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Information Geometry and Population Genetics

The Mathematical Structure of the Wright-Fisher Model

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Preface

Population genetics is concerned with the distribution of alleles, that is, variants at a genetic locus, in a population and the dynamics of such a distribution across generations under the influences of genetic drift, mutations, selection, recombination and other factors [57]. The Wright–Fisher model is the basic model of mathematical population genetics. It was introduced and studied by Ronald Fisher, Sewall Wright, Motoo Kimura and many other people. The basic idea is very simple. The alleles in the next generation are drawn from those of the current generation by random sampling with replacement. When this process is iterated across generations, then by random drift, asymptotically, only a single allele will survive in the population. Once this allele is fixed in the population, the dynamics becomes stationary. This effect can be countered by mutations that might restore some of those alleles that had disappeared. Or it can be enhanced by selection that might give one allele an advantage over the others, that is, a higher chance of being drawn in the sampling process. When the alleles are distributed over several loci, then in a sexually recombining population, there may also exist systematic dependencies between the allele distributions at different loci. It turns out that rescaling the model, that is, letting the population size go to infinity and the time steps go to 0, leads to partial differential equations, called the Kolmogorov forward (or Fokker–Planck) and the Kolmogorov backward equation. These equations are well suited for investigating the asymptotic dynamics of the process. This is what many people have investigated before us and what we also study in this book.

So, what can we contribute to the subject? Well, in spite of its simplicity, the model leads to a very rich and beautiful mathematical structure. We uncover this structure in a systematic manner and apply it to the model. While many mathematical tools, from stochastic analysis, combinatorics, and partial differential equations, have been applied to the Wright–Fisher model, we bring in a geometric perspective. More precisely, information geometry, the geometric approach to parametric statistics pioneered by Amari and Chentsov (see, for instance, [4, 20] and for a treatment that also addresses the mathematical problems for continuous sample spaces [9]), studies the geometry of probability distributions. And as a remarkable coincidence, here we meet Ronald Fisher again. The basic concept

of information geometry is the Fisher metric. That metric, formally introduced by the statistician Rao [102], arose in the context of parametric statistics rather than in population genetics, and in fact, it seems that Fisher himself did not see this tight connection. Another fundamental concept of information geometry is the Amari–Chentsov connection [3, 10]. As we shall argue in this book, this geometric perspective yields a very natural and insightful approach to the Wright–Fisher model, and with its help we can easily and systematically compute many quantities of interest, like the expected times when alleles disappear from the population. Also, information geometry is naturally linked to statistical mechanics, and this will allow us to utilize powerful computational tools from the latter field, like the free energy functional. Moreover, the geometric perspective is a global one, and it allows us to connect the dynamics before and after allele loss events in a manner that is more systematic than what has hitherto been carried out in the literature. The decisive global quantities are the moments of the process, and with their help and with sophisticated hierarchical schemes, we can construct global solutions of the Kolmogorov forward and backward equations.

Let us thus summarize some of our contributions, in addition to providing a self-contained and comprehensive analysis of the Wright–Fisher model.

- We provide a new set of computational tools for the basic quantities of interest of the Wright–Fisher model, like fixation or coexistence probabilities of the different alleles. These will be spelled out in detail for various cases of increasing generality, starting from the 2-allele, 1-locus case without additional effects like mutation or selection to cases involving more alleles, several loci and/or mutation and selection.
- We develop a systematic geometric perspective which allows us to understand results like the Ohta–Kimura formula or, more generally, the properties and consequences of recombination, in conceptual terms.
- Free energy constructions will yield new insight into the asymptotic properties of the process.
- Our hierarchical solutions will preserve overall probabilities and model the phenomenon of allele loss during the process in more geometric and analytical detail than previously available.

Clearly, the Wright–Fisher model is a gross simplification and idealization of a much more complicated biological process. So, why do we consider it then? There are, in fact, several reasons. Firstly, in spite of this idealization, it allows us to develop some qualitative understanding of one of the fundamental biological processes. Secondly, mathematical population genetics is a surprisingly powerful tool both for classical genetics and modern molecular genetics. Thirdly, as mathematicians, we are also interested in the underlying mathematical structure for its own sake. In particular, we like to explore the connections to several other mathematical disciplines.

As already mentioned, our book contains a self-contained mathematical analysis of the Wright–Fisher model. It introduces mathematical concepts that are of interest and relevance beyond this model. Our book therefore addresses mathematicians

and statistical physicists who want to see how concepts from geometry, partial differential equations (Kolmogorov or Fokker–Planck equations) and statistical mechanics (entropy, free energy) can be developed and applied to one of the most important mathematical models in biology; bioinformaticians who want to acquire a theoretical background in population genetics; and biologists who are not afraid of abstract mathematical models and want to understand the formal structure of population genetics.

Our book consists essentially of three parts. The first two chapters introduce the basic Wright–Fisher model (random genetic drift) and its generalizations (mutation, selection, recombination). The next few chapters introduce and explore the geometry behind the model. We first introduce the basic concepts of information geometry and then look at the Kolmogorov equations and their moments. The geometric structure will provide us with a systematic perspective on recombination. And we can utilize moment-generating and free energy functionals as powerful computational tools. We also explore the large deviation theory of the Wright–Fisher model. Finally, in the last part, we develop hierarchical schemes for the construction of global solutions in Chaps. 8 and 9 and present various applications in Chap. 10. Most of those applications are known from the literature, but our unifying perspective lets us obtain them in a more transparent and systematic manner.

From a different perspective, the first four chapters contain general material, a description of the Wright–Fisher model, an introduction to information geometry, and the derivation of the Kolmogorov equations. The remaining five chapters contain our investigation of the mathematical aspects of the Wright–Fisher model, the geometry of recombination, the free energy functional of the model and its properties, and hierarchical solutions of the Kolmogorov forward and backward equations.

This book contains the results of the theses of the first [60] and the third author [113] written at the Max Planck Institute for Mathematics in the Sciences in Leipzig under the direction of the second author, as well as some subsequent work. Following the established custom in the mathematical literature, the authors are listed in the alphabetical order of their names. In the beginning, there will be some overlap with the second author's textbook *Mathematical Methods in Biology and Neurobiology* [73]. Several of the findings presented in this book have been published in [61–64, 114–118].

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Contents

Chapter 1
Introduction

1.1 The Basic Setting

Population genetics is concerned with the stochastic dynamics of allele frequencies in a population. In mathematical models, alleles are represented as alternative values at genetic loci.

The notions of allele and locus are employed here in a rather abstract manner. They thus cover several biological realizations. A locus may stand for a single position in a genome, and the different possible alleles then are simply the four nucleotides A, C, G, T. Or a locus can stand for the site of a gene—whatever that is—in the DNA, and since such a gene is a string of nucleotides, say of length L, there then are 4^L different nucleotide combinations. Of course, not all of them will be realized in a population, and typically there is a so-called wildtype or default gene, together with some mutants in the population. The wildtype gene and its mutants then represent the possible alleles.

It makes a difference whether we admit finitely many or infinitely many such possible values. Of course, from the preceding discussion it is clear that in biological situations, there are only finitely many, but in a mathematical model, we may also consider the case of infinitely many possibilities. In the finite case, they are drawn from a fixed reservoir, and hence, there is no possibility of genetic novelty in such models when one assumes that all those alleles are already present in the initial population. In the infinite case, or when there are more alleles than members of the population, not all alleles can be simultaneously present in a finite population, and therefore, through mutations, there may arise new values in some generation that had not been present in the parental generation.

We consider here the finite case. The finitely many possible values then are denoted by $0, \ldots, n$. The simplest nontrivial case, $n = 1$, on one hand, already shows most of the features of interest. On the other hand, the general structure of the model becomes clearer when one considers arbitrary values of n.

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We consider a population of N diploid individuals, although for the most basic model, the case of a population of $2N$ haploid individuals would lead to a formally equivalent structure. (Here, "diploid" means that at each genetic locus, there are two alleles, whereas in the "haploid" case, there is only one.)

We start with a single genetic locus. Thus, each individual in the population carries two alleles at this locus, with values taken from $0, \ldots, n$. Different individuals in the population may have different values, and the relative frequency of the value i in the population (at some given time) is denoted by p_i. We shall also consider p as a probability measure on $S_{n+1} := \{0, \ldots, n\}$, that is,

$$\sum_{i=0}^{n} p_i = 1. \tag{1.1.1}$$

The relationship between the deterministic concept of a frequency and the stochastic concept of a probability of course requires some clarification, and this will be addressed below, through the passage to a continuum limit.[1]

The population is evolving in time, and members pass on genes to their offspring, and the allele frequencies p_i then change in time through the mechanisms of selection, mutation and recombination. In the simplest case, one has a population with nonoverlapping generations. That means that we have a discrete time index t, and for the transition from t to $t + 1$, the population V_t produces a new population V_{t+1}. More precisely, members of V_t can give birth to offspring that inherit their alleles. This process involves potential sources of randomness. Most basically, the parents for each offspring are randomly chosen, and therefore, the transition from the allele pool of one generation to that of the next defines a random process. In particular, we shall see the effects of *random genetic drift*. *Mutation* means that an allele may change to another value in the transition from parent to offspring. *Selection* means that the chances of producing offspring vary depending on the value of the allele in question, as some alleles may be fitter than others. *Recombination* takes place in sexual reproduction, that is, when each member of the population has two parents. It is then determined by chance which allele value she inherits when the two parents possess different alleles at the locus in question. Depending on how loci from the two parents are combined, this may introduce correlations between the allele values at different loci.

Here is a *remark* which is perhaps obvious, but which illuminates how the biological process is translated into a mathematical one. As already indicated, in the simplest case we have a single genetic locus. In the diploid case, each individual carries two alleles at this locus. These alleles could be different or identical, but for the basic process of creating offspring, this is irrelevant. In the diploid case, for each individual of the next generation, two parents are chosen from the current generation, and the individual inherits one allele from each parent. That allele then is

[1] In a certain sense, we shall sidestep the real issue, and in this text, we do not enter into the issue of objective and subjective probabilities.

randomly chosen from the two that parent carries. The parents are chosen randomly from the population, and we sample with replacement. That means that when a parent has produced an offspring it is put back into the population so that it has the chance to be chosen for the production of further offspring. To be precise, we also allow for the possibility that one and the same parent is chosen twice for the production of an individual offspring. In such a case, that offspring would not have two different parents, but would get both its alleles from a single parent, and according to the procedure, then even the same allele of that parent could be chosen twice. (Of course, when the population size N becomes large—and eventually, we shall let it tend to infinity—, the probability that this happens becomes exceedingly small.) But then, formally, we can look at the population of $2N$ alleles instead of that of N individuals. The rule for the process then simply says that the next allele generation is produced by sampling with replacement from the current one. In other words, instead of considering a diploid population with N members, we can look at a haploid one with $2N$ participants. That is, for producing an allele in the next generation, we randomly choose one parent in the current population of $2N$ alleles, and that then will be the offspring allele. Thus, we have the process of sampling with replacement in a population of size $2N$. The situation changes, however, when the individuals possess several loci, and the transmission of the alleles at different loci may be correlated through restrictions on the possible recombinations. In that case, we need to distinguish between gametes and zygotes, and the details of the process will depend on whether we recombine gametes or zygotes, that is, whether we perform recombination after or before sampling. This will be explained and addressed in Chap. 5.

Since we want to adopt a stochastic model, in line with the conceptual structure of evolutionary biology, the future frequencies become probabilities, that is, instead of saying that a fraction of p_i of the $2N$ alleles in the population has the value i, we shall rather say that the probability of finding the allele i at the locus in question is p_i. While these probabilities express stochastic effects, they will then change in time according to deterministic rules.

Although we start with a finite population with a discrete time dynamics, subsequently, we shall pass to the limit of an infinite population. In order to compensate for the growing size, we shall make the time steps shorter and pass to continuous time. Obviously, we shall choose the scaling between population size and time carefully, and we shall obtain a parabolic differential equation for the deterministic dynamics of the probabilities in the continuum limit.

1.2 Mutation, Selection and Recombination

The formal models of population genetics make a number of assumptions. Many of these assumptions are not biologically plausible, and for essentially any assumption that we shall make, there exist biological counterexamples. However, the resulting

gain of abstraction makes a mathematical analysis possible which in the end will yield insights of biological value.

We consider a population V_t that is changing in discrete time t with nonoverlapping generations, that is, the population V_{t+1} consists of the offspring of the members of V_t. There is no spatial component here, that is, everything is independent of the location of the members of the population. In particular, the issue of migration does not arise in this model.

Moreover, we shall keep the population size constant from generation to generation.

While we consider sexual reproduction, we only consider monoecious or, in a different terminology, hermaphrodite populations, that is, they do not have separate sexes, and so, any individual can pair with any other to produce offspring. We also assume random mating, that is, individuals get paired at random to produce offspring.

The reproduction process is formally described as follows. For each individual in generation $t+1$, we sample the generation t to choose its one or two parents. The simplest case is to take sampling with replacement. This means that the number of offspring an individual can foster is only limited by the size of the next generation. If we took sampling without replacement, each individual could only produce one offspring. This would not lead to a satisfactory model. Of course, one could limit the maximal number of offspring of individuals, but we shall not pursue this option.

Each individual in the population is represented by its genotype ξ. We assume that the genetic loci of the different members of the population are in one-to-one correspondence with each other. Thus, we have loci $\alpha = 1, \ldots, k$. In the haploid case, at each locus, there can be one of $n_\alpha + 1$ possible alleles. Thus, a genotype is of the form $\xi = (\xi^1, \ldots \xi^k)$, where $\xi^\alpha \in \{0, 1, \ldots, n_\alpha\}$. In the diploid case, at each locus, there are two alleles, which could be the same or different. We are interested in the distribution of genotypes ξ in the population and how that distribution changes over time through the effects of mutation, selection, and recombination.

The trivial case is that each member of V_t by itself, that is, without recombination, produces one offspring that is identical to itself. In that case, nothing changes in time. This baseline situation can then be varied in three respects:

1. The offspring is not necessarily identical to the parent (mutation).
2. The number of offspring an individual produces or may be expected to produce varies with that individual's genotype (selection).
3. Each individual has two parents, and its genotype is assembled from the genotypes of its parents (sexual recombination).

Item 2 leads to a naive concept of fitness as the realized or the expected number of offspring. Fitness is a difficult concept; in particular, it is not clear what the unit of fitness is, whether it is the allele or the genotype or the ancestor of a lineage, or in groups of interacting individuals even some higher order unit (see for instance the analysis and discussion in [70]). Item 3 has two aspects:

(a) Each allele is taken from one of the parents in the haploid case. In the diploid case, each parent produces gametes, which means that she chooses one of her two alleles at the locus in question and gives it to the offspring. Of course, this choice is made for each offspring, so that different descendents can carry different alleles.
(b) Since each individual has many loci that are linearly arranged on chromosomes, alleles at neighboring loci are in general not passed on independently.

The purpose of the model is to understand how the three mechanisms of mutation, selection and recombination change the distribution of genotypes in the population over time. In the present treatise, item 3, that is, recombination, will be discussed in more detail than the other two.

These three mechanisms are assumed to be independent of each other. For instance, the mutation rates do not favour fitter alleles.

For the purpose of the model, a population is considered as a distribution of genotypes. Probability distributions then describe the composition of future populations. More precisely, $p_t(\xi)$ is the probability that an individual in generation t carries the genotype ξ. The model should then express the dynamics of the probability distribution p_t in time t.

For mutations, we consider a matrix $M = (m_{\xi\eta})$ where ξ, η range over the possible genotypes and $m_{\xi\eta}$ is the probability that genotype η mutates to genotype ξ. In the most basic version, the mutation probability $m_{\xi\eta}$ depends only on the number $d(\xi, \eta)$ (d standing for distance, of course) of loci at which ξ and η carry different alleles. Thus, in this basic version, we assume that a mutation occurs at each locus with a uniform rate m, independently of the particular allele found at that locus. Thus, when the allele i at the locus α mutates, it can turn into any of the n_α other alleles that could occur at that locus. Again, we assume that the probabilities are equal, and so, it then mutates with probability $\frac{m}{n_\alpha}$ into the allele $j \neq i$. In the simplest case, there are only $n + 1 = 2$ alleles possible at each locus. In this case,

$$m_{\xi\eta} = m^{d(\xi,\eta)}(1-m)^{k-d(\xi,\eta)}. \tag{1.2.1}$$

When the number $n + 1$ of alleles is arbitrary, but still the same at each site, we have instead

$$m_{\xi\eta} = \left(\frac{m}{n}\right)^{d(\xi,\eta)}\left(1-\frac{m}{n}\right)^{k-d(\xi,\eta)}. \tag{1.2.2}$$

In contrast to mutation, recombination is a binary operation, that is, an operation that takes two parent genotypes η, ζ as arguments to produce one offspring genotype ξ. Here, a genotype consists of a linear sequence of k sites occupied by particular alleles. We consider the case of monoecious individuals with haploid genotypes for the moment. An offspring is then formed through recombination by choosing at each locus the allele that one of the parents carries there. When the two parents carry different alleles at the locus in question, we have to decide by a selection rule which one to choose. This selection rule is represented by a mask μ, a binary string

of length k. An entry 1 at position α means that the allele is taken from the first parent, say η, and a 0 signifies that the allele is taken from the second parent, say ζ. Each genotype is simply described by a string of length k, and for $k = 6$, the mask 100100 produces from the parents $\eta = \eta_1 \dots \eta_6$ and $\zeta = \zeta_1 \dots \zeta_6$ the offspring $\xi = \eta_1\zeta_2\zeta_3\eta_4\zeta_5\zeta_6$. The recombination operator

$$R_{\xi\eta\zeta} = \sum_{\mu} p_r(\mu) C_{\xi\eta\zeta}(\mu) \tag{1.2.3}$$

is then expressed in terms of the recombination schemes $C_{\xi\eta\zeta}(\mu)$ for the masks μ and the probabilities $p_r(\mu)$ for those masks. In the simplest case, all the possible 2^k masks are equally probable, and consequently, at each locus, the offspring obtains an allele from either parent with probability $1/2$, independently of the choices at the other loci. Thus, this case reduces to the consideration of k independent loci.

Dependencies between sites arise in the so-called cross-over models (see for example [11]). Here, the linear arrangement of the sites is important. Only masks of the form $\mu_c = 11 \dots 100 \dots 0$ are permitted. For such a mask, at the first $a(\mu_c)$ sites, the allele from the first parent is chosen, and at the remaining $k - a(\mu_c)$ sites, the one from the second parent. As a can range from 0 to k, we then have $k + 1$ possible such masks μ_c, and we may wish to assume again that each of those is equally probable.

In the diploid case, each individual carries two alleles at each locus, one from each parent. We think of this as two strings of alleles. It is then randomly decided which of the two strings of each parent is given to any particular offspring. Therefore, formally, the scheme can be reduced to the haploid case with suitable masks, but as we shall discuss in Chap. 5, there will arise a further distinction, that between gametes and zygotes.

With recombination alone, some alleles may disappear from the populations, and in fact, as we shall study in detail below, with probability 1, in the long term, only one allele will survive at each site. This is due to random genetic drift, that is, because the parents that produce offspring are randomly selected from the population. Thus, it may happen that no carrier of a particular allele is chosen at a given time or that none of the chosen recombination masks preserves that allele when the mating partner carries a different allele at the locus under consideration. That would then lead to the ultimate extinction of that allele. However, when mutations may occur, an allele that is not present in the population at time t may reappear at some later time. Of course, mutation might also produce new alleles that have not been present in the population before, and this is a main driver of biological evolution.

For these introductory purposes, we do not discuss the order in which the mutation and recombination operators should be applied. In fact, in most models this is irrelevant.

Finally, we include selection. This means that we shall modify the assumptions that individuals in generation t are randomly selected with equal probabilities as parents of individuals in generation $t + 1$. Formally, this means that we need to

change the sampling rule for the parents of the next generation. The sampling probability for an individual to become a parent for the next generation should now depend on its fitness, that is, on its genotype, according to the naive fitness notion employed here. Thus, there is a probability distribution $p_s(\xi)$ on the space of genotypes ξ. Again, the simplest assumption is that in the haploid case, each allele at each locus has a fitness value, independently of which other alleles are present at other loci. In the diploid case, each pair of alleles at a locus would have a fitness value, again independently of the situation at other loci. Of course, in general one should consider fitness functions depending in a less trivial manner on the genotype. Also, in general, the fitness of an individual will depend on the composition of the population, but we shall not address this important aspect here.

The preceding was needed to the set the stage. However, everything said so far is fairly standard and can be found in the introduction of any book on mathematical population genetics. We shall now turn to the mathematical structures underlying the processes of allele dynamics. Here, we shall develop a more abstract mathematical framework than utilized before in population genetics.

Let us first outline our strategy. Since we want to study dynamics of probability distributions, we shall first study the geometry of the space of probability distributions, in order to gain a geometric description and interpretation of our dynamics. For the dynamics itself, it will be expedient to turn to a continuum limit by suitably rescaling population size $2N$ and generation time δt in such a way that $2N \to \infty$, but $2N\delta t = 1$. This will lead to Kolmogorov type backward and forward partial differential equations for the probability distributions. This means that in the limit, the probability density $f(p,s,x,t) := \frac{\partial^n}{\partial x^1 \cdots \partial x^n} P(X(t) \le x | X(s) = p)$ with $s < t$ will satisfy the *Kolmogorov forward* or *Fokker–Planck equation*

$$\frac{\partial}{\partial t} f(p,s,x,t) = \frac{1}{2} \sum_{i,j=1}^{n} \frac{\partial^2}{\partial x^i \partial x^j} \left(x^i (\delta_j^i - x^j) f(p,s,x,t) \right) - \sum_{i=1}^{n} \frac{\partial}{\partial x^i} \left(b^i(x,t) f(p,s,x,t) \right), \tag{1.2.4}$$

and the *Kolmogorov backward equation*

$$-\frac{\partial}{\partial s} f(p,s,x,t) = \frac{1}{2} \sum_{i,j=1}^{n} p^i (\delta_j^i - p^j) \frac{\partial^2}{\partial p^i \partial p^j} f(p,s,x,t) + \sum_{i=1}^{n} b^i(p,s) \frac{\partial}{\partial p^i} f(p,s,x,t) \tag{1.2.5}$$

where the second order terms arise from random genetic drift, which therefore is seen as the most important mechanism, whereas the first order terms with their coefficients b^i incorporate the effects of the other evolutionary forces.

Again, this is standard in the population genetics literature since its original introduction by Wright and its systematic investigation by Kimura. We shall develop a geometric framework that will interpret the coefficients of the second order terms as the inverse of the Fisher metric of mathematical statistics. Among other things,

this will enable us to find explicit solutions of these equations which, importantly, are valid across loss of allele events. In particular, we can then determine all quantities of interest, like the expected extinction times of alleles in the population, in a more general and systematic manner than so far known in the literature.

1.3 Literature on the Wright–Fisher Model

In this section, we discuss some of the literature on the Wright–Fisher model. Our treatment here is selective, for several reasons. First, there are simply too many papers in order to list them all and discuss and compare their relevant contributions. Second, we may have overlooked some papers. Third, our intention is to develop a new and systematic approach for the Wright–Fisher model, based on the geometric as opposed to the stochastic or analytical structure of the model. This approach can unify many previous results and develop them from a general perspective, and therefore, we did not delve so deeply into some of the different methods that have been applied to the Wright–Fisher model since its inception.

