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Scientific Process and Social Issues in Biology Education

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Preface

This book is the product of the authors' teaching introductory biology and related science courses at several different colleges and universities, though primarily at Wesleyan University, Middletown, Connecticut (Baker) and Washington University, St. Louis, Missouri (Allen). One of us remembers in his earliest years of teaching having the distinct feeling that, more often than not, some of his most creative students received only mediocre grades: unmotivated by the presentation of a dazzling array of detailed factual information, they would often ask unexpectedly thoughtful and highly reflective questions. Conversely, students receiving As, while able to regurgitate biological "facts," (e.g., details of the Krebs citric acid cycle), were often totally incapable of mapping out a strategy for investigating even the simplest of research projects. A variation on this theme was the comment of one faculty colleague that he found himself becoming increasingly uncomfortable with the recognition that a few of his students could complete a basic introductory biology course satisfactorily yet still remain convinced of the intellectual validity of Creationism!

These and other such experiences convinced us that students may do well in a science course but fail completely to comprehend the nature of science itself, the underlying reasons for its immense power as an intellectual process, and the relationship between the natural sciences, social sciences, and humanities. Perhaps worse, when considering science at all, students seem to drift from one extreme to another, either buying into popular press versions of science as the ultimate source of all truth or viewing it as just one of many systems of intellectual thought, of no greater or lesser validity than any other. Unfortunately, this latter view is one often found even among the ranks of college faculty in the social sciences and the humanities, in which modern science may be referred to as "just another system of myths," "the predominant myth of the twentieth century," or other words to that effect. Such a view does a profound disservice to the meaning of both the terms "science" and "myth." If indeed modern science is to be viewed as a myth, then clearly it is by far the most powerful one yet devised by the human imagination!

It was in an attempt to deal with this confusion that, over the years, we began to incorporate material into our course designed to confront this and other such problems. Ironically, one of the anonymous reviewers of the manuscript for this book wrote a comment that reflects beautifully the sort of resistance one encounters to such efforts:

> As part of a debate with faculty over curricular issues some years ago, I asked one of my colleagues how our science students would fare if they were asked to distinguish between science and the humanities. . . . The response of my colleague was silence. This silence was born of what I believe to be a pervasive fact: that those of us who teach science rarely considered these issue so explicitly. . . . It is much easier to present the facts of normal science (what we know) than to consider how we know it.

In one of our earlier books we put forward what we think is the essence of a process approach to science: ". . . it is the process, not merely the content or "facts" of biology, that should form the basic thrust of introductory courses. By the process of science we mean *how we know what we know*; how experiments are designed, data analyzed and conclusions drawn—in short, the logic and method of science."[1] This approach is designed to stress to students that today's scientific "facts" may be tomorrow's errors. In our efforts over the past few years to produce an updated version of our approach, however, we found ourselves immersed in a publishing world far more concerned with the commercial success of encyclopedic and fact-driven textbooks and much less in scientific process. Beyond that, the introduction of full color to both art and photographs has driven the cost to the student of such textbooks to astronomical heights, in some cases, well over $100! As lovely as these books may appear, in this day and age of widespread student access to color TV, photography and the Internet, one cannot help but wonder if such an expense is justifiable. Thus when the Fitzgerald Science Press originally expressed interest in the underlying philosophy of our work and in publishing it as a series of low cost yet high quality, two-color volumes, we felt that a genuine meeting of the minds had occurred.

The format of this book is designed specifically to address the nature of science in general and of the biological sciences in particular. Chapter 1 deals with the historical development of the life sciences and looks ahead to what the field might be like in the next century. It also uses examples of current research in the field to stress that biology, like all the natural sciences, has many unsolved problems researchers today are still trying to understand and is therefore a field no less dynamic now than in the past.

Chapter 2 begins with an in-depth look at biology as a science in the context of hypothesis formulation and the underlying inductive and deductive logic involved. Here we stress the differing types of hypotheses, the role that conscious and unconscious bias may play in both formulating questions and evaluating answers, as well as the strengths and limitations of science as an intellectual discipline.

Chapter 3 deals with how scientific hypotheses are tested and how the logic involved may be analyzed in terms of its inductive and deductive framework. We have often elected here and elsewhere in this book to use older studies from the

[1]Preface, *The Study of Biology,* 4th, edition, Baker, Jeffrey J. W., and Allen, Garland E. Reading, MA. Addison Wesley Publishing Company, 1982, p. v.

seventeenth, eighteenth, and nineteenth centuries. So doing enables us to avoid having to provide a great deal of subject matter background and, since the student reader more than likely already knows the “answer,” he or she is forced to concentrate instead on the underlying intellectual structure involved. We then apply insights from these older case studies to contemporary issues: e.g., conflicting hypotheses concerning the cause of the AIDS epidemic now sweeping many developed and developing nations. For those instructors interested in introducing early the concept of statistical analysis in hypotheses evaluation, we provide an appendix dealing with some of the essential concepts and techniques and means used to illustrate experimentally established correlation.

Chapter 4 compares three case studies, the first an example of research carried out in the laboratory and the second an example of research in the field, with all the difficulties in terms of controlling variables that such studies entail. The third case study deals with problems inherent in evolutionary studies in which events have occurred that cannot be observed directly.

Finally, Chapter 5 is concerned with the interrelationship of science and the society within which it develops and the social responsibility of scientists to the society that funds their research. Using Creationism as our example, we end with issues raised by the still all-too-powerful attraction of pseudoscience and its misuse to further a particular political agenda. Doubtless here instructors may wish to bring in other examples of their own.

It is only appropriate here that we express our gratitude for the assistance provided us by the late Irma Morose, Teresa L. Tate (née Lowe), and Cindy Marks. All too often such valuable input goes unrecognized, despite the fact that little or nothing could be accomplished without it. It would be difficult to find greater justification for this book.

St. Louis, MO, USA — Garland E. Allen
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March 2014

Contents

Biology as a Process of Inquiry

1

Abstract

This chapter provides an overview of the nature of *process* in science, and biology in particular, with an emphasis on the fact that science is always an ongoing exploration of unsolved problems. After tracing the history of debates about the role of various methods and approaches to biology in the eighteenth and nineteenth centuries, the chapter proceeds to a discussion of a major revolution in biology during the twentieth century, with the introduction of new approaches associated with molecular and cell biology, and molecular genetics. The chapter concludes with three case studies of still-unsolved problems in biology: the annual migration of Monarch butterflies from the upper Midwest to Mexico in North America; the case in which chick embryos are induced to develop teeth, and what this tells us about genetic signals during embryonic development; finally, the vexing question of how life could have originated on Earth from non-living matter.

1.1 Introduction

Imagine yourself on a moonlit night in mid-August at the Marine Biological Laboratory in Woods Hole, Massachusetts. You are standing on a pier looking into the shallow waters below. The reflected moonlight rippling through the water, gives the appearance that the whole ocean is alive. As your eyes adjust to the darkness you realize that the water *is* teeming with life. You are observing the mating ritual, triggered by the full moon, of thousands of writhing, swirling polychete worms. A timeless event unfolds before you, drawing you back to primeval oceans where ancient progenitors of these polychetes repeated a similar ritual long before any human eyes were there to observe it. Here is an expression of life at its most

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fundamental, its most dynamic, its most breathtaking. You are witnessing a great saga: past, present and future all rolled into one spectacular moment.

Many who have witnessed this or similar events around the world have found in the activities of living organisms an inspiration to study, to investigate, to learn more about this wonderful phenomenon we call "life." Biology, the scientific study of life, builds on this inspiration to ask questions: Why, for example, does the polychete mating process occur only in late summer? How is it timed and what is it about the phases of the moon that triggers the mating behavior? Without this awe and wonder, there can be no sustained investigation. Without sustained inquiry, we look on as outsiders and do not gain access to life's mysteries. *Sustained inquiry is what biology as a science is all about*.

This book is about how biologists approach the study of life. How do we ask the right questions, questions to which it is possible to obtain answers? What distinguishes a useful from a not-so-useful question and one that can be tested from one that cannot? What are the respective roles of observations, facts, hypotheses and theories in science? How are experiments designed, carried out, and the resulting data analyzed? These and other issues implicit in asking "What is science" and "How do we know what we know" make up a central theme of this book.

1.2 The Growth of Biological Thought: The Nineteenth Century

If the nineteenth century witnessed the rise to pre-eminence of the physical sciences, the twentieth century has witnessed a similar rise to prominence of the biological sciences. As we stand in the early decades of the new millennium, biology represents one of the most rapidly developing and exciting areas of scientific investigation the world has ever known.

Throughout most of its earlier history, biology was a largely descriptive science, concerned with topics such as comparative anatomy and embryology, descriptions of the adaptations of organisms to their environments and the classification of species. Most of the early biologists had a strong background in natural history and field work. They studied their collected specimens in museums and laboratories and generally did not conduct experiments of the sorts carried out in chemistry and physics laboratories. It was for these reasons that biology was considered to be a distinctly second-class citizen among the academic community working in natural sciences such as physics, chemistry and geology.

Two areas of biological thought underwent major developments in the middle and later parts of the nineteenth century: physiology and the study of evolution. From the early 1850s on, both German and French physiologists pioneered the application of physical and chemical methods to the study of how organisms function. For example, Hermann von Helmholtz in Germany found ways to measure the speed of nerve impulses and to demonstrate its electrochemical nature. Claude Bernard in France studied the chemistry of the liver and demonstrated that it was able to manufacture animal starch from simple sugars, the first time such a synthesis had been demonstrated in animals (it was well-known in plants by this time). However, the most momentous scientific development in nineteenth century biology was undoubtedly the publication in 1859 of *On the Origin of Species by Means of Natural Selection* by Charles Darwin. Darwin not only promoted the idea, long well known but not well accepted, of evolution (or “transmutation of species” as it was called at the time) but also put forward a mechanism, natural selection, by which evolution might occur. He noted that in nature many more offspring are born than ever reach maturity, a result of competition for limited resources. Any variation an organism might have that gave it a slight edge in this competitive struggle. If that variation was genetically based, meaning inherited, the organism would therefore succeed in leaving more offspring. By natural selection, the favorable variation would spread throughout the population over successive generations, unfavorable variations eliminated, and the character of the population changed, i.e., evolution would have occurred. Although at the time Darwin’s theory was controversial among biologists and non-biologists alike, it has survived to become the most comprehensive organizing concept of modern biology.

Following Darwin’s lead, biologists in the later nineteenth century devoted themselves to working out descriptive aspects of evolutionary theory and, as noted earlier, it was this aspect of biology that came to dominate much of the work in the latter part of the century. An example of this descriptive biology was a field known as morphology, literally the “study of form.” In the 1870s and 1880s, morphology was primarily devoted to tracing evolutionary relationships based on evidence from comparative anatomy, embryology, physiology and the fossil record. The end product of such morphological work was the production of phylogenetic “trees” (Fig. 1.1). For example, to determine whether a group known as Annelids (earthworms and polychetes such as those described at the opening of this chapter) and Arthropods (insects, crayfish, spiders) might share a common ancestor, morphologists would compare the adult form’s anatomy. It was noted that both groups were segmented, possessed a similar nervous and circulatory systems, and developed from the fertilized egg in the same pattern of cell divisions and growth. This morphological similarity was strengthened by finding a species living today, *Peripatus* (Fig. 1.2) sharing characteristics of both groups. Like the Annelids, *Peripatus* is composed of repeated, nearly identical segments but has jointed appendages on each segment like Arthropods. *Peripatus* was thus thought to be the descendent of a form intermediate between the Annelids and Arthropods; to morphologists it represented something like what the common ancestor might have resembled.

A limitation of morphological work was that there was no way to test many of the ideas concerning evolutionary relationships with the methods available at the time. Thus the various scenarios remained highly speculative. (Such a limitation does not, of course, invalidate the attempt to determine evolutionary relationships by comparative methods; indeed, such efforts have gained a considerable following today, using a variety of molecular data unavailable in the past.) A break from the morphological tradition occurred in the 1880s and 1890s when German and French

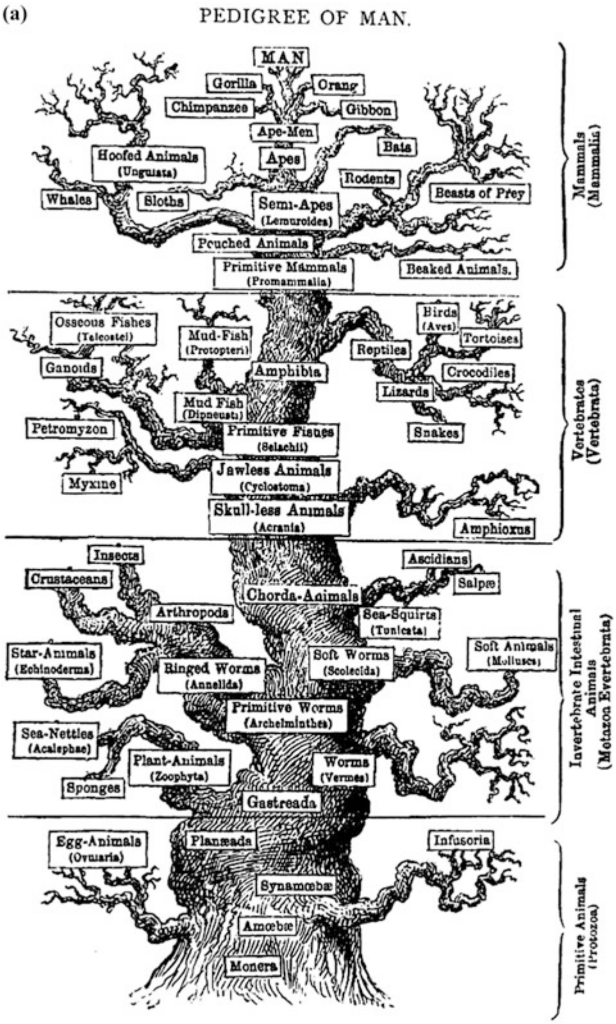

Fig. 1.1 Two versions of a phylogenetic tree, showing the evolutionary relationships thought to exist between the major animal groups (phyla). **a** A nineteenth century version, drawn for morphologist Ernst Haeckel's *The Evolution of Man* (1879). The tree shows not only the fascination of early morphologists with reconstructing the evolutionary relationships among organisms, but also their straight-line, progress-oriented, conception of evolution. The vertical tree trunk is shown as growing toward the ultimate product of evolution, human beings. Many of the relationships depicted here were based on evidence derived from embryological studies. **b** A more recent evolutionary tree. Note that it is more bush-like, with no single progression leading toward towards any one group

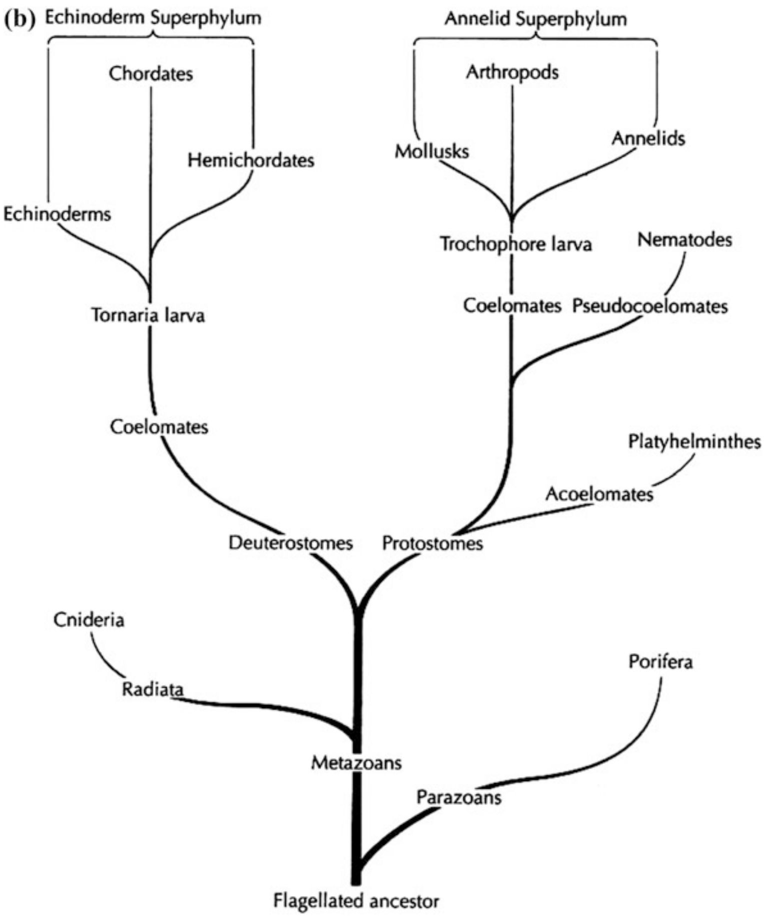

Fig. 1.1 (continued)

biologists became interested in studying the embryo for its own sake rather than only as a means to uncover clues about phylogeny. These biologists were also highly attuned to testing their ideas experimentally. For example, the German embryologist Hans Spemann (1869–1941) became interested in how the fertilized egg, after a number of cell divisions (cleavages), produces a variety of different cell types (muscle, nerve, bone, etc.). A common view at the time, known as the "mosaic theory," maintained that different parts of the egg contained different determiners or factors that became parceled out to different daughter cells as the egg divided. A cell would eventually develop into one special type according to the kind of determiner or factor it ended up containing.

Fig. 1.2 *Peripatus*, a member of the phylum Onycophora, is thought to be a modern-day descendant of a form ancestral to both the arthropods and annelids. The discovery of living or fossil forms intermediate between two quite divergent modern groups provides strong evidence for the Darwinian concept of evolution by natural selection. © Cabisco/visuals unlimited

Spemann worked with amphibian eggs (frog and salamander) because they are plentiful, can be kept alive in the laboratory with relative ease, and are large enough to be manipulated experimentally. Although most of the fertilized salamander egg look like a uniform mass of cytoplasm, there is one noticeably different region, called the gray crescent, that Spemann suspected might have something to do with directing the first phases of embryonic development. The salamander egg normally divides along a plane ensuring that each daughter cell gets part of the gray crescent. In a series of experiments using fine baby hair (from his infant son's head), Spemann carefully tied dividing salamander eggs in their normal plane of division so that the cells on each side of the constriction contained gray crescent material (Fig. 1.3a). Each part of the cells divided and gave rise to a more or less complete (though dwarf) embryos. Spemann reasoned that if material from the gray crescent is necessary for complete development, then tying the dividing egg in a plane perpendicular to the plane of cell division so that one side of the constriction received all the crescent while the other side received none, should result in only that part of the cell containing gray crescent material developing into a complete embryo. When he carried out this experiment (Fig. 1.3b) his prediction was borne out. The part of the cell lacking gray crescent material produced only a formless mass of cells, while the region containing the gray crescent formed a complete embryo. To Spemann these results were conclusive evidence that the way in which material—in this case, gray crescent material—was parceled out to daughter cells determined the overall course of development. Spemann's work demonstrated

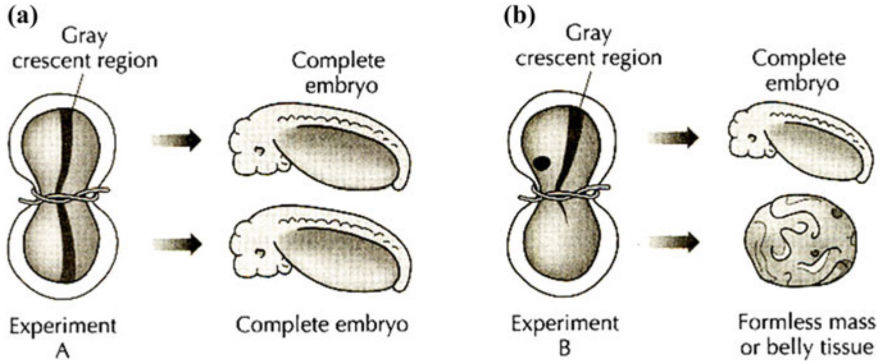

Fig. 1.3 Hans Spemann's experiments showing the importance of the gray crescent in the ability of the first two cells of an embryo to develop normally. **a** When Spemann experimentally constricted a dividing salamander egg so that gray crescent material was present in both cells, each cell would develop normally into a complete, though dwarf, embryo. **b** If the constriction were made in the same plane as the gray crescent, so that one side of the constriction received all the gray crescent material, only that cell produced a normal embryo; the other cell developed into a formless mass of cells. These experiments showed that specific determinants associated with the gray crescent were necessary for full development

experimentally that, in ways unknown at the time, the organization of the fertilized egg had an important effect on the future course of embryonic development.

As in the physical sciences, experiments such as Spemann's (for this and other work he was awarded a Nobel Prize in 1935) allowed biologists to obtain precise answers. It was through such experiments that biology began to acquire an image of becoming more rigorous and come into its own among the other experimental sciences.

1.3 The Twentieth Century Revolution in Biology

The rise of biology to its new scientific status coincided with the beginning of the twentieth century. In the year 1900, the original work on heredity by the Augustinian monk Gregor Mendel was rediscovered and, as a result, the new science of genetics was born. By 1950, genetics had become central to virtually all areas of modern biology. Questions about what the hereditary units called genes are and how they function led first to determination of the relationship between genes and the synthesis of proteins and eventually to determination of the double-helix structure of the molecule of heredity itself, deoxyribonucleic acid, or DNA, by James D, Watson and Francis Crick in 1953. Genes were now recognized as consisting of DNA. From this work there arose a whole field of molecular biology, the study of the atom-by-atom structure of biologically important molecules. The subsequent development of genetic engineering, including the cloning of agriculturally important animals and plants, has opened up new potentials for food production and management. Many genetic diseases, once thought incurable, are now open to the prospect of drug or gene therapy.

Perhaps most significant, genetics provided the mechanism of heredity that Darwin's theory of evolution had lacked, leading to new advances in understanding how species evolve over time. One of the weak points in the theory of natural selection as originally proposed by Darwin was that he had no clear idea how heredity worked. Like most of his contemporaries, he thought that characteristics acquired by an organism during its lifetime, especially changes induced by diet, temperature and changed habits, could be inherited by its offspring. He also thought that two different forms of the same trait (for example red and white flower color) would produce a blend in the offspring, thus diluting the trait in successive generations. In the late 1920s and early 1930s, various mathematically-oriented biologists began applying Mendelian genetics to the evolutionary process, creating the field of population genetics. Using the findings of Mendelian genetics, these investigators showed that traits generally do not blend and that favorable variations are not always lost to future generations. Since then, evolutionary biologists have worked out the dynamics of how natural selection works in a large variety of animal and plant populations. With its marriage to Mendelian genetics, the Darwinian theory of evolution by natural selection became thoroughly established as *the* central concept underlying all of modern biology and has become one of the most active areas of modern biological research.

Two aspects of evolutionary biology commanded the attention of biologists throughout much of the last half of the twentieth century. One is molecular evolution, the attempt to understand how evolution works at the molecular level. DNA guides the assembly of proteins—each DNA segment determining a very specific protein structure. As a result, changes in DNA (mutations) are many times reflected in variation in the structure and/or function of protein molecules, since protein structural differences can be determined with great precision, and, by comparing the same protein in different species, it is possible to test hypotheses about evolutionary relatedness more rigorously. The same can be done with DNA directly. Such studies have shown that proteins exist in "families"—for example, the proteins called cytochromes involved in cellular respiration—and, like organisms themselves, the members of these families may be thought of as having diverged from a common ancestral form. Proteins from very different families are now known to be composed in many instances of similar motifs or patterns that "highly conserved," i.e., used repeatedly, throughout evolutionary history.

Yet another aspect of evolutionary biology making great strides in the twentieth century was the study of human evolution. Excavations at Olduvai Gorge in East Africa in the 1950s and 1960s by Louis Leakey (1903–1972) and Mary Leakey (1913–1996) and in the Afar region of Ethiopia by Donald Johanson (b. 1943) in the 1970s brought to light much older fossil hominids (human-like forms) than had ever been discovered before. These finds suggested, among other things, that our ancestors walked upright long before our brain size expanded (or, as it has been said, our evolution was feet-first rather than head-first!). New finds are now made almost every year and, with computer-based studies of modern populations, physical anthropologists have concluded that it is most likely our own genus and species (*Homo sapiens*) originated in Africa and later migrated to all areas of Asia and Europe. Our closest relative in time, the Neanderthals (*Homo neanderthalensis*) are now believed to have roamed Europe as recently as 28,000 years ago. This much more recent estimate of their existence indicates that Neanderthals must have overlapped with our own species. Such discoveries have raised intriguing questions about how similar were the Neanderthals to us and what caused them to become extinct.

Toward the end of the twentieth century biologists embarked on their most ambitious project yet: the Human Genome Project (HGP), sometimes also referred to as the Human Genome Initiative. A large-scale international effort, the HGP's primary goal has been to map and sequence all of the base-pairs in the DNA of the human genome, a term referring to the complete set of genes contained in an organism. The purpose of this effort was to try and identify first the structure of all the genes and then determine their functions. Many different laboratories in the United States and Europe had been working since the early 1990s to complete the sequences. The technology developed to carry out this work increased dramatically the rate at which sequencing could be carried out. As a result, the isolation and molecular characterization of genes for several important human diseases, such as cystic fibrosis (a progressive build-up of mucus on the tissue lining the lungs and intestines leading in many cases to premature death) and Huntington's chorea (a gradual deterioration of the nervous and muscular systems). Genes affecting other rare diseases have already been mapped to specific regions of chromosomes, and many of these have been sequenced.

To help in understanding the function of many of these sequences, the genomes of several other experimental organisms have been analyzed: yeast (completed), a small roundworm *Caenorhabditis elegans* (completed), the weed *Arabidopsis* (completed), the mouse, and the fruit fly *Drosophila* and many others. What has already emerged from this comparative effort is the recognition that many of the same DNA sequences appear in a wide range of organisms. For example, one frequently encountered group of genes in the animal kingdom are known as the homeotic genes. These genes appear to be responsible for such fundamental processes in early embryonic development as establishing the anterior-posterior axis of the organism and the formation of the body segments found in insects or the vertebral column of vertebrates. Just as an architect may use a few basic modular blueprints that may be combined in different ways to produce quite different buildings, evolution has preserved batteries of genes that, in conjunction with other DNA sequences, build very different organisms from many of the same starting instructions.

Yet another area of biology that has shown enormous growth in the twentieth century is immunobiology, a field investigating how the immune system functions at the systemic, cellular and molecular levels to protect the body from invasion by foreign agents such as bacteria and viruses. Spurred on in part by new concepts in developmental biology in the 1960s, study of the immune process has expanded enormously in the past decade in response to the Acquired Immune Deficiency Syndrome (AIDS) epidemic rampant throughout the world. AIDS, a disease marked by decline in the ability of cells of the immune system (T-cells) to respond to infectious agents, is caused by a virus that has ribonucleic acid (RNA) instead of DNA, as its genetic material. People with AIDS lose the ability not only to fight off the AIDS virus itself, but all sorts of other infectious agents as well. Attempts to understand both the mechanism of infection and replication by the AIDS virus and the response to it by the antibody producing cells of the immune system have led to an explosion in research in the fields of virology and immunology. Drugs that interfere with the replication of the AIDS virus have revealed many details about the process of viral infection and host cell response. Although a cure is still in the future, considerable progress has been made in devising combinations of drugs that slow and even appear to stop the replication and spread of the AIDS virus within the host's body.

Other areas of biology that have flourished and expanded our horizons greatly during the twentieth century are neurobiology, cell biology and ecology. Neurobiology is a broad umbrella field that covers everything from the study of how individual neurons function to such issues as the nature of brain function, memory and consciousness. The twentieth century opened with a debate about whether the nervous system was composed of individual cells (neurons) or was a continuous, fibrous network, or reticulum, a debate resolved in favor of the neuron. Major advances were made between the 1930s and 1960s in devising techniques for studying single neurons and recording electrochemical changes between inside and outside the cell. In this work the marine squid (*Loligo peali*) figured prominently because of its widespread distribution and the fact that it has a very large neuron running along its dorsal (upper) surface that is easy to manipulate in the laboratory. So large is this neuron that it is possible to insert one microelectrode inside the cell and keep another on the outside, enabling the recording of voltage changes across the membrane as the neuron conducts an impulse. Along the same lines, much has also been learned about the process of transmission between neurons. Substances called neurotransmitters, which are released from one cell and stimulate (or inhibit) the other neurons with which it forms a junction, have proved to play very important roles in a wide variety of behaviors, including in humans the regulation of emotions.

The relationship between neuronal activity and behavior has been studied in exquisite detail in a variety of organisms, including the small roundworm (*Caenorhabditis elegans*), and the sea slug (*Aplysia*). Both of these organisms have simple nervous systems in which virtually every neuron has been described and the interconnections of all the neurons in the system have been mapped. Genetic or experimentally induced defects in particular neurons in the network have been correlated with specific behavioral changes and provide a glimpse into how simple nervous systems are organized and how they function in making specific responses. Top among the findings during the last two decades of the century was the role of a special class of neurotransmitters, the biogenic amines, including dopamine, epinephrine, norephinephrine and serotonin. These neurotransmitters have been found to play a role in increasing or inhibiting certain inputs to the brain and central nervous system. Serotonin, for example, is produced in highest quantities when the organism is awake and alert and lowest during sleep. In chimpanzees, serotonin levels change in response to changes in the animal's social position; increase in social position brings about a decrease in overall serotonin levels and vice versa.

The molecular basis of our conscious and altered states of mind, as well as of memory and thought, is increasingly yielding to biochemical analysis. This does not mean we are simply biochemical robots, since ever-changing inputs from the environment are constantly altering our physiological state. While our biology certainly determines our behavior, our behavior also determines our biology. The relationship is not a simple one, however, and overstated claims that complex behavior and personality traits are the product of one or two neurotransmitters or genes should be regarded with suspicion.

Our understanding of the structure and function of cells, the basic units of life, underwent a genuine revolution during the past century. In 1896, Edmund Beecher Wilson at Columbia University published the first edition of his book, *The Cell in Development and Inheritance*, which was to become a classic of cell biology throughout the first half of the twentieth century. Wilson's summary of cell structure and function of both adult and embryonic cells was derived mostly from observational studies with the light microscope. At the time, cells were still thought of as membrane-bound units with several specific internal structures such as a nucleus, chromosomes and vacuoles suspended in an amorphous medium known as "protoplasm" (Fig. 1.4a). With the advent of the electron microscope in the 1930s and its expanding use after World War II, protoplasm turned out to possess a complex structure of internal membranes, particle-like structures such as ribosomes (the sites of protein synthesis), organelles ("little organs") such as mitochondria and chloroplasts, each with its own complex structure, and a variety of structural components known collectively as the cytoskeleton (Fig. 1.4b). By the end of the century study of the structural and functional properties of cells using still more sophisticated imaging, such as the confocal microscope, have added further detail to our understanding of the molecular biology of the cell.

At the macroscopic (large-scale) rather than microscopic (small-scale) level of ecological processes, biologists have made some remarkable advances in the twentieth century. The field of ecology was effectively created in the second decade of the century, and the study of the world's major ecosystems (communities of organisms that interact in the some geographic space) has proceeded with great rapidity ever since. Yet, as we have learned more about the intricate interconnections that occur in most ecosystems, we have also learned how fragile they are. Human activities have had a major impact on ecosystems as diverse as the Atlantic Ocean and the tropical rain forests of South America. Writing at the end of the

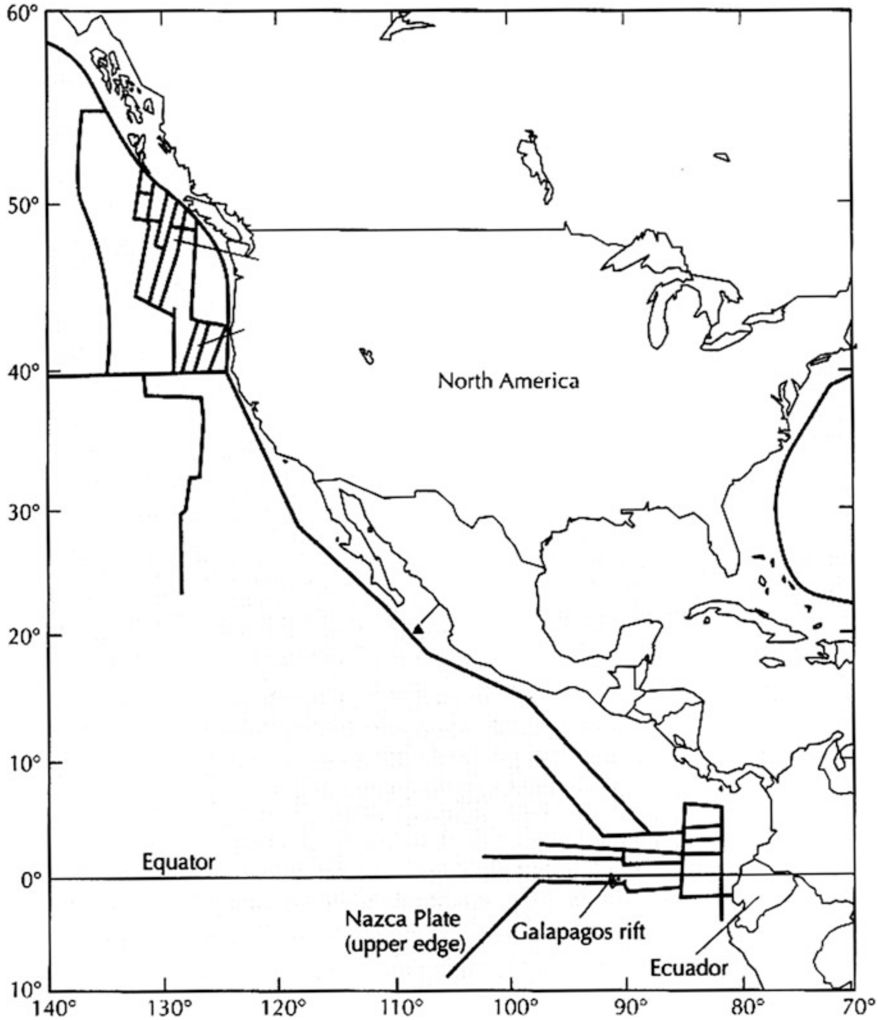

Fig. 1.4 Map showing the Galápagos Rift on the equator, and off the west coast of Ecuador. The rift is characterized by the emission of molten magma and hot gases from the earth's mantle into the ocean water. Except in the area at the rift center, waters at a depth greater than 1 mile are extremely cold (2 °C or 35 °F) and perpetually dark

twentieth century, Peter Raven, then Director and currently President *Emeritus* of the Missouri Botanical Garden in St. Louis, and an energetic spokesperson for the preservation of ecosystems and their diversity, emphasizes this point when he stated that:

> The most serious and rapidly accelerating of all global environmental problems is the loss of biodiversity. Over the past 300 years many species of organisms, including mammals, birds, and plants have been lost. In addition, habitat is vanishing rapidly, especially in the

> tropics. Scientists . . . have calculated that as much as 20 % of the world's biodiversity may be lost during the next 30 years. No more than 15 % of the world's eukaryotic organisms have been described, and a much smaller proportion of tropical organisms have been named. Thus, we may never even know of the existence of many of the organisms we are driving to extinction . . . This is a tragic loss for several reasons. First, many feel that on moral, ethical, and aesthetic grounds, we do not have the right to drive to extinction such a high proportion of what are, as far as we know, our only living companions in the universe. . . . Second, organisms are our only means of sustainability. If we want to solve the problem of how to occupy the world on a continuing basis, it will be the properties of organisms that make it possible. Organisms are the only sustainable sources of food, medicine, clothing, biomass (for energy and other purposes) . . ." [Peter Raven and George Johnson, *Biology* (William C. Brown, Fifth ed, 1999: p. 556)]

From tropical rain forests to oceanic reefs, we as humans depend on a variety of ecosystems for our survival in ways we are just beginning to recognize. In the twenty-first century we have already encountered the widespread effects of global warming, from receding glaciers and rising ocean levels, to the decimation of certain populations of organisms, both marine and terrestrial. The monarch butterfly, discussed later in this chapter, is just one example of a species whose numbers have decline precipitously in recent years due to a variety of human activities. Preserving our fragile ecosystems requires multiple levels of knowledge and rigorous hypothesis-testing—investigations of the sort we explore in this book.

1.4 The Spirit of Inquiry: Some Unsolved Problems in Biology

Science is not just about getting the "right answers", but also about learning how to ask the right questions. It is above all a process of *inquiry*. Children often make exceptionally good investigators, because inquiry is natural to them. Full of curiosity, they not only ask questions about the world they are experiencing, but also want to find the answers for themselves. For those who carry over the same high level of curiosity into adulthood and who prefer discovery over being handed authoritative "truths", science in general and biology in particular present challenging opportunities for exploration. Like all the sciences, biology is an organized exercise in human curiosity.

1.4.1 The Excitement of Unexpected Discovery

In October, 1977, while exploring and mapping a portion of a rift (large crack) on the floor of the Pacific Ocean near the Galápagos Islands (Fig. 1.4) geologists in a small research submarine discovered a new and unexpected world. Here, at a depth of 2650 m (1.5 miles), hot molten rock called magma rushes out of vents along the rift, meets the ice cold (2 °C) sea water, and solidifies into black lava. In the process, the surrounding water may be heated to 350 °C. The water cannot boil,

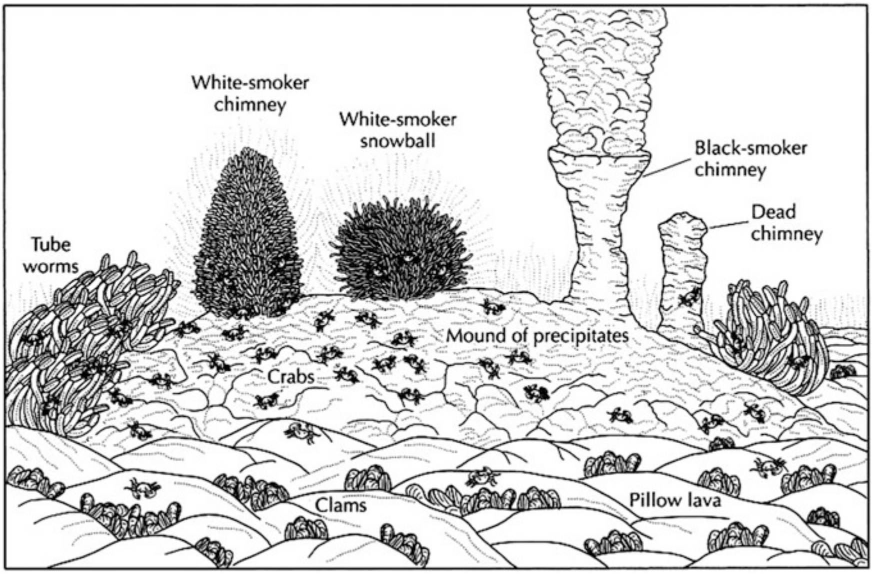

Fig. 1.5 Detail of community life surrounding a vent in the Galápagos Rift showing clams, crabs and tube worms. An active black smoker chimney, shown to the upper left of center, puts out extremely hot water (350 °C) containing hydrogen sulfide. White smoker chimneys, to the right of center, are built up out of burrows made by a little-understood organism, Pompeii worms, and emit water at a slightly lower temperature (300 °C). The entire community lives on energy extracted from the breakdown of hydrogen sulfide by chemosynthetic bacteria. There is thus no energy from the sun involved in maintaining this remarkable community

however, since the pressure at that depth is far too great. Because light cannot penetrate the ocean waters that far down, it is a world of perpetual night.

Given such conditions, the researchers were hardly prepared for what they saw when they turned on the submarine's powerful spotlights. Instead of a bleak, lifeless world, they were startled to find a large community of living organisms surrounding the vents (Fig. 1.5). Tube worms, some over a meter long, waved their reddish tentacles in the sea water; numerous shellfish, including huge clams were scattered across the ocean floor or attached to rocks; dandelion-like animals called siphonophores added yet another color, while scavenger crabs scurried around among them. The geologists used the word "astonishment" to describe their feelings as their spotlights revealed these organisms for the first time.

This same word—astonishment—is found in the diaries and journals of Western explorers of the eighteenth and nineteenth centuries as they described their journeys to distant regions and saw varieties of plant and animal species quite different from those of their homelands. The vent hydrothermal community presented a similar discovery and provided biologists with a new respect for the diversity and adaptability of life. Yet the vent community also presented a series of questions: Where do its organisms obtain their nutrients? How do they withstand the incredible pressure at such a depth? How many millions of years have they been living in these harsh conditions and from what ancestral forms did they evolve? Just at a time when biologists believed they had at least encountered all the major ecosystems on earth, the hydrothermal vent communities provided a startling and unpredicted new one.

This is what the sciences in general, and biology in particular, are all about: investigation and discovery. No one can know what new phenomena investigators will encounter, and no one can anticipate the questions that new observations will raise. One thing is certain, however: *scientific research always raises more questions than it answers*. In the case of the hydrothermal vent community, answers to some of the immediate questions were forthcoming. For example, further study showed that the tube worms, clams and several other animals feed by filtering water rich in bacteria and hydrogen sulfide (H_2S), an energy-rich compound produced by geothermal energy within the earth's interior and released in the vent's emissions. Inside the animals' body the bacteria live in association with certain specialized tissues of the animals or sometimes even within particular cell types. Not only do the bacteria not harm their hosts, they actually provide the animal with their basic nutrients by breaking down the hydrogen sulfide and releasing the energy it contains. This energy, in turn, is used by the bacteria to synthesize nutrients on which both the bacteria and its host depend. By the very act of this discovery new questions emerge: exactly how the thermal energy is coupled to the synthesis of the major nutrients in bacterial metabolism was not immediately apparent and that became the next question for the investigators to pursue.

In the remainder of this section we examine briefly three still unsolved mysteries of modern biology as a way to emphasize how much of science is based on inquiry and the pursuit of creative thinking: (1) The extensive migration of monarch butterflies from Canada to Mexico and back every year; (2) A remarkable investigation of the induction of teeth in chick embryos and what it has revealed about the process of embryonic development; and finally, (3) The question of the chemical origin of life, or how life could first have come into being by purely physical and chemical means on earth billions of year ago.

1.4.2 Butterfly Migration

Many organisms regularly travel hundreds or even thousands of kilometers to areas where they can feed and/or reproduce, a process known as migration. One of the most spectacular of such long-distance migrations is that of the monarch butterfly (Fig. 1.6). This insect's range includes most of North America and part of Southern Canada; its winter range is Central Mexico. During the early summer weeks, the adult monarchs mate, lay their eggs on milkweed plants, and soon die. The eggs hatch into caterpillars, feeding on the milkweed plants and multiplying their original weight 2700 times in two weeks. Every caterpillar sheds its outer covering approximately six times during this growth process and then enters a relatively dormant stage (pupa). During this stage, the internal organs of the caterpillar

Fig. 1.6 The monarch butterfly. © Gregg Otto/visuals unlimited

degenerate and are replaced by those of the adult butterfly. In about two more weeks, the case containing the organism (chrysalis) opens and the adult emerges.

Newly-hatched monarch butterflies attain adulthood in early to mid-summer and reproduce, completing the cycle. Their offspring, who become adults in late summer, remain temporarily infertile. As winter approaches and the daylight hours shorten, these late-hatching monarchs—hundreds of millions of them—begin a migration southward. This rather simple act was described in a recent popular account as follows:

> One afternoon at the end of last August a monarch butterfly, a robust, freshly hatched male who had been cruising around for a few days in a meadow in southern Manitoba, taking nectar from asters and goldenrods, abruptly decamped and started to make his way south in a frenzy of flapping. He was following a migratory urge and a specific flight plan that must have been inscribed in the genes of monarchs since well before the appearance of humans. [from Alex Shumatoff, "Flight of the Monarchs," *Vanity Fair* (November, 1999): p. 270]

Despite the fact that there are no adults of earlier generations to show them the way, monarchs return in droves to precisely the same region of Mexico where their ancestors wintered the year before (Fig. 1.7). Here the temperature drops sufficiently low to keep the insects in a state of semi-dormancy but not so cold that they freeze. As the temperature begins to rise in February and March, the monarchs become active again, gathering nectar for their return flight northward. As the days grow longer. the monarchs mate and they migrate *en masse* back north to the regions from which their parents came. When they reach their northern population centers they lay their eggs and the cycle begins again. Female monarchs often deposit some of their eggs along the way during their northward migration. When

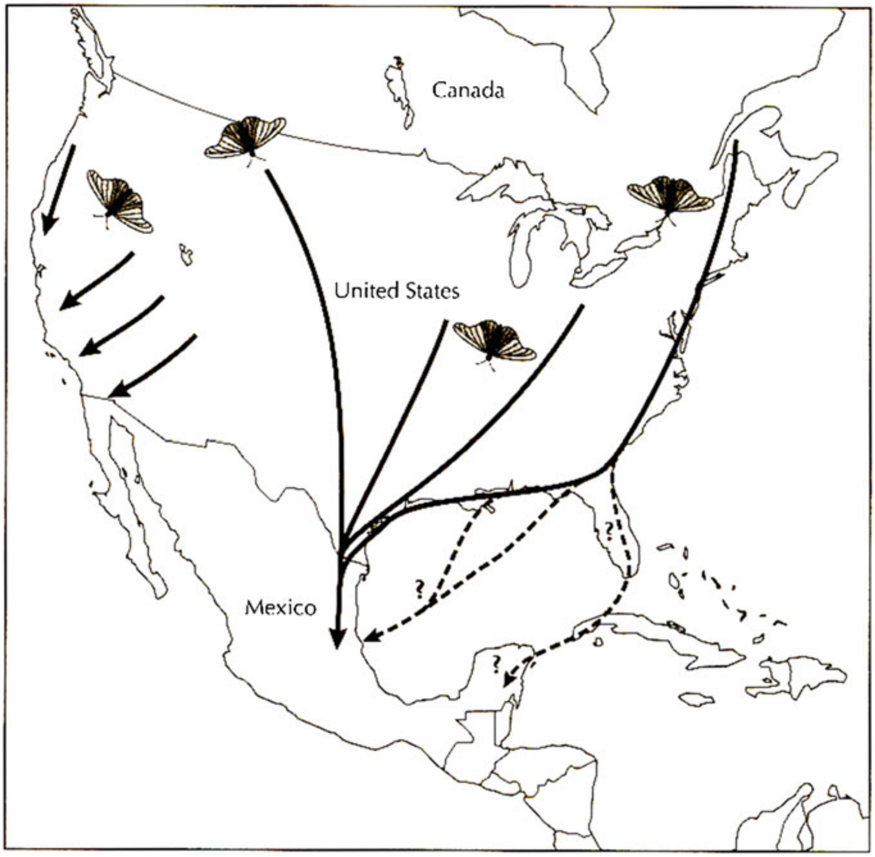

Fig. 1.7 Map of North America showing the projected routes followed by Monarch butterflies in autumn to their over-wintering site in Mexico. The majority of the butterflies migrating this route come from the upper midwest, but a significant population also comes from the northeast

the young hatch they continue the migration, often ending up in the same population centers as their parents.

Although the monarch migration has been known for over a century, little was understood about what triggered it or how the butterflies found their way when none of them had ever been on the journey before. Indeed, until 1975 it was not even known where the butterflies finally ended their southern migration: some thought Texas, others northern Mexico, Costa Rica or other parts of Central America. In the early 1970s two lepidopterists (biologists that study butterflies and moths, which are classified in the taxonomic order Lepidoptera), Fred A. Urquart of the University of Toronto, and the late Lincoln Brower, first at Amherst College (Massachusetts) and later at Sweetbriar College (Virginia), were both interested in the Monarch's migratory route. Urquart devised a system of placing a light-weight tag on the monarch's wing that would indicate where in the north an individual butterfly had been originally captured and would then determine where it might be found later in the south. Brower, meanwhile, had been getting information from various contacts in Texas who had spotted groups of Monarchs near Big Bend National Park during the early winter, but none of the groups were large enough to account for the massive emigration known to take place from the north; Urquart guessed they were strays that had gotten off course. More or less independently, Brown and Urquart were both trying to find the butterfly's over-wintering site.

Quite accidentally, as the result of an article Urquart's wife, Nora, had written for a Mexican newspaper describing their search for the over-wintering site, Kenneth Brugger, an American businessman working in Mexico City, gave them a call. Although at the time Brugger did not know one butterfly from another, he liked to drive and hike through the mountains in the vicinity of Mexico City and he offered to help look for the monarch site. He found nothing, however. Then, in 1974 Brugger married a Mexican woman, Catalina Aguado, who accompanied him on his weekend jaunts. Being a native, she was much better than he at asking questions of local people in the mountainous areas they visited. One day they received a call from a 73-year-old man who said he knew a place where "the trees are filled with butterflies." It was 100 miles west of Mexico City, on a rural common grounds distributed to the campesinos (peasant farmers) after the 1910 revolution. This land required permission from the farmers for access, a task for which Catalina proved to be an adept negotiator. The Bruggers obtained permission to visit the site and saw the massive encampment of monarchs that had eluded all previous investigators. Immediately the Bruggers called Urquart, who came with his wife to visit the site. In their subsequent reports and publications, the Urquarts refused to divulge the exact location of the site to Brower or anyone else on the grounds that too many visitors would disturb the fragile ecosystem that harbored the wintering insects, a decision that increased the growing rivalry between the two scientists. Urquart's decision to keep the location secret does raise an interesting methodological issue for science in general and biology in particular: How much does the investigator's activity disrupt the very system that he or she is trying to study? And what are the consequences of disrupting a system, especially something as large and extensive an ecosystem, compared the knowledge that can be obtained?

Discovering the site allowed Urquart to examine the monarchs and see if he could determine the location from which they had migrated. After inspecting thousands of insects, he discovered one that had been tagged in Wisconsin and so it was clear that this site was one of the places where the North American monarchs came (other sites were discovered subsequently). The site was spectacular, located on the slopes of an extinct volcano at a height of 1800 km (approximately 9000 feet) elevation. At least one part of the question about monarch migration was now answered.

The other part of the question was more intriguing: How do the monarchs locate this region and how do their offspring find their way back to the parents' starting-place in the north? What signals stimulate the monarchs to begin their migration south in late summer, or north in February and March: is it temperature, day-length, some combination of the two, or something totally different? Urquart himself marveled:

> . . . how such a fragile, wind-tossed scrap of life can find its way only once across prairies, deserts, mountain villages, even cities, to this remote pinpoint on the map of Mexico. [Quoted in Shoumatoff (1999), p. 295]

The mystery of monarch migration illustrates several important aspects of the wider nature of scientific work. Rivalries are common in science, yet they are a double-edged sword. While they may spur scientists on to work harder and faster than they otherwise might, they may also slow the research as two rival researchers impede each other's efforts: for example, by withholding information. Although Brower did eventually find the monarchs' over-wintering site on his own (much to Urquart's displeasure), it took a duplication of effort and resulted in even less chance that cooperative research between the two scientists would ever occur. This case also shows how important it is, especially in field studies, to enlist the help of local residents to gain access to research sites and other helpful information. A final feature of this story is the incredible passion, as exhibited by both Urquart and Brower, that often underlies work on a scientific problem. Passion helps keep investigators motivated even when progress is slow. It also drives their persistence at staying with a problem over extended periods of time. All of these factors were involved in solving at least one part of the mystery of monarch butterfly migrations.

Interestingly, monarch butterflies are once again come in the news, this time over a question of their very survival. In the past two decades monarch populations have been estimated to have declined by 90 %, raising questions about the causes for this change and suggesting that if something is not done the species may eventually become extinct. There are several possible factors responsible for the monarch's dramatic decrease. One is the rampant (and illegal) deforestation of the mountains of central Mexico where the monarchs over-winter. Over half of the forests remain in some areas where monarchs used to reside. Large-scale efforts by conservationists, biologists and Mexican officials have combined efforts to stop the large-scale deforestation, but for poor Mexicans, logging is a valuable resource, and neither the government nor other organizations can effectively police such large areas of mountainous terrain to stop the process. A second cause involves the expanded use of herbicides, pesticides and genetically modified crop plants in the central and eastern plains of North America, the very route over which the monarchs fly to and from Mexico. Pesticides kills monarchs directly, while herbicides kill the milkweed plants on which monarchs depend. In addition, the pollen from a particular variety of genetically modified corn (called Bt corn because the plants contain genetic elements engineered into it from a bacterium, *Bacillus thuringiensis*), blows onto milkweed leaves and be ingested by the monarch larvae. The *Bt* pollen slows down the growth of monarch larvae and eventually can kill them. More will be said about the widespread effect of genetically modified organisms in Chap. 5. But suffice it to note here that the decline in monarch populations in North America is due to multiple causes, but in concert they are highly problematic. While there are many sub-populations of monarchs around the world, including areas in the Caribbean and South America, so the species as a whole is not likely to become extinct. But the precipitous decline of the many populations in the midwest region of North America should give us pause to re-think how easily human activity can disruptive whole ecosystems in many unpredictable ways.

1.4.3 Hen's Teeth and Evolution

You have probably heard the phrase "scarce as hen's teeth," referring to the fact that hens and, indeed, all birds, lack teeth. This phrase seems at odds with the conclusion reached long ago by evolutionary biologists that birds and reptiles share a common ancestry.

Two possible evolutionary scenarios would still be consistent with the idea of a common ancestor: (1) The common ancestor had teeth, but the evolutionary line leading to birds lost them long ago; or, (2) The common ancestor did not have teeth and the evolutionary line to reptiles acquired them along the way. An ingenious way to distinguish between these two hypotheses was devised in the early 1980s by two biologists, E.J. Kollar and C. Fisher, working at the University of Connecticut Medical Center. Kollar and Fisher took the outer tissue layers of a chick embryo, in the region that normally produces the jaws, and grew it in a special culture with the middle tissue layers from a mouse embryo taken from the area where teeth normally develop (Fig. 1.8 top). In the normal embryonic development of the mouse, the enamel portion of the teeth develops from the outer tissue layer (called the ectoderm) while the underlying part of the tooth, the dentin, develops from the middle tissue layer (called the mesoderm). Moreover, in the mouse embryo, the outer layer does not form enamel unless it comes in contact with the underlying middle layer, which it normally does during mouse embryonic development. At the same time, the middle layer cannot form dentin unless it remains in contact with the newly differentiated enamel region.

The question Kollar and Fisher were asking is: What structures might be expected to develop if chick ectoderm and mouse mesoderm were allowed to develop together in a laboratory culture? Could the chick ectoderm produce a tooth, or could it only produce normal chick mouth parts? The experiment would provide a unique way to distinguish between the two evolutionary scenarios. If the chick ectoderm could be induced by mouse mesoderm to produce teeth, the investigators would know that the common ancestor to birds and reptiles possessed teeth, and that birds lost them in their divergence. If the chick tissue could not be induced to develop teeth it would be likely, but not certain, that the common ancestor may have lacked teeth, or at least that teeth had been lost very early in bird evolution.

When Kollar and Fisher performed the experiment, the results were startling: the chick ectoderm did indeed develop enamel and even the crown shape of a fully-formed tooth, while the mesoderm formed the dentin and the rest of the tooth

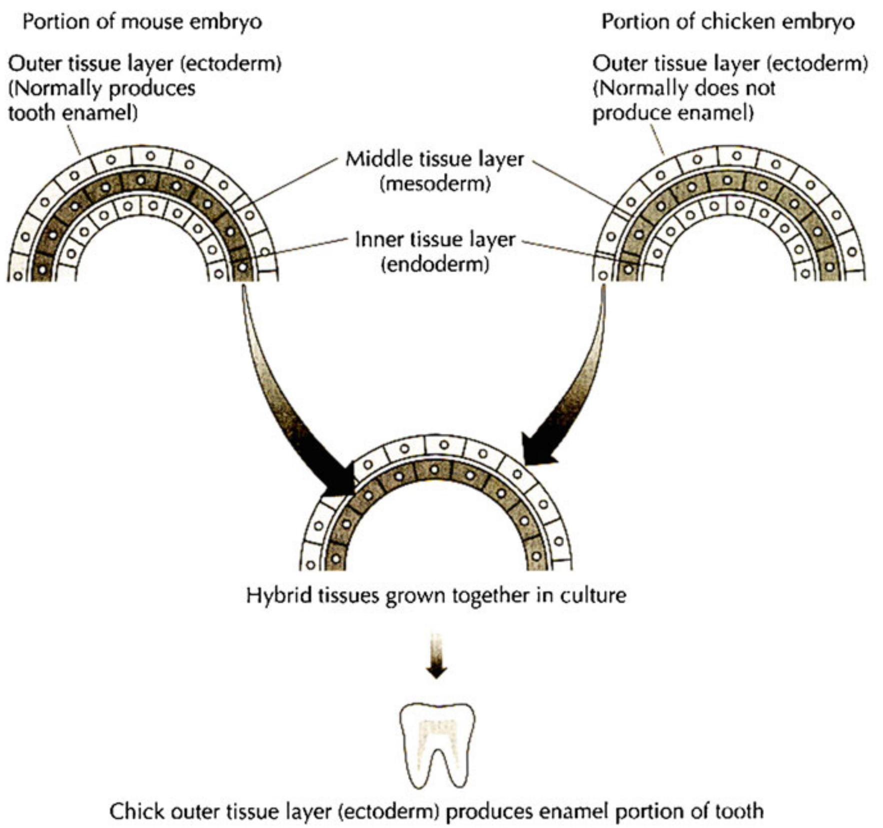

Fig. 1.8 Diagrammatic representation of the experiment by Kollar and Fisher in which they took tissue from the outer layer of a chick embryo (*right*) and grew it in culture with the middle tissue layer of a mouse embryo (*left*). The chick tissue, which normally does not produce teeth, was capable of generating the enamel and crown portion of a full-formed tooth in the presence of tooth-inducing middle tissue material from the mouse. Thus the chick's tooth-forming genes, latent for 60 million years, were induced to express themselves by the presence of the appropriate tooth-inducing middle layer from the mouse embryo

(Fig. 1.8 bottom, and Website 6). The evolutionary implication seems clear: the chick ectoderm, which had not produced tooth structures for 60 million years (the time at which the fossil record indicates divergence from a common ancestor probably occurred) still contained the genetic capability of producing teeth. All it needed was the right environmental stimulus, in this case one provided by teeth-inducing tissue from the mouse. The chick's own mesoderm had obviously lost the ability to stimulate enamel formation so that, in the normal course of development, the pathway for producing teeth was blocked. Also interesting was the fact that chick ectoderm, once induced to form enamel, still retained the ability to induce dentin formation in mouse mesoderm. Even more startling, the full tooth formed by the interaction of these two tissues is not a typical mouse tooth. Although we cannot be certain, the atypical appearance may very well represent an outline of the type of tooth found in a common, long-extinct reptilian ancestor of birds.

Like all scientific investigations, the re-emergence of the "hen's teeth" raises as many or more questions than it answers. One of the most intriguing of these unanswered questions is what keeps the tooth-forming gene or genes from expressing themselves in chickens and birds? How many other ancestral structures not only in birds but in other animals, including ourselves, lie hidden and never expressed? Why should genes that have been latent for so many millions of years still be present in birds? The fact that fossils of very primitive birds show distinct teeth (see for example, Chap. 5, Fig. 5.4), suggests that the common ancestor probably had teeth; but why did the line developing toward birds lose their teeth? Recent work in genetics has indicated that complex structures such as teeth are not controlled by single genes, but by groups of genes and control elements that regulate the genes' expression. These banks of genes often have multiple effects and are turned on or off by a variety of signals coming from other localized tissues and from the environment. Genes and their control elements can be thought of a modules like those used in the construction industry. The parts can be put together in a variety of ways to produce quite different outcomes, but the parts themselves are few and simple.

Many other questions arising from this sort of embryological investigation will continue to provide biologists with research projects for many years to come. Research in biology, as in all the sciences, is a never-ending process.

1.4.4 The Chemical Origin of Life

On the last page of *On the Origin of Species*, Darwin made his only published remarks about the origin of life when, in reference to the theory of evolution by natural selection, he wrote:

> There is a grandeur in this view of life, with is several powers, having been originally *breathed into a few forms or into one*; and that, whilst this planet has gone cycling on according to the fixed law of gravity, from so simple a beginning endless forms most beautiful and most wonderful have been, and are being, evolved. [1st ed, John Murray 1859: p. 490; italics added]

This was Darwin's deft attempt to side-step the crucial question of how the first forms of life may have arisen—the question of the origin of life itself. In a private letter written a few years later (1871), Darwin suggested that the process might have occurred by purely chemical means "in a warm little tide pool," but he never published that idea. Politically, this was a strategic decision on Darwin's part, because he knew the idea of evolution would be controversial enough in its own right and did not need to become more complicated by addition of another, even more controversial, idea.

However, many of Darwin's contemporaries immediately raised the issue of how life could have originated and indeed the flurry of controversies in the 1860s through the 1890s on "spontaneous generation" reflected the strong interest in this age-old question. Among the many claims, for example, were the assertions that maggots, the larval form of flies, were spontaneously formed from decaying meat or that bacteria were formed directly from the organic matter of beef broth (see Chap. 2). Certainly, if living organisms evolved by natural processes, then it was reasonable to argue that life might have originated by natural processes as well.

Two quite different explanations have dominated thinking about how life might have come to exist on earth: *abiogenesis*, that is, some sort of chemical processes occurring on the earth itself, and *panspermia*, the transportation of life to earth from somewhere else in the universe. Both views have had serious proponents since the late nineteenth century and both are still hotly debated today. In the twentieth century, abiogenesis has had more proponents, including the renowned biochemist and population geneticists J.B.S. Haldane (1892–1961) in the 1930s and the Russian biochemist A.I. Oparin (1894–1980) in the 1940s and 1950s. Panspermia has had some notable proponents, including one of the early Nobel laureates in chemistry, Svante Arrhenius (1859–1927), and currently by another Nobel laureate, Francis Crick (1916–2004). Today, although it is recognized that they are not mutually exclusive, both views are considered to be highly controversial.

The central question of abiogenesis is: Could the simple organic building blocks found in living organisms today have been produced by purely chemical means on the early earth? One of the first experiments to try and answer this question was carried out in 1952 by a young graduate student named Stanley Miller (1930–2007), then working in the laboratory of geologist Harold Urey (1893–1981) at the University of Chicago. From geochemical evidence, Urey and Miller hypothesized that the earth's early atmosphere was a chemically reducing one, that is, had little or no oxygen in it and consisted of compounds such as ammonia (NH_3), methane (CH_4), water vapor (H_2O) and molecular hydrogen (H_2) that were prone to pick up electrons from other molecules (chemically, the process of reduction involves the gain of electrons). Miller set up an enclosed, circulating gas system into which he introduced ammonia, methane and hydrogen, along with water, all of which he kept boiling in a flask at the bottom of the tubes (Fig. 1.9). Two electrodes produced periodic electrical discharges into a large bulbous chamber at the top of the apparatus. After a week, Miller collected and analyzed the residue from the lower arm of the tube. To his amazement, he found several amino acids (the building blocks of proteins), carbohydrates (mostly simple, 3-carbon sugars) and several other organic compounds, including urea (the basic component of urine, produced by mammals as the breakdown product of proteins) and acetic acid, the central component of vinegar, produced by bacterial metabolism). After allowing the materials in the system to circulate for several more weeks, Miller was able to accumulate over a dozen different compounds associated with living organisms today. Other investigators, using similar methods but with different energy sources or slightly different starting reactants, produced a variety of other simple organic

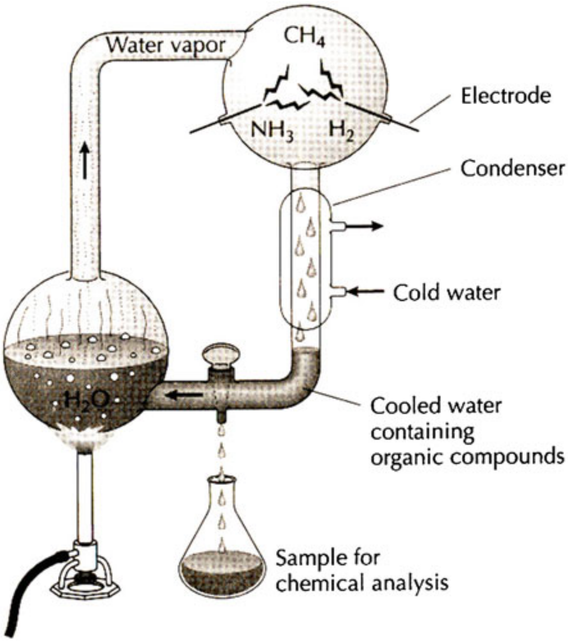

Fig. 1.9 The Miller-Urey experiment. Apparatus designed by Stanley Miller for the circulation of methane, ammonia, water vapor and hydrogen. Water is boiled in the flask at lower left. The products of the various chemical reactions that occur are collected once a week in the trap shown at center. Energy for chemical reactions comes from both heat and electric discharges in the large bulb at the upper right [From Richard E. Dickerson, "Chemical evolution and the origin of life," *Scientific American* (Sept. 1978)]

compounds. Such experiments supported the view that on the primitive earth, many of the basic molecular building blocks of life could have been formed abiotically, that is, without the agency of already-existing life forms. Subsequent work by Sidney Fox at the University of Florida showed that, once these basic building blocks were formed, they could join together spontaneously to form larger compounds such as simple proteins, carbohydrates and nucleic acids.

These results were exciting, but critics raised objections almost immediately. Some geochemists have questioned the assumption that the early atmosphere of the earth was a reducing one. Debates about the composition of the early atmosphere are not mere quibbles over detail. Miller's original experiment was based on the assumption of a reducing atmosphere. His results would have been very different if oxygen had been included within his original mixture of gases. This is because oxygen, though necessary for life as we know it today, is actually quite destructive to many of the macromolecules found in living cells. If oxygen had been prevalent in large quantities in the atmosphere of the early earth (it composes 18 % of the atmosphere today), it is likely that even the simplest organic molecules formed spontaneously would have been quickly broken down (oxidized). Other factors might have added to the problem, such as the turbulent conditions on the earth's surface, its excessive heat and the emission of gases like hydrogen sulfide from volcanic eruptions. Lack of an ozone layer, which normally filters out high-energy radiation like ultra-violet light from the sun, would have further contributed to the rapid degradation of any complex molecules that might have formed.

The original idea of panspermia was that some sorts of primitive microbes or even simpler living spores might have been transported to earth from elsewhere in the universe by way of meteorites or other cosmic "debris." This version of panspermia has been severely criticized because of the unlikely chance that a living, organized cell or spore could withstand a journey through space for perhaps thousands or millions of years, where the temperature is near absolute zero (−273 °C) and where there was also no protection from high energy radiation. In addition, as the meteorite containing the spores came into the earth's gravitational field and plummeted at thousands of miles per hour through the atmosphere, the enormous temperatures would incinerate any living thing. It thus seemed unlikely that life could have begun on earth by the transport here of highly-organized living structures from elsewhere in the universe.

Recently, however, an alternative to the old panspermia idea has been raised by several scientists, including Max Bernstein, Scott Sanford and Louis Allamandola at the National Aeronautic and Space Administration (NASA) Ames Research Center, Moffett Field, California. These investigators asked the following question: Could organic molecules, rather than fully formed spores or more highly-organized living entities, have been transported to earth after the surface had cooled down and at a time when those more complex molecules could have remained intact? The question could be broken down into two subsidiary questions: (1) Are organic molecules detectable in various extra-terrestrial sources? and (2) Is there any evidence that such molecules can enter the earth's atmosphere and reach the surface intact?

To answer the first question, the NASA team collected data from two sources: intergalactic clouds and material entering the earth's atmosphere at its outer reaches. To determine the composition of intergalactic clouds, the researchers analyzed light that passes through these clouds from more distant stars. They found that the wave-lengths of light that were filtered out were similar to those observed in laboratory analyses of "clouds" containing methane, cyclic hydrocarbons, ammonia and water. Thus, it is apparent that there would probably have been a considerable supply of carbon compounds, among others, for transport to the earth from outer space.

To answer the second question, the NASA team analyzed matter that had actually entered the earth's atmosphere from space either as "cosmic dust" or meteorites. Here, too, the results were striking. Modern meteorites contain a variety of organic molecules, including amino acids, carboxylic acid and ketones. Furthermore, microscopic dust particles from space collected by a research aircraft able to fly over 60 miles above the earth's surface contain more carbon compounds than in any other interstellar materials yet analyzed. The team estimated that some thirty tons of interstellar "dust," some particles of which are no larger than a grain of sand, filter down through the earth's atmosphere every day. Thus, both meteorites and dust particles could have provided a rich source of organic matter from which more complex organic molecules on the primitive earth might have been synthesized. Thus the new "panspermia" hypothesis is not so much about the transport of already living organisms to the earth, but instead about what raw materials might have been available from which those organisms could be evolved over millions of years.

