucus and ciliated cells on the upper respiratory passages (Figs. 100,101) and alveolar macrophages in the dependent regions (e.g., Brain

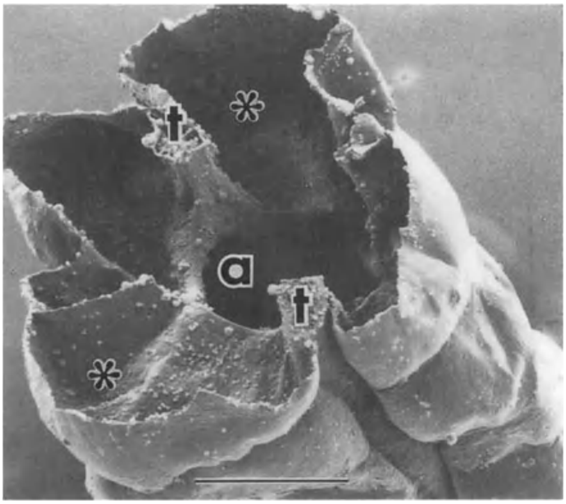


Fig. 99. View of the right lung of the caecilian, *Boulengerula (Afrocaecicilia) taitanus*, showing the central air duct, *a*, and peripheral gas exchange spaces, *. The rather simple lung is supported by two diametrically located trabeculae, *t*. *Bar* 115 μm. (Maina and Maloiy 1988)

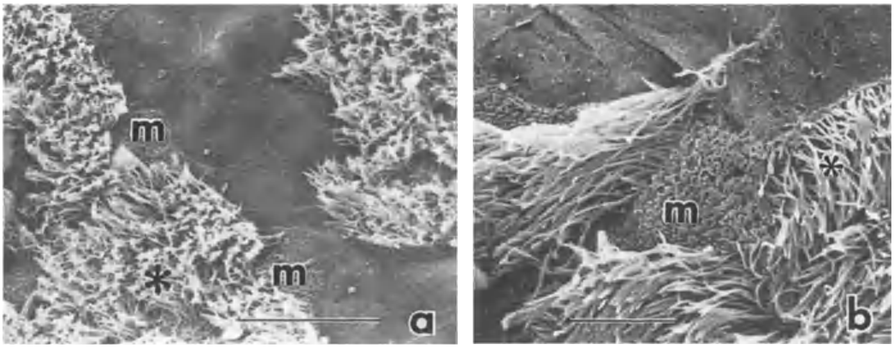


Fig. 100. a, b, Epithelial lining of the trachea of the respiratory system of the lung of the black mamba, *Dendroapis polylepis*, showing ciliated cells, *, and mucus cells, *m*. **a** *Bar* 2 μm; **b** 6 μm

1985; Fig. 102). In spite of the fact that the respiratory mucosa presents the largest interface between the external environment and the internal milieu, in absence of pulmonary disease, below the larynx, the respiratory system is virtually sterile (Skerret 1994; Agostini et al. 1995). In the amphibians (Welsch 1983; Maina 1989d; Goniakowska-Witalinska 1995) and probably in ectothems in general, lung macrophages are rare. The number of pulmonary macrophages appears to

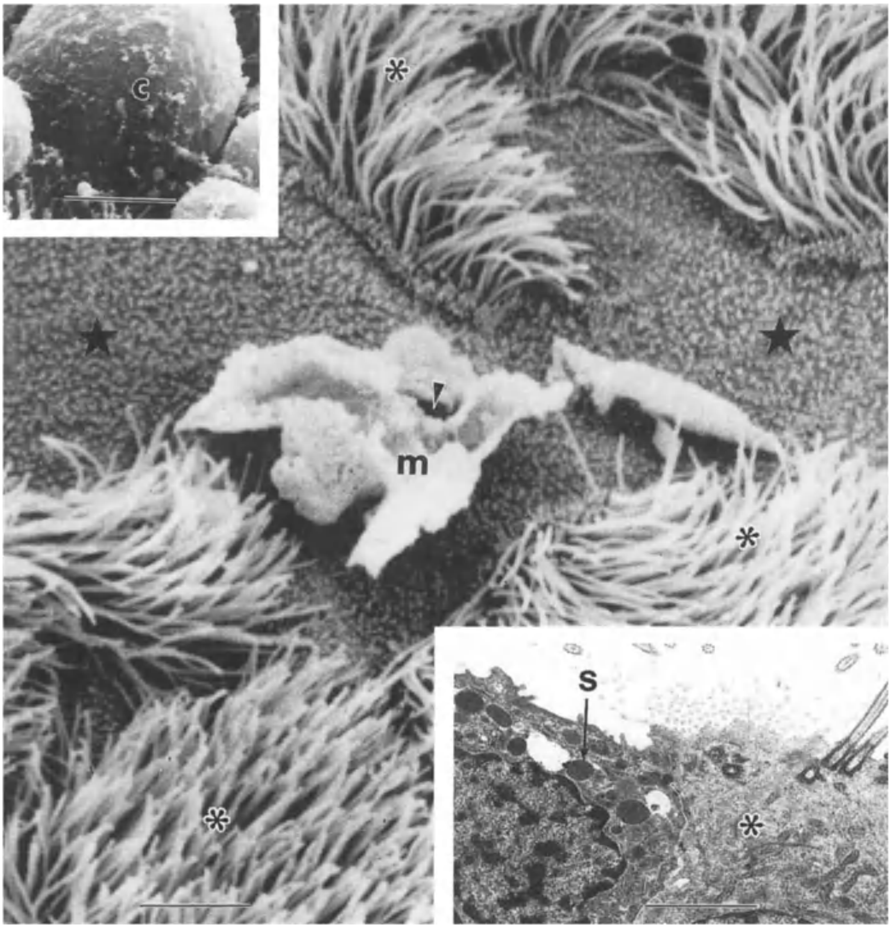


Fig. 101. Epithelial lining of the air passages of the lung of the vervet monkey, *Cercopithecus aethiops*: ✻ (*main figure*) ciliated cells; ★ mucus cells; *m* mucus debri; ➤ secretory pore of a mucus cell. *Top inset* Clara cells, *c*. *Bottom inset* a mucus cell with secretory granules, *s*, next to a ciliated cell, ✻. *Bar* (*main fig.*) 3.6 µm; *top inset* 0.5 µm; *bottom inset* 2 µm. (Maina 1988b)

correlate with the metabolic capacities of animals and the environment in which they live.

6.9 The Surfactant: a Versatile Surface Lining of the Gas Exchangers

While the insectan trachea, which are supported by helical cuticular taenidia, and the fish gills, whose filaments are physically separated by water, have little need for stabilization against surface forces, practically all evolved air-breathing

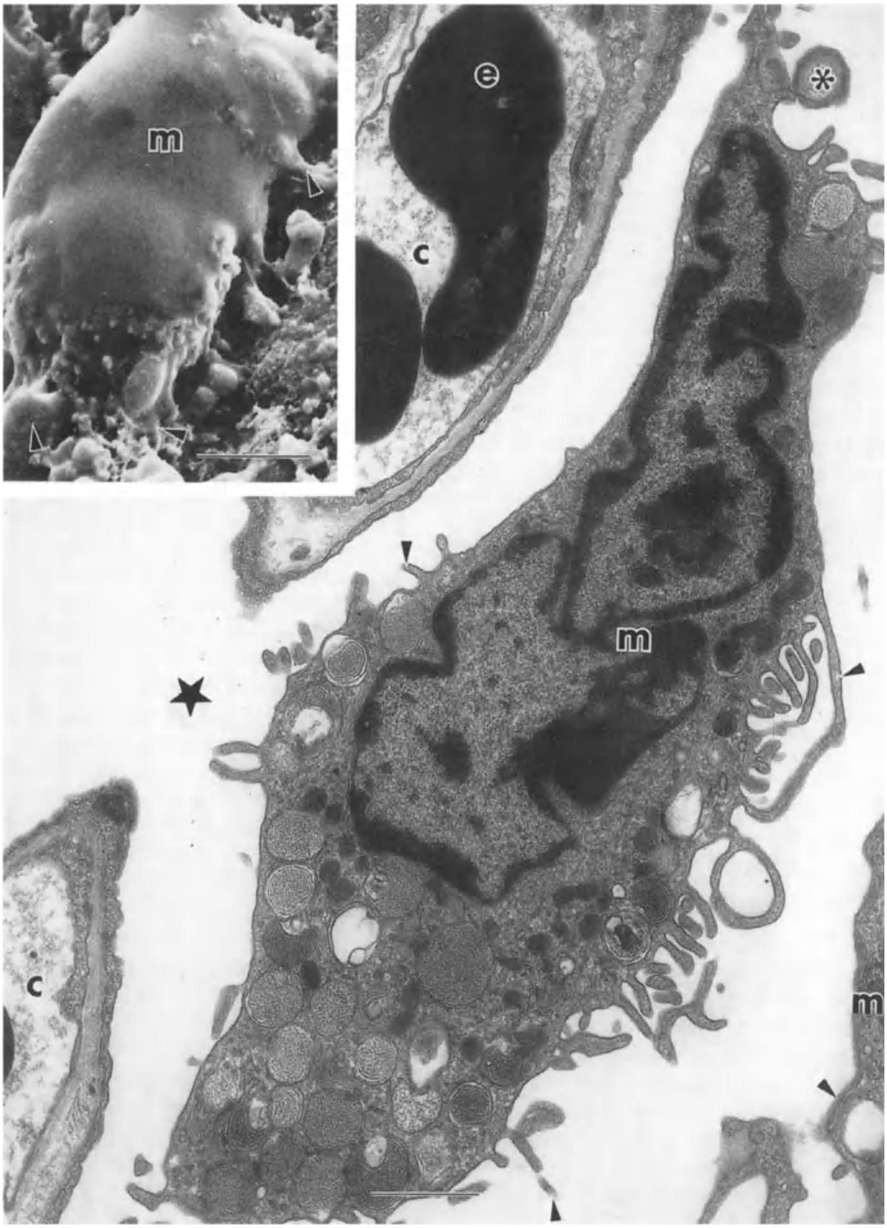


Fig. 102. Alveolar macrophages (*m*). *Main figure* (rat lung), * a particle about to be ingested; ➤ filopodia; ★ interalveolar pore; *c* blood capillary; *e* erythrocytes. The macrophage shown in the *inset* is from a lung of a tree frog, *Chiromantis petersi*: ➤ filopodia. *Bar* 0.6 μm; *inset* 6 μm. (*Inset* Maina 1989d)

organs require presence of an active surface film for stability (Stratton 1984). The process of increasing surface area by subdivision of the lung engenders an increase in the surface tension in the terminal respiratory units. The energy necessary to dilate the gas exchanger during inspiration (an important factor in the cost of breathing) rises. High surface tension affects fluid balance across the blood-gas barrier which coupled with the capillary blood pressure enhances filtration of fluids from the capillaries. The surfactant, a phospholipid material (dipalmitoylphosphatidylcholine) which lines the respiratory surfaces in all gas exchangers evolutionary derived from the lung, reduces the deleterious effects of surface tension at the air-water interface by spreading on the respiratory surface as a monomolecular phospholipid film (Cochrane and Revak 1991). By lowering the surface tension, the surfactant, at least in the mammalian lungs, stabilizes the extremely small terminal gas exchange spaces. In human premature newborn, inadequacy of the surfactant due to lack of type II cells leads to the respiratory distress syndrome which may be fatal. In the vertebrate lungs, the surfactant serves to smooth the alveolar air-liquid interface (Bastacky et al. 1995) and to promote the displacement of deposited particles into the aqueous subphase where they are cleared by the pulmonary macrophages and the mucociliary carpet (Schürch et al. 1990).