Actually, there exist some monographs on population genetics with a systematic mathematical treatment of the Wright–Fisher model that also contain extensive bibliographies, in particular [15, 33, 39], and the reader will find there much useful information that we do not repeat here.

But let us first recall the history of the Wright–Fisher model (as opposed to other population genetics models, cf. for example [17, 18] for a branching process model). The Wright–Fisher model was initially presented implicitly by Ronald Fisher in [46] and explicitly by Sewall Wright in [125]—hence the name. A third person with decisive contributions to the model was Motoo Kimura. In 1945, Wright approximated the discrete process by a diffusion process that is continuous in space and time (continuous process, for short) and that can be described by a Fokker–Planck equation. By solving this Fokker–Planck equation derived from the Wright–Fisher model, Kimura then obtained an exact solution for the Wright–Fisher model in the case of two alleles in 1955 (see [79]). Shortly afterwards, Kimura [78] produced an approximation for the solution of the Wright–Fisher model in the multi-allele case, and in [80], he obtained an exact solution of this model for three alleles and concluded that this can be generalized to arbitrarily many alleles. This yields more information about the Wright–Fisher model as well as the corresponding continuous process. We also mention the monograph [24] where Kimura's theory is systematically developed. Kimura's solution, however, is not entirely satisfactory. For one thing, it depends on very clever algebraic manipulations so that the general mathematical structure is not very transparent, and this makes generalizations very difficult. Also, Kimura's approach is local in the sense that it does not naturally incorporate the transitions resulting from the (irreversible) loss of one or more alleles in the population. Therefore, for instance the integral of his probability density function on its domain need not be equal to 1. Baxter et al. [14] developed

a scheme that is different from Kimura's; it uses separation of variables and works for an arbitrary number of alleles.

While the original model of Wright and Fisher works with a finite population in discrete time, many mathematical insights into its behavior are derived from its diffusion approximation that passes to the limit of an infinite population in continuous time. As indicated, the potential of the diffusion approximation had been realized already by Wright and, in particular, by Kimura. The diffusion approximation also makes an application of the general theory of strongly-continuous semigroups and Markov processes possible, and this then lead to a more systematic approach (cf. [43, 119]). In this framework, the diffusion approximation for the multi-allele Wright–Fisher model was derived by Ethier and Nagylaki [36–38], and a proof of convergence of the Markov chain to the diffusion process can be found in [34, 56]. Mathematicians then derived existence and uniqueness results for solutions of the diffusion equations from the theory of strongly continuous semigroups [34, 36, 77] or martingale theory (see, for example [109, 110]). Here, however, we shall not appeal to the general theory of stochastic processes in order to derive the diffusion approximation, but rather proceed directly within our geometric framework.

As the diffusion operator of the diffusion approximation becomes degenerate at the boundary, the analysis at the boundary becomes difficult, and this issue is not addressed by the aforementioned results, but was dealt with by more specialized approaches. An alternative to those methods and results some of which we shall discuss shortly is the recent approach of Epstein and Mazzeo [29–31] that systematically treats singular boundary behavior of the type arising in the Wright–Fisher model with tools from the regularity theory of partial differential equations. We shall also return to their work in a moment, but we first want to identify the source of the difficulties. This is the possibility that alleles get lost from the population by random drift, and as it turns out, this is ultimately inevitable, and as time goes to infinity, in the basic model, in the absence of mutations or particular balancing selective effects, this will happen almost surely. This is the key issue, and the full structure of the Wright–Fisher model and its diffusion approximation is only revealed when one can connect the dynamics before and after the loss of an allele, or in analytic terms, if one can extend the process from the interior of the probability simplex to all its boundary strata. In particular, this is needed to preserve the normalization of the probability distribution. In geometric terms, we have an evolution process on a probability simplex. The boundary strata of that simplex correspond to the vanishing of some of the probabilities. In biological terms, when a probability vanishes, the corresponding allele has disappeared from the population. As long as there is more than one allele left, the probabilities continue to evolve. Thus, we get not only a flow in the interior of the simplex, but also flows within all the boundary strata. The key issue then is to connect these flows in an analytical, geometric, or stochastic manner.

Before going into further details, however, we should point out that the diffusion approximation leads to two different partial differential equations, the Kolmogorov forward or Fokker–Planck equation on one hand and the Kolmogorov backward equation on the other hand. While these two equations are connected by a duality

relation, their analytical behavior is different, in particular at the boundary. The Kolmogorov forward equation yields the future distribution of the alleles in a population evolving from a current one. In contrast, the Kolmogorov backward equation produces the probability distribution of ancestral states giving rise to a current distribution. See for instance [94]; a geometric explanation of the analogous situation in the discrete case is developed in Sect. 4.2 of [73].

The distribution produced by the Kolmogorov backward equation may involve states with different numbers of alleles present. Their ancestral distributions, however, do not interfere, regardless of the numbers of alleles they involve. Thus, some superposition principle holds, and the Kolmogorov backward equation nicely extends to the boundary. For the Kolmogorov forward equation, the situation is more subtle. Here, the probability of some boundary state does not only depend on the flow within the corresponding boundary stratum, but also on the distribution in the interior, because at any time, there is some probability that an interior state loses some allele and turns into a boundary state. Thus, there is a continuous flux into the boundary strata from the interior. Therefore, the extension of the flow from the interior to the boundary strata is different from the intrinsic flows in those strata, and no superposition principle holds.

As we have already said, there are several solution schemes for the Kolmogorov forward equation in the literature. For the Kolmogorov backward equation, the situation is even better. The starting point of much of the literature was the observation of Wright [126] that when one includes mutation, the degeneracy at the boundary is removed. And when the probability of a mutation of allele i into allele j depends only on the target j, then the backward process possesses a unique stationary distribution, at least as long as those mutation rates are positive. This then lead to explicit representation formulas for even more general diffusion processes, in [25, 27, 35, 53, 54, 86, 105, 106, 112]; these, however, were rather of a local nature, as they did not connect solutions in the interior and in boundary strata of the domain. Finally, much useful information can be drawn from the moment duality [68] between the Wright–Fisher model and the Kingman coalescent [81], see for instance [26] and the literature cited there. The *duality method* transforms the original stochastic process into another, simpler stochastic process. In particular, one can thus connect the Wright–Fisher processes and its extension with ancestral processes such as Kingman's coalescent [81], the method of tracing lines of descent back into the past and analyzing their merging patterns (for a brief introduction, see also [73]; for an application to Wright–Fisher models cf. [88]). Some of these formulas, in particular those of [35, 106] also pertain to the limit of vanishing mutation rates. In [106], a superposition of the contributions from the various strata was achieved whereas [35] could write down an explicit formula in terms of a Dirichlet distribution. However, this Dirichlet distribution and the measure involved both become singular when one approaches the boundary. In fact, Shimakura's formula is simply a decomposition into the various modes of the solutions of a linear PDE, summed over all faces of the simplex; this illustrates the rather local character of the solution scheme.

Some ideas from statistical mechanics are already contained in the free fitness function introduced by Iwasa [67] as a consequence of H-theorems. Such ideas will be developed here within the modern theory of free energy functionals. A different approach from statistical mechanics which can also produce explicit formulae involves master equations for probability distributions; they have been applied to the Moran model [89] of population genetics in [65]. That model will be briefly described in Sect. 2.4.

Large deviation theory has been systematically applied to the Wright–Fisher model by Papangelou [96–100], although this is usually not mentioned in the literature. In Chap. 7, we can build upon his work.

As already mentioned, the Kolmogorov equations of the Wright–Fisher model are not accessible to standard stochastic theory, because of their boundary behavior. In technical terms, the square root of the coefficients of the second order terms of the operators is not Lipschitz continuous up to the boundary. As a consequence, in particular the uniqueness of solutions to the above Kolmogorov backward equations may not be derived from standard results.

In this situation, Epstein and Mazzeo [29–31] have developed PDE techniques to tackle the issue of solving PDEs on a manifold with corners that degenerate at the boundary with the same leading terms as the Kolmogorov backward equation (1.2.5) for the Wright–Fisher model in the closure of the probability simplex in $(\overline{\Delta}_n)_{-\infty} = \overline{\Delta}_n \times (-\infty, 0)$. Such an analysis had been started by Feller [43] (and essentially also [42]), who had considered equations of the form

$$\frac{\partial}{\partial t} f(x,t) = x \frac{\partial^2}{\partial x^2} f(x,t) + b \frac{\partial}{\partial x} f(x,t) \text{ for } x \geq 0 \tag{1.3.1}$$

with $b \geq 0$, that is, equations that have the same singularity at the boundary $x = 0$ as the Fokker–Planck or Kolmogorov forward equation of the simplest type of the Wright–Fisher model. Feller could compute the fundamental solution for this problem and thereby analyze the local behavior near the boundary. In particular, the case where $b \to 0$ is subtle; in biological terms, this corresponds to the transition from a setting with mutation to one without, and without mutation, the boundary becomes absorbing. For more recent work in this direction, see for instance [21]. In any case, this approach which focusses on the precise local analysis at the boundary and which only requires a particular type of asymptotics near the boundary and can therefore apply general tools from analysis, should be contrasted with Kimura's who looked for global solutions in terms of expansions in terms of eigenfunctions and which needs the precise algebraic structure of the equations. Epstein and Mazzeo [29, 30] then take up the local approach and develop it much further. A main achievement of their analysis is the identification of the appropriate function spaces. These are anisotropic Schauder spaces. In [31], they develop a different PDE approach and derive and apply a Moser type Harnack inequality, that is, the probably most powerful general tool of PDE theory for studying the regularity of solutions of partial differential equations. According to general results in PDE theory, such a Harnack inequality follows when the underlying metric and

measure structure satisfy a Poincaré inequality and a measure doubling property, that is, the volume of a ball of radius $2r$ is controlled by a fixed constant times the volume of the ball of radius r with the same center, for all (sufficiently small) $r > 0$. Since in the case that we are interested in, that of the Wright–Fisher model, we identify the underlying metric as the standard metric on the unit sphere, such properties are natural in our case. Also, in our context, their anisotropic Schauder spaces $C^{k,\gamma}_{WF}(\overline{\Delta}_n)$ would consist of k times continuously differentiable functions whose kth derivatives are Hölder continuous with exponent γ w.r.t. the Fisher metric (a geometric concept to be explained below which is basic for our approach). In terms of the Euclidean metric on the simplex, this means that a weaker Hölder exponent (essentially $\frac{\gamma}{2}$) is required in the normal than in the tangential directions at the boundary. Using this framework, they subsequently show that if the initial values are of class $C^{k,\gamma}_{WF}(\overline{\Delta}_n)$, then there exists a unique solution in that class. This result is very satisfactory from the perspective of PDE theory (see e.g. [72]). Our setting, however, is different, because the biological model forces us to consider discontinuous boundary transitions. The same also applies to other works which treat uniqueness issues in the context of degenerate PDEs, but are not adapted to the very specific class of solutions at hand. This includes the extensive work by Feehan [41] where—amongst other issues—the uniqueness of solutions of elliptic PDEs whose differential operator degenerates along a certain portion of the boundary $\partial_0\Omega$ of the domain Ω is established: For a problem with a partial Dirichlet boundary condition, i.e. boundary data are only given on $\partial\Omega \setminus \partial_0\Omega$, a so-called second-order boundary condition is applied for the degenerate boundary area; this is that a solution needs to be such that the leading terms of the differential operator continuously vanishes towards $\partial_0\Omega$, while the solution itself is also of class C^1 up to $\partial_0\Omega$. Within this framework, Feehan then shows that—under certain natural conditions—degenerate operators satisfy a corresponding maximum principle for the partial boundary condition, which assures the uniqueness of a solution. Again, our situation is subtly different, as the degeneracy behaviour at the boundary is stepwise, corresponding to the stratified boundary structure of the domain $\overline{\Delta}_n$, and hence does not satisfy the requirements for Feehan's scenario. Furthermore, in the language of [41], the intersection of the regular and the degenerate boundary part $\partial\partial_0\Omega$, would encompass a hierarchically iterated boundary-degeneracy structure, which is beyond the scope of that work.

Finally, we should mention that the differential geometric approach to the Wright–Fisher model was started by Antonelli–Strobeck [5]. This was further developed by Akin [2].

1.4 Synopsis

We now briefly describe, in somewhat informal terms, our approach and results.

Again, we begin with the case of a single locus. As already indicated, we consider the relative frequencies or probabilities $p^0, \dots, p^n$ on the set $\{0, 1, \dots, n\}$ of possible

alleles at our locus. This leads to the simplex

$$\overline{\Sigma}^n := \left\{ (p^0, p^1, \ldots, p^n) : p^i \geq 0 \text{ for all } i, \sum_{i=0}^{n} p^i = 1 \right\}$$

of probability distributions on a set of $n + 1$ elements. This means that when $p \in \overline{\Sigma}^n$ and we draw an allele according to the probability distribution p, we obtain i with probability p^i. The various faces of $\overline{\Sigma}^n$ then correspond to configurations where some alleles have probability 0. Again, when we take the probabilities as relative frequencies, this means that the corresponding alleles are not present in the population. Concerning the oscillation between relative frequencies and probabilities, the situation is simply that the relative frequencies of the alleles in one generation determine the probabilities with which they are represented in the next generation according to our sampling procedure. And in the most basic model, we sample according to the multinomial distribution with replacement.

A fundamental observation is that there exists a natural Riemannian metric on the probability simplex $\overline{\Sigma}^n$. This metric is *not* the Euclidean metric of the simplex, but rather the Fisher metric. *Fisher* here stands for the same person as the originator of the Wright–Fisher model, but this metric did not emerge from his work on population genetics, but rather from his work on parametric statistics, and apparently, he himself did not realize that this metric is useful for the model. In fact, the Fisher metric was developed not really by Fisher himself, but rather by the statistician Rao [102]. The Fisher metric is a basic subject of the field of information geometry that was created by Amari, Chentsov, and others. Information geometry, that is, the theory of the geometry of probability distributions, deals with a geometric structure that not only involves a Riemannian metric, but also two dually affine structures which are generated by potential functions that generalize the entropy and the free energy of statistical mechanics. We refer to the monographs [3, 10].

It will appear that the Fisher metric becomes singular on the boundary of the probability simplex $\overline{\Sigma}^n$. These singularities, however, are only apparent, and they only indicate that from a geometric perspective, we have chosen the wrong parametrization for the family of probability distributions on $n+1$ possible types. In fact, as we shall see in Chap. 3, a better parametrization uses the positive sector S^n_+ of the n-dimensional unit sphere. (This parametrization is obtained by $p^i \mapsto q^i = (p^i)^2$ for a probability distribution $(p^0, p^1, \ldots, p^n)$ on the types $0, 1, \ldots, n$.) With that parametrization, the Fisher metric of $\overline{\Sigma}^n$ is nothing but the Euclidean metric on $S^n \hookrightarrow \mathbb{R}^{n+1}$, which, of course, is regular on the boundary of S^n_+.

More generally, the Fisher metric on a parametrized family of probability distributions measures how sensitively the family depends on the parameter when sampling from the underlying probability space. The higher that sensitivity, the easier is the task of estimating that parameter. That is why the Fisher metric is important for parametric statistics. For multinomial distributions, the Fisher metric is simply the inverse of the covariance matrix. This indicates on one hand that the Fisher metric is easy to determine, and on the other hand that it is naturally

associated to our iterated sampling from the multinomial distribution. In fact, the Kolmogorov equations can naturally be interpreted as diffusion equations w.r.t. the Fisher metric. One should note, however, that the Kolmogorov equations are not in divergence form, and therefore, they do not constitute the natural heat equation for the Fisher metric, or in other words, they do not model Brownian motion for the Fisher metric. They rather have to be interpreted in terms of the dually affine connections of Amari and Chentsov that we mentioned earlier. From that perspective, entropy functions emerge as potentials. In particular, this will provide us with a beautiful geometric approach to the exit times of the process, that is, the expected times of allele losses from the population. When considering so-called exponential families (called Gibbs distributions in statistical mechanics), information geometry also naturally connects with the basic quantities of statistical mechanics. These are entropy and free energy. As is well known in statistical mechanics, the free energy functional and its derivatives encode all the moments of a process. We shall make systematic use of this powerful scheme, and also indicate some connections to recent research in stochastic analysis. In Chap. 7, we shall explore large deviation principles in the context of the Wright–Fisher model. Moreover, the geometric structure behind the Kolmogorov equations will also guide our analysis of the transitions between the different boundary strata of the simplex. This will constitute our main technical achievement.

As discussed, the key is the degeneracy at the boundary of the Kolmogorov equations. While from an analytical perspective, this presents a profound difficulty for obtaining boundary regularity of the solutions of the equations, from a biological or geometric perspective, this is very natural because it corresponds to the loss of some alleles from the population in finite time by random drift. And from a stochastic perspective, this has to happen almost surely. For the Kolmogorov forward equation, in Chap. 8, we gain a global solution concept from the equations for the moments of the process, which incorporate the dynamics on the entire simplex, including all its boundary strata. This also involves the duality between the Kolmogorov forward equation and the Kolmogorov backward equation. In Chap. 9, we then develop a careful notion of hierarchically extended solutions of the Kolmogorov backward equation, and we show their uniqueness both in the time dependent and in the stationary case. The stationary case is described by an elliptic equation whose solutions arise from the time dependent equation as time goes to infinity.[2] The stationary equation is important because, for instance, the expected times of allele loss are solutions of an inhomogeneous stationary equation. From our information geometric perspective, as already mentioned, we can interpret these solutions most naturally in terms of entropies.

[2] In fact, one might be inclined to say that time goes to minus infinity in the backward case, because this corresponds to the infinite past. With this time convention, however, the Kolmogorov backward equation is not parabolic. When we change the direction of time, it becomes parabolic, and we can then speak of time going to infinity. This mathematically natural, although not compatible with the biological interpretation.

In Chap. 10, we shall explore how the schemes developed in this book, namely the moment equations and free energy schemes, information geometry, the expansions of solutions of the Kolmogorov equations in terms of Gegenbauer polynomials, will provide us with computational tools for deriving formulas for basic quantities of interest in population genetics.

We mainly focus on the basic Wright–Fisher model in the absence of additional effects like selection or mutation. Nevertheless, we shall describe, in line with the standard literature, how this will modify the equations. Also, in Sect. 6.1, we shall systematically apply the moment generating function and energy functional method to those issues. The issue of recombination will be treated in more detail in Chap. 5 because here our geometric approach on one hand leads to an important simplification of Kimura's original treatment and on the other hand also provides general insight into the geometry of linkage equilibria.

Chapter 2
The Wright–Fisher Model

2.1 The Wright–Fisher Model

The Wright–Fisher model considers the effects of sampling for the distribution of alleles across discrete generations. Although the model is usually formulated for diploid populations, and some of the interesting effects occurring in generalizations depend on that diploidy, the formal scheme emerges already for haploid populations. In the basic version, with which we start here, there is a single genetic locus that can be occupied by different alleles, that is, alternative variants of a gene.[1] In the haploid case, it is occupied by a single allele, whereas in the diploid case, there are two alleles at the locus. Biologically, diploidy expresses the fact that one allele is inherited from the mother and the other from the father. However, the distinction between female and male individuals is irrelevant for the basic model. In biological terminology, we thus consider monoecious (hermaphrodite) individuals. Inheritance is then symmetric between the parents, without a distinction between fathers and mothers. Consequently, it does not matter from which parent an allele is inherited, and there will be no effective difference between the two alleles at a site, that is, their order is not relevant. Even in the case of dioecious individuals, one might still make the simplifying assumption that it does not matter whether an allele is inherited from the mother or the father. While there do exist biological counterexamples, one might argue that for mathematical population genetics, this could be considered as a secondary or minor effect only. Nevertheless, it would not be overly difficult to extend the theory presented here to also include such effects.

Generalizations will be discussed subsequently, and we start with the simplest case. In particular, for the moment, we assume that there are no selective differences between these alleles and no mutations. These assumptions will be relaxed later, after we have understood the basic model.

[1] Obviously, the term "gene" is used here in a way that abstracts from most biological details.

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In order to have our conventions best adapted to the diploid case, we consider a population of $2N$ alleles. In the haploid case, we are thus dealing with $2N$ individuals, each carrying a single allele, whereas in the diploid case, we have N individuals carrying two alleles each.

For each of these alleles, there are $n+1$ possibilities. We begin with the simplest case, $n = 1$, where we have two types of alleles A^0, A^1. In the diploid case, an individual can be a homozygote of type A^0A^0 or A^1A^1 or a heterozygote of type A^0A^1 or A^1A^0—but we do not care about the order of the alleles and therefore identify the latter two types. The population reproduces in discrete time steps. In the haploid case, each allele in generation $m+1$ is randomly and independently chosen from the allele population of generation m. In the diploid case, each individual in generation $m+1$ inherits one allele from each of its parents. When a parent is a heterozygote, each allele is chosen with probability $1/2$. Here, for each individual in generation $m+1$, randomly two parents in generation m are chosen. All the choices are independent of each other. Thus, the alleles in generation $m+1$ are chosen by random sampling with replacement from the ones in generation m. In this model, the two parents of any particular individual might be identical (that is, in biological terminology, selfing is possible), but of course, the probability for that to occur goes to zero like $\frac{1}{N}$ when the population size increases. Also, each individual in generation m may foster any number of offspring between 0 and N in generation $m+1$ and thereby contribute between 0 and $2N$ alleles.

In any case, the model is not concerned with the lineage of any particular individual, but rather with the relative frequencies of the two alleles in each generation. Even though the diploid case appears more complicated than the haploid one, at this stage, the two are formally equivalent, because in either case the $2N$ alleles present in generation $m+1$ are randomly and independently sampled from those in generation m. In fact, from a mathematical point of view, the individuals play no role, and we are simply dealing with multinomial sampling in a population of $2N$ alleles belonging to $n+1$ different classes. The only reason at this stage to talk about the diploid case is that that case will offer more interesting perspectives for generalization below.

The quantity of interest therefore is the number[2] Y_m of alleles A^0 in the population at time m. This number then varies between 0 and $2N$. The distribution of allele numbers thus follows the binomial distribution. When $n > 1$, the principle remains the same, but we need to work more generally with the multinomial distribution. We shall now discuss the basic properties of that distribution.

[2]The random variable Y will carry two different indices in the course of our text. Sometimes, the index m is chosen to indicate the generation time, but at other occasions, we rather use the index $2N$ for the number of alleles in the population, that is, more shortly, (twice) the population size.

2.2 The Multinomial Distribution

We consider the basic situation of probabilities $p^0, \dots, p^n$ on the set $\{0, 1, \dots, n\}$. That is, we consider the simplex

$$\overline{\Sigma}_n := \left\{ (p^0, p^1, \dots, p^n) : p^i \geq 0 \text{ for all } i, \sum_{i=0}^{n} p^i = 1 \right\}$$

of probability distributions on a set of $n+1$ elements. When we consider an element $p \in \overline{\Sigma}_n$ and draw one of those elements according to the probability distribution p, we obtain the element i with probability p^i.