As interesting as this work may be, it raises a whole host of new questions that may be even harder to answer: (1) How could these simpler organic compounds actually join together to form larger, more complex and varied molecules and how did they remain intact? (2) How did these more complex molecules eventually form higher-level associations having the properties, however primitive, of modern-day cells? And, finally, the greatest riddle of all: (3) How could these cells incorporate into their complex structures a process of self-replication? These and many other questions form the basis for the ongoing study of how life originated on earth. More than either of the two preceding examples, the origin of life has far more unanswered questions than it has answers. The field is just in its infancy. Yet it remains one of the most challenging and imaginative fields for investigation in the twenty-first century.

1.5 Conclusion

What is perhaps an apocryphal story has been told of the enigmatic and controversial American poet, Gertrude Stein (1874–1946). A graduate of Radcliffe College, an embryology student at the famous Marine Biological Laboratory in Woods Hole, and a medical student at Johns Hopkins University, Stein was one of the most innovative and acclaimed *avant garde* poets of the "lost generation" of the 1920s and '30s, a period that also included Ernest Hemingway and F. Scott Fitzgerald. In 1946, as she lay gravely ill and sedated for surgery, her mind wandered. She murmured to her long-time companion, Alice B. Toklas, "What is the answer?" Alice, thinking her friend was delirious, did not reply, Gertrude, always ready to fill a silence with a wry retort (sedated or not), answered her own query: "In that case, what is the question?"

This reply encapsulates the most basic aspect of science as well as any other form of human inquiry. Inquiry is about questions. Answers are certainly important—there is no need to ask questions if we do not care about the answers. Yet, the enduring part of inquiry is the way we formulate questions. The best questions in science are those that are limited in scope and thus can be answered by making specific observations or experiments. Like everything else, there is a process involved not only in answering but also in asking questions. It is with the asking of the questions that knowledge begins.

Further Reading

On the Development of Biological Thought (Nineteenth–Twentieth Centuries)

Allen, G. E. (1978). *Life science in the twentieth century*. New York: Cambridge University Press. (Chapters 1–4 specifically detail the change in the practice of biology from a descriptive to an experimental science).

Mayr, E. (1982). *The growth of biological thought*. Cambridge: Harvard University Press. (A long and detailed book that explores the nature of evolutionary theory as an example of the shift from "old" to "new" methods in biology).

On the General Topic of Methodology in Science

Goldstein, M., & Goldstein, I. F. (1978). *How we know. An exploration of the scientific process.* New York: Plenum Press. (Chapters 1 and 2, in particular, are concerned with the general process of science, including asking questions).

Jenkins, S. H. (2015). *Tools for critical thinking in biology*. New York: Oxford University Press. (This work is aimed at teaching the basics of biology with a focus of the scientific process, similar to that outlined in this chapter).

On the Discovery of the Galápagos Vent Communities

Cone, J. (1991). *Fire under the sea: The discovery of the most extraordinary environment on earth—volcanic hot springs on the ocean floor*. New York: Morrow. (A useful source for understanding the geology, ecology and organismic physiology of the vent community).

Macdonald, K. C., & Luyendyk, B. P. (1981). The crest of the east Pacific rise. *Scientific American, 244*: 100–116. (A discussion of both the geology of the ocean rift areas, and the biology of rift communities. Relates the formation of rifts and the geothermal activity to the geological theory of plate tectonics).

On Monarch Butterfly Migration

Larsen, T. (1993). Butterfly mass transit. *Natural History, 102*:31–38. (Describes migrations of butterfly species in other parts of the world than North America, particularly the Asian sub-continent and Africa).

Shoumatoff, A. (1999). Flight of the monarchs. *Vanity Fair*, 268–300. (A well-written popular account of the monarch butterfly problem, including a short discussion of the *Bt* corn problem).

Urquhart, F. A. (1987). *The monarch butterfly: International traveler.* Chicago: Nelson Hall. (An excellent book discussing the natural history, physiology, behavior, and experimental work on monarch butterfly migration. Contains many useful illustrations).

On "Hen's Teeth"

Gould, S. J. (1983). *Hen's teeth and Horses' toes*. New York: W.W. Norton. (Contains a number of interesting essays on evolutionary theory, including one for which the book is titled about the reactivation of long-lost ancestral traits in modern organisms).

On the Origin of Life

Bernstein, M. P., Sandford, S. A., & Allamandola, L. J. (1999). Life's far-flung raw materials, *Scientific American, 281*: 42–49. (A clear and comprehensive discussion of the modern panspermia idea, or organic material and water being transported to earth from intergalactic clouds and dust).

Knoll, A. H. (2003). *Life on a young planet: The first three billion years of evolution on earth*. Princeton, NJ: Princeton University Press. ISBN 0-691-00978-3. LCCN 2002035484. OCLC 50604948. (An excellent introduction to the topic by one of the world's long-standing experts on the origin and early history of life on earth).

Luisi, P. L. (2006). *The emergence of life: From chemical origins to synthetic biology*. Cambridge, UK: Cambridge University Press. ISBN 978-0-521-82117-9. LCCN 2006285720. OCLC 173609999. (A sweeping view of biology from the origin of life to the modern field of "synthetic biology" (the attempt to engineer new forms of existing life, approached from an engineering point of view)).

Schopf, J. W. (1999). *Cradle of life. The discovery of the earth's earliest fossils*. Princeton: Princeton University Press. (Although mostly about microfossils in the pre-Cambrian era (roughly 1–4.5 billion years ago), this book contains several good chapters (4–5) summarizing what is currently thought about abiogenesis).

Zubay, G. (2000). *Origins of life on the earth and in the cosmos* (2nd edn.). New York: Academic Press. (This textbook contains much useful reference material on aspects of the origin of life, including abiogenesis and modern versions of panspermia. Good introductory chapters on the origin of the universe, the elements, our galaxy and solar system, and the evolution of the atmosphere of the early earth).

The Nature and Logic of Science 2

Abstract

This chapter provides the basic foundation for understanding the logic involved in scientific/biological reasoning. Topics include: inductive and deductive logic, hypothesis formulation (*if ... then* reasoning), the concept of "proof" in science, and the difference between truth and validity. The interplay of these elements are illustrated by the "dissection" of a specific set of investigations by Italian biologist Lazzaro Spallanzani in the eighteenth century concerning what elements of the male semen were causally involved in fertilization and embryonic development in animals. The chapter then moves to a discussion of the way in which hypotheses are formulated as different kinds of explanations in biology, such as teleological *versus* causal explanations, all illustrated by the question of why warblers begin to migrate south from New England in the fall. This section also examines some of the recent philosophical studies on the nature of mechanisms in biology, and what elements are necessary for a mechanism to be successful as part of a scientific explanation. After discussing the nature of cause-and-effect in biology, and how causal relationships can be distinguished from simply correlations or accidental coincidences, the nature of bias in science is introduced to emphasize that science cannot eliminate all bias, and indeed that sometimes biases (or points of view) are extremely fruitful. The final part of the chapter is devoted to philosophical issues in biology: the nature of paradigms and paradigm shifts in biology, the materialist (as opposed to idealist) foundations of modern biology, and a review of both the strengths and weaknesses of science.

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2.1 Introduction

In the spring of 1985, a reporter for the British Broadcasting Company interviewed a biologist on the fertilization of human eggs and development of human embryos outside their mothers' body. "Surely," the reporter asked, "you must have done a lot of research to get this far?" The biologist nodded affirmatively. "Well, then," the interviewer asked, "don't you know everything you need to know?

The biologist was at a loss for words. It was a question no scientist would think of asking; one based on several widespread misconceptions about the nature of science. One such misconception is that science is largely a matter of collecting facts into a sort of encyclopedia of knowledge about a particular field, for example, biology, chemistry or physics. Related to the first, the second misconception is that the number of such facts is finite and, theoretically at least, we can expect to discover all of them if we search long enough. Yet it is doubtful that the reporter would have asked a historian if he or she knew enough about British or Russian history or a poet whether he or she had written enough poems. Science writer Ted Neild ended his report on the BBC interview with this observation:

> Science is about ideas … and because … the unifying ideas [of science] … are in constant need of revision as new facts come to light, and the insight of new ideas redefines the implications of the old knowledge, we can never 'know' enough. This is so obvious to scientists, yet apparently obscure to everyone else. [New Scientist March 7, 1985. p. 46.]

What, then, *is* science, and why is it so often misunderstood? These questions lead us into the main topic of this chapter: the nature and logic of science.

2.2 Science as an Intellectual Discipline

Defining Science

The term "science" was first coined in 1851 by the British philosopher William Whewell (1794–1866) to refer to the study of the natural world. The term "science" comes from the Latin *scientia*, meaning "knowledge" or "knowing." Prior to Whewell's time, people who studied nature were called natural philosophers, a term emphasizing the close historical connection once existing between the sciences and the humanities (Fig. 2.1).

In more recent times, however, science has become an increasingly separate pursuit. Yet, definitions clearly distinguishing science from other fields of human thought are difficult to formulate. This is partly because science is not a single enterprise but rather a collection of activities that often vary widely from one scientific discipline to the next. Furthermore, none of the methods associated with science are unique to science alone. A paleontologist who studies fossils and tries to reconstruct their evolutionary history is likely to have as much in common with a historian than with those biologists who carry out laboratory research in fields such

Fig. 2.1 Integration of sciences, social sciences and humanities as shown in a mid-18th century allegorical drawing, the frontispiece of Denis Diderot's *Encyclopedie* (1751 edition). At the top, center, is Truth, whose veil is being lifted off by Reason (wearing a crown) and it is being pulled away by Philosophy. Below are shown all the natural sciences: chemistry with a retort, botany with a cactus, astronomy with stars in her hair and math (center). The arts (poetry, literature, painting) are in the upper left and the mechanical arts, including agriculture, are shown at the bottom, receiving inspiration from above. At the upper left Imagination is preparing to adorn Truth with a garland of flowers [from I.B. Cohen, *Album of Science: From Leonardo to Lavoisier, 1450–1800* (N.Y., Scribners, 1980): #362): p. 266]

as genetics or physiology. Both paleontologists and historians are attempting to reconstruct the history of events which occurred in the past and both must draw their conclusions from the only evidence available to them. By contrast, biologists studying processes taking place in organisms that are alive today have available to them a variety of methods, most especially the use of experimentation, not available to paleontologists or historians. Despite these differences, few today would seriously question that paleontology is a science.

Characteristics of Science

Although we may not be able to define science as a unique activity, we *can* describe it as a specific combination of shared practices and assumptions. All science is based on **empirical knowledge** that is, knowledge obtained through our senses of sight, sound, touch, taste or smell. Empirical knowledge, even of the most tentative or casual sort—for example, observing a moth emerge from a cocoon—is often the starting point for any scientific investigation.

A second characteristic of science is its commitment to rationality. Rationality involves seeking explanations in terms of natural rather than supernatural causes. No astronomers today are satisfied with the medieval explanation that planets are moved through their orbits by angels and no biologists are satisfied with interpreting disease as the result of divine punishment. These latter explanations are considered *super*natural because they involve entities and activities that have no counterpart in our everyday world and because, by definition, they are beyond the rational and we cannot investigate them using rational methods.

A third characteristic of science is its emphasis on repeatability. Scientific results are always subject to confirmation by other investigators. Along with repeatability goes another related characteristic: reliability. Numerous persons have claimed to have seen the Loch-Ness monster, a supposedly prehistoric reptile living in a very deep and ancient lake in northwestern Scotland. Photographs claiming to have spotted the creature are routinely indistinct and "Nessie" as it has been named is so elusive that biologists have never been convinced that it has ever existed. The observations lack reliable confirmation and are thus suspect.

A fourth characteristic of science is its commitment to testability. No matter how interesting or imaginative an explanation might be, it is of no value if it cannot be tested. Untestable ideas provide no basis for asking further questions or for carrying out further research. As fascinatig as they might be, in science such ideas are usually an intellectual dead-end.

Following directly out of this fourth characteristic of science is a fifth: its commitment to the use, whenever possible, of experimentation. Experiments are planned interventions into a natural process to observe the effects of that intervention. For example, a biologist interested in how early stages in the development of frog embryos affect the later form of the adult may remove structures from embryos of different ages and record changes occurring as development continues. Such experiments allow the investigator to ask specific questions and obtain equally specific answers; they also allow him or her to make observations that might never be made under natural conditions. Of course, not all fields of science lend themselves to experimentation equally well. The films Jurassic Park I and II notwithstanding, evolutionary biologists cannot step back in time and experiment with dinosaurs, nor can astrophysicists experiment with stellar systems. Yet even in those fields where experimentation is less often applicable, it remains a goal whenever possible.

A sixth characteristic of science is its search for generality, the establishment of general principles operating in the natural world regardless of differences in time or place. Physicists are interested in principles of motion or gravity that apply not only at different places on the earth but throughout the whole universe. Biologists are interested in understanding living processes in *all* organisms, not merely mice, maple trees or bacteria. While it is true that each type of organism will respond to its own unique set of environmental conditions and its own internal make-up, the same basic biological principles are thought to apply throughout the living world.

It should be clear that none of the characteristics of science described above apply to science alone. They are, in fact, shared characteristics of all rational human attempts to understand the world we live in, its past as well as its present. It is another way in which we can reiterate a major theme of this book: that as proceses, that is, as ways of thinking, the sciences and the humanities are more similar than they are different.

The Relationship between the Sciences, Social Sciences and Humanities

The six characteristics listed in the previous section are not necessarily unique to science. Historians, writers, painters, musicians, auto mechanics and workers in many different fields often try to build more general concepts from specific and precise observations (the best poets, critics have noted, use the most concrete imagery) and all try to formulate these concepts in universally understandable terms. In the seventeenth century, for example, Sir Isaac Newton (1642–1728) formulated a concept of the universe as operating by mechanical principles: the solar system was depicted in terms of a common machine of the day, the clock. Indeed, the metaphor "clockwork of the universe" was commonly used to refer to the Newtonian model of the cosmos. Like writers, scientists use devices of language—analogies, metaphors, similies and often almost poetic descriptions—to convey their vision of the world. Take, for example, the final paragraph of Darwin's *On the Origin of Species*, first published in 1859:

> It is interesting to contemplate an entangled bank, clothed with many plants of many kinds, with birds singing on the bushes, with various insects flitting about, and with worms crawling through the damp earth, and to reflect that these elaborately constructed forms, so different from each other, and dependent on each other in so complex a manner, have all been produced by laws acting around us …. Thus, from the war of nature, from famine and death, the most exalted object which we are capable of conceiving, namely, the production of the higher animals, directly follows. There is grandeur in this view of life, with its several powers, having been originally breathed into a few forms or into one; and that, whilst this planet has gone cycling on according to the fixed law of gravity, from so simple a beginning endless forms most beautiful and most wonderful have been, and are being, evolved.

This passage contains a wide variety of literary devices that convey a particular vision of the natural world as Darwin was trying to present it. It opens with an a vivid and esthetically alluring description of the interrelatedness and complexity of nature ("an entangled bank"), while also emphasizing its harmonious qualities (the many different creatures so dependent on each other). Then Darwin the scientist steps in: These complex interactions have all come into being by everyday, observable "laws acting around us"—a direct appeal to our rational understanding. Darwin then introduces a new aesthetic, a more somber one, with a series of metaphors describing the processes of over-reproduction, competition, the resulting "war of nature, famine and death", all parts of his mechanism (natural selection) by which evolution occurs. Yet despite this very nineteenth-century view of the "war of all against all," Darwin concludes on a positive note: "There is a grandeur in this view of life", including a not-too-subtle comparison of his own laws of nature to those of Isaac Newton's laws of universal gravitation.[1] Darwin's prose is straightforward yet expressed with an almost poetic imagery. There is indeed a possible literary source for Darwin's descriptions of nature in his writings from his expedition on the HMS Beagle: One of the few books he took with him on that five-year trip was John Milton's *Paradise Lost*, and many passages describing the fascinating rain forests of South America are strikingly similar to Milton's descriptions of Adam and Eve in the Garden of Eden, as historian David Kohn notes in his book, *The Darwinian Heritage*. Science has as much room for creativity and imagination as do any of the arts. Creative efforts in science are like a painter's canvas that is constantly being reworked to obtain greater accuracy, completeness or aesthetic appeal. As physicist Albert Einstein (1879–1955) once stated: "After a certain high level of technical skill is achieved, science and art tend to coalesce in esthetics, plasticity, and form." In this view, the differences between the sciences and the humanities shrinks to a difference in technicalities, not major processes of thought.

The sciences, social sciences and humanities have long interacted in ways that lend support to one another. Questions about the use of atomic energy, the application of our knowledge of biology to preserve the environment, or the ethical implications of new discoveries in genetics often make us keenly aware of some of the ways in which science inspires our social and humanistic concerns and vice versa. Science has inspired many creative writers (the vast literature falling under the heading of science fiction is but one of many examples) and poets. The reverse is also true, however. Social, political, philosophical and even artistic developments often interact with, and directly affect, the course of scientific discovery. Historian Samuel Y. Egerton has argued that studies in visual perspective by early Renaissance painters such as Giotto de Bondone (1337–1376) initiated precise, quantitative and mechanical methods of viewing nature that served as a crucial stimulus for the scientific revolution in astronomy and physics in the sixteenth and seventeenth centuries (Fig. 2.2). The resulting view, that of an infinite universe working by purely mechanical principles, greatly altered human beings' view of themselves.

[1]That many of his contemporaries saw the comparison as apt is reflected in the fact that Darwin is buried next to Newton in Westminster Abbey.

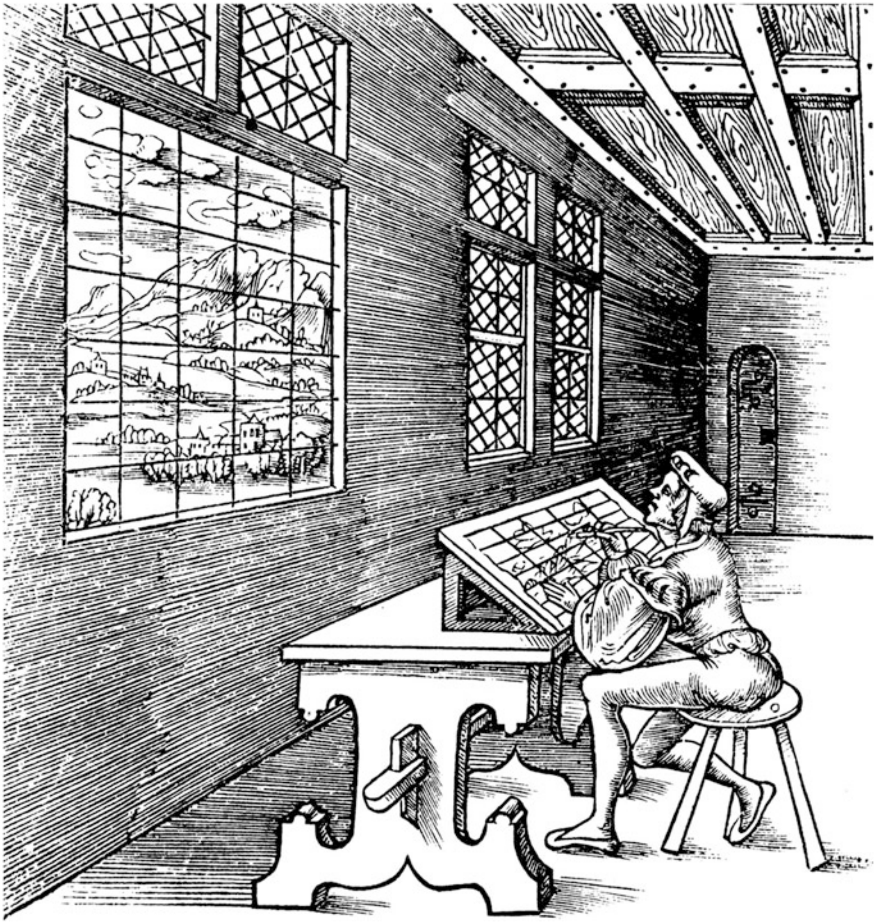

Fig. 2.2 The relationship between art and science. Woodcut demonstrating a technique developed by fifteenth-century sculptor-architect Filippo Brunelleschi (1377–1446). [From Leone Battista Alberti, *On Painting* (Florence, mid-1430's); taken from I.B. Cohen, *Album of Science, from Leonardo to Lavoisier, 1450–1800* (N.Y., Charles Scribner's Sons, 1980): Fig. 3]

Historian Robert Young has argued that if Darwin had not been familiar with the works on on political economy of Adam Smith (1733–1780), David Ricardo (1773–1833) and Thomas Robert Malthus (1766–1834), all of whom emphasized the scarcity of resources and competition as a natural part of the capitalist economic system, he quite possibly would never have come up with the idea of evolution by natural selection. Borrowing these ideas from the social and economic sciences of his day was one of Darwin's most creative efforts. For their part, Darwin's ideas stimulated another profound revolution in how human beings viewed themselves as having evolved like other organisms from previously-existing forms. Thus, our social views influence the way we form our picture of the natural world as much as our picture of the natural world influences our social views

Science, Common Sense and Intuition
A key feature of scientific thinking is that it tends to be highly suspicious of intuitively derived decisions lacking empirical backing; no matter how intuitively obvious an answer might seem, it must always be analyzed critically.

Consider the following problem. Imagine that you have ten marbles, identical in size and weight, of which eight are white and two are red. Now suppose you put these marbles into a brown paper bag and shake them up to randomize their distribution. Without peeking, you then reach into the bag and draw out a marble. If the marble is white, you put it aside and draw another. If that one, too, is white you put it with the other white marble you obtained on the first draw. You keep doing this until you draw a red marble. When that happens, you record the number of the draw on which you obtained the red marble—for example, the sixth draw. You then put all of the marbles you have drawn, both red and white, back into the bag with those remaining there and repeat the process 100 times or, better, 1000 times. The question to be answered is: *on which draw are you most likely to get a red marble*? Quite obviously it cannot be the tenth draw, since you will never get to it—if one draws eight white marbles in a row, there can only be two marbles left, both of which must be red. This leaves only draws one through nine as possibilities.

The correct answer to this problem is not intuitively obvious. Most people to whom we have presented this problem figure that if there are eight white marbles and two red marbles, then that is a 4:1 ratio of red to white marbles and therefore the chances of getting a red marble on the first draw are one out of five, or 20 %. This is most certainly correct. If you do get a white marble on the first draw, that leaves only seven white marbles in the bag to two red marbles and therefore the odds of getting a red marble on the second draw increases. Still more of an increase in the odds of getting a red marble on the third draw occurs if you get a white marble is drawn on the second draw, and so on. Generally overlooked, however, is the fact that, since the odds of getting a red marble on the first draw are 20 %, this means that *20 % of the time one never gets to the second draw*! If we enter that factor into the equation, it becomes quickly apparent that the first draw is the most likely one to get a red marble, the second the next most likely, the third the next most likely, with the odds decreasing down to the ninth draw, which makes getting to the ninth draw the least likely possibility.

Despite many examples in which intuition has turned out to be wrong, there are many cases in which it has turned out to be correct. Such famous scientific ideas as Einstein's theory of relativity and the molecular structure of the gene (DNA) were the result of a certain amount of intuition. However, neither these nor any other scientific concepts would have survived for long if they had not been subject to empirical verification (testing). It is no less so for much of ordinary human experience. Intuition may be highly useful both in analyzing problems and generating ideas but in science *it must always be confirmed or rejected by empirical tests.*

2.3 The Logic of Science

The elements of logic are at the heart of the methods employed in all rational thinking. To understand how we think logically, an examination of the components of empirical knowledge—observations, facts and conceptualizations—is in order.

Observation and Fact

The foundation of all empirical knowledge is a discrete item of sensory data known as an *observation.* The statement "The car is red," or "This robin's song consists of three notes," all represent observations. Each encompasses a single item of sensory data, in these cases, sight or sound respectively. In science, investigators often employ various instruments to make observations that none of our unaided senses is able to detect. Microscopes, for example, magnify objects too small to be seen with the unaided eye, high frequency audio detectors pick up and record sounds that our ears cannot hear, and electronic sensors amplify subtle chemical changes in living tissue that we cannot see directly. Of course, as any trial lawyer will attest, two observers do not always see the same object or event in the same way. A color-blind person may see a red car as a shade of gray, while someone who is tone-deaf may hear a bird's song as only a single tone rather than as three distinct notes. For observations to form the basis of our ideas they must be agreed upon by different observers. The criterion of repeatability discussed earlier means that any and all observations must be checked, not only by the original observer, but by other observers as well.

As they become repeated and agreed upon by some community of observers, observations often become established as facts. Facts, then, may be defined as individual observations that have been confirmed and accepted by consensus. For the group involved in that consensus, at least, the observations have been established as facts. It therefore becomes a fact that the car is red, or the bird's song consists of three notes *because and only because a group of observers has agreed it is so*. Facts are not some sort of inalterable "Truth" handed to us by an impersonal nature, but are rather negotiated agreements between individuals as they compare their observations.

Does the preceding make the term "fact" into something arbitrary. After all, if a color blind person sees a car as gray is that not a fact for that person, even if other people see it as red? The answer is yes in one sense but no in another. Since knowledge is always obtained and becomes ultimately useful only in a social context, communication and agreement about what is and is not a fact is critical in verifying observations and establishing facts. For example, a small group of Elvis Presley followers have claimed that they have seen the singer alive and that he has spoken to them. For this group, it is a "fact" that "Elvis lives." Similarly, for many, the existence of unidentified flying objects, or "UFOs," is also a fact. As either of these two circles of observers widens, however, the consensus dwindles and such former "facts" may eventually be regarded by the majority as unsubstantiated. This is where the empirical component of scientific knowledge becomes important in deciding what will or will not be accepted as fact. No matter how many people claim that some things are fact, if they cannot be observed repeatedly by a wider circle of observers, the "facts" become highly questionable.

One of the greatest strengths of science is its total commitment to putting observations or facts to empirical testing. It is this commitment that distinguishes science from areas such as religion or other forms of supernaturalism. Some advocates of the supernatural argue that it is necessary to be a "believer" in the phenomenon in order to be able to observe it. Such a claim amounts to little more than saying we can simply believe what we want to believe. One advantage of examining our thought processes is to be able to share with each other some common methods of understanding the world. Humans are social animals and the knowledge we generate is not merely individual knowledge. We could never exchange ideas if we did not employ some common methods of drawing conclusions and communicating with others about the phenomena we encounter.

Recognizing the social component involved in establishing observations and the facts that we derive from them does not lessen their value, but rather suggests that observations and facts are to some extent the product of a particular historical time and place. In other words, observations and the facts that derive from them are not independent of the observer, but rather are very much the product of humans interacting with the world and each other. Recognizing the social nature of observations and facts tells us that, if two or more people do not agree on the facts, they will have little success in discussing the conceptualizations that may be derived from those facts. It would be useless, for example, for two people to debate whether extra-terrestrial UFOs come from inside or outside of our solar system if they cannot agree that UFOs exist in the first place.

From Fact to Conceptualization

Human existence would be quite chaotic if our total experience consisted only of discrete observations, even if these were all quite well established. The agreed upon fact that the sun rose over the eastern horizon this morning would be relatively useless if we could not place it in some larger framework or conceptualization. Conceptualizations are abstract statements that go beyond individual facts and relate them to one another. Conceptualizations may be simple generalizations: "The sun always rises on the eastern horizon" or involve more complex explanations: "The sun rises in the morning and sets in the evening because the earth is turning on its axis." In either case, the most important characteristic of such conceptualizations is that they bring a group of specific facts together into a more general and useful relationship, allowing us to organize these facts into patterns of regularity about the world and to make accurate predictions. Indeed, it has been said that science is the search for patterns in nature.

If it is true that conceptualizations depend upon the observations and facts at hand, it is equally true that the kinds of conceptualizations we generate determine something about the observations we make. We tend to perceive readily only that which we are prepared by our conceptualizations to see. Seeing or observing is not an automatic activity. Art teachers are fond of saying that "art teaches you to see," which means that observation is something we all have to learn about as a process.

Our eyes or ears may be open but seeing and hearing involve the integrative mechanisms of our brain, which, in turn, is molded by our learning experience. Consciously or unconsciously, people often choose to overlook observations that do not fit with what they conceive to be true. The value of examining these philosophical issues is that it can make us more aware of how various factors influence the way we observe the world or put our observations together into conceptualizations. In turn, such awareness may help provide an antidote to any unintended biases that might influence our thinking.

Types of Conceptualizations

Although there are many categories of conceptualizations in science in science, we will limit our discussion here to three major types: generalizations, hypotheses and theories.

Generalizations. A generalization is a statement that is meant to apply to a large class of objects or set of phenomena. The example given previously that "The sun always rises in the east" is a generalization about a daily occurrence. Similarly, the statement that "all dogs have four legs" is a generalization about a set of objects, dogs. Generalizations are based on summarizing a number of specific observations of the same processes or object. Generalizations are highly useful because they point to a regularity among phenomena in the material world. They become problematic only when they are based on a very small number of cases which may not adequately represent the whole.

Hypotheses. Hypotheses are tentative explanations to account for observed phenomena. For example, if you flip the switch on a lamp and it does not go on, you might formulate several simple hypotheses as an explanation: (1) The bulb is burned out, or (2) The lamp is not plugged in. Both hypotheses lead to simple predictions: (1) Replacing the bulb or (2) plugging the lamp into an outlet should make the lamp light up again. In science, hypotheses always lead to predictions that can be verified or refuted. *The formulation and testing of hypotheses lie at the very heart of any scientific or rational inquiry.*

Theories. The term "theory" is often used in everyday language to mean something rather vague, more like a "guess" than any highly reasoned conceptualization. However, "theory" generally has a more precise meaning to scientists and philosophers of science. While philosophers often differ as to a universal definition of "theory," it is generally accepted among practicing scientists that a theory is an explanatory hypothesis that has stood the test of time and is well supported by the empirical evidence. Theories can be as simple as a generalization (all green apples are sour) or more complex causal statements such as nerve cells conduct impulses because electrically charged ions pass through the cell membrane. Theories are generally broader, more inclusive statements than hypotheses, and often relate two or more hypotheses to one another. The Darwin-Wallace theory of evolution by natural selection, for example, incorporates hypotheses dealing with the modifiability of organisms by selective breeding, the meaning of similarity of structure and function, the role of competition for food, territory and other natural resources, factors involved in mate selection, and so forth.

Observation, Fact and Conceptualization: A Case Study

At the turn of the century, biologists made numerous observations to determine the number of chromosomes (Gr. *chroma*, color; *soma,* body) present in the cells of most plants and animals, including humans. To see chromosomes it is necessary to stain cell preparations for viewing under the microscope. Chromosomes so treated appear as dark, oblong objects surrounded by other partially stained material in the nucleus.

Figure 2.3a suggests some of the problems observers encountered in trying to make accurate chromosome counts. First, the chromosomes are usually clumped together in such a way that it was not always easy to tell where one ends and another begins. Second, females appeared to possess one more chromosome in each body cell than did males. Third, chromosomes usually curl and twist toward or away from the plane of the field of vision. Consequently, it was easy to count as two chromosomes what was actually one chromosome appearing at different focal planes under the microscope.

In the early part of the twentieth. century, microscopists often used a device called a camera lucida for recording microscopic observations. The camera lucida projects what is observed under the microscope onto a flat surface and allows the observer to trace a pattern of the projected image (Fig. 2.3b). It was far easier to count chromosomes in camera lucida drawings than in the actual chromosome preparations. Yet even then, the same observers did not always see the same

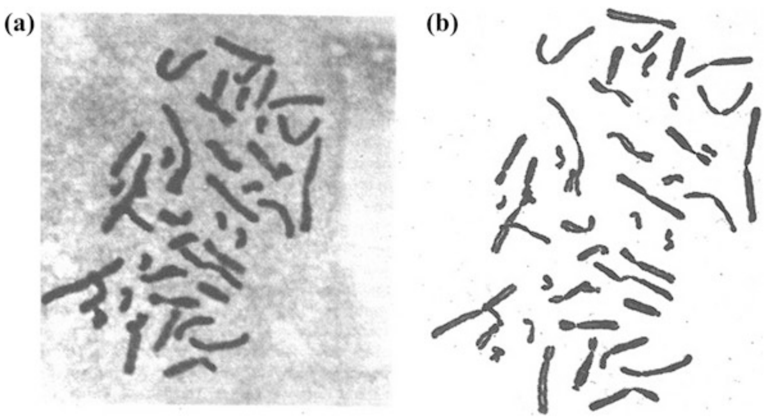

Fig. 2.3 **a** Photograph showing chromosomes from a stained spleen cell culture of a 17-week human fetus. Note how the chromosomes clump and overlap, making accurate counts difficult. **b** Camera lucida drawing of the same group of chromosomes. Such drawings help to elucidate detail more clearly, because they represent a composite of observationsat different depths of focus —something no single photograph can generate [from T.S. Hsu, *Journal of Heredity* 43 (1952): p. 168]

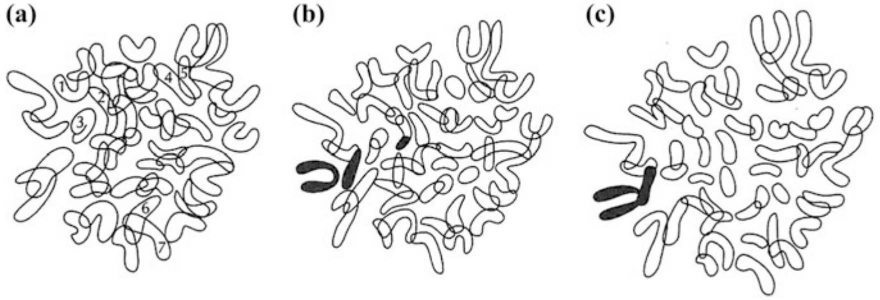

Fig. 2.4 Three different camera lucida drawings of the same chromosome group, as drawn by by three different observers. **a** Evans, **b** von Winniwarter, and **c** Oguma. Note the difficulty in determining whether some parts of chromosomes are attached to or separate from other parts. To see how tis affects actual counting, observe the chromosome labeled 2 in image A. Evans saw number 2 as a long, crescent-shaped chromosome, whereas both von Winiwarter and Oguma saw it as two shorter, separate chromosomes. On the other hand, Evans saw chromosome number 3 as a single chromosome, whereas von Winniwarter and Oguma saw it as two separate ones. Such problems greatly confused early attempts to get an accurate count of human chromosome numbers [From King and Beams, *Anatomical Record* 65 (1936): p. 169]

number of chromosomes (Fig. 2.4). In 1907, German cytologist H. von Winniwarter made the earliest counts of human chromosome counts, and reported 47 chromosomes as the total in humans: 23 pairs plus an extra, "accessory" chromosome, called the X chromosome. Between 1921 and 1924, however, T. S. Painter, then at the University of Texas, developed new techniques for preparing and observing chromosomes. Using these methods, he reported a count of 48 chromosomes, or 24 pairs. Between 1932 and 1952, at least five other observers confirmed Painter's count of 48 chromosomes. By the early 1950s, it was accepted that the correct chromosome number for the human species was 48 and all biology textbooks dutifully gave that number.

The certainty of Painter's count had two negative effects. First, it stifled further investigation; the count became authoritative and people simply stopped counting human chromosome preparations. Second, it prejudiced the few chromosome counts that *were* made. The conceptualization that 48 was the correct number caused observers to believe they saw 48. In the 1930s and 1940s, however, several new techniques were introduced. One of these was the preparation of karyotypes, in which the cell's chromosomes are first photographed and then the individual chromosomes are literally cut out of the photographic print. The chromosome images are then arranged on a sheet in a systematic fashion, making it possible to account for each individual chromosome and match it with its partner (Fig. 2.5). In 1955, Dr. Eva Hansen-Melander and her colleagues in Sweden had been studying the karyotypes of cancerous human liver tissue. They consistently counted 46 chromosomes. Eventually, after some doubts about the accuracy of their own observations, Dr. Hansen-Melander's group challenged in print the long-established

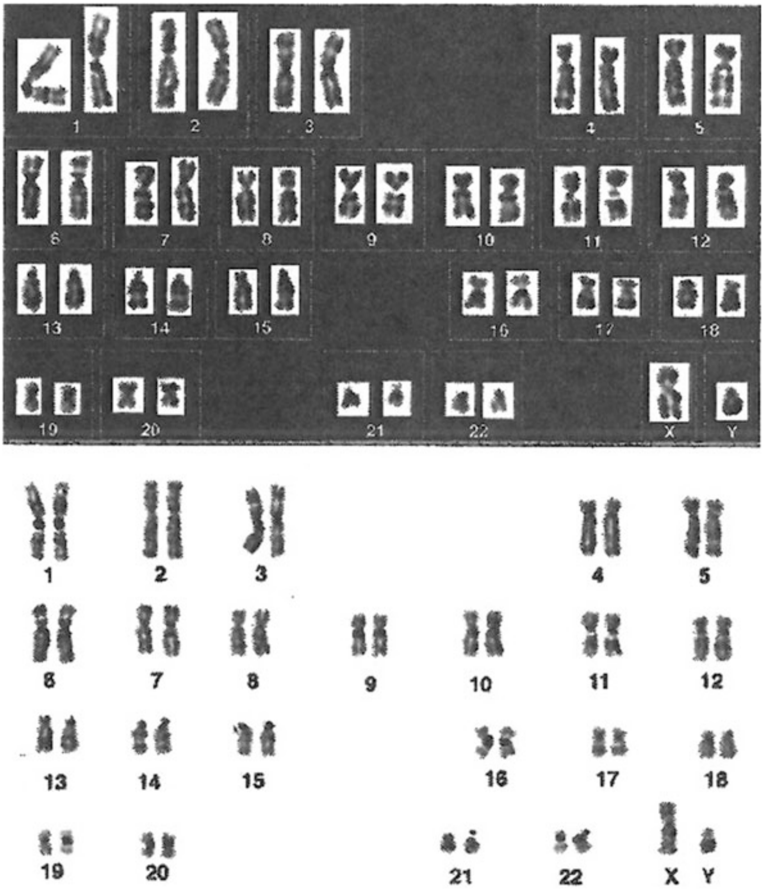

Fig. 2.5 Karyotype of a human male. The chromosomes are arranged in their natural pairs by number (numbers start with the larger chromosomes). Characteristically, the 23rd pair is the sex-0determining pair, shown here as XY for a male (females would be XX) [courtesy, Dr. Thomas Ried, M.D. and Dr. Hased. M. Padilla-Nash, Cytogenetics Laboratory, National Cancer Institute, NIH, Bethesda, Maryland]

notion that human beings have 48 chromosomes. By 1960, after many confirmations of the number 46, it was agreed that the older count of 48 was wrong.

What can we conclude about the process of observation from the history of establishing the chromosome count in humans? First, observation is not a passive process in which the observer simply lets sensory data flow into his or her brain. It is an active process that involves a good deal of input or active construction on the part of the observer. We have to "learn to observe." Second, since observations depend upon sensory data, if the material being observed is itself ambiguous (such as clumped chromosomes) the observations will reflect that ambiguity in one way or another, either in disagreements among different observers or failure of a single observer to confirm their own earlier findings. Third, observations generally contain some subjective input. Determining whether a particular stained mass represents one or two chromosomes is often a judgment call. Fourth, *people often find what they expect to find*. The expectation that human cells contain 48 chromosomes caused many workers actually to "see" 48 chromosomes. Thus even when something else is observed, the force of accepted dogma may cause investigators to disbelieve their own sensory impressions. Fifth, it should be pointed out that Painter was working with testicular samples taken from a patient at a Texas mental hospital. This individual may well have possessed an extra chromosome, a condition sometimes found associated with certain types of mental retardation. Thus, Painter's observations may have been accurate but his starting material atypical. This case also shows how the introduction of a new technique or procedure, in this case karyotyping, may change a conceptualization in science by improving the accuracy of observations.

This case also illustrates something about the role of gender context in scientific process. In the early twentieth century men far outnumbered women in the sciences, including biology. Men held the major faculty positions in research universities, had access to the most prestigious journals, and were major figures in professional societies such as the American Society of Naturalists or American Genetics Association. Many women went into science but often could obtain only low-paid positions as research assistants (to men) or technicians. In the face of claims by male authorities women often came to doubt their own observations or hypotheses when they found some disparities. In the chromosome case, Painter was a very well-known and authoritative figure, while Eva Melander was only a research assistant in a laboratory run by her male supervisor. The slow acceptance of her own count of 46 chromosomes may well have been the result of bias toward concepts advanced by authoritative men as opposed to those of less well-known women.

Creativity in Science

A popular stereotype maintains that creativity is a process reserved for poets, musicians and other artists, while science, by contrast, is coldly logical. In truth, science may be just as creative as any of the arts; the scientist as much an inspired creator as the poet. When Darwin and Wallace independently read Thomas Robert Malthus' *Essay on Population*, the concept of natural selection as a driving force in evolution occurred immediately to both of them. In each case it was an act of creativity resulting in the formulation of a bold new concept. Exactly *how* each individual arrived at this concept is impossible to pinpoint precisely; as in the artistic world, the process of creativity remains always elusive. The momentary insight, the creative flash of inspiration, often happens so quickly that even the individual involved may have difficulty in reconstructing the actual process. Thus, in our discussion of the nature of scientific thought, we will not be able to say much about the creative act of concept formulation itself. This should not be taken to mean, however, that creativity is unimportant in science. On the contrary, it often plays a central role. What we can understand more fully is the process of *verification*, that is, how we formulate and test hypotheses in a logical way.

2.4 The Logic of Science: Induction and Deduction

We now turn to the more formal aspects of hypothesis formulation and testing by examining the processes of induction and deduction.

Induction and Deduction

A major pattern of thought involved in forming conceptualizations is known as induction, or inductive logic. Induction is the process of making general statements based upon a set of individual observations. Consider for example, the series of integers below: 2 4 6 8 10 12 14 16 18, *et cetera*. Here, individual observations might lead to the formulation of a hypothesis proposing that the entire series, including any yet-to-be-revealed numbers indicated by the *et cetera*, is composed of the positive, even integers. Or, suppose a person tastes a green apple and finds it to be sour. If the same person tastes a second, third, and fourth green apple, and finds them to be sour also, he or she might reasonably hypothesize that *all* green apples are sour. The concepts that the entire number series is composed of positive even integers and that all green apples are sour are examples of hypothetical generalizations formed by inductive logic, that is, they are inductive generalizations. Such inductive generalizations not only summarize a set of observations, they may also serve to provide predictions concerning as yet unobserved events: for example, the identity of the next number in the series or the expected taste of the next green apple.

Going beyond the formulation of hypotheses by induction to test their validity involves the use of deduction or deductive logic. Often referred to as "*If* …, *then*" reasoning, deductive logic is the heart and soul of mathematics: for example, "*If* two points of a line lie in a plane, *then* the line lies in the same plane." Deduction is no less important in science. The "*if*" portion of the "*if* … *then*" format represents the hypothesis: the word "if" stresses the tentative, or conditional nature of a hypothesis, while the word "*then*" stresses that *the conclusion follows inevitably from acceptance of the hypothesis.*

A deduction is said to be valid if the conclusion follows necessarily from the original hypotheses from which it is derived. We can see this more clearly by laying out the logical sequence involved in what philosophers call a deductive syllogism, merely a formal sequence of if … then statements:

If … the number series consists of positive even integers
then … the next number to appear in the number series will be 20, and
If … all green apples are sour, and
if … this object is a green apple
then … this green apple must be sour.

Both syllogisms are valid: as a long as we accept the two hypotheses as stated, *we have no choice but to accept the conclusion.* The following, however, is an invalid syllogism:

If … all green apples are sour, and
if … this fruit is sour
then … it is a green apple

Here, the conclusion does *not* follow logically because "sour fruit" is a larger set than green apples and may include many other sour fruits in addition to green apples. Since the conclusion does not *necessarily* follow from the hypotheses, it is said to be invalid.

Note that the conclusion of a deductive syllogism is also a prediction—that is, it makes a statement about some future event. If a number series consists of positive even integers, then the number following 18 would be predicted to be 20; similarly, if all green apples are sour, the next green apple you taste should be sour. The fact that deductive syllogisms lead to predictions means that the conclusions can be tested. Testing hypotheses is one of the cornerstones of scientific investigation. This general method of reasoning is often referred to as the hypothetico-deductive method.

Thus far we have been talking about validity in a strictly logical sense. But what about the "truth" of a statement in the real world? The fact that the first syllogism concluding that this green apple must be sour does not mean that it *is* sour. *Validity and truth are not the same*. Validity has to do with logic; truth with our experience in the real world. For example, we can set up a perfectly valid deductive syllogism that has nothing to do with truth in terms of human experience:

If … all geometric figures have four corners, and
if … this circle is a geometric figure
then … this circle must have four corners

This syllogism is valid, yet clearly in the world of plane geometry it is not true that all circles have four corners.

Logic, Predictions and the Testing of Hypotheses

The use of either observations or experimentation to test hypotheses implies that there is a distinct relationship between hypotheses and the predictions they generate. This relationship is shown in the "truth table" (Fig. 2.6):

The "Truth Table"

Hypothesis	Conclusion (Prediction)
True	True
False	True or False

Fig. 2.6 The "Truth Table"

Note first that, barring an error in carrying out the experiment itself, obtaining a false prediction automatically implies that the hypothesis must also be false since, as the truth table shows, *a true hypothesis can never give rise to a false prediction*. This becomes obvious if we go back to our number series and sour green apples example. If the next number after 18 turns out to be 19 rather than 20, clearly the hypothesis proposing that the series consists of positive even integers is false. Similarly, if the next green apple is sweet, the hypothesis proposing that all green apples are sour must also be false. Logically speaking, therefore, we must reject both hypotheses. In the real world of formulating and testing scientific hypotheses, however, seldom does a single counter-example lead to the full-scale rejection of a hypothesis, especially if it is a widely accepted one. More likely, the "all green apples are sour hypothesis" would be modified, perhaps to "*Most* green apples are sour." There are good reasons why logic alone does not necessarily prevail here. A green apple that is sweet might be a different variety of apple that remains green when ripe; most certainly there are such varieties and their existence does not deny the reality that some other varieties of green apples are, indeed, always sour.

The truth table also shows that *only a false hypothesis can give rise to a false prediction*. The importance of this last statement cannot be overemphasized, for it is the only instance in which we can establish absolute certainty in evaluating scientific hypotheses. Note, on the other hand, that *obtaining a true prediction cannot achieve absolute certainty concerning the truth of scientific hypotheses, because false hypotheses may also give rise to true predictions*. The relationships outlined in the "Truth Table" are the logical basis for the claims by philosopher of science Karl Popper that the only *truly* scientific method is falsification. That is, to falsify a hypothesis is provides certainty, and is therefore logically rigorous: we must reject the hypothesis as originally stated if its predictions are falsified. Popper's claims have been controversial since many areas of science (for example, evolutionary theory) are not easily falsified, yet they are still considered by most practioners as science. Yet, falsification remains a goal of scientific work, even if sometimes unattainable.

The Concept of "Proof" in Science

As noted earlier, deductive logic is the heart and soul of mathematics. It is no less so for science. In mathematics, however, proofs by deduction are the standard. Scientific "proofs", on the other hand, are a combination of induction and deduction and as we have just seen, and therefore are *never more than probable*. Indeed, the word "proof" should not be used in the context of science at all.

Let us see why this is the case. You may recall from high school algebra the proof that the square root of two ($\sqrt{2}$) is an irrational number, that is, cannot be expressed as a ratio of two integers, e.g., 1/2 or 3/4. It is possible to *prove* this because the set of all numbers is divisible into two subsets, those that are rational, (that is, *can* be expressed as a ratio of two other numbers), and those that are irrational (that is, cannot be so expressed). The first step in the proof involves putting forth the hypothesis that the square root of 2 *is* a rational number, that is, is to be found in the set of rational numbers. The algebraic manipulations that follow lead eventually to a contradiction of this hypothesis, that is, to a false conclusion or prediction. As we know from the truth table, this means that, since the square root of two is not in the set of rational numbers, it can only be in the other set, that of the irrational numbers.

This situation of "if not *a*, then *b*" is usually not attainable in the real world of the scientist. The experimental disproof of any one scientific hypothesis does not mean that an alternative hypothesis must be true; instead, there may be large number of alternative hypotheses that might account for the phenomenon being researched such as the cause of a disease (there may be no *one* cause in all cases, but multiple causes). The conclusion here is an important one: *science cannot* ***prove*** *anything*. Popular reporting to the contrary, science has not "proved" that cigarette smoking causes such conditions as lung cancer, emphysema and/or heart failure. On the other hand, there exists a *vast* amount of evidence in support of the scientific hypothesis proposing a link between smoking and these conditions and it would be foolish to ignore this just because it cannot be "proven" in the mathematical sense —that is with utter certainty.

Many hypotheses that today we believe to be false today were once accepted by scientists and lay persons alike because they led to accurate predictions. For example, in the seventeenth and eighteenth centuries one of the most intriguing questions was how did an egg, like that of a frog or chicken, develop into a fully-formed organism with highly differentiated structures? Some naturalists believed in what was known as the theory of embryonic preformation. This theory held that that every egg or sperm (as we will see in the next section, at the time knowledge about fertilization and the role of egg and sperm in development was quite rudimentary) contained a minute, fully-formed organism, sometimes referred to as a "homunclusu" that simply grew into the more mature form during embryogenesis. Relying on a familiar process, growth, the theory of preformation explained what otherwise seemed incomprehensible: the formation of a complex organism out of unorganized matter (the alternative theoryat the time was known as epigenesis). This theory led to two predictions. The first was that if we could examine the egg (or sperm) microscopically we ought to be able to see the very tiny but fully-formed embryo inside. And in fact, some early microscopist claimed to have seen a tiny “homunculus” encased in the head of a sperm or within the egg. Many other observers failed to see a homunculus, but proponents of preformation calimed that the microscopes were not good enough to reveal the tiny individual. But as microscopes improved dramatically in the eighteenth century, it became clear that the predicted “homunculus” was simply not there. A second prediction was that in any series of generations of organisms, all the individuals back to the original progenitor, must have had every future offspring encased in their testes or ovaries. This prediction led to the absurd conclusion that the number of generations of every organism must be limited to however many preformed individuals were present in the original ancestor. Since both of these predictions turned out to be false, by the nineteenth century most naturalists had rejected the preformation theory. The alternative theory epigenesist, difficult as it was to imagine, seemed to offer a more fruitful path for research, and more predictive experiments in the long-run.

2.5 The “Dissection” of an Experiment

We turn now to an early example of a scientific investigation that demonstrates the logical nature of science in practice.

Today we know that a fluid called semen, produced by male animals, including humans, contains spermatozoa, or sperm. Sperm are living cells, possessing a headpiece and a tail and convey the inheritance factors (genes) of the male to the female ovum, or egg. In sexual reproduction, the sperm and egg unite in the process of fertilization, leading to the subsequent embryonic development of the resulting embryo.

This is what we know *today*. In the eighteenth century scientists were still uncertain as to just how the male semen managed to fertilize the egg. Two possibilities were recognized:

> **Hypothesis I**: The semen of the male must make actual contact with the egg before fertilization and embryonic development could begin, or,
> **Hypothesis II**: It is only necessary that a gas or vapor, arising from the semen by evaporation, make contact with the egg.

From their knowledge of the female reproductive system, as determined primarily through anatomical dissections, physicians could see that the semen must be deposited a considerable distance from the female ovaries where the eggs are produced. (Since the role played by the sperm cells was not understood, the fact that they were capable of swimming toward the egg was not taken into account.). Thus it seemed reasonable to hypothesize that only a vapor arising from the semen could possibly reach the egg and fertilize it.

In 1785, the Italian natural philosopher Lazaro Spallanzani (1729–1799) put the vapor hypothesis to an experimental test using the toad as his model organism. In the following presentation of this experiment, Spallanzani's own words, which provide an excellent example of the underlying logical structure of good scientific procedure, are printed in regular type, while our editorial commentary, which clarifies and emphasizes important aspect of Spallanzani's methodology is interspersed in *italics*.

Is fertilization affected by the spermatic vapor? It has been disputed for a long time and it is still being argued whether the visible and coarser parts of the semen serve in the fecundation [that is, here, in the early development] of man and animals, or whether a very subtle part, a vapor which emanates therefrom and which is called the aura spermatica, suffices for this function.

Here the problem is defined: Does the semen itself cause the egg to develop? Or, is it merely the vapor arising from the semen that does so?

It cannot be denied that doctors and physiologists defend this last view, and are persuaded in this more by an apparent necessity than by reason or experiments.

Here Spellanzanii points out the lack of experimental evidence to support the vapor hypothesis

Despite these reasons, many other authors hold the contrary opinion and believe that fertilization is accomplished by means of the material part of the semen.

In the full text of his report he cites some of the anatomical observations noted in the introductory part of this section.

These reasons advanced for and against do not seem to me to resolve the question; for it has not been demonstrated that the spermatic vapor itself arrives at the ovaries, just as it is not clear whether the material part of the semen that arrives at the ovaries, and not the vaporous part of the semen, is responsible for fertilization.

He next states the alternative hypothesis: that the semen must actually make contact with the egg for fertilization to occur. Two alternative hypotheses can be tested. The statement "it has not been demonstrated that" again shows Spallanzani's recognition of the lack of empirical evidence to support or refute either hypothesis.

Therefore, in order to decide the question, it is important to employ a convenient means to separate the vapor from the body of the semen and to do this in a way that the embryos are more or less enveloped by the vapor;

An experimental design is suggested. Some sort of apparatus must be constructed to properly test the two alternative hypotheses.

… for **if** they are born, [**then**] this would be evidence that the seminal vapor has been able to fertilize them; or [**if**] on the other hand, they might not be born, **then** it will be equally sure that the spermatic vapor alone is insufficient and the additional action of the material part of the semen is necessary [boldface ours, for emphasis].

Note the occurrence here of the if ... then format, as Spallanzani identifies the deductive logic behind his experiment. He had shown earlier that the semen coud be diluted several times, yet still remain capable of fertilization. In terms of what is known today, this is not surprising. However, Spallanzani interpreted these results *as support for the vapor hypothesis, since he considered vapor to be merely diluted semen. The next experiment, however, seems to have convinced him otherwise.*

In order to bathe the tadpoles [eggs] thoroughly with this spermatic vapor, I put into a watch glass a little less than 11 grains of seminal liquid from several toads. Into a similar glass, but a little smaller, I placed 26 tadpoles [he means eggs as explained below] which, because of the viscosity of the jelly [*a coating around the eggs*] were tightly attached to the concave part of the glass. I placed the second glass on the first, and they remained united thus during five hours in my room where the temperature was 18 °C. The drop of seminal fluid was placed precisely under the eggs. which must have been completely bathed by the spermatic vapor that arose; the more so since the distance between the eggs and the liquid was not more than 1 ligne [2.25 mm]. I examined the eggs after five hours and found them covered with a humid mist, which wet the finger with which one touched them; this was however only [the] portion of the semen which had evaporated and diminished by a grain and a half. The eggs had therefore been bathed by a grain and a half of spermatic vapor; for it could not have escaped outside of the watch crystals since they fitted together very closely …. But in spite of this, the eggs, subsequently placed in water, perished.

Like many of his day, Spallanzani believed in the preformation theory, hence the only role of the sperm for him was to initiate growth of the miniature form, that is, in the case of the frog the tadpole stage. This is why he refers to the unfertilized egg as a "tadpole" in the passage above. Spallanzani goes on to describe his next experimental set-up as shown in Fig. 2.7. The fact that development did not occur when the sperm were placed in the dish below, but not in contact with the eggs, meant that the prediction necessarily following from the vapor hypothesis was false; hence the hypothesis itself must be false.

Although the experiment overthrows the spermatic vapor theory … it was nonetheless unique and I wished to repeat it.

Spallanzani recognizes the need for further experimental evidence demonstrating that the vapor hypothesis is, indeed, incorrect. His results in this second series of experiments were the same.

Having previously used spermatic vapor produced in closed vessels, I wished to see what would happen in open vessels in order to eliminate a doubt produced by the idea that the circulation of the air was necessary for fertilization …

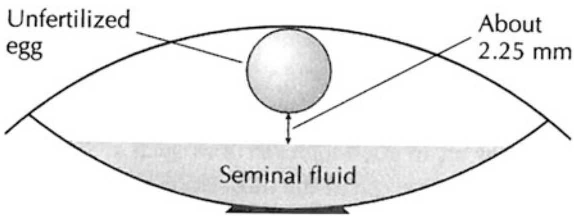

Fig. 2.7 Experimental set-up similar to the one used by Spallanzani to answer the question "Is fertilization effected by the spermatid fluid?" Vapor rising from the seminal fluid freely bathed egg, but no contact between the egg cell and fluid occurred. The egg did not become fertilized [from J.J. W. Baker and G.E. Allen, *The Study of Biology* (Addison-Wesley, 1st ed., 1967): p. 41]

He recognizes a variable factor is recognized that might influence the results; the experiment is modified to eliminate this variable i.e., If air plays a role in fertilization, then the eggs should develop if air is allowed to circulate, etc.

but fertilization did not succeed any better than in the preceding experiments. *Again, negative results. The prediction is shown to be false.*

The last experiment of this type was to collect several grains of spermatic vapor and to immerse a dozen eggs in it for several minutes; I touched another dozen eggs with the small remnant of semen which remained after evaporation, and which did not weigh more than half a grain; eleven of these tadpoles hatched successfully although none of the twelve that had been plunged into the spermatic vapor survived.

He performs yet another variation of the original experiment. This experiment yielded additional evidence against the vapor hypothesis: Even immersion in the condensed spermatic vapor did not result in fertilization! Certainly if the vapor hypothesis were valid, it would have predicted otherwise.

The conjunction of these facts evidently proves [supports the view] that fertilization in the terrestrial toad is not produced by the spermatic vapor but rather by the material part of the semen.

Expressed in deductive format, Spallanzani's results show the vapor hypothesis to be false. Despite his use of the word "proves" these results do not mean that the alternative hypothesis is correct, but only provide support for it

As might be supposed, I did not do these experiments only on this toad, but I have repeated them in the manner described on the terrestrial toad with red eyes and dorsal tubercles, and also on the aquatic frog, and I have also had the same results. I can even add that although I have only performed a few of these experiments on the tree frog, I have noticed that they agree very well with all the others.

Note also that Spallanzani is careful not to generalize beyond the species of animal used in his experiments.

Shall we, however, say that this is the universal process of nature for all animals and for man?

Spallanzani now wishes to extend his results to other organisms and so performs other experiments using different species. In other words, can the generalization be extended to other organisms not yet tested in these experiments?

The small number of facts which we have does not allow us, in good logic, to draw such a conclusion. One can at the most think that this is most probably so …

Spallanzani is properly cautious in considering an extension of his generalization about the necessity of contact with the semen (rather than its vapor) beyond the small group of species on which he actually carried out his experiments. He shows his awareness that while organisms of various types share many functional characteristics in common, they also show differences or variations that prevent the experimenter from automatically generalizing from one species to another.

… more especially as there is not a single fact to the contrary … and the question of the influence of the spermatic vapor in fertilization is at least definitely decided in the negative for several species of animals and with great probability for the others.

Spallanzani shows his awareness of the nature of scientific "proof" with this statement; no false predictions have been obtained in the experimental testing of this hypothesis (i.e., hypothesis I) but the conclusion can still only be expressed in terms of probability. *Note, too, Spallanzani's awareness that his negative results give him clear disproof of the vapor hypothesis, yet provide only probable verification rather than absolute demonstration for this being the case with other species.*

Spallanzani later performed other experiments that further contradicted hypothesis II, the vapor hypothesis. For example, he discovered that if he filtered the semen through cotton, it lost much of its fertilization powers and that the finer the filter the more those powers were diminished. He also found that several pieces of blotting paper completely removed the semen's ability to fertilize, but that the portion left on the paper, when put into water, *did* successfully fertilize eggs. Despite the obviousness (to us) of the role played by the sperm in fertilization—a role to which these experiments certainly point—Spallanzani had previously decided that semen without sperm *was* capable of fertilization and he was unable to shake this belief even in the light of his own experimental results. If nothing else, this demonstrates nicely that scientists are just as prone to overlook the obvious as anyone else and may often refuse to give up a preconceived notion despite clear evidence to the contrary. It was not until the nineteenth century that the distinct role of sperm in fertilization was first established.

[Excerpt from Spallanzani's account of his experiments is taken from M.L. Gabriel and S. Fogel, *Great Experiments in Biology* (Englewood Cliffs, NJ: Prentice-Hall, 1955]

2.6 The Logic of Science: Hypotheses as Explanations

Although generalizing hypotheses are important in science, hypotheses that actually *explain* a phenomenon are preferable. In case of the sour green apples, for example, a hypothesis might be developed to explain why they are sour. One such explanation might be that green apples contain high concentrations of a particular acid such as acetic or citric acid, components of many fruits. This explanation is readily testable by carrying out chemical analyses and comparing the amount of acid found in the sour green apples with the amount found in sweet apples. It is only those hypotheses that actually explain observed natural phenomena that may rise to the level of being considered theories.

Teleological versus Causal Hypotheses

Throughout the history of biology, there have been two types of explanatory hypotheses put forward. Teleological (Gr. *telos*, end or goal-oriented) hypotheses suggest that certain events or processes occur for some purpose or are directed toward some end. In contrast, causal hypotheses focus specifically on the direct factors that lead from event A to event B.

Consider the following example. In the 1970s, Harvard University biologist Ernst Mayr (1904–2005) observed that a warbler living all summer in a tree next to his house in New Hampshire began its southern migration on August 25. This single observation raised a question in his mind. *Why* did the warbler begin its migration on that date? A teleological answer to this question might be: "Because the warbler *decided* to move to a warmer climate where food was more abundant." Teleological explanations imply conscious or at least some form of pre-determined, goal-oriented behavior. Although it may be appropriate to ask teleological questions concerning human activities, it is not meaningful to ask such questions about other organisms. To ask "For what purpose did the warbler begin to migrate?" implies that the warbler made the same kind of conscious, goal-oriented choice that a person might make in deciding to go shopping for a particular item of merchandise. There is no way to test teleologicalhypotheses scientifically; one obviously cannot ask a warbler to tell us its reasons for leaving New Hampshire in late August! This is why biologists seek non-teleological, or causal explanations, ones that focus on more specific, testable reasons for why a bird might begin its migration at a certain time of year. Mayr's original question can be rephrased in a more precise manner: "What factor or factors caused the warbler to begin its migration on August 25?" It is possible to answer this question without making ungrounded assumptions concerning a conscious purpose on the part of the warbler in starting its migration.[2]

Before we try to answer Mayr's question, we need further clarification. His original question was phrased in the singular: "What caused *the warbler* to begin its migration on August 25?" In science, such questions are more likely to be posed in a general form: "What causes *warblers* to begin their migration *around* August 25?" No two warblers are exactly the same; no two August 25ths have absolutely identical conditions. Although biologists investigating such problems may have to deal with individual cases, it is important to frame the question in as broad a manner as possible. In general, scientists are more interested in explaining the principles underlying collections of events than in accounting for individual events such as the behavior of a single warbler. The greater the number of warblers studied, the more likely will be the validity of any hypotheses generated concerning the migratory behavior of warblers in general.

Types of Causal Explanations

In response to the general question regarding the causes of warbler migration, at least three different kinds of causal explanations are possible (Fig. 2.8):

(1) **An Internal Hypothesis**. Warblers begin migrating towards the end of August because a physiological mechanism (for example, a hormonal change) is activated, leading to migratory flight behavior. This explanation focuses on a physiological mechanism within the organism that may trigger migratory behavior.

[2]There are certain processes in biology that are teleological in the sense that from the initial events the end-point is pre-determined. The most obvious example is embryonic development, in which from the moment the sperm fertilizes the egg the subsequent course of events (barring outside disturbance) leading eventually tp the final goal, the formation of the adult organism.

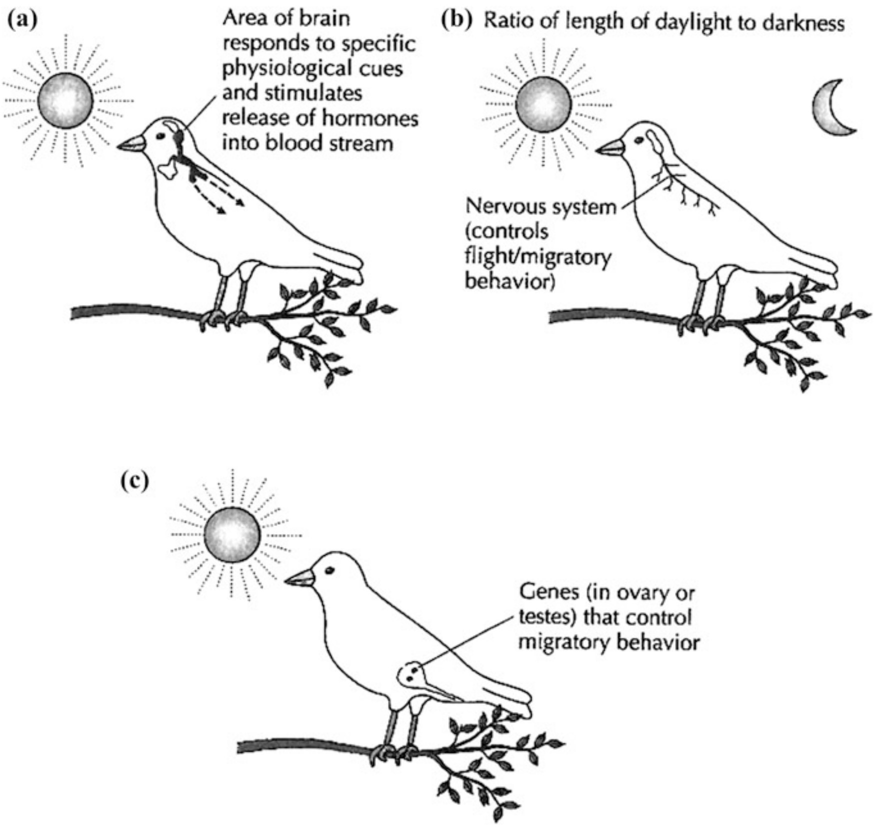

Fig. 2.8 Various ways to answer the question: Why did the warbler start its migration on August 25? **a** Internal cause, **b** External cause, **c** Historical cause [original art from authors]

(2) **An External Hypothesis**. One or more specific environmental factors, such as the short day-length associated with fall, or a decline in the insect population comprising the warbler's food supply, may activate the physiological trigger for migration described in explanation 1. This hypothesis emphasizes external factors that may trigger the onset of migratory behavior.

(3) **A Historical Hypothesis**. Warblers begin moving south because, through the course of evolution, they have acquired a genetic constitution that programs them to respond to certain environmental changes associated with the end of summer. This historical hypothesis relates warbler migration to an adaptive response to environmental changes developed through evolutionary processes over long periods of time.

These three types of explanations are not mutually exclusive, and the most complete explanation may well involve aspects of all of them.

Mechanisms in Biology

Most scientists, biologists among them, are interested in explanatory hypotheses that suggest a *mechanism* for how a given process actually works—for example, the physiological process that starts the birds' migration, or, the visual and physiological processes by which birds navigate in their migrations. Mechanisms in this sense have been described by philosophers of science Peter Machamer, Carl Craver and Lindley Darden as consisting of entities and activities that begin with some initial state and end with some outcome that is different from the initial state. For example, in bird migration the initial state might involve the birds' physiological and ecological (environmental) conditions on August 25; the entities might include its sensory apparatus (visual or temperature receptors) and specific hormones or enzymes that trigger a flight response; the activities would involve the means by which the hormones or enzymes actually caused an increase in response of flight muscles; and the outcome would be the initiation of migration.

The level of detail involved in describing any mechanism is obviously a function of the techniques available at any point in time. If it could be determined that changes in day-length as perceived visually by birds triggers a hormonal change that leads to migratory flight, but it as not possible to figure out how the hormone actually interacts with the nerve and muscle apparatus that causes the bird to start flying, that would still count as a mechanism—as far as it goes. If more refined analytical techniques were available to determine how hormone molecules interact with nerve or muscle cells that would make the mechanism more complete. Biologists, like all scientists, are constantly refining or reformulating the mechanisms for processes they are investigating.

It is sometimes tempting to think that the only mechanisms of importance in biology are those that can be traced to the biochemical and molecular levels. While having knowledge at the molecular level is always desirable, meaningful mechanisms can be put forward at *all levels* of biological organization, from the molecular to the cellular, tissue, organ, organismic, population or ecosystem levels. Indeed mechanisms for higher-level processes, for example the pattern formation of migratory birds (the familiar V-shape of a flock of geese, for example), may be *best* understood at the level of the population (flock) and not at the molecular level (though there would certainly be molecular mechanisms involved). The level at which mechanisms are proposed and investigated are appropriate for the question being asked.