In various forms and quantities, the surfactant is widely distributed in the vertebrate lungs (e.g., Clements et al. 1970; Hughes 1973; Pattle 1976; Dierichs and Dosche 1982; Hills 1988; McGregor et al. 1993). Lamellar bodies have been described in the lungs of the lungfishes (Hughes and Weibel 1976; Maina 1987a), those of fish such as bichirs, *Polypterus delhezi* and *P. ornatipinnis* (Zaccone et al. 1989), the gar-fish (*Lepisosteus osseous*) and the bowfin, *Amia calva* (Hughes 1973), in the epithelial lining of the fish swim bladder (Copeland 1969; Brooks 1970) and in the distal (respiratory) part of the intestine of the pond roach, *Misgumus fossilis* (Jasinski 1973). In the lungs of the higher vertebrates, it is secreted by the granular pneumocytes, the type II cells (Fig. 103). The composition of the surfactant and probably its function (at least in the human lung) may be regulated by the O_2 tension in the air spaces (Acarregui et al. 1995). The amphibian pulmonary type surfactant may or may not be discharged into the air space as tubular myelin type (Goniakowska-Witalinska 1980a,b; Bell and Stark-Vancs 1983), is mainly composed of phosphatidylcholine (e.g., Vergara and Hughes 1981), occurs in large quantities (Clements et al. 1970), and is not particularly surface-active like that of the higher vertebrates (e.g., Hughes and Vergara 1978; Daniels et al. 1989). The role of the surfactant, especially in the amphibian lung, is enigmatic, as even the most elaborate lungs have wide air cells which are not susceptible to collapse. Pattle et al. (1977) showed that in the lung of *Triturus vulgaris*, the surfactant only partly reduces the surface tension to $0.2\,\mathrm{mN\,m^{-1}}$ compared with the more efficient mammalian one which reduces it to $0.1\,\mathrm{mN\,m^{-1}}$ or less. In addition to the better-known roles of preventing atelectasis, edema, reduction of respiratory work, and stabilization of the terminal gas exchange components (e.g., Fishman 1972; Farrell 1982b), the surfactant plays several roles such as prevention of transendothelial transudation of substances across the blood-gas barrier, immune suppression, chemotaxis of macrophages (e.g., Daniels et al. 1993), and antioxidant function (Brooks 1970). The

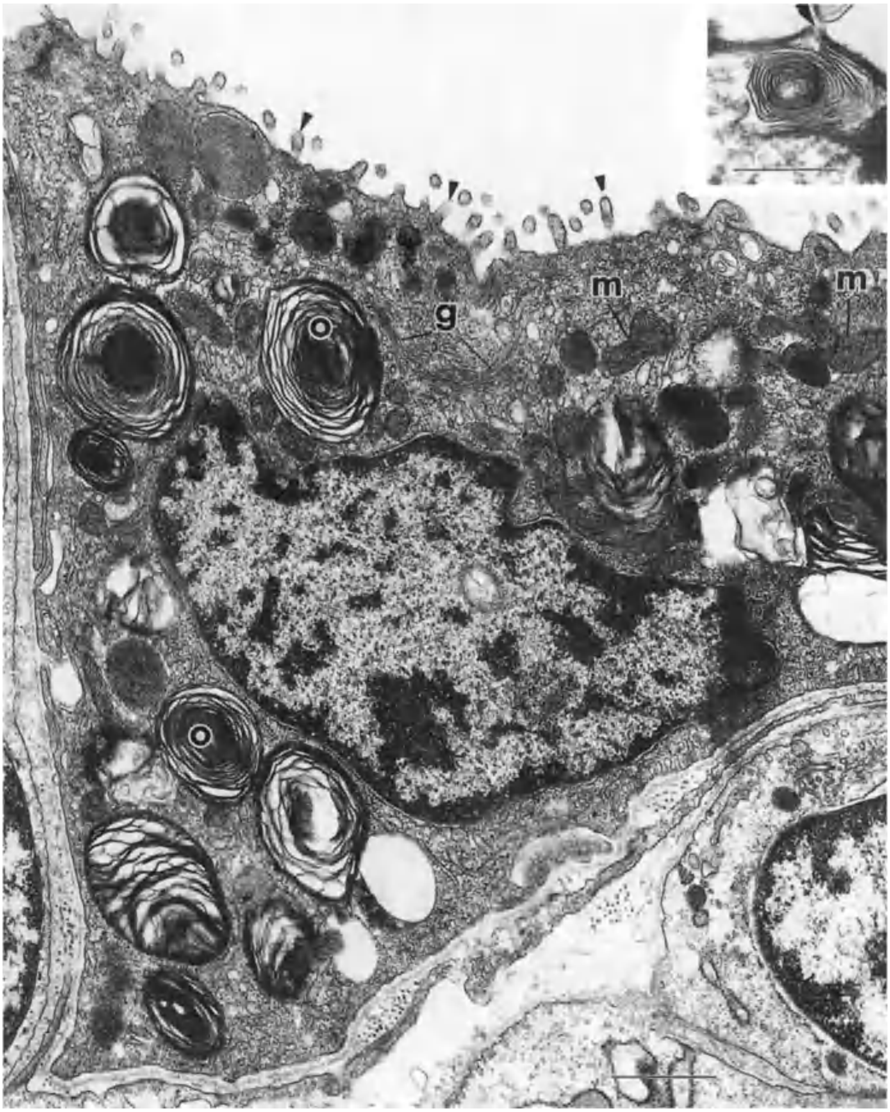


Fig. 103. A Type II cell from the lung of the tree frog, *Chiromantis petersi*, showing mitochondria, *m*, Golgi bodies, *g*, and osmiophilic lamellated bodies, *o*. ➤ microvilli. *Inset* a type II cell from the lung of a caecilian, *Boulengerula (Afrocaecicilia) taitanus*, showing secretion of the surfactant onto the surface of the lung. *Bar* 0.7 μm; *inset* 0.3 μm. (Main figure Maina 1989e; *inset* Maina and Maloiy 1988)

multifunctionality of the surfactant may help explain why the simple lungs, e.g., fish and amphibian lungs which have large air cells, possess the lining. In such animals, surface tension reduction may not be the primary role of the lining. In agamid lizard, *Ctenophorus nuchalis* (Daniels et al. 1990), the salamander, *Amphiuma tridactylum* (Stark-Vancs et al. 1984), and *Siren intermedia* (Guimond and Hutchison 1976; Martin and Hutchison 1979), the surfactant-like lipids are envisaged to act as an antiglue preventing epithelial adhesion after near total pulmonary collapse during apnea (Frappell and Daniels 1991; Daniels et al. 1993; McGregor et al. 1993). In aquatic amphibians this occurs during a dive when the hydrostatic pressure may lead to virtual pulmonary collapse (Daniels et al. 1994) and in mammals in cases of alveolar collapse at different points in a ventilatory cycle (Hills 1971; Weibel et al. 1973; Sanderson et al. 1976). In the Weddell seal, *Leptonychotes weddelli*, the alveoli are totally collapsed at depths of 30 to 35 m (Falke et al. 1985) but the lung of the dolphin, *Tursiops truncatus*, does not collapse, at least up to a depth of 70 m (Ridgway and Howard 1979). In the agamid lizard, the lung contains 70 times more surfactant per respiratory surface area than those of a comparable-sized mammal (Daniels et al. 1989). The antiglue role of the surfactant may be important in the lungs of those animals which lack well-configured intrapulmonary conducting airways and a diaphragm (e.g., amphibians, reptiles, and birds), where the lung is mechanically more susceptible to the displacements of the organs in the coelomic cavity (Daniels et al. 1994). The presence of the surfactant on the air capillaries of the bird lung (Fig. 40a), structures which are somewhat fixed in size, is most intriguing. While it may simply be a phylogenetic carryover from a primordial reptilian lung, especially the crocodile one (e.g., Perry 1992b), it may as well have evolved as a means of curtailing transendothelial filtration of fluids from the blood capillaries in order to prevent flooding of the air capillaries. It is interesting that there is no surfactant either in the fish gills or in the accessory respiratory organs of the bimodal breathing fish. The surfactant appears to be an innovation of the lung and its most immediate derivatives. As evident in most facets of respiration, exceptions pervade the field. Some air-breathing fish such as the gourami, which construct bubble nests, secrete a surface-active (surpellic) substance to reduce surface tension at the liquid-air interface (Phleger and Saunders 1978).

6.10 Nonrespiratory Roles of the Gas Exchangers

6.10.1 Trophic, Sensory, and Locomotory Functions

Owing to the fact that the respiratory system shares a common passage, the pharynx, with the digestive system, activities such as change in posture, eating, swallowing, drinking, and rumination affect ventilatory activity, but only momentarily. This results in moderate but noneventful asphyxia. In some animals, however, predominant activities such as feeding (in filter feeders), husbandry of young (e.g., in the mouth-brooding fish), and phonation greatly conflict with the gas transfer function. In some cases, respiration may be relegated in preference for a nonrespiratory role. Compared with *Chaetopterus variopedatus*, a filter-feeding marine annelid which ventilates its burrow continuously, the lugworm, *Arenicola marina*, a deposit feeder which swallows the detritus and regurgitates sand after extracting organic matter (Jacobsen 1967) has a ventilatory rate (at

15 °C) about ten times lower (Toulmond 1991): the O_2 extraction coefficient in *C. variopedatus* is 30%, while in *A. marina* the value is 80%. Debate has persisted (e.g., Willmer 1970) as to whether the initial task of the archetype respiratory organ, the gill, was respiratory or trophic. Filter feeders like sponges, ascidians, and lamellibranchs move water over their body surfaces, establishing a PO_2 gradient between the surrounding water and the body cells. In the process, microscopic unicellular organisms are entrapped (Hazelhoff 1939; Jorgensen 1955). Hazelhoff (1939) observed that at the same PO_2 in water, the O_2 extraction coefficient in the filter feeders is lower than that of the nonfilter feeders. This is presumably due to the necessary high flow rate of water needed to procure an adequate quantity of food. Jorgensen (1975) suggested that the rate of water flow over the gills is well synchronized with the O_2 and food concentration in a particular environment. In the polychaete worms, the irrigation of the branchial crown is $70\,\mathrm{ml\,g^{-1}\,h^{-1}}$ while that of the tube is only $12\,\mathrm{ml\,g^{-1}\,h^{-1}}$ (Dales 1961): O_2 utilization by the crown is about two times that of the skin. The marine polychaete, *Chaetopterus variopedatus*, a suspension feeder, continuously ventilates its burrow by body movements (Brown 1975, 1977), extracting O_2 and nutrients from the water current (McGinitie 1939). In organisms which use the same site for feeding and respiration, synchronization between gas transfer and feeding is most critical. The larva of the insect *Chironomus plumosus* exhibits cyclic behavior which changes from filter feeding to rest and from rest to respiration (water ventilation). Normally, the rest intervals are brief, with the two other episodes being of about the same duration: ventilation increases in a hypoxic condition at the expense of the feeding interval, the limiting external PO_2 for filter feeding being 2 kPa (Walshe 1950; Ewer 1959; Rubenstein and Koehl 1977). In aquatic animals such as the sea urchins, the respiratory organs (podia or tube feet) are utilized both for locomotion and sensory perception – in addition to their gas exchange role (Steen 1965). In the sabellid polychaete, *S. spallanzani*, a 60% drop in O_2 uptake was recorded by Fox (1938) after amputation of the branchial crown, a very active ciliary feeding structure and evidently an important respiratory one. In the bivalve mollusks, except for some Protobranchia, the ctenidia are greatly hypertrophied for their added role in extraction and transportation of food (e.g., Atkins 1936). In *Pholas dactylus*, particulate food is filtered from the large volumes of water (about 100 l) which pass through them per day (Knight 1984). The current of water created is far in excess of that needed for respiratory purposes in these rather sluggish, often sessile animals. The cephalopods, a toxon which traces its evolutionary lineage some 500 million years back, have conservatively utilized jet propulsion as the basic locomotor mechanism (e.g., Teichert 1988; Chamberlain 1990; O'Dor and Webber 1991). The ventilatory currents serve a locomotory role (Yonge 1947; Wells 1952). Oxygen extraction in cephalopods is variable, depending on the degree to which the animal uses jet propulsion for locomotion. In *Nautilus*, when in motion, O_2 extraction drops to as low as 4% and while at rest it is on average 5 to 10% (Wells and Wells 1985). *Sepia* and *Octopus*, which can uncouple locomotion from respiration, have O_2 extraction rates which are 35 to 45% or even much higher (O'Dor and Webber 1991). The volume of the water across the gills of swimming squids is so large that O_2 extraction is only 5 to 10% and on exposure to hypoxia and extreme exercise rises to a maximum of 17%

(Wells et al. 1988; Shadwick et al. 1990). The most aerobic muscle fibers in squids, which are located in the inner and outer surfaces of the mantle, contain as much as 50% mitochondria by volume (Bone et al. 1981; Mommsen et al. 1981), a value which compares with that of the insect flight muscle (Elder 1975; Ready 1983).