For each time step of the Wright–Fisher model, we draw $2N$ times independently from such a distribution p, to create the next generation of alleles from the current one. Call the corresponding random variables Y^i_{2N}, standing for the number of alleles A^i drawn that way. We utilize the index $2N$ for the total number of alleles here as subsequently we wish to consider the limit $N \to \infty$. For simplicity, we shall write i in place of A^i. When we draw once, we obtain a single element i, that is, $Y^i_1 = 1$ and $Y^j_1 = 0$ for all $j \neq i$. Since that element had probability p^i, we have

$$\mathrm{E}(Y^i_1) = \mathrm{E}((Y^i_1)^2) = p^i \text{ for all } i, \text{ and } \mathrm{E}(Y^i_1 Y^j_1) = 0 \text{ for } j \neq i \tag{2.2.1}$$

and hence

$$\mathrm{Var}(Y^i_1) = p^i(1-p^i), \quad \mathrm{Cov}(Y^i_1 Y^j_1) = -p^i p^j \text{ for } i \neq j. \tag{2.2.2}$$

When we draw $2N$ times independently from the same probability distribution p, we consequently get for the corresponding random variables Y^i_{2N}

$$\mathrm{E}(Y^i_{2N}) = 2Np^i, \quad \mathrm{Var}(Y^i_{2N}) = 2Np^i(1-p^i), \quad \mathrm{Cov}(Y^i_{2N} Y^j_{2N}) = -2Np^i p^j \text{ for } i \neq j. \tag{2.2.3}$$

By the same kind of reasoning, we also get

$$\mathrm{E}((Y^i_{2N})^{\boldsymbol{\alpha}}) = O(2N) \tag{2.2.4}$$

for all other moments (where $\boldsymbol{\alpha}$ is a multi-index with $|\boldsymbol{\alpha}| \geq 3$ whose convention will be explained below in Sect. 2.11).

We also point out the following obvious lumping lemma.

Lemma 2.2.1 *Consider a map*

$$\begin{aligned} \ell : \quad & \overline{\Sigma}_n && \to \overline{\Sigma}_m \\ & (p^0, \dots, p^n) && \mapsto (q^0, \dots, q^m) \\ \text{with } \ & q^j = \textstyle\sum_{i=i_{j-1}+1,\dots,i_j} p^i \ \text{ where } i_0 = -1,\ i_m = n, \end{aligned} \tag{2.2.5}$$

that is, we lump the alleles $A^{i_{j-1}+1}, \ldots, A^{i_j}$ into the single super-allele B^j. Then the random variable Z^j_{2N} that records multinomial sampling from $\overline{\Sigma}_m$ is given by

$$Z^j_{2N} = \sum_{i=i_{j-1}+1,\ldots,i_j} Y^i_{2N}. \tag{2.2.6}$$

□

2.3 The Basic Wright–Fisher Model

For the Wright–Fisher model, we simply iterate this process across several generations. Thus, we introduce a discrete time m and let this time m now be the subscript for Y instead of the $2N$ that we had employed so far to indicate the total number of alleles present in the population. Instead of the absolute probabilities of multinomial sampling, we now need to consider the transition probabilities.

That is, when we know what the allele distribution at time m is and when we multinomially sample from that distribution, we want to know the probabilities for the resulting distribution at time $m + 1$. We also not only want to know the expectation values for the numbers of alleles—which remain constant in time—and the variances and covariances—which grow in time in the sense that if we start at time 0 and want to know the distribution at time m, the formulas in (2.2.3) acquire a factor m—, but we are now interested in the entire distribution of allele frequencies.

We recall that we have $n+1$ possible alleles $A^0, \ldots, A^n$ at a given locus, still in a diploid population of fixed size N. There are therefore $2N$ alleles in the population in any generation, so it is sufficient to focus on the number $Y_m = (Y^1_m, \ldots, Y^n_m)$ of alleles $A^1, \ldots, A^n$ at generation time m. Assume that $Y_0 = \eta_0 = (\{\eta^1_0, \ldots, \eta^n_0\})$ and that, as before, the alleles in generation $m + 1$ are derived by sampling with replacement from the alleles of generation m. Thus, the transition probability is given by the multinomial formula

$$\mathrm{P}(Y_{m+1} = y | Y_m = \eta) = \frac{(2N)!}{(y^0)!(y^1)! \ldots (y^n)!} \prod_{i=0}^{n} \left(\frac{\eta^i}{2N}\right)^{y^i}, \tag{2.3.1}$$

where

$$\eta, y \in S^{(2N)}_n = \left\{ \eta = (\eta^1, \ldots, \eta^n) : \eta^i \in \{0, 1, \ldots, 2N\}, \sum_{i=1}^{n} \eta^i \leq 2N \right\}$$

and

$$\eta^0 = 2N - |\eta| = 2N - \eta^1 - \ldots - \eta^n; \qquad y^0 = 2N - |y| = 2N - y^1 - \ldots - y^n.$$

In particular, if $\eta^j = 0$ for some j, then also

$$\mathrm{P}(Y_{m+1} = y | Y_m = \eta) = 0 \text{ whenever } y^j \neq 0, \tag{2.3.2}$$

and

$$\mathrm{P}(Y_{m+1} = y | Y_m = \eta) = \frac{(2N)!}{(y^0)!(y^1)! \dots (y^{j-1})!(y^{j+1})! \dots (y^n)!} \prod_{i \neq j} \left(\frac{\eta^i}{2N} \right)^{y^i}, \tag{2.3.3}$$

for $y^j = 0$. Thus, whenever allele j disappears from the population, we simply get the same process with one fewer allele. Iteratively, we can let n alleles disappear so that only one allele remains which will then live on forever.

Returning to the general case, we then also have the probability

$$\begin{aligned} \mathrm{P}(Y_{m+1} = y | Y_0 = \eta) = \sum_{\eta_1, \dots, \eta_m} & \mathrm{P}(Y_{m+1} = y | Y_m = \eta_m) \, \mathrm{P}(Y_m = \eta_m | Y_{m-1} = \eta_{m-1}) \\ & \dots \mathrm{P}(Y_1 = \eta_1 | Y_0 = \eta). \end{aligned} \tag{2.3.4}$$

This is the probability for finding the allele distribution y at generation $m + 1$ when the process started with the distribution η at generation 0. In order to go from time 0 to time $m + 1$, we sum over all possibilities at intermediate times. This is also called the Chapman–Kolmogorov equation.

In terms of this probability distribution, we can express moments as

$$\mathrm{E}((Y_{m+1})^\alpha | Y_0 = \eta) = \sum_y y^\alpha \, \mathrm{P}(Y_{m+1} = y | Y_0 = \eta), \tag{2.3.5}$$

assuming that the process started with the allele distribution η at time 0.

From (2.2.3), we have

$$\mathrm{E}(Y_{m+1} | Y_m = \eta_m) = \eta_m, \tag{2.3.6}$$

and iterating (2.3.6), we get

$$\mathrm{E}(Y_{m+1} | Y_0 = \eta) = \eta. \tag{2.3.7}$$

In particular, by (2.3.6), the expected allele distribution at generation $m + 1$ equals the allele distribution at generation m, and the iteration (2.3.7) then tells us that it also equals the allele distribution at generation 0. Thus, the expected value does not change from step to step. This, or more precisely (2.3.6), is also called the martingale property.

In order to prepare for the limit $N \to \infty$, we rescale

$$t = \frac{m}{2N}, \text{ and hence } \delta t = \frac{1}{2N}, \quad X_t = \frac{Y_{2Nt}}{2N}. \tag{2.3.8}$$

We then get a discrete Markov chain X_t valued in $\left\{0, \frac{1}{2N}, \ldots, 1\right\}^n$ with $t = 1$ for X now corresponding to $2N$ generations for Y. With $X_{t+\delta t} = X_t + \delta X_t$, we then have from (2.3.5)

$$\mathrm{E}((X_{t+\delta t})^{\boldsymbol{\alpha}} | X_0 = x_0) = \sum_x x^{\boldsymbol{\alpha}} \, \mathrm{P}(X_{t+\delta t} = x | X_0 = x_0) \tag{2.3.9}$$

where

$$\mathrm{P}(X_{t+\delta t} = x | X_0 = x_0) = \mathrm{P}(Y_{m+1} = y | Y_0 = \eta) \tag{2.3.10}$$

and as in (2.2.3)

$$\mathrm{E}(\delta X_t^i) = 0, \tag{2.3.11}$$

$$\mathrm{E}(\delta X_t^i . \delta X_t^j) = X_t^i(\delta_{ij} - X_t^j)\delta t = \frac{1}{2N} X_t^i(\delta_{ij} - X_t^j), \tag{2.3.12}$$

noting that each time only one allele is drawn so that $\mathrm{E}(X_t^i X_t^j) = 0$ for $i \neq j$. Also, from (2.2.4) and (2.3.8),

$$\mathrm{E}(\delta X_t)^{\boldsymbol{\alpha}} = o(\delta t) = o(\frac{1}{N}) \quad \text{for } |\boldsymbol{\alpha}| \geq 3. \tag{2.3.13}$$

We now denote by $m_{\boldsymbol{\alpha}}(t)$ the $\boldsymbol{\alpha}$th-moment of the distribution at the tth generation, i.e.,

$$m_{\boldsymbol{\alpha}}(t) = \mathrm{E}(X_t)^{\boldsymbol{\alpha}} \tag{2.3.14}$$

Then

$$m_{\boldsymbol{\alpha}}(t + \delta t) = \mathrm{E}(X_t + \delta X_t)^{\boldsymbol{\alpha}} \tag{2.3.15}$$

Expanding the right hand side and noting (2.3.11)–(2.3.13), we obtain the following recursion formula, under the assumption that the population number N is sufficiently large to neglect terms of order $\frac{1}{N^2}$ and higher,

$$m_{\boldsymbol{\alpha}}(t + \delta t) = \left\{ 1 - \frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}| - 1)}{2} \right\} m_{\boldsymbol{\alpha}}(t) + \sum_{i=1}^{n} \frac{\alpha_i(\alpha_i - 1)}{2} m_{\boldsymbol{\alpha} - e_i}(t) \tag{2.3.16}$$

Under this assumption, the moments change very slowly per generation and we can replace this system of difference equations by a system of differential equations:

$$\dot{m}_{\boldsymbol{\alpha}}(t) = -\frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1)}{2} m_{\boldsymbol{\alpha}}(t) + \sum_{i=1}^{n} \frac{\alpha_i(\alpha_i-1)}{2} m_{\boldsymbol{\alpha}-e_i}(t). \tag{2.3.17}$$

2.4 The Moran Model

There is a variant of the Wright–Fisher model, the Moran model [89], that instead of updating the population in parallel does so sequentially. When we shall pass to the continuum limit below, the two models will have the same limits, and therefore succumb to the same analysis. The Moran model will be useful for understanding the relation with the Kingman coalescent below.

In order to introduce the Moran model, we slightly change the interpretation of the Wright–Fisher model. Instead of letting members of the population produce offspring, we simply replace them by other individuals from the population. Thus, at every generation, for each individual in the population, randomly some individual is chosen, possibly the original individual itself, that replaces it. If we do that for all individuals simultaneously, we obtain a process that is equivalent to the Wright–Fisher process. But then, instead of updating all individuals simultaneously, we can also do that sequentially. Thus, for the Moran model, at a random time, we randomly select one individual in the population and replace by some other random individual.

Thus, if there are η^k carriers of allele A^k in a population of haploid individuals of size $2N$, then the chance that a carrier of A^i is chosen for replacement is $\frac{\eta^i}{2N}$, and the chance that it is replaced by an individual of type A^j is $\frac{\eta^j}{2N}$. Thus, altogether, we have that the probability of having a transition from a carrier of A^i to one of A^j is

$$\frac{\eta^i}{2N}\frac{\eta^j}{2N}. \tag{2.4.1}$$

The expected number of individuals of type A^j after such a transition is

$$\sum_{i=0}^{n} \frac{\eta^i}{2N}\frac{\eta^j}{2N} = \frac{\eta^j}{2N}, \tag{2.4.2}$$

that is, this expected number is not affected by the transition. Thus, we can let the process run and each random time, selected at some rate λ, we can do such a transition.

More generally, the arguments leading to (2.2.1) and (2.2.2) apply, and we therefore get the same results for the variances and covariances as for the Wright–Fisher model when we do this random updating $2N$ times.

2.5 Extensions of the Basic Model

We return to the basic Wright–Fisher model and want to discuss how this model is modified when mutation and/or selection effects are included. From the discussion in Sect. 2.4 it is clear that we shall get analogous results for the Moran model.

In order to have a framework for naturally including mutation and selection, instead of (2.3.1), we write

$$\mathrm{P}(Y_{m+1} = y | Y_m = \eta) = \frac{(2N)!}{(y^0)!(y^1)!\dots(y^n)!} \prod_{i=0}^{n} \left(\psi^i(\eta)\right)^{y^i}, \tag{2.5.1}$$

where the ψ^i which replace $\frac{\eta^i}{2N}$ in (2.3.1) now should include those effects. The rationale is this. In the original model (2.3.1), $\frac{\eta^i}{2N}$ simply was the chance to find the allele A^i when randomly picking an allele from the pool. When the alleles can mutate before sampling (since we let the processes of sampling and mutation alternate, their order plays no role), that probability is increased or decreased according to the net contribution of mutations to the frequency of A^i. When selection operates, the chance to pick A^i is multiplied by a factor that expresses its relative fitness in the population. In other words, the fitter alleles or allele combinations have a higher chance of being chosen than the less fit ones. In order to incorporate selection effects in a simple mathematical model, we shall need to make some assumptions that simplify the biology.

Let us begin with mutation. Let $\frac{\vartheta_{ij}}{2}$ be the fraction of alleles A^i that mutate into allele A^j in each generation. (The factor $\frac{1}{2}$ is introduced here for convenience in Sect. 6.2 below.) For convenience, we put $\vartheta_{ii} = 0$. Then $\frac{\eta^i}{2N}$ needs to be replaced by

$$\psi^i_{\mathrm{mut}}(\eta) := \frac{2\eta^i - \sum_{j=0}^{n} \vartheta_{ij}\eta^i + \sum_{j=0}^{n} \vartheta_{ji}\eta^j}{4N}, \tag{2.5.2}$$

to account for the net effect of A^i mutating into some other A^j and conversely, for some A^j mutating into A^i. When there is no mutation, then all $\vartheta_{ij} = 0$, and we have $\psi^i_{\mathrm{mut}}(\eta) = \frac{\eta^i}{2N}$, and we are back to (2.3.1).

It turns that the case where the mutation rate depends only on the target, while biologically not so realistic, is mathematically particularly convenient. In that case,

$$\vartheta_{ij} =: \vartheta_j \text{ for all } i \neq j, \tag{2.5.3}$$

and (2.5.2) becomes

$$\psi^i_{\mathrm{mut}}(\eta) = \frac{(2 - \sum_{j=0, j\neq i}^{n} \vartheta_j)\eta^i + \vartheta_i \sum_{j=0}^{n} \eta^j}{4N}. \tag{2.5.4}$$

We model selection by assigning to each allele pair A^iA^j a fitness coefficient $1+\sigma_{ij}$. This includes the special case where the fitness of allele A^i has a value $1+\sigma_i$ that does not depend on which other allele it is paired with; in that case, $1+\sigma_{ij}=\frac{1}{2}(1+\sigma_i)+\frac{1}{2}(1+\sigma_j)=1+\frac{\sigma_i+\sigma_j}{2}$ is the average of the fitness values of the two alleles. Thus, our convention is that the baseline fitness in the absence of selective differences is 1. This will be convenient in Chap. 4. We shall assume the symmetry

$$\sigma_{ij}=\sigma_{ji}. \tag{2.5.5}$$

Although there do exist some biological examples where one may argue that this is violated, in general this seems to be a biologically plausible and harmless assumption.

When such selective differences are present, $\frac{\eta^i}{2N}$ needs to be replaced by

$$\psi^i_{\mathrm{sel}}(\eta):=\frac{\sum_{j=0}^n(1+\sigma_{ij})\eta^i\eta^j}{\sum_{j,k=0}^n(1+\sigma_{jk})\eta^j\eta^k}. \tag{2.5.6}$$

When there are no selective differences, that is, $\sigma_{ij}=0$, then since $\sum_{j=0}^n\eta^j=2N$, we are again back to (2.3.1).

We should note that the absolute fitness $1+\sigma_{ij}$ of an allele pair A^iA^j thus depends only that allele pair itself, but not on the relative frequencies of these or other alleles in the population. Only the relative fitness $\frac{1+\sigma_{ij}}{\sum_{j,k=0}^n(1+\sigma_{jk})\eta^j\eta^k}$ depends on the composition of the population. This is clearly an assumption that excludes many cases of biological interest. For instance, the relative fitness of males and females depends on the sex ratio in the population.[3]

The combined effect of mutation and selection may depend on the order in which they occur. A natural assumption would be that selection occurs before mutation and sampling. In that case, η^j in (2.5.2) would have to be replaced by $\psi^j_{\mathrm{sel}}(\eta)$. Later on, when we compute moments, however, this will play no role, as the two effects will simply add to first order.

In any case, instead of (2.3.1), we now have

$$\mathrm{P}(Y_{m+1}=y|Y_m=\eta)=\frac{(2N)!}{(y^0)!(y^1)!\dots(y^n)!}\prod_{i=0}^n\left(\psi^i(\eta)\right)^{y^i}, \tag{2.5.7}$$

where $\psi^i(\eta)$ now incorporates the effects of mutation and selection. When no mutations occur and no selective differences exist, then $\psi^i(\eta)=\eta^i$, and we have the original model (2.3.1).

[3]This was already analyzed by Fisher [47]. See [74] for a systematic analysis.

Analogously to (2.2.1), we have

$$\mathrm{E}(Y^i_{m+1}|Y_m = \eta) = 2N\psi^i(\eta), \tag{2.5.8}$$

or equivalently, with $X_t = \frac{Y_t}{2N}$, $\delta X_t = X_{t+1} - X_t$ as before,

$$\mathrm{E}(\delta X^i_t) = \psi^i(x) - \frac{x^i}{2N}, \tag{2.5.9}$$

We shall assume that the mutation rates satisfy

$$\vartheta_{ij} = O(\frac{1}{N}) \tag{2.5.10}$$

and the selection coefficients $1 + \sigma_{ij}$ likewise satisfy

$$\sigma_{ij} = O(\frac{1}{N}) \tag{2.5.11}$$

for all i, j and large N, and we consequently define

$$\begin{aligned} &\theta_{ij} := 2N\vartheta_{ij}, \quad \theta_j := 2N\vartheta_j, \\ &s_{ij} := 2N\sigma_{ij}. \end{aligned} \tag{2.5.12}$$

Thus, since the σ_{ij} are symmetric, so are the s_{ij}, that is,

$$s_{ij} = s_{ji}. \tag{2.5.13}$$

We then have

$$\psi^i(x) = \frac{1}{2N}(x^i(1 + \sum_j s_{ij}x^j - \sum_{j,k} s_{jk}x^j x^k) - \sum_j \frac{\theta_{ij}}{2}x^i + \sum_j \frac{\theta_{ji}}{2}x^j) + o(\frac{1}{2N}). \tag{2.5.14}$$

This implies

$$\begin{aligned} \mathrm{E}(\delta X^i_t) = \psi^i(x) - x^i &= \frac{1}{2N}(x^i(\sum_j s_{ij}x^j - \sum_{j,k} s_{jk}x^j x^k) - \sum_j \frac{\theta_{ij}}{2}x^i + \sum_j \frac{\theta_{ji}}{2}x^j) \\ &\quad + o(\frac{1}{2N}) =: \frac{1}{2N}b^i(x) + o(\frac{1}{2N}). \end{aligned} \tag{2.5.15}$$

The vector $b^i(x)$ will later on determine the drift terms in the Kolmogorov equations.

We also get from (2.5.10), (2.5.11)

$$\mathrm{E}(\delta X_t^i \delta X_t^j)) = \frac{1}{2N} x^i(\delta_{ij} - x^j) + o(\frac{1}{N}) =: \frac{1}{2N} a^{ij}(x) + o(\frac{1}{2N}). \tag{2.5.16}$$

The terms $a^{ij}(x)$ will become the coefficients of the diffusion term in the Kolmogorov equations.

We also have

$$\mathrm{E}(\delta X_t)^{\boldsymbol{\alpha}} = o(\frac{1}{2N}) \text{ for } |\boldsymbol{\alpha}| \geq 3. \tag{2.5.17}$$

Thus, under the assumptions (2.5.10) and (2.5.11), the second and higher moments are the same, up to terms of order $o(\frac{1}{2N})$, as those for the basic model, see (2.3.12), (2.3.13).

Besides selection and mutation, there is another important ingredient in models of population genetics, recombination. That will be treated in Chap. 5.

2.6 The Case of Two Alleles

Before embarking upon the mathematical treatment of the general Wright–Fisher model in subsequent chapters, it might be useful to briefly discuss the case where we only have two alleles, A^0 and A^1. This is the simplest nontrivial case, and the mathematical structure is perhaps more transparent than in the general case.

We let x be the relative frequency of allele A^1. That of A^0 then is $1-x$. Likewise, we let y be the absolute frequency of A^1; that of A^0 then is $2N-y$. The corresponding random variables are denoted by X and Y. The multinomial formula (2.3.1) then reduces to the binomial formula

$$\mathrm{P}(Y_{m+1} = j | Y_m = i) = \binom{2N}{j} (\frac{i}{2N})^j (1 - \frac{i}{2N})^{2N-j} \text{ for } i, j = 0, \ldots, 2N. \tag{2.6.1}$$

Thus, in the absence of mutations and selection, the formulas (2.3.11), (2.3.12) become

$$\mathrm{E}(\delta X_t) = 0, \quad \mathrm{E}(\delta X_t)^2 = \frac{1}{2N} X_t(1 - X_t). \tag{2.6.2}$$

The moments

$$m_k(t) = \mathrm{E}(X_t)^k \tag{2.6.3}$$

then satisfy

$$\begin{aligned}\dot{m}_k(t) &= \frac{k(k-1)}{2}\mathrm{E}\Big(X_t(1-X_t)X_t^{k-2}\Big)\\ &= \frac{k(k-1)}{2}m_{k-1}(t) - \frac{k(k-1)}{2}m_k(t).\end{aligned} \tag{2.6.4}$$

We next look at the case with mutation, and we put $\mu := \theta_{10}, \nu := \theta_{01}$, that is, A^1 mutates to A^0 at the rate $\frac{\mu}{4N}$, and in turn A^0 mutates to A^1 at the rate $\frac{\nu}{4N}$. Then (2.5.14), (2.5.15) become (writing $b(x)$ in place of $b^1(x)$)

$$b_{\mathrm{mut}}(x) = \frac{\nu}{2} - \frac{\mu+\nu}{2}x. \tag{2.6.5}$$

In the case of selection, when the fitness values of A^0A^0, A^0A^1, A^1A^1 are $1+\frac{s}{2N}$, $1+\frac{hs}{2N}$ and 1, resp., (for instance, $h=\frac{1}{2}$), we get

$$b_{\mathrm{sel}}(x) = x(1-x)(h-1+x-2hx)s, \tag{2.6.6}$$

and if we have both mutation and selection,

$$b(x) = b_{\mathrm{mut}}(x) + b_{\mathrm{sel}}(x). \tag{2.6.7}$$

The diffusion coefficient is

$$a(x) = x(1-x). \tag{2.6.8}$$

Thus, altogether we have

$$\begin{aligned}\mathrm{E}(\delta X_t|X_t) &= \Big(\frac{\nu}{2} - \frac{\nu+\mu}{2}X_t + X_t(1-X_t)(h-1+X_t-2hX_t)s\Big)\delta t + o(\delta t),\\ \mathrm{E}((\delta X_t)^2|X_t) &= X_t(1-X_t)\delta t + o(\delta t),\\ \mathrm{E}((\delta X_t)^\alpha|X_t) &= o(\delta t), \quad \text{for } \alpha \geq 3.\end{aligned} \tag{2.6.9}$$

2.7 The Poisson Distribution

The Poisson distribution is a discrete probability distribution that models the number of occurrences of certain events which happen independently and at a fixed rate within a specified interval of time or space. This may be perceived as a limit

of binomial distributions with the number of trials N tending to infinity and a correspondingly rescaled success probability $p_N \in \mathcal{O}(\frac{1}{N})$.