There are many cases in the history of biology, or science in general, in which a process can be described in considerable detail but for which no mechanism can be postulated at a given point in time. Ernst Mayr could determine with considerable reliability that his warblers in New Hmpshire started their southward migration on August 25 due to the interaction of day-length, temperature, and declining food supply, and yet have no hypothesis as to the mechanism by which this occurs in the birds' physiology. What happens within their bodies becomes a *black box*, that is, an unknown. A black box in science usually refers to a situation in which there is an input to a system leading to an outcome, but with as yet no understanding of how that outcome is generated. It relates *cause* (input) to *effect* (outcome), which is a valuable starting point for scientific research. A black box does not invalidate the empirical observations relating the input to the output, but it remains a region of the unknown, and therfore an area for future investigation.

Cause-and-Effect

As the preceding discussion suggests, modern science is built on belief in **cause-and-effect**: for every observed effect, there is some cause or set of causes. Yet, causal hypotheses have distinct limitations. One lies in our ability to test them. For example, the hypothesis proposing that warbler migration is the result of a delicate change in hormones is a reasonable one, but if a technique for measuring small hormonal changes within the organism is not available, the hypothesis remains untestable and is therefore of limited value (as pointed out above it can, of course, emphasize the need to develop new chemical techniques to detect slight hormonal changes and thus prove valuable in that sense). Further, many cause-and-effect relationships may be more apparent than real. Suppose, for example, that a cold air mass from Canada arrived in New Hampshire on August 25 just when the day-length was appropriate to trigger the warbler's migratory response. It might *appear*, therefore, that the primary cause for onset of migration was the drop in temperature, an example of a spurious cause. Such spurious relationships are common in nature, for many events occur simultaneously and thus may often *seem* to be causally related, when they are merely coincidences.

2.7 Bias in Science

Science is not an abstract process isolated within the ivory towers of colleges, universities or independent research institutions. Rather, science is always situated in a social context where economic, political and philosophical values influence everything from the precise nature of the research undertaken to the actual kinds of hypotheses considered acceptable. Like all people, scientists grow up within particular cultures and learn to accept certain values related their time and place in history. These values may often represent general biases that people in a given society may share. Individuals also have their own personal biases. For example, some biologists are biased against explanations that cannot be expressed in mathematical or molecular terms while others feel that such explanations lose sight of the fact that it is the whole organism that is the most significant unit of biological function. Religious and political biases may also play a role in influencing individual scientists. In the seventeenth and early eighteenth centuries, for example, religious convictions motivated many individuals to study natural history in order to reveal the wisdom of the Creator in generating so many intricate adaptations. Despite stereotypes to the contrary, individual scientists are no less prone to various kinds of biases than anyone else.

Two kinds of bias may appear in scientific work. One is conscious bias, a deliberate manipulation or alteration of data to support a preconceived idea. Conscious or intentional bias in science is, in reality, simple dishonesty. Although there *are* examples of such dishonesty, since science is based on repeatability, fraudulent work will eventually be uncovered by other investigators. So, while there are documented cases of such conscious dishonesty, they are relatively rare. Far more common, and important to understand, is unconscious bias, of which the individual may be totally unaware. Because science is a human activity, unconscious bias is almost inevitably present to some extent in all research. In order to present a more realistic view of the scientific process, it is important to examine the way in which biases of various kinds function in science.

First, let us clarify what we mean by "bias." In the English language, the term has a negative connotation, implying an undesirable component of the thinking process. When we say that a scientist may be "biased" we can also be saying that he or she may have a particular point of view that influences the selection and formulation of their hypotheses. Sometimes these points of view act as blinders, preventing scientists from seeing the value of new ideas. At other times, however, points of view may also act as catalysts, providing new insights or ways of looking at a problem. To understand both the positive as well as the negative role that bias can play in science, we will examine briefly one example involving conscious bias and another involving unconscious bias.

Conscious Bias. The inheritance of acquired characteristics is the idea that traits acquired by an organism in its own lifetime (for example, a large body musculature acquired by exercise) may be passed on to its offspring. A concept prominent from antiquity, by the twentieth century belief in the inheritance of acquired characteristics had been rejected by virtually all biologists. A few researchers, however, persisted in trying to show that acquired characteristics could be inherited. One was the Austrian biologist Paul Kammerer (1880–1936). In the years immediately after World War I (1914–1918), Kammerer studied inheritance in the "midwife toad" *Alytes obstetricans*.

Most toads and frogs mate in the water. In order to grasp onto the female during mating, the males develop rough "nuptial pads" on their palms and fingers during the mating season, enabling them to hold onto the slippery female. However, since midwife toads mate on land and the female's skin is rough and dry, there is no selective advantage in the males possessing nuptial pads, and they are absent in *Alytes*. Kammerer, who was very talented at raising and handling amphibians, was able to induce midwife toads to mate in water. After only a few generations, he claimed that the males showed nuptial pads and, far more significant, transmitted this trait to their male offspring.

Kammerer's results received criticism from many quarters. For one thing, for all his skillful experimental abilities, Kammerer was not a good photographer and many of the published photos of his specimen were difficult to see or appeared to be retouched. For another, visitors to Kammerer's lab in Vienna were never able to see live specimen with nuptial pads. The final blow to his hypothesis and to his reputation came when several biologists, including the American G. K. Nobel, finally examined the one surviving preserved specimen and he observed that the so-called nuptial pad was a blotch on the skin induced by what appeared to be the injection of India ink under the surface.

There was some evidence suggesting that Kammerer himself did not fake the data but that the injections were made by one of his assistants. Even so, had he not been such a zealous advocate for the idea of inheritance of acquired characters, Kammerer might have examined his own results more carefully and avoided becoming publicly discredited by the episode. Whether this revelation of fraud was responsible for his suicide some months later has never been established (Kammerer was also involved at the time in an unhappy love affair that was about to end), but it seems likely that the accusation of fraud must have played some role.[3]

Unconscious Bias. Unconscious bias is less straightforward than conscious bias and is far more common in scientific work. We will here discuss just one example.

In 17th century Italy it was a common observation that meat left out in the open would soon contain maggots, the larval stage of flies. The hypothesis put forward to explain this observation was that the maggots were spontaneously generated from the organic matter of the meat in contact with air. This hypothesis led to the prediction that any meat placed out in the open would soon show the presence of maggots, a prediction confirmed frequently by experience.

An alternative hypothesis, however, had also been proposed: the maggots develop from eggs laid by adult flies on the meat. This was not a trivial or purely academic issue, since the infestation of meat by maggots in open air markets in seventeenth-century Italy was a major economic and health problem. If maggots really came from flies, then a method of protecting meat immediately suggested itself. In light of this alternative explanation, the Italian naturalist Francesco Redi (1636–1697) realized that he could test the spontaneous generation hypothesis with a simple experiment:

Hypothesis	***If*** … spontaneous generation is responsible for the appearance of maggots in meat exposed to air, and***If*** … meat is exposed to air in a jar covered by gauze to exclude adult flies,
Prediction	***then*** … maggots should still develop in the meat

Redi set up the experiment a shown in Fig. 2.9. He used two jars, into each of which he placed the same amount and kind of meat of the same age obtained from the same butcher. One jar was left open (Fig. 2.9a) and the other was covered with gauze (Fig. 2.9b). The first jar served as the control jar, while the second served as an experimental jar. The experimental element in this experiment is that which has been modified (in this case covered with gauze) to test a particular hypothesis, while the control element remains unmodified and serves as a comparison. For example if it were very cold on the day of the experiment and there happened to be no flies around, then the control group should not develop maggots either. In setting up

[3]Kammerer's life and work has been treated a number of years ago sympathetically by writer Arthur Koestler in *The Case of the Midwife Toad*, and more recently, and critically by historian of science Sandor Gliboff.

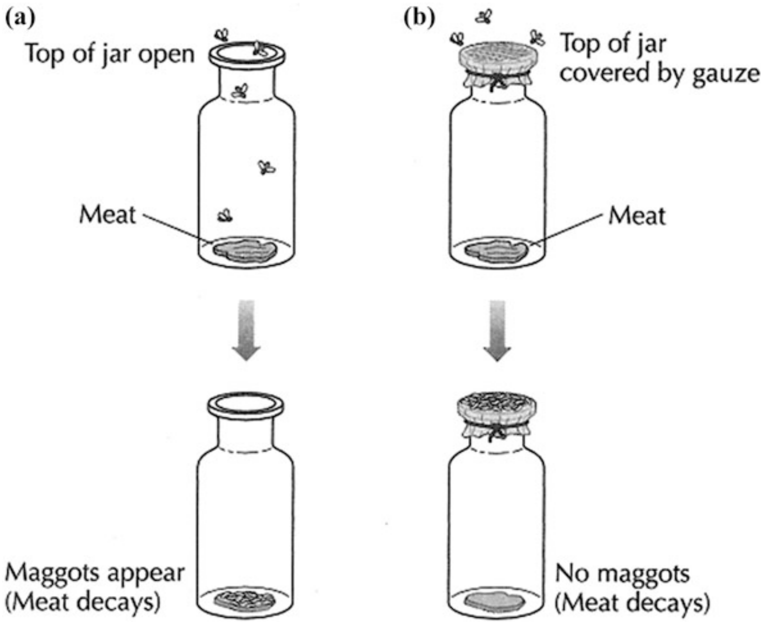

Fig. 2.9 Francesco Redi's experiment (1685) testing the hypothesis of spontaneous genetaction of maggots from meat exposed to air [original art from authors]

controls for experiments, it is important that all factors except the one being tested are kept the same. Thus, Redi used the same kind of meat of the same age from the same butcher (note that if the meat already contained fly eggs when it was bought it would obviously invalidate the experimental results). The two jars would all have to be placed in the same part of the room, kept at the same temperature, etc. As the experiment was proceeding Redi observed flies hovering around the top of both jars. Because jar A was uncovered they could enter and come in contact with the meat, but because of the gauze, they could not get inside jar B. The meat in B eventually spoiled through bacterial decay, but no maggots appeared, while the meat in A developed maggots. In this way Redi was able to show that the spontaneous generation hypothesis led to a false prediction and could therefore be rejected.

Or could it? History shows the outcome was not so simple. Proponents of the spontaneous generation hypothesis had a comeback. They argued that the gauze changed the quality of the air getting to the meat, thereby preventing the normal process of maggot generation from occurring. It required further experiments and observations; for example, observing flies actually laying eggs on the meat and microscopic observation of eggs developing into maggots before this modified version of the hypothesis of spontaneous generation could also be rejected.

Despite Redi's experiments, biologists in the 1860s were again debating the issue of spontaneous generation, this time in France. In this version, however, the debate occurred in a different context. Attention was now focused on the spontaneous generation of bacteria that routinely appeared in milk, beer and wine, causing them to sour. The germ theory of disease, championed by French microbiologist and chemist Louis Pasteur (1833–1895), and German microbiologist Robert Koch (1843–1910) was just gaining ground at this time. This theory proposed that the souring was caused by the presence of bacteria. An important component of Pasteur's championing of the germ theory was his opposition to spontaneous generation of any sort: all bacteria he claimed, came from the reproduction of previously existing bacteria, and were not spontaneously generated from non-living organic matter.

An opposing hypothesis, invoking spontaneous generation, was put forth by another French biologist, Felix A. Pouchet (1800–1873). He argued that although bacteria were certainly able to reproduce themselves, they could also be formed spontaneously from the right combination of organic materials. Pouchet performed a simple set of experiments that appeared to support his spontaneous generation hypothesis. He found that, if a series of flasks of hay infusion were heated to about 100 °C for a few minutes so as to sterilize their contents, and then were sealed and left at room temperature, after a short time they were seen under the microscope to be teeming with bacteria. In response to Pouchet's claims, and in defense of his own view, Pasteur countered that bacteria existed everywhere around us, on our hands, in our food, wine, beer and milk, and could be carried by the air from place to place. He argued that Pouchet had either not fully sterilized the original broth or had not plugged up the flasks quickly or carefully enough, thus allowing bacterial contamination of the liquid. This contention led Pouchet to repeat his own experiments several times, always with the same results.

The two scientists proceeded to exchange comments and letters in scientific publications. So intense was the debate that, in 1861, the French Academy of Sciences arranged a series of public presentations and a contest on the topic, with a cash prize to be awarded by a jury of scientists to the best presentation. Pasteur and Pouchet were the main contenders. For his part, Pasteur first demonstrated that boiling beef broth in a flask and then immediately sealing it by melting the glass at the top so that the contents were not allowed contact with air prevented the growth of bacteria and hence decay of the broth. (Bringing organic material close to the boiling point is the basis for "pasteurization," now used routinely to prevent the souring of milk, wine, beer and other foods.). However, Pouchet countered with a perfectly reasonable argument: he pointed out that boiling might have changed the chemical composition of the organic material in the broth, as well as the air inside the flask, rendering both unsuitable for the spontaneous generation of microbes.

In response to this claim, Pasteur performed another simple but elegant experiment. He boiled beef broth in a specially designed long necked flask (Fig. 3.11a) that allowed air to diffuse back and forth between the broth and the outside. The lower portion of the neck of the flask served as a trap for the heavier dust particles and bacteria carried in the air. This apparatus, what became known as the "swan-necked flasks", Pasteur reasoned, would allow air to come in contact with the broth but no airborne bacteria would make it beyond the trap. If spontaneous generation could occur, then it ought to do so under these circumstances. The results of Pasteur's experiment were quite dramatic. Even after several months, there was no decay in the flask. Moreover, he made another bold prediction: *If* bacteria were airborne and getting caught in the "trap," and *if* he tilted the flask so that some of the broth got into the trap and was returned to the main receptacle (Fig. 2.11b), *then* the broth in the receptacle should show bacterial growth. When he carried out this experiment, as his hypothesis predicted, bacteria appeared in the broth in just a few days. To Pasteur, this was strong support for his hypothesis and a clear rejection of Pouchet's. The French Academy of Sciences agreed and awarded the prize to Pasteur.

In the course of the debate, Pasteur *seems* to have shown by the sheer force of logic and ingenious experimental design that the theory of spontaneous generation of bacteria could be rejected and, indeed, this is the way the episode is presented in most biographical and textbook accounts. Pasteur himself promoted this interpretation and his work on spontaneous generation has often been used to illustrate the ideal of pure, unbiased science at work.

The story is not quite so simple as it might at first appear, however. Other factors also appear to have been at work in motivating the controversy, especially on Pasteur's part. Through a detailed study of Pasteur's published and unpublished writings, historians of science Gerald Geison (1943–2001) and John Farley have suggested that his position on spontaneous generation was very much influenced by his political and religious views. After the radical revolutions of 1848 that had spread throughout Europe, the period of the 1860s in France became one of growing political conservatism. Pasteur himself was especially conservative in his political and religious outlook. In the 1850s he had become an enthusiastic supporter of Emperor Napoleon III (nephew of the legendary Emperor Napoleon I) and the restoration of the French Empire, which stood for law and order, anti-radicalism, anti-socialism and for the suppression of ideas such as the separation of Church and State. Pasteur himself enjoyed the French government's financial support and, on several occasions, was an invited guest of the Emperor at one of his country estates.[4] Pasteur was also a member of the French Academy of Sciences, composed of the most pro-government, scientific elite of France. Pouchet was a Corresponding member of the Academy, working in the provincial town of Rouen and thus was not among the inner circle that dominated the Academy in Paris. Indeed, the Committee designated to judge the contest was so dominated by Pasteur's elite supporters that at one point Pouchet withdrew his entry, feeling the cards were stacked against him. He was finally persuaded by friends to re-submit the reports of his experimental work, but with some misgivings.

[4]At one point, Pasteur even ran for the French Assembly (analogous to the United States Congress) as a member of the Conservative Party.

On the religious side, Pasteur was a devout Roman Catholic. As early as 1850, he had enthusiastically supported Emperor Napoleon III's use of French troops to restore Pope Pius IX to the Papacy in Rome, from which the Pope had been driven by Italian insurgents. Pius IX was strongly interested in restoring the Church to its former place of political prominence in France. He became noted for his condemnation of all tendencies toward what he termed "religious tolerance" and "modernism" and for his convening the Vatican I Council meetings in Rome in the 1860s, at which he proclaimed the Dogma of Papal Infallibility (1870). By the early 1860s, both the Church and the French government had formed powerful allegiances to combat any tendencies, political, religious or intellectual that appeared to challenge orthodox views.

Geison and Farley suggest Pasteur viewed the idea of spontaneous generation as a serious challenge to the established religious views of "special creation" then officially supported by Church and State. Charles Darwin's *Origin of Species* had been published in 1859, just two years before the Pasteur–Pouchet debates began, and the same year that Pouchet had published a major work advocating the possibility of spontaneous generation and presenting some of his experiments. Darwin's book had raised the inevitable question of how the first forms of life had originated on earth and the theory of spontaneous generation of simple forms like bacteria *seemed* to provide an answer. A belief in the connection between Darwinism, philosophical materialism and atheism was further reinforced by the fact that the translator of Darwin's book into French, Clemence Royer (1830–1902), was herself an avowed materialist who saw *The Origin* as promoting a thoroughly naturalistic account of the formation of species. Although he explicitly denied any connection, Pouchet's ideas were viewed by many of his contemporaries, including Pasteur, as advancing the cause of materialism and therefore supporting attacks on the fundamental tenets of established religion.

In a lecture he gave in 1864 at the Sorbonne, perhaps the most famous of the French universities, Pasteur himself made clear his view of the relationship between the theory of spontaneous generation and liberal, "atheistic" ideas. The great question of the day, Pasteur began, was the permanence of species in contrast to the Darwinian idea of their slow transformation. "What a triumph it would be for materialism," Pasteur told his audience, "if it [the theory of evolution by natural selection] could claim that it rests on the [scientifically] established fact of matter organizing itself, taking on a life of its own … To what good, then, would be the idea of a Creator, God?" Although he goes on to tell his audience that questions of science cannot be decided by religious doctrine, it seems quite likely that Pasteur's own deep-rooted political and religious convictions played an important role in determining which side of the debate he supported. This interpretation is further strengthened by the fact that Pasteur did not bother to repeat Pouchet's most controversial experiments, asserting without providing experimental evidence that the apparent spontaneous generation of bacteria Pouchet observed must have been due to contamination of the broth.

The Pasteur *versus* Pouchet case illustrates that bias may have both a positive and a negative influence on scientific work. On the positive side, Pasteur's opposition to spontaneous generation led him to champion an opposing view, the germ theory of disease, which emphasized that disease may be transmitted by bacteria through personal contact between people or through the air. The germ theory was to have an enormously beneficial impact on medicine and public health in the ensuing decades. Yet Pouchet's view also had its positive side. By promoting the idea that the origin of life could be studied by chemical and physical means, he pioneered a line of research that has become increasingly fruitful and important in biological research today. Conversely, Pasteur's opposition to spontaneous generation prevented him from evaluating Pouchet's own evidence more carefully and from seeing that the question of the origin of life could be approached from a purely chemical and physical point of view. Ironically, although he privately entertained the *possibility* of a chemical explanation for the origin of life, Pasteur did not pursue such possibilities extensively, nor did he repeat them publicly. At the same time, Pouchet's advocacy of spontaneous generation led him to de-emphasize the importance of transmission of bacterial infection and thus the significance of the germ theory of disease.

Perhaps the greatest irony in this story is that *both* Pouchet and Pasteur were right. You may have noted in the description of their experiments that the two men were using different sources of organic matter: Pasteur's was beef broth while Pouchet's was a hay infusion, a liquid prepared by soaking hay in water. Because he did not repeat Pouchet's experiments using the hay infusion, Pasteur did not discover that the natural bacteria found in hay include some species that can form spores, which enable them to survive severe conditions like drought, cold or heat. The spores present in Pouchet's preparation were heat resistant enough to survive the short boiling time to which he subjected them, thereby being able emerge from their dormant stage and start reproducing once the flask cooled down. It was to be another several decades before the existence of heat-resistant spores was recognized by microbiologists.

2.8 The Concept of Paradigms

In June, 2000, the National Aeronautics and Space Administration (NASA) announced that new photographs, taken by an orbiting satellite, provided evidence that their might be sub-surface water on the planet Mars. This water is thought to occasionally break through the surface and erode the Martian surface, creating meandering, river-like channels revealed by satellite and other photographs.

Since the presence of water on Mars suggests strongly the possibility of past or present simple forms of life there, the NASA announcement received wide coverage in the popular press. However, as one astronomer noted, the discovery did not mark a major "paradigm shift" in his field. In essence, what the astronomer was conveying by this comment was that the announcement was "no big deal" and that, while the new pictures may have provided greater detail than before, the presence of channels on Mars (some of which, like those identified in the early part of the twentieth century resembling dried up riverbeds) had been known for decades. Thus the NASA announcement was not that new to anyone familiar with the field of Martian geography.

The expression "paradigm shift" is one that has received increasingly wide use over the past few decades. In his 1962 book, *The Structure of Scientific Revolutions*, historian Thomas Kuhn (1922–1996) introduced the term "paradigm" (Gr., *paradigma*, pattern) to refer to a broad collection of ideas, assumptions and methodologies that guide research in any field of science. Kuhn recognized that, once established, paradigms often resist change, even in the light of considerable contradicting empirical evidence. When the evidence against an established paradigm reaches a certain level, a "scientific revolution" or what Kuhn called a paradigm shift occurs, and a new way of viewing the world, or a particular set of problems, emerges. Kuhn noted that there may be large scale paradigm shifts—for example from the geocentric to the heliocentric view of the universe—and more restricted paradigm shifts—for example, from viewing the blood as ebbing and flowing in the body (as viewed in ancient times) to seeing it as circulating in a one-way path from arteries to veins back to arteries through the heart (from the 17th century onward). According to Kuhn, all paradigm shifts, large or small, share certain characteristics in common and reveal a number of important features about how science is practiced. Before listing some defining characteristics of paradigms and paradigm shifts, it will be useful to examine two historical examples.

Darwin and the Theory of Evolution by Natural Selection

One of the most profound shifts in our way of thinking about the living world came with the publication in 1859 of Charles Darwin's *On the Origin of Species*, in which he put forward his theory of the transformation of animal and plant species over time by the mechanism of **na**tural selection.

Since the earliest written records, human beings have wondered how the myriads of types of animals and plants found on earth—what we today refer to a biodiversity—could have arisen. In western culture from the ancient world through the nineteenth century, the traditional explanation for biodiversity has been the doctrine, (paradigm) of special creation. The various types of organisms, called *species* (borrowing Plato's terminology for ideal, fixed categories), were thought to be each a separate entity, created by God in their present forms, stable and unchanging (immutable) over time. Although species were recognized as separate entities, it was also apparent that they could be grouped into similar types (e.g. as members of the dog family, or the cat family, oak trees, pine trees), which shared many characteristics in common. Such groupings were interpreted under this older paradigm as representing God's plan for "Nature". As well as being part of religious dogma, this older paradigm of biodiversity also formed the basis for the work of important naturalists such as Karl von Linné (Carolus Linnaeus, in the Latinized name under which he wrote), whose widely used classification system grouped species by shared traits.

By 1800, however, the older paradigm (which we may call the Linnaean paradigm, since that is the explicit form in which most naturalists would have encountered it) was facing some unexplained observations. In his work on paradigms, Kuhn referred to such unexplained observations as *anomalies*. For one thing, geologists had unearthed multitudes of fossils. Some of these fossil forms were strikingly similar to forms still living today, while others (dinosaurs, feathered reptiles) were bizarre and had no living counterpart. Why should so many forms have perished? Why were large groups of organisms, like vertebrates, or flowering plants, all built on the same basic plan? Why were there certain patterns of the geographic distributions of organisms rather than a random distribution?

Between 1831 and 1836 Darwin traveled around the world as an unpaid naturalist on board a British exploratory vessel, the H.M.S. Beagle. He saw an enormous variety of life in an equally enormous range of habitats. From this experience and from copious reading, Darwin gradually came to accept the idea that species were not fixed and immutable, and that the species we see on earth today must have descended with modification from species that existed in the past. For example, species that share many characteristics in common, such as the orchids, must have all descended from a common ancestor. Darwin thus embraced the theory of transmutation of species (today known as evolution), which a few other naturalists had already put forth in one form or another, though not very successfully.

Darwin went on to propose a second theory, that of natural selection, as the mechanism for how evolution might occur. The theory of natural selection is based upon several observations: (1) More organisms are born than can survive, resulting in competition for scarce resources. (2) All organisms vary from one another; those organisms that have favorable variations will survive a little bit longer or be more vigorous, and as a result will be more fit for the environment in which they live. (3) The more offspring the individual leaves, the more fit that individual is said to be. (4) Many of these offspring will carry the favorable variations they inherited from their parents, and will in turn leave more offspring than other members of the population who lack this variation. In this way new and more favorable variations will spread gradually through the population, transforming its overall characteristics. (5) Since variations occur more or less randomly, if two portions of a single population are somehow isolated from each other for long periods of time, different variations will accumulate in each population, producing divergence in their characteristics. The result will be that eventually two species will have been derived from one common ancestral form, an evolutionary process known as speciation. Continuous speciation has led to the wide variety of organisms that have populated the earth in the past and today.

Darwin's paradigm challenged every aspect of the older Linnaean paradigm. Species were no longer viewed as fixed and immutable, but plastic and ever-changing; they arose not by a supernatural act of creation but by natural processes going on every day. Species were not composed of a single "type" representative of the whole, but by populations that exhibited a range of variability

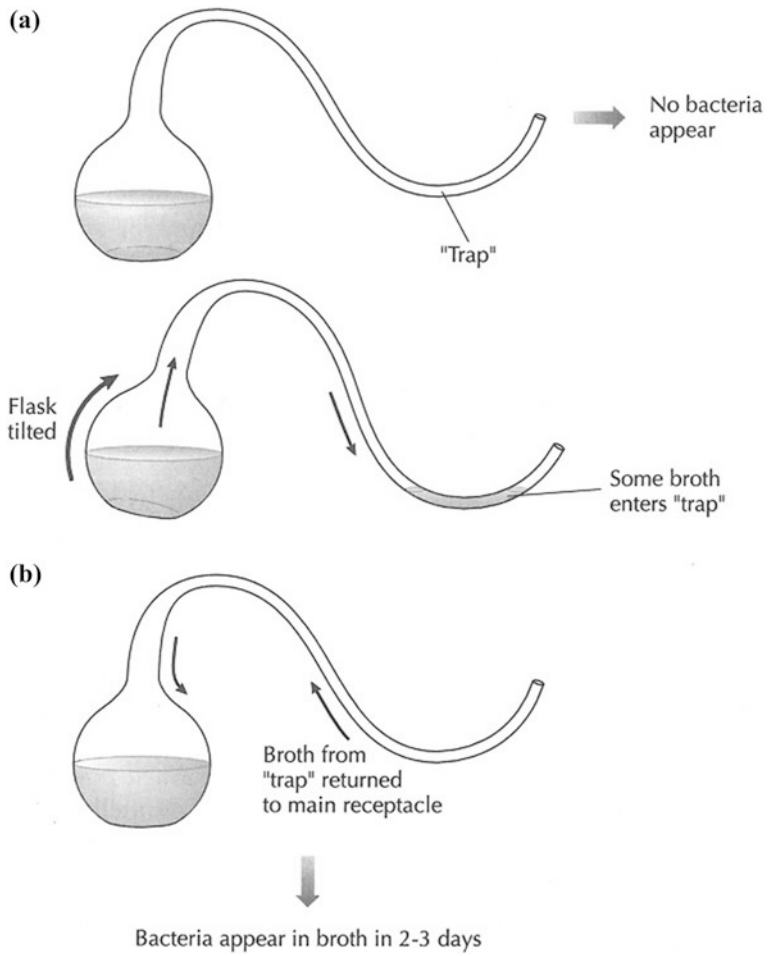

Fig. 2.10 Drawings of Louis Pasteur's swan-nceked flasks used for his studies on spontaneous generation of microbes (1860–61) [original art from authors]

for every trait. Extinction was not a result of God's displeasure with species, but of competition and the constant struggle for existence between various species for material resources. Most important, from the point of view of scientific methodology, Darwin's paradigm was thoroughly naturalistic (materialistic in the philosophical sense, as described in the previous section), and did not invoke any supernatural or occult causes.

The shift from the Linnaean to the Darwinian paradigm was neither easy nor quick. Many older naturalists simply could not accept the notion of species changing from one form to another; the idea of the fixity of species was too ingrained in their world-view. Others gradually accepted evolution—descent with modification from common ancestors—but could not accept the mechanism of natural selection, especially the idea that variations occurred by chance rather than in response to the needs of the organism. Though we often speak of a Darwinian "Revolution," it took until the mid-twentieth century for most of the initial objections to be resolved in favor of Darwin's basic paradigm.

From the start, the Darwinian paradigm encountered enormous opposition from organized religion. As we have seen, even so eminent a scientist as Louis Pasteur found the Darwinian paradigm unacceptable on religious and philosophical grounds. Although many religions found ways to reconcile the Darwinian paradigm with broad theological doctrines, many, especially those that emphasize the literal interpretation of the Bible, continue to object to the evolutionary paradigm right down to the present day (see Chap. 5, Section on "Scientific Creation" and "Intelligent Design"). As Kuhn emphasized, paradigm shifts do not come easily.

A Paradigm Shift in Molecular Biology: From the "Central Dogma" to Reverse Transcription

In the 1960s the major paradigm of how deoxyribonucleic acid, or DNA, the molecule that made up the genes of most organisms on earth, controlled hereditary traits was referred to as the "*Central Dogma*" of molecular biology. It was called "dogma" (despite the negative connotation of this term in scientific circles) because it was supposed to be a universal paradigm. The "central dogma" stated that DNA exerts its effects by serving as the template for transcribing a second form of nucleic acid, ribonucleic acid (RNA) that in turn guides the assembly of a specific protein molecule. The central dogma is often represented as a simple flow diagram:

$$\text{DNA} \xrightarrow{\text{Transcription}} \text{m-RNA} \xrightarrow{\text{Translation}} \text{Protein}$$

The first step (first arrow), in which messenger-RNA (mRNA) is synthesized from DNA is known as transcription, while the second phase (second arrow), in which mRNA guides the production of a specific protein, is known as translation. As it was conceived in the early 1960s, both phases of the process were thought to be unidirectional. The central dogma became the paradigm for how genes function chemically in all organisms.

In 1958 a young graduate student named Howard Temin was working with Rous sarcoma virus (RSV), a virus found in chickens and the first cancer-causing virus to be described. Viruses are very simple structures consisting, in this case, of a protein coat surrounding a nucleic acid core (Fig. 2.11a). It was widely known that RSV belonged to a special group of viruses, the retroviruses, whose hereditary material was made up of RNA rather than DNA. All viruses replicate themselves by attaching to a cell surface, injecting their DNA or RNA into the host cell, where the viral nucleic acid proceeds by one mechansm or another, to commandeer the cell's metabolic machinery to produce more viruses (Fig. 2.11b, c). One of the distinguishing features of RSV is that is does not usually kill the cell it invades but rather causes the cell to start dividing uncontrollably, thereby producing a sarcoma, or cancerous tumor. In 1964, while attempting to develop a chemical means of

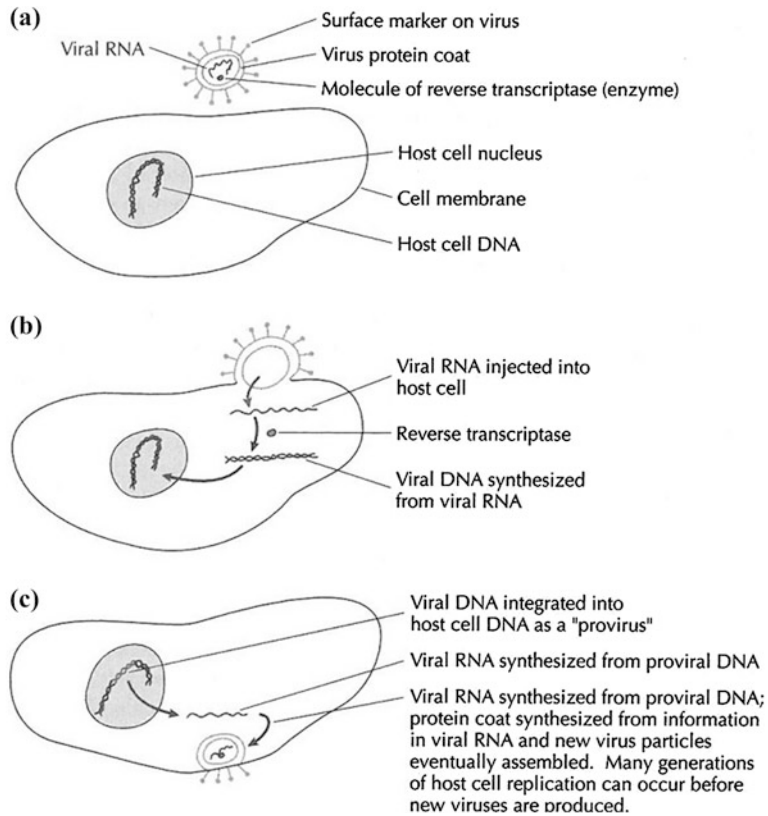

Fig. 2.11 Replication cycle of Rous Sarcome virus (RSV), showing the mode of infection of the host cell by the virus. RSV is an RNA virus, meaning its genetic material is RNA and DNA. By means of surface markers, the virus attached to the cell membrane and injects its RNA, along with a molecule of the enzyme reverse transcriptase, into the host cell. Reverse transcriptase, as Temin predicted, is able to catalyze the transcription of viral RNA into viral DNA, which is then integrated into the host cell genome as a "provirus." When the host cell's DNA is transcribed to make proteins, it also makes proviral proteins. Presence of these proteins stimulates uncontrolled cell division, producing a cancerous tumor. Moreover, the provirus replicates every time the cell divides, thus increasing dramatically the number of cells with provirus in them. Eventually, enough viral RNA and protein coat material is present and new viruses are assembled, breaking out of the cell and infecting other cells nearby. [original art from authors]

identification (assay) for cells infected with RSV, Temin made several interesting observations: (1) Cells infected with RSV showed recognizable modifications, which *were passed on to the progeny cells* even when no further viral replication inside the cell was observed. (2) Substances (such as cytosine rabinoside), known to block DNA synthesis prevent viral infection if applied within 12 h of the first contact between virus and susceptible cells. (3) Substances (such as actinomycin D) that inhibit the synthesis of RNA from DNA (transcription) allow infection to occur but block viral replication. These data suggested that RSV replication appeared to be a two-step process that somehow involved DNA replication, a rather surprising finding for an RNA-based virus.

To explain these results, Temin proposed what he called the **DNA provirus hypothesis**, which suggested that when RSV first enters a host cell it uses its own RNA as the basis for synthesizing DNA, DNA that now carries viral genetic information. Moreover, Temin argued, the new viral DNA becomes integrated into the DNA of the host cell (in which form it is known as a **provirus**), and is replicated with it every time the cell divides. The provirus DNA, when transcribed and translated into protein (by the central dogma pathway) leads to uncontrolled cell division, or cancer. What was so novel, and troubling, about Temin's new paradigm was that it postulated a reversal of the central dogma: in particular situations, RNA could guide the production of DNA.

The first reaction to Temin's paradigm was almost universal rejection. Not only did it go against the entrenched paradigm of the central dogma, but repeated attempts to detect the presence of proviral DNA in the host cell proved fruitless. Temin continued to search for ways to detect the presence of proviral DNA or other tell-tale signs of proviral activity. Then, quite independently, in 1970 Temin and another researcher, David Baltimore, discovered a new enzyme (enzymes are proteins that catalyze biochemical reactions in organisms) in RSV-infected cells. This new enzyme was called reverse transcriptase because it catalyzes the synthesis of DNA from an RNA precursor. Later, other varieties of reverse transcriptase were found as a normal component of animal cells not infected by RSV. These findings clinched the story and from the mid-1970s on, the provirus and reverse transcription paradigm has gained wide acceptance.

Characteristics of Paradigms

It may be useful to ask at this point why do we bother to talk about "paradigms" at all? Why not just refer to Darwin's "theory" of evolution by natural selection, or Temin's "theory" of reverse transcription? What has been gained by Kuhn's new terminology and analysis of scientific change?

Paradigms are more comprehensive than theories. A paradigm is a collection of theories; but also has embedded in it a variety of assumptions, particular methodologies, and is shared by a particular community of investigators. As we have seen, the Darwinian paradigm encompasses not just the theory of evolution, but also the theory of natural selection, theories about the nature of heredity and variation, about adaptation of organisms to particular environments, and about speciation, among others. An advantage of seeing a paradigm as consisting of a variety of theories is that it helps us understand how scientific ideas gain acceptance (or rejection). For example, Darwin's view that hereditary variations were always very small changes has been challenged by biologists at various points in the past (and even at present), although these critics do not oppose the concept of evolution or natural selection.

Paradigms embody certain methods that are agreed upon as appropriate by the community of investigators in the field. For example, molecular geneticists agreed that, if Temin's paradigm were to be accepted, it was necessary to use biochemical methods to identify an enzyme that would carry out reverse transcription. Agreement on the methods and instruments that are used in a field is one of the main components of a paradigm that knits its adherents together into a social as well as intellectual community. Agreement on methods is also crucial if workers are to evaluate each others' data and discuss its interpretation meaningfully.

Particularly important, paradigms, more than theories in the traditional sense, represent world views, or global ways of seeing nature. A Darwinian paradigm of species transformation is a very different view of the natural world than the old Linnaean view of static, immutable species. The Darwinian world is ever-changing, dynamic, never at rest. Change is both expected and celebrated, for it is the means by which organisms survive and adapt to an ever-changing environment. Similarly, the Temin paradigm presents a view of the cell that is more flexible, with a repertory of processes that can meet a larger variety of physiological needs. By contrast, the paradigm represented by the central dogma presents a view of the cell that is more rigid and mechanical. More than just discovering the nature of reverse transcription, Temin's paradigm suggests we should not so readily accept the idea that cells (or any biological system) have only one way of doing things. As one of the characters says in the movie *Jurassic Park* I, "Life will always find a way."

Kuhn's analysis is particularly helpful in understanding how scientific ideas change. Paradigm shifts are more difficult than merely substituting one theory for another, precisely because paradigm shifts involve a whole change in world view. In Darwin's case that world view encompassed not only naturalists' conceptions of species as fixed or immutable, but the religious doctrine of Special Creation and the role of God as Creator. It is no wonder that the reaction against the Darwinian paradigm was so violent, and has been so long-lasting. In a smaller way, the paradigm shift from central dogma to reverse transcription had its initially strong opponents, who ridiculed the idea that DNA could be made from an RNA precursor. The shift in world view to reverse transcription cast the fundamental relationship in molecular genetics between DNA (genes), RNA and proteins in a completely different light. Reorienting that relationship required a shift in world view, at least for those working in molecular genetics.

Indeed, in recent years, the idea that DNA can be made from RNA has had major implications for understanding the origin of life. This view suggests that the first living forms on Earth contained RNA as their basic genetic material, giving rise to what molecular biologist Walter Gilbert called the original "RNA World." The concept of RNA as a primordial self-replicating, genetic molecule[can be found in theoretical papers by Francis Crick (co-discoverer with James D. Watson of the structure of DNA), Leslie Orgel (1927–2007) Carl Woese (1928–2012) and others in the 1960s and 1970s. The fact the certain forms of RNA also have catalytic as well as self-replicating properties gave this hypothesis further credence. Scientists today hypothesize that DNA eventually became the molecule of heredity in most forms later, because of its overall greater chemical stability. The idea of reverse transcription thus allowed biologists working on the origin of life to formulate a much clearer picture of how earliest living forms could have evolved with a simpler form of hereditary molecule.

Old paradigms are replaced with new ones when "dead-ends" are reached; for example, when it is simply no longer intellectually satisfying to account for every aspect of species diversity or the fossil record by simply claiming that "God made it that way." Old paradigms also tend to get overthrown when they act to restrict rather than expand the scope of the questions being asked. One of the positive outcomes of a paradigm shift is that new areas of research open up, new sets of questions are asked and research projects designed to answer them. Resistance to paradigm shifts emanating from within the scientific community merely suggests that scientists, like other specialists, may get so hung up on their own tiny set of problems that they can see the world from only one viewpoint and are blinded to alternatives. In many historical examples, paradigm shifts occur not simply because scientists become intellectually convinced that new evidence is so overwhelmingly in favor of the new paradigm, but because the older scientists retire or die and younger scientists, with fewer ties to the old paradigm, take their place.

Kuhn's analysis has also provided a more realistic understanding of how science works. An older and more traditional view of science was that it changed by adding more and more information to its basic storehouse of facts and an increasing refinement of its conceptual foundations. In this view, science is cumulative, with each successive generation progressing toward a more accurate views of nature. Kuhn's view suggests that while the measurements and data of science may in fact accumulate in some sort of linear way, conceptualizations of science can undergo radical change. Old paradigms are completely discarded and are replaced lock, stock and barrel by new paradigms. A Darwinian view of species is not just a modified Linnaen view—after Darwin, species, even old data about any given species, were seen in a different light. To Linnaean taxonomists, variations among members of a species were a nuisance that they had to look beyond to make a proper classification. To Darwinians, variation is the crucial feature by which species evolve to meet new challenges from their environment. Far from being a nuisance, variation is now seen as a creative force in the history of life.

2.9 Modern Science, Materialism and Idealism

Mechanism and Vitalism

Distinct differences between living and non-living matter are obvious. The ability to move, ingest materials from the environment and convert it into more living material in the process we call growth; indeed, all of those properties we associate with living organisms, are clearly qualitatively different from anything observed in non-living matter. In the late nineteenth and early twentieth century, recognition of this fact led to a resurgence of a much older philosophical debate among biologists. The debate was between those who called themselves mechanists and those who called themselves vitalists. Vitalists explained the unique features of living matter by postulating the existence of a "vital force" (*élan vital*). This vital force was assumed to be wholly different from other known physical and chemical forces and ultimately to be unknowable, that is, not subject to physical and chemical analysis. The postulated vital force departs from a cell or an organism at death. It should be stressed that vitalists did not deny that chemical analyses of living organisms are valuable, but felt that what we call "life" involved something more than that which can be described by the principles of chemistry and physics

A classic example of vitalist thinking appears in the memoirs of Assistant Surgeon Edward Curtis of the Washington, D. C. Army Medical Museum. On April 14, 1865, president Abraham Lincoln was shot in Ford's Theater in Washington and died the next morning. An autopsy was performed in the Northeast Corner guest room of the White House. In the words of Dr. Curtis:

> Silently, in one corner of the room, I prepared the brain for weighing. As I looked at the mass of soft gray and white substance that I was carefully washing, it was impossible to realize that it was that mere clay upon whose workings, but the day before, rested the hopes of the nation. I felt more profoundly impressed than ever with the mystery of that unknown something which may be named "vital spark" as well as anything else, whose absence or presence makes all the immeasurable difference between an inert mass of matter owing obedience to no laws but those governing the physical and chemical forces of the universe and, on the other hand, a living brain by whose silent, subtle machinery a world may be ruled.

This example illustrates clearly a vitalistic belief in some sort of supernatural factor differentiating living from non-living matter. In brief, the vitalist philosophy may be expressed as one that viewed the whole as being greater than the sum of its parts.

Mechanists, on the other hand, maintained that organisms were simply physical and chemical entities composed of material parts whose functions could be investigated and ultimately explained by the ordinary laws of physics and chemistry. In contrast to vitalists, mechanists viewed organisms as merely complicated machines. Basic to the mechanist view was the idea that organisms are composed of separate parts (molecules, cells, organs) and that we need to merely study these parts in isolation to explain the working of the whole. In stark contrast to vitalists, mechanists maintained that the whole is equal to the sum of its parts, no more, no less. Thus to learn about how the heart works, for example, a physiologist might remove the heart from an experimental animal, place it in a perfusion chamber where it could be exposed to fluids with different hormones or chemical transmitters, and the effect on the rate of the heartbeat measured. By such procedures, mechanists thought that all the characteristics of the heart or, indeed, any component of the organism, could be understood.

Experiments by two German biologists played a role in the late nineteenth and early twentieth century will serve to illustrate how the vitalist-mechanist controversy played out in an actual research context. A major question of interest among embryologists at the time was what caused cells of the early embryo to eventually differentiate into the many different cell types (nerve, muscle, skin) that make up the adult organism. Wilhelm Roux (1850–1924) hypothesized that the fertilized egg was made up of particles that determined each cell type of the adult organism, and that as the cells divided during embryonic development these particles were parceled out differentially to daughter cells, so that ultimately each cell type ended up only the particles for its own characteristics. This was known as Roux's mosaic hypothesis and was obviously a very mechanical hypothesis to explain differentiation. However, it had the advantage of being testable. Roux worked with frog eggs, which he fertilized and allowed to undergo one cell division, creating a two-cell embryo (Fig. 2.10 left). According to the mosaic hypothesis the particles determining the right and left side of the organism should already be parceled out into the two separate cells. He then killed one of the cells with a red hot needle, predicting that if his hypothesis were correct, the resulting embryo should only develop one half of its body. The result was the formation of an incomplete, "half" embryo (Fig. 2.10 right). Roux interpreted these results to support the mosaic hypothesis, and the view that differentiation was indeed the result of a physical, mechanical process.

Hans Driesch (1865–1941), ayounger contemporary of Roux's, performed a similar experiment, but because he was working at a marine laboratory (the Naples Zoological Station), he used fertilized sea urchin eggs instead of frogs. However, after the egg divided into the two-cell stage, instead of killing one of the first two cells, Driesch separated them from one another by shaking the solution vigorously. The result was that both cells formed complete sea urchin larvae (Fig. 2.11). For Driesch, these results indicated that embryos were not merely some sort of mechanical entities but were harmonious systems that had the power of self-regulation and adjustment to altered circumstances. After a decade of using a variety of physical and chemical methods to investigate this problem, Driesch became a champion of vitalism, eventually giving up science completely and becoming a professor of philosophy. To him, the ability of the separated blastomeres to adjust to the new conditions imposed on them yet still undergo normal development, argued strongly in favor of the presence of some inherent, non-physical/chemical force that guided development. He was opposed vigorously in this view by Roux, who became one of the major exponents of the mechanistic view, developing a comprehensive research program known as "Developmental Mechanics." The written arguments between the two scientists became long and often highly polemical. Despite the controversy the two men remained cordial friends until Roux's death in 1924. However, the controversy their work engendered continued well into the first half of the twentieth century (Figs. 2.12 and 2.13).

The mechanist-vitalist debate was part of a much large philosophical dispute that has recurred in one form or another from the ancient Greeks to the present day between two broad, but mutually exclusive philosophical systems: idealism and materialism. These philosophical terms should be distinguished from their more familiar counterparts, in which "idealism" refers to an unrealistic and naïve view of the world and "materialism" to an undue concern with material possessions and wealth. Philosophical idealism and materialism have quite different meanings. Philosophical idealism derives much of its modern content from the writings of

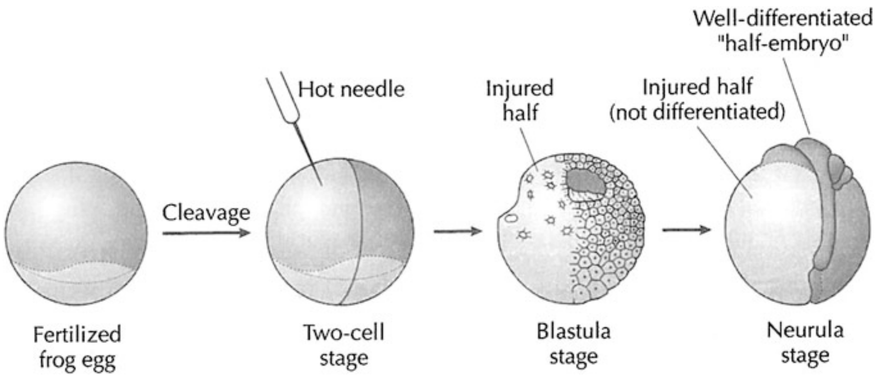

Fig. 2.12 Wilhelm Roux's experiment, in which he pricked one of the first two blastomeres of the frog egg with a hot needle, killing it. The result was development of a half-embryo that only reached partial development. These results supported Roux's mechanistic interpretation of development: each blastomere was already determined at the first cell division to produce half the embryo [from Viktor Hamburger, *The Heritage of Experimental Embryology* (N.Y., Oxford University Press, 1988): p. 10]

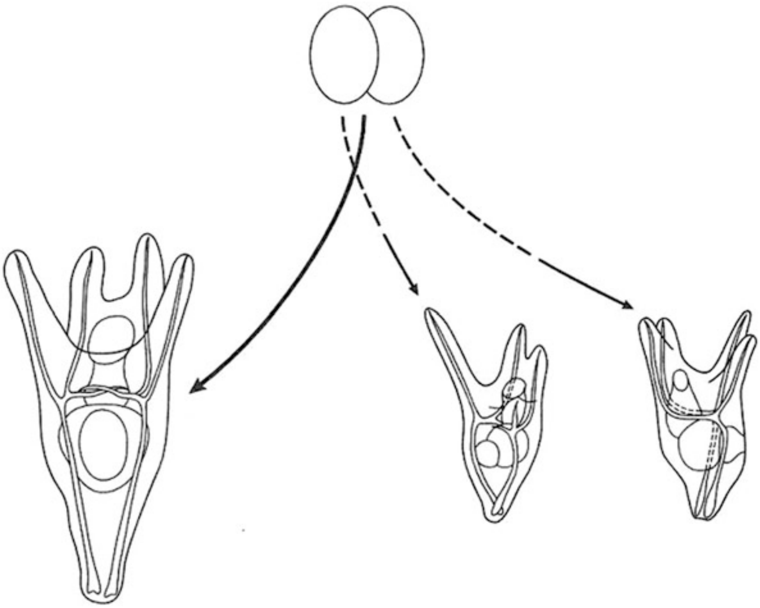

Fig. 2.13 Hans Driesch's experiment, separating the first two blastomeres (*top*) of the sea urchin egg. To the left a normal sea urchin larva developed from unseparated blastomeres, and to the right two slightly smaller but otherwise perfectly formed larvae developing from each separated blastomere. These results contradicted Roux's interpretation by showing that embryos have remarkable abilities to adjust to changed circumstances and are thus not mechanically determined in the way Roux had imagined [from Viktor Hamburger, *The Heritage of Experimental Embryology* (N.Y., Oxford University Press, 1988): p. 10]

Plato and the Platonic tradition in western philosophy. The basic claims are that ideas or non-material causes are the initial and prime movers in the world. Plato saw all material objects, for example, as crude reflections of the ideal object existing as a category, in the mind of the Creator. The Linnaean species concept described earlier is an example of idealist thinking in that each species existed in the mind of the Creator prior to its taking material form on Earth, e.g., all cats reflect the ideal or essential category of "catness." There are real cats in the world, of course, but the category of "catness" existed prior to and apart from the appearance of actual cats on the earth's surface and represents the idealized form underlying the group as a whole. Aspects of most contemporary religions are based on idealistic philosophy: for example, in the belief in a supernatural creator, in the power of prayer, or in miracles (see Chap. 5). Though they may not necessarily express their idealistic views in religious terms, vitalists are clearly idealists in this sense. Idealists do not deny the existence of material reality; they simply relegate it to a secondary role as a causal agent behind many biological processes.

By contrast, philosophical materialism is the view that all processes in the universe are the result of matter in motion. Matter is primary; everything else, including abstract ideas about matter and how it functions, are derived from that material reality through our interaction with it. Species, for example, do not exist as an abstract or idealized category apart from the material populations of organisms that form them in nature; we may, of course, create species categories, but they derive from observing actual organisms in nature, not from any a priori existence in themselves. Evolution does not occur because of God's plan or abstract "drives toward perfection" but because organisms are competing with one another for scarce material resources and their physical variations give them different survival and reproductive potentials. Materialists maintain that nothing is unknowable, though, of course, at any one point in time vast amounts remain unknown. For materialists, the methods of physics and chemistry are the proper tools for understanding the natural world. Modern science since the seventeenth century has rested firmly and increasingly, on a materialist foundation.

In the vitalist-mechanist debates, vitalists were clearly arguing from an idealist position and mechanists from a materialist position, Although both sides made important points, the debate ultimately became counterproductive. Mechanists saw clearly that since, by definition, vital forces were beyond the reach of scientific study, vitalism put limits on scientific research. They therefore rejected it. By the mid-twentieth century, however, many biologists came to the realization that the mechanistic view was too simplistic to account for many functions known to occur in living organisms: the self-replication of molecules, the self-regulation of physiological processes, embryonic development, and a host of other activities that had no counterpart in known machines of the day.

Is there an alternative to the mechanistic materialist approach other than vitalism? Biologists, and philosophers often inspired by biological examples, have developed a second form of materialism, holistic or dialectical materialism, which avoids the pitfalls of both idealism and of mechanism. The basic tenets of the holistic-dialecical approach are:

1. No part of any system exists in isolation. For example, one of the functions of the liver is to remove sugar from the blood and convert it to animal starch (glycogen) for storage. The liver is changed by removing sugar from the blood and the chemical conversion to starch, as is the blood by virtue of having sugar removed from it. Thus while both blood and liver may be described partially in isolation, neither can be understood fully except in their interactions with each other and other parts of the body.
2. Unlike machines, living systems are dynamic entities, constantly in a process of flux and change. This change results from the constant interaction of internal and external forces.
3. The internal processes of any living system undergo change as a result of the interaction of opposing forces. For example, all living organisms carry out both anabolic (build-up) and catabolic (breakdown) chemical reactions. The growth and development of a seed represents a change in which the overall effect of anabolic reactions is greater than that of catabolic reactions. Maturity occurs when the two are balanced and aging and death result from the dominance of catabolic over anabolic processes. Far from being accidental, this developmental process is programmed into the genetic makeup of the organism. At all stages, the overall process may be studied most fruitfully by investigating the interaction of anabolic and catabolic process, rather that either process alone. This is the part of the approach that is dialectical, meaning two opposing tendencies or processes.
4. The accumulation of many small quantitative changes may eventually lead to a large scale, qualitative change. For example, the heating of water from 90 to 91 °C represents a quantitative change since, although it is one degree warmer, the water is still a liquid. However, when the temperature goes from 99 to 100 °C, the water begins to boil and become the gas we call steam. This represents a qualitative change, since water and steam have quite different physical properties. Thus an accumulation of many quantitative changes has resulted in an overall qualitative change. This is as true of the biological as of the physical world. For example, if a nerve attached to a muscle is stimulated with a low voltage electric shock, the muscle may not respond. With an increase in voltage, a quantitative change, a qualitative change is eventually achieved in the nerve, an impulse is transmitted, and the muscle contracts.

If organisms are viewed as just described by these four tenets, the vitalists were correct: the whole is greater than the sum of its parts. Organisms do function as wholes, not as a mosaic of separate parts. In many respects, however, the mechanism-vitalism dichotomy is artificial. Vitalism and the idealistic philosophy it represents is limited because it presupposes a mystical, unknowable force in living organisms that, by definition, lies beyond scientific investigation. Mechanistic materialism, on the other hand, in trying to ground biological investigations in knowable but separate physical entities, has found it impossible to account for the holistic properties of complex systems like living organisms. Biologists are today developing new ways to understand the many interactions inherent in complex systems like organisms, including the mathematical theory of systems analysis combined with the power of modern computers. These new approaches do not preclude the mechanistic, analytical approach to studying individual components of organisms in isolation; in most cases this is the only way to begin to understand the parts that make up any complex system. But we now know this is not enough—it is only the first step. Biologists are increasingly adopting a more holistic, yet still materialist approach that transcends the old mechanist—vitalist debates.

2.10 Conclusion: The Strengths and Limitations of Science

Since its origins in the 17th century, modern western science has proven to be by far the most powerful way of understanding the natural world. As we have seen, one of the greatest strengths of science lies in its emphasis on logical thinking and on formulating testable hypotheses in ways that lead to accurate or refutable predictions. A second strength, growing out of the first, is the insistence that hypotheses and the predictions that follow from them must be testable. A third strength of science is its emphasis on repeatability. A single empirical test, even one repeated by the same experimenter many times, is seldom enough to convince most scientists; the results must be capable of being replicated under the same conditions by others. Thus a fourth strength of science lies in its critical, self-correcting nature. By checking their own results as well as those of others, any errors are far more likely to be uncovered.

Still, as powerful as it may be as an intellectual tool, science also has distinct limitations. For one, science is limited to dealing with observable phenomena; the empirical data on which hypotheses must ultimately be based. Without empirical data, even the most intriguing hypothesis has little value. Thus, science has absolutely nothing to say one way or the other about the existence of a God or gods, a human soul or vital forces; empirical data on such entities are simply not obtainable. Similarly, science is also limited by the availability of the tools and techniques by which scientific data are gathered. Prior to the development of the microscope, for example, we knew nothing of the sub-microscopic world; prior to the telescope, we could only speculate about the universe beyond what our eyes could directly see.

Through the self-critical process that characterizes their activity, scientists are forced to constantly modify and many times reject cherished hypotheses. This is *not* because scientists are necessarily more honest and conscientious than persons in other fields, but rather that honesty is reinforced in science by virtue of its system of peer review; all scientists are well aware that others in their field are monitoring their research to make certain that its results can be replicated. No scientific idea is likely to remain unchallenged or unchanged; indeed, scientists are probably as more often wrong than right. The 19th century physiologist Johannes Müller asserted that the velocity of a nerve impulse would never be measured; six years later, his student Hermann von Helmholtz measured it in a frog nerve only a few centimeters long.

The chemist Ernest Rutherford stated that the energy in the atomic nucleus would never be tapped; the first atomic bomb exploded just seven years after his death.

Clearly if scientists can be wrong, as we have seen, so can scientific hypotheses. Yet, although it may appear to be a limitation of science that it cannot "prove" anything and that its hypotheses and theories are always open to rejection or modification, in fact, this limitation is actually its greatest strength. As biologist Garrett Hardin (1915–2003) has put it:

> It is a paradox of human existence that intellectual approaches claiming the greatest certainty have produced fewer practical benefits and less secure understanding than has science, which freely admits the inescapable uncertainty of its conclusions.

Hardin is correct: the strength of science does not lie in any claim to infallibility but rather in being an ongoing intellectual process with no pretense of providing final answers or absolute truths. Nor does this strength lie solely in its logical underpinnings, for the conclusion of a perfectly logical argument may well be utter nonsense. The inherent self-criticism of science and its constant search for a better understanding of the natural world through the elimination of false hypotheses, is the source of its immense intellectual power.

2.11 Exercises

1. Distinguish between observation, fact, hypothesis and conceptualization in science.
2. Each statement below (a–e) can be described as either

- An observation
- A fact
- A conceptualization

Indicate which of the three above possibilities *best* characterizes each of the following statements:

(a) All 100 observers agreed that the sun rises in the east every day.
(b) This green apple is sour.
(c) Planets move from west to east against the background of fixed stars because they are revolving around the sun just like the earth.
(d) The United States fought in Vietnam to preserve democracy from communist aggression.
(e) All green apples are sour.
(f) The report said the witness was lying.

Explain your choices in each case.

3. Devise hypotheses to account for the following observations, and design an experiment or suggest further observations to test your hypotheses.

   (a) There are more automobile accidents at dusk than at any other time of day.
   (b) When glass tumblers are washed in hot soapsuds and then immediately transferred face downwards onto a cool, flat surface, bubbles at first appear on the outside of the rim, expanding outwards. In a few seconds they reverse, go under the rim, and expand inside the glass tumbler.
   (c) In mice of strain A, cancer develops in every animal living over 18 months. Mice of strain B do not develop cancer. If the young of each strain are transferred to mothers of the other strain immediately after birth, cancer does not develop in the switched strain A animals, but it does develop in the switched strain B animals living over 18 months.

4. A biologist reported the following set of observations:
   "While sitting on my porch during the afternoon and early evening, I could not help but notice the chirping of the crickets. I noticed that the rate of their chirping slowly diminished as the sun approached the horizon. I wondered why this should be so. At first I guessed that it was due to the loss of light as the sun disappeared and night came on. Accordingly, I counted the number of chirps given by ten individual crickets in the laboratory as they were exposed to less and less light intensity." The following data were obtained:

At 10 candlepower	48 chirps per minute
At 8 candlepower	46 chirps per minute
At 6 candlepower	49 chirps per minutes
At 4 candlepower	55 chirps per minute
At 2 candlepower	47 chirps per minute
At 0 candlepower	48 chirps per minute

   (a) Formulate the hypothesis being tested in a deductive syllogism (If … then format).
   (b) Do the results confirm or reject the second hypothesis? Explain your answer.
   "I then wondered if temperature might be affecting the number of chirps. I reasoned that as the sun set, the temperature would drop as night approached. Accordingly, in the laboratory I kept the crickets exposed to constant light, but exposed them to varying temperatures." The following data were obtained:

At 34 °C	55 chirps per minute
At 30 °C	48 chirps per minute
At 26 °C	39 chirps per minute
At 22 °C	20 chirps per minute
At 18 °C	8 chirps per minute
At 14 °C	no chirping

(c) In this second experiment what hypothesis is being proposed, and what prediction(s) is (are) made from it?
(d) Do the results confirm or reject the second hypothesis? Explain your answer.

5. Indicate for each of the following deductive syllogisms whether they are examples of valid or invalid reasoning, and whether each represents
   A true conclusion deriving from a true hypothesis(es)
   A true conclusion deriving from a false hypothesis (es)
   A false conclusion deriving from a false hypothesis (es)
   A false conclusion deriving from a true hypothesis (es)

(a) *If* … All residents of the USA are Martians and
    if … all Martians pay taxes,
    then … all residents of the USA pay taxes.
(b) *If* … All dogs have four legs and
    if … this animal is dog
    then … this animal has four legs.
(c) *If* … All residents of the USA are Martians
    if … all Martians are green and have tentacles
    then … all residents of the USA are green and have tentacles.
(d) *If* … All dogs are four-legged animals
    If … this animal is four-legged
    then … this animal is a dog.
(e) *If* … All Martians are residents of the USA and
    If … all humans are residents of the USA,
    then … all Martians are humans.

6. Think of something in your personal life that might represent a paradigm shift—for example, switching from a typewriter to a computer, learning a new language, or recognizing that a personal relationship is not going to work out. Describe some of the changing feelings, realizations and behaviors you encounter during this shift.

7. P.F. and M.S. Klopfer of Duke University have studied maternal behavior in goats. The following facts have been established: A mother goat (doe) will reject her young (kid) if deprived of it immediately after birth, even if it is given back an hour later. If allowed contact with her own kid for five minutes after birth and

then separated from it, the doe immediately accepts the kid and its littermates, if any, when returned an hour later. If allowed contact with her kid immediately after birth and then deprived of it, the doe shows obvious signs of distress. However, if this early contact is denied, the doe acts as if she had never mated or given birth to young.

(a) Propose a hypothesis to account for these observations, along with an experiment to test your hypothesis. Do not read the remainder of the exercise until you have finished this part.
Now consider the following additional facts about maternal behavior in goats established by the Klopfers: under the conditions described above, the doe will not accept a kid of the correct age that is not her own (an alien kid) if it, instead of her own kid, is returned to her. Denied her own kid immediately after birth, but allowed five minutes with an alien kid, the doe will not only accept the alien kid but also her own when returned. However, only the alien kid with which she is allowed contact will be accepted; all other alien kids are rejected.
(b) How do these facts affect your hypothesis? (Do not change your hypothesis as given in the previous question, even if it did not fare too well, only consistency with the facts given and experimental design are of primary importance.)
(c) If necessary, propose a new hypothesis to account for all the Klopfers' data as given above and suggest an experiment to test this hypothesis. If your original hypothesis stands, fine. If needs modifying, do so.

Further Reading

Conant, J. B. (Ed.) (1957). *Harvard case histories in experimental science* (Vol. 2). Cambridge, MA: Harvard University Press. (The Harvard Cast Histories *have been extremely useful in teaching the nature of science by selecting a series of controversies in the physical and life sciences. The cases include explanatory material setting the context (mostly intellectual rather than social or political) in which the controversy took place with extended excerpts from the writings of the scientists involved. This approach provides students with the chance to learn how to read and analyze material from primary sources as well as understand the scientific issues of earlier times in their own terms. Cases range from the verthrow of the phlogiston theory by Lavoisier's oxygen theory, to the nature of plant photosynthesis in the work of Joseph Priestly and others in the late eighteenth and early nineteenth centuries, and Pasteur's and John Tyndall's work on spontaneous generation in the 1860s and 1870s.*).

Geison, G. L. (1995) *The Private Science of Louis Pasteur.* Princeton, NJ: Princeton University Press. (*One of the most recent, and controversial biographies of Pasteur, because it questions some of the most cherished myths about Pasteur as a scientist), Geison's book provides ample evidence of Pasteur's political and religious biases in the spontaneous generation controversy. The specific Pasteur-Pouchet controversy has been summarized in Garland E. Allen, "That Louis Pasteur Disproved Spontaneous Generation on the Basis of Scientific Objectivity," in Kostas Kampourakis (ed)* Myths in Science *Cambridge, MA: Harvard University Press, 2015, pp ____.*).

Farley, J. (1977). *The spontaneous generation controversy from Descartes to Oparin.* Baltimore, MD: Johns Hopkins University Press. (*This book is a very readable introduction to the history of ideas of spontaneous generation from the seventeenth to the twentieth centuries. It includes discussions of Spallanzani, Redi and Pasteur-Pouchet.*).

Grinnell, F. (1987). *The scientific attitude*. Boulder, CO: Westview Press. (*Written by a practicing scientist for undergraduates and graduate students in science, this book is a simple, straightforward introduction to many aspects of science as a process. Topics include problems of observation, experimental design and interpretation, science as a collective activity and "thought-style," how scientific ideas are perpetuated and become entrenched.*).

Kuhn, T. S. (2012) *The structure of scientific revolutions* (4th ed.). Chicago, IL: University of Chicago Press. (*This edition contains revisions and was published on the 50th anniversary of the original appearance of the book in 1962. Kuhn's work has had a powerful effect on scientists, historians and philosophers of science alike, as well as in realms of social science and literary studies. In this book, Kuhn lays out his concepts of paradigm, normal science, puzzle-solving, anomalies and describes the development of science as a series of paradigm replacements, (shifts) or what he calls "scientific revolutions."*).

Longino, H. E. (1990). *Science as social knowledge: Values and objectivity in scientific inquiry*. Princeton, NJ: Princeton University Press. (*A clear introduction to problems of science as a social process, the author steers a solid course between the stereotype of science as objective truth and the view that it is nothing but subjective social construction. Longino deals with such issues as sex bias in research, the nature of evidence, values in science and science as social knowledge.*).

Mayr, E. (1961). Cause and effect in biology. *Science* 134,1502–1506.(*An elaboration of the example of the causes of bird migration discussed in Section 2.6.*).

Numbers, R. L., & Kostas Kampourakis (Eds) (2015). *Newton's apple and other myths about science*. Cambridge, MA: Harvard University Press. (*Contains a number of case studies of how science has been traditionally mythologized, and thus presented in an unrealistic way. Among other myths covered is a more detailed version of the Pasteur-Pouchet controversy.*).

Varmus, H. (1987, September). Reverse transcription. *Scientific American 257* (3), 56–64. (*A detailed account of the discovery and process of reverse transcription and the action of the enzyme reverse transcriptase as originally postulated by Howard Temin.*).

The Nature and Logic of Science: Testing Hypotheses

3

Abstract

The main focus of this chapter is the process of formulating and testing hypotheses. Two basic ways in which hypotheses are tested is by either observations and/or experiments. In both cases the importance of uniformity of conditions and sample size is a central point. Two in-depth case studies, emphasizing the testing of hypotheses by observation, form the core of the chapter: physician John Snow's mid-nineteenth century investigations into the cause of cholera and the search for the cause of the AIDS epidemic in the latter decades of the twentieth century.

3.1 Introduction

No matter how brilliant, a hypothesis that cannot be tested is of little use in science. There are two basic ways in which scientists test hypotheses: by making further observations of the phenomenon under consideration and by carrying out experiments. We will examine both of these methods in this chapter.

3.2 Testing Hypotheses: Some General Principles

3.2.1 Testing Hypotheses by Observation

In many scientific investigations, the only test for a given hypothesis is to make additional observations. A paleontologist cannot go back in time in order to recreate the sequence of stages in the evolution of present-day species. Instead, he or she

G.E. Allen and J.J.W. Baker, *Scientific Process and Social Issues in Biology Education*, Springer Texts in Education,
DOI 10.1007/978-3-319-44380-5_3

must infer it from already-existing data, or by making additional observations of the fossil record.