As a general rule, multifunctionality of a gas exchanger is an indication of primitiveness, especially where the roles greatly conflict, e.g., in designs for such processes as feeding, sensation, and respiration. Such exchangers must inherently be designed to accommodate remarkably different needs which cannot be compromised. Filter feeding occurs in fish such as the paddle fish, *Polyodon spathula*, anchovies, and menhaden (Durbin et al. 1981; Lazzaro 1987; James and Probyn 1989; Burggren and Bemis 1992) which utilize ram ventilation as they swim continuously. In the sabellid, *Schizobranchia insignis*, extirpation of the crown resulted in a 75% drop in O_2 consumption (Vo_2) while those worms which retained the crown but were prohibited from extending it into the water showed a 60% drop in Vo_2 (Dales 1961). The importance of the ciliary organs in respiratory function in polchaetes is remarkable. Assuming that the surgical procedure does not greatly interfere with the metabolic level, the total O_2 uptake by the two halves of a transversely bisected *S. pavolina* is not significantly lower than that of the whole worm but in *Myxicola infundibulum*, a dramatic drop in total O_2 uptake occurs on bisection. The posterior body part gives lower values compared with those of *S. pavolina* (Wells 1952). The differences show that in *S. pavolina*, which irrigates its tube through body movements, the ciliary crown does not contribute to the O_2 requirements of the rest of the well-ventilated body. However, in *Myxicola*, where the tube is not irrigated, dependence on the crown is much greater. The role of the respiratory organs in phonation and the physiological consequences on respiration and acid-base status of blood has been outlined by Dejours et al. (1967) and Bouhuys (1974), while the thermoregulatory aspects have been reported in mammals by Cunningham and O'Riordan (1957) and in birds by Calder and Schmidt-Nielsen (1968) and Lasiewski (1972).

6.10.2 Metabolic and Pharmacokinetic Functions of the Lung

The lung is best known for its role as the oxygenator of the blood and the provider of O_2 to the body tissues (e.g., West 1974; Weibel 1984a). This role is axiomatic from its design, which incorporates a large surface area and thin blood-gas barrier. The facts that the lung is mechanically ventilated with air by the ribs, perfused with blood by the heart, and gas exchange occurs by the passive process of diffusion is suggestive of an inert organ. For these reasons, the biochemical, pharmacological, and metabolic roles of the lungs are not as well recognized as the respiratory one (Heinemann and Fishman 1969; Vane 1969; Tierney 1974). This is despite the fact that as far back as over 70 years ago, Starling and Verney (1925) observed that isolated kidneys perfused with defibrinated blood quickly caused vasoconstriction but if the blood was passed through a heart-lung pump preparation, the vasoconstrictor response was absent. They concluded that the blood was "detoxified" in the lungs. Twenty five years later, Rappaport et al. (1948) identified the serum vasoconstrictor substance as 5-hydroxytryptamine (5-HT) and demonstrated that isolated lung preparations inactivated 5-HT. The processes of substrate handling by the lung was well documented by Eiseman et al. (1964) and the subject reviewed by, among others, Bakhle (1975). Though the complete spectrum of the roles the lung plays in physiological and pathological states remains largely unappreciated, it is now well recognized that the organ performs various important metabolic tasks. It is said to be "a peculiar immunological organ which can operate independently and synchronously with the general immune apparatus" (Agostini et al. 1995). Certain tasks are as important, if not more important, than the respiratory one. Bakhle (1975) asserts that "instead of referring to pharmacokinetics as one of the functions of the lung, we ought to refer to gas exchange as one of the nonpharmacokinetic functions of the lung". In some instances, the lung performs the nonrespiratory functions more efficiently than other organs which are considered more specialized (Table 27). The lung is an important source of biologically active agents, constitutes an important organ for defense, and, paradoxically, may initiate, actively participate in, or even sustain pathological processes such as allergy (Nicolet et al. 1975), emphysema (Kimbel and Weinbaum 1975), shock (Bleyl and Büsing 1971), pulmonary cancer (Cohen 1975), pulmonary necrosis (Reid et al. 1973), and hyaline membrane disease (Avery and Mead 1959). To carry out the roles which range from defense, clearance of mucus, and electrolyte transport, to the pharmacological ones, the lung has a large number of different cell types (e.g., Breeze and Wheeldon 1977; Andrews 1981; Weibel 1984b; Welsh 1987).

Anatomically, the lung is strategically located in the general circulation dividing the venous and the arterial circulations. Owing to its vast vascular transit distance, it contains the highest volume of blood per unit time of any other organ in the body. During the transit of blood through the lung, a fine balance between providing the essential metabolic nutriments to the tissue cells and limiting transport of salts and water into and out of vascular space must be maintained (Welsh 1987). More than in other tissues, the lung must make allowance for unhindered passage of some hormones and biologically active substances from the arterial to the venous side of circulation (Ryan and Ryan 1975). The adjust-

Table 27. N-demethylation rate of several drugs in rabbit microsomes prepared either from lung or liver. (Remmer 1975)

Substrate	Lung	Liver
	nmol HCOH formed mg^{-1} microsomal protein min^{-1}	nmol HCOH formed mg^{-1} microsomal protein min^{-1}
Aminopyrine	5.2	15
Ethylmorphine	2.2	3.5
N-Methyl-alanine	3.0	3.0
N-Methyl-p-chloroaniline	7.2	4.8
(+) - Benzphetamine	8.8	4.7

ments which take place after a substrate passes through the pulmonary circulation can be categorized into intrinsic ones, i.e., those which affect the activity of the substrate itself and the extrinsic ones, i.e., those which entail in situ production of biologically active factors (Bakhle 1975): the latter constitutes an endocrine function. The active factors are handled differently by the endothelial cells of the pulmonary vasculature particularly at the capillary level (e.g., Ryan and Ryan 1975). The endothelial cells of the lung have abundant caveolae cellulares (micropinocytotic vesicles; Figs. 29b,40a), most of which are in direct contact with the circulating blood and are irrefutably the sites of degradation, transformation, interaction, and biosynthesis of the macromolecules for which the lung has affinity and transendothelial transfer of the same to the alveolar surface (e.g., Bignon 1975). The lung has a very high pharmacokinetic specificity for the circulating biologically active enzymatic complexes. For example, the pulmonary circulation acts as a filter, letting adrenaline or histamine pass through but inactivating 5-HT, bradykinin, and synthesizing angiotensin II from angiotensin I (e.g., Bakhle 1975; Ryan and Ryan 1975; Nossaman et al. 1994) (Tables 28,29,30). A well-known example of the endocrine role of the lung is that of appearance of histamine in the lung perfusate when an antigen is passed through the pulmonary circulation of the isolated lungs from sensitized guinea pig (Bartosch et al. 1933).

Table 28. Pulmonary extraction of circulating 5-hydroxytryptamine (5-HT). (Junod 1975)

Species	Concentration of 5-HT	Extraction (%)
Man	Bolus injection of 7.6 $\mu g\,ml^{-1}$	65
Rat	5–100 $ng\,ml^{-1}$	92
	0.02 $\mu g\,ml^{-1}$	20–58
Dog	10–20 $\mu g\,ml^{-1}$	80–98
Rabbit	250 $ng\,ml^{-1}$	52.6
	500 $ng\,ml^{-1}$	56
Guinea pig	1–1000 $ng\,ml^{-1}$	48–60

Table 29. Pulmonary inactivation of bradykinin. (Friedli et al. 1973)

Group	Age of Gestation (Days)	Inactivation (% mean and standard deviation)
Ewes n = 5	Adult	93.4 ± SD 1.20
Lambs (n = 5)	Immature (12 Days)	68.0 ± SD 5.28
Fetal lambs at term (n = 4)	Term (144 Days)	46.5 ± SD 4.80
Premature fetal lambs (n = 4)	Immature (118 Days)	–

It is now well known that different pharmacologically active substances are released during anaphylaxis and that other stimuli are capable of causing the release of active substances from unsensitized lungs (e.g., Piper 1975). The lung secretes numerous active biochemical substances such as histamine (Bakhle 1975), slow reacting substance of anaphylaxis (Brocklehurst 1960), dipeptidyl carboxypeptidase (Roth and Depierre 1975), bradykininase, angiotensin I converting factor (Bakhle 1975), and prostaglandins (e.g., Änggård 1975; Piper 1973) in response to different stimuli which include anaphylaxis, physical deformation, biogenic amines, and peptides. Other than in anaphylaxis, the relevance of these experimental findings on isolated organs of laboratory animals to in vivo situations and particularly extrapolation to the human being is still a matter of speculation (Berry et al. 1971). More recently, however, the use of cardiopulmonary bypass as an investigative procedure (e.g., Parker et al. 1975) has corroborated some of the earlier assumptions. It is now well established that the metabolic and the pharmacokinetic functions of the lung are important for some crucial processes such as blood coagulation and inactivation and destruction of hormones and other biologically active factors. It is plausible that these processes may serve as an alternative safety system should other integral organs like the liver, or the kidneys be rendered ineffective. The nonrespiratory functions of the

Table 30. Effect of passage through the pulmonary circulation of biological activity. (Bakhle 1975)

Class of substance	Activation	Inactivation	No change in activity
Biogenic amines	–	5-Hydroxytryptamine Tryptamine Noradrenaline Acetylcholine	α-Methyl 5-hydroxytryptamine Adrenaline Isoprenaline Histamine
–	Angiotensin I Reno-active peptide	Bradykinin Reno-active peptide	Angiotensin Eledoisin Physalaemine Oxytocin Vasopressin
Prostaglandins	Arachidonic acid Other PG precursors	Prostaglandins of E and F type	Prostaglandins
Nucleotides	–	Adenosine monophosphate (AMP) Adenosine triphosphate (ATP)	–
Basic drugs	–	By absorption: Imipramine chlorocyclizine aphetamine By metabolism: methadone	–

lung are affected by factors such as age (Melmon et al. 1968), pregnancy (Bedwani and Morley 1974), and exposure to gaseous anesthetics (Naito and Gillis 1973).