The formal definition is that a discrete random variable X is said to be Poisson distributed with parameter $\lambda > 0$, if its probability mass function satisfies

$$P(X = k) = \frac{\lambda^k e^{-\lambda}}{k!} \quad \text{for } k \in \mathbb{N}. \tag{2.7.1}$$

We have

$$\begin{aligned} \mathrm{E}(X) &= \textstyle\sum_k k \frac{\lambda^k e^{-\lambda}}{k!} = \sum_k \lambda \frac{\lambda^{k-1} e^{-\lambda}}{(k-1)!} = \lambda \qquad (2.7.2) \\ \mathrm{E}(X^2) &= \textstyle\sum_k k^2 \frac{\lambda^k e^{-\lambda}}{k!} = \sum_k \lambda^2 \frac{\lambda^{k-2} e^{-\lambda}}{(k-2)!} + \sum_k \lambda \frac{\lambda^{k-1} e^{-\lambda}}{(k-1)!} = \lambda^2 + \lambda \end{aligned}$$

and hence

$$\mathrm{Var}(X) = \lambda. \tag{2.7.3}$$

2.8 Probabilities in Population Genetics

In this section we shall introduce some quantities which are important in population genetics and which we shall compute in Chap. 10 as applications of our general scheme. For the notation employed, please see Sect. 2.11.3 below.

2.8.1 The Fixation Time

In the basic Wright–Fisher model, that is, in the absence of mutations, the number of alleles will decrease as the generations evolve, and eventually, only one allele will survive. This allele then will be fixed in the population. One then is naturally interested in the time τ when the last non-surviving allele dies out. This is the fixation time, when a single allele gets fixed in the population. This fixation time is finite with probability 1, indeed, since we are working on a finite state space and the boundary is absorbing, that is,

$$\mathrm{P}(\tau < \infty) = \lim_{m \to \infty} \mathrm{P}(\tau \leq m) = \lim_{m \to \infty} \mathrm{P}(Y_m \in \{0, 2N\}) = 1. \tag{2.8.1}$$

2.8.2 The Fixation Probabilities

The calculation of the fixation probabilities of the individual alleles, that is, the probabilities with which each allele becomes the single surviving allele, is rather easy. In fact, from (2.3.7), we know that

$$\begin{aligned}\eta &= \mathrm{E}(Y_m|Y_0=\eta) = \mathrm{E}(Y_\tau\,\mathrm{P}(\tau<m)|Y_0=\eta) + \mathrm{E}(Y_m\,\mathrm{P}(\tau\geq m)|Y_0=\eta)\\ &\to \mathrm{E}(Y_\tau|Y_0=\eta) \text{ for } m\to\infty \end{aligned} \tag{2.8.2}$$

by (2.8.1). This means that the expected number of alleles A^j at τ is equal to η^j, and therefore their relative frequency is $\frac{\eta^j}{2N}$. Thus, the probability for finding allele A^j at the fixation time τ is $\frac{\eta^j}{2N}$.

2.8.3 Probability of Having $(k+1)$ Alleles (Coexistence)

Thus, when we start our population with $n+1$ alleles, eventually only one allele will survive, as all but one alleles will successively die out. Therefore, we would like to know, at an arbitrary generation, how many alleles are present. The corresponding probability is called the coexistence probability.

2.8.4 Heterozygosity

More precisely, we would also like to know the distribution of the alleles at each generation m. For that purpose, we consider the heterozygosity or genetic variability matrix with entries

$$h_m(i,j) = \frac{2Y_m^i Y_m^j}{2N(2N-1)} \tag{2.8.3}$$

which records the probability that two randomly drawn members of generation m carry the alleles A^i and A^j. When we have only two alleles A^1 and A^0 and Y stands for the number of A^1's, then the quantity reduces to

$$h_m = \frac{2Y(2N-Y)}{2N(2N-1)}, \tag{2.8.4}$$

the probability that two randomly drawn alleles are of different type. We then have $h_\tau = 0$ when τ is the fixation time.

2.8.5 Loss of Heterozygosity

In a diploid population, if an individual has two different alleles at a specific locus, we say the individual is heterozygous at that locus, and if the two alleles are the same, the individual is homozygous. The allele frequency is used to characterize the genetic diversity, or richness of the gene pool, in a population. The measure of the amount of heterozygosity across loci can be used as a general indicator of the amount of genetic variability. Loss of heterozygosity in the Wright–Fisher model results from the random genetic drift.

2.8.6 Rate of Loss of One Allele in a Population Having $(k+1)$ Alleles

When we are at a generation in which the population has only $k+1$ alleles, we would like to know how quickly one of the remaining alleles will be lost.

2.8.7 Absorption Time of Having $(k+1)$ Alleles

We denote by $T_{n+1}^{k+1}(p) = \inf\left\{t > 0 : X_t \in \overline{\partial_k \Delta_n} | X_0 = p\right\}$ the first time the population has at most $(k+1)$ alleles. $T_{n+1}^{k+1}(p)$ is a continuous random variable valued in $[0, \infty)$.

2.8.8 Probability Distribution at the Absorption Time of Having $(k+1)$ Alleles

$X_{T_{n+1}^{k+1}(p)}$ then is a random variable valued in $\overline{\partial_k \Delta_n}$. We consider its probability valued in $\Delta_k^{(\{i_0,\ldots,i_k\})}$, i.e., the probability distribution of the alleles in the population at the first time when at most $(k+1)$-alleles coexist. That is, we ask which alleles survive at that time and what their frequencies are.

2.8.9 Probability of a Particular Sequence of Extinction

Let $Q_{M,M-1,\ldots,2}(p^1, \ldots, p^M)$ be the probability that for a given initial allele frequencies $(p^1, \ldots, p^M)$, allele A^M becomes extinct first, followed by allele A^{M-1}, A^{M-2}

and so on, ending with fixation of allele A^1. This quantity encodes the order of the loss of alleles in a population.

2.9 The Kolmogorov Equations

In this section, we shall introduce the Kolmogorov equations which we shall derive in Sect. 4.2 as the diffusion approximations of Wright–Fisher models. There are two such equations, the Kolmogorov forward equation for the density function and the Kolmogorov backward equation for the ancestral state (cf. [82]).

Let us start with a brief description of the general theory. We consider a process $X(t) = (X^i(t))_{i=1,\dots,n}$ with values in $\Omega \subset \mathbb{R}^n$ and $t \in (t_0, t_1) \subset \mathbb{R}$ which satisfies the following conditions. Here, originally time t is discrete, but we want to pass to the continuum limit $\delta t \to 0$. The notation will be as in Sect. 2.3. In particular, we consider $2N \to \infty$ with $\delta t = \frac{1}{2N}$ as in (2.3.8).

$$\lim_{\delta t \to 0} \frac{1}{\delta t} \mathrm{E}_{\delta t}\big(\delta X^i \big| X(t) = x\big) =: b^i(x,t), \quad i = 1, \dots, n \tag{2.9.1}$$

and

$$\lim_{\delta t \to 0} \frac{1}{\delta t} \mathrm{E}_{\delta t}\big(\delta X^i \delta X^j \big| X(t) = x\big) =: a^{ij}(x,t), \quad i,j = 1, \dots, n \tag{2.9.2}$$

existing for all $(x,t) \in \Omega \times (t_0, t_1)$ and further

$$\lim_{\delta t \to 0} \frac{1}{\delta t} \mathrm{E}_{\delta t}\big((\delta X)^{\boldsymbol{\alpha}} \big| X(t) = x\big) = 0 \tag{2.9.3}$$

for all $(x,t) \in \Omega \times (t_0, t_1)$ and all multi-indices $\boldsymbol{\alpha} = (\alpha_1, \dots, \alpha_n)$ with $|\boldsymbol{\alpha}| \geq 3$. In the limit of continuous time and an infinite population, the probability density $f(p,s,x,t) := \frac{\partial^n}{\partial x^1 \cdots \partial x^n} P(X(t) \leq x | X(s) = p)$ with $s < t$ (if it exists and is smooth enough), then satisfies

- the *Kolmogorov forward equation* (also known as the *Fokker–Planck equation*)

$$\frac{\partial}{\partial t} f(p,s,x,t) = -\sum_{i=1}^{n} \frac{\partial}{\partial x^i} \Big(b^i(x,t) f(p,s,x,t) \Big) + \frac{1}{2} \sum_{i,j=1}^{n} \frac{\partial^2}{\partial x^i \partial x^j} \Big(a^{ij}(x,t) f(p,s,x,t) \Big), \tag{2.9.4}$$

- the *Kolmogorov backward equation*

$$-\frac{\partial}{\partial s}f(p,s,x,t) = \sum_{i=1}^{n} b^i(p,s)\frac{\partial}{\partial p^i}f(p,s,x,t) + \frac{1}{2}\sum_{i,j=1}^{n} a^{ij}(p,s)\frac{\partial^2}{\partial p^i \partial p^j}f(p,s,x,t) \tag{2.9.5}$$

with $(p,s),(x,t) \in \Omega \times (t_0,t_1)$ in each case.

The probability density function f as given here depends on two points in the state space (p,s) and (x,t) although either Kolmogorov equation only involves derivatives with respect to one of them (correspondingly, f needs to be of class C^2 with respect to the relevant spatial variables in Ω and of class C^1 with respect to the relevant time variable in (t_0,t_1)). In the theory of partial differential equations, the first order derivatives are called *drift terms* (with b^i being the *drift coefficients*), the second order derivatives *diffusion terms* (with *diffusion coefficients* a^{ij}). We should point out that this convention is the opposite of the biological interpretation, as the second order terms arise from random genetic drift whereas the first order terms represent diffusion effects due to such forces as mutation and selection. Nevertheless, we shall follow the PDE terminology.

By expressing the model through such partial differential equations for probability density functions rather than as a stochastic process, we shift from the consideration of random trajectories of the process to the *deterministic evolution* of a function which encodes the randomness of the process. This will allow us, in particular, a detailed treatment of the boundary behaviour and the hierarchical structure of the process.

2.10 Looking Forward and Backward in Time

When we have described the Wright–Fisher model in Sect. 2.3, we have essentially asked how a distribution of alleles in the population can be expected to evolve in the future. Let us normalize the starting time of the process to be 0, which we shall also call the present. We consider here the rescaled variables $X_m = \frac{Y_m}{2N}$, in order to be able to work on the probability simplex $\overline{\Sigma}_n$ (see (2.11.13)). Thus, given a frequency distribution $X_0 = x_0$, we ask about the probability distribution $\mathrm{P}(X_m|X_0 = x_0)$ for the random variable X_m for $m > 0$. Of course, instead of starting with a single value $X_0 = x_0$, we could also have a started with a probability distribution $\mathrm{P}(x_0)$ (see also (2.3.4)). The rescaling limit then yields the Kolmogorov forward equation. Its solution simply yields the probabilities for allele distribution at future times, in the rescaling limit of an infinite population evolving in continuous time. That is, it tells us the probabilities of the various possible future states when we know with which probabilities we started at time 0. And even if we start with a distribution with non-vanishing frequencies for all alleles $A^0,\ldots,A^n$, that is, with

an initial condition in the interior Σ_n of the probability simplex, after some time, one or more alleles may get lost, and we land in the boundary of the simplex. In the absence of mutations, we can then never come back into the interior. This happens almost surely along any sample path, and since the dynamics continues to follow the same pattern in any boundary face, the allele loss gets repeated, until only one allele survives, and we end up in one of the corners of the simplex. We can also look into the future at the population level. We can ask about the probabilities for the offspring of each population member several generations from now. But in the absence of selective differences, this is trivial. Each individual has the same chance of producing offspring. Since, in the finite population case, the size of the generation is fixed, when one individual produces more offspring, others can correspondingly produce only less. Eventually, the offspring of a single individual will cover the entire population.

But we can also look backward in time. Given again a current state at time 0, we can ask about the probabilities of various ancestral states to have given rise to that current state. Knowing the current state, we can neither determine its future nor its past precisely, but can compute only the probabilities of future and past states. Let us first look at the population level. Here, we can ask whether two individuals in the current generation had the same ancestor in some past generation, or more precisely, we can compute the probabilities for two or more individuals to have the same ancestor ℓ generations back into the past. And we can ask how many generation we have go back into the past at least so that all members of the current generation descend from a single ancestor, that is, to find the most recent common ancestor (MRCA). The resulting stochastic process is Kingman's coalescent [81]; see Sect. 4.4 for some more details (a concise discussion can also be found in [73]).

Again, we can also ask about probability distributions for the allele frequencies in the past. In the continuum limit, this is described by the Kolmogorov backward equation. Thus, when we assume a definite state at time 0, we can ask about the probabilities for its various ancestral states. The Kolmogorov backward equation will then show how those ancestral probabilities evolve as time is running backward, hence the name. This will reveal the same characteristics as in the forward case: When we let any particular ancestral state evolve in turn, then, with some probability, it will lose some alleles, that is, move into the boundary of the simplex before reaching the present. While in the forward case such allele is simply lost and does no longer influence the process, the backward case is somewhat asymmetric as the absorption into the boundary will also make itself felt in the interior. Hence, it is crucial whether our final condition, a probability distribution for relative frequencies at time 0, also encompassed boundary strata, that is, states where one or more alleles are lost. Of course, when the final condition is a definite state in the interior, that is, we assume in particular that no allele loss has happened, then nothing could have flown into the boundary. In general, however, the possibility of allele loss in the past leads to some difficulties in the analysis of the backward equation, see Chap. 9.

2.11 Notation and Preliminaries

In the last section of the current chapter, we systematically assemble some notation. Random variables have already occurred above when we formally introduced the basic Wright–Fisher model, but it should nevertheless be useful for the reader to have all relevant notations in a single place. We then collect the notation for moment generating functions which will also play an important role in subsequent chapters. Finally, we introduce some notation concerning the geometry of the standard simplex and its various faces, as well as for certain function spaces that are adapted to that geometry.

We often employ a multi-index notation. Thus, $\boldsymbol{\alpha} = (\alpha^0, \ldots, \alpha^n)$ is a multiindex with $n+1$ (the number of alleles present) nonnegative integer entries. We also put $|\boldsymbol{\alpha}| = \sum \alpha^i$. $X^{\boldsymbol{\alpha}}$ then stands for $\prod_i (X^i)^{\alpha^i}$, when $X = (X^0, \ldots, X^n)$.

2.11.1 Notation for Random Variables

We start with some notations.

We may have either integer times $m \in \mathbb{N}$ or real times $t \in \mathbb{R}^+$. Time is represented by a subscript. So, Z_m or Z_t is the value of the random process Z at time m or t.

We usually consider a population of N diploid individuals. Thus, in the single locus case, when every individual carries two alleles, we have a population of $2N$ alleles.

The random variable Y denotes allele frequencies, whereas X denotes relative frequencies. When we have alleles $A^0, \ldots, A^n$ at a single locus, their frequencies are given by $Y = (Y^0, \ldots, Y^n)$. Thus, $\sum_{i=0}^n Y^i = 2N$. The corresponding relative frequencies are given by $X^i = \frac{1}{2N} Y^i$. Thus, $\sum_{i=0}^n X^i = 1$.

We usually write $p(y^0, \ldots, y^n) = \mathrm{P}(Y^0 = y^0, \ldots, Y^n = y^n)$ for the probability that the components of the random variable Y take the values y^i. We shall employ the same notation for different random variables. Thus, p or P do not denote specific functions, but stand for the generic assignment of probabilities. Which random variable is meant will be clear from the variable names and the context.

When we have several loci $\mu = 1, \ldots, k$ and possible alleles $A_\mu^{i_\mu}$ at locus μ, we denote the (relative) frequencies by $Y^{i_1 \ldots i_k}$ ($X^{i_1 \ldots i_k}$). In contrast, when we consider the allele combinations at the loci of diploid individuals, we write Y^i_j or X^i_j for the (relative) frequencies of the combination of alleles i and j in an individual. We usually ignore the order, that is, we identify the combinations $\binom{i}{j}$ and $\binom{j}{i}$. Thus, $\sum_{i,j} Y^i_j = \frac{1}{2} \sum_\ell Y^\ell = N$ and $\sum_{i,j} X^i_j = 1$.

Turning to the special case of two loci with two alleles each, we denote the alleles at the first locus by A^0, A^1, and those at the second locus by B^0, B^1. Moreover, we

write for the allele combinations

$$G^0 = (A^0, B^0),\ G^1 = (A^0, B^1),\ G^2 = (A^1, B^0),\ G^3 = (A^1, B^1) \tag{2.11.1}$$

and thus get the corresponding relative frequencies $X^0 = X^{00}, X^1 = X^{01}, X^2 = X^{10}$, $X^3 = X^{11}$. We also put $i' = 0(1)$ if $i = 1(0)$ and write

$$D^{ij} = X^{ij}X^{i'j'} - X^{ij'}X^{i'j}.$$

When we use the G^ℓs, we also write $D^\ell := D^{ij}$ when $G^\ell = (A^i, B^j)$.

Subsequently, we shall often abbreviate

$$(A^i, B^j) =: (ij).$$

This notation possesses the advantage of a straightforward extension to the case of more than two loci.

2.11.2 Moments and the Moment Generating Functions

We recall some facts about moment generating functions. In particular, we shall discuss the moment generating function of the multinomial distribution.

Let $Y = (Y^1, \dots, Y^n) : \Omega \to \mathbb{R}^n$ be a tuple of random variables with joint probabilities $p(y^1, \dots, y^n) = \mathrm{P}(Y^1 = y^1, \dots, Y^n = y^n)$ for their values. The moment generating functions then is

$$M(s_1, \dots, s_n) := \mathrm{E}(e^{\sum_{i=1}^n s_i Y^i}) = \sum_{y^1,\dots,y^n} p(y^1, \dots, y^n) e^{\sum_i y^i s_i}. \tag{2.11.2}$$

M encodes the moments of the distribution p in the sense that the moment

$$\begin{aligned}\mathrm{E}((Y^1)^{\nu_1} \dots (Y^n)^{\nu_n}) &= \sum_{y^1,\dots,y^n} \prod_{i=1}^n (y^i)^{\nu_i} p(y^1, \dots, y^n) \\ &= \frac{\partial^{\sum \nu_i}}{(\partial s_1)^{\nu_1} \dots (\partial s_k)^{\nu_k}} M(s_1, \dots, s_n)_{|s_1=0,\dots,s_n=0}. \end{aligned} \tag{2.11.3}$$

We shall also need the following transformation rule. If

$$Y^i = \sum_{j=1}^{\ell} a^i_j Z^j \tag{2.11.4}$$

then

$$\mathrm{E}(e^{\sum_{i=1}^n s_i Y^i}) = \mathrm{E}(e^{\sum_{i=1}^n s_i \sum_j a_j^i Z^j}) = \sum_{z^1,\dots,z^\ell} p(Z^1 = z^1, \dots) e^{\sum_i s_i a_j^i z^j}. \tag{2.11.5}$$

In particular, when the Y^i are allele frequencies, and $X^i = \frac{1}{2N} Y^i$ are the corresponding relative frequencies, then

$$\mathrm{E}(e^{\sum_{i=1}^n s_i X^i}) = \mathrm{E}(e^{\sum_{i=1}^n \frac{s_i}{2N} Y^i}), \tag{2.11.6}$$

and where we have of course $\mathrm{P}(X^1 = x^1, \dots) = \mathrm{P}(Y^1 = y^1, \dots)$ with $x^i = \frac{y^i}{2N}$.

If Y is the sum of k independent random variables $Y_1, \dots, Y_n$ with moment generating functions M_j, then

$$M(s_1, \dots, s_n) = \prod_{j=1}^n M_j(s_j) = \sum_{y^1,\dots,y^n} p(y^1, \dots, y^n) e^{\sum_i y^i s_i}. \tag{2.11.7}$$

When we apply this to multinomial sampling where we sample $2N$ times independently, then the resulting random variable is the sum of $2N$ random variables obtained by sampling just once. Thus, when, as before, we have $n+1$ possibilities $\nu = 0, \dots, n$ occurring with probabilities p_ν, we obtain for the moment generating function

$$M(s_0, \dots, s_n) = (\sum_{\nu=0}^n p_\nu e^{s_\nu})^{2N}. \tag{2.11.8}$$

Thus, with (2.11.3), we recover the moments of the multinomial distribution,

$$\mathrm{E}(Y^i) = 2Np_i \tag{2.11.9}$$

$$\mathrm{E}(Y^i Y^j) = 4N^2 p_i p_j + 2Np_i(\delta_{ij} - p_j) \tag{2.11.10}$$

$$\begin{aligned}\mathrm{E}(Y^i Y^j Y^\ell) &= 2N(2N-1)(2N-2)p_i p_j p_\ell \\ &\quad + 2N(2N-1)(p_i p_j(\delta_{i\ell} + \delta_{j\ell}) + p_i p_\ell \delta_{ij}) + 2Np_i\delta_{ij\ell},\end{aligned} \tag{2.11.11}$$

where $\delta_{ij\ell} = 1$ if $i = j = \ell$ and $= 0$ otherwise. In particular, we have

$$\mathrm{Cov}(Y^i, Y^j) = \mathrm{E}(Y^i Y^j) - \mathrm{E}(Y^i)\mathrm{E}(Y^j) = 2Np_i(\delta_{ij} - p_j). \tag{2.11.12}$$

2.11.3 Notation for Simplices and Function Spaces

Since we plan to develop a hierarchical scheme for the solution of the Kolmogorov equations on the various boundary strata of the standard simplex, we need to develop some notation which allows for the recursive application of our scheme on different boundary strata. We also need suitable hierarchical products. That is the purpose of this section.