One problem with collecting new observations as the major means of testing a hypothesis is that it is not always possible to make the desired observations. For example, if a paleontologist cannot find some fossil predecessors of mammals, any hypothesis concerning their evolutionary origin will have to remain untested.[1] Sometimes we must simply wait for the right circumstances to present themselves, such as chance erosion of strata that exposes the relevant fossils. Whenever possible scientists prefer to test hypotheses by conducting an experiment. What are experiments and why are they preferable to naturally occurring observations?

3.2.2 Testing Hypotheses by Experiments

Experiments are direct interventions into nature that allow the investigator to force particular situations to occur that might otherwise occur only rarely, if at all, on their own. Experiments also make it possible to control the conditions under which a given effect occurs and thus allow the investigator to determine cause-and-effect relationships more precisely.

Suppose for example, we wish to see if light affects the growth of plant seedlings. It would be possible to roam the woods looking for examples of seedlings of the same species that germinated in the dark, perhaps under logs or under rocky ledges, and compare them with seedlings growing in an open field. Yet, under such conditions many additional factors or variables, might well be affecting rate of growth: for example differences in the amount of water received by the two groups of seedlings, differences in temperature or the amount of light. A more reliable answer to our question can be obtained by conducting an experiment in the laboratory, similar to ones often carried out in introductory biology courses at schools or university We might start by refining our question in line with the discussion of how to ask meaningful questions posed in Chap. 2. The broad question, "Does light affect the growth of plant seedlings?" might be posed more specifically as:

(1) Do plant seedlings need light to grow at all? Or,
(2) Do plant seedlings need light for normal growth?

The first is a simpler question, while the latter is more complex. For example, if we asked the second question, we would have to be prepared to know what was meant by "normal growth." In fact, we can answer both questions by one experiment, but the important point here is that, in framing the question initially, we need

[1]However, with the recent perfection of methods for collecting and analyzing ancient DNA (DNA from extinct organisms whose organic remains have been preserved as in freezing or in resin), paleontologists have come a major step closer to being able to recreat ancestry from the past. (see *Science* 349 (July24, 2015: pp 358–372).

to think through what sorts of information we want to get from an experiment to answer the question that we have posed.

If we formulate our question more broadly, as "Do plant seedlings need light for normal growth?," then we can formulate a hypothesis that is testable:

Hypothesis: ***If***… plant seedlings do not require light for normal growth,
Prediction: ***then***… seedlings grown in the dark should show the same amount and form of growth as those grown in the light.

The appropriate experiment to test this hypothesis would be as follows: Expose one group of seedlings to light and expose another group of the same species of seedlings to total darkness for a specified period of time. The experimental design and results of such an experiment are shown in Fig. 3.1. Recall from Chap. 2 that in

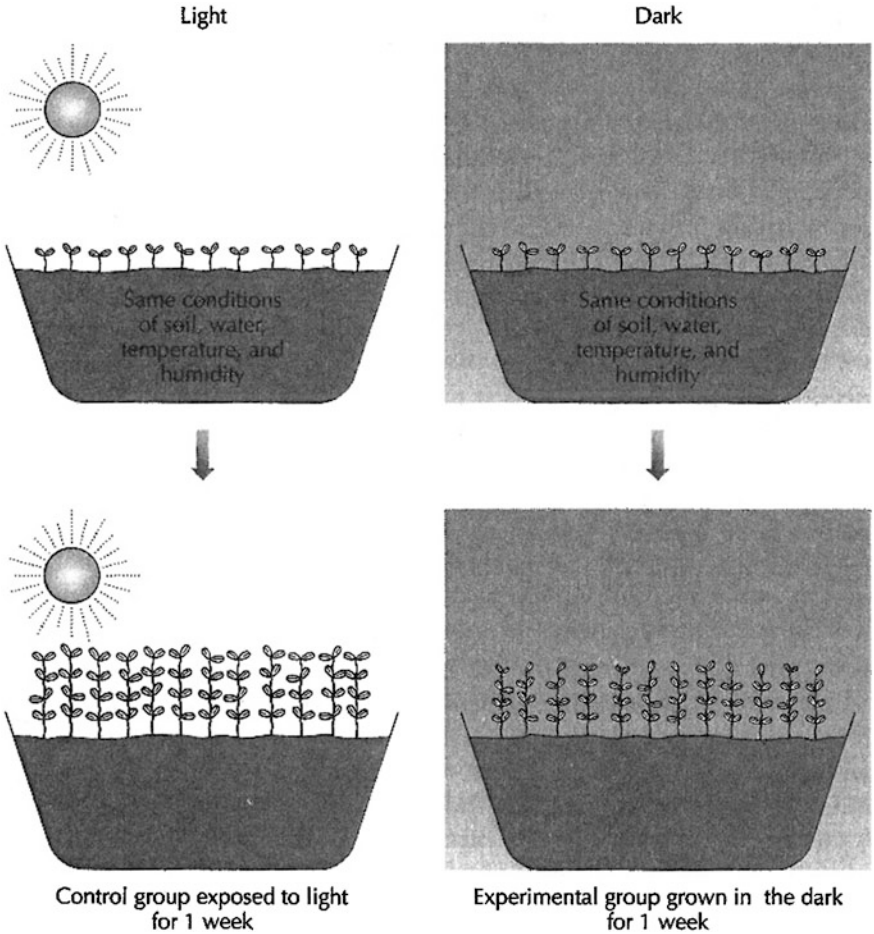

Fig. 3.1 Controlled experiment: plant seedlings grown in *light* and *dark* to test experimentally whether light is necessary for normal growth. [Original]

setting up experiments the group in which the variable (in this case light) is altered is called the experimental group while the group in which the variable was not altered (since seedlings normally develop in light) is called the control group. It would also be important to insure that all other known variable (temperature, composition of the soil, availability of water, etc.) are kept the same for both. Observing the two groups after a week, we might notice that plants in the experimental group are lighter in color and thinner than the controls grown in the light, which by comparison are green and robust. In this experiment, the data contradict the hypothesis proposing that light is *not* required for normal growth. Thus, we can conclude that light *is* necessary for normal seedling development. Because experiments allow us to manipulate external variables, we can draw more reliable conclusions from them than from observations alone.

Note that we expressed the hypothesis as a negative: "If plant seedlings *do not* require light for normal growth…," although we could just as easily have phrased the hypothesis as a positive: "If plant seedlings require light for normal growth…" While both forms of stating an hypothesis are acceptable, the negative form has one logical advantage. Recall from Chap. 2 that to disprove an hypothesis is more certain than simply to support one. Researchers often phrase their hypotheses in the negative, or null form, stating that there will be no effect of the factor (in this case, light) being investigated. The null hypothesis is analogous to the legal principle of presumed innocence until proof of guilt. Because the results of our experiment contradict the prediction based on the null hypothesis, we can reject it and conclude that the alternative, namely, light *is* necessary for normal growth, is at the very least highly probable. The null hypothesis is particularly useful in statistical tests applied to many experimental results where the aim is to determine if the difference observed between experimental and control groups is statistically significant or merely one to be expected by chance alone (see Appendix). Whenever possible, then, it is preferable to state hypotheses in the null form.

3.2.3 The Importance of Uniformity and Sample Size

It is not always possible to set up perfectly controlled experiments. Sometimes conditions cannot be controlled as rigorously the investigator would like. As anyone who has tried to grow house plants knows, different species of plants may have very different requirements for water, humidity, light or temperature. Indeed, there are often considerable variations between individuals *within* species. Thus, laboratory research is often carried out on organisms, such as mice or rats, that are inbred to make them as genetically, and thus overall biologically identical as possible. Organisms that have been "engineered" for experimental purposes are referred to as "model organisms", because, like any model, they are highly uniform, and introduce as few variables in their make-up as possible. Model organisms have several important advantages for biological research: (1) They can be obtained in large quantities and thus provide adequate sample sizes; (2) They have the advantage not only of uniformity within a single investigator's experiments, but also can be used by other investigators, guaranteeing (as much as possible) that the experiments are being carried out on the same biological material.

Another problem with obtaining large enough sample sizes is that sometimes the organisms being studied, for example large mammals or members of an endangered species, cannot be obtained in sufficient quantities to make a large-scale study possible. In our seedling experiment, the availability of seedlings was not a problem, but clearly one or two seedlings would not have been enough cases from which to draw any conclusions. Only by having a large number of plants as biologically uniform as possible, could we minimize the effects of individual differences. Even then, we obviously could not assume that this conclusion is valid for all plants, but only for the species with which we worked—recall from Chap. 2 Spallanzani recognized this problem in drawing his conclusions.

The problem of adequate controls is made more complex when the organisms under consideration are human beings. Ethical issues usually prevent investigators from doing fully controlled laboratory experiments on humans, though investigators do their best within certain limits. If we hypothesized, for example, that a substance X causes cancer, we could not ethically or legally divide a group of humans into experimental and control groups and administer X to one group and not the other. This is not to say, however, that scientific procedure has no role to play in studying the causes of human diseases or other issues of human biology. As noted in Chap. 2, clinical trials are common in medical studies among designated populations such as smokers or AIDS patients, where the individuals in the study are (1) volunteers carefully selected for the study and (2) for whom the results of the study might provide a corrective or cure to their habit or condition. Here, the ethical problem of asking a person to volunteer for an experimental study must be weighed against the chance that participation might pose a risk to their health or not benefit them directly. The question always exists: What is a true volunteer in any given case? Are patients suffering from a terminal illness truly volunteering, or acting out of desperation? Is a prison population, to whom certain privileges are granted for participation in a medical study, truly volunteers? Are elementary school children whose parents are paid a small fee to test behavior-controlling drugs truly volunteers?

Even if the ethical questions are resolved, clinical trials involving humans face other methodological problems among which finding adequate controls is probably the most important. Suppose we want to find out if Drug Y is effective in alleviating the effects of allergies. First there is the issue of matching an experimental and control group for all sorts of factors that might influence interpretation of the results. Allergies are influenced by geographic locality, and climate, especially dryness/humidity, presence of particular plants or soil types, drinking water supply, diet, life style, as well as age, state of health and socio-economic status. It is obvious that the effectiveness of a drug cannot be judged if it was tried on an experimental group whose average age was 35 and contained few smokers, while the control group was composed of people whose average age was 55 and contained large numbers of smokers. Finding comparable sample populations is one of the most difficult problems in constructing and carrying out clinical research.

However, even if all the above factors are matched between control and experimental groups, there is yet another problem in clinical studies the laboratory experimenter does not face: humans cannot be kept in a controlled environment for long periods of time. In most cases the individuals involved in such studies carry on routine daily activities, which may differ considerably from one person to the next. We might imagine the comparable situation for a laboratory investigator working with mice, who opened the cages every night and let the experimental and control groups run wild outside and then re-collected them in the morning. The investigator working with human populations can only hope that the variation in activity and lifestyle between subjects is not so great as to undermine the validity of any results obtained.

3.3 A Case Study in Hypothesis Formulation and Testing: How Is Cholera Transmitted?

Cholera is a highly contagious and often fatal disease. Its initial symptoms are painful muscle cramps, followed by nausea, vomiting and a severe diarrhea leading to extreme dehydration. In the past several centuries, cholera epidemics have swept Asia, Western Europe, Africa and North America. Before the development of the germ theory of disease by Louis Pasteur and Robert Koch (1843–1910) in the late nineteenth century, neither the cause of cholera nor its means of transmission were understood.

3.3.1 Disease: The Early Views

The Greek physician Hippocrates (460–370 BCE) argued that disease was the result of such environmental factors as polluted soil, water or air. Unfortunately in the past two or three thousand years humans turned to supernatural rather than natural explanations for disease: for example, that an epidemic or an individual's illness was the result of God's anger. Even today, this view occasionally surfaces; some television evangelists have attributed AIDS (see Sect. 3.4.3) as God's punishment for the supposed sin of homosexuality.

It was within a similar atmosphere that the British physician John Snow (1813–1858) practiced medicine in the mid-nineteenth century. While Snow is probably best known for being among the first to administer chloroform as an anesthetic during childbirth (twice for Queen Victoria), his greatest contribution to medicine lay in establishing the means by which cholera is transmitted. Snow's investigations stemmed from two cholera outbreaks in London, the first in 1848–49 and the second in 1853–54. In 1854, Snow published his findings in a monograph entitled "On the Mode of Communication of Cholera." Snow's work, which led ultimately to a method for controlling and preventing cholera epidemics, is a simple yet elegant example of scientific investigation.

Cholera outbreaks occur on massive proportions, raising the major question of how the disease is transmitted. Although microscopic organisms (or "animalcules," as they were then called) had been known to exist since the seventeenth century, solid clinical and experimental support for the germ theory of disease only began to be accepted in the 1870s. Thus, the role of microbes in the transmission of communicable disease was unknown during Snow's investigations of cholera. The most prevalent view at the time was the "effluvia hypothesis," which held that cholera was transmitted by poisoned air (effluvia) exhaled by cholera patients or emanating from the corpses of those who had died of the disease.

3.3.2 Snow's Observations

Snow had made a number of observations cholera that led him to doubt the effluvia hypothesis. He first recorded "certain circumstances" associated with the spread of cholera:

> It travels along the great tracks of human intercourse [interaction] never going faster than people travel, and generally much more slowly. In extending to a fresh island or continent, it always appears first at a sea-port. It never attacks the crews of ships going from a country free from cholera, to one where the disease is prevailing, till they have entered a port, or have [interacted] with [people on] the shore.[2]

Snow next describes several cases of the disease with which he had personal experience and that, to him, cast further doubts on the effluvia hypothesis:

> I called lately to inquire respecting the death of Mrs. Gore, the wife of a labourer, from cholera… I found that a son of the deceased had been living and working at Chelsea. He came home ill with a bowel complaint, of which he died in a day or two. His death took place on August 18th. His mother, who attended on him, was taken ill on the next day, and died the day following (August 20th). There were no other deaths from cholera registered in any of the metropolitan districts, down to the 26th August, within two or three miles of the above place…
>
> John Barnes, aged 39, an agricultural labourer, became severely indisposed on the 28th of December 1832; he had been suffering from diarrhea and cramps for two days previously. He was visited by Mr. George Hopps, a respectable surgeon at Redhousek, who… at once recognized the case as one of Asiatic cholera…
>
> While the surgeons were vainly endeavouring to discover whence the disease could possibly have arisen, the mystery was all at once, and most unexpectedly, unraveled by the arrival in the village of the son of the deceased John Barnes. This young man was apprentice to his uncle, a shoemaker, living at Leeds. He informed the surgeons that his uncle's wife (his father's sister) had died of cholera a fortnight before that time, and that as she had no children, her wearing apparel had been sent to [John Barnes] by a common carrier. The clothes had not been washed; Barnes had opened the box in the evening; the next day he had fallen sick of the disease.

[2]Bracketed inserts in the quotations are our editorial additions for clarification.

For Snow, the implication of these observations was that cholera seemed to be passed from a sick to a healthy person by some sort of direct contact between individuals, that is, by some material agent that could even be transmitted by way of a patient's clothes. It seemed clear that John Barnes had not been in his sister's presence during her illness and hence could not have come in contact with any sort of poisoned effluvia. He had, however, handled her unwashed clothing. After pointing out that the medical literature was full of additional cases similar to the ones he cited, Snow concluded that

> … the above instances are quite sufficient to show that cholera can be communicated from the sick to the healthy; for it is quite impossible that even a tenth part of these cases of consecutive illness could have followed each other by mere coincidence, without being connected as cause and effect…

Snow made yet another observation. Many people, such as doctors and nurses who dealt regularly with cholera patients and thus should have been constantly exposed to effluvia, did not usually become afflicted with the disease. He also noted that doctors usually washed their hands routinely after handling patients or their clothes. We might formulate Snow's doubts about the effluvia hypothesis deductively:

> Hypothesis: ***If*** cholera is spread by effluvia emanating from the body of an afflicted individual, and ***if*** healthy individuals are exposed to these effluvia…
>
> Prediction: ***then*** *all* persons in close contact with effluvia emanating from afflicted patients or their bodies should get cholera.

3.3.3 An Alternative Hypothesis

Snow further observed that cholera begins with intestinal symptoms rather than the skin lesions, coughing, or respiratory ailments that the effluvia hypothesis would have predicted. To Snow, this observation implied that the infectious agent must be ingested through the mouth, from which it then entered the digestive system directly. He therefore proposed an alternative to the effluvia hypothesis. Noting that the clothes and bed linens of cholera patients

> … nearly always become wetted by the cholera evacuations, and as these are devoid of the usual colour and odour, the hands of persons waiting on the patient become soiled without their knowing it; and unless these persons are scrupulously clean in their habits, and wash their hands before taking food, they must accidentally swallow some of the excretion, and leave some on the food they handle or prepare…

Snow was clearly moving toward a hypothesis proposing that the agent causing cholera was transmitted primarily, if not exclusively, from infected to healthy persons by ingestion of contaminated food or water. A further set of observations supported this view. Noting that cholera was particularly prevalent among the "working classes," a term often used for urban laborers during the industrial revolution, who lived crowded together in vast slums, Snow made the following observations:

> Mr. Baker, of Staines, who attended 260 cases of cholera and diarrhea in 1849, chiefly among the poor, informed me… that where a whole family live, sleep, cook, eat and wash in a single room, that cholera has been found to spread when once introduced, and still more in those places termed common lodging-houses, in which several families were crowded into a single room.

By contrast, Snow noted that

> When, on the other hand, cholera is introduced into the better kind of houses… it hardly spreads from one member of the family to another. The constant use of the hand-basin and towel, and the fact of the apartments for cooking and eating being distinct from the sick room, are the cause of this…

Since in Victorian England the poor, especially those with cholera, had little direct contact with the rich, how would the wealthy ever contract the disease, as some of them certainly did? Snow offered an explanation:

> … there is often a way open for it [cholera] to extend itself more widely, and to reach the well-to-do classes of the community; I allude to the mixture of the cholera evacuations with the water used for drinking and culinary purposes, either by permeating the ground, and getting into wells, or by running along channels and sewers into the rivers from which entire towns are sometimes supplied with water…

Noting that, especially in areas of poor sanitation such as the London slums, the "cholera evacuations" might also get into the groundwater, Snow was ready to advance a more general form of his hypothesis: cholera spreads within a community not only by contact between individuals but by way of the local water supply. The sewers of London emptied into the Thames River, which also supplied the city's drinking water (Fig. 3.2). Although there was no direct evidence that cholera was carried by water, additional observations provided support for Snow's alternative hypothesis:

> (1) In Manchester, England, Hope Street residents using water from one particular well were subjected to a severe cholera epidemic; 25 out of 26 perished from the disease. Residents in the same neighborhood who used water from another well showed no cholera. Examination of the first well showed that a sewer which passed only nine inches from it had leaked into the well.
>
> (2) In Essex, in 1849, cholera attacked every house in a row except one. This house turned out to be occupied by a washerwoman. She noted that the water [from the local well] gave her laundry a bad smell, and so used water from another part of town for washing, cooking and drinking.
>
> (3) In Locksbrook, cholera appeared in several tenement houses. The tenants had complained about the water to the landlord, who lived in the nearby town of Bath. He sent a surveyor, who could find nothing wrong. The tenants continued complaining. This time the landlord came. He smelled the water and pronounced it fine. Challenged to try it, he drank a glassful. This was Wednesday; by Saturday he was dead. His was the only case of cholera [in Bath].

Fig. 3.2 "Monster Soup, commonly called Thames water," 1828 etching in Philadelphia Museum of Art. London residents were aware of the pollution of the Thames, though they did not connect it with the spread of diseases like cholera [Image reproduced from Martin Goldstein and Inge F. Goldstein, *How We Know* (N.Y., Plenum Press, 1978: p. 35]

3.3.4 The Case of the Broad Street Pump

In London, in 1849, a severe outbreak of cholera occurred in the vicinity of Broad and Cambridge Streets. At that intersection, a pump supplied water to the neighborhood. Snow quickly noted that the epidemic appeared to be centered at the pump. To verify that impression, he mapped the occurrence of the disease house-by-house (Fig. 3.3). The results were startling. Within 250 yards of the pump there were almost 300 fatalities in ten days, a result quite consistent with his hypothesis. However, Snow had to deal with what appeared to be a contradictory observation. Seventy workers in a Broad Street brewery, located very near the pump, remained free of cholera. This contradiction was resolved, however, when Snow learned that, if the workers were thirsty, they drank water from the brewery's own deep well rather than from the Broad Street pump. On September 7, Snow convinced a citizens' group about the danger of the Broad Street pump and on September 8 its handle was removed. However, the epidemic had already reached its peak, the number of deaths had begun to decline, and most of the inhabitants had fled the area. Thus, removal of the pump handle came too late to be viewed as a means of testing Snow's water-borne hypothesis.

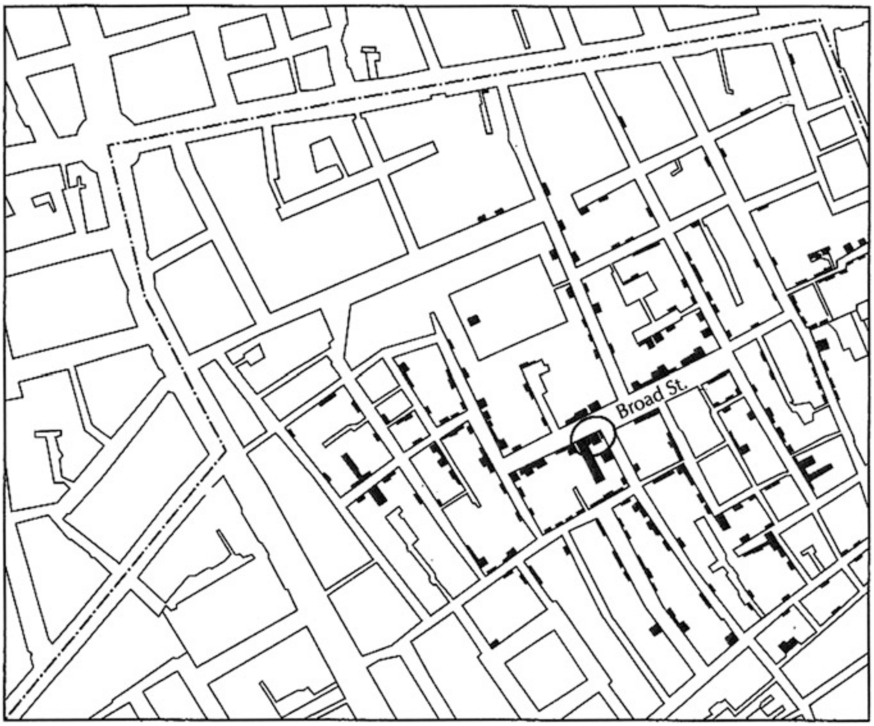

Fig. 3.3 Map of the area of the broad street pump showing location of cholera cases, 1849. The clustering of cases in the vicinity of the pump first alerted Snow to the possible contamination of water from this well by the cholera agent. [From Charles Rosenberg, *King Cholera* (London, Hamish Hamilton, 1966): Facing p. 204]

3.3.5 Objections to Snow's Water-Borne Hypothesis

Several objections were raised to Snow's water-borne hypothesis. Some people argued that not everyone who drank the polluted water got sick, precisely the same objection Snow himself had used against the effluvia hypothesis.

Snow's reply made two important distinctions that showed considerable sophistication on his part. The first distinction was that between a simple and complex cause-and-effect relationship. For his water-borne hypothesis to be supported it was not necessary that every person who drank from the same contaminated well come down with the disease. For various reasons, including state of health of the individual or amount of water consumed, not all individuals would be expected to respond identically. The second distinction was between what Snow called a "chemical" and a "biological" cause. Here, his reasoning is particularly insightful. *If* the infective agent of cholera were simply a chemical, Snow noted, *then* it would tend to be diluted in drinking water after a time and thus would not persist with continued virulence for weeks at a time. On the other hand, *if* the infecting agent were a biological one capable of reproducing itself, *then* it would not be diluted over time but spread over wider and wider areas. Clearly, he remarked, the pattern of infection showed that as long as people were in contact with one another, the cholera spread rapidly and showed no signs of becoming diluted. Therefore, Snow reasoned, it must be a biological rather than chemical agent.

3.3.6 The Critical Test

How could Snow test his hypothesis in a way that would distinguish clearly between the two alternatives? As we noted earlier, it is difficult and often unethical to carry out controlled experiments with human beings, especially if the point is to determine susceptibility to a fatal disease. However, in 1853, another cholera epidemic in London provided the experiment that allowed Snow to test his water-borne hypothesis directly.

Two water companies, the Lambeth Company and the Southwark and Vauxhall Company, both delivered water to a single district in London. As a consequence of the 1849 cholera epidemic, however, the Lambeth Company moved its waterworks upstream from the city, where the Thames was free of city sewage, while the Southwark and Vauxhall Company continued to take water downstream. This situation provided the opportunity for a critical test of Snow's hypothesis. As Snow reported it:

> Each Company supplies both rich and poor, both large houses and small; there is no difference either in the condition or occupation of the persons receiving the water of the different Companies… it is obvious that no experiment could have been devised which would more thoroughly test the effect of water supply on the progress of cholera than this… The experiment, too, was on the grandest scale. No fewer than 300,000 people of both sexes, of every age and occupation, and of every rank and station, from gentlefolks down to the very poor, were divided into two groups without their choice, and, in most cases, without their knowledge; one group being supplied with water containing the sewage of London… the other group having water quite free from such impurity.

Stated deductively in the null form, Snow's hypothesis predicted that ***If*** cholera were not borne by water, ***then*** there should be no difference in cases of cholera between those houses receiving Southwark and Vauxhall water and those receiving water from the Lambeth Company. His preliminary data determined that, of 44 deaths from cholera in the district, 38 occurred in houses supplied by Southwark and Vauxhall. The null hypothesis was contradicted.

What about the other six cases? Although most of the data supported Snow's water-borne hypothesis, he recognized that the six cases represented a false prediction and thus a possible negation of his hypothesis. Rather than abandon his hypothesis, however, Snow did what most scientists do. He tried to find variables that might explain the six exceptions. He found that, in many cases, the city residents (especially tenants whose landlords paid the water bill) did not know which water company supplied their house. How could he correct for this possible source of error? Snow found that he could distinguish the source of the water by a simple chemical test based on the fact that the two water supplies possessed different levels of sodium chloride. The difference in the amount of sodium chloride in the two water supplies was great enough to provide a reliable and objective way for Snow to determine which company supplied water to each house. After testing the water in the six exceptional households, his results showed that all six actually received their water from Southwark and Vauxhall, precisely as would be predicted by the water-borne hypothesis.

Note that Snow's use of data from the two water companies allowed him to control for other variables that might have affected spread of the disease. As Snow noted, "Each company supplies both rich and poor, both large houses and small; there is no difference either in the condition or occupation of the persons receiving the water of the different companies… "Thus all the various social and economic factors that might have influenced the spread of the disease were eliminated as causal factors, as best they could be in such a large scale and naturally occurring experiment. This left the one major factor—polluted or clean water—as the one difference between two large groups of subjects. By chance, Snow had been able to devise a controlled experiment without actually having to intervene directly and divide his subjects into experimental and control groups.

3.3.7 A Wider Applicability and the Role of Chance

Snow's work on cholera demonstrates two other factors often characteristic of scientific investigations. One is that hypotheses often apply to more than the phenomenon they were originally designed to explain. For example, Snow noted that typhoid fever killed even more people than did cholera, suggesting that typhoid fever might also be corrected by improved sanitation. This turned out to be the case, and typhoid fever, too, was eventually brought under control. Another factor is that new ideas often emerge in scientific investigations but are equally often overlooked. In his strong focus on the question of how cholera was transmitted, Snow missed an obvious therapeutic treatment coming directly from his own work. In making his case for the oral transmission of cholera Snow wrote:

> If any further proof were wanting [that] all the symptoms attending cholera, except those connected with the alimentary canal, depend simply on the physical alteration of the blood and not on any cholera poison circulating in the system, it would only be necessary to allude to the effects of a weak saline solution injected into the veins [of a patient] in the stage of collapse. The shrunken skin becomes filled out, and loses its coldness and lividity; the countenance assumes a natural aspect; the patient is able to sit up, and for a time seems well. If the symptoms were caused by a poison circulating in the blood depressing the action of the heart, it is impossible that they should thus be suspended by an injection of warm water, holding a little carbonate of soda in solution.

Note the deductive reasoning here: ***If*** the symptoms were caused by a poison circulating in the blood…, *then* it is impossible they could be alleviated by a simple injection of warm water. Snow overlooked here a potentially powerful treatment for cholera. We know today that the disease kills, not by the effect of bacterial toxins directly, but by dehydration. If a cholera patient drinks enough fluids or if fluids are given intravenously by injection, as Snow described, the disease is rarely fatal. It is ironic that Snow was so focused on finding the cause of cholera that he overlooked a possible treatment, even when it was directly in front of him.

3.3.8 The Mechanism of Cholera Action: A Modern Perspective

Modern-day studies on the nature of cholera infection have revealed how the bacterium, responsible for the disease, *Vibrio cholerae*, works its lethal effects on the human body. The bacterium produces a toxin during the course of its metabolism that affects the ability of epithelial (lining) cells, such as those lining the inside of the intestines, to control the flow of water out of the cells. As a result of cholera infection, the individual loses so much water (thus the symptoms of extreme diarrhea) that the body becomes dehydrated, resulting eventually in death. This modern understanding of the mechanism by which cholera operates now makes it perfectly clear why Snow's observation that when cholera patients were injected with saline solution their condition improved: the injection was re-hydrating them. One therapy routinely applied today with cholera patients is to give them massive injections of water, thus keeping them alive so the body's immune system has time to fight off the bacterial infection.

3.4 A Modern-Day Epidemic: The AIDS Crisis, 1981–2000

3.4.1 Background: The Origin of the AIDS Crisis

What cholera was to the nineteenth century, Acquired Immune Deficiency Syndrome (AIDS) has become for the twentieth. AIDS is a particularly deadly disease. It involves a breakdown of the body's immune system, whose job it is to ward off outside infections and to constantly survey the body's tissues for cancerous cells. People with AIDS die not from the disease directly, but from any number of infectious diseases or cancers that healthy people easily ward off. Epidemiological data from the U.S. government Centers for Disease Control (CDC) in Atlanta shows that in the United States the number of reported cases of AIDS went from less than 100 prior to 1981 to over 79,000 per year in the peak year of 1992–1993 (Fig. 3.4). Today in the United States, the CDC estimates that over 1.2 million persons ages 13 and over are living with HIV infection; surprisingly, about 12.8 % appear not to even know they have the infection. Although the rate of increase began to fall off by the mid-1990s, and has been stable for the past 15 years in the United States and other industrialized nations, it has simultaneously escalated in the rest of the world, particularly in Africa and Asia. In 1997, nearly 6 million people came down with

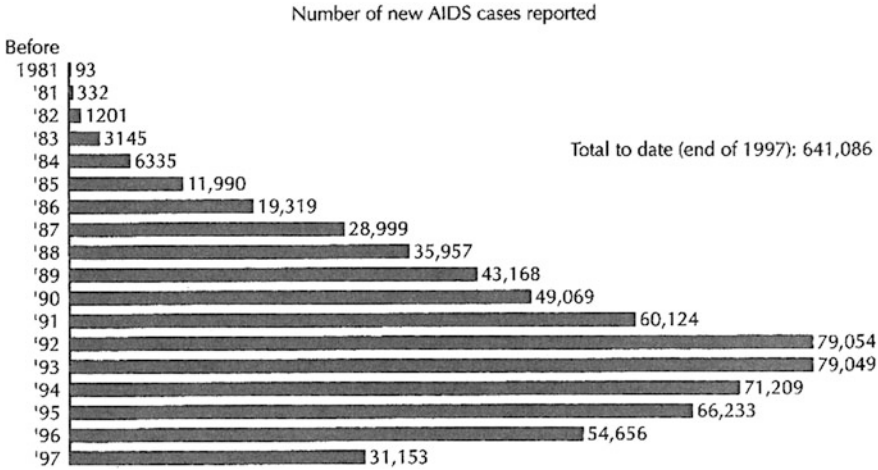

Fig. 3.4 Bar graph showing increasing incidence of AIDS in the United States, 1981–1997. The noticeable drop off after 1995 reflects the use of new drug combinations rather than use of single drug as had been common up to the mid-1990s. After 1997 the level of existing and new cases levelled off and remained stable up to the present. Statistics from Centers for Disease Control, Atlanta [From Peter Raven and George Johnson, *Biology* (William C. Brown, McGraw-Hill, 5th ed): p. 1089

AIDS worldwide and over 2 million died of the disease, some 460,000 of them children. AIDS has moved from epidemic (localized outbreaks) to pandemic (affecting whole continents) proportions. Today, with such a high degree of mobility, the spread of disease can occur much more rapidly and extensively than at any other time in human history. The causes of AIDS and methods of treating it have challenged medical science and public health policies in unprecedented ways.

What causes AIDS and how can scientists help fight back against this deadly disease? Since it made its first official appearance as a recognizable disease in 1981, AIDS has been the source of controversy regarding both origin and treatment. Some of the basic observational data regarding AIDS are:

1. No one comes down with AIDS without being in contact with someone who already has the disease; like cholera, AIDS meets all the criteria of a transmissible disease.
2. Although AIDS is transmissible, it not *easily* transmissible. It cannot be caught by simple physical contact between people, as in touching or kissing. Its only major portal into the human body is by way of the blood stream. While it is most frequently thought of as a sexually transmitted disease, because, during sexual intercourse some capillaries in epithelial tissue lining the reproductive tract or other body areas may be torn, providing a direct passageway into the blood stream. The disease may also be transmitted among intravenous drug users who

use non-sterile needles and much more rarely by the medical transfusion of blood and blood-derived products or by accidental needle pricks in a hospital setting.

3. What came to be called AIDS was initially identified in western, industrialized countries within the homosexual community, where it first became highly visible (for a while it was called the "gay disease"). AIDS later showed up in the heterosexual community and among drug users and prostitutes in both industrialized and non-industrialized countries.
4. Persons who have sexual or intravenous contact with individuals infected with AIDS often experience a long latent period of anywhere from a few months to 10 years or more, during which time they show no signs of the disease.
5. Persons who have contracted AIDS show a reduction in the number of $CD4^+$ T-cells (also called helper T-cells), components of the human immune system whose job it is to recognize foreign invading elements and mobilize other parts of the immune system to eliminate the invaders before they do significant harm. AIDS patients therefore lack this first line of defense against a whole host of infective agents.
6. Persons who show clinical symptoms of AIDS also have elevated levels of a virus know as Human Immunodeficiency Virus (HIV) in their blood streams.
7. Until 1995, anyone who began to experience the overt symptoms of AIDS was likely to be dead within 2-3 years. Since 1995, however, various combinations of drugs have staved off this previously inevitable fate. Research scientists and clinicians now have hope that, even if AIDS cannot be cured, it can at least be managed so that people with the disease can live a relatively normal and extended life.

To try and cure or control AIDS effectively, medical and public health officials sought very hard in the period after 1981 or 1982 to determine what *causes* the disease. Three major types of explanatory hypotheses were initially advanced since that time to account for the AIDS pandemic:

1. AIDS is God's punishment for homosexuality or intravenous drug use. Representatives of the religious right, including various radio talk show hosts and some television evangelists, have promoted this hypothesis.
2. AIDS is a result of a degenerate lifestyle that involves compromising the immune system through excessive sex, drug (especially amyl nitrate, inhaled as "poppers") and alcohol use, lack of proper diet, etc. Infective agents associated with AIDS are thus "fellow travelers" of an unhealthy lifestyle and not the direct cause of the disease. Dr. Peter Duesberg, a biochemist at the University of California, Berkeley, was one of the major proponents of this view.
3. AIDS is caused by infection from the HIV virus, which specifically attacks (enters) $CD4^+$ -T cells. $CD4^+$ cells are killed as the virus replicates itself inside of them and, as the virus spreads throughout the entire population of $CD4^+$ T-cells, the body's whole immune system is slowly rendered ineffective.

It is possible to distinguish between these alternative explanations. Hypothesis 1 can be eliminated immediately because it postulates a mystical, supernatural cause and is therefore untestable. Hypotheses 2 and 3, on the other hand, may be distinguished from one another by experimental and observational means. For example:

> ***If***… AIDS is the result of a harmful lifestyle (rather than as a direct effect of HIV infection),
> ***then***... people who live a healthy lifestyle should not come down with AIDS.

Medical records show, however, that health care workers and others who have led a perfectly healthy life style still contracted the disease if they experienced needle punctures while caring for AIDS patients. A healthy life-style, therefore, does not appear to be a guarantee against contracting AIDS. The prediction was not borne out, thus weakening hypothesis (2). A more direct prediction can be made from hypothesis 3:

> ***If***... AIDS is the direct result of infection by the HIV virus,
> ***then***… Infecting cells in laboratory tissue cultures or whole organisms with HIV should produce AIDS-related effects.

Laboratory experiments show that the HIV virus readily infects $CD4^+$ T-cells in vitro (that is, in a culture dish) and destroys them, while not affecting other kinds of T-cells (Fig. 3.5). Furthermore, an animal model of AIDS provides a test for hypothesis 3: Monkeys carry related viruses known as siminian immunodeficiency

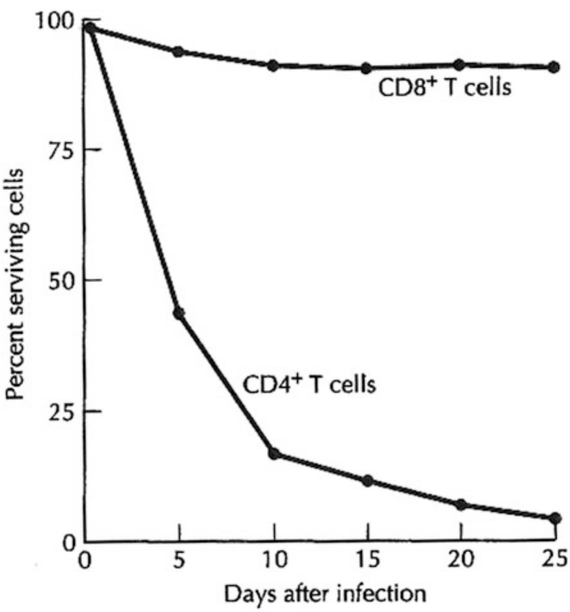

Fig. 3.5 Graph of HIV infecting and destroying $CD4^+$ T-cells but not $CD8^+$ T-cells. These data show the specificity of the virus for certain cells and not others in the immune system. [From Peter Raven and George Johnson, *Biology* (William C. Brown, McGraw-Hill, 5th ed): p. 1088]

viruses (SIV). When SIV is injected into healthy monkeys, they soon begin to experience an AIDS-like immune response (monkeys, however, do not usually progress to having the disease itself). By all counts, then, hypothesis 3 seems most strongly supported: AIDS appears to be directly caused by infection from the HIV virus.

Where did AIDS come from and how did it make its appearance in human populations starting around 1981? Again there are several hypotheses to explain this rather recent and sudden appearance of the disease:

1. HIV is a cousin of SIV, and evolved from SIV that had been transmitted to human populations through contaminated polio vaccines produced from infected monkey kidney cells. A widespread polio vaccination campaign was waged in central Africa in the 1950s, and thus it is postulated that an early form of HIV began to enter the human population at that time, becoming visible as an epidemic only a generation (30 years) later. This hypothesis was championed by Edward Hooper in a 1999 book, *The River: A Journey to the Source of HIV and AIDS*.
2. HIV was transmitted from African chimpanzees to humans, probably through bites or through hunting of chimps for food, rather than infected polio vaccine, with the virus adapting to exploit the human immune system.

Since both hypotheses rest on circumstantial evidence, it is not easy to distinguish between them. Hypothesis 1 may be true, but it is difficult to determine whether any of the polio vaccines produced in the 1950s involved monkey kidney cell cultures that were contaminated with HIV. Hypothesis 2 seems more likely at the present time, but we may have to be reconciled to the fact that it is difficult to determine the true origin of this disease.[3]

3.4.2 The Nature of HIV Infection

The front line of the body's defense system against invasion by foreign agents (principally bacteria, viruses and fungi) are several types of cells of the immune system, including $CD4^+$ helper T-cells. Helper T-cells respond to the presence of foreign bodies in the blood and body tissues by activating other types of cells of the immune system (B-cells and cytotoxic T-cells) that attack the invader. HIV viruses specifically infect the helper T-cells. The HIV virus is able to target these cells in particular because the virus has certain markers (glycoproteins) embedded in the lipid (fatty) envelope that covers it; the glycoprotein markers recognize cell surface molecules on $CD4^+$ T-cells and bind to the cell surface. The specificity is emphasized by the graph in Fig. 3.5, which shows that in the course of three weeks after infection by HIV, virtually 100 % of the $CD4^+$ T-cells in a laboratory culture have been eliminated from the body while another kind of T-cell, $CD8^+$ T-cells

[3]Two other hypotheses propose that HIV originated in Caribbean pigs eaten by North American tourists to Haiti in the early 1980s or that it is the result of a military germ warfare program gone awry. There is no firm evidence supporting either of these hypotheses, however.

remain virtually unaffected. Once the HIV virus particle attaches itself to a specific cell surface marker, the process of infection begins.

Like all viruses, HIV is very simple in structure, consisting of its lipid envelope (not all viruses have a lipid envelope, but only a protein coat) (inside of which is a capsid containing two long molecules of nucleic acid, the virus' genetic information system for making new viruses) and two molecules of the enzyme reverse transcriptase (Fig. 3.6). The envelope serves two purposes in the viral life cycle. It protects the nucleic acid from being destroyed by other molecules in the body or in the outside environment, while the glycoprotein fits specifically onto the surface molecules of T-cells, initiating the process of infection.

The infection cycle of HIV begins with attachment of the virus to the T-cell surface (Fig. 3.7a). Once attached, the virus injects its nucleic acid into the interior and the work of infection begins (Fig. 3.7b). Infection involves the viral nucleic acid commandeering the machinery of the host cell to produce not what the host cell needs, but hundreds of new viral particles (Fig. 3.7c). The virus is like a saboteur who invades a factory and turns the production process in the factory toward the saboteur's own ends. Finally, the new virus particles are assembled and pass through the membrane of the destroyed helper T-cell, each forming its new envelope from the lipid membrane of the cell (Fig. 3.7d). With each single virus being able to produce hundreds of progeny within one host cell, it is easy to see how the infection can spread rapidly throughout the body.

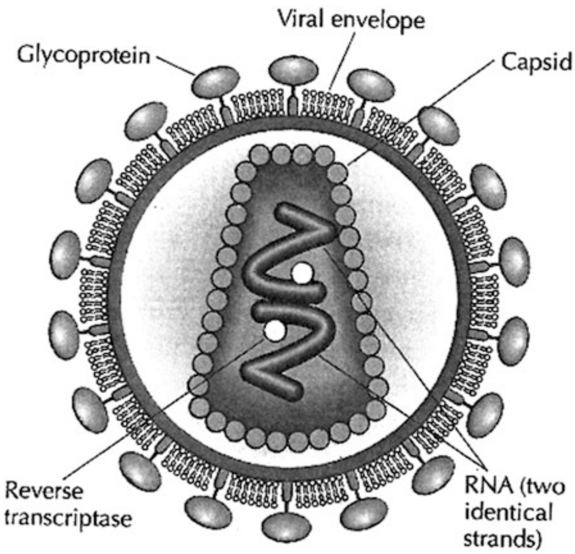

Fig. 3.6 Diagram of HIV, showing capsule (protein coat) with surface glycoproteins, capsid, and interior with two identical molecules of RNA and two molecules of the enzyme reverse transcriptase. [From Neil Campbell, *Biology* (Menlo Park, Addison, Wesley-Benjamin-Cummings, 6th ed): p. 336]

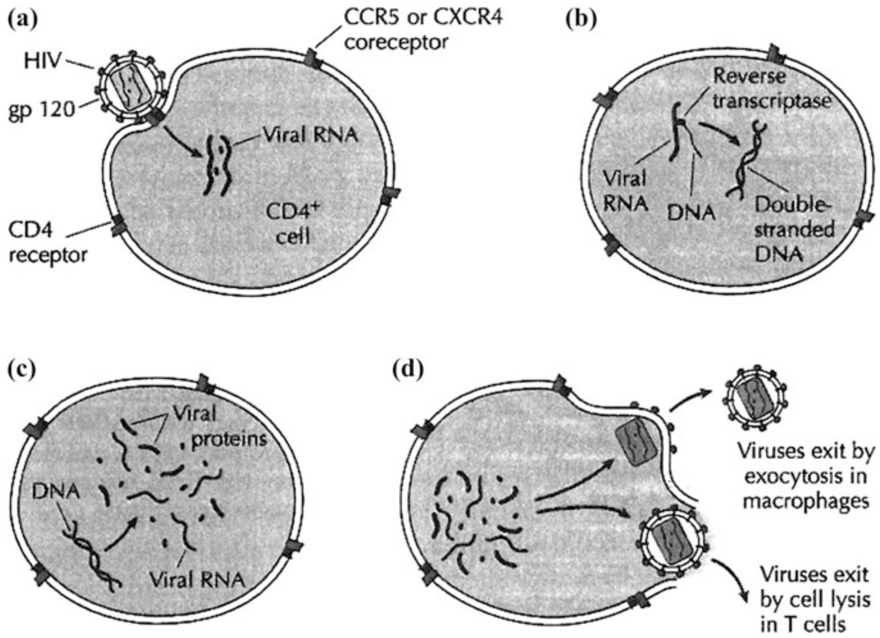

Fig. 3.7 Infective cycle of HIV, shown in four stages. **a** The gp 120 glycoprotein on the surface of HIV attaches to $CD4^+$ Helper T cells and one of two co-receptors on the surface of a $CD4^+$ cell. The viral contents enter the cell by endocytosis (being engulfed). **b** Reverse transcriptase makes a DNA copy of the viral RNA. The host cell then synthesizes a complementary strand of DNA. **c** The double-stranded DNA that has just been synthesized directs the synthesis of both HIV RNA and HIV proteins, which self-assemble inside the cell. **d** Complete HIV particles bud out from the cell by exocytosis (extrusion) in the *white blood* cells known as macrophages, or by lysing (breaking open) the cell in the $CD4^+$ cells. [Modified from Peter Raven and George Johnson, *Biology* (William C. Brown, McGraw-Hill, 5th ed): p. 581]

HIV is among a group of viruses known as retroviruses (see Chap. 2), whose nucleic acid consists ribonucleic acid (RNA) rather than deoxyribonucleic acid (DNA). Most viruses, like bacteria and all multicellular organisms, have DNA as their genetic material. Thus the host cell's metabolic machinery is set up to take instructions from DNA for whatever proteins and other molecules it synthesizes. Because they possess RNA as their genetic material, retroviruses must carry a specific enzyme, reverse transcriptase, that allows their RNA, once inside the cell, to first be transcribed into DNA. Once this transcription has taken place, the new DNA, carrying viral genetic information, can then provide instructions to the cell's machinery to produce viral RNA and proteins.

During the early period of infection, patients may be diagnosed as HIV-positive (meaning the virus can be detected in their body) but show no other signs of illness. Medically speaking, they do not have AIDS. AIDS itself is said to occur when visible signs of the breakdown of the immune system are apparent. These signs can include repeated opportunistic infections by yeasts, the appearance of certain rare cancers associated with immune system deterioration, etc. Some individuals have remained HIV-positive for years without showing any major symptoms of the disease.

For reasons that biologists still do not understand, HIV sometimes adopts a second strategy in its infectious process. Once it has transcribed DNA from its RNA inside the cell, the viral DNA becomes integrated into the chromosomes of the host, replicating as that cell replicates for many generations and producing a so-called latent period. Suddenly, for reasons equally mysterious, the viral DNA may become active and start the process of replicating HIV proteins and RNA. This latent phase of the the cycle (called the lysogenic phase, which means the virus has the potential to lyse [break open and kill] the cell, but does not do so immediately, may account for the fact that people can be HIV-positive for many years before experiencing the symptoms of AIDS itself. Suddenly, however, for reasons equally mysterious, the viral DNA may become active and start the process of replicating HIV proteins and RNA/

The HIV virus itself is quite fragile. It cannot exist outside of a host cell or the blood stream for any length of time. In this sense, therefore, it should be a difficult disease to contract. Why, then, has AIDS become the major epidemic disease of the last three decades? The answer lies in several characteristics of this virus compared to most other viruses or bacteria with which medical practitioners have had to contend. The first is that, because HIV attacks the immune system, which is supposed to ward off such invasions, it paves the way for complete takeover of the body. The infected person becomes helpless as their immune system breaks down. Second, HIV has the ability to mutate quite rapidly, especially in genes coding for the structure of the glycoprotein markers in the envelope. The immune system depends on being able to recognize invading microorganisms (including viruses) as foreign elements by detecting specific markers on their surfaces. If a particular HIV-strain enters the body and the immune system learns to recognize it and eliminate it before it can reproduce, the strain will be kept at a low level or eliminated altogether. However, in the course of its replication within the body of a single host, HIV may undergo numerous mutations of its glycoproteins. As a result, after several generations of replication, it is no longer recognizable to the immune system as the original strain and is therefore seen as a brand new invader. Antibodies now are made to this new HIV-strain, but in the meantime a number of T-cells have been destroyed and the immune system weakened. This downward spiral is repeated until the whole immune system has collapsed.

AIDS has also spread rapidly, and on a global basis, for social as well as biological reasons. Widespread increase in drug traffic and unregulated prostitution, and unsafe sex practices in general, have contributed to the spread of this disease. Although the rate of increase in spread of the disease has diminished in industrialized countries, the situation is particularly tragic in impoverished areas of the Third World. In these areas, where sex for money and drug trafficking often appear as the only roads out of poverty, or even of mere survival, the future is grim no matter what. As a prostitute in Harare, Zimbabwe stated, "I can choose to die of starvation now, or of AIDS later." Reports in October 2000 from the Thirteenth International AIDS Conference in South Africa, produced some startling, and disturbing facts: 15 million people have already died of the disease, another 34 million are HIV-positive, including 25 million in sub-Saharan Africa alone; it is projected that in some African countries 67 % of today's teenagers will die of AIDS in the next decade. The available drug mixtures (see below) necessary to counter retroviral activity in infected persons cost an average of $ 10,000 a year, and can buy survival. In most Third World countries, however, the average expense on total health care is $ 80 per person per year. The gap between the rich and poor countries of the world makes the difference between life and death.

3.4.3 Treatment and/or Cure for AIDS

Until the mid-1990s anyone diagnosed as HIV-positive was almost certain to die within a few years. The progress of the disease is horribly debilitating, with one infection following on top of the other, the appearance of rare cancers, loss of weight and the breakdown of organs such as the kidney and the liver. Various drugs have been tried, most notably one known as AZT that inhibits the action of the enzyme reverse transcriptase. If this enzyme were inhibited, it was hoped, viral replication would be halted at the outset. However, AZT has some serious side effects and it seemed that the virus could mutate so fast that its reverse transcriptase enzymes (which are coded by its own RNA) soon evolved to circumvent the drug's effects. Thus AZT could retard the progress of the disease temporarily, but nothing seemed to work permanently. Hopes for a vaccine seemed even more remote. It appeared this was a virus that had the perfect strategy for survival.

However, starting around 1995, clinicians began a new regimen known as "combination drug therapy." The idea here was to hit the virus hard at two different points in its replication cycle: once at the reverse transcriptase phase by using analogs of AZT, and second at the end of the replication cycle, with drugs known as protease inhibitors. A drug analog has a molecular structure that resembles that of the original drug bu with sufficient differences so that the side effectsare reduced. The analogs of AZT that had been developed proved not to have so many side effects as AZT itself. The protease inhibitors slow or stop the action of viral enzymes that cut into small pieces the viral protein produced during infection (these proteins serve as part of the protein coat and also as enzymes such as reverse transcriptase). Together, these combination drugs have produced some remarkable effects. A combination of two AZT analogs and protease inhibitor, for example, have lowered the level of HIV in patients' blood below the level of detection. There are still some side effects, such as diarrhea, and it is not clear whether the virus, with its high mutation rate, will evolve to circumvent the drugs. Yet clearly the combination has made it more difficult for the virus to replicate as extensively, and mutate to resistant strains and so for the moment it offers a way of staving off the disease while other strategies are explored. Among those newer strategies is a drug BMS-955176, known as a maturation inhibitor: That is, it prevents HIV from producing complex proteins that are cut up by protease enzymes and assembled into new virus particles. BMS-955176 would thus be the first HIV medication to work by preventing virus assembly, maturation, and release from infected cells. BMS-955176, in combination with a protease inhibitor, could potentially be a new option for people who cannot tolerate or are resistant to reverse transcriptase inhibitors. The new drug is being examined but as of 2015 has not yet been approved for release.

One exciting finding in the late 1990s was that a few patients from Australia had been HIV-positive for 14 years and had never shown any sign of the disease. Isolation and study of the virus from these individuals has revealed that they are infected by a strain of HIV that has a genetic defect in a gene called "negative factor" (*nef*). The normal protein product of this gene appears to play a role in regulating the rate of viral replication. The defective gene produces a defective protein that down-regulates viral reproduction to the point that it stops, or at least proceeds so slowly that the immune system can produce enough antibodies to keep the virus at bay. What is exciting about discovery of the *nef* mutant is that it offers a possible way of producing a vaccine. Because the *nef* strain appears to have the usual protein structure of the HIV viral coat, it might be used to stimulate the immune system to produce antibodies without the risk of debilitating infection. Thus with so low a reproductive rate, the *nef* itself is not be able to infect the body.

3.5 Conclusion

We began this chapter by focusing on how to formulate hypotheses and test them by either observation or experimentation. Testing hypotheses by observation is characteristic of many sciences, for example astonomy or paleontology, where the investigator cannot usually intervene in the phenomenon under consideration. Although the requisite observations are not always readily available (a particular fossil, for example), new observations are critical to the testing of many hypotheses. Where possible, however, experimentation is preferable. Experiments allow the investigator to intervene in the phenomenon under consideration in a direct and controlled way. We discussed the process of setting up control and experimental groups that were matched in all respects except for the factor being investigated (for example, the role of light in growth of plant seedlings). We also pointed out the advantage of formulating hypotheses in the null form (for example *If* light has *no* effect on seedling growth, *then* . . .), because rejection of the hypothesis yields a more certain conclusion than merely supporting it.

We then examined the process of formulating and testing hypotheses in two real-life attempts to understand the cause of human disease: cholera in the nineteenth century and AIDS in the late twentieth century. In both cases direct experimentation with human subjects to study mechanisms of transmission was not possible. To follow the spread of the disease researchers in both cases had to work with what "experiments" nature or social circumstances. In the cases presented here where human subjects were involved, procedural issues such as comparing populations matched for age, sex and socio-economic status were important aspects of setting up control groups. Ethical issues, too, are critical matters when studying human disease and testing possible cures.

3.5.1 Questions for Critical Thinking

1. Explain why it is always important to put forth hypotheses that can be tested, as opposed to those that, for whatever reason, cannot be tested.

2. Give an example of one or more hypotheses that could be tested primarily (or only) by observation. Why are hypotheses that can be tested by experimentation to be preferred over those testable only by observation?

3. A number of years ago a study was carried out attempting to correlate body shape in adolescent males to a tendency toward criminal behavior. The researchers assembled two study populations: boys in a Massachusetts reformatory (average age 16.5 years), and boys in a fashionable public school in Boston, Boston Latin School (average age 15.5 years). The hypothesis being tested was that a more muscular (mesomorphic was the technical term) body form was associated with criminality, while both thin, wiry (ectomorphic) and fat (endomorphic) body shapes were not. The researchers found that their prediction was borne out: the body form of the reformatory population was on average more mesomorphic than the population in Boston Latin School.

   (a) In terms of experimental design, what problems do you see with this research plan?
   (b) What ethical concerns might you raise about this sort of investigation?

4. Discuss why the solution to the spread of epidemic disease is never just a matter of the technicalities of biology or medicine, but also involves social dimensions. Use the cases of cholera or AIDS to illustrate your points.

5. Taking off from the last answer to question 4, discuss the issues of how to balance individual rights *vs* collective good in a community (city, state, nation) where an epidemic is in progress. Should people with the diease (assuming it is contagious) be quarrantined (this issue has come up with regard to AIDS patients, where some voices within the community called for quarrantine). Should drugs be legalized to reduce the number of intravenous users who get their injections in back-alley settings where there is no control over sanitation? Should those entering a community (as at immigration ports, for example) be required to have medical tests for communicable diseases before being allowed entry? (At the height of a cholera epidemic in the Mississippi valley in the late 1840s – where it had come from Europe – steamships planning to dock in St. Louis were required to stop a number of miles below the city and be searched for patients with cholera, who were then prevented from disembarking).

Further Reading

On the Process of Science in General

Goldstein, M., & Inge, G. (1978). *How do we know?* New York: Plenum Press (Contains a number of case studies from many areas of science, illustrating various aspects of how we know what we know. One chapter focuses on Snow's investigations on cholera.).

On John Snow's Study of Cholera

Rosenberg, C. (1966). *King Cholera*. London: Hamish Hamilton (A series of very well-written essays about the cholera epidemics in London in the nineteenth century.).

On Aids and Transmission of HIV

Duesberg, P. (1995). *Infectious AIDS: Have we been misled?* Berkeley, CA: North Atlantic Books (Historically speaking this book is interesting because it presents Duesberg's unorthodox view that AIDS is not a direct result of infection by HIV, but by an unhealthy lifestyle that leads to a breakdown of the immune system, allowing infection by HIV to take hold (see also websites 5 and 6).).

Hooper, E. (1999). *The river: A journey to the source of HIV and AIDS*. Boston: Little, Brown and Co. (Hooper presents a history of the AIDS epidemic as well as speculations on its possible origins; the author leans toward the infected polio vaccine theory but presents its limitations fairly).

Montagnier, L. (1999). *Virus*. New York: W.W. Norton (A more biologically oriented discussion of the origin of AIDS, Montagnier's book contains detailed discussions about how the virus itself infects T-cells and the various drug strategies that have been employed to try and stop it.).

Joint United Nations Programme on HIV/AIDS (UNAIDS). (2011). *Global HIV/AIDS response, epidemic update and health sector progress towards universal access* (PDF) (A useful website based on the work of UNAIDS, a major world-wide effort to educate people about AIDS and prevent its spread.).

Doing Biology: Three Case Studies

4

Abstract
This chapter is built around three case studies of biological investigations carried out not only in three very different areas of biology, but also in three different settings: the experimental laboratory, the field under natural conditions, and in historical time using paleontology and the fossil record to answer questions about the evolutionary development of life on earth. The first, laboratory-based case concerns the investigation into the mechanism by which nerve fibers growing out from the central nervous system "find" their way to very specific target sites (muscles, for example) in the peripheral areas of the animal body. This work led to the discovery of Nerve Growth Factor (NGF) in the 1950s–1970s. The second, field-based case comes from a long-term investigation into the homing behavior in salmon: namely, an attempt to find out how adult salmon find their way from the ocean to the precise stream in which they hatched three or four years earlier. The third, historical case, involves the quest of evolutionary biologists to understand the causal factors in the extinction of the dinosaurs as part of a larger phenomenon known as "mass extinction", during which numerous groups of organism all become extinct in a relatively short period of geological time.

4.1 Introduction

The various procedures for asking questions, framing hypotheses, designing experiments and analyzing their results discussed in the first three chapters of this book, are major components of the process of doing science. Many are involved in virtually all scientific research, while others are appropriate only in specific investigations. In this chapter, we turn to three specific case histories in which the various processes of science are brought into play in solving specific problems.

G.E. Allen and J.J.W. Baker, *Scientific Process and Social Issues in Biology Education*, Springer Texts in Education,
DOI 10.1007/978-3-319-44380-5_4

In carrying out scientific research, it is critical to choose the best methods for answering any given question, since a large portion of science involves good judgment about the most practical yet fruitful approach. Using an organism that is difficult to work with, or where adequate controls are impossible to maintain, may produce ambiguous if not largely meaningless results. In the 1930s and 1940s, for example, scientists attempted to use the fruit fly *Drosophila* to study the mechanism of how genes exert their various effects during embryonic development. This effort proved largely unsuccessful because the insects are too small to carry out the dissections and transplantation of embryonic parts necessary for working on a complex, multicellular organism. Some fascinating work did result, but progress was slow and allowed the answering of only a limited repertory of questions. Microorganisms such as bacteria and yeast later proved much more effective for investigating more precisely the nature of gene action.

In this chapter, we examine three rather different types of research projects, each requiring a different assemblage of organisms and methods in order to carry out the investigation. Each of these case studies comes from ongoing areas of biological research and, despite the differing methods each employs, all show an underlying similarity in logic and design.

4.2 Formulating and Testing Hypotheses in the Laboratory: The Discovery of Nerve Growth Factor

In the developing embryonic nervous system of vertebrates such as the chicken, nerve cells (neurons) develop from undifferentiated precursors, the neuroblasts. These first appear in the region of the embryo that will become the central nervous system, composed of the brain and spinal cord. As neuroblasts differentiate, the axon appears as a long extension of the cell, ultimately growing outward to form connections that innervate tissues such as muscles or secretory glands. In the twentieth century, two basic questions emerged concerning how the nervous system develops. First, how does the axon form? Second, once formed, how do the axons find their way so precisely to their target tissues? These two questions are obviously interrelated, since the answer to the first provides clues to the second.

The development of the central and peripheral nervous systems was studied in 1905 and 1906 by the Yale University embryologist Ross G. Harrison (1879–1959). In the nineteenth century, three hypotheses had been put forward to account for the origin of the axon. One of these hypotheses maintained that the growing axon is formed by Schwann cells, a chain of cells that produce the myelin sheath providing insulation around the axon. The location of the Schwann cells would therefore determine the location of the future neuron. A second hypothesis proposed that the growing nerve fiber was formed along a pre-existing “protoplasmic bridge” that acted as a kind of roadway or guideline. A third hypothesis suggested

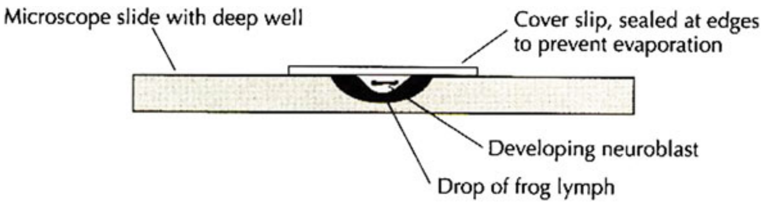

Fig. 4.1 Ross Harrison's culture preparation for observing growth and differentiation of an isolated neuroblast (1907). A deep-well microscope slide provides a miniature culture chamber on the top of which is placed a cover slip that can be sealed at the edges to prevent drying out. The undifferentiated neuroblast is placed in a drop of sterile frog lymph and observed every few hours for a period of 8–10 h [original drawing]

that each nerve fiber was an outgrowth of a single neuroblast, extending outward without the aid of either Schwann cells or protoplasmic bridges.

In 1905 Harrison set out to test these three hypotheses. In order to do so, he needed to find a way to observe neuroblast development outside the embryo's environment where Schwann cells or the postulated protoplasmic bridges could exert their influence. Harrison isolated neuroblasts from frog embryos and placed them in a drop of sterilized frog lymph fluid, which served as a culture medium. He then suspended this drop from the underside of a deep-well slide (Fig. 4.1), which he could examine under the microscope.

When first placed in the hanging drop, the neuroblasts had not yet begun to differentiate. If the first and second hypotheses were correct, the neuroblast should show relatively little differentiation in terms of axonal outgrowth, since neither Schwann cells (Hypothesis 1) nor protoplasmic bridges (Hypothesis 2) were present. Only if Hypothesis III were correct would normal development of a recognizable axon be predicted. The deductive logic of Harrison' experiment may be stated as follows:

If … neuroblasts do not require Schwann cells or protoplasmic bridges to form axons, and

if … neuroblasts are grown in a culture medium in which Schwann cells and protoplasmic bridges do not exist,

then … neuroblasts should develop normal axons.

Harrison observed his neuroblast cultures for periods of up to nine hours. The results of one preparation, observed at 2:50 p.m., 4:45 p.m., and 9:15 p.m. on the same day, are shown in Fig. 4.2. Note that axonal development occurs as a distinct outgrowth of the neuroblast cell body. Clearly neurons possess their own program for growth and differentiation of the axon. The results contradict Hypotheses 1 and 2 and support Hypothesis 3.

Harrison's work, which was nominated once and considered twice for the Nobel Prize, was technically and conceptually brilliant. (The Nobel Committee decided against awarding Harrison the prize because he himself did not follow up on the technique or use it beyond his work on this one set of experiments.) Nonetheless, Harrison's approach to the problem laid the foundation for techniques of culturing

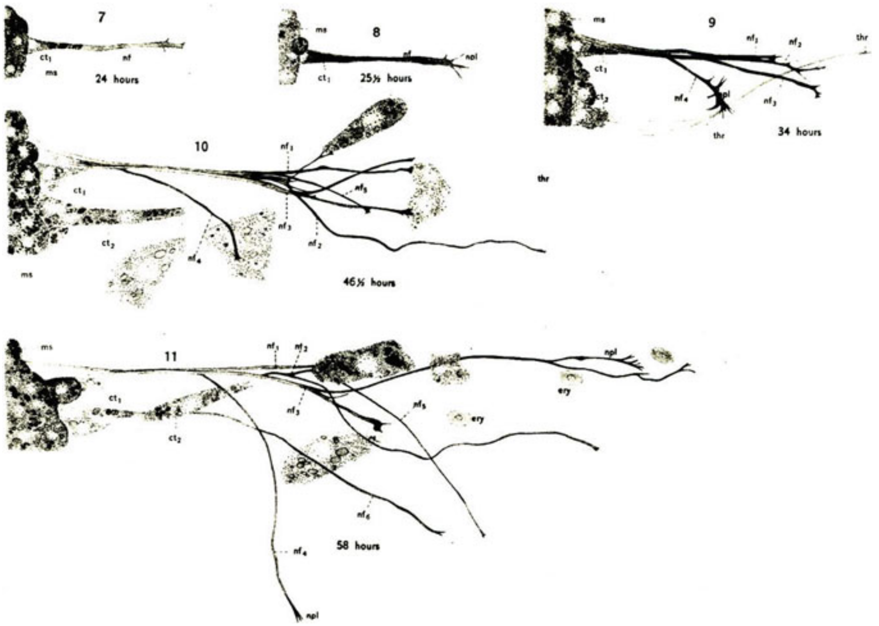

Fig. 4.2 Development of a living nerve fiber (the axon of the neuron or nerve cell as observed by Harrison. This drawing comes from a 1910 publication. The top drawing **a** shows the axon growth at 2:50 p.m., the middle **b** at 4:40 p.m. and the bottom **c** at 9:15 p.m. the same day. The observations clearly show the outgrowth of the axon from the neuroblast with no help from guiding "protoplasmic bridges" or Schwann cells. The other cells shown are scraps that were transplanted along with the neuroblast from the frog egg [from Ross G. Harrison, *Journal of Experimental Zoology* 9, 1910: 787–846, from Benjamin Willier and Jane Oppenheimer, eds., *Foundations of Experimental Embryology*. New York, Hafner/Macmillan, 2nd ed., 1974: p. 102]

living nerve cells in the laboratory. However, as often happens in science, Harrison's results raised a second closely related question: How do the outgrowing axons find their way to their appropriate target sites?

One of the first insights into this question came in 1909 from the work of Mary L. Shorey. She found that removal of a chick limb bud, that portion of the embryo destined to become a leg or wing, caused a failure of the neuroblasts that normally innervate the bud to develop. For the next 25 years nothing much was made of this observation. Then, in 1933, Viktor Hamburger (1900–2001), a German emigré working in the laboratory of Frank R. Lillie (1870–1947) at the University of Chicago, approached the same problem in the reverse direction. Instead of removing the limb bud, he implanted a limb bud from one chick embryo into the limb bud region of another, producing an embryo with two limb buds in the same place. The result was that this second embryo produced far more nerve growth extending into the limb region than occurred in the controls, that is, embryos with only one limb bud. Both Shorey's and Hamburger's findings suggested that nerve growth is somehow regulated by stimuli from the peripheral target zones, such as a developing limb bud. The precise nature of this stimulus remained a mystery. However, in concluding his 1934 paper, Hamburger had put forth a model consisting of several associated hypotheses suggesting how this influence might occur. He proposed that: (1) The developing peripheral regions produced some sort of specific chemical that stimulated neuroblasts to grow in the direction of the developing tissues; (2) The effect must be transmitted from the peripheral region by way of the out-growing ends of the neurons back up the axon to the cell body, where growth was controlled; and (3) The stimulating effect of the limb bud tissue was quantitative, that is, the amount of stimulating effect is directly proportional to the quantity of limb bud tissue present.