The diversity of the functions carried out by the lung compares with the well-established multifunctional ones of the fish gills which, in addition to respiration, include osmoregulation, acid-base balance, nitrogen excretion, and modification and conditioning of plasma hormones before perfusion of the systemic circuit (e.g., Olson 1996). The lung is also known to greatly modify biological activity of many substances endogenous and exogenous to the pulmonary circulation (Alabaster and Bakhle 1972; Remmer 1975). Smooth muscle contractility in the femoral arterial blood of cats was much less (after infusion of bradykinin) when the chemical was infused into the right ventricle than when the infusion was made into the aorta just distal to the aortic valve (Alabaster and Bakhle 1972; Levine et al. 1973): an inactivation factor of bradykinin ranging from 75 to 99.9% during the passage from the right ventricle to the heart was determined. The degradation of bradykinin in the lung was shown by Ryan et al. (1970) to be very fast. A peptidase from the pig lung has been shown to split the COOH-terminal dipeptide from bradykinin (Igic et al. 1972; Dorer et al. 1974). The ability of the lungs to inactivate bradykinin, a hypotensive factor, while converting (activating) angiotensin I to angiotensin II, a potent hypertensive agent (Nossaman et al. 1994; Table 30) indicates the central role of the lung in blood pressure regulation. Thomas and Vane (1967) showed that 98% of the biological activity of 5-HT was lost during its passage through the pulmonary circulation (Table 28). The disappearance of 5-HT from the circulation results from its uptake by the lung tissue which is followed by fast oxidative deamination yielding 5-OH indole acetic acid (Junod 1975). The extraction process seems to be: (1) saturable when the concentration of the substrate is increased (Junod 1972; Iwasawa et al. 1973); (2) limited by transport rather than metabolism (Junod 1972); and (3) an active temperature-dependent process (Junod 1975). 5-HT, which is exclusively found in endothelial cells of the pulmonary circulation from large vessels to capillaries (Strum and Junod 1972; Iwasawa et al. 1973) and norepinephrine which, compared with 5-HT, is extracted to a lesser extent (40%) (Hughes et al. 1969b; Iwasawa and Gillis 1974) are the only naturally occurring amines affected to a significant extent by the lung and show similar uptake behavior. Histamine, dopamine, 1-dopa, and norepinephrine are not significantly retained or degraded (Vane 1969). The level of P_{450} in the sheep lung is 0.092 nmol per mg protein (Burns et al. 1975). Besides other possible functions, P_{450} has been implicated with O_2 transfer in the lung (Burns and Gurtner 1973; Burns et al. 1975) and the placenta (Burns and Gurtner 1973; Gurtner et al. 1982).

In summary, the central position of the lung in the circulatory system and the fact that among all organs in the body it contains the largest number of endothelial cells (Junod 1975; Ryan and Ryan 1975) as well as the greatest diversity of constituent cells (Ballard and Ballard 1974), of which as many as 20 types are in place as early as the 14th week of gestation (Avery 1968), to a large extent enables the pulmonary system to protect itself as well as the arterial circulation from the influences of locally produced and exogenous biologically active molecular factors. The large number of different cells provides the necessary receptor sites over which the different functions of the lung are carried out (Conolly and Greenacre 1975). The pulmonary endothelial cells are known to be the active sites of metabolic and biosynthetic functions of the lung (Ryan et al. 1968; Smith and Ryan 1970). It is possible that the number of endothelial cells exposed to the circulating blood can be varied during different states (Ryan and Ryan 1975). Prostaglandins are released from isolated perfused lungs of several species by diverse stimuli which may be immunological, chemical, or mechanical (Saeed and Roy 1972; Änggård 1975), the possible sites of production being the perivascular cells, type II alveolar cells, and macrophages (Smith and Ryan 1973a,b). Under experimental and pathological conditions such as septicemia, improper transfusion of blood, trauma, or poisoning, the lung is highly susceptible to disseminated extraneous intravascular coagulation. Blockage of blood flow may be a secondary cause of death.

6.11 The Implications of Liquid Breathing in Air Breathers

The commonality of the mechanisms of gas exchange by diffusion across the tissue barriers and the ventilatory and circulatory adjustments evoked to meet the metabolic needs independent of the milieu an animal lives in raises a fundamental theoretical and practical question as to whether air breathers can survive by breathing water or any other liquid, especially if such fluid is charged with O_2 (Kylstra 1968, 1969). This would hopefully reveal why the air- and water-breathing organs are structurally so different in spite of the fact that their basic functions are the same. It is now well recognized that in utero, the lungs are not collapsed but are distended by aspirated and secreted fluid measuring at about 30 ml per kg in the human fetal lung. Presence of an appropriate volume of liquid is thought to be necessary for normal intrauterine lung growth and development (Moessinger et al. 1990). Immediately before birth (e.g., Dickson et al. 1986), during labor, and/or soon after (e.g., Brown et al. 1983), pulmonary filtration ceases (as the respiratory epithelium stops secreting Cl^- ions and starts to absorb Na^+ from the lumen of the lung) (e.g., Bland 1990; Chapman et al. 1994). The two process are regulated by levels of circulating catecholamines (e.g., Mortola 1987). Efficient removal of liquid from the air spaces during and after birth is vital for normal switching from placental to pulmonary gas exchange. Liquid is thus not an entirely alien factor to the respiratory surfaces of aerial gas exchangers, at least during the early stages of development. It is of profound interest to know to what extent the structural and functional modifications of the aerial gas exchangers, the lungs, have lost the capacity of utilizing the primordial respiratory medium - water.

In an applied sense, liquid breathing, if and when perfected, will overcome the serious obstacles which human beings would experience for successful survival in deep subaquatic habitats and in the outer space. If a diver breathes a suitable liquid enriched with O_2 instead of air, since the liquid in the lungs would resist the external pressure without significantly changing in volume, it would be possible to descend to depths and ascend to the surface rapidly without the risk of decompression sickness (bends) (Paulev 1965). The ultimate obstacle in the conquest of speed apparently will not be technology but the fragility of the human body to withstand the stresses and strains that have to be endured during such states. Only a few people have "gone supersonic" without the aid of an air craft and survived (Cameron 1990). In future space travels enormous accelerations will be necessary to escape from the gravitational pulls of the much larger celestial bodies. Though constant displacement (speed), irrespective of how fast, produces little stress on the human body, accelerations, decelerations, and sudden maneuvers exert strong forces on the body. Such stresses and strains may not be tolerable to the delicate parts of the human body such as the lungs (e.g., Bullard 1972). The destructive effect could be minimized or even totally eliminated if a whole animal is externally supported by a respirable liquid of the same specific gravity as the body fluids (instead of air). Furthermore, fluid-filled lungs should be able to bear much greater stresses and strains (e.g., Margaria et al. 1958). Absence of gas in the body would equalize the density throughout the body, preventing relative inertial movements of the heart, lungs and other visceral organs while pulmonary arterio-venous shunting would be prevented (Sass et al. 1972). Experimentally, dependent pulmonary atelectasis, arterio-venous shunting and downward displacement of the heart brought about by gravitational-inertial force exposure were prevented in dogs breathing oxygenated liquid fluorocarbon in a whole-body immersed respirator (Sass et al. 1972). Liquid lavage has been used successfully in treating pulmonary conditions such as asthma, bronchiectasis, and mucoviscidosis (Kylstra et al. 1971), in treatment of acute lung injury (e.g., Richman et al. 1993), and management of respiratory failure (Rogers et al. 1972). The pioneering experimentation on breathing O_2-saturated liquids was carried out by, among others, Kylstra and Tissing (1963), Clark and Gollan (1966) and Kylstra et al. (1966).

Due to the remarkably different physicochemical properties of water and air (Tables 4,9), water breathing poses distinct problems to an air breather. The primary limitations are that: (1) water under normal atmospheric pressure contains too little dissolved O_2, and (2) the differences in the ionic composition of water compared with that of blood upsets ionic equilibrium with the body fluids (e.g., Lowe et al. 1979). Owing to its greater viscosity, the maximum flow rate of water from isolated dog lungs is much lower than the maximum expiratory flow rate of air at equal lung volumes (Leith and Mead 1966). Furthermore, the driving pressure affordable for maximum expiratory flow, which is limited by the lung's static recoil pressure in liquid filled lungs (Mead et al. 1967) is less than in an air-filled one (Wood and Bryan 1971). Aquatic organisms have evolved within the physical constraints of their relatively O_2-deficient medium. Most of them possess highly specialized gas exchange systems (gills) which promote extraction of the available O_2. When saline is inhaled into a lung, it physically destroys the delicate terminal gas exchange components (e.g., Curtis et al. 1993), dissolves and mechanically displaces the surfactant (Lewis et al. 1993), osmotically interferes with the composition of the body fluids, causes pathological changes such as interstitial edema, produces intrapulmonary froth and atelectasis (Blenkarn and Hayes 1970), causes loss of macrophages and rupture of the alveolar cell and basement membrane (Huber and Finley 1965), and upsets the integrity of the blood-gas barrier (Reidbord 1967). Direct interference with the surfactant production reduces or even totally eliminates surface tension. This lowers the driving pressure available for maximum expiratory flow to a value no greater than that produced by the elastic recoil of the lung tissue, which is only a small portion of the total static recoil pressure available during air breathing (Kylstra and Schoenfisch 1972). Presence of liquid in the airways increases airway constriction (Yager et al. 1989). With the dissolving of the surfactant and other alveolar hypophase liquid materials, the viscosity and density of the saline increases tremendously, elevating the cost of the ventilatory effort (Blenkarn and Hayes 1970). Addition of exogenous surfactant to liquid ventilated lungs reduces maximal inflatory pressures (Tarczy et al. 1996).

By using isotonic solution supercharged with O_2 to a pressure equivalent to that of air at sea level, it has been possible to keep rats (Pegg et al. 1963), mice (Kylstra 1962), and dogs (Kylstra et al. 1966) alive breathing water for hours. The eventual survival times have depended on factors such as the experimental temperature and the chemical composition of the fluid used. Death during liquid ventilation in a normothermic cat (Clark and Gollan 1966) and the dog (Kylstra et al. 1966) did not result from anoxia but from difficulties in removing CO_2 at the necessary rate. This limitation resulted in acidosis, thought to be secondary to a high arterial PCO_2 (e.g., Shaffer et al. 1976). It was not until mechanically assisted liquid breathing systems were designed (e.g., Saga et al. 1973; Shaffer and Moskowitz 1974) and the effect of CO_2 overloading minimized that the significance of acidosis was fully appreciated as a particular metabolic complication during liquid breathing: unequivocally, O_2 delivery to the tissues during liquid breathing is more than adequate (Shaffer and Moskowitz 1974; Shaffer et al. 1976). The exhaled breath of a mammal on average contains 50 ml of $CO_2\,l^{-1}$ while at the same temperature and PCO_2, a solution with the same salt concentration as blood contains only about 30 $ml\,l^{-1}$. This indicates that to remove as much CO_2 through the water as that eliminated via the air, a water-breathing mammal would have to exhale about twice as large a volume of water as of air (Kylstra and Tissing 1963). This is practically made difficult by the narrowness of the bronchial passages and the greater viscosity of water which requires about 36 times more power to move than air. In a state of laminar flow, a process which appeared to occur in saline breathing dogs (Kylstra et al. 1966), a liquid breather would have to expend 60 times the energy required in breathing air. The maximum expiratory flow of a liquid has been estimated to be 40 to 100 times lower than air ventilation (Leith and Mead 1966). Liquid-breathing mice died as a result of exhaustion of the respiratory muscles and accumulation of CO_2 to toxic levels (Kylstra 1962), a complication which has been reported in other animals (e.g., Clark and Gollan 1966; Modell et al. 1970).