We recall the simplex

$$\overline{\Sigma}_n := \left\{ (x^0, x^1, \ldots, x^n) : x^i \geq 0 \text{ for all } i, \sum_{i=0}^{n} x^i = 1 \right\}. \tag{2.11.13}$$

This is the standard n-simplex in $\mathbb{R}^{n+1}$ representing the probabilities or relative frequencies $x^0, x^1, \ldots, x^n$ of alleles $A^0, A^0, \ldots, A^n$ in our population. Thus we have the normalization $\sum_{j=0}^{n} x^j = 1$, and we therefore have $x^0 = 1 - \sum_{i=1}^{n} x^i$. Often, however, it is advantageous to work in $\mathbb{R}^n$ instead of $\mathbb{R}^{n+1}$, we shall therefore work with the (open) *n-dimensional standard orthogonal simplex*

$$\Delta_n := \left\{ (x^1, \ldots, x^n) \in \mathbb{R}^n \middle| x^i > 0 \text{ for } i = 1, \ldots, n \text{ and } \sum_{i=1}^{n} x^i < 1 \right\}, \tag{2.11.14}$$

or equivalently,

$$\Delta_n = \left\{ (x^1, \ldots, x^n) \in \mathbb{R}^n \middle| x^j > 0 \text{ for } j = 0, 1, \ldots, n \text{ and } \sum_{j=0}^{n} x^j = 1 \right\}. \tag{2.11.15}$$

Its topological closure is

$$\overline{\Delta}_n = \left\{ (x^1, \ldots, x^n) \in \mathbb{R}^n \middle| x^i \geq 0 \text{ for } i = 1, \ldots, n \text{ and } \sum_{i=1}^{n} x^i \leq 1 \right\}. \tag{2.11.16}$$

In order to include time $t \in [0, \infty)$, we shall also use the notation

$$(\Delta_n)_\infty := \Delta_n \times (0, \infty).$$

The boundary $\partial\Delta_n = \overline{\Delta}_n \setminus \Delta_n$ consists of various subsimplices of descending dimensions called *faces*, starting from the $(n-1)$-dimensional *facets* down to the *vertices* (which represent 0-dimensional faces). Each subsimplex of dimension $k \leq n-1$ is isomorphic to the k-dimensional standard orthogonal simplex Δ_k. For an index set $I_k = \{i_0, i_1, \ldots, i_k\} \subset \{0, \ldots, n\}$ with $i_j \neq i_l$ for $j \neq l$.

We put

$$\Delta_k^{(I_k)} := \left\{(x^1,\dots,x^n) \in \overline{\Delta}_n \middle| x^i > 0 \text{ for } i \in I_k; x^i = 0 \text{ for } i \in I_n \setminus I_k\right\}. \tag{2.11.17}$$

We note that $\Delta_n = \Delta_n^{(I_n)}$.

For a given $k \le n-1$, there are of course $\binom{n+1}{k+1}$ different such subsets I_k of I_n, each of which corresponds to a certain boundary face $\Delta_k^{(I_k)}$. We therefore introduce the *k-dimensional boundary* $\partial_k\Delta_n$ of Δ_n by putting

$$\partial_k\Delta_n^{(I_n)} := \bigcup_{I_k\subset I_n} \Delta_k^{(I_k)} \subset \partial\Delta_n^{(I_n)} \quad \text{for } 0 \le k \le n-1. \tag{2.11.18}$$

With this notation, we have $\partial_n\Delta_n = \Delta_n$, although this is not a boundary component. The concept of the k-dimensional boundary also applies to simplices which are themselves boundary instances of some $\Delta_l^{(I_l)}$, $I_l \subset I_n$ for $0 \le k < l \le n$, thus

$$\partial_k\Delta_l^{(I_l)} = \bigcup_{I_k\subset I_l} \Delta_k^{(I_k)} \subset \partial\Delta_l^{(I_l)}. \tag{2.11.19}$$

In the Wright–Fisher model, Δ_n corresponds to the state of all $n+1$ alleles being present, whereas $\partial_k\Delta_n$ represents the state of exactly (any) $k+1$ alleles being present in the population. The individual $\Delta_k^{(\{i_0,\dots,i_k\})}$ comprising $\partial_k\Delta_n$ correspond to the state of exactly the alleles $i_0,\dots,i_k$ being present in the population. Likewise, $\partial_{k-1}\Delta_k^{(\{i_0,\dots,i_k\})}$ corresponds to the state of exactly one further allele out of $i_0,\dots,i_k$ being eliminated from the population. Eventually,

$$\overline{\partial_k\Delta_n^{(I_n)}} \equiv \bigcup_{I_k\subset I_n} \overline{\Delta_k^{(I_k)}}$$

corresponds to the state of at most (any) $k+1$ alleles being present in the population.

We shall also need the function spaces

$$H_n := C^\infty(\overline{\Delta}_n), \quad H_n^0 := C_0^\infty(\Delta_n), \text{ and}$$
$$H := \left\{f : \overline{\Delta}_n \to [0,\infty] \text{ measurable such that } [f,g]_n < \infty, \forall g \in H_n\right\},$$

More generally,

$$H_k^{(\{i_0,\dots,i_k\})} := C^\infty\left(\overline{\Delta_k^{(\{i_0,\dots,i_k\})}}\right),$$
$$H_k := C^\infty(\overline{\partial_k\Delta_n}), \quad k \in \{1,\dots,n\}.$$

We shall also use the L^2-product

$$(f,g) := (f,g)_n := \int\limits_{\Delta_n} f(x)g(x)d\boldsymbol{\lambda}_n(x), \tag{2.11.20}$$

where $\boldsymbol{\lambda}_n(x)$ is the Lebesgue measure on the simplex Δ^n. (We shall leave out the index n when the dimension is clear from the context.)

Finally, we need a notion of hierarchical L^2-product over a simplex and all of its boundary simplices:

$$\begin{aligned} {}_n &:= \int\limits_{\overline{\Delta}_n} f(x)g(x)d\boldsymbol{\lambda}(x) = \sum_{k=0}^{n} \int\limits_{\partial_k\Delta_n} f(x)g(x)d\boldsymbol{\lambda}_k(x) \\ &:= \sum_{k=0}^{n} \sum_{\{i_0,\ldots,i_k\}} \int\limits_{\Delta_k^{(\{i_0,\ldots,i_k\})}} f(x)g(x)d\boldsymbol{\lambda}_k^{(\{i_0,\ldots,i_k\})}(x), \end{aligned} \tag{2.11.21}$$

and correspondingly

$$\begin{aligned} L^2\Big(\bigcup_{k=0}^{n}\partial_k\Delta_n\Big) := \Big\{ f\colon \overline{\Delta}_n \longrightarrow \mathbb{R} \,\Big|\, & f|_{\partial_k\Delta_n} \text{ is } \boldsymbol{\lambda}_k - \text{measurable and} \\ & \int_{\partial_k\Delta_n} |f(x)|^2\, d\boldsymbol{\lambda}_k(x) < \infty \text{ for all } k = 0,\ldots,n \Big\}. \end{aligned} \tag{2.11.22}$$

Here, $\boldsymbol{\lambda}_k$ again stands for k-dimensional Lebesgue measure, but when integrating over some $\Delta_k^{(I_k)}$ with $0 \notin I_k$, the measure needs to be replaced with the one induced on $\Delta_k^{(I_k)}$ by the Lebesgue measure of the containing $\mathbb{R}^{k+1}$, which is denoted by $\boldsymbol{\lambda}_k^{(I_k)}$. However, will also just write $\boldsymbol{\lambda}_k$ as it is clear from the domain of integration $\Delta_k^{(I_k)}$ with either $0 \in I_k$ or $0 \notin I_k$ which version is actually used. We will use $\boldsymbol{\lambda}$ without a sub- or superscript for the measure on the closed simplex composed of the hierarchical family of Lebesgue measures on all its subsimplices.

In order to define an extended solution on Δ_n and its faces (indicated by a capitalised U) in Sect. 9.2, we shall in addition need appropriate spaces of pathwise regular functions. Such a solution needs to be at least of class C^2 in every boundary instance (actually, a solution typically always is of class C^∞, which likewise applies to each boundary instance). Moreover, it should stay regular at boundary transitions that reduce the dimension by one, i.e. for $\Delta_k^{(I_k)}$ and a boundary face $\Delta_{k-1} \subset \partial_{k-1}\Delta_k^{(I_k)}$. Globally, we may require that such a property applies to all

possible boundary transitions within $\overline{\Delta}_n$ and define correspondingly for $l \in \mathbb{N} \cup \{\infty\}$

$$U \in C_p^l\big(\overline{\Delta}_n\big) :\Leftrightarrow U|_{\Delta_d^{(I_d)} \cup \partial_{d-1}\Delta_d^{(I_d)}} \in C^l(\Delta_d^{(I_d)} \cup \partial_{d-1}\Delta_d^{(I_d)}) \quad \text{for all } I_d \subset I_n, 1 \le d \le n \tag{2.11.23}$$

with respect to the spatial variables. Likewise, for ascending chains of (sub-)simplices with a more specific boundary condition, we put for index sets $I_k \subset \ldots \subset I_n$ and again for $l \in \mathbb{N} \cup \{\infty\}$

$$U \in C_{p0}^l\Big(\bigcup_{d=k}^{n} \Delta_d^{(I_d)}\Big) :\Leftrightarrow \begin{cases} U|_{\Delta_d^{(I_d)}} \text{ is extendable to } \bar{U} \in C^l(\Delta_d^{(I_d)} \cup \partial_{d-1}\Delta_d^{(I_d)}) \text{ with} \\ \bar{U}|_{\partial_{d-1}\Delta_d^{(I_d)}} = U\chi_{\Delta_{d-1}^{(I_{d-1})}}\chi_{\{d>k\}} \text{ for all } \max(1,k) \le d \le n \end{cases} \tag{2.11.24}$$

with respect to the spatial variables.

Finally, we put $e_0 := (0, \ldots, 0) \in \mathbb{R}^n$, $e_i := (0, \ldots, \underbrace{1}_{i\text{th}}, \ldots, 0) \in \mathbb{R}^n$ for $i \in \{1, \ldots, n\}$.

2.11.4 Notation for Cubes and Corresponding Function Spaces

For the regularising blow-up scheme of Sect. 9.7.2, we furthermore introduce some notation for cubes and their boundary instances: In conjunction to the definitions for Δ_n in Sect. 2.11.3, we define for $n \in \mathbb{N}$ an *n-dimensional cube* $\square_n$ as

$$\square_n := \big\{(p^1, \ldots, p^n) \big| p^i \in (0,1) \text{for } i = 1, \ldots, n\big\}. \tag{2.11.25}$$

Analogous to Δ_n, if we wish to denote the corresponding coordinate indices explicitly, this may be done by providing the coordinate index set $I'_n := \{i_1, \ldots, i_n\} \subset \{1, \ldots, n\}$, $i_j \neq i_l$ for $j \neq l$ as upper index of $\square_n$, thus

$$\square_n^{(I'_n)} = \big\{(p^1, \ldots, p^n) \big| p^i \in (0,1) \text{for } i \in I'_n\big\}. \tag{2.11.26}$$

This is particularly useful for boundary instances of the cube (cf. below) or if for other purposes a certain ordering $(i_j)_{j=0,\ldots,n}$ of the coordinate indices is needed. For $\square_n$ itself and if no ordering is needed, the index set may be omitted (in such a case it may be assumed $I'_n \equiv \{1, \ldots, n\}$ as in Eq. (2.11.25)). Please note that a primed index set is always assumed to not contain index 0 (resp. $i_0 = 0$, which we usually stipulate in case of orderings) as the cube does not encompass a 0th coordinate.

In the standard topology on $\mathbb{R}^n$, $\square_n$ is open (which we always assume when writing $\square_n$), and its closure $\overline{\square}_n$ is given by (again using the index set notation)

$$\overline{\square_n^{(I'_n)}} = \left\{(p^1, \ldots, p^n) \middle| p^i \in [0,1] \text{ for } i \in I'_n\right\}. \tag{2.11.27}$$

Similarly to the simplex, the boundary $\partial\square_n$ of $\square_n$ consists of various subcubes (faces) of descending dimensions, starting from the $(n-1)$-dimensional facets down to the vertices (which represent 0-dimensional cubes). All appearing subcubes of dimension $0 \leq k \leq n-1$ are isomorphic to the k-dimensional standard cube $\square_k$ and hence will be denoted by $\square_k$ if it is irrelevant or given by the context which subcube exactly shall be addressed. However, we may state $\square_k^{(I'_k)}$ with the index set $I'_k := \{i_1, \ldots, i_k\} \subset I'_n$, $i_j \neq i_l$ for $j \neq l$ stipulating that I'_k lists all k 'free' coordinate indices, whereas the remaining coordinates are fixed at zero, i.e.

$$\square_k^{(I'_k)} := \left\{(p^1, \ldots, p^n) \middle| p^i \in (0,1) \text{ for } i \in I'_k; p^i = 0 \text{ for } i \in I'_n \setminus I'_k\right\} \tag{2.11.28}$$

down until $\square_0^{(\varnothing)} := (0, \ldots, 0)$ for $k = 0$.

For a given k, there are of course $\binom{n}{k}$ different (unordered) subsets I'_k of I'_n, each of which corresponds to a certain boundary face $\square_k^{(I'_k)}$. Moreover, for each subset I'_k with k elements, altogether $2^{(n-k)}$ subcubes of dimension k exist in $\partial\square_n$, which are isomorphic to $\square_k^{(I'_k)}$ (including $\square_k^{(I'_k)}$) depending on the (respectively fixed) values of the coordinates with indices not in I'_k. Thus, if necessary, we may rather state a certain boundary face $\square_k$ of $\partial\square_n$ for $0 \leq k \leq n-1$ by only giving the values of the $n-k$ fixed coordinates, i.e. with indices in $I'_n \setminus I'_k$, which may be either 0 or 1, hence

$$\square_k = \left\{p^{j_1} = b_1, \ldots, p^{j_{n-k}} = b_{n-k}\right\} \tag{2.11.29}$$

with $j_1, \ldots, j_{n-k} \in I'_n$, $i_r \neq i_s$ for $r \neq s$ and $b_1, \ldots, b_{n-k} \in \{0,1\}$ chosen accordingly. In particular for dimension $n-1$, it is noted that we have $n-1$ faces, which each appear twice; in zero dimension, there are 2^n vertices. If we wish to indicate the total *k-dimensional boundary of* $\square_n$, i.e. the union of all k-dimensional faces belonging to $\overline{\square}_n$, we may write $\partial_k\square_n$ for $k = 0, \ldots, n$ with analogously $\partial_n\square_n := \square_n$.

Lastly, when writing products of simplex and cube which do not span all considered dimensions, we indicate the value of the missing coordinates by curly brackets marked with the corresponding coordinate index, i.e. for $I_n = \{i_0, i_1, \ldots, i_n\}$ and $I_k \subset I_n$ with $i_{k+1} \notin I_k$ we have e.g.

$$\begin{aligned}&\Delta_k^{(I_k)} \times \{1\}^{(\{i_{k+1}\})} \times \square_{n-k-1}^{(I'_n \setminus (I'_k \cup \{i_{k+1}\}))} \\ &\quad := \left\{(p^{i_1}, \ldots, p^{i_n}) \middle| p^i > 0 \text{ for } i \in I_k, p^{i_{k+1}} = 1, p^j \in (0,1) \text{ for } j \in I'_n \setminus (I'_k \cup \{i_{k+1}\})\right\}\end{aligned} \tag{2.11.30}$$

with $p^{i_0} = p^0 = 1 - \sum_{j=1}^{k} p^{i_j}$. If coordinates are fixed at 0, the corresponding entry may be omitted, e.g. we may just write $\Delta_k^{(I_k)}$ for $\Delta_k^{(I_k)} \times \{0\}^{(I_n \setminus I_k)}$.

Furthermore, we also introduce a (closed) cube $\overline{\square_k^{(I'_k)}}$ with a removed base vertex $\square_0^{(\varnothing)}$ somewhat inexactly denoted by $\overline{\boxtimes_k^{(I'_k)}}$, i.e.

$$\overline{\boxtimes_k^{(I'_k)}} := \overline{\square_k^{(I'_k)}} \setminus \square_0^{(\varnothing)} = \left\{ p^{i_1}, \dots, p^{i_k} \in [0,1] \,\middle|\, \sum_{j=1}^{k} p^{i_j} > 0 \right\}. \tag{2.11.31}$$

For functions defined on the cube, the pathwise smoothness required for an application of the yet to be introduced corresponding Kolmogorov backward operator (cf. p. 242) may be defined as with the simplex in equality (2.11.23); hence, we put

$$\tilde{u} \in C_p^l(\overline{\square}_n) \;:\Leftrightarrow\; \tilde{u}|_{\square_d \cup \partial_{d-1}\square_d} \in C^l(\square_d \cup \partial_{d-1}\square_d) \text{ for every } \square_d \subset \overline{\square}_n \tag{2.11.32}$$

with respect to the spatial variables, implying that the operator is continuous at all boundary transitions within $\overline{\square}_n$. This concept likewise applies to subsets of $\overline{\square}_n$ where needed.

Chapter 3
Geometric Structures and Information Geometry

3.1 The Basic Setting

We consider the probability simplex

$$\overline{\Sigma}^n := \left\{ (x^0, \ldots, x^n) : \sum_{i=0}^{n} x^i = 1 \right\}. \tag{3.1.1}$$

The x^i will stand for relative allele frequencies or probabilities that were denoted by p^i in (1.1.1). When the total number of alleles present in the population is $2N$ (i.e., a population consisting of N diploid individuals), we have

$$x^i \in \left\{ \frac{0}{2N}, \frac{1}{2N}, \ldots, \frac{2N}{2N} \right\}, \tag{3.1.2}$$

but in the infinite population size limit that we shall mainly consider, the x^i can take any values between 0 and 1. The normalization

$$\sum_{i=0}^{n} x^i = 1 \tag{3.1.3}$$

induces correlations between the x^i, $i = 0, \ldots, n$, that will be captured by the Fisher metric introduced below. On this space of relative frequencies or probabilities, we shall consider probability distributions $p(x)$. As probability distributions, they need to satisfy the normalization

$$\int_{\overline{\Sigma}^n} p(x)dx = 1, \tag{3.1.4}$$

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or in the discrete case

$$\sum_{x=x^0,\ldots,x^n} p(x) = 1. \tag{3.1.5}$$

In the sequel, we shall equip the probability simplex $\overline{\Sigma}^n$ with various geometric structures. Of course, it already possesses a geometric structures as an affine linear subset of $\mathbb{R}^{n+1}$. Another geometric structure is obtained by projecting it to the positive sector of the unit sphere in $\mathbb{R}^{n+1}$. Simple as these structures may seem, they, and in particular the relation between them, will provide us with a lot of structural insight. This is the content of information geometry. In order to treat information geometry, we need to develop some basic concepts from Riemannian geometry. A reader who is either familiar with that or not interested in geometry per se may skip the next sections and continue with Sect. 3.5. In any case, those next sections only provide a survey. For detailed proofs, the reader is referred to [71].

3.2 Tangent Vectors and Riemannian Metrics

Let M be an n-dimensional differentiable manifold M. Such a manifold can be locally described by coordinates taking their values in $\mathbb{R}^n$. They are therefore written as $x = (x^1, \ldots, x^n)$. Properties like smoothness can then be checked in local coordinates. In particular, all objects considered in the sequel will be assumed to be smooth.

The tensor calculus works in such local coordinates and employs indices that run from 1 to n, the dimension of our manifold. Since the coordinates are arbitrary, geometric quantities should not depend on the choice of coordinates. Therefore, tensor calculus incorporates certain rules for switching between different coordinate systems. Even though most of our constructions will only involve a single coordinate system, as the simplex or the positive spherical sector can be covered by a single coordinate system, nevertheless the types of geometric objects, as they show themselves by their transformation behavior, will also be important for our analysis. Therefore, we shall introduce here the basic aspects of tensor calculus.

We usually write $x = f(y)$ when we replace the coordinates x by other coordinates y. The corresponding conventions include the Einstein summation convention that a summation sign is omitted when the same index occurs twice in a product, once as an upper and once as a lower index, that is, for instance

$$v^i w_i := \sum_{i=1}^{n} v^i w_i. \tag{3.2.1}$$

Thus, in this chapter, unless explicitly stated otherwise, indices will range from 1 to n, and such index pairs as in (3.2.1) will be summed over from 1 to n.

There also exists a convention for inverses of tensors which we shall describe here for the metric tensor, an important object to be defined below. When $G = (g_{ij})_{i,j}$ is a metric tensor, the inverse metric tensor is written as $G^{-1} = (g^{ij})_{i,j}$, that is, by raising the indices. In particular

$$g^{ij}g_{jk} = \delta^i_k := \begin{cases} 1 & \text{when } i = k \\ 0 & \text{when } i \neq k. \end{cases} \tag{3.2.2}$$

More generally, the metric tensor is employed for raising and lowering indices, that is,

$$v^i = g^{ij}v_j \text{ and } v_i = g_{ij}v^j. \tag{3.2.3}$$

A tangent vector for M is a rule for computing directional derivatives of functions at some point x_0. In local coordinates x, a tangent vector is written as

$$V = v^i \frac{\partial}{\partial x^i}. \tag{3.2.4}$$

For a function $\varphi(x)$, we can then compute the directional derivative as

$$V(\varphi)(x_0) = v^i \frac{\partial \varphi}{\partial x^i}\Big|_{x=x_0}. \tag{3.2.5}$$

The tangent vectors at a point $p \in M$ form an n-dimensional vector space, called the tangent space T_pM of M at p. When p varies in M, the tangent spaces T_pM constitute a vector bundle over M, called the tangent bundle TM of M. That is, the fiber of TM at $p \in M$ is the vector space T_pM. We shall need this vector bundle below in Sect. 3.4 when we introduce connections.

The rule for how to transform the local expression (3.2.4) for V into a different coordinate system, that is, when we change coordinates from x to y, is

$$V = v^i \frac{\partial y^k}{\partial x^i} \frac{\partial}{\partial y^k}. \tag{3.2.6}$$

Thus, the coefficients of V in the y-coordinates are $v^i \frac{\partial y^k}{\partial x^i}$. Of course, this transformation rule is set up in such a way that the result of the operation of the tangent vector V on a function φ, $V(\varphi)$, is independent of the choice of coordinates. Expressed more shortly, (3.2.5) does not depend on the choice of coordinates.

A vector field assigns to each point p of M a vector in T_pM. In local coordinates, we can write a vector field as $V(x) = v^i(x)\frac{\partial}{\partial x^i}$. The space of vector fields on M is denoted by $\Gamma(TM)$.

The transformation behavior (3.2.6) is called contravariant. There are also objects that transform covariantly, that is, in a manner opposite to (3.2.6). The basic such

objects are the covectors $\omega = \omega_i dx^i$. With the basic rule

$$dx^i\Big(\frac{\partial}{\partial x^j}\Big) = \delta^i_j, \tag{3.2.7}$$

we can apply a covector ω to a vector V, yielding

$$\omega_i dx^i\Big(v^j \frac{\partial}{\partial x^j}\Big) = \omega_i v^j \delta^i_j = \omega_i v^i, \tag{3.2.8}$$

or written more shortly as $\omega(V)$. The covariant transformation behavior

$$\omega_i dx^i = \omega_i \frac{\partial x^i}{\partial y_k} dy^k \tag{3.2.9}$$

ensures the invariance of $\omega(V)$.

We can then also form other tensors, with more than one index. A lower index always indicates covariant, an upper one contravariant transformation. For example, the metric tensor, written as $g_{ij}dx^i \otimes dx^j$, with $g_{ij} = \langle \frac{\partial}{\partial x^i}, \frac{\partial}{\partial x^j} \rangle$ being the product of those two basis vectors, operates on pairs of tangent vectors. It therefore transforms doubly covariantly, that is, when we change coordinates from x to y via $x = f(y)$, $g_{ij}(x)dx^i \otimes dx^j$ becomes

$$g_{ij}(f(y)) \frac{\partial x^i}{\partial y^k} \frac{\partial x^j}{\partial y^\ell} dy^k \otimes dy^\ell. \tag{3.2.10}$$

The metric tensor provides a Euclidean product of tangent vectors,

$$g(V, W) := \langle V, W \rangle := g_{ij} v^i w^j \tag{3.2.11}$$

for $V = v^i \frac{\partial}{\partial x^i}, W = w^i \frac{\partial}{\partial x^i}$. (Here, $g(.,.)$ and $\langle .,. \rangle$ are alternative notations for the same object.) In this formula, v^i and w^i transform contravariantly, while g_{ij} transforms doubly covariantly so that the product as a scalar quantity remains invariant under coordinate transformations.