After reading Hamburger's paper, a young medical researcher in Italy, Rita Levi-Montalcini (1909–2012), decided to determine exactly how removal of the target tissues affected growth of developing neuroblasts. Although she had received an MD degree, Levi-Montalcini could not obtain a university or government position in Benito Mussolini's fascist Italy because she was Jewish. She therefore had to perform her experiments in her own home with fertile chicken eggs obtained from a local dealer. Repeating Hamburger's experiments, Levi-Montalcini found that if the limb buds of a developing embryo are removed before neurons enter them, large numbers of the neurons heading for the target area actually degenerate. She suggested that the peripheral target tissues may serve the function of *maintaining* rather than stimulating neuronal growth. Published during the war in 1942 and 1944, Levi-Montalcini's papers eventually came to Hamburger's attention. In the best spirit of scientific collaboration, he invited Levi-Montalcini in 1946 to join him in his laboratory, which was then located at Washington University in St. Louis, Missouri. In their first experiments together, Hamburger and Levi-Montalcini confirmed that removal of the target areas does, indeed, cause an increasing deterioration and death of developing neurons. This confirmation supported Shorey's and Hamburger's earlier suggestion that the target tissues must provide some sort of signal for neural development, direction and survival.

What was the nature of that signal? Some insight into that question came from an unexpected source. One of Hamburger's former doctoral students, Elmer Bueker (1903–1996), then at Georgetown University in Washington, D.C., had removed limb buds from chick embryos and replaced them with mouse tumors. The purpose of the experiment was to determine whether a homogeneous tissue like a tumor would produce the same or a different effect on neuronal growth from that produced by the more complex differentiating tissues of a limb bud. Bueker found that one of his mouse tumors, sarcoma 180, grew quite well in chick embryos and that adjacent developing nerves quickly invaded the tumor mass, causing the nerve cell bodies to increase in number by about 30 %. When Bueker sent Hamburger his paper describing this work, Hamburger and Levi-Montalcini obtained his permission to use mouse sarcoma 180 to investigate how peripheral tissue might provide a specific signal for neuronal growth. They found first that the mouse sarcoma was far more effective than limb bud tissue in stimulating neuronal growth in embryos to which it had been transplanted. They also found that the effect was highly specific: The sarcoma affected primarily sensory neurons. Finally, they found that this effect could be produced even when the tumor was placed outside the major membranous coverings of the egg, through which no cells or large structures could pass. The latter result suggested clearly that the tumor must be producing some substance that diffused through the membrane thereby affecting neuronal growth.

To identify what that substance might be, Hamburger was able to hire a post-doctoral fellow, Stanley Cohen (b. 1922), then at the biochemistry department at Washington University School of Medicine, to work with Levi-Montalcini. First, the investigators prepared cell-free extracts from the tumor. They found this extract stimulated neuron growth in precisely the same fashion as the intact tumor and contained a mixture of proteins, nucleic acids and other macromolecules. The active component, whatever it might be, was named "nerve growth factor" (NGF).

To determine the specific nature of NGF, Cohen and Levi-Montalcini began a process of eliminating the various possible components of the mixture. They first treated their extract with snake venom, which contains an enzyme that degrades nucleic acids, reasoning that, if the extract lost its ability to stimulate neuron growth after treatment, then NGF must be a form of nucleic acid. These experiments involved growing nerve cells in culture medium dishes with NGF, NGF+ venom and venom alone (Fig. 4.3). To their complete surprise, Cohen and Levi-Montalcini found that neuronal growth was greater in the control (i.e., venom alone) than in the culture medium containing venom plus tumor extract. It was therefore clear that NGF was not a nucleic acid. In fact, it turned out that snake venom itself is a rich source of NGF. The results also supported Levi-Montalcini's hypothesis that NGF serves primarily a maintenance role in neuronal development. Many neurons begin to grow out from the central nervous system. Most, however, degenerate before reaching a target site. The difference between which ones degenerate and which ones continue to grow has to do with whether or not they come into contact with NGF early in their differentiation. Additional studies showed that NGF was also found in the mammalian anatomical counterpart of snake venom glands, the salivary glands. As it turned out NGF could be found especially easily in the salivary glands of male mice.

Armed with these rich sources of NGF, Cohen and Levi-Montalcini began an all-out assault on its precise identity. Hamburger, meanwhile, returned to his main interest, factors determining nerve growth patterns during chick development. During the mid and late 1950s, Cohen and Levi-Montalcini showed that NGF was a protein and its amino acid sequence was eventually determined. More recently, the DNA for NGF has been sequenced and cloned for a number of species. Before leaving St. Louis for Vanderbilt University in Nashville, Tennessee in 1960, Cohen discovered yet another growth factor, known as epidermal growth factor (EGF). This discovery, along with NGF, suggested that vertebrate development might be guided by a series of growth factors emanating from various peripheral tissues.

Although the exact mechanism of NGF action is still under investigation, it is clear that neurons do not find their way to target tissues unaided. NGF plays an important role in enabling them to get there. For their work on NGF and its extension to EGF and to other growth factors, Levi-Montalcini and Cohen were awarded the 1986 Nobel Prize in Physiology and Medicine.

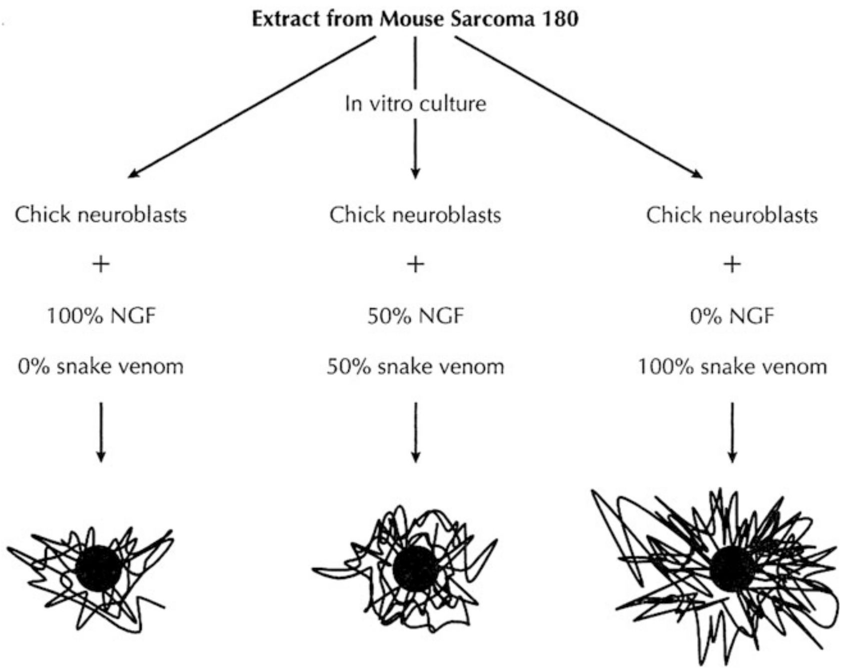

Fig. 4.3 Experimental design for the experiment performed by Rita Levi-Montalcini and Stanley Cohen to demonstrate the effects of NGF on chick neuroblast proliferation. An extract of mouse sarcoma 180 was prepared containing NGF. This was then administered by itself to chick neuroblasts in cell culture (experiment at left, 100 % sarcoma NGF) to chick neuroblasts in combination with snake venom (middle experiment, 50 % mouse sarcoma NGF and 50 % venom), and without any mouse sarcoma NGF and only snake venom (experiment at right, 0 % NGF, 100 % venom). The experiment showed clearly not only that NGF has an effect on proliferation, but also that snake venom has an even more powerful effect, a surprising outcome. In this set-up, each experiment serves as a control for the others [original]

4.3 Research in the Field: Homing in Salmon

The research on nerve growth factor is a classic case of laboratory based research in the biological sciences. The experiments were all performed under conditions allowing for the control of all variables that might have affected the outcomes.

At times, however, experiments must be carried out under conditions where it is not possible to control all of the variables that might influence the outcome of a research study. Such experiments are often referred to as being carried out "in the field." Here we will analyze one such field research project: that of determining how salmon find their way from the ocean to mate in the same freshwater streams where they were hatched.

4.3.1 The Organism

There are few better known fish than the salmon. Its characteristic pink meat has been enjoyed by untold millions of humans. Riverside archeological discoveries of human habitats dating back thousands of years suggest that this enjoyment is very old. The Atlantic salmon (*Salmo salar*) can be found in the waters of virtually every European country bordering the Atlantic ocean, as well as those of countries forming a great arc westward across the Atlantic (Iceland, Greenland, Newfoundland, Canada) to the northeastern portion of the United States (Maine). The silver salmon (*Oncorhyncus kisutch*) is prized by both sport and commercial interest groups and may be found in waters extending from the northwest corner of the United States into western Canada and Alaska.

Besides the pink color of their meat, both Atlantic salmon and the Pacific silver salmon share certain other features in common. One of these shared characteristics is that both are migratory species. Atlantic salmon hatch in freshwater streams and, after reaching a certain size, in response to some as yet undetermined stimulus the fish swim downstream to the Atlantic ocean for several years of feeding and increasing in body weight from five to more than twenty pounds. Upon reaching sexual maturity, they then return to freshwater streams to lay their eggs (spawn), with the males then fertilizing them. After hatching, the cycle begins all over again. Similarly, silver salmon hatch in the freshwater streams of the Pacific Northwest. The young fish swim downstream to the Pacific Ocean, where they may spend five or more years attaining full size and sexual maturity. They then return to freshwater streams, often jumping incredible heights up waterfalls to lay their eggs (Fig. 4.4). As in the case of the Atlantic salmon, the females lay their eggs and the males fertilize them. The adult fish then die.

The second characteristic both species of salmon share is an unfortunate one: a drastic decline in both populations (Fig. 4.5). Exactly *why* this is the case remains unclear. Numerous hypotheses have been put forth: overfishing, changing water temperatures as a result of global warming, disease and/or parasites introduced by escaped farm-raised fish (whose caged and thus denser populations tend to encourage transmission of diseases and parasites). More recently, fish and wildlife personnel have noted a variety of direct human alterations to the rivers themselves through which the salmon migrate. In particular in the northwest, pollution by mining and logging activities in tributary streams leading to the larger rivers, leeching of pesticides and fertilizers from large-scale agricultural production, and clearing river channels for navigation (especially the removal of wood debris, called snags), has deprived the salmon of quiet, backwater eddys where they can rest on their arduous journey. An even more disruptive practice by loggers has been to erect a temporary “flash dam” that builds up a reservoir of water behind it, which is periodically unleashed to “shoot” logs downstream, with devastating effects when it hits a population of migrating salmon. As *Smithsonian Magazine* put it in 2014 with

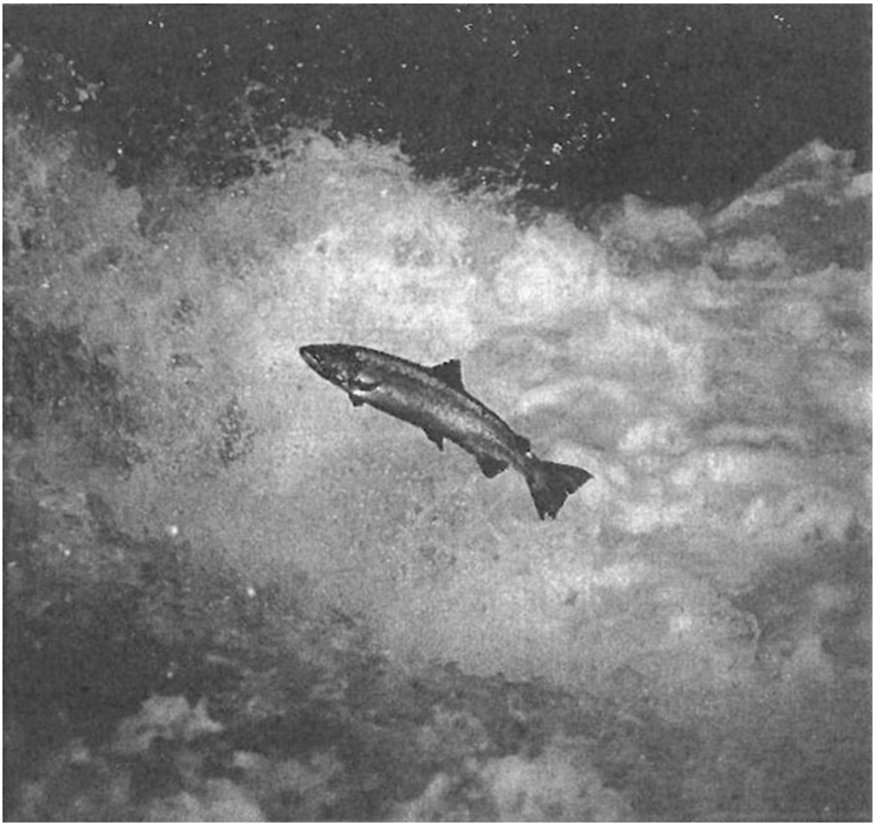

Fig. 4.4 Silver salmon leaping up a waterfall as they swim toward the freshwater streams where they will reproduce. In the case of the Alaskan sockeye salmon, it has been estimated that only about one fish out of 1000 make it successfully to its spawning grounds [© B. and C. Alexander/Photo Researchers]

respect to the silver salmon, the growth of “industrial capitalism and its enterprises wreaked havoc on the wild salmon of the Pacific Northwest.”[1]

Biologists also found out something quite remarkable about the migration of salmon, similar to the migration of the monarch butterflies that was discussed in Chap. 1. By tagging two to three year-old silver salmon at the stage (smelt) when they are ready to go from their home streams to the ocean to mature, biologists found that, to begin the life cycle over again, *salmon return to exactly the same stream from which they hatched*. Geneticists have also found that each home stream has its own genetically-distinct sub-population, a feature that enhances the overall

[1]See, Priscilla Long, “Swimming Upstream: Can Human Ingenuity Help Salmon Navigate the Dangers of One of their Last Srongholds in the Northwest?” *Smithsonian Magazine* (October 2014): pp. 35–38; quotation p. 37.

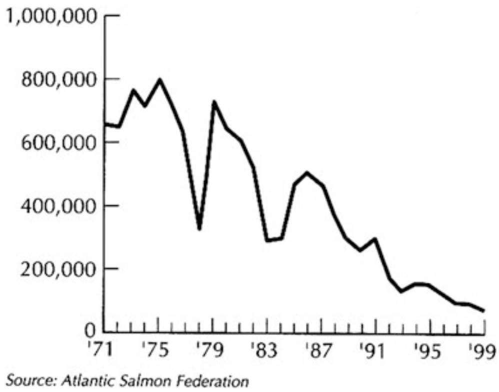

Fig. 4.5 Decline in the population of the Atlantic salmon, *Salmo salar*, from 1971 to 1999. Similar population declines have been documented for its western relative, the silver salmon, *Oncorhyncus kisutch*. The precise cause or causes of this decline remain uncertain

genetic diversity of the species across its range. In terms of scientific process, note that the observation that salmon migrate back to their original home stream is based on a finite number of observations, that is, a sampling of the silver salmon population studied. It is therefore an inductive generalization (see Chap. 2). Assuming this generalization is correct, a new question now arises: *How* do the salmon find their way to the stream where they hatched? In other words, what is the causative factor involved in leading adult silver salmon to return precisely to their home streams instead of any other freshwater stream?

4.3.2 Two Possible Hypotheses

There are at least two possible explanatory hypotheses that might account for the ability of salmon to locate their home streams:

Hypothesis 1: Salmon find their way back by the sense of sight; that is, by recognizing certain objects they saw several years before when they passed downstream on their way to the sea.

Hypothesis 2: Salmon find their way back by their sense of smell, that is, by detecting certain substances and/or proportions of those substances which characterize their home streams.

Several other hypotheses are also possible, of course. Indeed, it may well be that *both* of the above hypotheses are correct and that salmon use their sense of sight *and* smell in locating their home stream. However, it is more practical at least to begin by working with just these two alternative hypotheses and designing experiments to test them. For example, if Hypothesis 2 is correct, then salmon with shields placed over their eyes should be unable to find their way home. This reasoning may be expressed deductively as follows:

If … Silver salmon use visual stimuli alone to find their way to their home streams to spawn …,

then … blindfolded salmon of this species should not be able to find their way home.

In fact, blindfolding experiments reveal that the fish find their way home just as well as they did before. If we assume that no variables which might have influenced the experimentally-obtained results have been overlooked, have these blindfolding experimental results *disproved* our hypothesis? Yes. Suppose, on the other hand, that the blindfolded fish did *not* find their way to their home streams. Would these results *prove* the hypothesis? No: As we stressed in Chap. 2, it lies beyond science to "prove" anything. The experimental results could only be said to *support* hypothesis 1 or, at the very least, to be consistent with it. However, even if the results had supported the visual hypothesis, they would not rule out the role of smell.

Now let us test Hypothesis 2:

If … Silver salmon find their way to their home stream by following its distinctive chemical characteristics upstream …,

Then … blocking the olfactory sacs with which fish detect odors or tastes should prevent salmon of this species from locating their home streams.

This experiment was performed in the mid-1960s by biologist Arthur D. Hasler (1908–2001) and his associates of the University of Wisconsin, working with silver salmon from two streams near Seattle, Washington, the Issaquah Creek and its East Fork (Fig. 4.6). Note that these streams join together just before they empty into Lake Sammanish. A total of 302 salmon were captured for the experiment. Approximately equal numbers came from each stream. The fish were then divided into four groups. Two control groups were established, one from the Issaquah Creek and one from the East Fork. Each fish from the control groups was tagged to indicate the stream from which it came. The experimental groups were also tagged. In addition, however, their olfactory sense was disrupted by the insertion of cotton plugs coated with petroleum jelly or the application of benzocaine ointment (an anesthetic) into their olfactory pits (Fig. 4.7), where the sensory nerve endings responsible for the sense of smell are located. The experimental group fish were then released three-quarters of a mile downstream from where the Issaquah Creek and the East Fork join and subsequently recaptured at traps set in each fork approximately one mile above the junction.

4.3.3 Tabulating the Results

As Table 4.1 shows, not all the released fish were recaptured upstream. Some swam downstream after release, while others swam upstream but missed the traps. Only

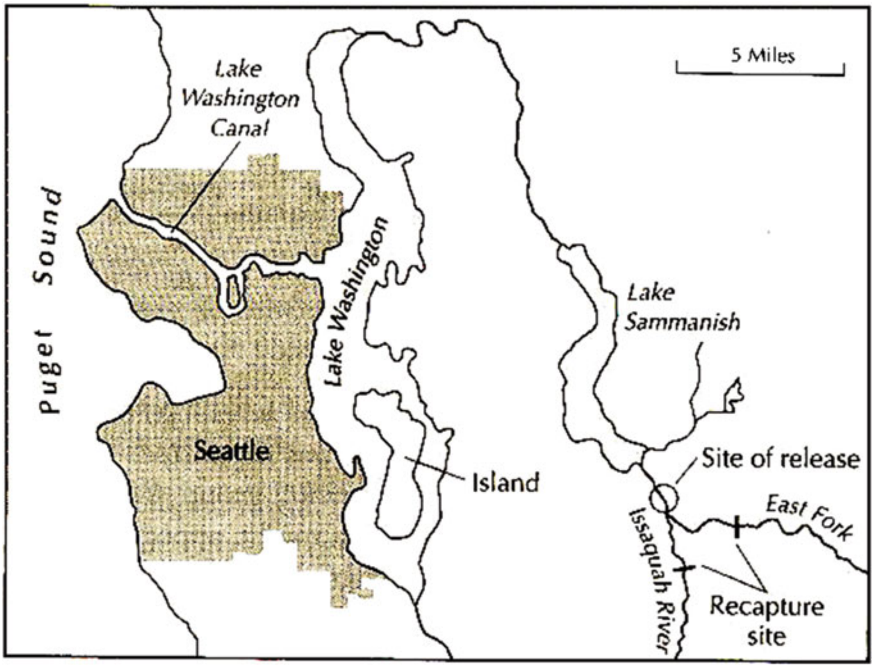

Fig. 4.6 A map showing the region near Seattle, Washington, where A.D. Hasler and his research team did his field studies on factors influencing homing behavior in the silver salmon [after Hasler (1966, p. 39). Copyright 1966 by the University of Wisconsin Press and reproduced with permission]

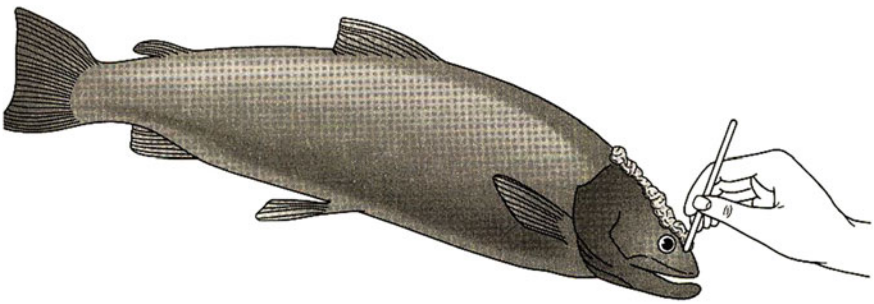

Fig. 4.7 Inserting a cotton wad (visible above the eye of the fish) permeated with petroleum jelly of benzocaine ointment into the olfactory pit of an anaesthetized and tagged silver salmon. After Hasler (1966, p. 39). Copyright by the University of Wisconsin Press and reproduced with permission

Table 4.1 Total silver salmon tagged compared to number captured from experimental and control groups

		Recaptures		Not captured	
	Total tagged	Actual number	Percent	Actual number	Percent
Control	149	73	49.6	76	50.4
Experimental	153	70	45.0	83	55.0

Table 4.2 Distribution of recaptured silver salmon, comparing experimental and control groups

Capture site	Recapture site			
	Issaquah		East Fork	
	Actual number	Percent	Actual number	Percent
Control				
Issaquah (46 fish)	46	100	0	0
East Fork (27 fish)	8	29	19	71
Experimentals				
Issaquah (51 fish)	39	77	12	23
East Fork (19 fish)	16	84	3	16

50 % of the controls and 45 % of the experimental fish were recaptured. More important, however, were the results of the distribution of fish according to their stream of origin. As Table 4.2 indicates, there was a significant difference between the control and experimental groups in terms of finding their way home. Among the controls, 100 % of the Issaquah Creek and 71 % of the East Fork salmon were able to find their way back to their home streams. In the experimental groups, however, only 77 % of the Issaquah Creek and 16 % of the East fork salmon found their stream of origin. Thus Hypothesis II, maintaining that the olfactory sense is responsible for salmon being able to identify their home streams was supported.

Note that *some* fish from each experimental group *did* find their way back to their home streams, a result that might appear to contradict Hypothesis II. Here, however, the laws of chance and probability come into play. A certain number of the fish would be expected to return to their home streams purely by chance. In Hasler's experiment, the small number of experimental animals that actually found their way home was approximately what would be expected based on chance alone. Thus, Hypothesis II can still be considered valid.

4.3.4 Further Questions

The salmon experiment demonstrates a characteristic of any scientific problem-solving activity: the answer to one question often raises many more. For example, it would be useful in fish management practices as well as interesting from a scientific perspective, to determine what is it in their home streams that the salmon detect by their sense of smell? What sort of factor or factors in the stream provide serve as a guide? A number of hypotheses come to mind:

Hypothesis I: Silver salmon detect discrete combinations of dissolved inorganic substances (minerals) in the water of their home streams.

Hypothesis II: Silver salmon detect discrete combinations of dissolved organic compounds characteristic of their home streams.

Hypothesis III: Silver salmon are somehow able to recognize other salmon of their own home stream population and follow them.

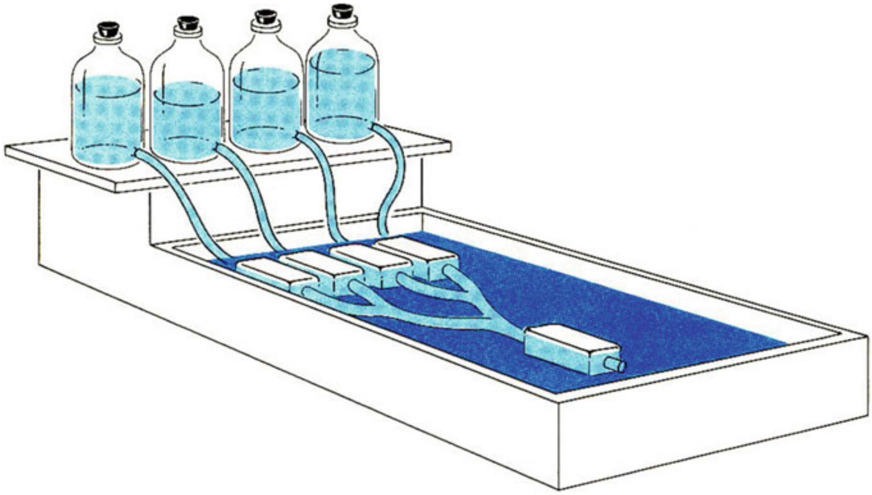

Fig. 4.8 Whenever possible, biologists attempt to construct an apparatus which allow testing hypotheses in the laboratory rather than in the field. By so doing, variables which might influence the results are more easily controlled. This apparatus tests the ability of eels, another migratory fish, to detect minute amounts of dissolved substances in water. The object is to see whether these substances play a role in young eels' ability to find their way home from the Sargasso Sea, a region in the Atlantic Ocean south of Bermuda where they hatched, to the freshwater streams in Europe where they spend most of their lives. It was shown young eels show no preference for tap water over sea water, but had a strong preference for natural inland water to sea water, being able to detect certain organic compounds in the water even when diluted to 3×10^{-29} parts per million. This means they must be reacting to the presence of only two or three molecules of the substance! Since eels are a different species of fish than salmon, such results provide only indirect support for the olfactory hypothesis concerning how silver salmon are able to locate the stream where they hatched

Again, using deduction, each of these hypotheses lead to specific predictions that may, in turn, be verified or refuted experimentally. Studies with other closely related migratory organisms may also help. For example, it has been shown that eels, which also migrate from freshwater to saltwater where they spawn and then return, are enormously sensitive to dissolved minerals and organic material in water. A single eel is able to detect the presence of a substance dissolved in water and diluted to the extent that only two or three molecules of the substance were present per liter (Fig. 4.8), an observation lending support to Hypotheses I and II in the case of the silver salmon.

Fortunately, there are some experimental data available to help distinguish between Hypotheses I, II and III. Dr. D.J. Solomon of the Ministry of Agriculture, Fisheries and Food in Great Britain, studied Atlantic salmon migration around three rivers, the Usk, Wye and Severn. These rivers empty into the Bristol Channel, located on the west coast of England (Fig. 4.9). The adult salmon breed and the young fish mature in the upstream portions of each of these rivers. However, several other rivers also empty into the Bristol Channel yet they do not contain salmon populations.

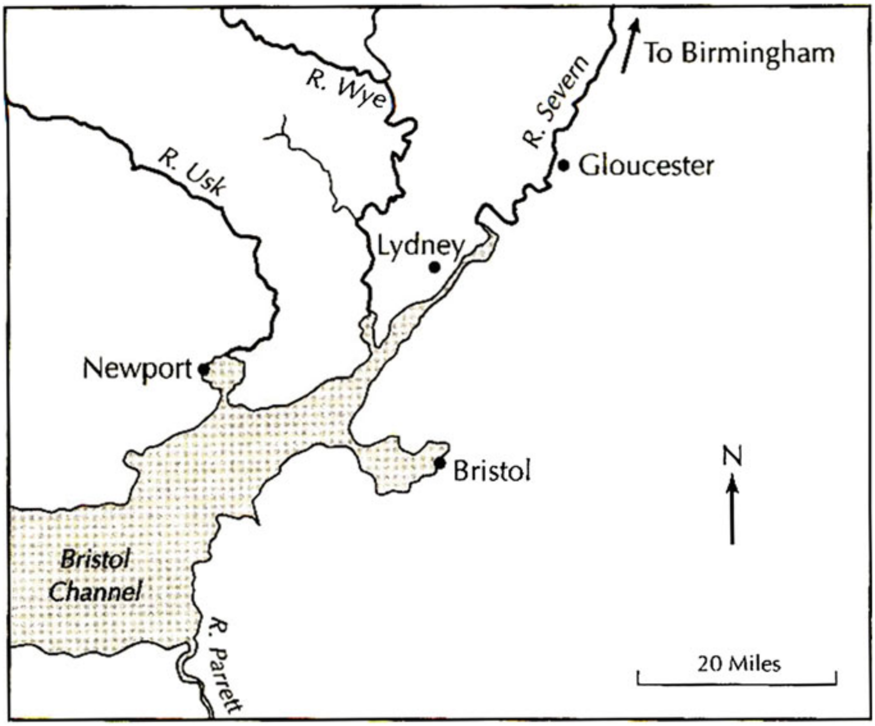

Fig. 4.9 A map of the west coast of England showing the Bristol Channel with the rivers Usk, Wye and Severn emptying into it. These three rivers normally contain salmon, yet other rivers also emptying into the Bristol channel generally do not [from *Nature* 244, July 27, 1973, p. 231. Crown Copyright. Reproduced by permission of the Controller of Her Britannic Majesty's Stationery Office]

Solomon became curious about what attracted adult salmon into the Bristol Channel and thence into the Usk, Wye and Severn and yet, conversely, kept them from invading other available rivers. He reasoned that, if something as general as dissolved minerals and organic matter were the attractant, then one would expect to find Bristol Channel salmon swimming selectively into the point of entrance of freshwater from *all* the rivers emptying into the channel's salt water estuaries. Since ocean water contains far more dissolved minerals and organic matter of the same general type found in freshwater rivers, fish would have to swim part of the way up a river to be able to determine whether it was "home". Yet in a survey of 23,000 tagged fish, only six were found entering into those rivers. What Solomon *did* notice, however, was that only a few (six) salmon swam into rivers where there were no other salmon. This observation led Solomon to formulate another hypothesis: The main factor attracting salmon to a river is the presence of other salmon. He knew that many animal species are known to produce distinctive substances called pheromones by which members of each species recognize one another. Solomon hypothesized that the factor attracting salmon to one salmon-containing river over another are the pheromones produced by that river's particular population of young salmon. But he needed a way to test this hypothesis. Designing an experiment in nature with such a huge fish population would be difficult and involve innumerable practical obstacles, not the least of which would be expense. However, in going through the research literature, Solomon discovered data from a 20-year-old breeding experiment that provided a test for his hypothesis. In the 1950s, the British government had financed an attempt to establish a salmon breeding ground in a tributary of the Parrett River, which also empties into the Bristol Channel. The attempt ultimately met with failure when no salmon population became established in the Parrett. However, records showed that in the three years immediately after the first breeding population was introduced, the number of adult salmon found swimming up the Parrett increased several fold. Most significant here, these fish had not come from the newly established fishery population, but rather from the Usk, Wye, and Severn populations. The fish appeared to have suddenly found the Parrett interesting! Using deduction, in this case retroactively, Solomon could see that a prediction based upon his pheromone hypothesis had already been supported by the Parrett River study done 20 years before. Expressed hypothetico-deductively:

If … Atlantic salmon recognize pheromones produced by other salmon
then … introducing young salmon into a river ordinarily without salmon ought to increase the chances of adult salmon swimming into that river.

As already noted, the Parrett River data supported Solomon's hypothesis. As we know from Chap. 3, however, a true prediction does not necessarily mean a true hypothesis. Nonetheless, the data *do* lend support to the hypothesis by verifying one of the predictions which follow from its acceptance.

4.3.5 Testing the Pheromone Hypothesis Further

It had been shown as long ago as 1938 that salmon transplanted at the pre-migratory stage from their native river to a second river returned as adults to the second river. In a contrasting set of experiments, salmon were kept in a hatchery until well past the age at which they would have begun their journey from natural home streams to the ocean. When these salmon were then released into different streams, they failed to return as adults to their transplant stream, but rather returned in a random pattern to a number of different streams. These results suggest that a critical period must exist in a young salmon's life during which it "learns" to recognize the stream where it hatched. Further experiments, conducted between 1955 and 1971 by a number of investigators, found that young salmon are especially receptive to recognizing the chemical characteristics of their home stream just at the time they enter the stage of their life at which they begin to migrate towards the ocean. In fact, during this critical period, exposure of a young salmon to the chemical odors for as short a time as 4 h is long enough for it to "remember" this odor for life, a phenomenon referred to as *imprinting*. Thus, it could be hypothesized that, at a critical period in life, young salmon become imprinted with the specific chemical composition of their home streams and later use this imprinted memory to guide them back as adults.

In the mid-1970s, Hasler, along with several associates, decided to study the imprinting process directly. They exposed a group of young salmon at the pre-migratory stage to a non toxic organic substance called morpholine (C_4H_9NO). They then selected two groups of salmon that had been raised in a hatchery until the pre-migratory stage. The experimental group they exposed to low dosages of morpholine (1 × 105 mg/L) for a month. The control group received no morpholine. Both groups remained in the hatchery for ten more months, after which they were brought to the laboratory, placed in tanks with morpholine, and their brain waves recorded. As the research team had predicted, the experimental group that had been exposed to morpholine showed a significantly higher amount of brain wave activity than did the controls that had not been exposed.

Hasler and his co-workers then proceeded to resolve another question: Will fish exposed to morpholine actually swim toward streams into which the compound has been placed? They took the experimental and control groups of salmon described above and released them into Lake Michigan at a point equidistant between the outlets of two creeks. Into one (Owl Creek), they placed a concentration of morpholine about equal to that maintained in the hatching tanks. The other stream was left undisturbed. The fish were marked and eighteen months later the investigators carried out recapturing procedures so as to see which fish were found in each stream. In Owl Creek, out of a starting population of 16,000, a total of 246 tagged fish were recaptured, about the expected percentage of recapture in other such experiments. Of the 246 fish recaptured, 218 were those that had been exposed to morpholine, while only eighteen were from the control group. In the other creek, most of the fish were from the control group. It seemed clear that the cue that had attracted such a disproportionate number of the experimental group to Owl Creek was the presence of morpholine in the water.

Could something else in Owl Creek have served as a cue to the experimental fish, masking the effects of morpholine? In a follow-up experiment, representatives of the control and experimental groups were released near the two streams, but no morpholine was added to either stream. If the experimental fish had found their way into Owl Creek because of the presence of some other cues, they ought to do so in this second experiment in the same approximate numbers as in the first one. When the investigators carried out this experiment, they found about equal numbers of both control and experimental fish in each creek. Therefore the hypothesis proposing that salmon became imprinted to a specific chemical compound (or group of compounds) early in life seemed well supported.

In yet another experiment, Hasler and his associates attempted to track the movement of adult salmon through the water in response to the presence of morpholine. They implanted ultrasonic transmitters to serve as tracking devices into forty salmon, twenty of which had been imprinted on morpholine and twenty of which had not. After releasing the fish into Lake Michigan, the researchers set up an "odor barrier" by pouring a line of morpholine in the water along the shore. It was found that the fish exposed to morpholine would stop swimming when they encountered the odor barrier and mill around for up to 4 h within the barrier until the scent had been washed away by the current. The control salmon, not exposed to morpholine, swam through the barrier without stopping.

From all of these results, Hasler felt that he could draw three major conclusions:

1. Salmon use their olfactory sense to detect the presence of familiar substances in water in identifying their home streams.
2. Salmon become imprinted to the familiar chemical odors of their home streams when in their early pre-migratory stage.
3. The specific chemical odors to which young salmon become imprinted guide them as adults in returning to their home streams.

4.3.6 "Dissecting" the Experiments

Hasler's and Solomon's work with salmon illustrates several important features of testing hypotheses in science. Note that both investigators framed their questions in ways that were testable. They did not put their question in a general form such as, "How do salmon find their way home?" Instead, they broke this large question down into several smaller, more directly answerable questions: among them, "Do salmon use their olfactory sense to find their way home?" and "Will salmon become imprinted to an artificial substance if they are exposed to it early in life?" Both of these questions suggest observations or experiments that might provide answers.

A second point about scientific research illustrated by this case is the importance of approaching a given problem from a number of different directions. Hasler and his research team were not content to simply do one or two experiments testing the olfactory hypothesis. They showed not only that adult salmon use their olfactory sense to find their way home, but also that salmon become imprinted to specific substances early in life, show a distinct neurological reaction to substances to which they have become imprinted, and select streams containing these substances when they return to spawn. All these lines of evidence converge to support the initial Hypothesis 2, which proposed that young salmon are able to use their olfactory sense to "recognize" the chemical peculiarities of their home streams and use this recognition to guide them back to these streams as adults.

A final point concerning scientific methodology illustrated by these salmon experiments comes from Solomon's work. It is not always possible in science to perform an experiment to test a hypothesis. Yet it often happens that an observation or group of observations that already exist will serve the same purpose. Solomon's observation that adult salmon appeared in the Parrett River only after young fish had been introduced there supported one aspect of the olfactory hypothesis, in this case the idea that part of the olfactory stimuli to which adult salmon react may be pheromones or some similar substance or substances resulting from the presence of other salmon. Solomon did not do an experiment to come to this conclusion; in a way, the experiment had already been done for him. He simply took advantage of data already collected relevant to the question he was asking.

4.3.7 Statistical Significance

Quantitative data are a cornerstone of modern science (see Appendix A). Yet it is obvious that a large collection of such data is of little or no value if it is not arranged in such a way as to demonstrate important relationships. The individual data for each tagged fish in Hasler's experiments yield little information if they are presented randomly, for example in the order in which each fish was recaptured. In collecting data in the field, of course, Hasler and his associates had to tabulate it as it came in; that is, as they captured a fish they would record where it was from, whether it belonged to the experimental or control group, and the stream in which it had been caught. Their field notebooks might have contained information arranged as is shown in Table 4.3. Note that these data are both quantitative and qualitative. Hasler's first experiment involved quantitative data: he counted the number of each fish population recaptured in each river and expressed the number in terms of percentages of those released.

As presented thus far, these data do not allow us to determine readily whether the odor hypothesis (Hypothesis II) has been confirmed or disproven. By arranging the data to allow a comparison between the experimental and control groups, however, Hasler was able to determine that a difference did exist between them. As shown in Table 4.2, silver salmon with their olfactory sacs plugged found their way back home less frequently than those with their olfactory sense left unimpaired. What, then, is the function of the data shown in Table 4.1? This table records the difference between the number of fish released in each group and the number recaptured. Note that, for both groups, the percent of fish recaptured (or conversely,

Table 4.3 Hypothetical table of raw data as it might have been recorded by A.D. Hasler and his research associates

Fish number (in order of recapture)	Recapture site			
	Control group		Experimental group	
	Where released	Where recaptured	Where released	Where recaptured
1	Issaquah	Issaquah		
2	East Fork	Issaquah		
3			Issaquah	East Fork
4	East Fork	East Fork		
5			East Fork	East Fork
6			East Fork	Issaquah
7	Issaquah	Issaquah		
8			Issaquah	East Fork
Etc.				

not recaptured) is approximately the same (49.6 % of controls, 45 % of experimentals). This is vitally important information. If a significant decrease in the percentage of silver salmon in the experimentals and controls had been found, comparison of the data shown in Table 4.2 would not be very useful. If a statistically significant decrease in the percentage of silver salmon in the experimental group, compared to the controls, had found their way home, we would have to conclude that the plugging of their olfactory pits must not have affected the general ability of the fish to navigate. The similar recapture rate recorded for both experimental and control fish, however, indicates that the two groups must have had an approximately equal ability to navigate.

Table 4.1 also informs us whether or not both experimental and control groups were subject to the same sampling error. Suppose, for example, that only 10 % of the total experimental group had been recaptured as compared to, say, 50 % of the controls—obviously a very large difference. A 10 % recapture rate is very small and thus might well be unrepresentative of the whole. Because Hasler was dealing with a total of only about 150 fish in each group, control and experimental, a large difference in recapture rate between the groups could easily lead to sampling error in the smaller group. Determining that the recapture rates were similar for both groups eliminated this problem.

Recall, however, that *some* of the experimental fish *did*, in fact, end up in streams that were not their homes. Only in the case of the Issaquah Creek control group did 100 % of the fish manage to get back to the stream where they hatched. Among the East Fork controls, only 71 % returned to the East Fork. This confirms that the inductive generalization "salmon return to their home stream to spawn" is accurate only in a statistically significant number of cases. Precisely the same applies to most situations in the real world. Although from a strictly logical point of view a single exception to an inductive generalization is enough to make it invalid, in nature this is not the case. The generalization that salmon find their way home by the use of environmental clues obtained through their olfactory sense does not necessarily mean that other factors may not also be involved. The presence of predators, water currents, fatigue, the behavior of other nearby fish, may also have contributed to the direction Hasler's silver salmon took when they came to the juncture of the Issaquah and East Fork. Thus, although it may generally be correct that silver salmon find their way home by the use of their olfactory sense, this does not mean that other factors may not also influence an individual salmon's migratory direction.

Here again is where the statistical significance of the difference enters into the equation. Table 4.1, for example, shows that of all the fish released, about 50 % of the control group and 45 % of the experimental group were recaptured. Is this difference statistically significant? Under some circumstances it might be. To Hasler, knowing the conditions under which fish were tagged, released and recaptured, such a difference appeared to be insignificant. He was confident that the rate of recapture between the experimental and control groups was virtually the same. A statistical significance test verified this conclusion, but that does not mean that Hasler was absolutely right. Sometimes small, unexpected differences between what is predicted and what is actually found to be the case leads to new discoveries. A highly subjective element in science lies partly in knowing when to ignore and when to pay attention to such differences.

The same test of statistical significance may be applied to the data in Table 4.2. If the olfactory hypothesis were correct, for example, we might expect that, with very large samples, approximately 50 % of the Issaquah Creek control group would actually end up in Issaquah Creek and 50 % of the East Fork control group would end up in the East Fork. Howether, with no olfactory sense to guide them, silver salmon in the experimental group should enter streams more or less at random. The data show that, among the experimental groups, more Issaquah Creek fish ended up in the Issaquah Creek than in the East Fork (77 % as compared to 23 %), an approximately 25 % error between the actual and the expected results. Among the East Fork experimental subgroup, the situation was very different. Here, 84 % ended up in their non-home stream (Issaquah Creek), whereas only 16 % arrived at their home stream (East Fork). Are these differences from expectation (50:50 in both cases) statistically significant? The situation is most clear-cut in relation to the East Fork experimental group. Of these fish, 84 % ended up in their non-home stream, whereas by chance we would expect about 50 % to do so. Comparing the East Fork experimental with their control group counterparts, we see that in the latter only 29 % ended up in the wrong stream. Here, no statistical test is necessary to state conclusively that the difference between 29 and 84 % is significant. However, data from the Issaquah Creek experimental and control groups, presents an interesting twist. It is certainly an unusual result that 100 % of the Issaquah Creek controls were recaptured where they were predicted to be. Among the experimental group, only 77 % were recaptured in their home stream, a figure also considerably higher than the 50 % we might expect on the basis of chance alone. Indeed, the Issaquah Creek experimental group with no olfactory sense actually did *better* than the East Fork controls whose olfactory sense was fully functional! Quite obviously, Hasler's conclusion that the data still support the olfactory hypothesis comes to some extent from considerations other than hard data. This example emphasizes the many arbitrary and often subjective elements that may often enter into data analysis and the evaluation of scientific hypotheses based on these data even if obtained by rigorous and quantitative processes.

4.4 An Evolutionary Historical Case: Mass Extinctions and the End of the Dinosaurs: The Nemesis Affair

In the late 1970s, geologist Walter Alvarez (b. 1940), at the University of California, Berkeley, became interested in events occurring at major transition points in the earth's history. One such transition was that between the Cretaceous and Tertiary periods, known as the K-T boundary (the letter "K" is used to avoid confusion with the "C" of the Cenozoic era, which marks the beginning of the Tertiary period) approximately 65 million years ago. The K-T boundary marks the end of the

Mesozoic and beginning of the Cenozoic eras, a time known not only for the rapid extinction of the dinosaurs but also of many other forms of life. It is the best-known example of mass extinctions in geological history. Alvarez was working on a site in northern Italy near the town of Gubbio, where the actual boundary layer is exposed, when he noted an unusual, thin layer of clay between the two thicker rock strata. To determine how long it took to deposit this thin clay layer, Alvarez, along with his father, Luis Alvarez (1911–1988), a physicist also at the University of California, Berkeley, noted and measured the amount of the rare metal iridium (Ir) in the clay. Iridium is found in very small concentrations on earth, but is known to be far more plentiful in meteorites and other extra-terrestrial objects. Iridium enters the earth's atmosphere at a fairly regular rate in the form of a shower of cosmic dust, and thus its concentration in a layer of sediment would provide a good estimate of sedimentation rate. When the clay was analyzed, it was found to have abnormally high concentrations of iridium: 10 parts per billion (ppb) compared to 3 ppb in the rock strata on either side. Further information on other K-T boundary sites around the world showed iridium to be abnormally high in these sediments as well (Fig. 4.10).

What could have caused such an unusual and widespread deposition of iridium 65 million years ago? In a 1980 paper in the journal *Science*, the Alvarez team hypothesized a novel explanation: the high level of iridium was due to the impact of a giant asteroid, roughly 10 km (6 miles) in diameter, that collided with Earth, stirring up clouds of dust and ash and causing widespread volcanic activity. The resulting atmospheric ash reduced sunlight and thus photosynthesis, leading to the

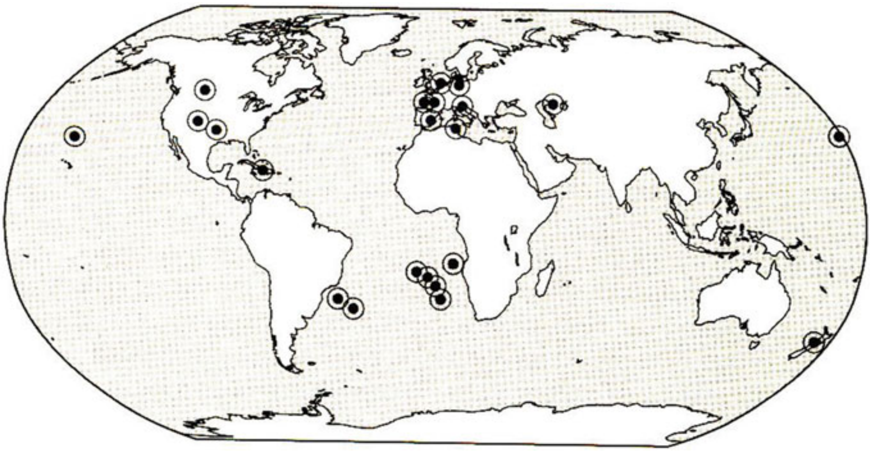

Fig. 4.10 Location of the most important sites where iridium anomalies occur at K-T boundaries, tabulated as of mid-1983. The map shows the global distribution of the sites as well as the variety of environments involved: marine, swamp and land. The chemical analyses come from laboratories in Switzerland, Holland, the former Soviet Union and the United States. From Raup (1986, p. 85); originally from Walter Alvarez et al. in *Science* 223, 1984: 1183–1186, Fig. 1

mass extinctions that characterized the late Cretaceous period. Thus, from an initial anomaly, the unexpected finding of high levels of iridium at the K-T boundary, a new hypothesis to account for the mass extinctions was born.

4.4.1 Testing the Impact Hypothesis

An obvious way to test the asteroid hypothesis would be to use the sequence of dinosaur fossils in the geological record to trace the time of extinction with respect to the K-T boundary layer. We can set up a deductive syllogism as follows:

If … extinction of the dinosaurs was primarily due to a meteoric impact that also produced the iridium layer,

then…. dinosaur and other large animal fossils should be prevalent below the K-T boundary and scarce or non-existent above it.

One particular fossil bed was known to exist where the prediction could be tested, the Hell Creek formation in Montana, where fossil-rich strata existed above and below the K-T boundary. Examination of this site, however, revealed that the most recent dinosaur remains were well below the iridium layer—in fact, *too far below*! There were a full three meters (approximately 10 ft) of sediment between the last dinosaur remains and the iridium layer. This "three meter gap" as it was termed, suggested that the dinosaurs had become extinct long before the hypothesized meteorite impact, thus falsifying predictions stemming from the Alvarez hypothesis and rendering it invalid.

In defense of their hypothesis, the Alvarez team argued that the lack of dinosaur fossils in the three-meter gap did not necessarily mean that the animals had died out at that time, but only that they were not fossilized in this particular locality during that period. The logic here is straightforward: the presence of dinosaur fossils *above* the boundary layer would have indicated clearly that the animals continued to live in the area after the impact and thus invalidate the impact hypothesis. On the other hand, given the accidental nature of fossil formation, the lack of fossils in the three meter gap did not necessarily mean that the dinosaurs had become extinct in that period. In this case, negative evidence is not as logically binding as positive evidence. (As forensic experts say, "The absence of evidence is not evidence of absence.") The impact hypothesis remained viable, although still wholly speculative. While it was well documented that large meteorites had struck the earth periodically in the past, leaving tell-tale craters, none of these craters seemed to be large enough nor of the right age to support the Alvarez hypothesis.

A dramatic breakthrough would soon occur. In the early 1990s, geologists discovered the remains of a gigantic impact crater in the Yucatan peninsula and determined its age to be precisely that demanded by the Alvarez hypothesis, 65 million years. Even with this impact event strongly confirmed, however, the paleontological data concerning a mass extinction at that time remained problematical.

4.4.2 Extinctions and the Paleontological Record

One major problem in determining if a mass extinction has occurred involves two intertwined questions: (1) What counts as a mass extinction as compared to the ordinary occurrence of extinctions over a specific time frame? (2) What taxonomic levels should be used in computing extinction rates: species, genus, family, order, or phylum? Both questions involve setting some consistent, though ultimately arbitrary, criteria.

Determining what counts as a mass extinction may *seem* simple, but it is far from being a straightforward matter. Is a mass extinction equivalent to 90 %, or 40 %, or 20 % of *all* species? Should a distinction be made between animals and plants or between terrestrial organisms more vulnerable to drastic climatic changes and marine organisms that are protected by the shielding effect of ocean waters? Therefore, part of the debate about the meteoric impact hypothesis was that different investigators had different criteria for what counted as a mass extinction. For example, at the K-T boundary extinction, 60–80 % of all marine species became extinct, but only about 15 % of all marine animals. On the other hand, microscopic marine animals (zooplankton) were particularly hard-hit, while microscopic marine plants (phytoplankton) were not. Organisms living as part of coral reef ecosystems were major victims but the animals that built and lived within the coral reefs themselves survived well. Deep sea organisms survived better than surface water organisms, while terrestrial plants survived better than terrestrial animals. The selectivity of extinction makes it difficult to decide on which group or groups of organisms to focus in determining whether an extinction is truly "mass" in character.

At first glance it might seem that choosing the taxonomic level at which to examine extinctions is obvious: the species. However, using species in the fossil record is not as easy as it might sound. One of the major problems is that it is often far more difficult to draw clear demarcations between fossil species than between living species. With living species the taxonomist has available evidence not only from anatomy but also ecology, physiology, behavior and reproductive capacity. Except for certain kinds of invertebrate species such as shellfish, possessing easily fossilized parts, most of the characteristics of fossils are obscured so that the paleontologist has much less information to go on. Also, paleontologists often do not have a sufficiently large population of fossils, especially of larger organisms, to determine whether their collection represent a single species with lots of variation or two or more species that are distinct from each other. Moving up the taxonomic scale to class or phylum includes so many varied forms, tracking each group through time would probably not reveal much fine detail about extinction rates. Most of the species of the class Reptilia, to which dinosaurs belong, might have become extinct but still the entire class might not. Thus paleontologists have more or less compromised on the family as the taxonomic level that yields the most useful information about extinction. Families have enough diversity to withstand various climatic and other changes, yet they are a small enough grouping to reflect more serious environmental events, such as a meteoric impact. Family-level differences are also easier to distinguish in the fossil record than are genus or species-level differences.

However, there is a problem inherent in using any taxonomic category higher than the individual species. A family, for example, may contain one genus and species (such as the family Hominidae, which includes humans as the only surviving species), or it may contain, as do some insect families, hundreds of species. Yet, single-species families and multispecies families each count as one unit in tallying up extinctions. As a result of this problem, critics of mass extinction theories argue that it is possible to make anything a mass extinction by choosing the taxonomic category to be used that will give the desired results. It is for just this reason that paleontologists negotiated the family as an agreed-upon taxonomic category and which they use when trying to assess the severity of most extinction events.

A second problem encountered by the impact hypothesis is that of determining the age of fossils and geological strata accurately. Depending on the dating methods used, estimates of the age of specimens have changed dramatically over the past 40–50 years. To make estimates of precisely when a species became extinct over the long periods of the geological record it is necessary to use several different data bases.

4.4.3 Periodic Mass Extinctions

In 1983, paleontologists David Raup (1933–2015) and Jack Sepkoski (1948–1999) at the University of Chicago became intrigued with the Alvarez impact hypothesis. In a paper published in the journal *Science* in 1984, they argued that a mass extinction event had not only occurred at the K-T boundary but appeared to be periodic, occurring on the average of every 26 million years.

Such a periodicity seemed remarkable, and very much a surprise. The methodology of determining periodicity, to say nothing of extinction rates, seemed fraught with difficulties. First, there is the problem of periodicity itself. Probability theorists know that many purely random events often give the appearance of cycles. Suppose, for example, you take a deck of cards and draw out one card every day. If you do this every day for 250 days, noting on a calendar the days on which you draw a black ace, you would expect to make a mark on the average of twice every 52 draws, or once every 26 days. In reality, however, you do not get such a neat distribution. Five such drawings, each covering 250 days, were simulated on a computer and the distribution of black aces calculated (Fig. 4.11). Note that, even though the process of generating the draws is random, black aces appear in clusters, rather than being evenly spaced. These clusters are separated by long periods where no black aces are drawn at all. Here, the periodicity is simply the result of chance. However, Raup demonstrated that the clustering shown in Fig. 4.12, the 26 million year cycle, is more regular than that of the black aces shown in Fig. 4.11, suggesting that extinction events might not be the result of mere chance. In other words, while randomness *might* have generated the 26-million year cycle, its

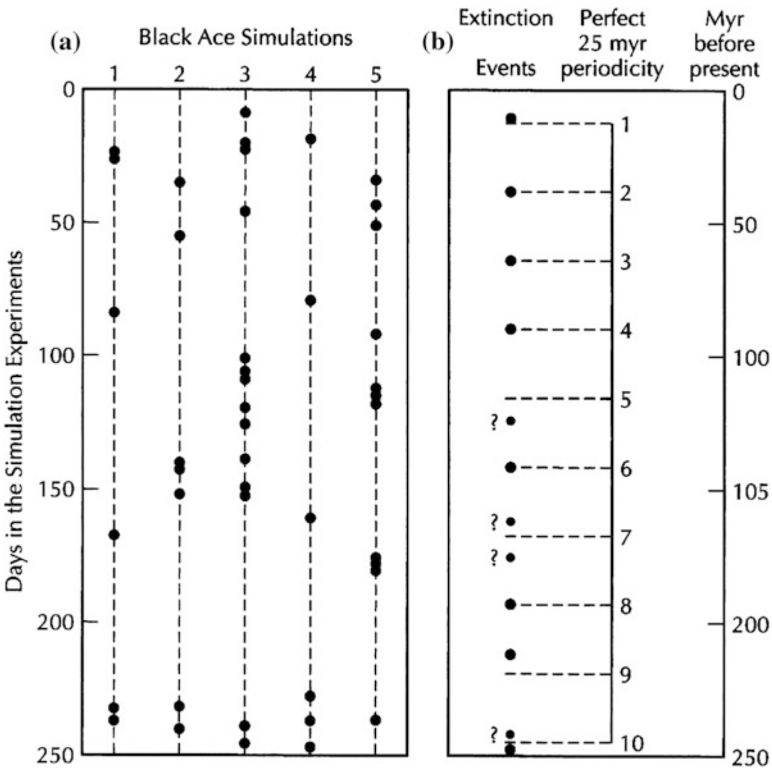

Fig. 4.11 Results of a computer-simulated black ace experiment (**a**) compared to the periodicity established for mass extinction events (**b**). Both series show some degree of clustering, with events bunched together and then separated by intervals where no events occur. In **a** the periodicity is generated completely by chance and the cycles are somewhat irregular. In **b** the periodicity is more regular, but its cause is not known. The point of the experiments is to demonstrate that even completely random events may show periodicity, suggesting that the mere existence of a cycle does not indicate it is caused by some regular, as opposed to a random, phenomenon. From Raup (1986, p. 117)

greater regularity argues for a more persistent causal agent. Raup and Sepkoski were thus surprised and delighted to learn that Walter Alvarez and astrophysicist Rich Muller had found a 26-million year cycle in the occurrence of asteroid craters identical to that found for mass extinction events. A periodicity discernible from three different kinds of data, iridium sampling, dating of meteorite craters and extinction events, greatly increased the likelihood that these were not purely chance events, but might well have some fundamental connection with each other. Therefore, the Alvarez hypothesis, devised originally to explain only a single extinction at the end of the Cretaceous, might be extended to a whole series of extinctions occurring roughly every 26 million years.

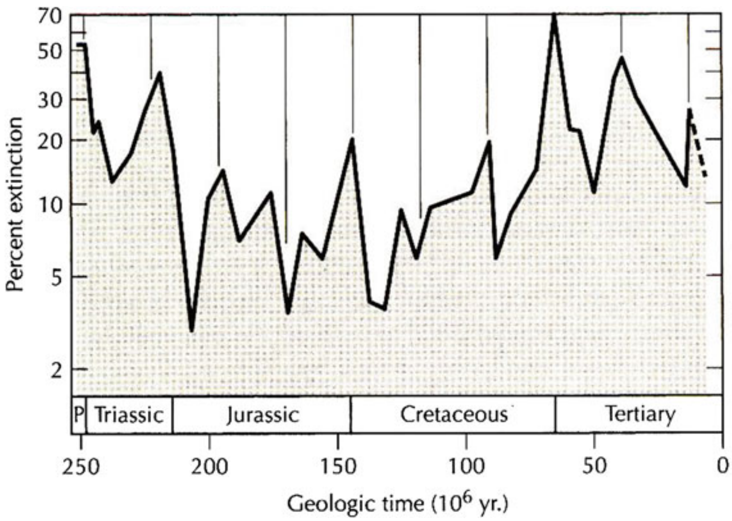

Fig. 4.12 Cyclic recurrence of mass extinction events over the past 150 million years for families of extinct marine organisms. The relative heights of the various peaks are approximations. Note that the peaks appear to recur on approximately 26 million year cycles [from RAUP and SEPKOSKI, "Periodicity of extinctions on the geologic past." *Proceedings of the National Academy of Sciences* 81, 1984: 801–805; Fig. 1, p. 802]

4.4.4 The Nemesis Hypothesis

After 1984, a number of hypotheses were advanced to explain the periodicity of the extinction and impact events: sunspots cycles, cosmic dust clouds through which the sun passes periodically in its journey around the galaxy, oscillation of the sun above and below the galactic plane and even the existence of an unknown planet beyond Pluto. For a variety of reasons, none of these hypotheses seemed satisfactory.

One hypothesis, however, remained among the most ingenious, controversial, and enduring: the "Nemesis hypothesis." Named for the Greek goddess who continually followed the rich and powerful, tormenting them, the Nemesis hypothesis proposed that a dark companion star, Nemesis, revolves around a common center of gravity with the sun. Nemesis was hypothesized to have a highly eccentric orbit that takes it from the inner reaches of the solar system to the realm of the outer planets every 26 million years. Beyond the orbit of Pluto, Nemesis passes through the Oort Cloud, a hypothetical ring of millions of comets surrounding the solar system. During this passage, Nemesis causes immense gravitational disturbances, sending many comets and the debris that make up their heads hurtling through the solar system. It is this material that was hypothesized to impact the earth, creating immense heat, ash and dust, thereby blocking out the sunlight and, ultimately, causing mass extinctions.

The Nemesis hypothesis is intriguing. It draws on a number of scientific disciplines—geology, paleontology and astrophysics—and seems to account for data derived independently from them all. Yet it has one major difficulty: no astrophysicist has any hard evidence that either a dark companion star to the sun or the Oort Cloud actually exist. Prior to the interest in mass extinction, some circumstantial evidence had suggested the existence of the Oort Cloud, but it has yet to be detected directly. Hypothesizing a dark companion to the sun and existence of the Oort Cloud is an example of ad hoc hypothesis; that is, hypotheses that explain existing data, possess no independent supporting data of their own, but that may eventually find support beyond the data they were originally designed to explain. Such hypotheses are useful in science to the extent that they suggest new lines of research not considered before. The Nemesis hypothesis has stimulated a number of astrophysicists to begin a systematic search for the hypothesized dark companion star and a more intensive search for evidence of the Oort Cloud.

Such research ventures are often chancy, however. If a nemesis is found, it will constitute one of the great discoveries of this century. If it is not found, we will never know with certainty whether a dark companion star is just a convenient figment of the scientific imagination, or actually exists but is too difficult to detect with our present methods. Thus the issue of mass extinctions and the possibility that they possess a periodic nature, is likely to remain an unresolved question for years to come.

4.5 Conclusion

As just suggested, the nemesis hypothesis represents a very different sort of hypothesis from the laboratory and field research examined earlier in this chapter. Nemesis deals with a hypothesized historical event or series of events that cannot be investigated directly, and therefore all the evidence is necessarily indirect and circumstantial. The impact crater discovered in the Yucatan is the right size and age for the event that might have caused the extinction at the K-T boundary, but we have no direct way of determining conclusively a cause-and-effect relationship between that event and the disappearance of the dinosaurs and other species 65 million years ago. Furthermore, the Nemesis hypothesis is really not a single hypothesis but rather a series of separate hypotheses combining observations from the fields of geology, paleontology, geochemistry and astrophysics. Such synthetic hypotheses certainly play an important role in science. However, though fruitful in stimulating research in the areas with which they are concerned, it is not possible to expect the same level of rigor in testing them than is possible in laboratory and field studies.

Questions for Consideration

1. Three examples of scientific research have been presented in this chapter.

   (a) Laboratory research on nerve growth factor.
   (b) Field research on salmon migration.

(c) Paleontological studies concerning the sudden disappearance of the dinosaurs and other species occurring in the late Cretaceous.

In terms of our discussion of science historian Thomas Kuhn's concept of paradigm shifts (Sect. 2.8), rank these three studies in terms of the extent of their results and how they might, or might not, represent a paradigm shift.

2. In this chapter we noted that Elmer Bueker had found that mouse cancerous tumors grew quite readily in chick embryos. We also noted that Stanley Cohen and Rita Levi-Montalcini found that snake venom and male mouse salivary glands were a rich source of nerve growth factor (NGF). Beyond the research on NGF and other growth factors, what might bethe significance of this work be for the Darwin-Wallace concept of evolution?
3. Assume it has just been reported in a scientific journal that high levels of iridium have been found in a layer of rock formed in a geologic period in which there is no evidence from the fossil record that there were any extinctions at that time, nor any evidence of a meteoritic impact on the earth. What would be the effect of such a discovery on the Alvarez K-T boundary hypothesis? And how might proponents of the K-T hypothesis respond to such findings?
4. Using the three case studies in this chapter, discuss how hypotheses were tested by both experimentation and observation. In which case study was observation the most prominent means of hypothesis testing, and why?

Further Reading

On Neuronal Growth and Nerve Growth Factor (NGF)

Allen, G. E. (2015). Viktor Hamburger, 1900–2001. *Biographical Memoirs of the National Academy of Sciences* (National Academy of Science), 1–39. Available on-line at: www.nasonline.org/memoirs

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The Social Context of Science: The Interaction of Science and Society

5

Abstract

This chapter focuses on how science is embedded in various economic, social and cultural contexts. The chapter emphasizes that context is important in understanding both why a given scientific question is important at a given time and place, as well as how that context affected the content of the particular theory. The chapter turns to the "social construction" of science, that is, the process by which scientists (biologists in his case) construct a view of nature using models, metaphors and analogies, along with certain philosophical perspectives derived from their cultural circumstances. This view of science is contrasted to the older "treasure hunt" view, which sees the natural world and its relationships (laws or concepts) already existing, only to be "discovered" by the scientist. The chapter then moves on to consider four case studies dealing with the question of social responsibility of scientists and the use of their work: "eugenics," the use of genetics to try and improve the social and mental qualities of the human population in the early twentieth century; the use of herbicides, developed initially for agricultural purposes, to defoliate forests in Southeast Asia during the Vietnam war; issues revolving around the use of human embryonic stem cells for biomedical research; and the development of genetically modified organisms (GMOs), including their impact on agriculture and farming practices. The ethical issues in the use of humans as subjects in research is illustrated by the history of the long-term Tuskegee Syphilis Experiment in the United States (1930–1970). The final two sections of the chapter focus on the relationship between science and religion, including teaching some form of "creationism" or Intelligent Design in public schools alongside Darwinian evolution. Here, the chapter emphasizes the very different philosophical bases on which religious explanations of events in the natural world are built (philosophical idealism), compared to those in the sciences (philosophical materialism).

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5.1 Introduction

The atomic bombs that exploded over Hiroshima and Nagasaki, Japan, on August 6 and 9, 1945, quickly brought World War II (1941–45) to a close. The physicists who had worked on theoretical aspects of the project leading to production of the atomic bomb (known as the Manhattan Project) had some sense of the immense destructive power that the splitting atoms might unleash. Until it was actually put to military use, however, most had no conception of how they would feel about the role they played in developing this new technology The resulting massive destruction of life and property jolted scientists into a realization they had not encountered before in such a dramatic way. The deployment of the atomic bomb served as a wake-up call for scientists to consider the technological uses to which their theoretical ideas might ultimately be put.

Biologists and medical researchers were soon to be confronted with their own versions of this moral dilemma. Revelations of human medical experimentation in Nazi Germany indicated how far some scientists were willing to go in order to obtain funds for their research and advance their own scientific or professional careers. Genetically identical twins were subjected to deadly injections of drugs or microorganisms to test whether their genetic make-up gave them the same or different susceptibilities to disease. Mendelian genetics was used to justify the involuntary sterilization or killing of people claimed to have inferior heredity: Jews, Gypsies, gay men, lesbian women and persons with mental problems. When such scientific work was exposed at the war crimes trials held in Nüremberg, Germany after the war, biologists around the world began to wonder "Could it have happened here?"

This chapter explores both sides of the science in society coin: how science affects society and how society may affects and determines the direction of science. Recognizing the interactive relationship between science and the society in which it is pursued helps to shed light on the complex factors that influence how new scientific ideas develop and how they are used and sometimes misused.

5.2 Science and Technology—The Public Confusion

Watching the evening news on national television, an announcement is often made that the next segment will be turned over the network's "science correspondent," John Doe. However, John Doe's reports are more often than not about science but about a new artificial heart valve or the latest space shuttle launch. Such topics are more commonly regarded as technology rather than science.

There is, of course, a great deal of science behind the development and production of artificial heart valves and space shuttle launches. These technological developments are the result of a great deal of theoretical research in physics, chemistry and biology. So, too, are the many technological marvels we now take for granted, televisions and computers designed by electronic engineers being perhaps the most obvious examples. Modern medicine, too, is a technology based upon laboratory and clinical research in the biological sciences. In this case, physicians, rather than engineers, are the technological practitioners. Engineers and physicians are highly skilled professionals who take advantage of the latest advances in science so that they may apply these findings in their own respective fields of interest (for example, new and more effective artificial heart valves). They are sometimes referred to as "applied scientists" in that they apply general principles in a field to the solution of particular, practical problems. While in the past there was a tendency to denigrate the role that applied scientists played with respect to theoretical scientists, that distinction no longer appears as a real or important one. Most scientists usually have some general, practical problems in mind when they choose a research project, while most applied scientists have a general interest in broad theoretical concepts, even when not trying to solve particular technological solutions.

Whether they are working on a more practical problem of one of more theoretical nature, engineers and physicians use scientific reasoning in carrying out their daily work; a great deal of the diagnostic medicine involved in pinpointing an illness by analyzing symptoms and clinical tests (e.g., urinalysis, blood tests, etc.) utilizes precisely the inductive and deductive processes described in Sect. 3.4. So, for that matter, do good automobile mechanics … the underlying logic involved in scientific research, far from being limited to scientists, is often practiced by all of us in many different walks of life.