To demonstrate the inadequacy of CO_2 elimination during liquid breathing, the survival time of mice was increased to 18 h by addition of tris(hydroxymethyl) amino methane (a substance that minimizes the harmful effects of CO_2 accumulation) to the experimental solution (Kylstra 1962; Nahas 1962). An anesthetized dog cooled to 32 °C was kept alive for 24 min and resuscitated, and normothermic dogs were able to breath liquid for 45 min, 40% of them surviving the exposure well (Kylstra et al. 1966; Mathews et al. 1978): during the experiment, the blood pressure was lower than normal, the heart and respiratory rates were below normal but regular, the arterial blood was fully saturated with O_2 (arterial PO_2, 6.8 to 39 kPa) but the CO_2 content of the arterial blood increased gradually from 5.7 to 10.7 kPa, indicating that the dog's respiratory efforts were not enough to eliminate adequate amounts of CO_2 from the body. West et al. (1965) and Kylstra et al. (1966) observed that the overall pulmonary gas exchange in liquid-filled lungs is diffusion-limited and remarkably large gas tensional gradients occur within the liquid-filled terminal gas exchange components due to the slow rate of diffusion in water. In dogs subjected to lavage with hyperbarically oxygenated saline (PO_2 in the inspired air, 387 kPa), arterial oxygenation was 32 kPa after 15 min, but a severe respiratory acidosis (arterial PCO_2, 9.3 kPa; pH, 7.2) developed.

6.12 Physical Gill and the Plastron: a Unique Underwater Respiratory Strategy

The insectan tracheal system (Sect. 6.6.1) evolved fundamentally as a means for air breathing and hence as an adaptation for terrestrial habitation. A large number of species in the taxon have, however, many times successfully secondarily invaded wet and even aquatic environments. The retention of atmospheric respiration in such cases is a clear manifestation of the advantages derived from air breathing in the taxon and animals in general. In being able to carry air with them in form of gas bubbles (Fig. 104), the insects have retained the major advantage of extracting O_2 from air while subsisting in water. They have gained access to new resources in water and escaped from surface predators. The simplest mode of aerial respiration in aquatic insects is the snorkel one utilized by many larval forms, e.g., the mosquito larva *Culex*, where a breathing tube opening to a spiracle placed on one end of the body is brought into contact with the surface

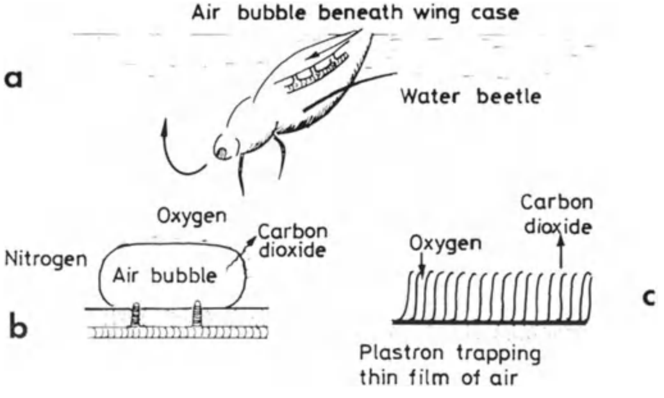
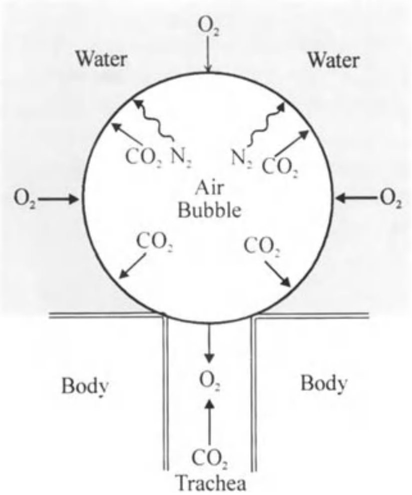


Fig. 104a–c. Underwater air-breathing in insects. **a** An air bubble entrapped underneath a wing of a beetle. **b** A physical gill. **c** Gas exchange in a plastron. (Hughes 1982)

Fig. 105. Schematic diagram of a compressible (physical) gas gill. Oxygen diffuses into the bubble from the surrounding water ( ) to replace the amount consumed in the body. The CO_2 released from the body dissolves into the surrounding water. The partial pressure of nitrogen decreases, leading to eventual collapse of the bubble

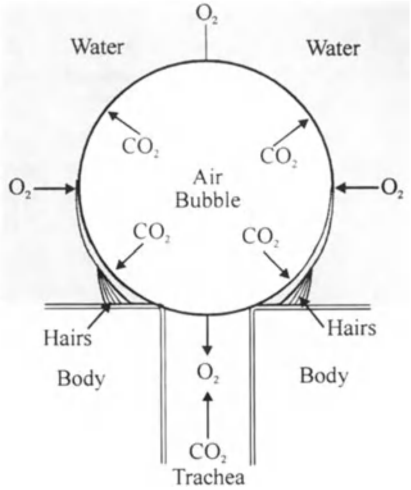


of the water. The air is transferred to the body by diffusion, the surface film being utilized for support using hydrofuge hairs. Amazingly, the underwater gas bubble utilized by the insect is comparable to the air held in the lung of a pneumonate gastropod (Hunter 1953), providing a micromileu which facilitates exchange of O_2 and CO_2 across the water-gas interface (Wolvekämp 1955; Rahn and Paganelli 1968).

Two modes of underwater air breathing have evolved in insects especially in the Hemiptera and Coleoptera. In the "compressible gas-gill" (Rahn and Paganelli 1968; Fig. 105), gas pockets or bubbles of air adherent to the body parts (Fig. 104) are utilized as sources of O_2. Groups such as the diving beetles (*Dytiscids*), the black swimmers (*Notonectids*), and water boatman (*Corixa*) (Ege 1918; Crisp 1964) utilize this mode of gas exchange where gas transfer is effected between the trachea, the gas-gill, and the water. In a compressible gas-gill, the pressure of the gases is dependent on the prevailing hydrostatic pressure, i.e., the depth at which the insect operates. Depth shortens the duration of the dive by increasing the rate of O_2 loss into the water due to the increased PO_2 (Rahn and Paganelli 1968): a dive of 2 m increases the PO_2 in the gas-gill to 25 kPa, creating a partial pressure gradient of 4 kPa in favor of loss of O_2 from the gas-gill. Oxygen is extracted by the trachea through the spiracles which open into the bubble. The discharged CO_2 rapidly dissolves into the surrounding water. As the PO_2 in the bubble decreases, in well-oxygenated waters, O_2 diffuses inwards from the surrounding water. Due to the increase of the partial pressure of nitrogen in the bubble, indirectly through loss of CO_2 into the surrounding water and directly through the hydrostatic pressure which increases at a rate of 1 atm per 10 m, N_2 is slowly lost. This results in a steady decrease in the size of the bubble and its eventual collapse at a critical diameter (Rahn and Paganelli 1968; Liew 1970). To increase the rate of diffusion of O_2 into the bubble, some insects actively ventilate the gas-gill by moving water currents around it. The frequency at which an insect makes periodic visits to the surface to pick up fresh air is dependent on: (1) the pressure prevailing in the gas bubble, which in turn is determined by the working depth (the PN_2 between the gill and water increases at a rate $9.9\,kPa\,m^{-1}$); (2) O_2 uptake by the tissues which indirectly leads to an in situ elevation of the concentration of N_2 enhancing its efflux; and (3) the PO_2 in the surrounding water and hence the rate of O_2 recharge of the gas gill from the surrounding water or is even lost from the air bubble when the animal is in hypoxic water. Before the collapse of the gas gill, however, the insect will have extracted a volume of O_2 from the water which is 7 to 13 times greater than that in the bubble at the beginning of the dive. This extends the dive duration 8 to 13 times (Ege 1918; Rahn and Pagannelli 1968). In a *Corixa*, Ege (1918) observed that the insect obtains enough O_2 out of the water by diffusion into the air bubbles covering its body, a supply which extends its underwater stay 10 to 30 times longer than would be possible if it were to rely only on the initial amount of O_2 in the gas bubble(s) at submergence. The spider, *Argyroneta*, which always carries a layer of air around the entire abdomen and part of the thorax, is highly adapted for underwater gas gill respiration, with the air sometimes lasting for several days in summer (Braun 1931). Interestingly, an insect can stay underwater longer when the gas gill is filled with air (in air-saturated water) than when the gill is filled with pure O_2. A backswimmer survives for only 35 min in O_2 saturated water but for as long as 6 h in air-saturated water. When a *Notonecta* was put in O_2-saturated water and also made to breathe from a pure O_2 bubble, the animal became heavier than water in 14 min and succumbed in 35 min. When breathing ordinary air (at the same temperature), however, it could survive for 6 h without surfacing (Ege 1918). This is due to the fact that the presence of N_2 enables the gas gill to function as a physical gill, i.e., it allows O_2 and CO_2 transfer between the water and the gas gill. During winter when the surface of water is covered with ice, a number of species of the Dytiscidae family are highly active, catching air bubbles arising from aquatic plants or from the mud (Krogh 1941). Although such bubbles may contain relatively little O_2, they should replenish the quantity of N_2 in the air bubbles carried by the insect and hence prolong the survival of the gas gill. While the spiracles and hydrophobic hairs may act as barriers, it is intriguing how the insects totally keep the trachea from flooding with water through capillarity. If the trachea are filled with water, the transfer of O_2 would decrease 10 000-fold and the insect would almost certainly drown. This has found a practical application in destruction of mosquito larvae by applying oil on the surface of standing water, a process which eliminates the supporting surface tension. Denney (1993) contemplates that the trachea are lined by a waxy substance which repels water.

In insects which possess "incompressible gas gill" (Fig. 106), a layer of gas is held firmly (over the epicuticle which covers those parts of the body onto which the spiracles open) by stiff hydrophobic hairs or a cuticular meshwork of hairs, the plastron (e.g., Hinton 1966) (Fig. 107). The hairs are about $5\,\mu m$ long. In the bug, *Aphelocheirus*, the hairs number about $2.5 \times 10^6\,mm^{-2}$, are about $0.5\,\mu m$ apart, have a diameter of about $0.2\,\mu m$, and are strong enough and adequately hydrophobic to withstand 4 to 5 atm of external pressures before the wetting of the cuticle can occur (Thorpe 1950; Crisp 1964). The surface tensional forces

Fig. 106. Schematic diagram of an incompressible gas gill (plastron). The gas air bubble is firmly attached to the body by hydrofuge hairs. As O_2 is consumed and PO_2 drops in the bubble, the gas diffuses inwards from the surrounding water ( ). Carbon dioxide dissolves into the surrounding water. Owing to the firm physical support of the bubble, the pressure of nitrogen in the bubble is not a factor in the longevity of a plastron. Theoretically, the bubble may last indefinitely