Equipped with a Riemannian metric, one can introduce all the notions and carry out all the constructions that are familiar from Euclidean geometry. For instance, two vectors V, W are called orthogonal if $\langle V, W \rangle = 0$.

When we put

$$g := \det(g_{ij}), \tag{3.2.12}$$

we obtain the volume element $\sqrt{g} dx^1 \dots dx^n$ of a Riemannian metric. We can then integrate functions. Again, the transformation behavior of the volume element (3.2.12) is such that the result will not depend on the choice of coordinates.

Definition 3.2.1 A differentiable manifold M that is equipped with a Riemannian metric g is called a *Riemannian manifold*.

In particular, when we change the local coordinates the tensor (g_{ij}) representing the Riemannian metric has to transform according to (3.2.10).

The standard operations for differentiable manifolds are compatible with Riemannian metrics. In particular, we have

Lemma 3.2.1

1. *Let (N, g) be a Riemannian manifold, and let M be a (smooth) submanifold of N. Then g induces a Riemannian metric on M.*
2. *Let $(M_1, g_1), (M_2, g_2)$ be Riemannian manifolds. Then their Cartesian product becomes a Riemannian manifold $(M_1 \times M_2, g_1 \times g_2)$.*

Proof

1: Let $x \in M \subset N$. Then the tangent space T_xM is a linear subspace of the tangent space T_xN. Thus, for $V, W \in T_xM$, we can form the product $g(V, W)$. This then yields the Riemannian metric on M.

2: Let $x = (x^1, x^2) \in M_1 \times M_2$. Every $V \in T_x(M_1 \times M_2)$ can be uniquely decomposed as $V = V^1 + V^2$ with $V^i \in T_{x^i}M_i$, $i = 1, 2$. We then put

$$(g_1 \times g_2)(V, W) = g_1(V^1, W^1) + g_2(V^2, W^2) \tag{3.2.13}$$

to define our product metric. □

Furthermore, let (M_1, g_1) and (M_2, g_2) be Riemannian manifolds of dimensions n and m, and let $g_1 \times g_2$ be the product metric on $M_1 \times M_2$. Taking the representation in local coordinates of the metrics, i.e. $(g_{1\,ij}(x_1))_{i,j=1,\dots,n}$ with $x_1 = (x_1^1, \dots, x_1^n)$ and $(g_{2kl}(x_2))_{k,l=n+1,\dots,n+m}$ with $x_2 = (x_2^{n+1}, \dots, x_2^{n+m})$, we have

$$\left((g_1 \times g_2)_{rs}\right)_{r,s=1,\dots,m} = \begin{pmatrix} (g_{1\,ij}(x_1))_{i,j=1,\dots,n} & 0^{n,m} \\ 0^{m,n} & (g_{2kl}(x_2))_{k,l=n+1,\dots,n+m} \end{pmatrix} \tag{3.2.14}$$

with $0^{n,m}$ being the $n \times m$ null matrix. For the inverse metric, we correspondingly obtain

$$\left((g_1 \times g_2)^{rs}\right)_{r,s=1,\dots,m} = \begin{pmatrix} (g_1{}^{ij}(x_1))_{i,j=1,\dots,n} & 0^{n,m} \\ 0^{m,n} & (g_2{}^{kl}(x_2))_{k,l=n+1,\dots,n+m} \end{pmatrix} \tag{3.2.15}$$

as for a block matrix $M = \left(\begin{smallmatrix} A & B \\ C & D \end{smallmatrix}\right)$ like $\big((g_1 \times g_2)_{rs}\big)_{r,s=1,\dots,m}$, we have

$$M^{-1} = \begin{pmatrix} A^{-1} + A^{-1}B(M/A)^{-1}CA^{-1} & -A^{-1}B(M/A)^{-1} \\ -(M/A)^{-1}CA^{-1} & (M/A)^{-1} \end{pmatrix} \tag{3.2.16}$$

with $(M/A)^{-1} := (D - CA^{-1}B)^{-1}$ being the *Schur complement of A in M* (cf. [127, pp. 17 f.]). Clearly, these considerations extend straightforwardly to product metrics with more than two factors.

3.3 Differentials, Gradients, and the Laplace–Beltrami Operator

The differential of a function φ is

$$d\varphi = \frac{\partial \varphi}{\partial x^i} dx^i, \tag{3.3.1}$$

which does not depend on the metric. This is a covector. When we want to have a vector instead, the gradient of φ, we need the metric:

$$\operatorname{grad} \varphi = g^{ij} \frac{\partial \varphi}{\partial x^j} \frac{\partial}{\partial x^i}. \tag{3.3.2}$$

We also want to differentiate vector fields. The divergence of a vector field $Z = Z^i \frac{\partial}{\partial x^i}$ is the function

$$\operatorname{div} Z := \frac{1}{\sqrt{g}} \frac{\partial}{\partial x^j} \big(\sqrt{g} Z^j\big) = \frac{1}{\sqrt{g}} \frac{\partial}{\partial x^j} \Big(\sqrt{g} g^{ij} \Big\langle Z, \frac{\partial}{\partial x^i} \Big\rangle\Big). \tag{3.3.3}$$

We can then define the Laplace–Beltrami operator

$$\Delta_g \varphi := \operatorname{div} \operatorname{grad} \varphi = \frac{1}{\sqrt{g}} \frac{\partial}{\partial x^j} \Big(\sqrt{g} g^{ij} \frac{\partial \varphi}{\partial x^i}\Big). \tag{3.3.4}$$

Here, $\sqrt{g}$ is the determinant of the metric tensor, see (3.2.12). Let us point out that the sign convention adopted here differs from that of [71].

This is a self-adjoint operator in the sense that for any two smooth functions φ, ψ (compactly supported if the manifold M is not compact itself)

$$\int \varphi \Delta_g \psi \sqrt{g} dx^1 \dots dx^n = \int \psi \Delta_g \varphi \sqrt{g} dx^1 \dots dx^n. \tag{3.3.5}$$

A function φ is called harmonic if

$$\Delta_g \varphi = 0. \tag{3.3.6}$$

3.4 Connections

Definition 3.4.1 Let M be a differentiable manifold with tangent bundle TM. A *covariant derivative*, or equivalently, a *connection* is a map

$$D\colon \Gamma(TM) \otimes \Gamma(TM) \to \Gamma(TM) \tag{3.4.1}$$

$$(V, Z) \mapsto D_V Z \tag{3.4.2}$$

satisfying

(i) D is tensorial in V:

$$D_{V+W}Z = D_V Z + D_W Z \qquad \text{for } V, W, Z \in \Gamma(TM), \tag{3.4.3}$$

$$D_{fV}Z = f\, D_V Z \qquad \text{for } f \in C^\infty(M, \mathbb{R}),\ V \in \Gamma(TM). \tag{3.4.4}$$

(ii) D is $\mathbb{R}$-linear in Z:

$$D_V(Z + Y) = D_V Z + D_V Y \quad \text{for } V, Z, Y \in \Gamma(TM) \tag{3.4.5}$$

and it satisfies the following product rule:

$$D_V(f\, Z) = V(f) \cdot Z + f\, D_V Z \qquad \text{for } f \in C^\infty(M, \mathbb{R}). \tag{3.4.6}$$

Thus, when we multiply V by a smooth function f, we can simply pull that function out, but when we multiply Z, we also need to differentiate that function f.

Again, tensor calculus expresses things in local coordinates. Thus, for a connection D, we define the *Christoffel symbols* Γ_{ij}^k $(i, j, k = 1, \ldots, n)$ by

$$D_{\frac{\partial}{\partial x^i}} \frac{\partial}{\partial x^j} =: \Gamma_{ij}^k \frac{\partial}{\partial x^k}. \tag{3.4.7}$$

The Christoffel symbols, however, do not transform as tensors, in contrast to the curvature tensor to be defined below.

Definition 3.4.2 The *curvature tensor* R of a connection D is defined by

$$R(X, Y)Z = D_X D_Y Z - D_Y D_X Z - D_{[X,Y]}Z \tag{3.4.8}$$

for vector fields X, Y, Z on M. Here, $[X, Y]$ is the vector field that operates on functions φ via $[X, Y]\varphi = X(Y\varphi) - Y(X\varphi)$.

A connection whose curvature tensor vanishes is called *flat*.

We define the components $R^k_{\ell ij}$ of the curvature tensor by

$$R\left(\frac{\partial}{\partial x^i}, \frac{\partial}{\partial x^j}\right)\frac{\partial}{\partial x^\ell} = R^k_{\ell ij}\frac{\partial}{\partial x^k} \tag{3.4.9}$$

$(i, j, k, \ell \in \{1, \ldots, n\})$. (Note the convention about the position of the indices; this is taken from [71] and may differ from the convention employed in some other textbooks.) These components can be expressed in terms of the Christoffel symbols via

$$R^k_{\ell ij} = \frac{\partial \Gamma^k_{j\ell}}{\partial x^i} - \frac{\partial \Gamma^k_{i\ell}}{\partial x^j} + \Gamma^k_{im}\Gamma^m_{j\ell} - \Gamma^k_{jm}\Gamma^m_{i\ell}\,. \tag{3.4.10}$$

The curvature tensor is antisymmetric in X and Y, i.e.,

$$R(X, Y) = -R(Y, X), \tag{3.4.11}$$

or with indices,

$$R^k_{\ell ij} = -R^k_{\ell ji} \;\forall\, i, j, k, \ell\,. \tag{3.4.12}$$

Definition 3.4.3 The *torsion tensor* of a connection D on TM is defined as

$$T(X, Y) := T_D(X, Y) := D_X Y - D_Y X - [X, Y] \quad (X, Y \in \Gamma(TM)). \tag{3.4.13}$$

D is called *torsion free* if

$$T \equiv 0. \tag{3.4.14}$$

In terms of our local coordinates, the components of the torsion tensor T are given by

$$T_{ij} = T\left(\frac{\partial}{\partial x^i}, \frac{\partial}{\partial x^j}\right) = D_{\frac{\partial}{\partial x^i}}\frac{\partial}{\partial x^j} - D_{\frac{\partial}{\partial x^j}}\frac{\partial}{\partial x^i} = (\Gamma^k_{ij} - \Gamma^k_{ji})\frac{\partial}{\partial x^k}. \tag{3.4.15}$$

Thus, the connection D on TM is torsion free if and only if

$$\Gamma^k_{ij} = \Gamma^k_{ji} \quad \text{for all } i, j, k. \tag{3.4.16}$$

So far, there was no relation between a connection D on a differentiable manifold M expressed in local coordinates by the Christoffel symbols Γ^k_{ij} and a Riemannian

metric $\langle \cdot, \cdot \rangle$ expressed in local coordinates by a metric tensor g_{ij}. We now impose a compatibility condition in terms of a product rule for the differentiation of the Riemannian product of two vector fields. Given a metric, for a connection D on M, we may define its dual connection D^* via

$$Z\langle V, W\rangle = \langle D_Z V, W\rangle + \langle V, D^*_Z W\rangle \tag{3.4.17}$$

for all vector fields V, W, Z.

Definition 3.4.4 A connection D on M is called *metric* when it is self-dual in the sense that $D = D^*$.

That means that

$$Z\langle V, W\rangle = \langle D_Z V, W\rangle + \langle V, D_Z W\rangle \text{ for all } V, W, Z \in \Gamma(TM) \tag{3.4.18}$$

For a metric connection, we have

$$R^k_{\ell ij} = -R^\ell_{kij} \quad \text{for all } i, j, k, \ell \in \{1, \ldots, d\} \tag{3.4.19}$$

(Compare this symmetry with (3.4.12) which holds for every connection, not necessarily metric.)

Theorem 3.4.1 *On each Riemannian manifold M, there is precisely one metric and torsion free connection ∇, called the Levi-Civita connection of M. It is determined by*

$$\begin{aligned}\langle \nabla_X Y, Z\rangle = \frac{1}{2}\big\{&X\langle Y, Z\rangle - Z\langle X, Y\rangle + Y\langle Z, X\rangle \\ &- \langle X, [Y, Z]\rangle + \langle Z, [X, Y]\rangle + \langle Y, [Z, X]\rangle\big\}.\end{aligned} \tag{3.4.20}$$

for vector fields X, Y, Z.

For the Levi-Civita connection, the Christoffel symbols can be expressed in terms of the metric g_{ij}:

$$\Gamma^k_{ij} = \frac{1}{2} g^{k\ell}(g_{i\ell,j} + g_{j\ell,i} - g_{ij,\ell}), \tag{3.4.21}$$

where $g_{ik,j} := \frac{\partial g_{ik}}{\partial x^j}$. When we have a metric, we can also use it to pull down the upper index of the Christoffel symbols of a connection D; with the convention (3.2.3), we get

$$\Gamma^D_{kij} = g_{k\ell}\Gamma^\ell_{ij} = \langle D_{\frac{\partial}{\partial x^i}} \frac{\partial}{\partial x^j}, \frac{\partial}{\partial x^k}\rangle \tag{3.4.22}$$

where we now indicate the connection by a superscript for later purposes. In particular, we obtain (3.4.21) by putting $X = \frac{\partial}{\partial x^i}, Y = \frac{\partial}{\partial x^j}, Z = \frac{\partial}{\partial x^k}$ in (3.4.20) and use the fact that coordinate vector fields commute, e.g. $[\frac{\partial}{\partial x^i}, \frac{\partial}{\partial x^j}]\varphi = \frac{\partial^2\varphi}{\partial x^i \partial x^j} - \frac{\partial^2\varphi}{\partial x^j \partial x^i} = 0$. Also, (3.4.21) then becomes

$$\Gamma_{ijk} = \frac{1}{2}(g_{ik,j} + g_{jk,i} - g_{ij,k}), \tag{3.4.23}$$

Let us then consider a pair (D_1, D_2) of connections, as well as the Levi-Civita connection ∇. Comparing (3.4.17) and (3.4.18) yields the following condition for D_1 and D_2 to be dual in the sense of (3.4.17)

$$\Gamma^{D_1}_{kij} + \Gamma^{D_2}_{kij} = 2\Gamma^{\nabla}_{kij} \quad \text{for all } i, j, k. \tag{3.4.24}$$

Not surprisingly, the curvature tensor R of the Levi-Civita connection ∇ satisfies some additional identities. R is given by

$$R(X, Y)Z = \nabla_X \nabla_Y Z - \nabla_Y \nabla_X Z - \nabla_{[X,Y]} Z$$

(cf. (3.4.8)). In local coordinates, as in (3.4.9),

$$R\left(\frac{\partial}{\partial x^i}, \frac{\partial}{\partial x^j}\right)\frac{\partial}{\partial x^\ell} = R^k_{\ell ij}\frac{\partial}{\partial x^k}. \tag{3.4.25}$$

We use again the convention (3.2.3) to pull down an index with the help of the metric tensor and put

$$R_{k\ell ij} = g_{km}R^m_{\ell ij},$$

i.e.

$$R_{k\ell ij} = \left\langle R\Big(\frac{\partial}{\partial x^i}, \frac{\partial}{\partial x^j}\Big)\frac{\partial}{\partial x^\ell}, \frac{\partial}{\partial x^k}\right\rangle. \tag{3.4.26}$$

We point out that the indices k and l appear in different orders on the two sides of (3.4.26), following the convention of [71].

For vector fields X, Y, Z, W, we then have

$$R(X, Y)Z = -R(Y, X)Z, \quad \text{i.e. } R_{k\ell ij} = -R_{k\ell ji}, \tag{3.4.27}$$

$$R(X, Y)Z + R(Y, Z)X + R(Z, X)Y = 0, \quad \text{i.e. } R_{k\ell ij} + R_{kij\ell} + R_{kj\ell i} = 0, \tag{3.4.28}$$

$$\langle R(X, Y)Z, W\rangle = -\langle R(X, Y)W, Z\rangle, \quad \text{i.e. } R_{k\ell ij} = -R_{\ell kij}, \tag{3.4.29}$$

$$\langle R(X, Y)Z, W\rangle = \langle R(Z, W)X, Y\rangle, \quad \text{i.e. } R_{k\ell ij} = R_{ijk\ell}. \tag{3.4.30}$$

From the preceding, we recall that (3.4.27) holds for any connection, (3.4.28) for a torsion free one, and (3.4.29) for a metric one. (3.4.28) is the *first Bianchi identity.*

Definition 3.4.5 The *sectional curvature* of the (linearly independent) tangent vectors $X = \xi^i \frac{\partial}{\partial x^i}, Y = \eta^j \frac{\partial}{\partial x^j} \in T_x M$ of the Riemannian manifold M is

$$\begin{aligned} K(X,Y) :&= \langle R(X,Y)Y, X\rangle \frac{1}{|X \wedge Y|^2} \\ &= \frac{R_{ijk\ell}\xi^i\eta^j\xi^k\eta^\ell}{g_{ik}g_{j\ell}(\xi^i\xi^k\eta^j\eta^\ell - \xi^i\xi^j\eta^k\eta^\ell)} \\ &= \frac{R_{ijk\ell}\xi^i\eta^j\xi^k\eta^\ell}{(g_{ik}g_{j\ell} - g_{ij}g_{k\ell})\xi^i\eta^j\xi^k\eta^\ell} \end{aligned} \tag{3.4.31}$$

with the normalization factor $|X \wedge Y|^2 = \langle X, X\rangle\langle Y, Y\rangle - \langle X, Y\rangle^2$.

With (3.4.10), we obtain

$$R_{klij} = g_{km}R^m_{lij} = \partial_i\Gamma_{jlk} - \partial_j\Gamma_{ilk} - \Gamma^s_{ki}\Gamma_{jls} + \Gamma^r_{kj}\Gamma_{ilr}$$

as $g_{km}g^{mb} = \delta^b_k$ and where we have used the metric to pull down the upper index of the Christoffel symbols, i.e., $g^{as}\Gamma_{jls} = \Gamma^a_{jl}$. And with (3.4.21), we can further rewrite this as

$$R_{klij} = \frac{1}{2}\left(\partial_i\partial_l g_{jk} + \partial_j\partial_k g_{il} - \partial_i\partial_k g_{jl} - \partial_j\partial_l g_{ik}\right) + g^{rs}\left(\Gamma_{kjs}\Gamma_{ilr} - \Gamma_{kir}\Gamma_{jls}\right), \tag{3.4.32}$$

which we will use for calculating sectional curvatures.

We also observe the following scaling behavior of the curvature.

Lemma 3.4.1 *If the metric g Riemannian metric is scaled with a factor $\lambda > 0$, then the corresponding sectional curvatures are scaled by $\frac{1}{\lambda}$.*

Proof In (3.4.31), g appears twice in the denominator, while R_{klij} in the enumerator according to (3.4.32) only contains either $\partial\partial g$ or terms of the form $g^{-1}\partial g\partial g$, which both contribute only one factor λ. □

Lemma 3.4.2 *Let $(M_1 \times M_2, g_1 \times g_2)$ be a Riemannian product as in Lemma 3.2.1. Let $x = (x^1, x^2) \in M_1 \times M_2$. Let $V \in T_{x^1}M_1, W \in T_{x^2}M_2$. Then*

$$K(V, W) = 0. \tag{3.4.33}$$

Proof Since the metric $g = g_1 \times g_2$ is a product metric, we have in product coordinates $g_{ik} = 0 = g^{ik}$ whenever the index i corresponds to a direction tangent to M_1 and k to a tangent direction of M_2. Therefore, by (3.4.21), also $\Gamma^k_{ij} = 0$ if, for instance, i, j represent directions tangent to M_1 and k a direction tangent

to M_2. Thus, from (3.4.32), also $R_{k\ell ij} = 0$ when k, i correspond to directions tangent to M_1, whereas ℓ, j stand for tangent directions of M_2. Equation (3.4.31) then yields (3.4.33). □

3.5 The Fisher Metric

One can always equip a smooth manifold with some Riemannian metric. As such, this is somewhat arbitrary, and this becomes more useful when that manifold carries some additional structure that constrains or even determines such a Riemannian metric. This is the case, as we shall now explain, for families of probability distributions. In this and the following sections, we develop the basic structures of information geometry which deals with the geometry of families of probability distributions. A more detailed treatment can be found in [3, 10]; the latter will be our main reference. Information geometry was originally developed by Amari and Chentsov.

Let us consider a smooth family of probability distributions on some domain Ω parametrised by $s = (s_1, \ldots, s_n) \in S \subset \mathbb{R}^n$ with probability density functions $p(\omega|s)\colon \Omega \longrightarrow \mathbb{R}$. When the sample $\omega \in \Omega$ is not important, we shall simply write $p(s)$ in place of one of the more detailed alternatives $p(\omega|s)$, $p(\omega; s)$ or $p(.|s)$.

The *Fisher information metric* of such a family is given by (cf. [4, p. 27])

$$g_{ij}(s) := \mathrm{E}_{p(s)}\Big(\frac{\partial}{\partial s_i}\log p(s)\frac{\partial}{\partial s_j}\log p(s)\Big) \qquad \text{for } i,j \in \{1,\ldots,n\}, s \in S \tag{3.5.1}$$

$$= \sum_{\omega\in\Omega}\frac{\partial}{\partial s_i}\log p(\omega;s)\frac{\partial}{\partial s_j}\log p(\omega;s)\; p(\omega;s) \tag{3.5.2}$$

$$= \sum_{\omega\in\Omega}\frac{1}{p(\omega;s)}\frac{\partial}{\partial s_i}p(\omega;s)\frac{\partial}{\partial s_j}p(\omega;s) \tag{3.5.3}$$

where the expectation E is taken with respect to $p(s)$. Of course, when the sample space Ω is infinite, the sums in (3.5.2) and (3.5.3) have to be replaced by integrals.

It may be checked that this defines a Riemannian metric on the parameter space S, indeed. The Fisher metric measures the sensitivity of the parameter s to sampling from Ω. That is, in statistics, one takes samples ω from the sample space Ω, and one wants to find that parameter s_0 for which the distribution $p(.|s_0)$ best matches the statistics of the samples. Of course, the more sensitive the parameters are to the sample statistics, the easier the task.

We first consider probability distributions that depend linearly on their parameters. Thus, let us take a probability distribution on a collection of points α of the form

$$q^\alpha(\pi) := g_0^\alpha + \sum_{i=1}^{I} g_i^\alpha \pi^i, \quad \alpha = 0, \ldots, A. \tag{3.5.4}$$

The important assumption here is that the q^α be *linear* functions of the parameters, which we now denote by π^i instead of s^i, with the index range $i = 1, \ldots, I$.