Research such as that carried out in medical schools is often called clinical research, since it may involve patients showing particular symptoms and who may participate in studies designed to learn more how to improve treatment of a specific disease. Clinical research is but one example of applied science, i.e., research designed to solve a particular problem. An engineer working on a problem encountered in trying to get a space probe onto the planet Mars or to program a fly-by of the distant planet Pluto, provides another example of applied research. By contrast, the work of a biologist studying the development of nerve cells in the wings of bat embryos is an example of what is called basic research: that is, it is not aimed at solving any one specific problem, though it is always hoped that it will contribute to practical outcomes at some later point in time. Indeed, as most historians and sociologists of science now recognize, even the most "basic" scientific research is often motivated, at least in general, by the recognition of some practical questions that need a solution. Research on nerve cell development, for example, has been motivated by the medical problem of finding ways to stimulate adult nerve cells to regenerate after damage by injury or disease. Historically, the practical benefits derived from such "basic" research have proven to be widespread.

5.3 The Social Construction of Science

The scientifically based technology of military weapons development or the scientific research that produces a new vaccine to cure or prevent an illness demonstrate clearly the diverse effects of science on society. By contrast, it is far less common to think of society affecting the practice of science. Of course, as noted earlier, when it comes to the funds made available for scientific research by granting agencies or the type of research those agencies are willing to fund, societal influences are obvious. At a much deeper level, however, social influences may well impinge on science at every level, influencing the way in which we formulate our most far-reaching paradigms. We have already noted in Chap. 2, for example, that by being socially conditioned to "see" 48 chromosomes in the human genome, countless observers *did* think they observed 48 instead of the 46 that actually exist. Even as a result of the language we use, our broader social experience inevitably becomes a part of our science. Thus the cell may be referred to as being similar to a "factory," taking in "raw materials" and synthesizing new "products." The body may be likened to a "machine" and aging referred to as the "wearing out" of body parts. Artificial heart valves, knee joint or hip replacement prosthetics are often referred to as "spare parts." The natural world is sometimes called "mother nature." Adenosine triphosphate (ATP) the so-called "high energy compound" involved in powering biochemical reactions, is often referred to as the energy "currency" of the cell. Evolution is described in terms of organisms devising "strategies" for survival, with the evolution of prey-predator relationships likened to a military "arms race." Social values, metaphors and concepts pervade science at the level of theory construction far more thoroughly than many scientists care to acknowledge.

A standard view of science is often what might be termed the "treasure hunt model," in which the scientist is seeking the hidden treasure of nature's secrets. According to this view, the treasure already exists, ready-made and waiting. The scientist's job is merely to "discover" it. This view is associated with an older positivist philosophy, which saw science as completely objective and uninfluenced by social, political or philosophical "biases" and ultimately able to describe nature as it really is. In recent years, the positivist view of science has been critiqued by some philosophers and historians of science as being naïve, presenting an unreal picture of how science works. An alternative way of understanding the scientific process is known as the "social constructionist" view. This view takes as its starting point the idea that we do not so much *discover* nature as we *construct views* of it. This does not imply that we can simply make up any ideas we want: all scientific hypotheses must stand up to empirical testing. As just noted, however, in constructing our view of the natural world we may often use ideas, metaphors, analogies and terminology that reflect both our social as well as scientific experience. In this way we construct a view that makes sense to ourselves and others.

The social constructionist view suggests that particular scientific paradigms may reflect the social values of the time and place in which they were developed because science, far from being independent of time and place, is actually both culturally situated and influenced. To a greater or lesser degree, therefore, both in the topics chosen for investigation and in the construction of paradigms, science may differ from country to country and century to century. Two examples will illustrate the way in which social values and assumptions may influence the construction of scientific paradigms.

The Origin of "On The Origin of Species": Charles Darwin and the Political Economists

Charles Darwin was not the first to advocate the evolution of species. He was, however, among the first to propose a mechanism for the way in which evolution might occur: the hypothesis of natural selection. As we noted in Chap. 1, this hypothesis states that:

1. More organisms of a species are born than can survive to reproduce;
2. This over-reproduction engenders competition between organisms for available resources (including food, water, habitat, breeding sites, etc.);
3. All organisms vary slightly from other members of their species. Some of these variations are inherited and may be passed on to that organism's offspring;
4. Any inherited variation that provides an organism with some slight advantage in the competitive struggle for survival will tend to be preserved, while any variation that confers a disadvantage on an organism will tend to be eliminated. This process of preservation and/or elimination is what Darwin referred to as natural selection;
5. As a result of natural selection, the physical and physiological characteristics of a species will change over time, that is, they will evolve.

Darwin published his theory in 1859 in a milestone book with a typically long Victorian title: *On the Origin of Species by Means of Natural Selection, or the Preservation of the Favoured Races in the Struggle for Existence.* The second part of he title is revealing. He had been working on the ideas behind the book since the 1830s. Others who had proposed something similar to his idea concerning the possibility that species might not be fixed and unchanging were also, like Darwin, living and working out their ideas in Victorian England from the mid-1830s through the 1880s. It has been suggested, therefore, that the concept of natural selection was a product of the economic, social and political developments of the period in which industrial capitalism was reaching its peak and the British empire was expanding around the globe. Although Darwin and his family were strong abolitionists, he could not help recognizing that everywhere the British or other European colonists expanded, they were able to overwhelm and conquer the indigenous peoples. Darwin's expanded title for his book at once explained, and for those who accepted it, justified the practice of slavery. Indeed, recent historical studies have argued that the industrial revolution as we know it, based on the rapid expansion of the textile (most especially cotton) industry, could not have occurred without an extensive slave system in the New World.

Moreover, this was also the period in which the theory of political economy, dealing with the rules by which the capitalist system operated, were being developed. The writings of Adam Smith (1723–1790) in the 1750s, Thomas Robert Malthus (1766–1834) in the early 1800s, and David Ricardo (1815–1820), among others, laid a foundation for a theory of monetary accumulation, including the importance of competition, the consequent struggle engendered by this competition, the necessity of constant innovation to keep ahead of the competition and the importance of a division of labor. The outcome of the interaction of all these factors was that some entrepreneurs would succeed and others fail. This process was viewed as the natural outcome of free enterprise and was considered to lead to the progress and improvement of society.

A number of historians have pointed to the similarity between Darwin's mechanism for natural selection and the basic economic theories of the time. In 1836, after returning from his five-year voyage on the H.M.S. Beagle, Darwin read ("for amusement," he said) Thomas Robert Malthus' *Essay on Population*, first published in 1798 (because of its popularity it went through some sixteen editions by the time Darwin read it). Malthus was a country clergyman and a Professor of Political Economy at the East India Company College in Hertfordshire. He was particularly concerned with the increasing poverty visible in England during the first phase of the industrial revolution. In his *Essay*, Malthus made the assumption that populations of people tend to grow exponentially (2, 4, 8, 16, 32, 64…) while their food supply tends to grow only arithmetically (2, 4, 6, 8, 10…). Because no reliable census data yet existed in England, he had no strong statistical support for this assumption, although he did use some limited data from North America. Nevertheless, from this assumption Malthus deduced that populations would always tend to outrun their food supply and that the only way to prevent famine was for those who did not have the means to support large families to practice birth control (abstinence). Malthus was writing only a few years after the French Revolution, and his expressed purpose was to discover the "laws" of human society that would prevent such cataclysmic social upheavals in the future. The cause of poverty, he argued, was that the poor, yielding blindly to their passions, had more children than they could support. Darwin immediately saw the application of this principle to nature, and as suggested above, it became a cornerstone of the theory of natural selection.

To highlight the general applicability of the social constructionist hypothesis in this case, it is worth noting that in the 1850s the other naturalist who independently came up with the idea of natural selection, Alfred Russell Wallace (1823–1913), had also just read Malthus's *Essay* while recuperating from malaria on a specimen-collecting trip in the Malay archipelago. For him, as for Darwin, the idea of population pressure and competition seemed to provide a perfect mechanism for the way in which evolution might occur. Another contemporary, Karl Marx (1818–1883), although highly impressed with *The Origin* on first reading it in 1860, nonetheless saw immediately that it could be viewed as a projection of Darwin's society onto the animal and plant world:

> It is curious that Darwin recognizes among beasts and plants his English society with its division of labour, competition, opening of new markets, inventions, and the Malthusian "struggle for existence." [Letter from Karl Marx to Friedrich Engels, June 18, 1862. From Donna Torr, ed. *Marx-Engels Selected Correspondence*. New York, NY, International Publishers, 1934: 128]

Does the possibility that Darwin may have attained his initial insight into a mechanism of evolution by reading a treatise on political economy necessarily invalidate his conclusion? Most certainly not. One advantage of understanding science in its social context is to recognize that constructing nature according to our social models or visions may often provide a creative step forward in hypothesis formulation. However, it is also important to recognize that these same social insights can also act as blinders, obscuring our vision of alternative, and quite different explanations. The notion of competition for scarce resources was valuable in developing the theory of evolution. Yet, until late in the twentieth century, it blinded many biologists to other mechanisms by which evolution may also occur; for example, by cooperative or symbiotic interactions. Viewing science as a social construct makes explicit a process that has been part of scientific creativity from the outset: the use of metaphors, analogies and models for interpreting nature. By making this part of the process of science explicit, it allows us to examine the metaphors and models we use and determine if they are helping or hindering our thinking concerning the phenomenon at hand. The idea of social construction of science neither diminishes the value of that science nor does it elevate science to a supra-human level. It simply sees science as part of a social fabric, to which we all—scientists and non-scientists alike—are heirs.

Homeostasis: Walter Bradford Cannon and The New Deal
In the 1850s, French physiologist Claude Bernard postulated that complex organisms like vertebrates, especially mammals, have a variety of built-in mechanisms that control their internal environment (*milieu intérieur*), keeping it constant despite changing outside conditions (temperature, types of food intake, etc.). The mechanism by which this constancy is attained, however, was largely unknown at the time.

During World War I (1914–1918), Harvard University physiologist Walter Bradford Cannon (1851–1945) was assigned to work in England and France on the problems of physiological shock that often followed severe injury and trauma. One of the observations Cannon made was that shock involves the breakdown of many of the body's regulatory processes, for example those that maintain constant acidity or alkalinity (pH) and sugar levels in the blood, or a constant body temperature. His subsequent investigations of shock in dogs suggested that most regulatory processes involve the endocrine (hormone-producing) and nervous systems, particularly that part of the nervous system known as the sympathetic system. Both systems operate without any conscious action on the part of the individual. In a remarkable series of experiments, Cannon removed parts of the sympathetic nervous systems of animals and found that, under normal laboratory conditions, the animals continued to function perfectly well. It was only when conditions were changed dramatically (for example high or low temperatures or injections with high concentrations of glucose) that the lack of regulatory ability became noticeable. Cannon found that the nervous system controls a number of regulatory responses directly, for example, the muscles that open and close blood capillaries, thereby regulating blood flow into peripheral tissues (Fig. 5.1). The nervous system also controls a number of processes indirectly through the endocrine system, for example, the changes that accompany the "fight-and-flight" response of animals to perceived danger.

Cannon called the process of maintaining a constant internal environment "homeostasis." The concept of homeostasis has now become a major paradigm of modern physiology. As framed by Cannon, homeostasis was viewed as a dynamic

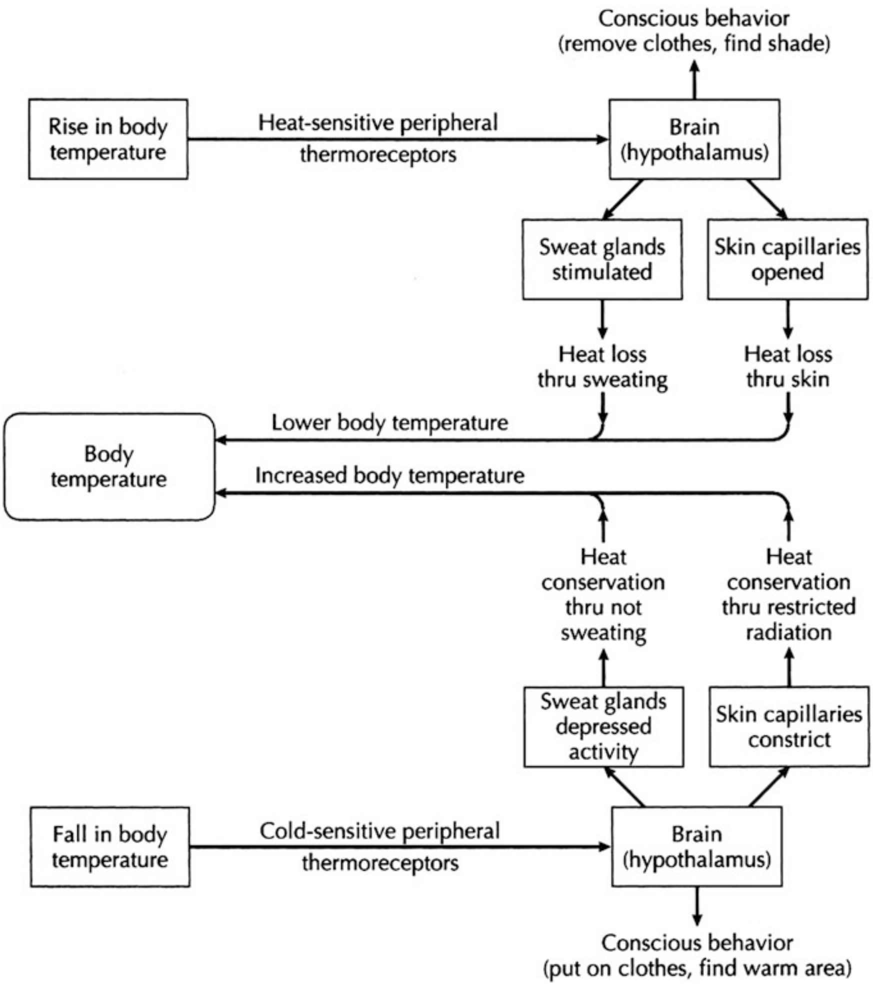

Fig. 5.1 Diagram of a homeostatic system for the maintenance of a constant body temperature in mammals such as humans. The human body temperature is kept at approximately 98.6 F (37.5 ° C), despite changing outside conditions, by a number of components that interact in a series of self-regulating feedback systems. Body temperature, the condition being controlled, is shown in the *middle, left*. If the temperature rises, due to exercise or an increase in outside temperature, this increase is detected by receptors in the skin or other parts of the body and a signal is sent to the brain (to a region known as the hypothalamus), which responds by ending signals to the sweat glands to release perspiration and to the skin capillaries to expand. Both processes produce a cooling effect. Response to falling body temperature works the same way, though in the opposite direction (lower half of diagram). As is the case with all other homeostatic systems, temperature regulation works by negative feedback loops; the loops are negative because the body's response has the effect of negating the initial stimulus [*Rights granted to authors by John Wiley & Sons, Letter of June 20, 2013*]

process. Constancy of the internal environment is maintained despite the fact that substances constantly enter and leave the body and external conditions change. Homeostasis describes the complex and continual interchange between organism and environment that preserves this constancy. Cannon saw homeostasis as a series negative feedback processes in which input and output is constantly monitored by the endocrine and sympathetic nervous systems to maintain this physiological balance.

It has been suggested that, just as in the case of Darwin, Cannon's concept of homeostasis may have drawn heavily on societal factors at several levels. The most obvious and direct was that traumatic shock was a process, known from antiquity, that Cannon had studied primarily because of its wartime occurrence. Had Cannon not been forced to observe the repeated breakdown of physiological control systems among numbers of badly wounded soldiers, he might not have recognized the central role that such control mechanisms play in maintaining normal physiological responses.

At the same time Cannon was developing his paradigm of homeostasis in the late 1920s and 30s, he was also influenced by a seminar he attended conducted by several of his friends in the Department of Social Relations at Harvard University. That seminar was devoted to the work of an Italian economist and social theorist, Vilfredo Pareto (1848–1923), a strong opponent of classical *laissez-faire* economics in which market forces alone, unaided by governmental intervention, controlled wages, prices and profits. Pareto was an advocate of a strong, centralized government that would regulate monetary and other social policies. Pareto's philosophy had drawn considerable attention in the post-World War I period and even more so after the 1929 stock market crash that had rocked western capitalist societies. To Cannon, the resulting economic depression and the failure of existing social processes by which economic behavior was regulated, seemed remarkably analogous to the total breakdown of the body's normal physiology during shock. The idea that built-in regulatory processes in government (for example, institutions like the Federal Reserve Bank, which regulates interest rates and a wide variety of other economic parameters) could stabilize society against future "shocks" seemed eminently reasonable, given the effects of boom-and-bust cycles such as that experienced before and after the 1929 depression. Similar thinking motivated United States president Franklin Delano Roosevelt's "New Deal" programs in the 1930s, in which many regulatory agencies and policies were instituted at the level of the federal government.

Reading Pareto and discussing issues of economic control suggested to Cannon that he might look deeper into the regulatory processes at work within the organism. Although we can never be certain, of course, it is plausible that had he not become interested in Pareto or lived through the economic uncertainties of the post-war period and the Great Depression, Cannon might not have seen physiological shock as a breakdown in homeostatic processes. Nor might he have formulated an explanation of homeostatic control in terms of centrally organized regulatory mechanisms. It is certainly possible that this influence may have greatly strengthened his conviction that, in French physiologist Claude Bernard's words, "The maintenance of the constancy of the internal environment is the condition for a free life."

5.4 The Social Responsibility of Science

As noted at the beginning of this chapter, many nuclear physicists, including Albert Einstein (1879–1955) were concerned that their work had been used to unleash a bomb of immense destructive power. Similarly, many American biologists were horrified to learn that some of their German colleagues, under the Nazi regime, had conducted experiments on human beings or advocated theories of racial inferiority that were used to justify the enslavement or murder of millions of human beings. Such concerns raised an issue that had not been discussed to any extent previously: What responsibility do scientists have for the use to which their research is put? Can individual scientists be held responsible for the way or the context in which their work is applied? Should scientists inquire into the objectives of those who fund their research or, as is more traditional, assume that their main responsibility is to produce sound, verifiable results? If their own motives are beyond reproach, is this as far as their responsibility goes?

These are difficult questions to which no simple answers can be given. The least productive response is to assume that the misuse of science or lack of ethical concerns are products of other times and places in history and that they "can't happen here." In fact, misuses of science can and do happen everywhere. The following four examples will illustrate some of the moral and ethical issues raised by scientific work in the United States both before and after World War II.

5.4.1 "Breeding Better People": Genetics and Eugenics, 1900–1945

It was not long after the rediscovery of the work of Mendel's work in 1900 that biologists began finding that a number of genetically controlled traits in human beings all appeared to follow basic Mendelian principles. These included red-green color blindness, hemophilia, eye color, the basic A-B-O blood groups and Huntington's disease. In their enthusiasm for these findings, however, some geneticists also claimed that personality and behavioral traits were also determined largely by Mendelian inheritance. Included in this wide range of traits were alcoholism, manic depression, pauperism (the tendency to be chronically poor), rebelliousness, nomadism ("wandering" impulse), and "feeblemindedness" (judged by low scores on intelligence tests). Family pedigree studies, in which a trait was followed in as many generations as the investigator could trace (Fig. 5.2), were used to support the notion that such traits were hereditary. The fact that the trait could be seen to recur in generation after generation was taken at face value to indicate its genetic nature. Because most of these conditions were viewed as negative and because no methods of

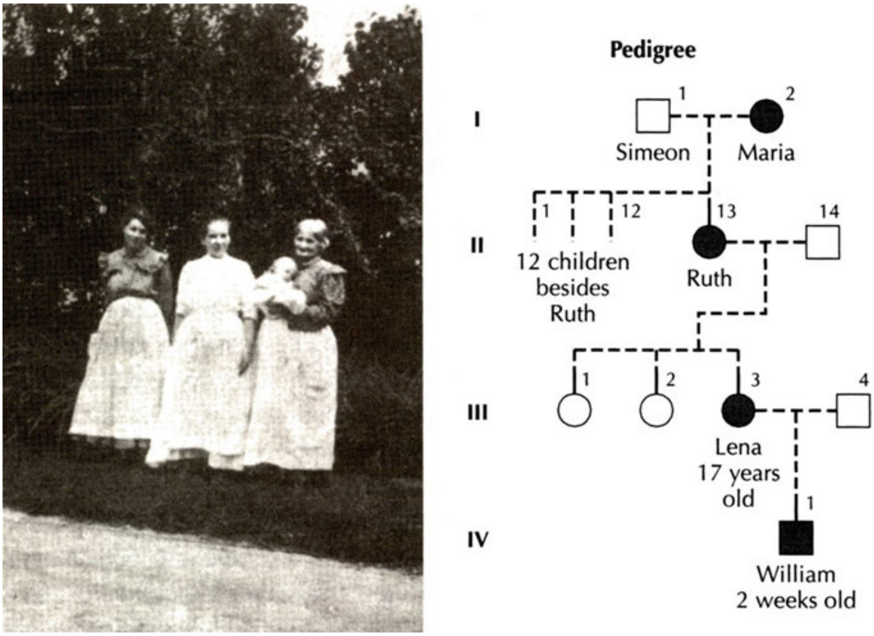

Fig. 5.2 A family pedigree chart for the trait known as "pauperism," a presumed genetic tendency to always remain poor. Four generations are shown here, all housed in one almshouse (poorhouse) in New York state. In these pedigree charts, squares represent males and circles females. The filled-in squares or circles indicate individuals who have the trait in question, while blank squares or circles are individuals who do not display the trait. As can be seen here, pauperism appeared in every generation shown in the chart, with the latest addition to the family, two week old William, held in the arms of his great-grandmother on the right, having already been diagnosed as a pauper! This chart was drawn up and published in a pamphlet by the Sterilization League of New Jersey in 1937 [From Marison S. Norton, "Selective Sterilization in Primer Form," (Princeton, NJ: Sterilization League of New Jersey, 1937) *Organization no longer exists, pamphlet published and distributed by author, Marion S. Norton*]

treatment were known, some geneticists and social reformers argued that individuals who showed these traits (or might be assumed to carry the trait even though they did not show it), should be prevented from reproducing. Such claims were brought together and organized loosely into a reform movement known as eugenics, defined in 1910 by its major American proponent, Charles B. Davenport (1866–1944), as "the science of the improvement of the human race by better breeding."

Using the principles of Mendelian inheritance and family pedigree analysis, eugenicists often made highly simplistic claims that one or a few genes controlled complex social behaviors and mental traits. Eugenicists thought that they could cure many of the ills of society simply by eliminating defective genes. They were, in fact, partly motivated by the prospect of using cutting-edge biology to solve persistent social problems that traditional methods of reform seemed unable to solve.

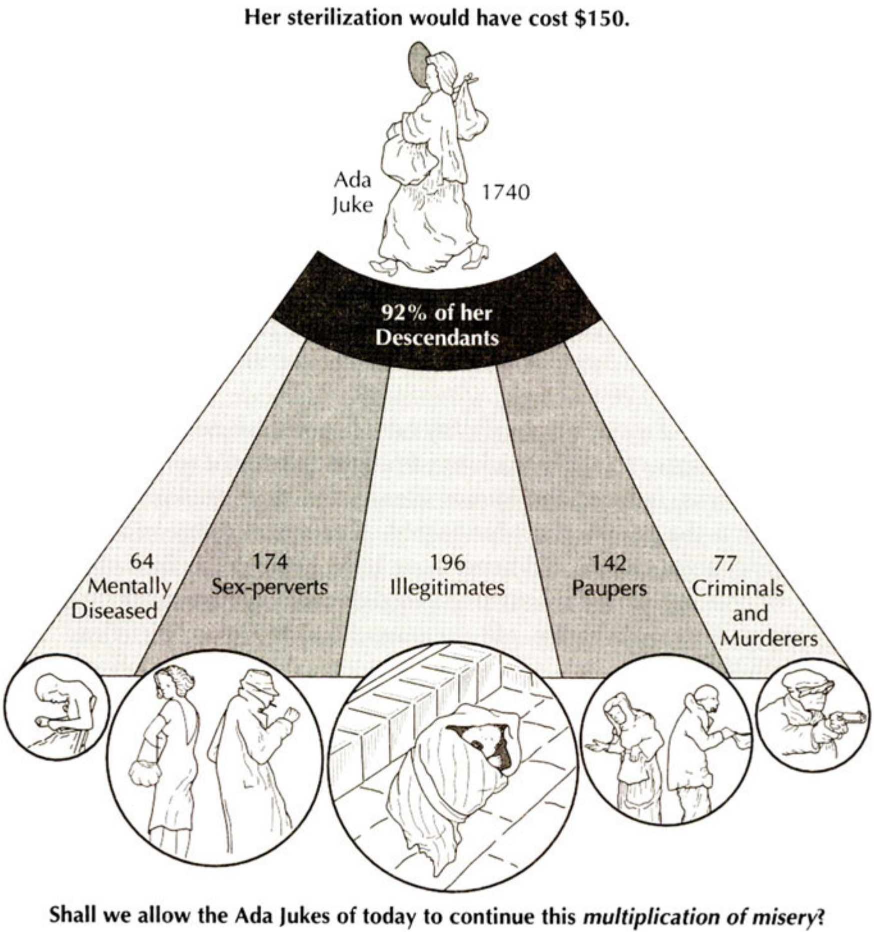

Fig. 5.3 A cartoon calling for the sterilization of "degenerates" to prevent them from passing on their "defective genes" to future generations. Among those advocating sterilization the argument brought to public attention was that too much tax money was being spent on supporting defectives who should never have been born. Ada Juke was an eighteenth century American woman who had a number of offspring, many of whose descendants became wards of the state. The economic message here is clear: if Ada Juke had been sterilized in 1740, none of her hundreds of defective descendants would have been born and the state would have been spared millions of dollars in needless expense. This cartoon also appeared in the pro-sterilization booklet published by the Sterilization League of New Jersey in 1937 [From Marison S. Norton, "Selective Sterilization in Primer Form," (Princeton, NJ: Sterilization League of New Jersey, 1937) *Organization no longer exists, pamphlet published and distributed by author, Marion S. Norton*]

To achieve their aims, eugenicists in the United States lobbied for the passage of compulsory sterilization laws, to be applied to people judged to have undesirable traits and capable of passing those traits on to their children (Fig. 5.3). Between

1905 and 1935, over 30 states in the United States passed eugenically-based sterilization laws that allowed the compulsory sterilization of prison inmates, juveniles in reformatories, or patients in state hospitals and asylums who were judged to be genetically "defective." In 1933, a major sterilization law based on the American model was put into full force in Germany under the National Socialist (Nazi) government, leading to the involuntary sterilization of over 400,000 people. In addition, eugenicists in the United States lobbied successfully for passage of the 1924 Reed-Johnson Immigration Restriction Act. This law selectively restricted immigration by establishing quotas from countries and/or ethnic groups eugenicists claimed harbored many of what they considered to be genetically defective people (Poland, Austria-Hungary, Italy, Russians of Jewish descent and others). In the early 1940s the *St. Louis*, a ship carrying mostly German Jewish immigrants to the United States, was turned back because the Jewish immigrant quota set by this 1924 law had been reached. Forced to return to Europe, many of the passengers would end up being exterminated in Nazi death camps. In all countries that passed sterilization or immigration laws during this time, it was usually the poorest and most defenseless individuals who were the targets.

Eugenics as both theory and practice did not escape scientific criticism. Nobel Laureate Thomas Hunt Morgan (1866–1945) was the geneticist at Columbia University who introduced the fruit fly (*Drosophila*) as the model organism for genetic studies in 1908. He pointed out in 1925 that many of the behaviors eugenicists claimed were genetically determined were so vague and ill-defined it would be impossible to demonstrate that they had any significant component. Morgan also noted that the family pedigree data on which eugenicists based their analyses were obtained in such haphazard and uncontrolled ways that they were completely unreliable. A few years later (1932) Morgan's student, Hermann J. Muller (1890–1967), then at the University of Texas and a future Nobel Laureate himself, emphasized that until socio-economic factors were equalized for all people there was no way to distinguish the effects of biology from those of the environment in assigning causes to social behavior or socio-economic status. Given the economic disparities that existed after the 1929 depression, Muller argued, eugenics would only be used by the rich and powerful against the poor and weak. By the time such criticisms were gaining force, however, eugenics laws of various sorts had already been passed and the damage had been done. Many of the sterilization laws were not repealed until the 1960s.

The issue of social responsibility here lies with those eugenicists who, in their enthusiasm to apply the latest findings of science to the solution of social problems, ignored the human element in their studies. Eugenicists assumed that the people they designated as genetically defective were less than fully human and therefore should never have been born in the first place. The Nazis, of course, carried this attitude to the extreme, first sterilizing and then annihilating those they claimed were defective and labeled as "lives not worth living."

5.4.2 Herbicides in Southeast Asia

The presence of U.S. military troops in South Vietnam in the early 1960s was officially aimed at preserving the division of that country into North and South Vietnam that had been created after World War II. The conflict, known as the Vietnam War, arose over the attempts of the North, supported by China and the Soviet Union, to reunite the country under their communist leadership, and attempts by the South, supported by the United States and its allies, to keep South Vietnam independent under western, capitalist leadership. During the course of the war, the United States Air Force sprayed chemical "defoliants" over five million acres of South Vietnamese forests and croplands, as a way to clear the heavy vegetation cover in which guerilla forces from the North could hide. As a result of this spraying program, however, some 35 % of South Vietnam's dense tropical forest was defoliated, leading to a significant reduction in plant and, consequently, animal life. Spraying of the coastal mangrove swamps further resulted in total annihilation of the vegetative cover where many species of fish and other marine food sources lived. The chemical agents used, principally 2,4-D (2,4 dichlorophenoxyacetic acid) and 2,4,5-T (2,4,5-trichlorophenoxyacetic acid) in mixtures known as "Agent Orange" and "Agent White," are called "defoliants" because they cause plants to lose their leaves. Depending on dosage and how often spraying of the same area occurs, defoliants may eventually kill the plants. In addition to reducing vegetation cover through which soldiers from the North could move undetected, the purpose of massive spraying of agricultural areas was to kill crop plants and thus destroy the ability of the affected regions to feed guerrilla forces, a strategy referred to by critics as "ecocide."

How does the proceeding relate to the issue of scientific responsibility? Arthur W. Galston (1920–2008), a plant physiologist at Yale University for most of his career, pioneered research into the nature of plant growth hormones. In the 1940s while a graduate student at the University of Illinois, he discovered that a chemical substance known as TIBA (2,3,5-triiodobenzoic acid) not only increased the rate of flowering in soybeans but also, in higher concentrations would defoliate the plant by increasing the rate at which the abscission layer at the base of the leaf formed (the abscission layer allows the leaf to detach from the stem). This work led to development of 2,4 D by chemical companies, principally Dow, in the United States. In the mid-1960s, Galston was horrified to find that his chemical studies on the hormonal control of abscission had formed the basis for developing Agents Orange and White. After learning about the destructive purposes to which his research had been put, Galston became an active opponent not only of the military's defoliation policy, but also an outspoken critic of the Vietnam war itself. Together with other scientists, including Matthew Meselson of Harvard University and Ethan Singer of MIT, he petitioned the military to cease using Agents Orange and White. Not only were these substances wreaking havoc on the ecology of the whole Southeast Asia region, they were also shown to have a number of deleterious physiological effects in animals, including birth defects. This problem later surfaced in a variety of medical problems among U.S. veterans who had served in the area at the time the defoliants were being used. The scientists' campaign eventually led then-President Richard M. Nixon to discontinue the spraying program.

In the course of his involvement with the anti-defoliant campaign, Galtson realized (but only after the fact) that *scientists generally have no say concerning the use of their work*. After retiring from his faculty position at Yale, Galston went on to work as a bioethicist, writing and lecturing widely about the need for scientists to take more responsibility, including a more active political role, in determining how their work could possibly, or actually is being, used. The Galston case emphasizes that, while it was impossible to predict what the uses of any new research might be, it is important for scientists to give at least some thought to this issue rather than assume naively that science always leads to beneficial applications. Like the geneticists who criticized eugenics, Galston realized the extent of the damage his research had brought only after the damage had been done. His case came to demonstrate, however, that it is the political and social context in which research is carried out and used, rather than the research itself, that often determines whether the results are desirable or undesirable.

5.4.3 Stem Cell Biology: The Ethical Concerns

In the past two decades a controversy has arisen within the biomedical community and sectors of the general public concerning the use of human "stem cells", particularly embryonic stem cells, both in research and clinical treatment. This controversy became an explicit public issue in the United States when, in 2001, President George W. Bush argued that no federal funds should be used for research on embryos, even in their very earliest stages of development. This ban included embryonic stem cell research.

What is so controversial about stem cells and their use in biomedical research and therapy? Why should this seemingly straightforward area of developmental biology receive so much attention among public and political leaders? Before examining this question further, it will be helpful to look at the development of the early embryo and, explicitly, the formation of embryonic stem cells.

Stem cells are those cells in multicellular organisms that are able to differentiate into a variety of specialized cells and/or new stem cells. In mammals, for example, there are two types of stem cells: embryonic stem cells that can be isolated from a very early stage of the developing embryo (the blastocyst, which in humans is 4–5 days old and has not yet implanted in the uterine wall), and adult stem cells, located in various organs and tissues throughout the body. In adults, stem cells serve to replace cells that die from normal aging processes, disease, or injury. In mammals in particular, the fertilized egg (a zygote) and those cells up through about the 8-cell stage (called blastomeres) are largely undifferentiated and are capable of developing into all of the tissues of the future body (Fig. 5.4a–c). Such cells are said to be *totipoten*t in their capacity for full differentiation. Soon, the 8-cell-stage embryo undergoes a process in which the cells begin to collect more closely as a mass (a process called *compaction*), forming the 16-cell *morula* stage (Latin for

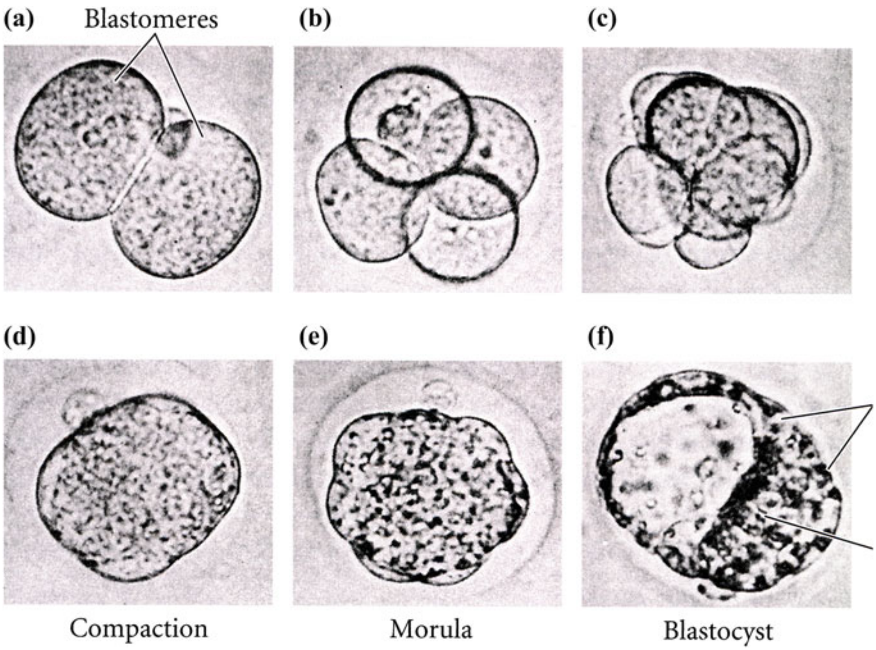

Fig. 5.4 Early stages in the development of a mammalian embryo, similar to those through which a human passes from the two-cell to the 150-cell blastocyst stage. Cells from (**a**) through (**c**) are totipotent, while cells of inner, compact mass making up the blastocyst have already become restricted: they can form all the cells of the body but not the outer group of cells that surround them, the trophoblast, which are said to be pluripotent. It is the cells of the inner mass of the blastocyst that researchers want to be able to clone and use for research or implantation in defective organs for medical treatment [Photo from Scott Gilbert, Anna L. Tyler, and Emily J. Zackin. 2005. *Bioethics and the New Embryology: Springboards for Debate*. Sunderland, MA: Sinauer Associates; photo originally supplied by J.G. Mulnard; *Permission needed*]

"blackberry", which this mass resembles, Fig. 5.4d, e). As the morula continues to grow (to the 150-cell stage), it differentiates into an inner cell mass, the *blastocyst* and an outer cell layer, the *trophoblast*, which serves to attach the young embryo to the uterine wall (Fig. 5.4f).

Cells of the blastocyst are able to differentiate into all the major cell types in the body except they can no longer produce trophoblast tissue, and are thus referred to as being *pluripoten*t ("*pluri*", meaning "many," i.e. they are *almost* totipotent, but not completely). After the embryo has become fully formed and developed all its major tissue types, some cells may still retain stem-cell-like characteristics. Although these cells cannot differentiate into *all* of the other cell types in the body, they *can* differentiate into several different types, and are therefore referred to as being *multipotent*, *multi*-, many). Hematopoietic stem cells in bone marrow are an example of multipotent stem cells, since they are able to differentiate into any of the various types of blood cells found in that particular organism, but not into other kinds of tissues such as skin or muscle. Multipotent cells are responsible for the normal regeneration of tissue types in organs such as the liver that constantly renew the various types of cells of which they are composed.

Since the 1960s, stem cells have been identified in almost all of the body organs of adult mammals, including humans. Once a stem cell line has been extracted from its source, from either adult or embryonic tissues, and methods developed for culturing it in the laboratory, it can be used for both research on how differentiation and de-differentiation is controlled, as well as in therapeutic procedures for re-implanting these cells in the body to replace those damaged by disease, injury or aging. The factors involved in differentiation and de-differentiation appear to be tied to the ability of stem cells to respond to signals, usually chemical messengers from other cells or the environment, that make the cell "receptive" to development in a specific direction. Thus, differentiation of a pluripotent cell into a given cell type (for example, into brain cells) is a property of both the cell's own potency and the nature of the signals it receives. Re-implanting pluri- or multi-potent cells into ailing or deteriorating tissue provides great potential for treating such debilitating conditions as Alzheimer's disease, a highly degenerative process in which certain cells in the adult brain and central nervous system begin to cease their normal functioning and die, leading to cognitive deterioration, loss of motor function and eventual death. If stem cells from the brains of embryos or healthy adults could be transplanted into the brains of affected patients and stimulated to grow and differentiate, they might be able to slow down or even reverse the progression of the disease. Other conditions that might potentially be treated by pluripotent stem cells include a number of blood and immune-system genetic diseases, cancers, juvenile diabetes, Parkinson's disease and spinal cord injuries. The obvious advantage of using embryonic stem cells is that, while adult stem cells can differentiate in only a few lines of development, stem cells are pluripotent and therefore are capable of differentiating in virtually any direction.

Currently, the technology for extracting and culturing (cloning) human embryonic stem cells involves obtaining the blastocyst from in vitro fertilization processes, that is, where egg cells are fertilized by sperm outside the body and cultured as a clone to the early blastocyst stage. (If the cloning process is aimed at producing a child, called reproductive cloning, the blastocyst is transferred to a prospective mother's uterus where it can implant and develop to term). Yet another method for producing blastocysts is to remove the nucleus from an unfertilized egg and replace it with the nucleus from an adult cell of an intended recipient of stem cell therapy. The egg is then stimulated to start development and form an embryo that can provide embryonic stem cells at the blastula stage. The advantage of this method for therapeutic purposes is that when the stem cells are transplanted and differentiate, they will be genetically the same as those of the recipient, and therefore not be rejected by the body's immune system as foreign tissue.

Because methods of cloning embryonic stem cells still face many technical problems, there is a strong push within the biomedical community to continue and expand research in this area. But here is where the controversy comes in. Opposition from various religious and "right-to-life" groups has grown over the years, and was instrumental in the success of President George H.W. Bush's moratorium on all embryonic stem cell research in 2001. The issues focus around how the stem cells are obtained. Adult stem cells are easier to extract, grow well in tissue culture, and do not harm the individual from which they are obtained. Harvesting embryonic stem cells from the blastocyst stage, however, destroys the embryo and thus has encountered a great deal of opposition from the Roman Catholic Church and various versions of Evangelical Protestantism, both of whose teachings generally view a fertilized human egg (ovum) or an early stage embryo, such as the 8-cell or blastocyst stage, as being already a "human being." Theologically, this means that at some stage the fertilized egg or the blastocyst has been endowed with a "soul" (a process referred to theologically as "ensoulment") and therefore is considered to be equivalent in every respect to a post-natal human being.

The central theological and philosophical issue here is the definition of when the "life" of an individual organism (in this case, human) can be said to begin. In other words, while it is clear that the fertilized egg and all the early stages of embryonic development are alive in a biological sense, at what point do we grant them full status as a human being? Theologians have debated this question for centuries, and the specific point at which "personhood" has been granted to embryos has changed over time, for example, from the moment of conception to the time the mother feels the first signs of movement (known as "quickening", usually around 40 days) to when the newborn infant takes its first breath. Some religions, such as Islam, have set the time at 40 days after conception, but although there have been many variants over time, the more strictly Christian traditions have declared that human life begins at conception. It is clear that setting any particular turning point at which a cell, small group of cells, or fully-formed fetus is viewed as "human" is an arbitrary decision based upon particular philosophical and/or religious predispositions, and that biology can provide no definitive answer. Therefore, the question of whether a blastocyst is a human being, and therefore its destruction for use as a source for embryonic stem cells counts as "murder" is tied into the definition one accepts as to when a human life can be said to begin.

The claim that life begins at conception is reflected in a 2008 book, *Embryo: A Defense of Human Life* (New York, Doubleday-Knopf), co-authored by Robert P. George, Professor of Political Science at Princeton University, and Christopher O. Tollefsen, Professor of Psychology at the University of South Carolina. Both authors are self-professed religious conservatives (George is a Roman Catholic, Tollefsen is a "born-again" Protestant). Early in the book, the authors express a highly anthropocentric view of the biotic world, describing human beings as representing the "the central modes of moral significance." (This would appear to mean that all moral and ethical decisions are to be related to humans and humans only—one wonders what environmentalists and conservationists would think of such a position). Later, they pose for their readers a hypothetical dilemma. Suppose, they describe, a woman is trapped in a burning building, presumably one in which there is a fertility clinic, and she must choose between saving a five-year-old child or a container of her own frozen embryos? The authors then go on to state their view that "no one would label her immoral if she chose to save the container." (The response to this statement by reviewer Emily Brazelon in *The Washington Post* was an astonished "*Really*?"). Admittedly, the dilemma as presented is ambiguous in that it is not clear whether the five-year-old is the woman's own daughter or someone else's, possibly under the woman's care at the moment. However, the central question in either case is whether a partially-developed early embryo, or an already well-developed child, should take priority for rescue. The example is hypothetical, but the moral dilemma as presented is quite clear. To dismiss it so easily, as he authors did, without probing into the deeper meaning behind the difference between frozen embryos and a fully-developed child, seems highly simplistic. Although heartily welcomed in the ranks of the political and religious right of both Protestant and Catholic "pro-life" groups, the authors' views were sufficiently embarrassing that the publishers eventually withdrew the book from bookstore shelves.

One of the clear points that comes out of the stem cell controversy (and others that depend on defining when human life begins) is that *any* definition is going to be arbitrary, whether it is made by biologists, philosophers, or theologians. Biologists can tell us that a fertilized human egg, under proper conditions, will develop the form of a human embryo and then of a newborn infant. But when that infant is deemed a "human" worthy of all the legal and social protections that society offers, is an issue that must be decided by informed social, philosophical and moral perspectives. But what about babies seriously deformed at birth with debilitating conditions such as hydrocephalics, or Tay-sachs disease, both of which are incurable and lead to death within a few months or a few years? How "human" are these infants? Yet, whether to keep such children alive when there is no hope for any normal development is also a social and moral question, and the answers vary from one society to another, and indeed, even in the same society, over time.

It is in such a light—having a full understanding of the science of human development—that decisions about whether creating a 150-cell blastocyst in order to obtain embryonic stem cells must be understood.

5.4.4 Genetically Modified Organisms (GMOs)

The term "genetically modified organisms, or GMOs, refers technically and legally to "any living organism that possesses a novel combination of genetic material obtained through the use of modern biotechnology"[1] (which is also referred to as "genetic engineering"). In a looser sense, all of today's important agricultural crops and domesticated animals are genetically modified, that is, humans have been altering the genetic make-up of domesticated organisms for thousands of years, However, the genetic engineering techniques used for creating GMOs are based on a wholly different technology. Traditional breeding approaches include: (1) Selecting desired variants that arise largely by chance in breeding populations such as a

[1]The official definition according to the Congena Protocol on Biosafety, an international agency that regulates trade in GMOs.

flock of chickens or field of corn, and then selecting these variants as parents for the next generation; (2) Crossing (hybridizing) two varieties and then selecting from the offspring those organisms with a desired trait or combination of traits for further breeding. These methods have produced some major improvements in domesticated animals and plants over the last several centuries, but they are slow and tedious, especially since most agriculturally important organisms produce only one or two generations per year and because they are limited to varieties that can interbreed, that is, they are members of the same species.

The production of GMOs, on the other hand, is based on a relatively new technology, molecular biology, developed from the mid-1950s onward. It was with the discovery of the structure of deoxyribonucleic acid (DNA), the molecule that makes up genes, and the associated mechanisms for translating its coded information into specific proteins that biotechnology was born. Through methods of excising and splicing genes, hereditary information can be directly transferred from one organismo another, even between different species, thus short-cutting the usual reproductive process. Its potential for genetically engineering organisms for agriculture and medicine (especially drug production) was seen from the very start. This method can produce results much more quickly and effectively than traditional breeding practices. For example, in 1978, molecular biologists isolated the gene responsible for producing human insulin, the hormone regulating sugar levels in the blood and thus controlling diabetes. Although it would have been ideal to be able to insert that gene into the tissue (the beta-cells of the pancreas) that normally make insulin (but are defective in patients with certain types of diabetes), the technology has proven to be extremely difficult. Alternatively, molecular biologists were able to insert the human insulin gene into bacteria, which were cultured in large vats and then used to produce insulin in industrial quantities, making the drug more readily available and at lower cost.

In addition to producing new drugs, GMO technology has found a wide variety of biological and medical applications. In agriculture, GMO technology has led to production of a wide variety of plant varieties that are herbicide-resistant (for example, Monsanto's "Roundup-Ready corn, which is resistant to Monsanto's weed-killer Roundup, meaning fields can be sprayed with herbicides that kill weeds but do not affect the crop), or pesticide-producing corn (Bt corn and potatoes, that do not have to be sprayed with commercial pesticides because the crop has a bacterial gene that allows the plant to produce its own pest-killer), rice that can synthesize Vitamin A, and thus become a source of this vitamin for a large percent of the world's population for whom rice is a major dietary staple. Some genetically modified agricultural animals have been produced as well, including pigs that excrete 70 % less phosphorus than conventional pigs and thus reduce pollution of groundwater, sheep with genes for a human protein that helps prevent damaging lung symptoms in cystic fibrosis patients, and goats that produce a high-fiber milk that alleviates certain human digestive problems. In biomedical research, genes have been inserted into bacteria or viruses to help find ways to deliver them from healthy humans to patients whose own genes are defective (a process in known as "gene therapy"). The majority of these various types of GMO varieties are still in the experimental stage. The primary ones that are commercially available are those that are herbicide-resistant or produce their own pesticide. While the only genetically modified animal to have been approved by the United States Food and Drug Administration (FDA) to date for food consumption is Aqua Advantage salmon, which mature twice as rapidly as their natural counterparts, proponents expect that it will only be a matter of time before they will be developed and approved. Increasingly, farmers have adopted GM technology around the world. Between 1996 and 2013, the total surface area of land cultivated with GM crops increased by a factor of 100. In the United States alone, by 2014, 94 % of the planted area of soybeans, 96 % of cotton and 93 % of corn were genetically modified varieties. In recent years GM crops expanded rapidly in developing countries, so that by 2013 approximately 18 million farmers grew 54 % of worldwide GM crops in Asia, Africa and Latin America. Thus, the introduction of genetically modified plants as food for both animals and humans, has been growing steadily since the mid-1970s (Fig. 5.5).

Despite these developments, the production and distribution of GMOs has generated a world-wide controversy leading to the requirement in many countries to

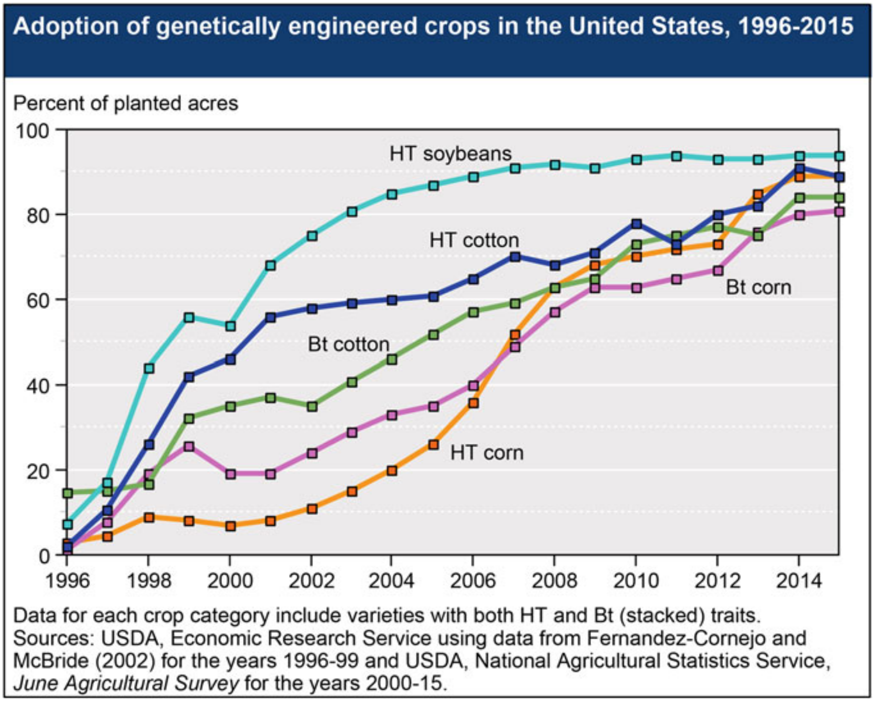

Fig. 5.5 Adoption of a variety of GMO plants in United States agricultural production since the mid-1970s for five major crops: soybeans, HT cotton, Bt cotton, Bt corn, and HT corn (*bottom line*). HT plants are engineered to be herbicide resistant, while Bt plants are engineered to be insect-resistant. As the graph shows, by 2012 between 70 and 90+ % of acreage devoted to these crops were planed with GMO varieties [*Source* USDA (See caption above)]

label those intended for food as "Genetically Modified." Before examining why this should be such a controversial topic, it will be useful to examine exactly how GMOs are produced.

The Genetic Engineering of GMOs

The basic principles of genetic engineering used in generating GMOs involve techniques that remove segments of DNA (a gene or gene complex) from a donor organism and transfer them into recipient cells of a host organism. Inserted genes can come from the same species (in which case the modified organisms are call-ed*cis-genic organisms*) or from a different species (in which case they are called *trans-genic* organisms). In either case the process, known as "horizontal transfer", is successful if the newly inserted genes in the donor express a protein that leads to development of a desired characteristic. Horizontal transfer is known to occur in nature by a variety of agents, particularly insects, which feed on a number of different plants in succession and carry bits of DNA along with the other plant tissues they ingest.

In the laboratory, however, the process of horizontal gene transfer is usually accomplished by several different techniques, each of which is adapted to the particular donor and recipient organisms involved. While some methods work best for plants and others for animals, the basic principles for most common genetic modification are the same:

1. Identifying and isolating the gene of interest from a host organism;
2. Inserting the gene of interest into the host cell, using either a biological vector (bacterium or virus), or a physical process such as a "gene gun" or micro-syringe to inject the gene directly into a host cell such as a fertilized egg.
3. Using various means to activate the newly-transferred gene.

To simplify our discussion, we will focus on the example of transferring genes in plants by way of bacterial vectors, since that is one of the most widespread and successful methods currently in use (Fig. 5.6).

In step (1) above, DNA is isolated from the host organism and cut into segments by enzymes known as restriction endonucleases, or restriction enzymes. A mixture of the DNA fragments is subjected to a procedure that separates the different fragments by weight, size and overall electrical charge. Based on previous experience, molecular biologists identify the fragment(s) likely to contain the gene of interest. This DNA fragment is purified and multiple copies generated by an enzyme known as DNA polymerase (the process known as polymerase chain reaction, or PCR). The newly-isolated gene is now ready for insertion into the host organism.

For transporting genes into plant cells, one of the most common vector used is the soil bacterium *Agrobacterium tumefaciens*. In nature, *Agrobacterium* has the ability to induce tumors (called "crown galls") in plants it infects, by transferring tumor DNA to the host plant's cells. This transfer is mediated by a plasmid (the T_i

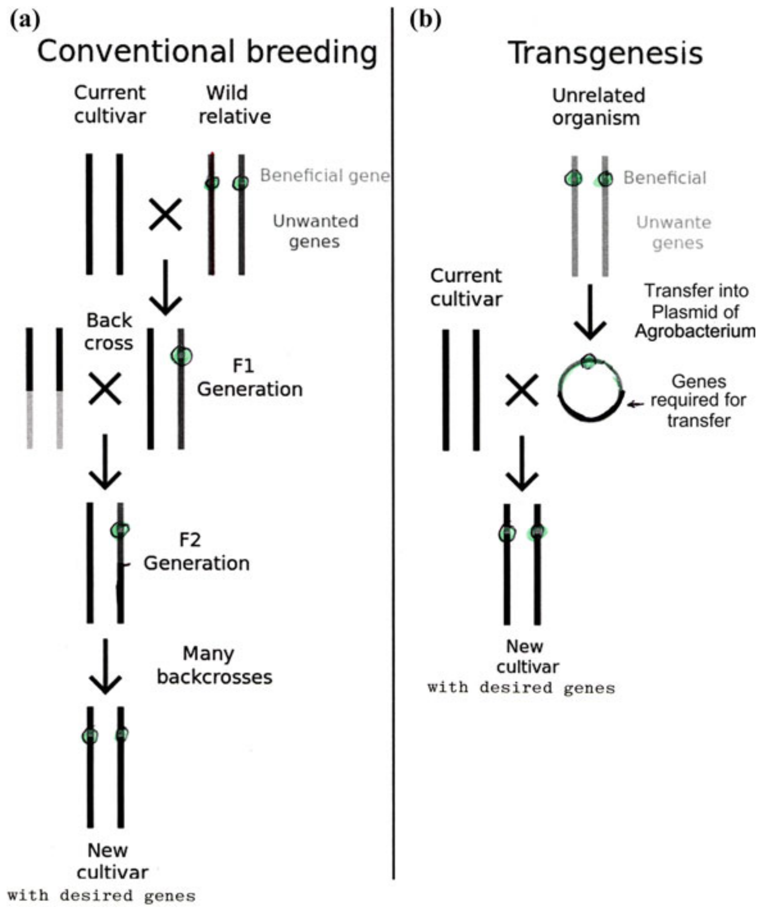

Fig. 5.6 Methods for modifying the genetic make-up of agricultural crops by combining desirable genes from one variety of plants into an existing form (cultivar). **a** The conventional method of hybridizing two genetically related forms (usually varieties of the same species) by conventional breeding practices. **b** The process of transgenesis or "transgenic modification," which involves removing desired genes from an organism of one species and introducing them (by a variety of different techniques) into the cells of a host of another species, where they can be expressed. The method of introducing the desired genetic elements into the host shown here is by way of a bacterial plasmid, a small circular bit of DNA that is separate from the bacteria's main chromosome. Along with a (virus not shown here), the plasmid acts as a vector, or transmitting agent. **c** Cisgenesis uses the same approach (attaching desired genes in one existing variety into a bacterial plasmid) but between closely related species. Both trans- and cis-genic processes produce GMOs [*Art original, based on Wikipedia article,* "*Cisgenesis*"]

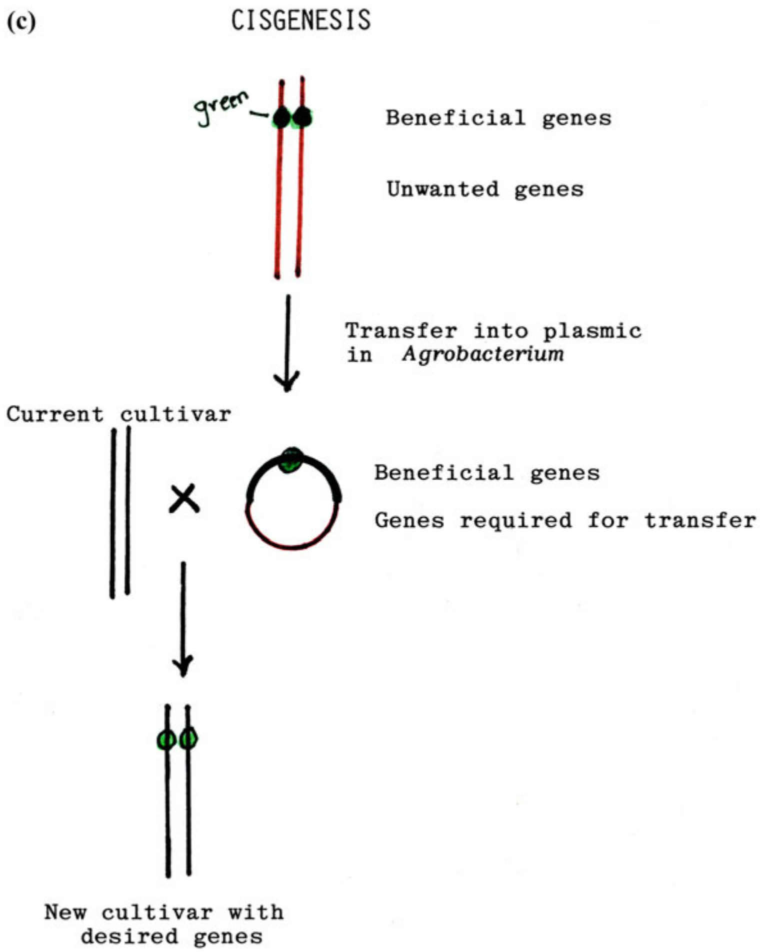

Fig. 5.6 (continued)

or tumor-inducing plasmid) that exists in the bacterium separate from the cell's main chromosome. The tumor-forming DNA is flanked by regions of DNA on both sides that are important for its integration into the plasmid. *Agrobacteria* thus modify plants genetically by "natural" means, that is, by a process that occurs in nature without human intervention. What is most fortunate for genetically engineering new plants, the process works even when the original DNA containing the information for tumor formation is removed from tthe plasmid and replaced with the desired foreign DNA. In this way, the *Agrobacterium* can be used to introduce new genes into crop plants.

The third step involves activation of the inserted gene to form the desired new protein. Since most DNA segments (genes) that code for specific proteins are under some sort of genetic regulation, affecting when they function to form proteins, it is important that the specific regulatory elements be transferred into the plasmid along with the gene of primary interest. This can be a tricky part of the process, since it is important for the newly-introduced gene not to *over*-produce as well as *under*-produce its protein product.

In animals, the process is more complex, and usually involves harvesting unfertilized eggs from the future host organism, fertilizing them in vitro (that is, in laboratory culture dishes) with sperm of males of the same host species. This primes the egg to begin its development. Before the egg starts dividing, however, donor DNA of interest is injected into the cell, either by microinjection techniques or, more reliably, by using viruses as a vector (Fig. 5.7). The most common viral vectors are from a family of *lentiviruses*, retroviruses containing RNA as their genetic substance very similar to the HIV virus discussed in Chap. 3 (see Fig. 3.6). As shown in Fig. 5.7, the lentivirus attaches to particular receptors on the cell surface and injects its RNA, which can be integrated into the host cell's genome (in this case a fertilized egg). The egg is then transferred to the uterus of a surrogate mother of the host species where it can undergo full development. If the process is successful the trait of interest will be expressed in the developing embryo. Since the first transgenic mouse was produced by Stanford's Paul Berg in 1981, a variety of transgenic animals (including mice, sheep, pigs and a primate, the marmoset) have been genetically engineered in this manner. Despite their use in transforming animal cells, lentiviruses have several disadvantages compared to bacteria like *Agrobacterium*. These include difficulty in expressing the foreign DNA and long-term stability (that is, the new gene may be shut down after a period of time by the host cell). As a result bioengineering in animals has proceeded more slowly than in plants.

A much newer technology, developed beginning in 2011, takes advantage of a gene-editing/splicing system known as Crispr-Cas9, found naturally in 40 % of the bacteria whose DNA has been sequenced to date. The Crispr-Cas9 system appears to serve as a bacterial "immune system", allowing bacterial cells to recognize foreign DNA to which they have been previously exposed, such as that from viruses that prey on bacteria. If the bacteria survives the first infection, its Crispr-Cas9 system can recognize and attach to any new invading viral DNA of the same strain and quickly cut it into specific pieces, rendering it ineffective. Crispr-Cas9 has already proven to be a powerful gene-editing technique that can be applied to animals and plants, including ourselves and our agricultural crops and stock. This new technology can quickly speed up the process of designing genes that produce desired effects in genetically modified organisms, but like all such technologies there are concerns about its potential misuse. Already, there have been questions about the use of Crispr-Cas9 to produce "designer babies", a suggestion fraught with various biological, social and ethical concerns. For engineering GMOs, it does not pose problems different from those involved with using older methods. It simply holds the prospect of making that process much easier and more rapid.

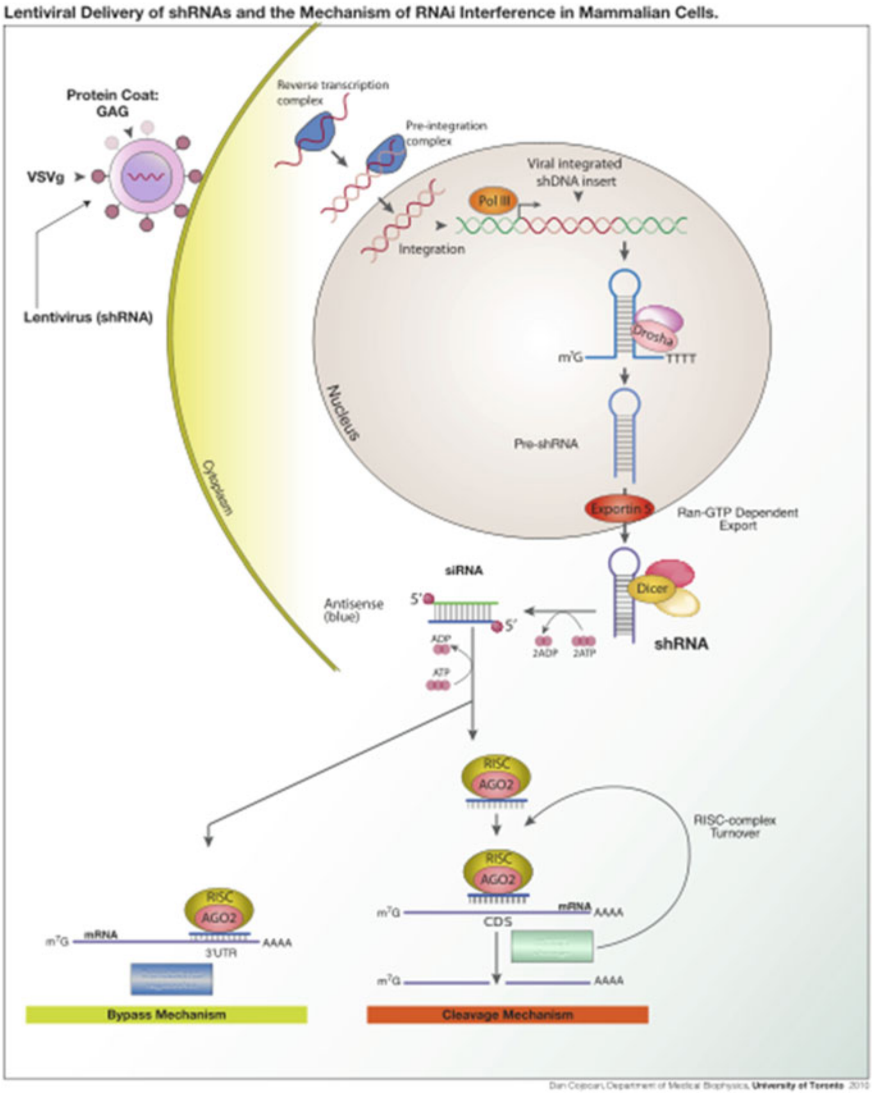

Fig. 5.7 Infectious cycle of a lentivirus used as a vector for gene transfer in animal models. Lentiviruses are retroviruses containing RNA instead of DNA as their hereditary molecule. The RNA can integrate into the host cell's DNA and be replicated and transcribed for multiple cell generations. The lentivirus, shown at the *upper left*, contains surface markers that match those on the animal egg surface. After attachment, the virus injects its DNA (shown in *brown*) into the host cell's DNA (shown in *green*) and can then function to guide the synthesis of proteins using a series of the host cell's organelles and viral RNAs (shown on the *right-hand side* of the diagram) [Needs to be redrawn from Wikipedia, "Lentiviruses" (October 2015)] (Color figure online)

What is important to keep in mind in examining the controversial elements of GMOs is that desired genes are transferred from the genome of one organism to the genome of another organism, either related or unrelated, directly rather than through breeding the organisms and waiting to see if the desired genes are passed on to the offspring. To many people this process introduces an unnatural element into the transgenic (or even cisgenic) organism that can lead to complex ecological and health issues that proponents and the commercial producers have not adequately addressed. We turn to these controversies in the next section.

Controversial Issues with the Development of Transgenic Organisms

Although both transgenic and cisgenic organisms have been controversial, it is the transgenic forms that have attracted most attention. The disputes involve biotechnology companies, individual consumers, research scientists, farmers, environmental activists and government regulators. Overall, the scientific community has claimed to have reached a consensus that there is no well-documented threat to human health from consumption of genetically modified food. According to the American Medical Association's *Report 2 of the Council on Science and Public Health* (2012), "Bioengineered foods have been consumed for close to 20 years, and during that time, no overt consequences on human health have been reported and/or substantiated in the peer reviewed literature."[2] At the same time, however, the AMA has also called for mandatory pre-market safety testing for all GMO foods, which is currently only voluntary on the part of biotechnology companies. What is particularly problematic here is that GMOs are being treated as a single category, as if they were all the same regardless of the particular genes that have been engineered into them. One of the major lessons of biology is that all species and varieties are different, and that blanket generalizations about characteristics such as safety are likely to be meaningless when applied across the board (we would certainly not make such a statement about all naturally-occurring plants). As philosopher of biology Roberta Millstein at the University of California, Davis, has noted: "Context matters" for the growing and consuming of GMO foods (Millstein 2016). Crop plants such as Bt corn or Bt cotton, in particular are notorious for producing very different results in different localities or under varied types of planting and maintenance practices. As geneticists have known for almost a century, to understand the full range of a gene system's effect on the organism's characteristics, the organisms must be raised under a variety of environmental conditions. While this issue relates more to overall productivity of a variety, it could

[2]The safety of genetically-engineered foods was partly put to rest in the mid-1970s when a group of molecular biologists, convened by the U.S. National Academy of Sciences at Asilomar State Beach in California, met to discuss regulations on recombinant DNA research (as we have seen, an early step in attaching together DNA from one organism with that of another). The conference drew up a series of measures to ensure the safety of recombinant research, especially since the public became highly concerned by the use of bacteria and viruses as vectors and the possibility these could get loose into the general environment. The conference also affirmed the need for molecular biologists carrying out recombinant DNA work be as open and transparent to the general public as possible.

also apply to potential toxic effects that do not appear under one set of conditions but could appear under others.

Advocates of the use of GMOs also point to a recent study (2015) found that in nearly 300 samples of strains of cultivated sweet potato, bacterial DNA sequences have been identified, the result of lateral gene transfer during naturally-occurring infection by *Agrobacterium*. Since the cultivated sweet potato has been a staple in human diets for millenia, proponents argue that human engineered genetic modification most likely poses no risk whatsoever. Advocates also point out that in the last 20 years that GMO crops have been available, they have virtually taken over many markets, especially corn (maize), which in various forms is now grown in 14 countries, and in 2012 twenty-six varieties of herbicide resistant GM corn were authorized for import by the European Union (EU). In that same year the EU imported overall 30 million tons of GMOs. There have been no human medical conditions that have been directly linked to GMOs in any of those countries.