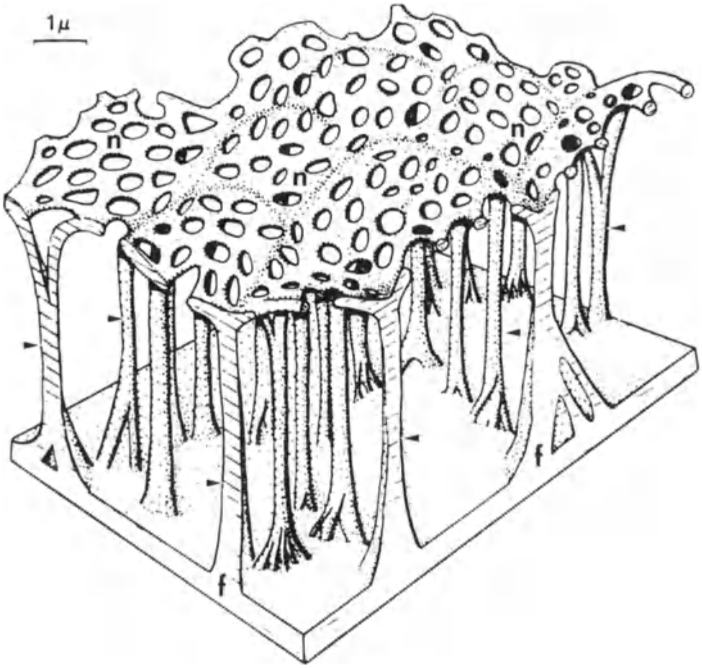


Fig. 107. Schematic drawing of the hairs of a plastron of a cranefly larva, *Dicranomyia*, that consists of narrow spaces delineated by a roof made up of a thin holey cuticle, *n*, and thick basal cuticle, *f*. Vertical struts, ➤, connect the roof to the floor. The air contained in the interstices is not directly subjected to hydrostatic pressures at natural depths. (Hinton 1976)

augmented by the support provided by the hairs counteract the hydrostatic pressure preventing compression of the gas phase, making the volume of the plastron remain fairly constant (Rahn and Paganelli 1968): the PN_2 in the bubble is equal to that in the water and the rate of O_2 uptake by the insects is the same as that diffusing in from the water. Consequently, the loss of the inert gases, mainly N_2, which sets the limit of the gas-gill existence, is avoided. Theoretically, this should allow an insect to remain submerged indefinitely (Thorpe and Crisp 1949; Hinton 1976; Rahn and Paganelli 1968). Strictly, the insects endowed with "compressible" (physical gas gill) or "incompressible" gas bubbles are essentially air breathers as they actually exchange O_2 and CO_2 with a gas phase which, in turn, exchanges gases with the surrounding water. The empiric changes of the gas profiles within the tracheal system and air sacs of an insect utilizing such devices are fundamentally similar to those in an insect breathing free air.

The compressible gas-gill is suitable for insects which operate close to the water surface. In such cases, large energetic costs are not involved for surfacing and diving. Incompressible gas gills, within limits, act well at depths and serve those insects which stay under the water for long periods of time well. While the compressible gas gill requires no definite structural adaptations, plastron respiration demands a greater degree of anatomical specializations in form of hydrophobic hairs and/or other cuticular modifications. The typical environment inhabited by insects with a plastron is that which has well-aerated water and one which dries up at times, exposing the insect to the atmosphere. Plastrons are also quite common on insect eggs which are liable to being covered by water when it rains (Hinton 1953, 1966; Crisp 1964). Such eggs have areas which consist of an intricate meshwork of air channels lined by hydrophobic substances.

A plastron is a highly versatile respiratory organ which functions as an efficient underwater gas exchanger and when the insect is exposed to air provides a satisfactory pathway for gas transfer while minimizing risk of desiccation (Hinton 1966). The insectan plastron corresponds with the fine hydrophobic air channels of many aquatic plants which prevent entrance of water while allowing in air. This makes such plants relatively more buoyant. Of particular interest is the mode of respiration in the larva of the bot-fly, *Gastrophilus intestinalis* which subsists in the virtually anoxic stomach of the horse. In a more or less plastron manner, O_2 is extracted from the air bubbles (which are swallowed during feeding) through a special organ made up of large cells around an array of trachea (Krogh 1941). A totally different mechanism of maintaining a permanent gas-gill has evolved in the volant aquatic elmid beetle: before diving, the beetle carries a large bubble of air which extends from the first femora back over and past the dorsum. In calm water, the beetle has to surface from time to time to replenish the air but in the torrential mountain stream waters, where the currents are faster than $70\,\mathrm{cm\,s^{-1}}$, the Bernoulli-Venturi effect generated by the flow of water across the convex face of the bubble causes the pressure in the bubble to fall below the atmospheric. This effects an inward flux of O_2. The tracheal (air) gills which comprise of an air-filled tracheal system sealed off from water, e.g., the highly tracheated flaps or filamental outgrowths from the thoracic and/or abdominal segments of the body in nymphal Plecoptera and Ephemeroptera and larval Trichoptera constitute an extreme retrogressive transformation which allows permanent aquatic habitation: O_2 diffuses from the surrounding water into the trachea which serve as internal plastrons and CO_2 is discharged and dissolved by the surrounding water.

Remarkable behavioral, morphological, and physiological convergencies in underwater respiration occur. Some high-latitude winter-diving mammals are known to use gas pockets trapped between the water-ice interface (e.g., Hart and Fisher 1964; Mitchell and Reeves 1981; MacArthur 1992). Such air pockets may arise from air entering through natural fissures in the ice, from exhaled gases released by the diving animals (e.g., Harrison et al. 1972), from the hair, or from photosynthetic activity of the aquatic plants. In nature, diving muskrats, *Ondatra zibethicus* (Errington 1963), and experimentally submerged gray seals, *Halichoerus grypus* (Harrison et al. 1972), are reported to breath in air in these gas pockets. Since CO_2 is more soluble (30 times) in water than O_2, the PCO_2 in the air in the bubbles discharged from the lung or from the surface of the body should drop with time. Depending on the PO_2 in the surrounding water, the bubbles trapped under ice may be charged with O_2. A high concentration of O_2 (26.67 to 29.04%) was determined in the air bubbles collected under ice by MacArthur (1992). The investigator, however, attributed it to photosynthetic activity of submerged macrophytes. In addition to the O_2 contained in the intrapulmonary air and the body tissues, the air bubbles in the water/ice interface could provide an important auxiliary source of O_2 during prolonged dives. In the muskrat, *O. zibethicus*, dive duration was increased by 31% when the animals were allowed access to underwater gas pockets (MacArthur 1992).

6.13 The Cleidoic Egg: a Fascinating Gas Exchanger

The evolution of the cleidoic (self-contained) egg in reptiles and birds was a monumental advance in the attainment of terrestriality. For once, the land invaders were able to totally dissociate themselves from water for fundamental activities such as reproduction. In the about 9000 species of birds, in addition to the presence of the ubiquitous feather, oviparity, the mode of reproductive which involves formation of fertilized eggs encased in an egg shell, is a unifying feature. While viviparity has variably evolved in most other vertebrate groups, e.g., amphibians like the caecilian *Typhlonectes compressicauda* (Garlick et al. 1979), reptiles like the lizard, *Sphenomorphorus quoyii* (Grigg and Harlow 1981), and teleost fish like *Zoarces viviparous* (Hartvig and Weber 1984; Weber and Hartvig 1984), *Embiotoca lateralis* (Ingermann and Terwilliger 1981), and *Clinus superciliosus* (Veith 1980), birds constitute the only vertebrate class which is exclusively oviparous. Debate ranges on the reasons for retention of this ancestral reproductive condition (e.g., Blackburn and Evans 1986; Anderson et al. 1987; Lewin 1988): it has been suggested that viviparity in birds would inhibit flight due to the increased pay load, during pregnancy. Such an argument is clearly untenable if it is recalled that bats have evolved both flight and viviparity and of the at least 15 families of birds which have given up flight, none has evolved viviparity.

Simple cost-benefit analysis may explain the case. Being ectothermic, birds can incubate their eggs outside the body – they do not need to retain them in the body for development. Since the eggs are formed at different times (one every 25 h or so), if retained in the oviduct and/or uterus (space allowing), it would mean that embryos would have to be delivered at different times (even when the bird is still laying!) depending on the incubation period and the period of laying (clutch size). The benefits of retaining oviparity perhaps outweigh the costs and risks. Due to its intrinsic self-sufficiency, some authorities (e.g., Bender 1992) consider the egg to be a "cell". In birds, the 1.5-kg ostrich (*Struthio camelus*) egg is hence the largest extant cell while the dinosaur eggs, e.g., those of the sauropod, *Hypselosaurus priscus* (Kerourio 1981), which had a volume of about 2 l (about 40 times the volume of a chicken egg) and the 10-kg ones of the now extinct 500 to 1000-kg elephant bird, *Aepyornis* (Amadon 1947, Rahn et al. 1975; Feducia 1980), are some of the largest cells which ever formed.

Both theoretically and practically, the egg is a marvel of morphogenetic engineering (e.g., Ar et al. 1974). The microcosmos contains all the necessary factors needed for embryonic development such as nutriments, minerals, and water: the only factor missing is O_2, a resource which must be procured from outside. The products of metabolism, CO_2 and water, must be removed while the nongaseous ones (e.g., products of nitrogen metabolism) are stored in the allantois. The shell must be strong enough to mechanically and physically protect the developing chick from trauma during brooding and from toxic, infectious, and parasitic agents: O_2 must be allowed in and CO_2 let out, excessive water loss must be avoided, while the shell must be adequately weak for the chick to break out at the end of incubation (Ar et al. 1979; Schmidt-Nielsen 1984). The eggshell is made up of calcium carbonate ($CaCO_3$) arranged in orderly crystalline arrays embedded in a protein matrix separated by fine air spaces, the pores. The differences in the pattern of deposition of $CaCO_3$ crystals accounts for the disparities in the eggshell conductances of newly laid eggs for O_2 (Tazawa 1987). The conductances of the eggshell of the African parrot, *Enicognathus ferrugineus*, differs by a factor of 7 (Bucher and Barnhart 1984) and in the turkey, *Meleagris gallopavo*, the number of pores in the eggshells changes during a laying cycle, increasing during the late stages of laying (Rahn et al. 1981). The shell of a 60-g chicken egg has a surface area of about 70 cm^2 and about 10 000 pores which are 17 μm in diameter and 0.35 mm in length (Wangensteen et al. 1971; Tazawa 1987). Much as it is a rigid structure, the shell does not completely isolate the developing chick from the external environment. The embryo receives information in form of sound or mechanical movements from the parent(s) and the adjacent eggs, cues used to synchronize hatching in a clutch of eggs (Drent 1975). The need to reconcile remarkably different requirements has led to what appears like near-optimization of the gas transfer capacity of the avian eggshell. Wangensteen and Weibel (1982) observed that the diffusing capacity of the chorioallantois of a 16-day-old egg was equal to the physiological diffusing capacity. Weibel (1984a) attributed the optimal state of the avian eggshell to its transient nature since it does not add immense cost to support and maintain. It is instructive to note that the placenta (Sect. 4.7), an equally ephemeral organ, maintains a substantial functional reserve during most of the gestation period (Karsdorp et al. 1996).