We therefore require first of all

$$\sum_\alpha g_0^\alpha = 1, \quad \sum_\alpha g_i^\alpha = 0 \text{ for } i = 1, \ldots, I, \tag{3.5.5}$$

in order to have

$$\sum_\alpha q^\alpha = 1, \tag{3.5.6}$$

that is, q is indeed a probability distribution. We now want to choose the coefficients in (3.5.4) so that the π^i become the expectation values of certain observables f^i for the probability distribution q. For this purpose, we require

$$\sum_\alpha f_\alpha^i q^\alpha(\pi) = \pi^i \text{ for } i = 1, \ldots, I. \tag{3.5.7}$$

We compute the Fisher metric (3.5.3) of the family (3.5.4) as

$$g_{ij} = \sum_\alpha \frac{1}{q^\alpha} g_i^\alpha g_j^\alpha, \quad \text{for } i, j = 1, \ldots, I. \tag{3.5.8}$$

We now look at the important special case that captures the basic Wright–Fisher model. For $\alpha = 0, \ldots, n$ and $i = 1, \ldots, n$ ($A = I = n$), we simply take as our observables the probabilities $p^\alpha \equiv q^\alpha$, i.e. $f_\alpha^i = \delta_\alpha^i$. The expectation value π^i of the ith observable then is q^i, so that we get the special case $\pi^i = q^i$ of (3.5.4). We then have

$$p^\alpha(\pi) = \pi^\alpha \quad \text{for } \alpha = 1, \ldots, n \tag{3.5.9}$$

$$p^0(\pi) = \pi^0 = 1 - \sum_{\beta=1}^{n} \pi^\beta, \tag{3.5.10}$$

and accordingly

$$g_0^\alpha = \delta_0^\alpha \quad \text{and} \quad g_i^\alpha = \delta_i^\alpha - \delta_0^\alpha, \quad \text{for } \alpha = 0, \ldots, n \text{ and } i = 1, \ldots, n. \tag{3.5.11}$$

The Fisher metric (3.5.8) then becomes

$$g_{ij} = \sum_{\alpha=0}^{n} \frac{1}{p^\alpha} g_i^\alpha g_j^\alpha = \frac{\delta_{ij}}{p^i} + \frac{1}{p^0}. \tag{3.5.12}$$

We shall discuss the geometric interpretation of this formula in Sect. 3.8.

When we compute the inverse metric tensor of (3.5.12), we obtain

$$g^{ij} = p^i(\delta_i^j - p^j), \tag{3.5.13}$$

which is nothing but the covariance matrix of the probability distribution p, see (2.2.2).

3.6 Exponential Families

In fact, (3.5.13), that the inverse metric is the covariance matrix, is not a coincidence, but a general phenomenon. In order to elucidate that phenomenon, we now consider a different class of families of probability distributions.

These are the *exponential families* with probability density function

$$p(\omega;\theta) = g(\omega)\exp\Big(\sum_{i=1}^{n} \theta_i f^i(\omega) - F(\theta)\Big) \tag{3.6.1}$$

Here, the $f^1,\ldots,f^n$ are again *observables*, and their values are checked on samples $\omega \in \Omega$, and one wants to find a probability distribution on Ω that best recovers the statistics of those observables. In statistical mechanics, such distributions are also called Gibbs distributions.

The factor $g(\omega)$ will not play any important role in the sequel. In contrast $F(\theta)$ is needed to ensure the normalization

$$\sum_{\omega\in\Omega} p(\omega;\theta) = 1 \text{ for all } \theta, \tag{3.6.2}$$

which yields

$$F(\theta) = \log \sum_{\omega} \Big(g(\omega)\exp\Big(\sum_{i=1}^{n} \theta_i f^i(\omega)\Big)\Big). \tag{3.6.3}$$

(In statistical mechanics, F is called the free energy.)

Differentiating (3.6.3) w.r.t. θ yields

$$\frac{\partial}{\partial\theta_i}F(\theta) = \sum_{\omega\in\Omega} g(\omega)f^i(\omega)\exp\Big(\sum_{i=1}^n \theta_i f^i(\omega) - F(\theta)\Big) = \mathrm{E}_{p(\theta)}(f^i), \quad i = 1,\dots,n, \tag{3.6.4}$$

the expectation value of the observable f^i. In the sequel, we shall sometimes leave out the subscript $p(\theta)$ when computing expectation values.

Such computations become clearer when, instead of F, we work with

$$Z(\theta) = \exp F(\theta) = \sum_{\omega} g(\omega)\exp\Big(\sum_{i=1}^n \theta_i f^i(\omega))\Big). \tag{3.6.5}$$

Z, called the Zustandssumme or partition function in statistical mechanics, satisfies

$$\frac{\partial^k Z(\theta)}{\partial\theta_{i_1}\cdots\partial\theta_{i_k}} = \sum_{\omega} g(\omega)f^{i_1}\cdots f^{i_k}\exp\Big(\sum_{i=1}^n \theta_i f^i(\omega)\Big), \tag{3.6.6}$$

whence

$$\mathrm{E}_{p(\theta)}(f^{i_1}\cdots f^{i_k}) = \frac{1}{Z(\theta)}\frac{\partial^k Z(\theta)}{\partial\theta_{i_1}\cdots\partial\theta_{i_k}}, \tag{3.6.7}$$

for $i_1,\dots,i_k \in \{1,\dots,n\}$.

We now consider the special case where

$$\mathrm{E}_{p(\theta)}(f^i) = 0 \text{ for all } i. \tag{3.6.8}$$

In that case, (3.6.7) yields

$$\frac{\partial^k F(\theta)}{\partial\theta_{i_1}\cdots\partial\theta_{i_k}} = \frac{\partial^k \log Z(\theta)}{\partial\theta_{i_1}\cdots\partial\theta_{i_k}} = \mathrm{E}_{p(\theta)}(f^{i_1}\cdots f^{i_k}). \tag{3.6.9}$$

In the general case, that is, when (3.6.8) need not hold, this becomes

$$\begin{aligned}\frac{\partial^k F(\theta)}{\partial\theta_{i_1}\cdots\partial\theta_{i_k}} &= E_{p(\theta)}((f^{i_1} - \mathrm{E}_{p(\theta)}(f^{i_1}))\cdots(f^{i_k} - \mathrm{E}_{p(\theta)}(f^{i_k})))\\ &= E_{p(\theta)}((f^{i_1} - \frac{\partial}{\partial\theta_{i_1}}F)\cdots(f^{i_k} - \frac{\partial}{\partial\theta_{i_k}}F)),\end{aligned} \tag{3.6.10}$$

because $f^i - \mathrm{E}_{p(\theta}(f^i)$ in place of f^i satisfies (3.6.8) and we can use (3.6.4).

In particular, the Fisher metric satisfies

$$g_{ij}(\theta) = \frac{\partial^2 F}{\partial\theta_i \partial\theta_j} \tag{3.6.11}$$

$$= \mathrm{E}_{p(\theta)}\Big(\Big(f^i - \frac{\partial}{\partial\theta_i}F\Big)\Big(f^j - \frac{\partial}{\partial\theta_j}F\Big)\Big) \tag{3.6.12}$$

$$= \mathrm{E}_{p(\theta}(f^i f^j) - \mathrm{E}_{p(\theta}(f^i)\mathrm{E}_{p(\theta}(f^j), \quad i,j = 1,\ldots,n. \tag{3.6.13}$$

Thus, the Fisher metric is nothing but the covariance matrix of the corresponding distribution. Also, since the metric is positive definite, (3.6.11) implies that $F(\theta)$ is strictly convex.

Now, in (3.5.13), the covariance matrix was the inverse of the Fisher metric, whereas here it is the metric tensor itself. As we shall now explain, the reason for this is a duality between linear and exponential representations of families of probability distributions. We therefore return to the family (3.5.4) and consider

$$S(\pi) := \sum_\alpha q^\alpha(\pi)\log q^\alpha(\pi), \tag{3.6.14}$$

the negative of the entropy of statistical mechanics, and compute

$$\frac{\partial^2}{\partial\pi^i\partial\pi^j}S(\pi) = \sum_\alpha \frac{1}{q^\alpha}\frac{\partial q^\alpha}{\partial\pi^i}\frac{\partial q^\alpha}{\partial\pi^j} = \sum_\alpha \frac{1}{q^\alpha}g_i^\alpha g_j^\alpha, \quad \text{for } i,j = 1,\ldots,I. \tag{3.6.15}$$

Thus, we recognize the formula (3.5.3) for the Fisher metric. In particular, since this is positive definite, S is a strictly convex function. Since strict convexity is invariant under *affine linear* coordinate transformations, the particular form of (3.5.4) is not important, as long as we represent our family of probability distributions as a linear family.

We can therefore consider the Fisher metric

$$g_{ij} = \frac{\partial^2 S(\pi)}{\partial\pi^i\pi^j}, \quad \text{for } i,j = 1,\ldots,I. \tag{3.6.16}$$

as a metric on an affine space.

Since $S(\pi)$ is a convex function, we can perform a Legendre transformation. That means that we put

$$\tau_i := \frac{\partial S(\pi)}{\partial\pi^i} = \sum_\alpha g_i^\alpha \log q^\alpha \text{ for } i = 1,\ldots,I \tag{3.6.17}$$

and

$$\begin{aligned} F(\tau) :&= \max_{\bar{\pi}} \left(\sum_{i=1}^{I} \tau_i \bar{\pi}^i - S(\bar{\pi}) \right) \\ &= \sum_{i=1}^{I} \pi^i \frac{\partial S(\pi)}{\partial \pi^i} - S(\pi) \\ &= \sum_{i=1}^{I} \pi^i \left(\sum_{\alpha} g_i^\alpha \log q^\alpha + \underbrace{\sum_{\alpha} g_i^\alpha}_{=0} \right) - \sum_{\alpha} q^\alpha \log q^\alpha \\ &= \sum_{\alpha} \left(\sum_{i=1}^{I} g_i^\alpha \pi^i - q^\alpha \right) \log q^\alpha \\ &= -\sum_{\alpha} g_0^\alpha \log q^\alpha, \end{aligned} \tag{3.6.18}$$

since the maximum is realized when (3.6.17) holds.

From the properties of the Legendre transformation, we also obtain

$$\left(\frac{\partial^2 F(\tau)}{\partial \tau_i \tau_j} \right)_{i,j=1,\ldots,I} = \left(\left(\frac{\partial^2 S(\pi)}{\partial \pi^i \pi^j} \right)_{i,j=1,\ldots,I} \right)^{-1} = \left(\sum_{\alpha} \frac{1}{q^\alpha} g_i^\alpha g_j^\alpha \right)^{-1}, \tag{3.6.19}$$

see (3.6.15).

We then have

$$g^{ij} = \frac{\partial^2 F(\tau)}{\partial \tau_i \tau_j} = \frac{\partial \pi^j}{\partial \tau_i}, \tag{3.6.20}$$

again by the properties of the Legendre transform. That is, (3.6.20) is the inverse of the Fisher metric.

We recall (3.6.16)

$$g_{ij} = \frac{\partial^2 S(\pi)}{\partial \pi^i \pi^j} = \frac{\partial \tau_i}{\partial \pi^j}. \tag{3.6.21}$$

In fact, we have

$$\begin{aligned}\sum_{i,j} g^{ij} d\tau_i d\tau_j &= \sum_{i,j} g^{ij} \sum_{k,l} \frac{\partial \tau_i}{\partial \pi^k} \frac{\partial \tau_j}{\partial \pi^l} d\pi^k d\pi^l \\ &= \sum_{i,j} g^{ij} \sum_{k,l} g_{ik} g_{jl} d\pi^k d\pi^l \\ &= \sum_{k,l} g_{kl} d\pi^k d\pi^l,\end{aligned} \tag{3.6.22}$$

that is, the inverse metric tensor g^{ij} in the τ-coordinates is the same as the tensor g_{ij} in the π-coordinates.

We also put

$$\tau_0 := \sum_{\alpha} g_0^{\alpha} \log q^{\alpha}, \tag{3.6.23}$$

and

$$f_{\alpha}^0 = 1, \quad \text{for all } \alpha. \tag{3.6.24}$$

We can see that (f_{α}^i) is an *left inverse* of (g_i^{α}). In fact, for $i = 1, \ldots, I$, we have

$$\begin{aligned}\pi^i &= \sum_{\alpha} f_{\alpha}^i q^{\alpha}(\pi), \quad \text{due to (3.5.7)} \\ &= \sum_{\alpha} f_{\alpha}^i \left(g_0^{\alpha} + \sum_{j=1}^{I} g_j^{\alpha} \pi^j \right), \quad \text{due to (3.5.4)} \\ &= \sum_{\alpha} f_{\alpha}^i g_0^{\alpha} + \sum_{j=1}^{I} \left(\sum_{\alpha} f_{\alpha}^i g_j^{\alpha} \right) \pi^j.\end{aligned} \tag{3.6.25}$$

Therefore

$$\sum_{\alpha} f_{\alpha}^i g_0^{\alpha} = 0, \quad \text{for } i = 1, \ldots, I$$

and

$$\sum_{\alpha} f_{\alpha}^i g_j^{\alpha} = \delta_{ij}, \quad \text{for } i, j = 1, \ldots, I.$$

Moreover, from (3.5.5) and (3.6.24) we have

$$\sum_\alpha f_\alpha^0 g_0^\alpha = \sum_\alpha g_0^\alpha = 1,$$

and

$$\sum_\alpha f_\alpha^0 g_i^\alpha = \sum_\alpha g_i^\alpha = 0, \quad \text{for } i = 1, \dots, I.$$

It implies that

$$\sum_\alpha f_\alpha^i g_j^\alpha = \delta_{ij}, \quad \text{for } i, j = 0, \dots, I.$$

Remark We note that in this case, we do not need the condition $A = I$.

Now, we can left invert (3.6.17) and obtain

$$\log q^\alpha = \sum_{j=0}^{I} f_\alpha^j \tau_j, \tag{3.6.26}$$

that is,

$$q^\alpha = \exp\left(\sum_{j=0}^{I} f_\alpha^j \tau_j\right) = \exp\left(\sum_{j=1}^{I} f_\alpha^j \tau_j\right) e^{\tau_0}. \tag{3.6.27}$$

The normalization $\sum_\alpha q^\alpha = 1$ and (3.6.18), (3.6.23) yield

$$F(\tau) = -\tau_0 = \log \sum_\alpha \exp\left(\sum_{i=1}^{I} f_\alpha^i \tau_i\right) \tag{3.6.28}$$

so that we can rewrite (3.6.27) as

$$q^\alpha(\pi) = \exp\left(\sum_{i=1}^{I} f_\alpha^i \tau_i - F(\tau)\right) =: p_\alpha(\tau). \tag{3.6.29}$$

We have thus obtained the exponential family (3.6.1), and in particular, F turns out to be the free energy (3.6.3). From (3.6.22), we see that the Fisher metric w.r.t. the exponential parameters is the inverse of the Fisher metric w.r.t. the linear ones. That is, the metric g_{ij} considered in Sect. 3.5 has turned into the inverse metric g^{ij} in this section.

From (3.6.13), we also see that the expectation value π^{ij} of the product $f^i f^j$ for the distribution q is given by

$$\pi^{ij} = \pi^i \pi^j + g^{ij}, \tag{3.6.30}$$

that is,

$$g^{ij} = \mathrm{Cov}(f^i, f^j).$$

3.7 The Multinomial Distribution

We finally discuss how this applies to the multinomial distribution $\mathcal{M}(2N; p^0, p^1, \ldots, p^n)$, $p \in \Delta_n$ introduced in Sect. 2.2. First of all, we see that when we sample only once, this is simply the situation of the simple linear family with $p^i = q^i$ for which we get the metric tensor (3.5.12). As we have seen, the inverse metric tensor is given by the covariance matrix, (3.5.13), and the covariance matrix of the multinomial distribution for arbitrary $2N$ is given by (2.2.3). We should note, however, that in (2.2.3), we have computed the covariance matrix for the random variables Y^i that count the number of events of type i, but here we consider the normalized variables p^i, which differ by a factor $\frac{1}{2N}$ from the Y^i. Therefore, we need to multiply the covariance matrix by a factor $\frac{1}{(2N)^2}$, and we obtain the inverse metric tensor of the multinomial distribution therefore as

$$g^{ij} = \frac{1}{2N} p^i (\delta_i^j - p^j), \tag{3.7.1}$$

and the metric tensor is then given by

$$g_{ij} = 2N \left(\frac{\delta_{ij}}{p^i} + \frac{1}{p^0} \right). \tag{3.7.2}$$

We can also check this by expressing the multinomial distribution as an exponential family in their *natural parameters*

$$\theta_i := \log \left(\frac{p^i}{1 - \sum_{j=1}^n p^j} \right), \quad i = 1, \ldots, n \tag{3.7.3}$$

and with $g(\omega) = \binom{2N}{f^1(\omega), \ldots, f^n(\omega), 2N - \sum_j f^j(\omega)}$ and $F(\theta) = 2N \log \left(1 + \sum_{j=1}^n \exp(\theta_j)\right)$, the Fisher metric g thus defines a Riemannian metric on the space of natural parameters Θ of the multinomial distribution with $(g_{ij}(\theta))$ coinciding with the corresponding covariance matrix (cf. Eq. (3.6.11)). However, this is only true

for (g_{ij}) given in the θ-coordinates, whereas the Ohta–Kimura formula and its derivations are rather formulated in terms of the p-coordinates (see (5.6.4)).

Carrying out the corresponding coordinate change, the Fisher metric of the multinomial distribution in the coordinates $p^1, \dots, p^n$ (the parameter p^0 does not appear as coordinate due to $\sum_{i=0}^{n} p^i = 1$) becomes, according to the transformation rule (3.2.10) for the metric tensor,

$$g_{kl}(p) = \sum_{i,j=1}^{n} g_{ij}(\theta) \frac{\partial \theta_k}{\partial p^i} \frac{\partial \theta_l}{\partial p^j} = (2N)^2 \sum_{i,j=1}^{n} g_{ij} (g_{ki})^{-1} (g_{lj})^{-1} = (2N)^2 g^{kl}(\theta(p))$$
$$\text{for } k, l = 1, \dots, n, p \in \Delta_n. \tag{3.7.4}$$

Here, we have used

$$2N \frac{\partial p^i}{\partial \theta_j} = \frac{\partial}{\partial \theta_j} \mathrm{E}(f^i) = \frac{\partial^2}{\partial \theta_i \partial \theta_j} F(\theta) = \mathrm{E}(f^i f^j) - \mathrm{E}(f^i)\mathrm{E}(f^j) \equiv g_{ij}(\theta), \tag{3.7.5}$$

where the first equality is a special property of the multinomial distribution. Thus, the Fisher metric on the parameter space Δ_n in the p-coordinates is the inverse of the metric on the parameter space in the θ-coordinates Θ (up to the factor $(2N)^2$; cf. [73]). For the inverse metric, this further implies

$$g^{kl}(p) = \frac{1}{(2N)^2} g_{kl}(\theta(p)) = \frac{1}{2N} p^k (\delta_{kl} - p^l) \quad \text{for } k, l = 1, \dots, n, p \in \Delta_n, \tag{3.7.6}$$

and consequently we obtain (3.5.12),

$$g_{kl}(p) = 2N \Big(\frac{\delta_{kl}}{p^k} + \frac{1}{p^0} \Big) \quad \text{for } k, l = 1, \dots, n, p \in \Delta_n. \tag{3.7.7}$$

Note that the parameter $2N$, which is the number of independent drawings, only affects the Fisher metric in terms of a scaling factor.

As another example, let us also compute the Fisher metric for the Poisson distribution (2.7.1) depending on the scalar parameter λ. From (2.7.1), we have

$$\log P(k|\lambda) = k \log \lambda - \lambda - \log k!$$

and hence

$$\begin{aligned} g(\lambda) &= -\sum_k \frac{d^2 \log P(k|\lambda)}{d\lambda^2} p(k|\lambda) \\ &= \sum_k \frac{\lambda^{k-2} e^{-\lambda}}{(k-1)!} \\ &= \frac{1}{\lambda} \sum_k P(k-1|\lambda) \\ &= \frac{1}{\lambda}. \end{aligned} \tag{3.7.8}$$

3.8 The Fisher Metric as the Standard Metric on the Sphere

In this section, we interpret the formulae (3.5.12), (3.5.13) for the Fisher metric in geometric terms. We first use $p^0, \cdots, p^n$ as coordinates on the simplex. Note that we are using here $n+1$ coordinate functions on an n-dimensional space, an issue to be addressed shortly. The Fisher metric tensor (in the mathematical biology literature, also called the Shahshahani metric) then becomes

$$\left(\gamma_{\alpha\beta}\right)_{\alpha,\beta=1}^{n}(p) = \begin{pmatrix} \frac{1}{p^0} & 0 & \dots & 0 \\ 0 & \frac{1}{p^1} & \dots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \dots & \frac{1}{p^n} \end{pmatrix}. \tag{3.8.1}$$

Equation (3.8.1), however, is not yet the expression for a Riemannian metric because, as mentioned, we have $n+1$ coordinates $p^0, \dots, p^n$ on an n-dimensional space. This can be easily corrected, however, by expressing

$$p^0 = 1 - \sum_{j=1}^{n} p^j. \tag{3.8.2}$$

This means that we consider the Fisher metric as a metric on the n-dimensional simplex

$$\overline{\Sigma}^n = \left\{ (p^0, \dots p^n) : p^i > 0, \sum_{i=0}^{n} p^i = 1 \right\}. \tag{3.8.3}$$

By the transformation behavior (3.2.10) for a Riemannian metric,

$$g_{ij}(y) = \gamma_{\alpha\beta}(x)\frac{\partial x^\alpha}{\partial y^i}\frac{\partial x^\beta}{\partial y^j}, \tag{3.8.4}$$

when transforming between the coordinates y and $x = x(y)$ (here we take $y = \bar{p} = (p^1, \ldots, p^n)$, $x = p = (p^0, \ldots, p^n)$), and using

$$\frac{\partial p^0}{\partial p^j} = -1 \text{ for } j = 1, \ldots, n, \tag{3.8.5}$$

we obtain the metric tensor g_{ij} in the coordinates $p^1, \ldots p^n$ as

$$(g_{ij}(\bar{p}))_{i,j=1}^n = \begin{pmatrix} \frac{1}{p^1} + \frac{1}{p^0} & \frac{1}{p^0} & \cdots & \frac{1}{p^0} \\ \frac{1}{p^0} & \frac{1}{p^2} + \frac{1}{p^0} & \cdots & \frac{1}{p^0} \\ \vdots & \vdots & \ddots & \vdots \\ \frac{1}{p^0} & \frac{1}{p^0} & \cdots & \frac{1}{p^n} + \frac{1}{p^0} \end{pmatrix}, \tag{3.8.6}$$

with p^0 given by (3.8.2). The inverse metric tensor g^{ij} then becomes

$$(g^{ij}(\bar{p}))_{i,j=1}^n = \begin{pmatrix} p^1(1-p^1) & -p^1p^2 & \cdots & -p^1p^n \\ -p^1p^2 & p^2(1-p^2) & \cdots & -p^2p^n \\ \vdots & \vdots & \ddots & \vdots \\ -p^1p^n & -p^2p^n & \cdots & p^n(1-p^n) \end{pmatrix}. \tag{3.8.7}$$

We can also compute the Christoffel symbols of this metric as (see [5])

$$\begin{aligned} \Gamma^i_{ii} &= \tfrac{1}{2}\left(\tfrac{p^i}{p^n} - \tfrac{1-p^i}{p^i}\right) \\ \Gamma^i_{jj} &= \tfrac{1}{2}\left(\tfrac{p^i}{p^n} - \tfrac{p^i}{p^j}\right) \quad \text{for } i \neq j \\ \Gamma^i_{j\ell} &= \tfrac{1}{2}\tfrac{p^i}{p^n} \quad \text{for } j \neq \ell. \end{aligned} \tag{3.8.8}$$

We can also rewrite the metric in spherical coordinates, by simply putting

$$q^i := \sqrt{p^i}, \quad \text{for } i = 1, \ldots, n. \tag{3.8.9}$$

Applying the transformation rule (3.8.4) with $\frac{\partial p^\alpha}{\partial q^j} = 2\delta^\alpha_j q^j$ for $j, \alpha = 1, \ldots, n$, we obtain $\hat{\gamma}_{ij}(q) = 4\delta_{ij}$ in the q-coordinates, that is, simply the Euclidean metric. As before, however, we need to satisfy the normalization constraint (3.8.2) which now

becomes $q^0 = \sqrt{1 - \sum_{j=1}^n (q^j)^2}$. Using $\frac{\partial q^0}{\partial q^j} = -\frac{q^j}{q^0}$ for $j = 1, \ldots, n$, we obtain

$$\left(h_{ij}(\bar{q})\right)_{i,j=1}^n = \frac{4}{(q^0)^2} \begin{pmatrix} (q^1)^2 + (q^0)^2 & q^1 q^2 & \ldots & q^1 q^n \\ q^1 q^2 & (q^2)^2 + (q^0)^2 & \ldots & q^2 q^n \\ \vdots & \vdots & \ddots & \vdots \\ q^1 q^n & q^2 q^n & \ldots & (q^n)^2 + (q^0)^2 \end{pmatrix} \tag{3.8.10}$$

and

$$\left(h^{ij}(\bar{q})\right)_{i,j=1}^n = \frac{1}{4} \begin{pmatrix} 1 - (q^1)^2 & -q^1 q^2 & \ldots & -q^1 q^n \\ -q^1 q^2 & 1 - (q^2)^2 & \ldots & -q^2 q^n \\ \vdots & \vdots & \ddots & \vdots \\ -q^1 q^n & -q^2 q^n & \ldots & 1 - (q^n)^2 \end{pmatrix} \tag{3.8.11}$$

Since this has been obtained as the restriction of the Euclidean metric to the unit sphere, this must simply be the standard metric on the unit sphere S^n, up to the factor 4 that emerged in our computations. Since the standard metric on the sphere has sectional curvature $\equiv 1$, and since by Lemma 3.4.1, the sectional curvature of a Riemannian metric scales with the inverse of a scaling factor, our factor 4 leads to

Lemma 3.8.1 *The Fisher metric on the standard simplex $\overline{\Sigma}^n$ is 4 times the standard metric on the unit sphere S^n, and its sectional curvature is $\frac{1}{4}$.*

Remark Compare this with the state space of recombination (Proposition 5.6.1), where the Fisher metric has been multiplied by four implying that the sectional curvature will be divided by four.