On the humanitarian side, proponents of GMOs point out that they hold the potential for feeding millions of starving people in sub-Saharan Africa and elsewhere in the Third World. Companies involved in producing GMOs, such as Monsanto, DuPont and Syngenta, in the United States and Plant Genetic Systems and Crop Design in Belgium have launched huge promotional campaigns to sell GMOs worldwide.

Opponents of the widespread distribution of GMOs, such as the Oregon Consumers Association, the Union of Concerned Scientists, and Greenpeace argue that the long-term effects of consuming bioengineered foods have not been tested thoroughly, and that it is irresponsible to release them into the environment—agricultural and ecological—without better data on their consequences. Concerns have been expressed along several lines: biomedical (human health), environmental disruption, and the legal and social issues associated with "intellectual property" rights.

On the biomedical side, there is fear that the use of bacteria and viruses with foreign genes could lead to the widespread dissemination of pathogens into the human population. There have also been claims that diseases such as cancer could be linked to GMOs and that these possible cause-effect relationships have not been explored over long enough periods of time to be detected. Geneticists have increasingly found that genes interact, an that the introduction of completely foreign genes into the genome of an established animal or plant variety could have a variety of unpredictable effects. More broadly, claims that genetically-engineered hormones for cattle have been shown to affect the health of the animals themselves, since GMO cows can get udder infections more readily than their non-modified counterparts. Udder infections could, it is argued, introduce sources of infection for humans who consume that cow's milk. introducing additional sources for human infection. There are also concerns that the proteins produced in GMO plants and animals could undergo deterioration after time and produce toxic by-products not present in standard organisms. Underlying these biomedical claims is a general fear that, as a result of this new and poorly-understood technology, people simply do not know what they are putting in their bodies when they eat genetically-modified foods. An indicator of the fear associated with GMOs is that they have been referred to by some as “Frankenfoods”, a reference to Frankenstein, the human-engineered monster of Mary Shelley’s 1818 novel about a human robotic creation gone wrong.

Consumer groups also question the impartiality of the regulatory agencies that are supposedly watchdogs over GMOs, such as the Food and Drug Administration and the Environmental Protective Agency, both in the United States, which routinely seem to approve distribution of GMOs without long-term testing. A GMO Watchdog group, the “Laissez Faire Club” has pointed out that with so much of the agricultural acreage in the United States devoted to GMO plants, we are being bombarded on all sides by chemicals whose effects we do not understand. They point out that GMO foods are highly profitable and that the rush to put them into the farmer’s fields, and thus produce quick profits for biotech companies and their investors, has taken precedence over adequate testing. For example, the increase in GMO production between 2000 and 2012 is highly correlated with Monsanto’s corporate profits in the same period, which rose 12-fold, from $10 to $120 per share.

But as critics claim, what about the consumer’s right to know? To counter the increasing distribution of unlabeled GMOs, opponents have called for mandatory labeling. To date, while most European Union countries have required some form of labeling, only one state in the United States (Vermont) has actually adopted such a measure (aimed to go into effect in 2016, pending a lawsuit against it). Maine and Connecticut have also passed such laws but they would only be enacted if neighboring states pass similar legislation. In November, 2014, a legislative proposal to require labeling in Oregon lost by a narrow margin. The industry has fired back with a bill, House of Representative (HR) bill 1599 that would make it illegal for any state to require foods to have a GMO label (this bill has been called the “Deny Americans the Right to Know” or “DARK Act” by its opponents).

On the environmental side, opponents of GMOs fear that genes placed into crop plants could be spread to non-crop plants either through hybridization (if the crop can hybridize with its wild relatives), or through lateral gene transfer by bacteria or viruses acting as natural vectors. Spread of genetically modified genes, such as those conferring pesticide-resistance (that is, plants that produce their own pesticides) or herbicide resistance, might produce “super weeds” that could be difficult to control. Ecologists point to a particular case in which the widespread use of a GMO product in agriculture, Bt corn, affecting Monarch butterfly larvae that feed on milkweed (as described in Chap. 1), has led to unanticipated ecological problems that might have been avoided if the corn had been tested thoroughly in the field. The bacterium, *Bacillus thuringiensis*, has a gene that produces a protein, delta endotoxin, that is particularly effective in controlling infestation by the European corn borer in corn fields. The Bt genes were genetically engineered into the corn where they expressed the endotoxin in many plant parts, including especially the leaves. When corn borer larvae hatch on corn and start eating the leaves, they consume the endotoxin, which soon forms a poison that binds to the intestinal wall and causes perforations. The larvae stop eating and eventually die. Bt delta endotoxin is particularly useful because it only affects the larvae of butterflies, moths and their relatives, whose larvae are the most destructive to corn in the early spring. Studies to date, however, show that the endotoxin does not affect the larvae of other insects such as beetles, wasps or bees, nor does it affect humans and other mammals.

In the late 1990s it was discovered that pollen from Bt corn, which contained the Bt-toxin gene, was carried by wind as far as 60 m from corn fields. Some of these pollen grains fell on other plants, including the milkweed plant (*Asclepias*), which is the sole food source for larvae of the Monarch butterfly (*Danaus plexippus*). As discussed in Chap. 1, the dramatic decrease in the Monarch population in the past several decades was thought to be tied, at least in large part, to the presence of Bt-pollen on the leaf surfaces of the milkweed. In 1999, a team at Cornell University in New York carried out a controlled experiment to determine whether the genetically-engineered pollen was a causal factor in the death of the butterfly larvae. The researchers set up three groups of five Monarch larvae each: One, a control group consisting of larvae and milkweed leaves to which no pollen of any kind has been applied; a second consisting of larvae and milkweed leaves to which non-GMO corn pollen had been applied; and a third, with larvae and milkweed leaves to which Bt-engineered corn pollen was applied. The results are shown in Fig. 5.8. When the milkweed leaves were ingested by the Monarch larvae, they slowed down or stopped eating altogether and eventually died in larger numbers than in a control group. Note that not all larvae exposed to Bt-engineered pollen were killed, but that by the fourth day (when the experiment ended) the survival rate of the group consuming the Bt-pollen was only half (56 %) that of the control group which consumed no pollen of any sort. It is also interesting to note, however, that in

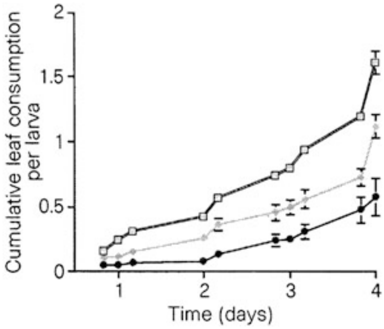

Fig. 5.8 Effects from a study on the exposure of Monarch Butterfly larvae (*Danaus plexippus*) to genetically-engineered corn pollen carrying an insecticide, Bt delta endotoxin, inserted into a bacterim (*Bacillus thuringiensis*). The gene that codes for the insecticide molecule is transmitted experimentally to corn or other plants using the bacterium, where it enters leaf cells (primarily) and integrates into the cell's own genome. The effects of Bt delta endotoxin are shown in three growth curves from a laboratory experiment carried out at Cornell University: *Top curve*, larvae exposed to milkweed leaves on which no Bt pollen has been applied; *middle curve*, larvae exposed to milkweed leaves on which non-Bt pollen was applied; and *lower curve*, larvae exposed to milkweed leaves to which Bt pollen was applied. Horizontal axis (x-axis) represents time in days after larvae start feeding, while vertical axis (y-axis) measures the amount of leaf material consumed per day per larva [Modified from *Nature* 399 (May 20, Losey 1999): p. 214;]

the second control group, those larvae that consumed non-engineered pollen, the feeding and survival rate was also lower than those that consumed no pollen, at least for the first three-and-a-half days. By the fourth day, however, it appears they were catching up to the group that were exposed to no pollen.

The implications of this study are important in that they suggest how the use of GMOs can have effects on a large number of non-target organisms. Since milkweed is the sole food on which Monarch larvae feed, and since the use of Bt corn has spread over large areas of the midwestern section of North America, the Bt endotoxin has been implicated in the dramatic decline of the Monarch butterfly population noted in Chap. 1. There is also no emerging evidence that Bt corn pollen, which is chemically sprayed with a neonicotinoid pesticide, affects bee reproduction, which may account for the significant reduction in bee pollinators that has been documented in North America. Because we do not know how many other species might be affected in these ways, critics of GMOs oppose their release and use on a large scale until they can undergo thorough testing in the field.

In response to such criticism, the biotech industry has responded that there is still no evidence that GMO plants and animals affect human health directly. Biomedical critics have observed that, compared to Europe, the increase in a number of human diseases such as cancer, diabetes, gastrointestinal infection and many others has risen dramatically in the United States in the last three decades, during which GMO crops have become most widespread. Defenders of GMOs have argued that correlation does not necessarily indicate a direct cause-effect relationship (see the Appendix, section on "Correlations"). It can be argued that many other changes have been occurring in this same time period that could be the cause of increased disease incidence in the United States: rising cost of health care, including pharmaceuticals, increased water and air pollution, or job-related stress to name a few. Both companies and the government regulators that oversee them continue to argue that lack of any clear-cut negative effects makes it reasonable to continue using and developing GMOs. Opponents claim that this very lack of clear-cut evidence should be a warning sign not to move ahead too quickly with mass distribution.

The Legal, Economic and Social Problems Surrounding GMOs

The issue of patenting crop plants and their seeds has had a long history in the capitalist west, going back to early agricultural concerns about the intellectual property rights of traditional breeders in the eighteenth century: that is, the issue of patents. The key value of patents is that they give the developer of some new invention or process exclusive rights to exploit any income that may result from their work for some definite period of time. Up until the 1930s, in many countries, including the United States, it was argued that plants and animals, even those modified by practical breeders over time, were still "products of nature" and thus could not be patented in the same way as a mechanical invention. The Plant Patent Act of 1930 in the United States was among the first successful pieces of legislation to provide some coverage for those who developed new plant products. The Act allowed plant breeders to patent non-sexually-reproducing varieties of crops, particularly fruit trees that can be propagated by grafting or other non-sexual means.

However, it excluded sexually-reproduced plants, and thus their seeds, which were still considered "natural." With the rapid growth of biotechnology and recombinant DNA techniques in the 1970s, there was pressure to expand the law to include genetically-engineered organisms, including bacteria and eventually higher plants (specifically their seeds) and animals.[3] With the new legislation, large biotech corporations such as biotech giants Monsanto, Dow and Dupont rushed to patent seeds, various strains of microbes and even individual DNA sequences and their control elements.

This is when the legal controversies began. To understand the nature of the controversy, we will take a look at the case of Monsanto and the question of proprietary rights over its genetically-modified crops, particularly Bt corn, which in addition to its insecticide trait is also resistant to the powerful herbicide, "Roundup", which, coincidentally, Monsanto also produces. Thus, large fields of Bt Roundup-Ready corn can be sprayed with Roundup, killing the other weeds but leaving the corn unaffected.

Traditionally, farmers have saved seeds from each year's harvest to plant the next year's crop. When Monsanto developed a series of herbicide-resistant and pesticide-producing strains, such as Bt corn, they sold them to farmers for use in one particular season only. The problem, from Monsanto's point-of-view was that, since the basis for resistance was now engineered into the plant's genome, it would replicate itself in the seeds and thus could technically be used to grow another season's crop. This of course would mean that farmers could buy the seeds only once and from there on use their held-over seeds for all future plantings. It should be pointed out that Monsanto stood to profit in two ways from selling its Bt corn: the seeds themselves, and then the herbicide to which their engineered plants were resistant.

One possible way to circumvent the problem of the re-use of seeds was to employ what became known as Genetic Use Restriction Technology (GURT), or "terminator genes," which render the seeds of the second generation sterile. This technology had already been developed in the 1990s by the United States Department of Agriculture and several multinational seed companies. However, because of widespread opposition across the globe, in 2000 the United Nations Convention on Biological Diversity (UNCBD) recommended a moratorium on the distribution or use of terminator technology. In addition, some countries, such as India and Brazil, passed their own laws to prohibit the use of terminator genes. Thus it is not surprising that when news leaked to the public that Monsanto was considering engineering terminator sequences into it Bt corn, there was such an outcry from the general public, environmentalists and farmers, that Monsanto backed down. They turned instead to a legal route, requiring all farmers who bought their GMO seeds, to sign a contract

[3]The first higher animal, the Oncomouse, was patented by Harvard University in 1988 for work carried out by Philip Leder and his associates. The OncoMouse is a genetically modified mouse that carries oncogenes (*Onco*, Greek for tumor) and their control elements that, when activated, significantly increases the mouse's susceptibility to cancer. The Oncomouse has become a widely-used model organism for cancer research. The DuPont company later obtained the patent, which it held until its expiration in 2005.

that they would not save any seeds for use in future plantings. This arrangement led to two separate legal issues: (1) Confronting and prosecuting farmers who purposefully violated their contract and knowingly grew second generation GM crops without paying Monsanto; and (2) Dealing with farmers who had never bought Monsanto seeds but whose crops were accidentally cross-fertilized by pollen from nearby fields that were planted with the Monsanto's GMO seeds.

The first problem was the easiest to resolve, since it involved the direct violation of a contractual arrangement, which the farmers had entered into willingly, whatever one might think about the moral or ethical status of such contracts. The second problem, however, became more contentious when Monsanto began suing a series of farmers, especially small, often organic, farmers opposed in principle to growing GMOs, whose fields were "contaminated" unknowingly by the GM pollen. As a result, in 2010 a coalition including the Oregon Seed Growers' Association, individual United States and Canadian family farmers, independent seed companies and agricultural organizations, sought in turn to sue Monsanto for its aggressive stance on this issue. The problem was complicated by the fact that in stating its policy, Monsanto had pledged not to sue farmers whose crops were found to contain 1 % or less of the company's genetic modifications. This clause notwithstanding, by the time of the suit Monsanto had brought over 100 individual farmers to court, and settled some 700 cases out-of-court. In June, 2013, the case was heard by the U.S. Federal Court of Appeals for the Federal Circuit in Washington D.C. which ruled that, while it was inevitable that *some* contamination from cross-fertilization would occur, the plaintiffs (the farmers and grower's associations) had no basis for prohibiting Monsanto from bringing suit since "the company has made binding assurances that it will not take legal action against growers whose crops might inadvertently contain traces of Monsanto biotech genes…" The decision thus left open the likelihood that Monsanto could continue suing farmers, which would be costly for the farmers as well as raise difficult questions what about amounted to "a trace," or even 1 % (1 % of what?) of GMO contaminants. To make matters more confusing, corn is naturally prone to moving genes around both within an individual plant and between plants (movable, or transposable genes were first discovered in corn in the 1940s), making it highly susceptible to spontaneous gene transfer. Nevertheless, the United States Supreme Court upheld the lower court ruling in January, 2014.

Another issue that at first glance might seem less controversial, relates to claims from large corporations such as Monsanto and Dupont that their GMOs will help "feed the world" (refer back to Fig. 5.9). This sounds like a humanitarian goal worth striving for, even if we do not have the technology to accomplish it at the moment. However, according to many sociologists, economists and demographers who study changes in population structure, growth and migration, the problem is far more complex than can be solved by a technological fix such as better engineered GMOs. According to this view, the real problem is an economic and social, rather than a biological one. For example, critics such as Vandana Shiva, an environmental activist in Delhi, India, has argued that increasing acreage devoted to producing GM crops in developing countries could actually increases rather than

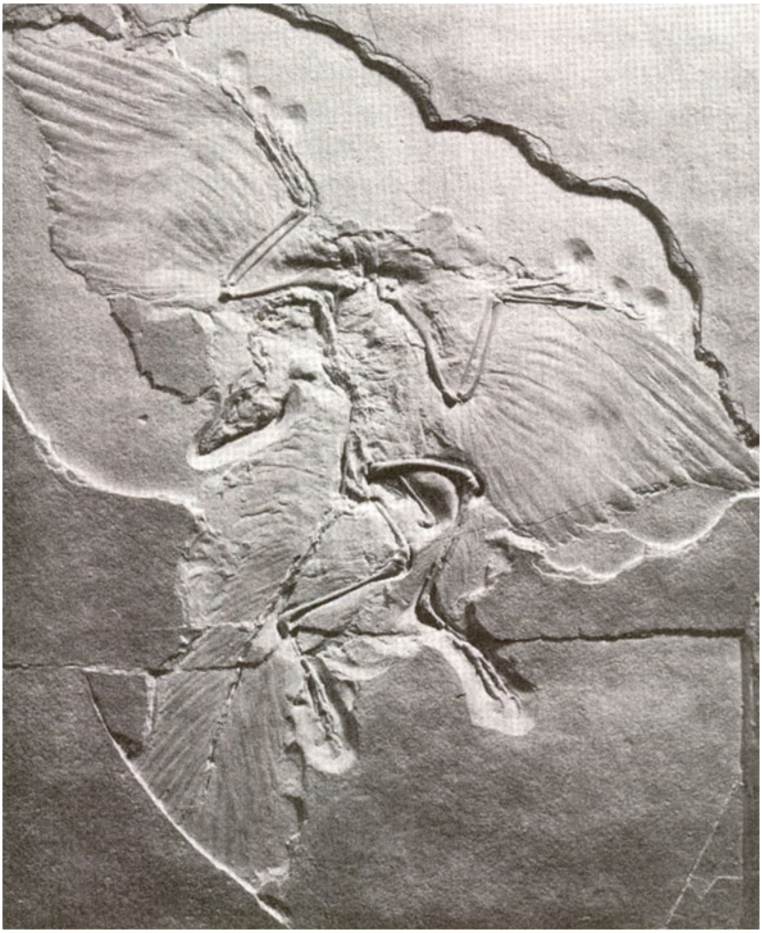

Fig. 5.9 Fossil of the primitive *Archaeopteryx,* a true intermediate between modern birds and reptiles. Note the long tail, claws on the appendages, and teeth, all of which are reptilian characteristics, yet the perfectly formed feathers and front limb structure are characteristics of modern birds. While *Archaeopteryx* is not considered a direct ancestor of modern birds (it shared a common ancestor with a form that did give rise to modern birds), it clearly represents the sort of intermediate data from the fossil record that Darwinian theory would predict. In fact, without the feathers, *Archaeopteryx* would probably be classified as a small, bipedal dinosaur [Photograph courtesy, American Museum of Natural History, from J.J.W. Baker and G.E. Allen, *The Study of Biology* (4th edition, Addison-Wesley Publishing Co, 1982). *Rights transferred to authors, December 13, 2002*]

decreases hunger and famine in those regions. Her claim is that the planting of large areas with expensive GMO seeds results in the displacement of small farmers by larger ones who can actually afford to buy the new seeds and the chemicals needed to grow and maintain them. To recoup the original investment, the farmer must then sell the GMO crops on the international market, which essentially moves food out of the local areas where it is most needed and transports it to areas where people can afford to buy it (i.e., the industrialized countries). The problem, then, is one of the vast differentials in income around the world, not necessarily the need for increased food production. This position gains some credence from a report as long ago as 1996 by the United Nations Food and Agricultural Organization (UNFAO), which reported that world-wide food production was keeping pace with population growth and that enough food was then being grown to supply every person on earth with 4.3 lb of food per day: 2.5 lb of grain, beans and nuts, a pound of fruits and vegetables, and nearly one more pound of meat, milk and eggs per year.[4] The real cause of famine, in this view, is the lack of *money* to buy and grow food on the part of millions of the world's poorest, and hungriest populations, rather than the inability to produce the food itself.

As the proceeding suggests, there are thus many ancillary issues involved at the economic, social and political levels associated with genetically modified organisms: the question of property rights (in this case, ownership of GMOs) for commodities considered to be necessities of life such as food; the safety and nutritional value of organic versus bioengineered foods; a rising suspicion about the amount of control, often unseen, that large corporations, which must make profits for their shareholders, have over so many facets of people's lives, especially the production and distribution of food; and the role GMOs play in global agriculture, especially in regard to hunger and malnutrition in countries where GMOs are being grown and the industrialized countries where they are being manufactured and sold. We cannot hope to explore all of these questions (and many others) in this book, but they are real issues, especially in a world that is becoming ever-more globalized and polarized between the haves and have-nots. The opposition to this new technology may well arise as much or more out of a much larger set of cultural concerns than it does out of skepticism about the foods themselves.

Ethical Concerns in Science Today

Other examples abound concerning the ethical questions that arise in scientific work. For example, as geneticists in the 1990s worked fast and furiously to sequence the human genome, questions were already being raised about who should have access to that information? Can insurance companies refuse coverage of (or employers jobs to) people with genetic diseases? Should geneticists encourage the testing of newborn infants for genetic diseases if there are no therapies, let alone cures, for most of the conditions? Should a researcher working on bat sonar navigation accept research funds from the military, not knowing how that work will eventually be used? If a young Ph.D. is having difficulty finding a job, should he or she accept a job with a biological weapons unit or even a large corporation producing GMO seeds to grow in developing countries?

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[4]UNFAO, *State of the World's Plant Genetic Resources for Food and Agriculture*. Background Document for the Fourth International Technical Conference on Plant Genetic Resources, Leipzig, Germany, June 1996: pp. 17–23. These figures are cited in Andrew Kimbrell (ed), *Fatal Harvest: The Tragedy of Industrial Agriculture* (Washington, D.C., Island Press, 2001: p. 50).

One of the most controversial issues to emerge in light of new technologies surrounds the prospects of cloning animals. Cloning is a process in which stem cells are implanted in the female reproductive tract and allowed to develop. “Dolly,” the sheep that was successfully cloned in 1998, represented one of the first of these new technological breakthroughs. Immediately, however, the question arose about whether cloning, even of animals, had moral and ethical implications. For example, a company was formed in New York to use stem cells from pets to clone a replacement when the original pet dies (the company was named “Copy Cat”). This enterprise gave owners the false impression that they were going to get a perfect replic of their deceased pet, personality, behavior and all. What are the implications for the cloning of human beings. Suppose, for example, a child is killed; would cloning that child be legal and ethical as a replacement for the grieving parents? What about cloning human bodies for organ replacement? These are very serious issues and they raise a host of problems. None are easy to resolve, but difficult questions must be asked now and means devised to guide us toward making ethical and humane decisions in the future. Such issues cannot be put aside if scientists are to take any responsibility for preventing future misuse of their research.

5.5 Ethical and Social Issues in the Use of Human Subjects for Research

In the wake of the Nüremberg Trials in Germany in 1945, one of the most startling revelations was the extent to which German scientists, supported by grants from the National Socialist (Nazi) government, had carried out brutal forms of human experimentation. Subjects were placed in ice-cold tanks until they died, an experiment designed to assess survival rates of pilots downed in the icy waters of the North Sea. Other subjects were given poisonous gases in a effort to determine strategies for military personnel in gas warfare attack. Still others were used as guinea pigs for transplantation of various organs at a time when such procedures were merely speculative experiments. The list is distressingly long.

The issue of human experimentation has always raised difficult ethical questions. Clearly, if we are to make any medical progress, at some point new medications or new surgical procedures have to be tried on *somebody*. The question always is: How much risk is ethically acceptable, who are the people used in such experiments (prisoners, poor people, or the affluent), and how much benefit will come to the subjects of such experiments? No simple formula can answer these questions, but it is critical that scientific investigators keep ethical considerations foremost in their minds as they plan clinical trials that involve human subjects.

The Tuskegee Study, 1932–1972

The fact that scientists and medical personnel do not always carefully consider the ethical implications of their work is illustrated by a project conducted between 1932 and 1972 by the United States Public Health Service (USPHS) in Macon County, Alabama, a rural, cotton-farming region. The project was referred to as the "Tuskegee Study," after the name of one of the larger towns in the area and home to the renowned Tuskegee Institute founded in 1881 by George Washington Carver (c. 1860–1943) to promote higher education for southern blacks.

The purpose of the experiment was to study the long-term effects of syphilis infection. Syphilis is a venereal disease caused by a spirochete, a corkscrew-shaped bacterium that can be passed from one person to another during sexual intercourse, as well as from an infected mother to her developing fetus. If infected persons are not treated, they may harbor the parasite for the rest of their lives, often leading to a premature death. The spirochetes may invade virtually all of the body tissues, producing skin lesions, debilitating pain in the joints and muscles, and liver deterioration; invasion of the central nervous system and brain, can result in paralysis and dementia. Spirochetes may sometimes remain dormant in the human body for years before re-emerging and continuing to spread throughout the body. In other cases, the organism has no latent period, moving from one part of the body to another immediately after infection. Clinically, syphilis is usually described as passing through three stages, primary, secondary and tertiary, the latter representing the last, usually fatal stage.

Although syphilis had been a long-standing problem throughout the world, in the United States it became a particularly severe public health issue both during and after World War I (1914–1918). Attempts to study the problem systematically were hampered by strong religious and moralistic attitudes that shunned any open discussion of sex or sexually transmitted diseases. As a result of religious lobbying, congressional appropriations to the USPHS for such studies were continually cut during the 1920s, and even more drastically reduced after the stock market crash of October, 1929.

One of the questions physicians and researchers needed to know in order to learn how to treat syphilis was how, if left untreated, it progressed over long periods of time. Why was it, for example, that some people progressed immediately from one stage of infection to another while other cases showed varying periods of latency? Was this the result of differences in the strain of spirochete or differences in the people involved? Could knowledge of those differences provide a clue to discovering a possible cure?

To answer these questions, the USPHS initiated a long-term study in 1932. It was generally assumed, (though with no hard statistical evidence) that syphilis was especially rampant among African-Americans. Indeed, in some medical circles African-Americans were referred to as a "syphilis-soaked race," an indication of the racist attitudes prevalent both inside and outside the medical community at the time. A project was therefore conceived to follow a syphilitic population of 399 rural African-American men to describe the long-term progression of the disease. The project was managed out of the Centers for Disease Control (CDC) in Atlanta, and involved a number of local doctors as well as interns and medical officers from the PHS in Washington. The Tuskegee University's hospital was also involved both in providing facilities and administrative support. African-American nurse Eunice Rivers (1899–1986) who had trained at Tuskegee University, was hired to act as a local contact with the subjects and as an intermediary between the all-white doctors and the African-American community.

USPHS officials, with the help of Nurse Rivers, went to the fields and homes of rural sharecroppers in Macon County, talking to individuals and selecting for the study those who could be diagnosed in the tertiary stage of syphilis. Potential subjects were told they would get periodic free medical exams, a hot lunch on the day of each exam, transportation to and from the examination site, and burial expenses (a rather macabre but economically attractive incentive). They were also told they would receive treatment for various illnesses. None of the subjects in the project knew what the real purpose of the study was. Many of the subjects thought they were being examined for "bad blood," a general term for a variety of diseases including rheumatism, fatigue and various gastro-intestinal ailments. The study was organized with the aid not only of the USPHS but also the major administrators of the Tuskegee University Hospital. Nurse Rivers handled most of the negotiations and the day-to-day work of chauffeuring subjects to and from the study.

The control group consisted of 201 men who were free of the disease, and who were also examined regularly by USPHS doctors. Funding aimed at providing eventual treatment for the men who had syphilis was initially obtained from the Rosenwald Fund, a Chicago-based philanthropy. Treatment at the time consisted of giving the patient a drug called silversan and combinations of mercury and bismuth, all of which had highly toxic side-effects. However, the stock market crash in October, 1929 and its long-term financial effects drove the Rosenwald Fund to withdraw its support before any treatment could be offered, but subjects in the study were never told the treatment option no longer existed. Indeed, because the point of the study was to examine the long-term effects of syphilis, there was never any clear indication if or when treatment, might be made available to the subjects. As a part of the experimental control for the study, some subjects were given "placebos," a fake pill that subjects were told was a treatment that would make them feel better. (Placebos are used all the time as a legitimate aspect of clinical trials, since they insure that improvement in a condition is really a result of the treatment administered and not a psychological effect of the subject's *thinking* he or she is being cured. However, major ethical issues arise about administering placebos to a control group with a serious and life-threatening condition.)

Reports of the Tuskegee research were made in major medical journals periodically during the course of the study. Thus, it would have been clear to anyone who read the literature carefully what the Tuskegee Experiment was about. There was no attempt to conceal the study or keep the findings secret. Approximately 100 (25 %) of the men in the syphilitic group died directly from the effect of the disease and the lack of treatment. The whistle was finally blown on the Tuskegee Study in 1972 at a time when issues of civil rights and African-American consciousness were at a new high. The first exposure of the study came from a reporter at the Associated Press. Other newspapers quickly picked up the story. Under pressure from the press, USPHS officials (of the initial planners only Nurse Rivers still remained with the project) sought in vain to find a written protocol for how the study was designed, or for any form showing that subjects had given official or informed consent for their participation.

Responses were immediate and angry, especially from the African-American community. While most newspapers stopped short of calling the project a Nazi-like experiment, some African-Americans considered it another example of genocide. The Tuskegee study was abruptly terminated, but the questions it raised stimulated a major reassessment of USPHS protocols for studies involving human subjects. In 1974 the United States Congress passed the National Research Act and formed a Commission to make recommendations for all future studies involving human subjects. The National Institutes of Health (NIH), which provides funding for such investigative work, along with the USPHS, now require elaborate reviews of all projects where human subjects are involved, not only to protect the subjects' health and well-being, but also to insure that privacy and other matters of personal concern are respected. To bring some closure to the story, in 1994 a multi-disciplinary symposium was held on the Tuskegee study at the University of Virginia. Following that symposium, interested parties formed the Tuskegee Syphilis Study Legacy Committee to develop ideas that had arisen at the symposium and publicize the issues to a broader public. As a result in May of 1997 U.S. President Bill Clinton formally apologized to the subjects and their families at a ceremony at the White House:

> What was done cannot be undone. But we can end the silence. We can stop turning our heads away. We can look at you in the eye and finally say on behalf of the American people, what the United States government did was shameful, and I am sorry… To our African American citizens, I am sorry that your federal government orchestrated a study so clearly racist.

Five of the eight study survivors were able to attend and be honored at the White House ceremony.

The Tuskegee Study raises serious questions about the ethics of human experimentation. In the first place, the doctors conducting the study deliberately withheld treatment from individuals who might have benefited, or at least might have experienced less suffering, had they been given medication. By the 1950s penicillin was widely available and known to help reduce the effects of syphilitic infection. Yet the whole project was conceived with the purpose of making observations on untreated individuals, an issue with enormous ethical implications that were apparently not seriously considered by any of those who designed or participated in the study. That the study was carried out by medical personnel makes the question even more problematic. A part of the Hippocratic Oath, which all physicians take upon being admitted into the medical profession, states that the physician must be dedicated to "doing no harm." Those carrying out the Tuskegee study are not the only ones at fault however. More than a dozen peer-reviewed journal articles reporting on the Tuskegee Study appeared in the medical literature over a 40-year period, with no questions raised about the ethics of the study design, especially concerning the issue of withholding treatment. The moral question simply did not seem to exist, just as it did not exist for many physicians and scientists in Germany under the Nazi regime at the same time.

The Tuskegee study also revealed the attitudes of the USPHS and its staff. The very fact that it was assumed that most black men had syphilis and that therefore they would be a ready-made population for such investigations indicates the deep racist biases that underlay the study design. While most African-American physicians knew that syphilis was not rampant in their communities in the 1930s and 1940s, the fact that they were not allowed to be members of the American Medical Association (AMA) meant they had little chance to interact with or explain to their white counterparts the lack of basis for this myth. Furthermore, the use of poor blacks from the rural south presumed that no one would question the methods or raise the same kind of issues that would be raised if the study were to be done on middle-class white men (this was further insured by keeping the real purpose of the study secret from the subjects). That the experimental group was an impoverished and desperate segment of American society made them all the more likely subjects. As one reporter put it, the fact that these men agreed to be in the study because they got a free exam, a hot lunch and "burial expenses" shows just how marginal their lives were at the time.

Medical researchers have learned much from the public exposure of the Tuskegee study and other cases where human experimentation has been carried out with less-than-sound ethical considerations. Yet neither scientists nor the public can become complacent and assume that something like Tuskegee will never happen again. The right to investigate must always be balanced against the rights of the individuals participating in any given study. Scientists can easily get so caught up in enthusiasm for their research that they may fail to consider the ethical questions involved, or of their subjects as human beings with fears, rights and concerns. Ethics is not a philosophical hobby that scientists can think about only in their spare time. It must be an ongoing aspect of the research, as integral to the process of science as other aspects of research that we have discussed in earlier chapters of this book.

5.6 Science and "Pseudoscience": "Scientific Creationism" and "Intelligent Design"

Pseudosciences (Gr. *pseudes*, false) are activities or forms of thought that wish to be identified as being "scientific," yet lack strict adherence to the traditional intellectual structure that characterizes mainstream science. What actually counts as a "pseudoscience," however, is a much-debated issue among scientists, historians, philosophers and sociologists of science. One set of characteristics of pseudoscience put forward a few year ago included the proponents' usual isolation from the scientific community, their vigorous resistance to criticism, exaggerated claims about their revolutionary findings, the invocation of supernatural processes and inability (at the time, anyway) for their claims to be tested and, specifically, to be falsified. Yet by these criteria, a number of admitted scientific claims such as Einstein's theory of relativity (for example his claim that light rays can be bent by a gravitational field and the interconversion of matter and energy) could have been rejected as pseudoscience when they were first published. Furthermore, the process can go in reverse: practices that in earlier times were considered legitimate sciences such as alchemy and astrology in the sixteenth and seventeenth centuries were later cast into the dustbin of pseudoscience. The fact that astrology has failed consistently to show any statistically significant predictive accuracy over what would be expected by chance alone, relegates it to the realm of a relatively harmless pseudoscience. In the next section, however, we will deal with a series of claims, known as "Scientific Creationism" and "Intelligent Design", that are today considered pseudo sciences by members of the scientific community in particular, yet have been able to wield considerable political power, especially in the area of public educational policy.

5.6.1 "Scientific" Creationism

In August, 1999, the State of Kansas Board of Education voted to remove the requirement that evolution be taught in biology classes in the public school curriculum. References to the concept of evolution of new species from older forms (macroevolution) were to be eliminated from textbooks and classroom discussions. They also voted to remove from the curriculum the currently accepted "big bang" theory concerning the origin of the visible universe. This vote occurred despite letters from the presidents of the State's six public universities warning the Board that the new standards would "set Kansas back a century and give hard-to-find science teachers no choice but to pursue other career fields or assignments outside of Kansas." Only a June, 2000 public vote (which threw out two of the three "Creationists" on the Kansas State Board of Education) appears to have reversed matters in terms of educational policy in that State.

Yet what happened in Kansas has happened in many other places in the United States. Attempts to either have Creationism taught as a scientifically acceptable alternative hypothesis to evolution in high school biology classrooms or to eliminate evolutionary theory altogether have taken legal form in Tennessee (1925, 1973), Minnesota (1978), Louisiana (1981), and Arkansas (1981). Although most of these measures either failed to pass in the state legislatures or were immediately challenged and found to be unconstitutional, the reccurrence of such efforts clearly represent the deep-seated anxiety that, historically, such paradigm shifts have often elicited: as Thomas Kuhn emphasized, even within science, such shifts do not come about easily. Where emotionally-loaded religious views are concerned, the changes become especially volatile and contentious.

Some Historical Background

The vote of the State of Kansas Board of Education is a modern-day example of an intellectual conflict between science and religion that has been going on for over 500 years. In the modern era it had its beginnings with the publication in 1543 of the book, *De revolutionibus orbium celestium* (L. "On the Revolution of the Heavenly Bodies") by Nikolas Copernicus' (1453–1543), throughout most of his life a Canon of the Catholic Church in Poland. In this work, Copernicus rejected the old astronomical paradigm of an Earth-centered universe, claiming instead that the sun was at the center, with earth and the other planets orbiting about it. The struggle of the Copernican system for acceptance, especially the confrontation between Galileo Galilei (1564–1642) and the Roman Catholic Church in the early seventeenth century over advocacy of the new system, is well known and has been described in a number of sources (see the reading list at the end of this Chapter).

A similar version of that confrontation occurred in the nineteenth and twentieth centuries over evolution. Although the details are no doubt somewhat apochrophyl, the first volley in the battle came at the annual meeting of the British Association for the Advancement of Science in Oxford, England, in 1860 (the year after publication of Darwin's *On the Origin of*). At that meeting, the Reverend Samuel Wilberforce (1805–1873), Bishop of Oxford and an accomplished naturalist in his own right, ridiculed Darwin's theory by asking Thomas Henry Huxley (1825–1895), a young naturalist and Darwin supporter, whether he was descended from an ape on his grandmother's or grandfather's side! Huxley, who had only been persuaded to attend the meeting at the last minute, is said to have replied that he would rather be descended from an ape than from a "man of high position" who used his talents to such poor effect. From this point onward, the "warfare between science and religion" (to use Huxley's phrase) focused on the theory of evolution, especially human evolution. The debate continues today with great intensity, although almost entirely in the United States. The current form of the controversy centers on the issue of evolution *versus* Creationism, and the arena has been the public school curriculum.

Creationism: What Is It?

Creationism is the belief of fundamentalist Christians, primarily but not exclusively Protestants, that the description of the creation of the Earth and all life upon it occurred in six days, precisely as described in the book of Genesis. Estimates of how long ago this event occurred tends to vary from one group of Creationists to another. Some support the calculation based on the ages of the prophets listed in the Old Testament. Using this method, Archbishop James Ussher (1581–1656), claimed that these fateful six days occurred 4004 years BCE. Others seem willing to accept a considerably older Earth without life on it, but hold steadfast to the belief that the six days of creation can be no longer than 6000 years ago. Still others now seem willing to accept a figure as high as 25,000 years. The precise number does not really matter, since all fall so far short of geologists' current estimates of the earth's age (current estimates place the earth at least 4.5 billion years old) that they are not even comparable. As for living organisms, Creationists maintain that God created each species as separate and distinct groups and, while they are now willing to grant that some variations may be produced *within* species, as in selective breeding (microevolution), they steadfastly deny that new species may emerge from older species over time (macroevolution). Thus, it is the concept of the evolution of species from previously-existing species that is the main focus of their attack.

The vote of the Kansas State Board of Education described at the start of this section marks a return to a policy, once widespread in the United States, of trying to probit the teaching of Darwin's theory of evolution in public schools. In a famous

1925 trial in Dayton, Tennessee, science teacher John Scopes (1900–1970) was accused of violating a state law designed to enforce this prohibition. In a face-to-face contest between science and religion the famous Chicago lawyer Clarence Darrow (1857–1938), argued for the defense, and fundamentalist, two-time U.S. Presidential candidate William Jennings Bryan (1860–1925), argued for the prosecution. The trial received massive publicity, becoming the first ever to be broadcast nationally by radio. The result, as reported by the press, was that Darrow, who, as the trial revealed, knew as much or more about the Bible than Bryan, "made a monkey of the man." Scopes was convicted—his guilt in teaching evolution was never denied—but fined only a token $100 (which was never paid). The courtroom confrontation between Darrow and Bryan, which was later the subject of a Broadway play (*Inherit the Wind*) and at least four films, would forever be known as "the monkey trial."

Educational change was slow in coming, however. In fact, the net effect of the Scopes trial was that evolution, which had previously been included in high school biology texts, was gradually dropped by all major publishers after 1925. This omission continued through the early 1960s, when massive increases in the amount of federal aid to education was aimed at raising the level of science literacy in the United States. As a result, evolution gradually assumed a central role in modern biology education. The Tennessee law under which John Scopes had been convicted was finally repealed in 1965.

Before the Scopes trial and even after, Creationism was simply seen from within and without for what it was: a religious view held by many groups, particularly Christian fundamentalists, in the United States. However, in the post-World War II period, the reintroduction of evolution into school curricula (if not textbooks) led dedicated proponents of Creationism to change their tactics. On April 30, 1953, Senate Bill 394 became law in the State of Tennessee. Unlike the earlier Tennessee bill, this law did not prohibit the teaching of evolution, but did require that "Scientific Creationism" be presented in the biology classroom as an alternative scientific hypothesis to the Darwinian view. Similar legislation was considered in several other states. In 1980, a law resembling that of Tennessee and mandating the teaching of "creation science" (also referred to as "Scientific Creationism") was passed as Act 590 in the Arkansas state legislature.

"Scientific" Creationism versus Evolution

On the surface, the idea of teaching "scientific" Creationism side-by-side with the teaching of evolution seems like an acceptable compromise, if only in the spirit of "fair play" for opposing viewpoints. Unfortunately, doing so presents several problems. The first of these is the most important with respect to understanding science as a "process." Creationists present no testable paradigm of their own. Their tactic has changed from overt support of Biblical creation to trying to be "scientific" by criticizing the evidence on which modern evolutionary theory is based.

There is absolutely nothing wrong with criticizing an existing paradigm, of course. Scientists criticize each others ideas all the time; this is an essential part of the scientific endeavor. However, in making such criticisms two points are important. First, it is necessary to understand the nature of the problem, whether it is a theoretical concept or a methodological practice. Second, the most useful criticism has to be matched by an alternative hypothesis for the phenomena in question. Moreover, the alternative hypothesis must be *testable*, as we have emphasized throughout this book. In criticizing evolutionary theory, Creationists have targeted what they see as both conceptual and methodological problems with the Darwinian paradigm, without presenting a testable alternative.

One of the primary targets of the Creationists has been the existence of gaps in the fossil record between earlier forms of species and their descendants. Since it takes a rare combination of environmental factors for fossils to form (to say nothing of being able to find them!), one would *expect* the fossil record to be incomplete. Furthermore, some organisms are better candidates than others for fossilization: for example, animals possessing skeletons in contrast to those, such as jellyfish, which do not. Despite these problems, however, the existence of transitional forms between groups of animals and plants is far more complete than Creationists like to admit (Fig. 5.9). As Eugenie Scott, Executive Director of the National Center for Science Education has put it, "there are [many] transitional fossils … the problem is [antievolutionists] will never tell you what they would accept as a transitional form." No matter how many are discovered, it will never enough to satisfy the Creationists, who can always point to whatever gaps may remain.

Yet another point that Creationists often raised against evolution is that living organisms, including humans, are far too complex to have evolved by chance. Consider, for example, the following typical examples from a Creationist publication:

> … will the [chemical] elements of the earth, left to themselves, ever produce an automobile, or even a simple gear? To the contrary, the elements remain as they are. [From a contemporary volume published by the Watchtower Bible and Tract Society, Brooklyn, NY: International Student Association, no date.]

Again, quoting from the same Creationist source:

> Take a large barrel and put into it bits of steel, glass, rubber and other materials. Turn this barrel thousands of times and open it. Would you ever find that the materials by themselves had produced a complete automobile?

The answer to both questions is obvious: of course the elements or pieces of a car would not come together automatically, nor would any biologist claim otherwise. However, according to the Darwinian paradigm, simple molecular components or "pieces" of the organism also do not come ready-made, but rather have evolved together in combinations of various complexity over long periods of time. Little by little, as these organic complexes became able to replicate themselves, they may be shaped, in conjunction with one another, by natural selection. Indeed, it is the action of natural selection that keeps evolution from being a strictly chance or random affair (though the mechanism of most genetic change, mutations, *is* a random matter). By arguing as they have in the passages quoted above, creationists are using the tactic of setting up a straw man argument, one that serves only to demonstrate their own complete lack of understanding of the evolutionary process, to say nothing of the scientific process itself.

As noted earlier, creationists admit that change may occur *within* species, but maintain that selection has never produced divergence of two or more new species from a common ancestral species. They note that the many varieties of dogs, the result of selection by humans over hundreds of years, are still the same species and able to interbreed. Because, in nature, the evolution of most species has required long periods time, far longer than any age of the earth accepted by most creationists, this would seem to be a difficult objection for biologists to counter. Yet, in the early 1980s biologist Jeffrey Powell at Yale University produced genetically isolated populations of fruit flies in the laboratory by selecting two different lines and keeping them apart for multiple generations (14 months at 1–2 generations/month). These experiments demonstrated clearly that reproductive barriers, one of the defining characteristics of a difference between two species, can develop from a common ancestor in a relatively short period of time.

Another object of attack by creationists are the methods used by geologists and paleontologists to estimate the age of the Earth as well as that of fossils and the geologic strata in which they are found. Creationists point to the fact that the estimates of the earth's age have changed radically in the last century, from somewhere around 300 million years in Darwin's day to about 4.5 billion years at present. With such constant changes in the figures quoted, creationists argue that the methods of estimating the age of the earth or fossils are so faulty as to be unusable. Here, however, they *totally* miss a main aspect of the nature of scientific investigation: to continue to obtain more precise data and evaluate new ideas. The revision of data bases and resulting concepts marks a strength of modern science, not a weakness.

Creationists also claim that because different radioactive isotopes (Carbon-14, Uranium-238, etc.) give different readings from the same rock sources or fossils, the methods are unreliable and therefore cannot be used to make any meaningful estimate of the Earth's age. As advocates of a "young Earth" theory, creationists have a stake in discounting dating methods that emphasize the vast age of the planet. Their argument is based on a misunderstanding of the technology of radioactive dating. It is true that results sometimes vary, since fossils or rock samples may contain secondary isotope deposits (perhaps washed onto the sample after it was exposed to the air in its initial setting) and some samples contain only small amounts of isotopes, introducing the possibility of measurement error. However, geologists are able to check one radioactive dating method against another and against an independent method such as geomagnetic data (comparing the orientation of metal particles in a sample to known orientations of the Earth's magnetic field at different periods of geological history). Such comparisons show a high degree of agreement between age estimates using these different methods.

Creationists claim that another weakness of evolutionary theory is apparent in the disagreements that often surface among biologists about specific issues, such as the rate of evolution, or the importance of small or large mutations in creating the variation on which natural selection acts. For much of the first half of the twentieth century most evolutionary biologists agreed that the evolutionary process was slow and constant, leading to gradual change over time. In the early 1970s, however, evolutionary biologists Stephen Jay Gould (1940–2002) and Nils Eldredge (b. 1943) suggested from both genetic and paleontological data that species may evolve by alternating periods of rapid evolutionary change followed by longer periods of stasis, during which there was little or no significant change. This theory, often referred to as "punctuated equilibrium," was hotly debated from its inception (1972) until the mid-1990s, at which point it became regarded as a more accurate way to understand many long-term developments in the fossil record. Creationists, however, jumped on the issue and claimed immediately that such debates showed the incoherence and weakness of the Darwinian paradigm. In fact, as with the age of the Earth disputes, it shows that one of the greatest strengths of science is that it fosters questioning of even the most established ideas and brings them up for scrutiny. The debates on punctuated equilibrium helped clarify many questions about evolutionary mechanisms and rates of change that otherwise may not have come to light.

Creationism as a Science

Because creationists have attempted to claim that creation theory is a science, it will be worthwhile to examine how it measures up to other sciences in this regard. Keep in mind that to qualify as a scientific hypothesis there must be some way to test predictions deriving from that hypothesis.

One problem in examining the creation hypothesis is that of deciding which of the creation stories described in the book of Genesis represents the proper creationist view to test. For example, Chap. 1 of Genesis states that after creating all the other forms of life, God creates both Adam and Eve simultaneously: "Male and female created he them." Chapter 2, however, describes a quite different order of events. In this version, the creation of "every beast of the field and fowl of the air" occurs *after* Adam. Later, God is described as putting Adam into a "deep sleep," during which Eve is formed out of one of his ribs. This second creation myth has given rise to the mistaken belief, once held by many fundamentalist Christians, that human males have one less rib than females. Religious and ancient history scholars have noted that both of these stories have different origins and are variations of far older creation myths to be found in ancient Babylonian and Egyptian mythology. Since the Hebrew Bible relates in Exodus how the Israelites lived for many generations in ancient Egypt, it is hardly surprising that they would incorporate variations of Egyptian mythology into their own creation stories.

However, let us take just the first story of creation appearing in the book of Genesis and test it as if it were a scientific hypothesis. Doing so is not completely a lost cause for creationism; in fact, this "Genesis I" hypothesis may be said to generate predictions just as accurate as those of evolution by natural selection. For example, the order in which God creates the various species in the hypothesized six days of creation is a rough approximation of the order in which the fossil record shows them appearing in the evolutionary scheme of things (though the whale, a mammal, is listed with fish, a common and quite understandable error during the time the book of Genesis was written). The anatomical similarities between humans and our closest relatives, the great apes, as well as those between other groups of similar species, may be said to be equally well predicted by both the evolutionary and creationist hypotheses. The latter accounts for these similarities on the seemingly reasonable grounds that God used similar plans in making the various kinds of organisms in close succession. Yet this is a purely ad hoc hypothesis, that is, one that is added onto an original hypothesis to explain what the original hypothesis still does not account for.

There is yet another contradiction that creationists encounter if they try to claim their hypothesis is "scientific." If creationism is a science worthy of being taught in a science classroom, it must be willing to play by the rules of science. One of these rules is that hypotheses in one field of science must, as far as possible, align with well-established hypotheses in other fields of science. In the case of creationism, the conflict comes with physics and geology and estimates of the age of the earth. Staunch creationists have wedded their hypothesis to a young earth theory, presumably to keep it in close agreement with literal interpretation of Scripture. But as we have noted, when creationists deny the validity of contemporary evolutionary theory, they are also denying the validity of geology, physics and chemistry as well. This places the creation hypothesis in a very awkward position when it claims to be "scientific."

As we stressed in Chap. 2, science tests its hypotheses by attempting to disprove them, either by designing experiments or making further observations. This being the case, would it be possible for evidence to be presented that would reject the evolutionary hypothesis, thereby forcing biologists to look elsewhere for an explanation for the origin of species? Absolutely. Conversely, would it be possible to produce evidence that rejects predictions by the creationist hypothesis? The answer is "No." Since creationists rely on creation of species by an omniscient being, a supernatural power, which by definition cannot be investigated by rational means, there is no evidence, no prediction, that can falsify their claims. In trying to be scientific by falsifying the evolutionary hypothesis, they reveal their inconsistency in not being able to apply the same criterion to their own hypothesis.

Writing a review criticising a quite different sort of hypothesis (one dealing with a supposed genetic basis for the existence of rape!), Dr. Jerry A. Coyne, of the Department of Ecology and Evolution at the University of Chicago, notes that such theses lack

> … the defining property of any scientific theory—the property of falsifiability, the ability to be disproven by some conceivable observation. An unfalsifiable theory is not a scientific theory. It is a tautology, *an article of faith.* [italics added; *New Republic,* April 3, 2000, p. 29.]

In stating to the Kansas State Board of Education that "The Bible is the sole authority on creation" the creationists nicely confirm Coyne's words. Creationism is based on an article of faith that is not questioned. It is not only not a scientific hypothesis, it is not a hypothesis of any sort. Recall from Chap. 1 of this book that hypotheses are always proceeded by he conditions "*If*", meaning they are tentative suppositions, not dogmatic declarations. Creationists rarely, if ever, state the creation process as an "*If*" clause. It therefore remains immune to scientific analysis. Most certainly Judeo-Christian, as well as other accounts of creation might be taught in the schools in history, philosophy or comparative religion classes. But they should be presented as religious teachings and *not* as science in a biology class.

In their comments to the Kansas State Board of Education, it is interesting to note that creationists themselves made the case for the unscientific nature of creationism by stating that evolution and morality were incompatible. Science, of course, does not and, indeed, by its very nature *cannot* make moral pronouncements. As the late Cornell University biologist William Keeton (1933–1980) and his Princeton University colleague James Gould (b. 1945) put it:

> … science … cannot make value judgments: it cannot say, for example, that a painting or a sunset is beautiful. And science cannot make moral judgments: it cannot say that war is immoral. It cannot even say that a river should not be polluted. Science can, however, analyze responses to a painting; it can analyze the biological, social, and cultural implications of war; and it can demonstrate the consequences of pollution. It can, in short, try to predict what people will consider beautiful or moral, and it can provide them with information that may help them make value judgments about war or pollution. But the act of making judgments itself is not science. [William T. Keeton and James Gould. *Biological Science.* New York: Norton, 4th. ed., 1986.]

By proclaiming evolutionary theory and morality to be incompatible, creationists once again demonstrate a total misunderstanding of science and its limitations. In the late 1990s some creationists have even blamed the teaching of evolution for a perceived decline in moral values, citing the tragic 1999 shooting at Columbine High School in Littleton, Colorado or other similar, and more recent tragedies. Because creationists view the theory of evolution as contradicting their version of Biblical "Truth," and since the Bible is their authority on both "Truth" and morality, they therefore view the teaching of evolutionary theory in public schools as threatening "traditional values." In this argument, they seem to forget that both ethics and moral questions have been discussed and debated by philosophers for thousands of years in a completely secular context. There is no necessary connection between moral and ethical principles and any particular religious teaching.

There is, however, another view that suggests precisely the reverse: that creationist views are actually a hindrance to a moral view of humanity and its proper relationship to the natural world. Ecologist Paul R. Ehrlich (b. 1932), Professor of Biology *emeritus* at Stanford University, expressed this view in 1995 when he wrote:

> Evolution is a necessary background for understanding anything about the real world, because our perceptual systems evolved. It is the way I make sense of biology at any level, and it surely is a critical background for any ecologist. I believe the current ascendancy of creationism among the public in the United States (and, interestingly, *just* in the United States among western countries), is an important factor in worsening the human predicament. The decline in the teaching of evolution in schools cuts most Americans off from knowledge about their origins and the origins of the ecosystems in which they operate, and

> generally encourages a feeling of human exceptionalism. It has contributed to the misuse of both antibiotics[5] and pesticides, resulting in the deaths of tens of thousands of human beings and increasing the odds of much more extensive disasters. Creationists are not, as many seem to believe, harmless—they help make the world a more dangerous place. [*A World of Wounds: Ecologists and the Human Dilemma,* 1995, in, *Excellence in Ecology*, #8, Ecology Institute, D-21385, Oldendorf/Luhe, Germany.]

It is often said that creationists simply do not understand evolution. As we have seen, this is certainly correct in terms of understanding the nature of its strong scientific underpinnings. Yet, as in the case of the Church with Galileo in the seventeenth. century, creationists *do* understand the philosophical implications of evolution in terms of its view of the proper place of humankind within nature. The Church-approved seventeenth century view of humankind in the universe was a limited, self-centered one that placed ourselves at this center, as the culmination of creation. Being a human organization, the Church used the power derived from its close union with the State to lash out at those like Galileo who dared to burst this illusionary bubble. It was a similar human arrogance that was challenged once again by Charles Darwin. In this case, however, the paradigm shift moved humankind not just from the center of the universe but to being only one small part of the living world; in Paul Ehrlich's words, it overthrew the concept of "human exceptionalism." As paleontologist Stephen Jay Gould put it, Darwin's work suggested that humans were merely "a fortuitous cosmic afterthought, a tiny twig on the enormously arborescent bush of life," rather than a species especially created and favored "in the image of God." It is perhaps not surprising, therefore, that Darwin's paradigm, like that of Copernicus Galileo and Newton, unleashed a new storm of religious protest. In the case of Copernicus and Galileo, it became increasingly evident that science was right, the Church wrong, and Christian theology has gradually adjusted to this new view. In the case of Darwin and the theory of evolution by natural selection, we live in an age analogous to that which followed Galileo, in that there are still those, like the creationists, who wish to turn the theological clock backward rather than forward. Failing to convince the general population, like the medieval Church they turn to using the power of the State (e.g., and its public education apparatus) to force their views upon society at large.

Although creationists may understand evolution and its philosophical limitations, they very distinctly do *not* understand the nature of science from either a philosophical or practical standpoint. As we noted earlier, it is not only biology but, in fact, the intellectual foundation of all the other sciences that is threatened by creationism. The October 1999 issue of the popular scientific magazine, *Geotimes*,

[5]Populations of infectious organisms include mutant forms which possess immunity to antibiotics and, when exposed, are therefore selected for survival over the non-mutant forms. Pharmaceutical research laboratories are therefore constantly having to produce new variations and/or combinations of antibiotics to which the new forms may not be immune. Ironically, even the most ardent Creationist (doubtless including even congressman DeLay!), when ill, will not hesitate to take advantage of antibiotics developed in response to resistant forms of infectious organisms that developed this resistance by the very processes—mutation and natural selection—which direct evolution!.

was devoted to the Kansas School Board matter. In a series of articles appearing in this issue, several geologists and science educators reacted to the Board's decision. Linda Selvig, president of the National Earth and Space Science Teachers Association, expressed her view that:

> The proponents of removing evolution from the science classroom indicate that, because evolution is only a "theory" it holds no validity. Where they are wrong is that in the scientific community the term "theory" does *not* mean a "guess or hunch." Scientific theories are based upon a preponderance of evidence. The unique aspect of a scientific theory is that as new evidence emerges theories are modified or discarded. It is through knowledge of evolution and this questioning and process of self correction, for example, that we are able to openly discuss and understand the possibility of life on early Mars. Science is still looking for the "evidence for," not "proof of." [*Geotimes,* 44 (October, 1999): p. 21]

One could hardly find a better statement pinpointing the precise manner in which creationists fail to comprehend the intellectual process of science. They seem not to understand that someday a scientist might well come up with a better paradigm than Darwinian natural selection for the driving force behind evolution or, for that matter, one to replace the concept of evolution itself. Instead, Creationist literature has portrayed evolution as a godless theory dreamed up by atheistic scientists in order to lead students away from religion. During "The Cold War" between the United States and the former Soviet Union, creationist literature described evolutionary theory as a Communist plot designed to accomplish precisely this end!

In fairness to religion, it should be pointed out that creationism represents an anti-intellectual phenomenon that is limited largely to the continental United States, though versions of it are currently being exported to other countries around the world. Even here, few if any modern-day Christian theologians find any difficulty in accepting evolution. Testimony in 1982 against the Arkansas law requiring the teaching of "creation science" was led by both scientists *and* Christian theologians. In fact, many Christian scholars seem embarrassed by the various creationist movements. In the same issue of *Geotimes* cited previously the Reverend James W. Shehan, S.J., Professor of Geology and Geophysics at Boston College, referred to the Kansas School Board Creationist vote as a "strategy of 'dumbing down' science teaching, not to mention beliefs fundamental to the Jewish and Christian religions." Nor is any conflict between evolution and religion to be found in Judaic theology, possibly because of its long tradition of respect for the intellectual process. This last point is especially significant since, as noted, the Biblical passages cited by creationists as relating the "true" story of creation are found in Genesis, the first book of the Old Testament, the Hebrew Bible. Finally, it should also be noted that Eastern religions, many far older than Christianity, express a viewpoint of humankind and its relationship with nature that is not only not in conflict with modern science but instead reasonably compatible with it. This is quite likely because, as Tibet's Dalai Lama stated in 1997: "If scientific research proved certain Buddhism teachings to be incorrect, I would agree that the teachings should be changed accordingly." Had similar attitudes prevailed earlier, the humiliation suffered by the both the Roman Catholic and fundamentalist Protestant Churches in the cases of Galileo and Darwin, might well have been avoided.

The Struggle Continues: The Rise of the "Intelligent Design" Movement, 1995-Present

Even though none of the attempted passage of state laws prohibiting the teaching of evolution or requiring the simultaneous teaching of "Scientific Creationism" in public school classrooms have stood the legal challenges mounted against them, new attacks on the Darwinian paradigm have emerged since the mid-1990s in the form of a view known as "Intelligent Design" (ID). Intelligent Design has been defined by its supporters as the theory that "certain features of the universe and of living things are best explained by an intelligent cause, not an undirected process such as natural selection." Having learned from the earlier creationist movements to avoid appearing to promote a religious argument, ID supporters have reverted to the eighteenth-century "Natural Theology" of the Reverend William Paley (1743–1806), as put forth in his book *Natural Theology: or, Evidences of the Existence and Attributes of the Deity*. Paley introduced what is known as the "argument from design," the idea that the many marvelous adaptations we see in nature are evidence of the existence of God as the great and omniscient designer.

Paley's example has resonated with readers for two centuries. He argued that if a person was walking across a field he [or she] might find a rock and recognize that, in its simplicity, it arose from natural causes. However, if one found a watch lying in the field, its functional complexity would indicate it must have been designed, and thus the work of a designer. For Paley, that designer was God, and the study of nature was one important way to understand the mind of the Creator. Today's Intelligent Design advocates do not make the argument so explicitly, and never mention God. But their claim amounts to the same thing. Pointing to adaptations like the vertebrate eye or the flagellar apparatus in bacteria (an elaborate molecular assembly that helps certain bacteria move about and one of the "Intelligent Design" proponents' favorite examples), they argue that such intricate structures are evidence of an "intelligent" design process that cannot be accounted for by natural selection acting on chance variations. When questioned, advocates of intelligent design claim they do not invoke God or any traditional theological processes. They simply claim that in some way an element of "design" has to be involved in the origin of the many adaptations observed in nature. They try to make the argument sound like a rational alternative to the elements of chance that are a part of the Darwinian paradigm.

There is no question that there are myriads of remarkable adaptations in nature, both anatomical and physiological. Not only the vertebrate eye, but the close fit between insect mouth parts and the shape of the flowers on which they feed, the talons of the eagle or hawk for catching and holding their prey, the intricate spinning of the spider's web and many other examples, clearly show how organisms are marvelously adapted to their ecological niches and their place in nature. However, Intelligent Design as an alternative to the Darwinian paradigm, faces the same philosophical problems as "Scientific Creationism" before it. "Design" and "Designer" are purposefully left as extremely vague concepts, and, like "Scientific Creationism" are equally untestable. Despite these major limitations, beginning in the 1990s Intelligent Design advocates tried to get the concept introduced into high school biology classes as a viable scientific alternative to Darwinian natural selection.

Perhaps the most important legal test case for introducing Intelligent Design in high school biology classes occurred in the small town of Dover, Pennsylvania in 2004–2005. At the time, several politically powerful members of the community along with sympathetic members of the Board of the Dover Area School District, teamed up to write and then vote to include a statement that would require teaching "Intelligent Design" as an alternative to evolution by natural selection in the high school biology curriculum. Originally, the proponents of Intelligent Design had wanted Creationism taught in the schools. However, the earlier legal outcomes in states such as Kansas, where Creationism had been found to be unconstitutional, forced them to turn to the design argument instead. Advocates argued that Intelligent Design, unlike the clearly theologically-based "Scientific Creationism," was a *scientific,* rather than a religious view, and one that would account equally well, or perhaps better, for the existence of adaptations in nature. The wording of the proposal couched the requirement to teach ID along with evolution as a means of teaching critical thinking, and of encouraging students to keep an "open mind." The statement also subtly noted that Darwin's theory was "only a theory" and therefore always being revised. In this manner of argument, they claimed that ID was also a theory deserving equal consideration.

In response, a group of parents challenged the Board's ruling and brought the case to court (as *Kitzmiller v Dover Area School District*) in late 2005. To defend the School Board's position, lawyers for the defense argued that the lack of any theological language in ID statements or in their literature indicated it was not a religious view and therefore could be taught legitimately in science classes. Lawyers for the plaintiffs (the parents), however, were able to produce in court the revised manuscript of a creationist high school biology textbook (*Of Pandas and People*) originally published in 1989. They pointed out that in the revised manuscript wherever the word "creationism" appeared in the original text, the words "intelligent design" had been inserted in its place! This blatant bit of dishonesty appears to have exposed the intellectual level (to say nothing of the lack of integrity) of the Intelligent Design advocates. As a result of this court case, U.S. District Judge John E. Jones III ruled that Intelligent Design is *not* science, that it "cannot uncouple itself from its creationist, and thus religious, antecedents," and that the school district's promotion of it therefore violated the Establishment Clause of the First Amendment to the United States Constitution, establishing the separation of church and state. Since Dover, the controversy, at least in terms of the appearance of other such Court cases, seems to have been settled at least for the time being. The comment of a Professor of Biology at Brown University, a devout Christian, to the effect that "A Creator who created millions of species, 99.9 % of which became extinct, could surely not have been intelligent!" seems an appropriate way to bring closure to the Creationist-ID controversies.

5.7 Science and Religion: An Underlying Difference

One might well ask: Why have conflicts between science and religion, persisted since the rise of modern science in the seventeenth century? Almost certainly it is because, popular press accounts to the contrary, there are major and important differences between the way the fields of science and religion approach our understanding the universe.

There is a story concerning a meeting in the early nineteenth century between Emperor Napoleon I of France and the noted astronomer Pierre Simon de Laplace (1749–1827). Laplace was explaining to Napoleon his hypothetical model of the solar system incorporating the sun and the six then-known planets. The Emperor is alleged to have remarked: “But Monsieur Laplace, I see no mention of God in your model.” Laplace’s reported reply was: “God? I have no *need* of that hypothesis”! The story is probably apocryphal, but it is illustrative of a major historical shift in philosophical thinking since that time. Chemist Gilbert N. Lewis (1875–1946) once noted that scientists “do not aim to seek [the] ultimate but [the] proximate [causes].” Ultimate causes are those that are concerned with “why” questions, while proximate causes are concerned with “what” or “how” questions. Explaining planetary motion or the circulation of the blood as being the result of God’s plan are examples of ultimate causes, whereas explaining the same phenomena by gravitational forces or the beating of the heart, respectively, are examples of proximate causes. Indeed, the rise of modern science in the seventeenth century may be said to have marked quite precisely a philosophical move from focusing on ultimate to proximate causes. This was *not* because of a rejection of a belief in God on the part of early scientists; on the contrary, many, if not most, were religious to one degree or another. Sir Isaac Newton (1642–1787), for example, saw the study of proximate causes as leading to revelations about the most ultimate of all causes, the mind of God. In brief, then, the rise of modern science marked a shift toward leaving the determination of ultimate causes to philosophers and theologians and concentrating instead on those proximate causes open to scientific investigation.

The continued conflict between science and religion does rest on major philosophical differences between the two systems of thought. At various points in time these systems may achieve a peaceful coexistence, but only by ignoring their inherent differences. As we saw in Chap. 2, science is based on philosophical materialism, the view that all phenomena in the universe are the result of matter in motion, that is, the interaction of material entities in conjunction with known and measurable forms of energy (mechanical, chemical, electrical, etc.). As a philosophy, materialism admits no unknowable forces, no theoretically unmeasurable forms of energy, and no mystical or occult causes. Religion, on the other hand, is based on philosophical idealism, a view that stresses the primacy of ideas, non-material entities and abstract causes as significant agents operating in the universe. For example, in dealing with the origin of life itself, philosophical materialists would argue that matter has within its make-up the potential to form complex associations (for example, molecules), that these can form still more complex associations (membranes, cell organelles, etc.), and that the formation of higher level interactions does not need input from some mystical power. The known forces of nature—matter, energy and their interactions—are all that is necessary to understand how life might have originated. Philosophical idealists would argue that something more than mere matter and energy must have been involved in putting together the pieces of even the simplest form of life, whether that is expressed in a secular form as a "vital force" or in a religious form as the "will of God."

On the philosophical level, these are rather different ways of approaching an explanation of events in the world. Thus a quiet truce has been established between science and religion by maintaining that the two approaches deal with different aspects of human experience. As just noted, Newton and others in the seventeenth century solved the dilemma by arguing that science deals with proximate and religion with ultimate causes. For many people, such a truce works in a practical, everyday sense; we may seek guidance and comfort in spiritual matters from literature, art or religion yet still turn to science or medicine to figure out how our bodies work and what is a healthy life style. Many if not most people can accept belief in a higher power in guiding their lives, yet do not step out of a window because they have just prayed for gravity to be suspended. Thus the truce works, though it may often come at the expense of a rigorous philosophical consistency. For many people this appears as not too high a price to pay. It does emphasize, however, the underlying difference in philosophical outlook. This difference can and does surface on occasion, however, when matters such as religious control of public education, legislation concerning abortion rights, embryonic stem cell research or other controversial issues are involved. Under these circumstances it is critical that informed scientific information and a clear understanding of the nature of science as a process, be a central part of such discussions.

5.8 Conclusion

As we have stressed, none of the preceding material concerning creationism and the ascendancy of materialist over idealist views concerning the origin of species should be interpreted as implying that religious views can play no positive role in society. Religion has always been concerned with ethics and values, though as we also noted, it has never been the only route to grappling with these issues. However, when we look to religious leaders, philosophers, or any others claiming expertise in ethical matters, it is imperative that they be scientifically informed about the natural world within which our moral and ethical choices are made. As philosopher Max Otto (1876–1968) noted in 1945:

> The universe is run by natural forces and laws, not by moral laws. However, human societies which live in the natural world must live by moral laws. If those moral laws contradict or ignore the natural laws, it will be the human societies, not the physical universe, which suffer the consequences of such defiance.

There could be no better way to end this book than to underscore the importance Otto's words. It is *precisely* those natural forces and laws with which modern science is concerned and to which, by its very nature, it is limited. Limited as it may be, however, *science remains humankind's most powerful intellectual tool.* As Otto noted, we ignore its findings at our own peril.