Since the capacity to conduct the respiratory gases is somewhat fixed at the formative stage of the eggshell, i.e., before incubation starts (Wangensteen et al. 1971; Kayar et al. 1981; but see dissenting views e.g., Kutchai and Steen 1971; Lomholt 1976a; Tullet and Board 1976), the design must somewhat adaptively preempt the maximum O_2 and CO_2 flux at the peak of embryonic development. Unique to all gas exchangers, where both CO_2 and O_2 are transported with balanced facility, in the chorioallantois of the bird egg, gases are transported at different rates corresponding with their molecular weights. Unique to all other gas exchangers, each gas has its own diffusion coefficient. On this basis, Rahn and Paganelli (1982) suggested that while the convective transport of the lung can be described as an egalitarian transport, that in the avian egg should be considered an elite transport system. Throughout the incubation period, a time when O_2 consumption increases by a factor of about 800 times (Kutchai and Steen 1971; Rahn et al. 1974; Table 32), the bird embryo is encased in a rigid shell of invariable area and thickness (Table 31). Kutchai and Steen (1971) estimated that O_2 and CO_2

Table 31. Morphometric parameters of the eggs of several species of birds. (Romanoff and Romanoff 1949)

Species	Body wt. (approx – kg)	Egg wt. (g)	Shell thickness (mm)	Mean pore diameter (mm)	Thickness of the membranes (mm)
Aepyornis	500	12000	4.40	–	–
African ostrich	150	1400	1.95	0.035	0.200
Australian swan	17	700	0.69	0.34	0.165
Holland turkey	8	80	0.41	0.040	–
Chickens	3.3	53.7	0.31	0.018	0.065
Pheasant	3.0	32	0.26	0.012	–
Quail	2.0	9	0.13	–	0.067
Finch	0.01	1	0.09	–	0.005
Hummingbird	0.008	0.5	0.06	–	–
Auk	–	–	–	0.041	–
Duck	–	–	–	0.023	–
Gull	–	–	–	0.013	–

Table 32. Day of incubation (DI), cardiac output (CO), oxygen consumption (Vo_2), hemoglobin content (cHb), oxygen capacity (O_2C), transport capacity (TC), and oxygen utilization coefficient (O_2UC) of the chicken during development. (Romanoff 1967; Bartels et al. 1996)

DI	CO	Vo_2	cHb	O_2C	TC	O_2UC
3	20	3.8	0.015	0.0201	0.4	950
5	120	9.4	0.028	0.0375	4.5	210
12	4800	121	0.069	0.0926	445	27
17	6800	305	0.098	0.1310	826	37
17	6800	305	–	0.1100	750	41

permeabilities of the shell and the membranes of a newly laid egg are not adequate to support gas exchange needs during the last stages of the development of the embryo. The megapodes, birds of the Southern-Pacific area, e.g., the Australian malee fowl, *Leipoa ocellata*, and the brush turkey, *Alectura lathami* (Brom and Dekker 1992; Dekker and Brom 1992; Jones and Birks 1992), deposit their eggs deep in the soil among putrefying organic matter and on rare occasions in geothermal heat to provide natural warmth for incubation (e.g., Fleay 1937; Frith 1956). In the egg mound, the eggs must face critical levels of hypoxia and hypercapnia especially during the last stages of incubation. Furthermore, the developing embryos are exposed to a moisture-saturated environment where there is minimal water loss. In most birds, water loss, which may constitute as much as 20% of the initial mass of the egg, is essential for proper development of the eggs (Rahn and Ar 1974; Ar and Rahn 1980; Simkiss 1980). Within a short period, the hatchlings must find their way to the surface or face suffocation. The shells of the eggs of the megapodes are remarkably thin, allowing rapid outward diffusion of metabolic water, out flux of CO_2, and influx of O_2 (Drent 1975). The eggs of the painted turtle, *Chrysemys picta* (Emydidae), present another interesting mode of development: though the eggs hatch in late summer or early autumn, the neonates do not emerge from their subterranean nests until the following spring, i.e., 6 to 9 months after hatching (e.g., Linderman 1991; Constanzo et al. 1995). Though the great mortality of the neonates has been associated with hypothermia (Packard and Packard 1997), hypoxia and hypercapnia (especially when the ground is covered with ice) may be significant contributing factors to the fatalities. Whereas turning of the eggs during incubation is critical for proper embryonic development (e.g., Romanoff 1960; Metcalfe et al. 1979), the eggs of the megapodes develop normally without it (Seymour and Rahn 1978; Seymour and Ackerman 1980). In some reptiles, the sex of the embryo is determined by the ambient temperature (e.g., Ferguson 1992). In fixed incubating eggs, concentration of the albumen occurs arresting the development of the chorioallantoic vessels (Romanoff 1960) and that of the albumin sac (Randles and Romanoff 1950). The normal clutch of about 100 eggs laid at a depth of about 1 m by the green turtle, *Chelonia myda*, face extreme hypoxia and hypercapnia at the end of incubation. The O_2 level falls to 12% and that of CO_2 rises to above 2.24% (Prange and Ackerman 1974). The dinosaurs, e.g., the sauropod, *Hypselosaurus priscus*, are thought to have deposited their eggs in small groups (e.g., Kerourio 1981) instead of about 50 in one clutch, as such a mass of eggs would have consumed O_2 faster than it could diffuse through the walls of the nest (Seymour 1979).

Birds have been able to adapt to a wide variety of nestling conditions by adjusting the eggshell microarchitecture to provide optimal gas exchange for the special needs in their habitats. The incubation period of the bird eggs is inversely related to metabolic rate and the eggshell conductance (Rahn et al. 1974). Pathological conditions which affect the shells of the bird eggs occur frequently especially in cases of malnutrition, e.g., when laying birds experience calcium deficiency. The shells are poorly formed and fragile. A recent environmental problem which has lead to extensive eggshell deformation in birds has resulted from use of pesticides such as DDT (Cooke 1976; Fox 1976; Risenbrough 1986).

During the 21-day incubation period, a 60-g chicken egg will take 6 l (8.6 g) of O_2, give off 4.5 l (8.8 g) of CO_2, lose 9 g in weight (= 11 l of water vapor) and by the end of incubation, about 30 kcal of the initial 100 kcal energy in the egg will have been consumed to form the 39 g of the chick (e.g., Carey et al. 1980; Rahn and Ar 1980). In the species which nest at high elevations (see Rahn 1977), the respiratory demands of the eggs are daunting. Not only do the eggs of such species have to cope with the prevailing hypoxia but must also experience low ambient temperatures and excessive water loss due to the low vapor pressure prevalent at elevation (Rahn et al. 1976). Hatchability of chicken and turkey eggs decreases with altitude (Weiss 1978), the mortality rate being particularly more pronounced during the second week of incubation. Incubated under the same conditions, the eggs of species from wet habitats lose mass at a higher rate than those from drier habitats (Lomholt 1976b). Eggs laid by chickens acclimatized to an altitude of 3.8 km showed a reduction in the total pore area (Wangensteen et al. 1974; Packard et al. 1977; Carey 1980a,b), a feature which should curtail water loss (Tazawa 1987). In eggs that are laid at higher altitude, the number of pores in the shell is less, the shells are thicker, and the water content is higher (Rahn et al. 1977; Carey 1980a,b). The eggs of the birds which nest over water, e.g., the pied-billed grebe, *Podilymbus podiceps*, have a high density of pores which allows them to lose water to the relatively humid air around them (Drent 1975). The hatchability of the eggs laid by high-altitude (3.8 km) hens improves with the generations of residence at elevation (e.g., Carey et al. 1982). The total effective pore surface area of eggshells decreases with the barometric pressure (Packard et al. 1977). Increased diffusivity of gases through the eggshell due to enhanced gas-phase diffusion compensates for the prevailing hypoxia but results in hypocapnia due to increased CO_2 efflux (Rahn and Ar 1974). The PCO_2 in the air cell drops from 4.3 to 2.9 kPa when sea level eggs are exposed to 0.5 atm of a gas mixture containing 40% O_2 in N_2, to prevent hypoxia. Hyperoxia has a damaging effect on the development of the chick embryo. Exposure of O_2 at 5 atm for 3 h on 72-h-old chick causes a more than 50% mortality and 20 to 30% of those chicks which hatch have deformities of the brain, eyes, upper jaw, legs, feet, and heart (Pizarello and Shircliffe 1967). Due to the gas diffusion changes which occur at altitude and the fact that the measure of egg shell conductance is somewhat fixed once an egg is laid, fertile eggs laid at sea level but incubated at altitude require specific changes in the composition of gases such as enrichment with O_2 and CO_2 in the incubator for normal hatching to occur (Visschedjik and Rahn 1981). Incubation of eggs laid at sea level at an altitude of between 3.1 and 3.8 km results in reduced metabolic rates, prolonged incubation periods, low body mass at hatching, and unpredictable hatchability (Beattie and Smith 1975). To achieve the same conductance, the shells of the large eggs are relatively thicker than those of small eggs but are much more porous (e.g., Ar et al. 1974). The pores occupy 0.02% of the area of a chicken's egg shell but 0.2% of the area of that of an ostrich.

Gas exchange in the avian egg from the ambient air to the chorioallantoic capillary blood takes place by diffusion in the gas phase. The pathway through which O_2 diffuses from outside comprises of: (1) a variably thick cuticle (a noncellular mucinous coat closely applied on the surface of the eggshell); (2) a shell (a hard calcaneous and porous structure); (3) outer and inner shell membranes; and

(4) allantoic capillary blood (Fig. 108). The thickness of the eggshell (0.3 mm in the domestic fowl) varies among species (Table 31), depending on factors such as body and egg size and nutrition and nutritional status (Romanoff and Romanoff 1949). The inner shell membrane surrounds the albumin and the outer one is cemented to the shell. While the inner shell membrane has been presumed to be "wet" and hence presents significant resistance to O_2 transfer (e.g., Kutchai and Steen 1971; Wangsteen 1972; Tullet and Board 1976; Lomholt 1976a), morphometric determination of the diffusing capacity of the egg by Wangensteen and Weibel (1982) indicated that the membrane is "dry" and offers negligible resistance to O_2 flux. Of the three components of the chorioallantoic blood-gas barrier, the blood-gas barrier itself of which the harmonic mean thickness is 0.40 μm offers 10%, the plasma layer about 2%, and the O_2 binding rate 88% of the total resistance to O_2 flow (Wangensteen and Weibel 1982). Feeding acidic salts such as ammonium chloride (Hunt and Aitken 1962) and exposure to high concentrations of CO_2 for half a day for about 2 days (Helbacka et al. 1963; Hunt and Simkiss 1967), factors which lead to metabolic acidosis, decrease shell thickness. Pore geometry and the diffusion coefficient of a particular gas determine the permeability of the eggshell. With the onset of incubation when the embryonic heart starts beating, the circulation of the blood through the capillaries of the embryo

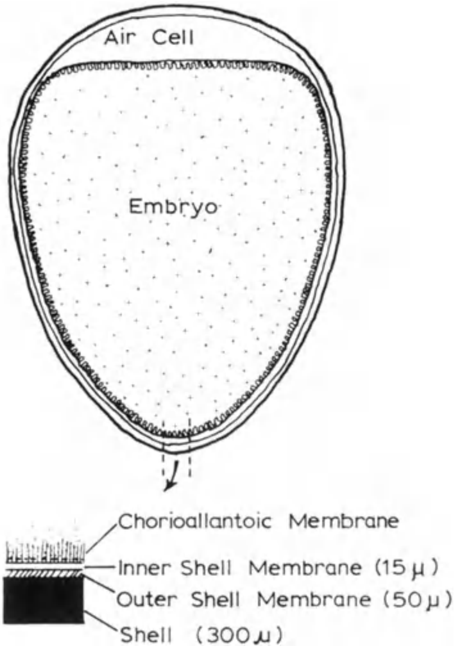


Fig. 108. Cross-section of an avian egg at an advanced stage of development. The dimensions of the main components which form the gas exchange pathway are shown. (Wangensteen et al. 1971)