5.9 Exercises

1. Distinguish between the "treasure-hunt:" and "social constructionist" views of science. In what ways might you argue that both points of view are involved in understanding the factors influencing how science works?
2. How might social constructionist claims be tested? That is, even if such claims are true, how can those adhering to this view as a way of describing science, test their claims against reality?
3. Political action groups supporting the movement known as "Right to Life" in favor of a Constitutional Amendment outlawing abortion, often use statements in defense of their position such as "Science has proved that life begins at conception." Analyze this statement in terms of the nature of science and its limitations.
4. Sociologist Troy Duster at the University of California, Berkeley, has argued that pre-natal testing for supposed genetic defects in a fetus, with an eye to abortion if the fetus exhibits any such defects, represents a "back door to eugenics." What might he mean by that phrase? Could such testing introduce eugenic practices back into society?
5. As more human clinical diseases become known to have a significant genetic basis, drug companies and Health Management Organizations (HMOs) are requiring pre-natal diagnosis before agreeing to cover a newborn on the parent's medical coverage plan. The HMOs' argument is that genetically determined traits are "prior conditions" and can be excluded on the same grounds that they can exclude someone who applies for a policy after having a heart attack. What are the ethics of such claims, and how should society respond to the accumulation of this sort of new knowledge?
6. How do GMOs differ biologically from plants or animals bred by traditional methods of mating and hybridization? Why do some people fear the former so much more than the latter.
7. Two strains of cattle have been produced that contain special high protein content, one by traditional methods of hybridization among existing breeds, and the other by recombinant DNA technology that imports DNA from a pig into a cow's genome. What might be the biological differences between these two strains of cows and why might that matter, or not matter, in discussions about the development of GMOs?

8. What are the moral and ethical issues surrounding intellectual property rights, especially concerning such necessities of life as food? Should any private individuals be allowed to control the creation and distribution of food? Why or why not?
9. If you were a reporter for a reputable magazine and were interviewing a plant biotechnology company executive who claimed that GMOs were going to solve the problem of hunger in the world, what questions would you want to ask about this claim? What information might you want to find out before writing your article?

Further Reading

Much has been written on all the areas of science and its social interactions as touched upon in this chapter. A few items for further exploration are listed here by chapter sub-headings.

The Social Construction of Science

Dear, P. (1995). Cultural history of science: An overview with reflections. *Science, Technology and Human Values*, 20, 150–170. (A thorough discussion of what it means to try and interpret science in its cultural and social context).

Jones, R. (1989). The historiography of science: Retrospect and future challenge. In M. Shortland & A. Warwick (Eds.), *Teaching the history of science* (pp. 80–99). Oxford: Blackwell. (This is a good review of various methods of interpreting science over the past half century, from the "traditional approach" to social constructionism).

Young, R. (1985). Malthus and the evolutionists: The common context of biological and social theory. In R. Young (Ed.), *Darwin's metaphor: Nature's place in Victorian culture* (pp. 23–55). Cambridge: Cambridge University Press. (A classic essay showing the influence of Victorian social and economic metaphors on Darwin's thinking).

The Social Responsibility of Science

Allen, G. E. (1999). Genetics, eugenics and the medicalization of social behavior: Lessons from the past. *Endeavour, 23*, 10–19. (A discussion of the development of eugenics and its political consequences with special reference to the relationship between the movement in the United States and that in Germany after the rise of power of the National Socialists).

Benedek, T. G., & Erlen, J. (1999). The scientific environment of the Tuskegee study of syphilis, 1920–1960. *Perspectives in Biology and Medicine, 43*(1), 1–23. (A more sympathetic discussion of the Tuskegee study, trying to argue that in the context of its day, the study was neither racist nor unconcerned with the health of its participants).

Galston, A. (1971). Education of a scientific innocent. *Natural History, 80*, 16–22. (Arthur Galston details his unwitting involvement in developing herbicides that wreaked havoc on the ecosystems of Southeast Asia during the Vietnam war).

Jones, J. H. (1981). *Bad blood. The Tuskegee syphilis experiment.* New York: Free Press. (A detailed, well-written popular account of the Tuskegee experiment).

Lombardo, P. A., & Dorr, G. M. (2006). Eugenics, medical education, and the Public Health Service: Another perspective on the Tuskegee syphilis experiment. *Bulletin of the History of Medicine, 80*(2), 2006): 291–316. (Provides a detailed discussion of the three major organizers of the Tuskegee experiment in the early 1930s, and their direct involvement with the then-current eugenics movement).

Paul, D. (1995). *Controlling human heredity.* Atlantic Highland, New Jersey: Humanities Press. (A very readable book that provides a good overview of the whole eugenics movement and its social consequences).

The Ethics of Stem Cell Research

Baker, J. 2013. *Shall we laugh or shall we cry? The abortion issue: Scientific information, religious nonsense, political mayhem*. Amazon, ISBN-13: 978-1479243587. (A broader exploration of the issues surrounding right-to-life issues, including abortion, women's rights and reproductive policies in general).

Maienschein, J. (2003). *Whose view of life? Embryos, cloning and stem cells.* Cambridge, MA: Harvard University Press. (Contains a thorough historical review of embryological approaches to understanding the development of human life, and attempts to determine when life begins, especially from both the biological and theological point of view, ranging from Aristotle to the present day).

Genetically Modified Organisms

Carter, C., Moschini, G.-C., & Sheldon, I. (Eds.). (2011). *Genetically modified food and global welfare*. Vol. 10 of Frontiers of Economics and Globalization Series. Bingley, UK: Emerald Group Publishing. (An edited volume with a wide-ranging collection of articles on both health and safety of GMOs).

External Link: "Everything You Wanted to Know about GM Organisms": http://www.newscientist.com/channel/life/gm-food. A compendium provided by the magazine *New Scientist*.

Finochario, M. A. (2009). That Galileo was imprisoned and tortured for advocating copernicanism. In Numbvers, R. L. (Ed.), *Galileo goes to jail and other myths about science and religion* (Chapter 8: pp. 68–78). Cambridge, MA: Harvard University Press. (An up-to-date assessment and debunking of the traditional portrayal of Galeilo's trial and its aftermath. The same volume also contains reassessments of many other "mths" about science and religion).

Jon Entine, "GMOs, Yes!" (pp. 15–32), and Robert Millstein, "GMOs? Not So Fast." (pp. 33-46). These articles are simply and clearly written and together provide a good forum for discussion. They could easily be used as the basis for debate in classrooms and elsewhere. Can be found on-line at commonreader.wustl.edu.

Kingsbury, N. (2009). *Hybrid: The history and science of plant breeding.* Chicago: University of Chicago Press. (Although this book covers the history of plant breeding over a much longer period of time than the advent of GMOs, it also places recent developments in biotechnology in a useful historical perspective).

Millstein, Roberta. (2016). GMOs? Not so fast. *The Common Reader: A Journal of the Essay*, 1(1), 33–46. (Abrief simple summary of some of the issues, and answers, raised by opponents of GMOs to their widespread distribution).

Losey, John E., Linda S. Rayor and Maureen E. Carter (1999). Transgenic pollen harms monarch larvae. *Nature* 399 (20 May), 214.

Scientific Creationism and the Relations between Science and Religion.

Nelkin, D. (1982). *The creation controversy.* New York: W. W. Norton. (This is a brief but useful summary of the creationist debate especially with respect to the Arkansas law of 1981).

Numbers, R. L. (1992). *The creationists: The evolution of scientific creationism*. Berkeley: University of California Press. (Provides a valuable historical context for the development of various Creationist movements in the United States over the past 150 years. The author places the modern Creationist movement in a long line of evangelical tradition that has taken refuge in Biblical literalism).

Two articles, published back-to-back in *The common reader: A journal of the essay*, Vol. 1 (No. 1, 2016) succinctly summarize the opposing views.

Appendix A: The Analysis and Interpretation of Data

A.1 Introduction

For John Snow's analysis of cholera and more recently for researchers studying AIDS, observational information was critical in coming to conclusions about the causes of diseases and methods of transmission. Testing competing hypotheses requires the use of both observational and experimental data. Yet, a large collection of data is of limited value if it is not arranged in such a way as to reveal possible relationships. For example, Snow's collection of mortality data on cholera in 1849 would not have yielded any significant conclusions had he not organized it by pinpointing the location of each death on a street map of London. This organization of the data enabled him to see that the greatest number of deaths occurred in the vicinity of the Broad Street pump. How investigators choose to collect, organize and display data determines to a large extent what information they think is needed to answer the question at hand, and what conclusions they wish to communicate.

A.2 Collecting Data and the Problem of Sampling Error

Many types of measurements in biology involve sampling small amounts of data from the vast collections potentially available. For instance, from a practical point of view it would be impossible to measure the height of all the individuals in a large city in order to determine the average height of the city's population. Not only would such an undertaking be time-consuming and laborious, it would also be unnecessary, since by choosing a sample of individuals from the population at large an accurate set of data can be collected far more easily.

However, gathering that sample is not without some potential problems. The most important problem is that of bias in the sample. If we sample 100 people from a city of 500,000, that sample must be representative of the population at large if it is to tell us anything meaningful about the population as a whole. If we sampled only people who happened to be basketball players, their average height would

G.E. Allen and J.J.W. Baker, *Scientific Process and Social Issues in Biology Education*, Springer Texts in Education,
DOI 10.1007/978-3-319-44380-5

obviously be considerably different than if we sampled people from a senior center. Thus, the sample would need to take into consideration all sorts of factors that might affect height: sex, age, ethnic background and so forth.

A.3 Seeking Relationships: Collecting and Organizing Data

Data is collected, organized and presented using many methods. Because these methods have to be related to the question being asked, the nature of the phenomenon being studied and the purpose of the investigation in the first place, researchers do not have one formula or set of rules for the process of collecting or organizing data.

A.3.1 Qualitative and Quantitative Data

Data collected directly from observations or experiments is called raw data. In Snow's study, for example, the raw data collected were the number of cholera fatalities as recorded hour-by-hour or day-by-day. Raw data may be collected and/or expressed in two forms: qualitative and quantitative. Qualitative data is that which is expressed in a general, non-numerical form. For example, the statement, "a lot of people died of cholera in London on September 3, 1849" is qualitative data, because it simply conveys the information that many people died. Qualitative data is useful in certain circumstances, but it can be misleading because they are by definition imprecise. For instance, what is "a lot" to some people may be only a few to others.

On the other hand, stating that "58 persons died in London on September 3, 1849" represents quantitative data. Quantitative data are expressed numerically and are therefore more precise. It is also possible for other investigators to test the accuracy of quantitative data more easily than qualitative data. Quantitative data may also be arranged into tables and charts, plotted into graphs and subjected to statistical tests that tell something more about their reliability or reveal relationships not otherwise apparent. Quantitative results from different experiments may also be compared more accurately than can qualitative data. In testing his water-borne hypothesis by comparing differences between the two water companies, for example, it was important for Snow to know how many people came down with cholera after drinking the water supplied by each company. If his results had merely stated that people supplied by Southwark and Vauxhall showed more cases of cholera, it would be difficult to know if the difference were big enough to be significant.

By emphasizing the value of quantitative data, we are not suggesting that qualitative data are of no use in scientific research. For example, Snow found he could tell instantly the company from which each water sample came if he added silver nitrate to the sample, since it produced a milky precipitate, silver chloride, that could be identified immediately. This was a qualitative judgment: The degree of cloudiness between water from the two companies was sufficient to identify from which source the water had come. He could have made the test more quantitative by measuring the exact amount of silver chloride precipitate, but this was not necessary. Simply being able to distinguish the source of the water is all he needed to know to test his hypothesis. Because qualitative data can often be collected more easily and quickly, it plays an important role in scientific research.

A.3.2 Measurement and Precision in Data Collection

Collecting quantitative data obviously involves some type of measurement. In Snow's case, the measurements with which he was dealing were counts of the number of fatalities resulting from cholera *per* 1000 persons. Collecting such data is not as easy as it might seem. Snow had to be sure that the fatalities were due to cholera since, even during the worst of cholera epidemics, people die of other causes. If Snow had failed to separate out all other deaths, his data would have been worthless in determining the cause of cholera or its means of transmission. Attention to the detail of measurement procedures is absolutely necessary if measurements are to be of any value. If data are not obtained reliably in the first place, the most brilliant analysis may produce unreliable or meaningless conclusions. The computer science expression "garbage in, garbage out" applies to all scientific investigation.

A.3.3 Variations in Measurement by Different Observers

No two people see the same event or phenomenon in exactly the same way. Making a measurement always requires some human judgment and can be prone to introducing small amounts of error. For example, in measuring a sample from a population of deer mice for tail length, three different biologists compiled the data shown in Table A.1 (only 10 organisms in the sample are shown here). In no case did all three observers get the exact same measurement on the same organism. Where, for example, does the tail actually start on a mouse? This means that if a team of investigators is working together making measurements, they must establish a clear criterion among themselves for how to make those measurements. Establishing clear criteria increases the reliability of the data. Reliability simply means that the data are consistent and can be repeated by other observers. Reliability is a key feature of scientific data because it means that other investigators can use the data without having to repeat all the measurements themselves.

Table A.1 Measurements of tail length in a sample of deer mice (*Peromyscus*)

Organism number	Observer 1 (mm)	Observer 2 (mm)	Observer 3 (mm)
1	60.5	60.2	60.3
2	61.0	59.9	61.1
3	62.2	62.0	63.0
4	68.1	68.0	67.9
5	60.7	60.6	60.2
6	58.3	58.4	58.5
7	66.6	66.7	66.3
8	56.7	56.6	56.5
9	62.5	62.6	62.5
10	60.8	50.9	60.5

A.4 Seeking Relationships: The Presentation of Data

A first step in the analysis of data is to arrange the data into one of several forms for inspection and display: distribution maps, tables and graphs.

A.4.1 Displaying Data

Distribution Maps. Distribution maps show the localization of the objects, organisms, or events being studied. For Snow, such a map showed the spread of cases of cholera over a given spatial area. Snow's distribution map of the location of households in which cholera fatalities had been reported made it possible for him to reveal clearly that the source of contamination was the Broad Street pump.

Tables. Tables represent another common way of displaying and analyzing data. A table consists of data arranged in two or more columns, enabling one to see how items in one column relate to items in the other(s). For example, in following the course of the 1849 cholera epidemic, which began in late August and ran through mid-September, Snow collected the data shown in Table A.2. These data show clearly the quantitative progression of the epidemic.

One of the characteristics of any set of data such as that shown in Tables A.1 and A.2 is that they exhibit a *range* of values, from the highest to the lowest. For the data in Table A.2, number of deaths during the period August 29 through September run from 1 to 145. The range therefore defines the outer limits of the measurements in any given sample.

Graphs. The data in Table A.2 may be presented graphically as well. Graphs show the relationship between two or more factors arranged along two (or more) axes on each of which is plotted a particular scale of measurements. Figure A.1 shows a bar graph of the data in Table A.2. The horizontal, or *x*-axis, measures an independent variable, a variable not (usually) affected by the other factor or factors

Table A.2 Number of deaths due to Cholera in the Vicinity of Broad Street, South London, 1849

Date	Deaths due to Cholera
August 29	2
30	10
31	58
Sept 1	45
2	120
3	57
4	50
5	35
6	20
7	29
8	15
9	14
10	8
11	8
12	2

under consideration. The independent variable in Fig. A.1 is time expressed in terms of days of the month (which pass with regularity, after all, regardless of whether cholera cases occur or not). The vertical, or y-axis, measures the dependent variable. As its name suggests, dependent variables are dependent on, that is, a function of, independent variables. The number of deaths due to cholera is a

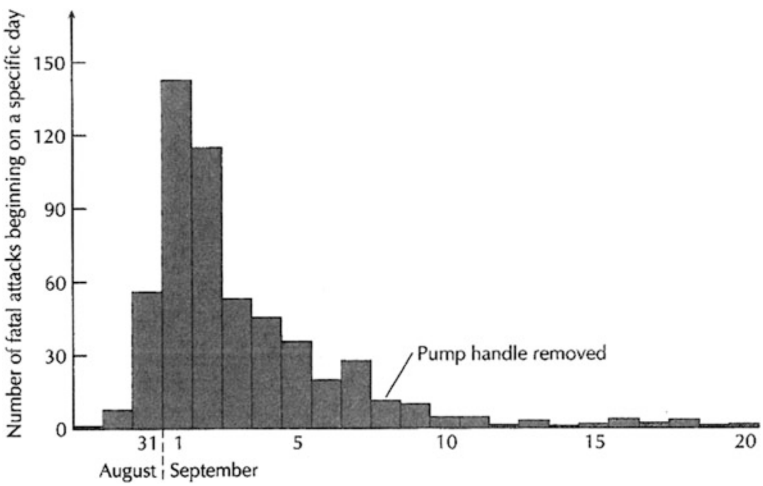

Fig. A.1 Bar graph of data on the number of deaths due to cholera between August 29 and September 20, 1849 [From Snow (1855), summarized in Martin F. Goldstein and Inge F. Goldstein, *How Do We Know? An Exploration of the Scientific Process* (New York, Plenum Press, 1978: p. 40)] dependent variable because it is a function of the time since the infectious agent arrived in the community. The point of intersection of the x- and y-axes is called the origin. The height of the bars in Fig. A.1 illustrates the difference in number of cases from one day to the next. Bar graphs often make a quantitative point far more clearly and often dramatically than a simple presentation of numbers in a table.

In a line graph, points representing the data collected are connected to one another by a line. Figure A.2 shows a line graph for the same data as that in the bar graph in Fig. A.1. Each data point on a line graph relates a value on the *x*-axis to its corresponding value on the *y*-axis. The data points are plotted by finding the *x*-axis

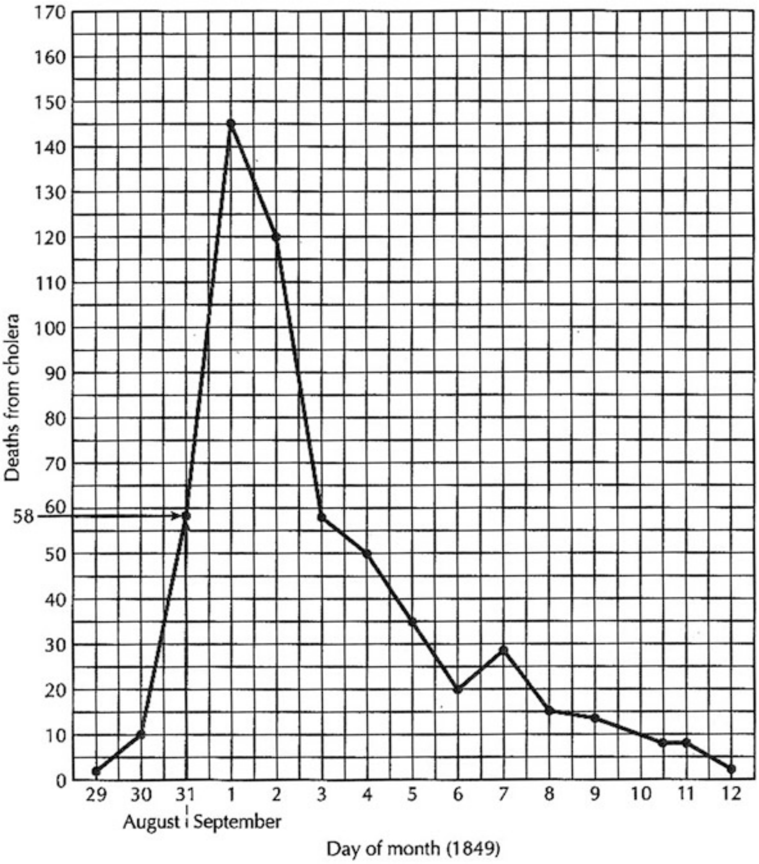

Fig. A.2 Line graph showing the number of deaths that occurred in London due to cholera from August 29 to September 12, 1849 (same data as in Fig. 5.1) [From Snow, 1855, as summarized in Goldstein and Goldstein, Ibid.]

value (in this case, a particular day, for example, August 31), and then moving sufficiently high on the y-axis to find the y-axis value, in this case 58, the number of deaths occurring on that day.

Although both bar and line graphs show the change in death rate from one day to the next, in the bar graph the data for each day stand visibly separate from the others. The line graph, on the other hand, conveys a sense of continuity from one day to the next and thus emphasizes a trend over time. Both forms of presenting graphical material may be equally useful, depending on the phenomenon being studied and the point the investigator most wishes to emphasize.

A.4.2 Scales and Scalar Transformation

It is important to consider the scale on which the axes of graphs are arranged. Snow's data on number of deaths per day during the 1849 epidemic (Fig. A.1) show clearly the daily change because the y-axis on which number of deaths is plotted is laid out in units of 30. If the same scale had been laid out in units of 100 or 500, however, the graph would have looked quite different and shown much less of the magnitude of the day-to-day changes.

The scales on which the data in Fig. A.1 are plotted are arithmetic scales, since both are based on numerically constant increments. Scientists sometimes use a logarithmic scale, in which each unit on the scale represents an increase by multiples, such as a two-fold or ten-fold increase: for example, 2, 4, 8, 16, 32, 64 … , or 1, 10, 100, 1000, 10,000, 100,000. A logarithmic scale is valuable in plotting data with a wide range of values or in which the rate of change in one factor is much greater than in the other: for example, human population growth from pre-historic times to the present, where the numbers range from 1 million to 5.5 billion. Because the numbers with which Snow was dealing ranged over a small scale (0–150 deaths over 15 days), an arithmetic scale was perfectly suitable. Scalar transformations, changing the scale of one or both axes of a graph, either from one arithmetic scale to another or from an arithmetic to a logarithmic scale, are often an important aid to analyzing data. They can also be used to convey very different messages (Fig. A.3).

A.4.3 Interpolation and Extrapolation

Scientists employ two techniques in constructing and interpreting graphs. Interpolation refers to the process of filling in, or generalizing, between two items of data in a table or graph. We employ interpolation whenever we draw a line on a graph connecting two data points. Suppose, for example, that Snow had recorded cholera deaths on an every-other-day basis (Fig. A.4). A solid line connecting data points for August 31 and September 2 would suggest that the

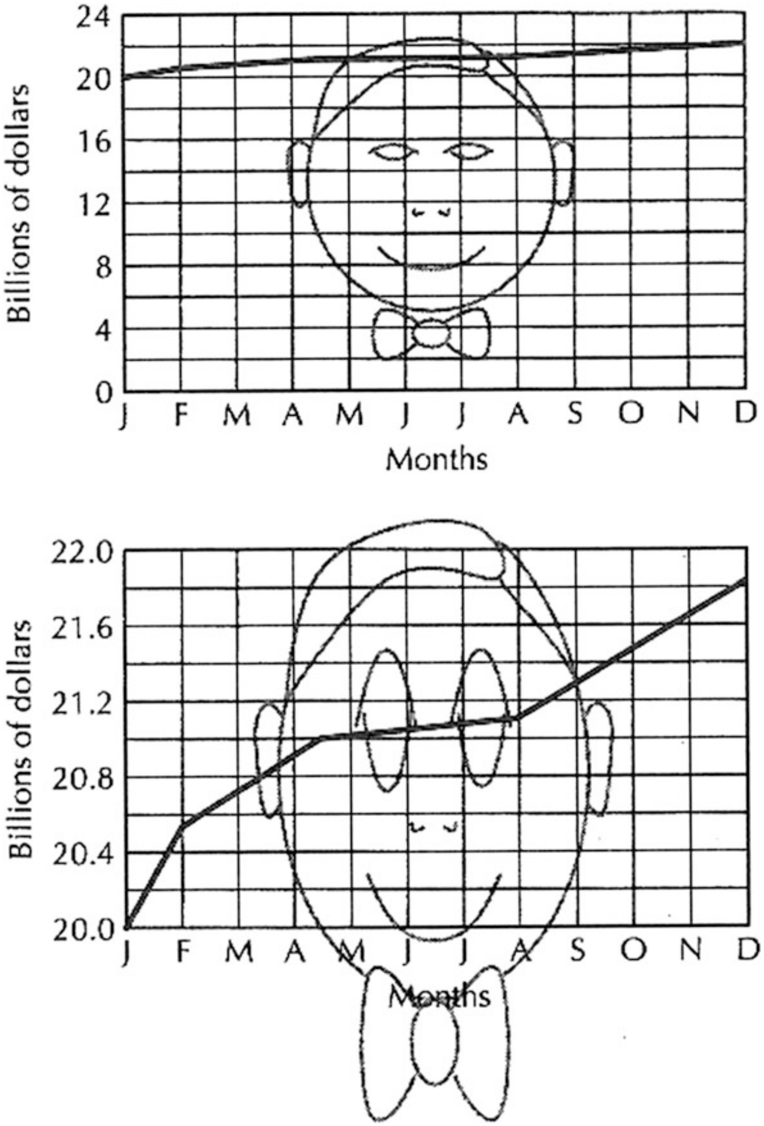

Fig. A.3 It's all in what you want to show: changing scales on a graph may convey quite different messages (Modified from Darrell Hufff, *How to Lie with Statistics*)

number of deaths for September 1 should have been somewhere around 88–90. Thus one function of drawing lines connecting data points on a graph is to interpolate predictions for cases not measured directly.

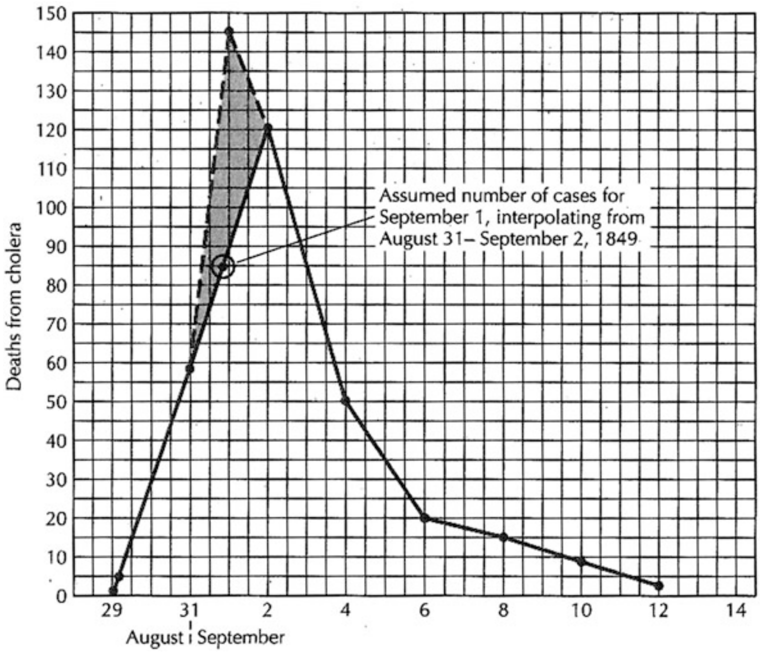

Fig. A.4 Graph showing interpolation of data. Interpolation is an important part of generalizing any set of data, but it has the danger of misrepresentation. If only data on the number of deaths between August 31 and September 2 are taken into account, the interpolated value for September 1 would be 85 deaths. In reality, the number of deaths on that date was 145

Interpolation may not always be accurate, however. Sometimes the discrepancy is trivial; at other times, it may be critical. As the dotted line in Fig. A.4 indicates, if Snow had based his analysis on data gathered every other day, he would have made two errors. First, he would have given the maximum number of deaths as 120 on September 1 rather than the actual 145. This could be a significant difference to public health officials trying to track the course of an epidemic. Second, he would have erroneously dated the peak of the epidemic as occurring on September 2 rather than September 1. This, too, might have been an important difference in later analyses of the time frame within which cholera epidemics develop. The interpolation in Fig. A.4 gives the impression that the epidemic developed more slowly than was actually the case.

Extrapolation involves making predictions beyond the limits of the data available, and is based on trends revealed by the data set at hand. Extrapolation of data in Fig. A.2 or A.4 involves predicting what the number of cholera cases might have been on September 13. The trend from September 6 or 8 to September 12 shows a steady decline. It would thus be reasonable to extrapolate, that on September 13, there might be only one or no deaths. Such an extrapolation would suggest that the epidemic was essentially over by September 13.

A.5 The Analysis and Interpretation of Data

Once a collection of data is organized into a table or plotted onto a graph, it can be more readily analyzed. There are several common statistical approaches that aid in the analysis and interpretation of data.

A.5.1 Correlation

In addition to showing the change of one quantity with respect to another, tables and graphs may also reveal a correlation. A correlation is a relationship between two factors in which one factor changes in some regular, or patterned way with respect to a change in the other. For example, from the map shown in Fig. 3.3, Snow could have plotted a correlation between distance people lived from the Broad Street pump and the number of cases of cholera. Such a plot is given in tabular form in Table A.3 and graphically in Fig. A.5. Inspection of Table A.3 indicates that number of deaths declines with distance from the pump. The exact nature of the decline, that is, the degree of correlation, is not clear from the numbers alone, however. The graph in Fig. A.5 shows the relationship more clearly. The fact that the points of data form a fairly a straight line suggests that the correlation between the two factors is a strong one. In this particular case, the correlation is said to be negative, in that as the numerical values for distance (the independent variable) increase, the numerical values for number of deaths (the dependent variable)

Table A.3 Number of deaths declines with distance from the pump

Distance from Broad Street Pump (in yards)	Deaths due to Cholera Reported (Aug. 29–Sept. 12, 1849)
0–50 yds	130
100–150	100
150–200	80
200–250	55
250–300	45
300–350	30
350–400	15
400–450	1
450–500	0
Total	573

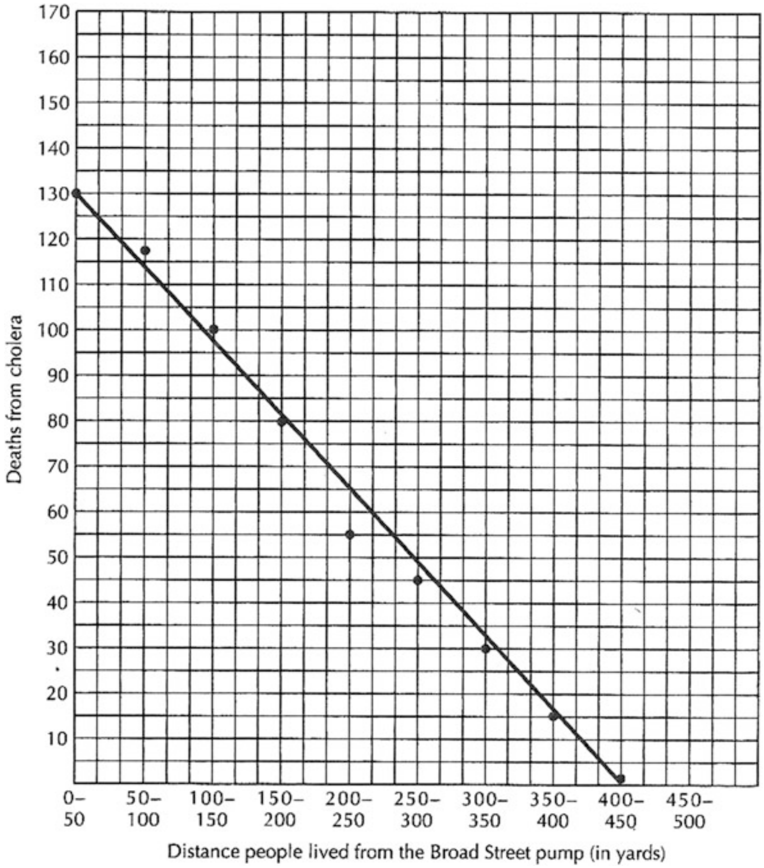

Fig. A.5 Graph showing correlation between distance people lived from the Broad Street pump and deaths due to cholera in 1849. In this case the correlation is said to be a negative one, since as one factor, the independent variable (distance from the pump) increased, the other factor, the dependent variable (deaths from cholera) decreased

decrease. If the number of deaths from cholera had increased as distance from the pump increased, the correlation would be said to be positive. It would also be possible to show the relationship between number of deaths from cholera and distance from the pump as a positive correlation, by plotting *proximity* to the pump (rather than distance from the pump) on the x-axis. The choice of how to display the data would depend completely on what the investigator wanted to emphasize.

The slope of a graph line also tells us the precise quantitative way in which the two factors correlate with one another. When the slope is at a 45° angle, as shown in Fig. A.5, the correlation is said to be 1:1; that is, as one factor increases by a specific unit, the other factor changes by a comparable unit. For example, with every 50-yard increase in distance from the pump, number of deaths decreases by about 15. The lines on a graph of correlation may, however, be of any slope. As long as the units are the same from one graph to another, a slope steeper than 45° means that as the independent variable changes by one unit, the dependent variable changes by more than one unit. Conversely, a slope of less than 45° means that as the independent variable changes by one unit the dependent variable changes by less than one unit.

It should be apparent that graphical representations of correlations can be compared to one another only if they are plotted in comparable units. For example, we might alter the slope of the line simply by choosing a different scale on which to plot number of deaths, while leaving the distance at the same scale. If, instead of plotting deaths in units of tens (10, 20, 30, 40 …) as shown in Fig. A.5, we were to plot it in terms of twenties (20, 40, 60 …) as shown in Fig. A.6, the slope of the line would be much less steep but the correlation itself would not be changed. What *would* be changed would be the perception of the viewer.

Other than by visual inspection of the distributions of points on a graph, how can we determine whether a particular correlation is strong or weak? To get an estimate of how closely the trend in one factor is associated with that in the other factor, statisticians calculate a value known as the correlation coefficient. A correlation coefficient expresses the ratio of change in the two factors being compared in any given data set. Correlation coefficients run from −1 to 0, and from 0 to +1, with values on the minus side representing negative and those on the plus side representing positive, correlations. A correlation coefficient of 0 indicates no relationship between the two entities being measured. For example, using Snow's data correlating the number of cases of cholera with the distance people lived from the Broad Street pump, we get a correlation coefficient of −0.8. This represents a

Fig. A.6 Same data as Fig. 5.5 but with data on the y-axis plotted in intervals of 20 rather than intervals of 10, as in Fig. 5.5

strong negative correlation: that is, the greater the distance the fewer the cases. As pointed out above, we could also calculate the correlation as a positive one if we compared proximity to the pump.

The method of calculating correlation coefficients is sufficiently complex that it will not be included here, but knowing correlation coefficients gives an immediate, and quantitative indication of the degree of association between the entities being compared. Correlation coefficients also make it possible to compare sets of data that may be based on different units or types of measurements. For example, we could still compare results if other studies of the Broad Street pump had measured distance in meters rather than yards or in amount of water consumed from the pump by individuals rather than distance they lived from it.

It must be stressed that *correlations do not by themselves tell us anything about cause-and-effect*. For example, the data given in Table A.3 and plotted in Fig. A.5 do not necessarily tell us that the water from the Broad Street Pump was the actual cause of the deaths from cholera. Recall that Snow had difficulty convincing people of the correctness of his water-borne hypothesis. Proponents of the effluvia hypothesis could always argue that, since the pump was a center of activity and the area around it was usually crowded, effluvia from infected individuals meeting at the pump, rather than water from the pump itself, was the cause of infection. Thus the existence of a correlation alone was not enough to establish a causal agent. Snow needed, in addition, the data obtained by comparing the populations using water from the two different water companies to demonstrate a strong cause-effect connection between source of water and occurrence of cholera. By showing that only people who drank water from the Southwark and Vauxhall Company contracted cholera, Snow was able to establish a plausible connection between polluted water and the spread of cholera.

Correlations may be quite seductive by suggesting what looks like an obvious cause-and-effect relationship that is completely spurious (for example, the almost perfect 1:1 correlation between the increase in a person's age from 1950 to 1980 and increasing levels of pollution in major urban areas in the United States). In other cases, however, suggested correlations might well turn out to be accurate. Indeed, one of the great benefits of establishing correlations in the first place is that they suggest *possible* causal relationships. However, an actual causal relationship can only be established by doing further research and gathering additional data on the system or organism in question.

A.5.2 Rate and Change of Rate

When John Snow calculated deaths in the 1853 London cholera epidemic he presented his data not only as the absolute number of deaths (Table 5.2) but also as deaths *per* number of households, that is, as a death *rate*. Rate is a measure of change in quantity of the dependent variable *per* some standard unit of the independent variable, such as time, volume, *etc*. Snow's death rate measured number of deaths *per* standard unit of population, in this case *per* 10,000 households. Calculating rate makes it possible to compare different samples using the same common denominator; in Snow's case a per-capita basis or standard unit of population. For example, comparing the total number of deaths for houses supplied by each of the two London water companies would have been meaningless if given only in absolute numbers, since one company might have served a larger number of households than the other. As shown in Table A.3, by using death rate, however, Snow was able to demonstrate clearly that one company was associated with a far greater incidence *per capita* of cholera infections than the other.

A.5.2.1 Analysis of Distributions: Central Tendency and Dispersion

In trying to determine patterns of infection in cholera patients, Snow and others encountered considerable variation in the time required for the disease to run its course, recorded as the time required for a patient, once infected, to either die or recover from the effects of the disease. For some individuals, the time between infection and death or recuperation was very short: 1 or 2 days. In others, it took up to a week. The average, or mean, was around 3–4 days. If Snow had wanted to represent this variation quantitatively he might have tabulated the results from a number of individual cases and plotted them on a distribution graph (Fig. A.7). Distribution graphs plot a range of measurements on the x-axis against the number or frequency of individuals in any particular category on the *y*-axis. They are generally used to show the distribution of measurements around a mean or average

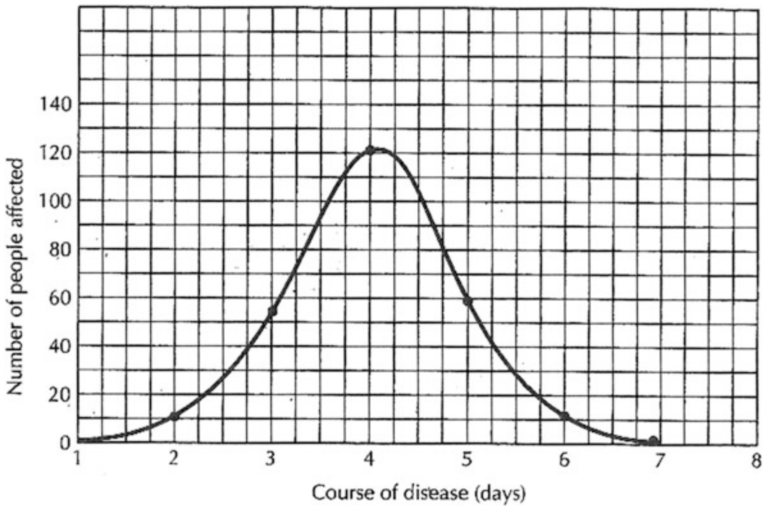

Fig. A.7 Normal distribution curve, showing frequency with which death occurred plotted against number of days since infection was first noted in an individual. The graph shows that death tends to occur around the fourth day after the infection was first noted

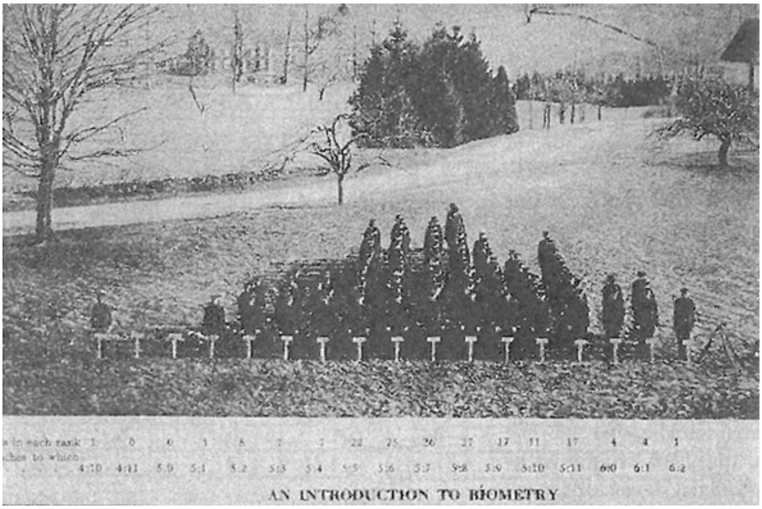

Fig. A.8 A photograph from a textbook of 1914 illustrating the normal curve of distribution for height in a group of 175 World War I recruits. Each small cross in front of a row of individuals indicates one particular height category (such as 5′ 8″, 5′ 9″, as indicated by the numbers below the photograph) [From A.F. Blakeslee, *Journal of Heredity* 5 (1914)]

for a population of individual organisms, for example, height in a group of people (Fig. A.8).

Two very useful means for describing characteristics of a data set of such measurements are the *central tendency* and the *dispersion* of the data. Central tendency is given by three values: the *mean, median and mode*. The mean is the *average* value for a group of measurements, and is calculated as:

$$\text{Mean} = x = \frac{\sum x_i}{n}$$

where x_i are the individual measurements, n is the total number of measurements, $\sum$ means "sum of" and x is the symbol for mean. The mode is the most common measurement in the sample and the *median* is the value above and below which lie equal numbers of measurements. Measurements of central tendency often give a bell-shaped, or curve of "normal distribution", as shown in Fig. A.8. Early statisticians were fascinated to discover that measurements of an extremely wide variety of samples showed some variant of the normal distribution curve. What the measures of central tendency do *not* show, however, is the dispersion—that is, how widely or narrowly the sample is dispersed around the mean. Variance and standard deviation are both measures of dispersion, that is, how much the sample as a whole deviates from the mean. In calculating variance we cannot simply average the deviations from the mean, since the negative deviations will be cancelled out by the positive (in a normal curve) and the result will be *zero*, not a very useful number! It is possible, however, to average the squares of the deviations, using the following calculation:

$$\text{variance} = \frac{\sum (x_i - x)^2}{n - 1}$$

Squares of the deviations are divided by n − 1 since dividing by n alone tends to underestimate the variance especially if the population is relatively small. Variance is a useful measure, but it is more common to estimate dispersion by calculating the square root of the variance, or what is called *standard deviation*, as follows:

$$\text{Standard deviation(s)} = \sqrt{\frac{\sum (x_i - x)}{n}}$$

One major reason for using standard deviation is that the units for variance itself (for example height squared) does not make physical sense (what, after all, is *squared* height?). However, by taking the square root of the variance, we come out with real units of measure (height in inches, number of days for individuals to show symptoms of cholera, etc). Taking the square root compensates for squaring the measurements in the first place. The value of standard deviation is that it tells us a great deal about dispersion of the data around the mean. For a normal distribution as shown in Figs. A.7 and A.8, 68 % of all the observations lie within one standard deviation on either side of the mean, and 95 % lie within two standard deviations on either side of the mean. Ninety-nine percent of the measurements lie within three standard deviations (Fig. A.9). In calculating standard deviation(s) for any set of data, the higher the value, the greater the dispersion of the data around the mean, and thus the greater the width of the bell curve.

All distributions do not follow a normal curve, however. Some distributions may be either skewed or bimodal. A bimodal curve (Fig. A.10a) is one in which there are two modal groups, indicating at least two major groupings of characteristics within the sample. Field naturalists often find bimodal distributions within a particular population of organisms in nature, for example a black and a brown form of ground squirrels, or of left- or right-coiling shells in snails from the same population. The two modal groups do not have to be equal in frequency for the distribution to be described as bimodal. They do, however, have to be distinctly demarcated from each other such that each has its own mean value. Skewed

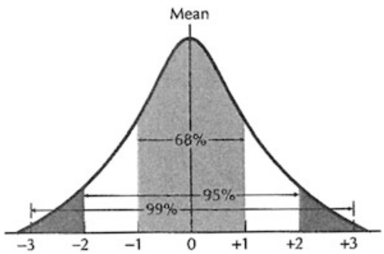

Fig. A.9 Bimodal distribution graph showing the two modal groups with the mean in the "valley" between distributions are those in which the mode is distinctly different from the mean, so that the peak of the curve is not symmetrically placed between the two extremes of the range (Fig. A.10b). The mode may be skewed to the right, above the mean or to the left below the mean. Skewed distributions simply indicate that a lot of individual measurements in the sample lie to one side of the other of the mean. A skewed mean in a population of organisms in a field setting might indicate that natural selection is at work moving the population from an earlier, normal distribution, toward the other end of the range.

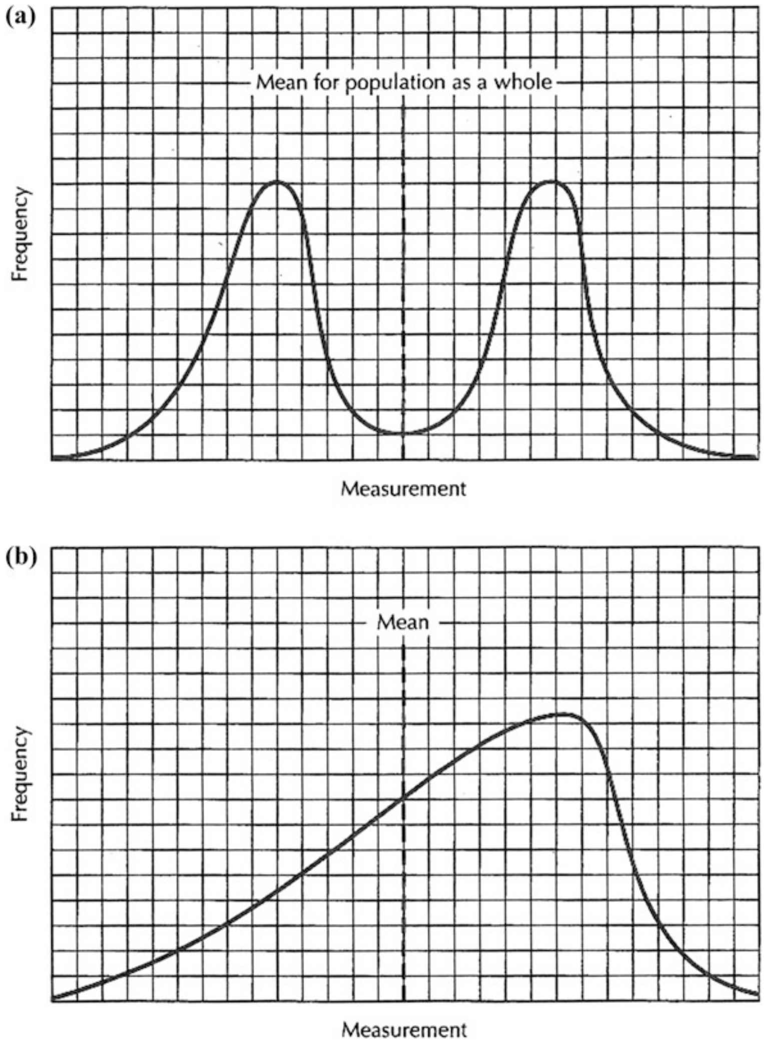

Fig. A.10 A skewed distribution graph, with the single modal group well to the right (toward the higher end of the measurement scale) of the mean

A.5.3 Levels of Significance

The question of significance deals with determining whether given measurements represent a meaningful as opposed to a chance departure from the expected. Suppose, for example, we measure height in a group of 100 college students on a campus in Minnesota, and get a normal curve, with a mean of 5′ 8″. Now, suppose that we then get another, much smaller sample of 10 students from a college in California, and find that the mean height is 6′ 4″. The difference might reflect actual differences in the populations in the two localities, or it might reflect a bias resulting from the much smaller size of the second sample. The question investigators in this sort of situation would like to know is whether this measured difference is significant or not; or expressed another way, what is the probability that the difference we observe in the small sample from California occurred purely by chance?

Starting with the null hypothesis that there should be no significant difference between the two populations we then try to reject that hypothesis. If the probability of making a certain measurement or observation is less than 5 % (i.e., would occur in less than 5 instances out of 100), the results are considered to be significant, and the null hypothesis can be rejected. Knowing something about the system they are studying (in this case height in college students), investigators often set their standard of significance level prior to making their measurements. They decide ahead of time what the probability would be of obtaining, by chance alone, a difference as large or larger than the observed difference. For example, knowing that our second measurement of the California college students only consisted of 10 individuals, we could calculate by statistical methods what the chances are that we would get such a different mean by chance alone. A significance level of 0.05 (or 5/100) is the generally agreed-upon standard for stating that the results are not purely due to chance and therefore that the difference is a significant one. Investigators who wish to be more rigorous may analyze data to the 0.01 (1/00) significance level. These levels are somewhat arbitrary, but only in the sense that the values of 0.05 and 0.01 represent two agreed-upon standards for judging how likely it would be to get a significant difference in two sets of data by chance alone.

Appendix B

The Nature and Logic of Science

Possible Answer for Exercises

1. *An observation is a discrete item of sensory data (e.g., "the frog jumped"). A fact is an observation or set of observations that are agreed upon by a group of people. A conceptualization is a more general or abstract statement that goes beyond concrete facts and relates the facts to each other.*
2.
   (a) *Fact. An agreed-upon set of observations is a fact.*
   (b) *Observation. A specific item of sense data, visual in nature.*
   (c) *Conceptualization. The statement offers an abstract reason for why the planets move in the direction they are observed to move.*
   (d) *Conceptualization (same reason as c, above)*
   (e) *Conceptualization. The statement is a generalization going beyond the specific set of green apples the observer has tasted)*
   (f) *Observation. The statement is about the contents of the report derived from reading the document itself.*

3.
   (a) (*i*) *At dusk, the light is dim but not perceived as dim as it might actually be, so a person's vision is more impaired than they think; this hypothesis could be tested by testing a person's vision under various levels of illumination and also by gathering more precise data on degree of illumination compared to accident rate as afternoon wanes into dusk.* (*ii*) *An alternative is that dusk is also "rush hour" on certain days anyway, so traffic is higher and so are accidents; this hypothesis could be tested by measuring accident rate (number of accidents per total volume of traffic) for different periods during evening rush hour.*
   (b) *When the tumbler is warm, the air inside is expanding, forcing the bubbles to the outside. As the glass cools on the drainboard, the air begins to*

G.E. Allen and J.J.W. Baker, *Scientific Process and Social Issues in Biology Education*, Springer Texts in Education,
DOI 10.1007/978-3-319-44380-5

contract, drawing bubbles back inside. A test would be to wash the tumbler in cold soapy water, in which case it would be predicted that no bubbles would form [A student one suggested that there might be a fan on in the room at the time and that this created air currents that caused the air to exit the glass; cooling of the glass caused the air to re-enter. What might be some problems with this explanation? Could the explanation be tested?]

(c) *The results suggest that contact between offspring and the strain A mother is essential for cancer to develop. A likely transmitter at this stage of development is the mother's milk, which might contain a virus that inserted itself into cells of the young mice and later caused those cells to become cancerous. Several varieties of cancer are known to be associated with viruses or genes of viral origin that have inserted themselves into the cells of their host.*

4.

(a) *If ... diminishing light intensity causes cricket chirping to slow down, then ... Crickets placed in the laboratory when the light was successively diminished, should show decreased chirping.*
(b) *The results contradict the hypothesis/prediction. The slight variation in chirps at different intensities shows no trends.*
(c) *If ... diminishing temperature causes cricket chirping to slow down, then ... at successively lower temperatures crickets should show decreased chirping.*
(d) *The results confirm the second hypothesis, since the rate of chirping decreases markedly with decrease in temperature. The trend here is very clear.*

5.

(a) *Valid reasoning; a true conclusion deriving from (2) false hypotheses*
(b) *Valid reasoning; a true conclusion deriving from (2) true hypotheses*
(c) *Valid reasoning; a false conclusion deriving from (2) false hypotheses*
(d) *Invalid reasoning; false conclusion from (2) true hypotheses*
(e) *Invalid reasoning; false conclusion from (2) false conclusions*

6. *Basic feelings encountered when an old paradigm begins to provide problems or anomalies, are confusion and sometimes resentment or anger. Generally old paradigms are not abandoned until new ones are found to replace them; with the acceptance of a new paradigm there is often a sense of great discovery, illumination, excitement and relief.*

7.

(a) *It would be reasonable to hypothesize that if allowed contact with her kid for even five minutes a doe will establish a bond, perhaps based on sight or smell recognition cues; she will recognize the kid on return even after an* *hour or more; however, if she is not allowed to establish any sight-smell bond, she will reject the kid as foreign. Once the bond has been established in the first 5 min, the doe is distressed at the kid's removal, but if no bond is ever established, the doe's maternal behavior is never evoked and she behaves as if she never gave birth. This hypothesis could be tested by substituting a foreign kid for the doe's own natural kid immediately after birth, then removing it, and returning it an hour later. If the doe accepted the kid this would reinforce the smell-sight bond hypothesis. If she rejected the foreign kid an hour later this would tend to refute the smell-sight bond hypothesis.*

(b) *The second set of observations/experiments confirm the smell-sight bonding hypothesis, since the doe accepts even a foreign kid if she is allowed five minutes with it after birth.*

(c) *It would be possible to distinguish between sight and smell as the possible avenues of recognition used by the doe. The doe's nostrils could be plugged with scented cotton that would block her sense of smell and the two experiments above (using her own kid and then a foreign kid) repeated. The converse could be done by patching the doe's eyes. A third approach would be to rub a foreign kid with liquids from the placenta of the doe's natural kid, allow the doe to spend 5 min with her own kid and then remove it; the foreign kid, now smelling like the original kid, could be returned one hour later, with the following predictions as to the doe's behavior: If smell were the main means of recognition, the doe ought to accept the foreign kid; if smell is not involved or if sight is the main means of recognition, the doe ought to reject the foreign kid.*

The Nature and Logic of Science:Testing Hypotheses

Possible Answer for Exercises

1. *Hypotheses that cannot be tested, as interesting or imaginative (or far-fetched) as they may be, can never be either supported or rejected, and thus add nothing in the long run to our understanding of the world. Formulating hypotheses without the check of testability also gives free reign to sloppy and non-rigorous thinking. It is possible to propose anything if yoiu are not under any obligation to test it in the real world. On the other hand, many hypotheses that seemed untestable when first formulated turned out be imaginative enough to stimulate later experimenta. So, lack of immediate testability is not always a reason for dismissing a new hypothesis. (For example, many of the early theories about the genetic code were purely theoretical hypotheses that no one could immediately test, but they stimulated thinking about the code as a "language" and eventually led to very fruitful plredictions and biochemical tests).*

2. *Hypotheses about phylogenetic relationships, or past geological occurrences can only be tested by observation of fossils and geological strata. Other examples are involved) the hypothesis that smoking causes cancer; that Amerindians descended from Asian migrants who crossed the Behring Strait at some point in the past; that teenagers present a greter diriving risk than those who are 25 years old; that women inherently like to take care of children more than men, etc. Hypotheses testable by experimentation are preferred because the variables that might influence the outsome can be controlled, and the experimenter can set up conditions to his/her specifications. Experiments allow a more rigorous testing of alternative hypotheses by making predictions and then manipulating the system so as to observe whether the outcome does or does not fit the prediction.*

3. *There are many problems associated with this study. (a) First, and perhaps most obvious, the average age of the two populations is not the same, the reformatory group being on average a year older than the Latin school population. In adults a one-year discrepancy in age mjight not be all that serious, but during adolescence, when one year can make a huge difference in growth, especially where the characrteristic being measured is body form, the discrepancy can be significant. The two populations are also very likely not matched for socio-economic factors, which can have important influences on body growth and rate of development. It is also not clear whether there were ethnic differences taken into account, which clearly have some relation to body shape. Definition body forms is at best a vague and largely subjective process – looking around at your friends try to make such classifications; it borders on philosophical idealism to create such abstract categories into which actual individuals are supposed to fit. One more problem is that there is an underlying assumption that body shape somehow determines behavioral tendencies. Correlation of a physical trait with a behavior does not establish cause-and-effect. (b) Ethically, the study raises some problems in that if its conclusions were widely accepted (which they were for a time in the 1940s and 1950s) could lead to prejudging of boys just by superficial examinatioin of their appearance, leading to expectationi that they would have to delinquent behavior. Such expections often elicit the result, being what is known as a "self-fulfilling proplhecy." There was also no inidication that the boys in either group were asked to sign consent forms to have their physiques measured. This aspect of the issue emerged several years ago when an adult woman found a naked picture of herself as a college student in a published book, based on a similar body-form study from the 1950s. She was rightfully angered at what she considered a basic invasion of privacy.*

4. *Diseases are caused by infective agents such as bacteria, viruses, parasitic microorganisms (among others), and environmental toxins of various sorts. Understanding how these affect the human body is obviously one of the aspects of fighting disease. On the other hand, disease is spread by interaction between people, which includes a wide variety of social factors from individual and*

group behavioral practices (types of interpersonal contacts) as well as more widely organized applications such as public health facilities (how are wastes in a community disposed of, how are the rights of the individual to be balanced against the overall public health interests of the community)?

5. *This is always a delicate balance. Quarrantine has been used during many , but the extent to which it is employed needs to take into account (a) How easily transmissble the disease is, (b) The form of transmission (sexually, through water supply, soiled clothing, etc), and (c) Community mores.) to an area gets very difficult, especially when a community gives way to panic about an epidemic or possibility of an epidemic. At the height of in the United States (early 1990s) there was a call to the U.S. Immigration and Naturalization Service to bar admission to all immigrants who were HIV positive. Such a prohibition never became actual law, but there were attempts at many ports of entry to find out who might be infected.*

Doing Biology: Three Case Studies

Possible Answer for Exercises

1. *There are of course highly subjective judgments involved here. The authors would rank (c) first, (a) second, and (b) third. The had for so long been hypothesized as being due to climate change, with the resulting disappearance of the plants upon which the herbivorous dinosaurs fed (and thus, in turn, the loss of these dinosaurs as food for the carnivorous forms to prey upon), the Alvarez hypothesis, with its associated meteor impact crater , presented a whole new way of looking at things and suggested entirely new avenues of research. Nerve growth factor research was certainly vitally important in the fields of and neuroscience and also influenced the direction of research in the field, but did not represent as dramatic a shift in this direction. Hasler's salmon studies were significant contributions to the field of animal migration and of great practical value to the salmon industry, but only in providing experimental evidence for what had been suspected for some time—that the chemical composition of salmon home streams provided the clues enabling them to return to their home streams to spawn. In neither of the three cases, however, is the level of magnitude of paradigm shift even close to that of Dalton's atomic theory in chemistry, quantum mechanics in physics, or the Darwin-Wallace theory of evolution by natural selection in biology.*
2. *The findings suggest further support for the Darwin-Wallace paradigm in that such widely differing organisms possess molecular similarity at the tissue-cell level. Since snake venom glands are modified salivary glands their production of NGF suggests divergence from a common ancestor. That NGF is also found*

in the developing chick embryo suggests an ancestral relationship between all species discussed here.

3. *Since the Alvarez K-T boundary hypothesis associates a high level of iridium with meteoritic impact and suggests that event as the causative factor in mass , the new discovery amounts to a falseof the K-T hypothesis and thus that hypothesis itself must be false. Being human, however, scientists tend to be very fond of their hypotheses. Thus, for example, in defending their hypothesis, the Alvarez's might suggest that the fossil record during the reported time period was not complete enough to record of extinctions and that the meteoritic crater, like the one eventually found at the Yucatan Peninsula, had simply not yet been located.*
4. *The nerve growth factor (NGF) and salmon homing cases both involved the greatest amount of experimentation. In the case of NGF observation was involved not so much in testing but in formulating an hypothesis. The observation that mouse sarcoma greatly stimulated neuronal growth gave rise to the hypothesis that the sarcoma was producing a substance, later named NGF, that directly affected neuron growth and maintenance. Similarly, Hasler's work on homing in salmon began with the observation that salmon return to spawn in the same streams in which they were hatched. The Nemesis case is the one in which observation was used most regularly to test aspects of the hypothesis of meteoric impact: for example, searching for periodicity in the paleontological record or for remnants of an impact crater that would match the estimates of the meteor hypothesized to strike Earth 65 million years ago.*

The Social Context of Science: The Interaction of Science and Society

Possible Answer for Exercises

1. *The "treasure hunt" concept of science assumes there are real scientific laws in nature that have an existence independent of time and place. The scientist's job is to use clues to find the treasure, which will be the same no matter who discovered it or when. The social constructionist view is that scientists "construct" a view of nature using the tools of language, metaphors philosophy, analogies available to them, and that since these tools change from one culture to another, the resulting view of nature will necessarily reflect time and place. It could be argued that both points of view are important in assessing how science is pursued. There can be little doubt that our language, metaphors, comparisons and analogies play an important part in constructing and communicating to others our view of nature. However, if we assume there is a real world out there beyond our senses, then our socially constructed view of that world will still*

have to be tested in reality. In that way different constructions can be compared and contrasted and the most fruitful ones chosen to develop.

2. *Social constructionist and other such views cannot be tested directly, of course. For example, if we put forth as a scientific hypothesis that both Darwin and Wallace were influenced by the social, political and economic environment of nineteenth. century Great Britain to which both men were exposed, this hypothesis would predict that, had these two men lived in a socialist or a pre-capitalist society, their paradigm would have been expressed using different metaphors, emphasizing perhaps cooperative rather than competitive aspects of nature. Quite obviously, such an experiment cannot be performed. However, it is possible to make comparisons between hypotheses devised in different cultures and in that way gain some insight into how social and cultural factors affect how science is done. While such comparisons are subject to other interpretations, they provide one way to test from the social constructionist perspective.*

3. *As stressed in* Chap. 2, *science cannot* ***prove*** *anything: it can only establish its "truths" in terms of probabilities. The statement contains other errors as well. First, even if a "moment" were a precisely defined unit of time* (*as is a millisecond, for example*)*, there is no one "moment of conception." Fertilization of an egg by the sperm is a process, not an instantaneous event. Considerable time elapses between initial contact of sperm with the egg surface and the fusion of the male and female pronuclei, still more before the initiation of their combined genetic underpinnings of development, and still more before it is determined if the resulting fertilized egg (zygote) will finish its developmental journey down the Fallopian tube, with implantation in the uterine lining to initiate pregnancy or, as appears to be the case with as many as one half of successful fertilizations, be aborted naturally and pass out of the vagina unnoticed. Second, the statement also implies that "life" is a clearly defined entity. It is not. One has only to pick up a reasonably decent high school biology textbook to learn that, as early as the nineteenth century, biologists recognized that attempts to define life were fruitless. The Frenchman Claude Bernard* (*1813–1878*)*, considered by many to be the father of modern physiology, noted:* "… it is necessary for us to know that it is illusory and chimerical and contrary to the very spirit of science to seek an absolute definition of [life]. We ought to concern ourselves only with establishing its characteristics…" *In fact, all science can do is attempt to describe those characteristics that most (though by no means all) life forms display. This being the case, therefore, we can state with certainty that life most definitely does* ***not*** *begin at any "moment of conception," since clearly both egg and sperm are alive, as are their progenitor cells,* etc, etc.*, the so-called "beginning" of life thus being ultimately traceable back to the origin of forms meeting some threshold number of features characterizing living matter perhaps four and a half billion years ago.*

   We must stress here that we are not suggesting that one may not oppose abortion for any variety of reasons including, as is often the case, the religious *conviction that it is "immoral," but only that one cannot use science, most especially the mistaken concept of," in support of that position. As the quote from Keeton and Gould cited in this chapter makes clear, science can only provide information relevant to such decisions, but cannot itself make the social and/or moral decision.*

4. *Much depends on how "eugenics" is defined. The older, historical meaning was tied to state-sponsored programs and had a coercive quality about it. It was also tied to concerted efforts to "improve the race" through planned breeding. Today, more subtle forms of coercion, such as denial of health care coverage, could end up forcing families to make choices not unlike those they would have been forced to make under the older eugenic legislation. At the same time, the modern movement is not so motivated by overt claims to "improve the human species."*

5. *It could be argued that life in general in a "genetic disease" since we are all going to die of something at some point, and that what counts is how we maximize our potential in the time we do have and that this is more important than figuring out cost-benefit analyses of human worth. From another point of view, however, one might argue that genetic diseases are often very expensive to treat and even if the treatment allows the individual to contribute something to society, in balance it is an inefficient way to manage limited health care resources. Where diseases—genetic diseases in this case—can be prevented they should be; cure is only for that which cannot be prevented in the first place. This latter position comes back to the economic efficiency argument, and the juxtaposition of financial resources to human worth. It could also be argued, of course, that the real problem is the limitation imposed on health care availability and costs, and other competing societal interests such as education and/or military expenditures.*

6. *GMOs differ in several ways from organisms bred by conventional means. First, specific genes of interest can be transferred directly from the donor to the recipient or host organism. In conventional breeding, mutant genes are transmitted along with all the other genes in the parental genome, which may include undesirable ones as well. Second, the process of gene transfer with biotechnology is much quicker and more certain than conventional breeding, which involves waiting for a favorable variant to occur. In an even more significant way, GMOs can contain genetic elements such as trans-genes from totally unrelated organisms, which is not possible with conventional breeding practices. It is particularly concerning the latter process that some people are suspicious or hostile to GMOs, fearing that the "foreign genes" in the host organism will lead to disruption of the host organism's physiology with possible poisonous or detrimental effect on the consumer. Another reason, of course, is the fear that GMOs will have adverse effects on the environment as illustrated by the effect of Bt pollen development.*

7. *As in question 6, the introduction of "foreign" genes that would never be possible by traditional breeding methods is feared by some people to have a potential deleterious effect on the host organism that could make it harmful for human consumption. For example, milk produced from pig genes and supplanting, or interacting in some unpredictable way with the cow's own genes for milk production might contain different antibodies or types of sugars that could lead to an allergic reaction in humans drinking that milk. Such problems could, of course, be largely avoided if sufficient field testing of the new GMO products were carried out prior to release on the market.*

8. *Some might argue that food, like the air we breathe and the water we drink ought not be owned by anyone but dispensed and paid for by the collective community. Such an argument would be based on the idea that these are such basic necessities of life in our modern society, and that for individuals to make a personal profit on them is unethical. On a more specific level, many ethicists have argued that, especially in today's academic and business environment, ownership of new ideas or procedures ignores the reality of how science is being practiced. Grants from governments, philanthropic and public charities (like the March of Dimes) all provide the financial support necessary for the research in the first place so that granting intellectual property rights to an individual or even one specific institution ignores the many forms of support that went into the research process. Another argument might be that since science is a collective enterprise, often carried out by laboratory teams, to award property rights to one or a few of those involved (usually the head scientist or principal investigator) fails to acknowledge the work of others—graduate students, technicians, laboratory managers, or maintenance personnel who keep the physical facilities functioning and clean. Whose work is essential for the research to proceed. Proponents of intellectual property rights argue that it is the scientists' original ideas that make the whole research effort possible and that, without these, there would be no project at all. This view gives primary place to the intellectual aspect of research, whereas the former view includes the material aspect of research as an integral and thus inseparable aspect of the whole endeavor. The issue thus boils down to whether one wants to give primacy to the intellectual (theoretical) or to the integrated theory + practice concepts of the nature of scientific practice. Traditional accounts —textbooks, journalistic presentations and histories of science have traditionally emphasized the intellectual component of research and omitted, or only treated briefly, the other material components.*

9. *One question the reporter might want to ask is how are the new genetically-engineered crops going to be distributed? Are they going to be given away free, or at cost, and if so, how is the company going to justify to their investors that they are not getting a return on the expense of research and development. If the food is to be sold on the open, competitive market, how are malnourished people, who are almost always poor, going to be able to afford them?*

Further Reading

Barnard, C., Gilbert, F., & McGregor, P. (1993). *Asking questions in biology*. New York, NY: Wiley (*A well-written and clear presentation of many aspects of hypothesis formulation, data analysis and experimental design. Aimed at the undergraduate level, contains many good examples, especially from the field of animal behavior*).

Gilbert, N. (1989). *Biometrical interpretation: Making sense of statistics in biology*. Oxford, UK: Oxford University Press (*This is a concise, well-written and user-friendly introduction to a variety of statistical concepts, all using biological examples. Explanations are in simple language, and the book overall requires minimum mathematical background*).

Huff, D. (1954). *How to lie with statistics* (1st ed.). New York, NY: W.W. Norton (*Although over 60 years old, this is a clever, simple, and very well-written book that provides a good introduction to statistical thinking, and especially to methods of representing data. The author's sense of humor and the clear illustrations make the subject of statistics not only interesting but painless*).

Laake, P., Breien Benestad, H., & Reino Olsen, B. (Eds). (2015). *Research in medical and biological sciences.* Oxford, UK: Elsevier (*This comprehensive book covers a wide variety of topics all relevant to material in both Appendix 1 and other chapters in this book as well. Topics include designing experiments, types of data and data collecting, data analysis, ethics in scientific, especially human biomedical research, and philosophy of science. As the title suggests medical research is included. The primary audience is advanced undergraduate and graduate students*).

G.E. Allen and J.J.W. Baker, *Scientific Process and Social Issues in Biology Education*, Springer Texts in Education,
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