add a convective process to the earlier entirely diffusive one. The formation of blood starts about 25h after the start of incubation and hemoglobin containing erythrocytes appear by the 2nd day (Romanoff 1960). As occurs in the lungs of birds (Maina et al. 1989a), the greatest impedance to O_2 uptake in the egg lies in the reaction between O_2 and the hemoglobin. The process contributes 88% of the overall resistance, the plasma only 2%, and the remarkably thin blood-gas barrier 10% (Wangensteen and Weibel 1982). The concentration of the hemoglobin does not change significantly between the 12th day of incubation and hatching, when 90% of it is converted to the adult form (Sandreuter 1951). Similarly, over the greater part of the period, the O_2-carrying capacity of blood does not change considerably (Bartels et al. 1966). Erythropoiesis in the developing chick is suppressed by hyperoxia and enhanced by hypoxia (Jalavisto et al. 1965). In complete contrast to the mammalian placenta (Sect. 4.7) which adjusts its gas exchange capacity with gestation, i.e., as the metabolic requirements of the fetus increase, the gas exchange machinery of the egg especially regarding pore number, size, and geometry are somewhat fixed despite the gradual increases in O_2 demands with incubation (Wangensteen et al. 1971). Romijn (1950) and Kutchai and Steen (1971), however, observed that eggshell permeability increases with incubation and estimated that at day 20 of incubation, 575ml O_2 diffuse into the egg per day. Like the mammalian embryo, the avian one subsists under perpetual hypoxia. Towards the end of incubation, high PCO_2 and low PO_2 in the air space (Romijn 1948) may prompt the chick to break through the shell. A change in the O_2 dissociation curve of the blood of 20-day-old embryos was observed by Bartels et al. (1966): the P_{50} was only 4kPa in the embryonic blood compared with 6.7kPa after a few days of hatching. In the egg, the PO_2 and PCO_2 of the air cell is set by the O_2 uptake and CO_2 release (metabolism) of the embryo and the conductances of the egg shell (Wangensteen and Rahn 1970; Paganelli 1980). Throughout incubation, CO_2 permeability of the eggshell and membranes is two to three times higher than that of O_2, showing that diffusion occurs mainly through air-filled rather than fluid-filled pores (Kutchai and Steen 1971). Given the relatively low diffusion coefficient of O_2 in water, eggs with solid shells would theoretically have to be very small and possess a very high density of pores and low rate of O_2 consumption to survive in water. Such eggs occur in skates and rays (Denney 1993). In a water-saturated environment, the embryos in the larger avian eggs soon drown. The chorioallantoic membrane, a very well-vascularized organ which is closely applied to the inner shell membrane, is the only adaptable structural factor in the egg. It develops steadily and only completely underlies the whole shell towards the beginning of last half of the incubation period (Wangensteen and Rahn 1970; Wangensteen 1972). The degree of vascularization of the outer allantoic surface is increased when the eggs are incubated in a lower PO_2 (Remotti 1933).

The chorioallantoic membrane is considered to be a homolog of the mammalian placenta (Metcalfe and Stock 1993). The diffusing capacity of the chorioallantoic membrane for O_2 in chicks increases sixfold between days 10 and 18 of incubation. During late incubation, the mass-specific diffusing capacity and the capillary blood volume are similar to those of the human lung (Tazawa and Mochizuki 1977). Compared with the viviparous species, where the change from embryonic respiration is abrupt on the breaking of the umbilical cord, in the oviparous species, the change is a gradual process. Mainly owing to the fact that the metabolic rate of the developing embryo increases steadily while the permeability of the shell arguably remains almost constant (Kutchai and Steen 1971; Rahn et al. 1974), in bird eggs, a critical hypoxic phase occurs towards the end of embryogenesis (Freeman and Misson 1970; Girard and Muffat-Joly 1971; Wangensteen 1972). As incubation progresses, the PO_2 in the air cell decreases from 18.7 to 13.3 kPa and that of CO_2 increases from 0.67 to 5.3 kPa (Wangensteen 1972; Table 33). At about day 19, the concentration of O_2 is about 10 to 12% and that of CO_2 lies between 6 and 8% (Tazawa et al. 1983b). As the embryo uses the O_2 inside the shell's air space (Fig. 108), the PO_2 decreases. This increases the partial pressure gradient of O_2 between the ambient air and that inside the egg, enhancing the O_2 influx. Until the 8th day of incubation, the partial pressure gradient of O_2 between the outside of the shell and the air space is about 1.3 kPa, at the 16th day it rises to 6.0, and rises to 10 kPa by the 18th day (Metcalfe 1967). This indicates that as hatching advances, the PO_2 in the allantoic arterial blood must fall to very low levels, increasing the danger of the chick succumbing to hypoxia. Bartels et al. (1966) observed that after day 17, compared with the state after hatching, the chick embryo showed signs of respiratory acidosis: the CO_2 content of blood at a PCO_2 of 5.3 kPa is 54 ml per 100 ml of blood at the 17th day and decreases to about 36 ml after hatching. The autoregulating process of the PO_2 in and outside the developing egg ascertains that the embryo is well supplied with O_2 by diffusion. In regulating O_2 flux, the embryo is not a passive participant. The hypoxia which occurs during the late embryogenesis induces increase in the level of the catecholamines which improve the blood gas status (Wittman and Prechtl 1991). The permeability of the eggshell must adaptively be designed to provide the maximum amount of O_2 required by the embryo, regulating it around the

Table 33. Measured air cell gas tensions (mmHg)[a] of an incubated chicken egg. (Wangensteen and Rahn 1970)

Embryo age (days)	PAO_2	$PACO_2$
7	141.6	13.6
8	140.0	12.7
9	138.1	16.2
10	137.5	16.0
11	134.7	18.3
12	131.3	19.4
13	129.2	21.2
14	124.5	24.8
15	117.9	30.8
16	111.9	36.6
17	106.4	41.8
18	109.9	38.7
19	102.3	43.3

[a] To convert to kPa multiply by 0.013.

critical minimum arterial PO_2 needed for survival. Reciprocatively, the O_2 consumption of an embryo is determined by the conductance of the shell and the lowest tolerable arterial PO_2 (Wangensteen and Rahn 1970). The acid-base status of the embryo is regulated by increases in plasma concentration of the HCO_3^- ions in direct proportion with the changes in the PCO_2. This maintains a constant pH of about 7.45 (Erasmus et al. 1970/71). During incubation, the arterial PCO_2 reaches a value of about 5.3 kPa, which is about the same level as that in the lungs of the hatched chicks. Wangensteen and Rahn (1970) considered this to be a preparation for smooth transition to air breathing when the gas exchange process changes from diffusion respiration of the chorioallantois to the convective one of the lungs. The changeover from total chollioallantoic respiration to pulmonary respiration takes 22 to 30 h in the chicken (Visschedijk 1968a; Vince 1973). The time of pipping corresponds with increased PCO_2 or decreased PO_2 in the egg air space (Vince et al. 1975), the stimulating effect of CO_2 being two times more potent than that of O_2 (Visschedijk 1968b).

6.14 The Bottom Line

In nearly all evolved life forms, throughout their existence, molecular O_2 to varying extents has been in constant demand. Respiration has hence been integral in molding the complex morphologies in biology. As a terminal hydrogen acceptor in the ubiquitous scheme of intracellular oxidation by electron transfer, O_2 is involved in the vital energy-producing processes which sustain life. The gas exchangers have evolved and adapted in tandem with the respiratory requirements of whole organisms in different states, environments, and habitats. Once they were genomically inaugurated, the designs were continually fashioned by needs and circumstances. The shared morphological contrivances evident in the constructional plans of the gas exchangers indicate that similar pressures have inspired the congruous designs. The aphorism that necessity is the mother of invention is as relevant to evolution and adaptation to novel designs in biology as it is to human activities and needs in the contemporary world. Change in size and activity and subsistence in unique habitats has called for appropriate adjustments for efficient O_2 uptake, transfer, and utilization. Among many animals, solutions to these needs have differed only in details, and not in generality. For example, sheet flow of blood at the gas exchanger, closed circulation, double circulation, presence of respiratory pigments in blood and muscle tissue, etc., are some of such prevalent devices. There are no rules in the construction and working of the gas exchangers: means justify ends! Contingent upon the available resources and the specific requirements for survival, the final solutions are arrived at independently. For instance, in insects, the lengthy and costly developments that would have entailed formation of, e.g., a circulatory system, blood, carrier pigments, and blood cells were ingeniously circumvented simply by elaboration of a tracheal system which delivered O_2 directly to the tissue cells from the atmosphere. An animal's success in life is determined by the arsenal of vital adaptations it has creatively appropriated, devised, and harnessed along the way. In the formidable continuous forward momentum enforced by natural selection, befitting improvements in the respiratory processes are pivotal for survival. Our response to the question asked by Weibel (1983b) – is the lung built reasonably? – is yes, and to that by Dempsey (1986) – is the lung built for exercise? – is no. We hasten to qualify the latter response as follows: exercise is an extreme costly state of operation which in virtually all animals is endured only momentarily. Gas exchangers are designed to operate at the most economical levels but have inbuilt plasticity of making functional adjustments in response to moderate pressures.

As established in the laws of thermodynamics, a fundamental aspect integral to life's existence on Earth is that it survives on finite, diminishing resources. This rather fatalistic state of affairs calls for efficient means of procurement and economical utilization of the limited resources. It obliges optimal designs of biological systems. Strategies for thrifty use and maximization of the energy reserves and supply developed very early in evolution (e.g., Priede 1977; Szarski 1983). Through painstaking cost-benefit analysis of causes and effects and rationalization and appraisal of the utilities of the attributes that they are endowed with, animals are innately engineering and carefully crafted by natural selection to a high fidelity state from which they are able to ameliorate or overcome the external pressures which continually besiege them. The practical consequence of evolution and adaptation has been to fashion optimal systems where form and function associate harmonically. Nowhere else has this need been of more paramount importance than in the design of the gas exchangers. On a low-energy life-style animal, the snail, Ramsay (1968) observed that "the more one looks into the snail's way of life (plant food is abundant in near vicinity and when threatened it takes refuge in its shell) the more one sees that it has nothing to gain by stepping up its activity, and for its low level of activity a respiratory organ and a circulatory system of moderate efficiency are adequate". In extreme circumstances and when need has justified it, animals have adopted extreme measures of reducing their metabolic requirements, e.g., by going into programmed low energy retreats like estivation and cryptobiosis (e.g., Storey 1988, 1989; Storey and Storey 1990). When warranted, some animals have resolutely deconstructed organs and organ systems and, where need has justified it, readopted past simpler designs and more economic strategies of operation. In many cases, if not in most, when all else has failed, two or more animals (and even animals and plants!) have abandoned their genetically programmed evolutionary trajectories and adopted beneficial symbiotic (= cooperative) associations (e.g., Margulis 1979; Trench 1979; May 1981; Childress et al. 1989; Fenchel and Finlay 1991a,b; McFall-Ngai and Ruby 1991; Finlay and Fenchel 1993; Rennie 1992; Vogel 1997). By pooling their capabilities, the partnership ensured access to resources which otherwise would be unreachable to the individuals alone. Identifying and reconciling the factors that enforce the different or similar morphologies and lifestyles on organisms remains an interesting and challenging aspect in biology. It calls for a vast synthesis of different disciplines of science. Cognizance of the effects past events have engendered on present life is both theoretically engaging and practically useful. It is hopefully by understanding how we got here that we may be able to better anticipate where we are going. The very survival of the humankind may rest squarely on understanding and considerate management of our single most important resource – biodiversity. The opinion offered by Thomas Thomson in 1802 is as valid now as it was some two centuries ago. It is an appropriate closing introspection.

> *"As soon as man begins to think and to reason, the different objects which surround him on all sides naturally engage his attention. He cannot fail to be struck with their number, diversity, and beauty; and naturally feels a desire to be better acquainted with their properties and uses. If he reflect also, that he himself is altogether dependent upon these objects, not merely for his pleasures and comforts, but for his very existence, this desire must become irresistible. Hence (it is) that curiosity, that eager thirst for knowledge, which animates and distinguishes generous minds." A system of chemistry, by Thomas Thomson, 1802 – quoted in Holmyard and Palmer (1952)*

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