3.9 The Geometry of the Probability Simplex

The simplex $\overline{\Sigma}^n$ of (3.8.3) possesses a hierarchical structure. That is, its boundary consists of $n+1$ copies $\overline{\Sigma}_j^{n-1} := \{(p^0, \ldots, p^n) \in \overline{\Sigma}^n, p^j = 0\}$ of the simplex $\overline{\Sigma}^{n-1}$. In turn the boundary of each $\overline{\Sigma}_j^{n-1}$ consists of n copies of $\overline{\Sigma}^{n-2}$, and so on.

According to what we have discussed in the preceding, the simplex $\overline{\Sigma}^n$ (and analogously each of its subsimplices) carries a hybrid structure. On one hand, we have the affine structure underlying (3.8.3). By (3.8.3), we also obtain a measure $\boldsymbol{\lambda}_n$ induced by the Lebesgue measure of $\mathbb{R}^n$. On the other hand, we have the Riemannian metric (3.8.10) of the spherical sector, becoming (3.8.6) in our affine coordinates.

For the inverse metrical tensor (3.8.7) (as expressed in the coordinates $p^1, \ldots, p^n$), its normal component vanishes on the boundary whereas the tangential

component restricts to the corresponding Fisher metric on the boundary simplices. This is simply seen by putting $p^j = 0$ in (3.8.7).

The simplex $\overline{\Sigma}^n$ of (3.8.3) also possesses a dually flat structure. That is, a Riemannian metric g together with two flat connections ∇, ∇^* that are dual with respect to g. This means that they satisfy (3.4.17), i.e.,

$$Zg(X,Y) = g(\nabla_Z X, Y) + g(X, \nabla_Z Y), \quad \text{for all vector fields } X, Y, Z.$$

Such dually flat structures have been introduced and investigated by Čensov [20] and Amari [3, 48].

In fact, we can construct the flat connections from g as follows (also see [75]): For $-1 \leq s \leq 1$, we define the s-connection through

$$\Gamma_{ijk}^{(s)} = \Gamma_{ijk}^{(0)} - \frac{s}{2} \frac{\partial^3 S}{\partial \pi^i \partial \pi^j \partial \pi^k} \tag{3.9.1}$$

where $\Gamma_{ijk}^{(0)}$ represents the Levi-Civita connection $\nabla^{(0)}$ for g_{ij}, i.e., recalling (3.4.22),

$$\Gamma_{ijk}^{(0)} = g\left(\nabla^{(0)}_{\frac{\partial}{\partial \pi^i}} \frac{\partial}{\partial \pi^j}, \frac{\partial}{\partial \pi^k}\right) \tag{3.9.2}$$

Also, from (3.4.23) and $g_{ij} = \partial_i \partial_j \varphi$, we infer

$$\Gamma_{ijk}^{(0)} = \frac{1}{2} \frac{\partial^3 S}{\partial \pi^i \partial \pi^j \partial \pi^k}, \tag{3.9.3}$$

we have

$$\Gamma_{ijk}^{(s)} = \frac{1}{2}(1-s) \frac{\partial^3 S}{\partial \pi^i \partial \pi^j \partial \pi^k}, \tag{3.9.4}$$

and since this is symmetric in i and j, $\nabla^{(s)}$ is torsion free. Since (3.4.24) is satisfied, i.e.,

$$\Gamma_{ijk}^{(s)} + \Gamma_{ijk}^{(-s)} = 2\Gamma_{ijk}^{(0)},$$

it implies that $\nabla^{(s)}$ and $\nabla^{(-s)}$ are dual to each other with respect to g.

In particular, $\Gamma_{ijk}^{(1)} = 0$, and so $\nabla^{(1)}$ defines a flat structure, and the coordinates π are affine coordinates for $\nabla^{(1)}$.

The connection dual to $\nabla^{(1)}$ then is $\nabla^{(-1)}$ with Christoffel symbols

$$\Gamma_{ijk}^{(-1)} = \frac{\partial^3 S}{\partial\pi^i\partial\pi^j\partial\pi^k} \tag{3.9.5}$$

with respect to the π-coordinates. We can then obtain dually affine coordinates τ by

$$\tau_i = \frac{\partial S}{\partial\pi^i}, \tag{3.9.6}$$

and so also

$$g_{ij} = \frac{\partial\tau_j}{\partial\pi^i} = \frac{\partial^2 S}{\partial\pi^i\partial\pi^j}. \tag{3.9.7}$$

The corresponding local potential is obtained by a Legendre transformation, as we have seen in Sect. 3.5,

$$F(\tau) = \max_{\pi}(\pi^i\tau_i - S(\pi)), \quad S(\pi) + F(\tau) - \pi\cdot\tau = 0, \tag{3.9.8}$$

and

$$\pi^i = \frac{\partial F(\tau)}{\partial\tau_i}, \quad g^{ij} = \frac{\partial\pi^j}{\partial\tau_i} = \frac{\partial^2 F(\tau)}{\partial\tau_i\partial\tau_j}. \tag{3.9.9}$$

It is easy to see that $\nabla^{(-1)}$ defines a flat structure, and the coordinates τ are affine coordinates for $\nabla^{(-1)}$. Therefore $\left(\overline{\Sigma}^{k-1}, g, \nabla^{(1)}, \nabla^{(-1)}\right)$ is a dually flat manifold.

3.10 The Affine Laplacian

Remark The operator A defined here will be our $2L^*$, see (3.12.4).

Given an affine structure with coordinates $\pi^i, i = 1,\dots,n$ on $\overline{\Sigma}^n$ as above and a metric

$$g_{ij}(\pi) = \frac{\partial^2 S(\pi)}{\partial\pi^i\partial\pi^j}, \quad i,j = 1,\dots,n.$$

we formulate

Definition 3.10.1 The operator given by

$$A := \sum_{i,j=1}^{n} g^{ij}(\pi)\frac{\partial^2}{\partial\pi^i\partial\pi^j} \tag{3.10.1}$$

is called the affine Laplacian (see also [75]), where the Kähler affine structure is in the sense of Cheng–Yau (see [22]).

A solution of

$$Af = 0 \tag{3.10.2}$$

is called an affine harmonic function.

Lemma 3.10.1 *For the function*

$$S(\pi) = \sum_{\alpha} q^{\alpha}(\pi) \log q^{\alpha}(\pi) \tag{3.10.3}$$

of (3.6.14), we have

$$AS = k \equiv \text{const.} \tag{3.10.4}$$

The *proof* is obvious from the definition (3.6.16) of the Fisher metric.

This result will play a useful role below when we want to understand exit times of genetic drift.

We now compute the transformation behavior of the affine Laplacian under non-affine coordinate changes. Let us recall the general transformation formula for a linear second order differential operator of the form

$$Mu(x) = \sum_{i,j} a^{ij}(x) \frac{\partial^2}{\partial x^i \partial x^j} u(x) + \sum_i b^i(x) \frac{\partial}{\partial x^i} u(x) + c(x)u(x). \tag{3.10.5}$$

Lemma 3.10.1 *The partial differential operator (3.10.5) transforms under a change of the coordinates* $(x_i)_i \mapsto (\tilde{x}_i)_i$ *into*

$$M\tilde{u}(\tilde{x}) = \sum_{k,l} \tilde{a}^{kl}(\tilde{x}) \frac{\partial^2}{\partial \tilde{x}^k \partial \tilde{x}^l} \tilde{u}(\tilde{x}) + \sum_k \tilde{b}^k(\tilde{x}) \frac{\partial}{\partial \tilde{x}^k} \tilde{u}(\tilde{x}) + \tilde{c}(\tilde{x})\tilde{u}(\tilde{x}) \tag{3.10.6}$$

with $\tilde{u}(\tilde{x}(x)) = u(x)$ *and*

$$\tilde{a}^{kl}(\tilde{x}) = \sum_{i,j} a^{ij}(x) \frac{\partial \tilde{x}^k}{\partial x^i} \frac{\partial \tilde{x}^l}{\partial x^j}, \quad \tilde{b}^k(\tilde{x}) = \sum_i b^i(x) \frac{\partial \tilde{x}^k}{\partial x^i} + \sum_{i,j} a^{ij}(x) \frac{\partial^2 \tilde{x}^k}{\partial x^i \partial x^j}, \quad \tilde{c}(\tilde{x}) = c(x). \tag{3.10.7}$$

Proof Let $\tilde{x}$ be a coordinate change and $u(x) = \tilde{u}(\tilde{x}(x))$. The chain rule yields

$$\begin{aligned}\sum_{i,j} a^{ij}\frac{\partial^2}{\partial x^i \partial x^j}u &= \sum_{i,j}\sum_k a^{ij}\frac{\partial}{\partial x^i}\Big(\frac{\partial \tilde{x}^k}{\partial x^j}\frac{\partial}{\partial \tilde{x}^k}\tilde{u}\Big)\\ &= \sum_{i,j}\Big(\sum_{l,k} a^{ij}\frac{\partial \tilde{x}^l}{\partial x^i}\frac{\partial \tilde{x}^k}{\partial x^j}\frac{\partial^2}{\partial \tilde{x}^l \partial \tilde{x}^k}\tilde{u} + \sum_k a^{ij}\frac{\partial^2 \tilde{x}^k}{\partial x^i \partial x^j}\frac{\partial}{\partial \tilde{x}^k}\tilde{u}\Big)\\ &= \sum_{l,k}\sum_{i,j} a^{ij}\frac{\partial \tilde{x}^l}{\partial x^i}\frac{\partial \tilde{x}^k}{\partial x^j}\frac{\partial^2}{\partial \tilde{x}^l \partial \tilde{x}^k}\tilde{u} + \sum_k\sum_{i,j} a^{ij}\frac{\partial^2 \tilde{x}^k}{\partial x^i \partial x^j}\frac{\partial}{\partial \tilde{x}^k}\tilde{u}\end{aligned}$$

and

$$\sum_i b^i\frac{\partial}{\partial x^i}u = \sum_i\sum_k b^i\frac{\partial \tilde{x}^k}{\partial x^i}\frac{\partial}{\partial \tilde{x}^k}\tilde{u} = \sum_k\sum_i b^i\frac{\partial \tilde{x}^k}{\partial x^i}\frac{\partial}{\partial \tilde{x}^k}\tilde{u}. \tag{3.10.8}$$

Now putting $\tilde{a}^{lk}$, $\tilde{b}^k$ and $\tilde{c}$ as in Eq. (3.10.7), we have

$$\sum_{i,j} a^{ij}\frac{\partial^2}{\partial x^i \partial x^j}u + \sum_i b^i\frac{\partial}{\partial x^i}u + cu = \sum_{l,k}\tilde{a}^{lk}\frac{\partial^2}{\partial \tilde{x}^l \partial \tilde{x}^k}\tilde{u} + \sum_k \tilde{b}^k\frac{\partial}{\partial \tilde{x}^k}\tilde{u} + \tilde{c}\tilde{u}. \tag{3.10.9}$$

□

In particular, the coefficient matrix of the second order derivatives a^{ij} transforms like the coefficients g^{ij} of the inverse of the Riemannian metric $g = (g_{ij})$ under coordinate changes (i.e. twice contravariantly). This is, of course, in line with our geometric approach where we interpret a^{ij} as an inverse metric tensor g^{ij} of a Riemannian manifold. We should point out, however, that the transformation behavior of the second order terms also yields an additional first order term. Geometrically, this is due to the fact that the operator $M_g := \sum_{i,j} g^{ij}(x)\frac{\partial^2}{\partial x^i \partial x^j}$ is not the Laplace–Beltrami operator for the metric g_{ij}; that latter operator is given by $\Delta_g\varphi := \sum_{i,j}\frac{1}{\sqrt{\det g_{ij}}}\frac{\partial}{\partial x^i}\Big(\sqrt{\det g_{ij}}g^{ij}(x)\frac{\partial \varphi}{\partial x^j}\Big)$ for some function φ, see for instance [71]. In particular, M_g and Δ_g differ by a first order term. This will be elucidated in Sects. 3.11 and 3.12.

With (3.10.6) at hand, we can also transform the affine Laplacian from the coordinates π^i to the dual coordinates τ_i. Even though those dual coordinates also define an affine structure that is dual to the original one, this transformation is not affine itself, simply because the two affine structures are different. Therefore, in the τ-coordinates, A will acquire an additional first order term. We have

$$\frac{\partial^2}{\partial \pi^i \partial \pi^j} = \sum_{\ell,m}\frac{\partial \tau_\ell}{\partial \pi^i}\frac{\partial \tau_m}{\partial \pi^j}\frac{\partial^2}{\partial \tau_\ell \partial \tau_m} + \sum_\ell \frac{\partial^2 \tau_\ell}{\partial \pi^i \partial \pi^j}\frac{\partial}{\partial \tau_\ell}. \tag{3.10.10}$$

Here and in the sequel, all sums range from 1 to n.

We recall (3.6.20), i.e.,

$$g_{ij} = \frac{\partial^2 S(\pi)}{\partial \pi^i \pi^j} = \frac{\partial \tau_i}{\partial \pi^j} \tag{3.10.11}$$

and therefore obtain

$$A = \sum_{i,j} g^{ij} \frac{\partial^2}{\partial \pi^i \partial \pi^j} = \sum_{\ell,m} g_{\ell m} \frac{\partial^2}{\partial \tau_\ell \partial \tau_m} + \sum_{i,j,\ell} \frac{\partial^3 S(\eta)}{\partial \pi^i \partial \pi^j \partial \eta_\ell} \frac{\partial^2 \tau_\ell}{\partial \pi^i \partial \pi^j} \frac{\partial}{\partial \tau_\ell}. \tag{3.10.12}$$

Since $\frac{\partial^3 S(\eta)}{\partial \pi^i \partial \pi^j \partial \eta_\ell} = -\frac{1}{(\pi^i)^2} \delta_{ij} \delta_{i0}$ by (3.6.15), we obtain

$$A = \sum_{\ell,m} \left(\frac{\delta_{\ell m}}{\exp(\vartheta_\ell)} + \frac{1}{\exp(\vartheta^0)} \right) \frac{\partial^2}{\partial \tau_\ell \partial \tau_m} - \sum_{\ell} \frac{1}{(\exp(\tau_\ell))^2} \frac{\partial}{\partial \tau_\ell}. \tag{3.10.13}$$

Here, the τ_ℓ range between 0 and $-\infty$, and $\exp(\tau_0) = 1 - \sum_{\ell=1}^n \exp(\tau_\ell)$. Thus, we have transformed the singularity at the boundary, where some π^i become 0, to $-\infty$. Our operator, however, then will become singular at $-\infty$.

3.11 The Affine and the Beltrami Laplacian on the Sphere

Under the coordinate transformations from p^i on the simplex to the coordinates $q^i = \sqrt{p^i}$ on the sphere, the affine Laplacian becomes

$$\frac{\partial^2}{\partial p^i \partial p^j} = \sum_{\ell,m} \frac{\partial q^\ell}{\partial p^i} \frac{\partial q^m}{\partial p^j} \frac{\partial^2}{\partial q^\ell \partial q^m} + \sum_{\ell} \frac{\partial^2 q^\ell}{\partial p^i \partial p^j} \frac{\partial}{\partial q^\ell}. \tag{3.11.1}$$

Then on the sphere, the affine Laplacian is given by the form

$$A = \bar{g}^{\ell m}(q) \frac{\partial^2}{\partial q^\ell \partial q^m} + \frac{1 - (q^\ell)^2}{4 q^\ell} \frac{\partial}{\partial q^\ell},$$

where $\bar{g}^{\ell m}(q) = \frac{1}{4}\left(\delta_{\ell m} - q^\ell q^m\right)$ is the inverse metric tensor on the sphere.

The affine Laplacian is different from the Laplace–Beltrami operator, the natural divergence type operator derived from the Riemannian metric of the sphere, given by

$$\Delta_{\bar{g}}(q) = \bar{g}^{\ell m}(q) \frac{\partial^2}{\partial q^\ell \partial q^m} + \frac{(1-n) q^\ell}{4} \frac{\partial}{\partial q^\ell}.$$

As we see from this formula, the affine Laplacian has the same leading term as the Laplace–Beltrami operator, but differs from it by a first order term. That term with a factor $1/2$ has been called the *Christoffel force* in [5].

3.12 The Wright–Fisher Model and Brownian Motion on the Sphere

As in Sect. 3.8, we want to interpret the coefficients of the operators L and L^* as the inverse metric tensor of the standard sphere in simplicial coordinates $x^i, i = 1, \ldots, n-1$ with $0 \le x^i, \sum_{j=1}^{n-1} x^j \le 1$,

$$g^{ij} = x^i(\delta_{ij} - x^j). \tag{3.12.1}$$

We recall the Laplace–Beltrami operator (3.3.4)

$$\Delta_{\mathrm{g}} := \frac{1}{\sqrt{g}} \sum_{i,j} \frac{\partial}{\partial x^i} \left(\sqrt{g} g^{ij} \frac{\partial}{\partial x^j} \right). \tag{3.12.2}$$

We rewrite the Laplace–Beltrami operator as

$$\begin{aligned} \Delta_{\mathrm{g}} &= \sum_{i,j} g^{ij} \frac{\partial^2}{\partial x^i \partial x^j} + \frac{1}{\sqrt{g}} \sum_{i,j} \frac{\partial}{\partial x^i} \left(\sqrt{g} g^{ij} \right) \frac{\partial}{\partial x^j} \\ &= \sum_{i,j} g^{ij} \frac{\partial^2}{\partial x^i \partial x^j} - \sum_{i,j,\ell} g^{i\ell} \Gamma^j_{i\ell} \frac{\partial}{\partial x^j} \end{aligned} \tag{3.12.3}$$

after some computation.

When we apply this to the inverse spherical metric (3.12.1), we see that the first term on the right hand side of (3.12.3) is our affine Laplacian (3.10.1)

$$A = 2L^* = \sum_{i,j} g^{ij} \frac{\partial^2}{\partial x^i \partial x^j}, \tag{3.12.4}$$

or twice the generator L^* of the backward Kolmogorov equation for the Wright–Fisher model.

The lower order terms, however, are different, and we now wish to discuss this difference in geometric terms as in [5]. The Laplace–Beltrami operator (3.12.2) generates Brownian motion for the Riemannian metric g_{ij}. We shall explain in a moment what Brownian motion on a Riemannian manifold means (see [66]), but we first point out that the probability density $p(t, z, x)$ for Brownian motion, that is, the probability density for the position x at time t of a particle starting Brownian

motion at z at time 0, evolves according to

$$\frac{\partial}{\partial t}p(t,z,x) = \frac{1}{2}\Delta_{\mathrm{g}}p(t,z,x), \tag{3.12.5}$$

where Δ_{g} operates w.r.t. to the variable x. Since Δ_{g} is self-adjoint, see (3.3.5), also the expectation values of a function φ evolve according to (3.12.5),

$$\frac{\partial}{\partial t}\varphi(t,x) = \frac{1}{2}\Delta_{\mathrm{g}}\varphi(t,x), \tag{3.12.6}$$

that is, there is no difference between the corresponding forward and backward equations.

Comparing (3.12.3), (3.12.4), we obviously have

$$\begin{aligned} L^*f(x) &= \frac{1}{2}\Delta_{\mathrm{g}}f(x) + \frac{1}{2}\sum_{i,j,\ell} g^{i\ell}\Gamma^j_{i\ell}\frac{\partial f(x)}{\partial x^j} \\ &=: \frac{1}{2}\Delta_{\mathrm{g}}f(x) + \sum_j V^j\frac{\partial f(x)}{\partial x^j} \end{aligned} \tag{3.12.7}$$

for smooth functions f with a vector field V.

Recalling the formulae (3.8.8) for the Christoffel symbols,

$$\begin{aligned} \Gamma^i_{ii} &= \tfrac{1}{2}\left(\tfrac{x^i}{x^n} - \tfrac{1-x^i}{x^i}\right) \\ \Gamma^i_{jj} &= \tfrac{1}{2}\left(\tfrac{x^i}{x^n} - \tfrac{x^i}{x^j}\right) \quad \text{for } i \neq j \\ \Gamma^i_{j\ell} &= \tfrac{1}{2}\tfrac{x^i}{x^n} \qquad\quad \text{for } j \neq \ell, \end{aligned}$$

the above vector field V in (3.12.7) is given by

$$V^j = \frac{1}{2}\sum_{i,\ell} g^{i\ell}\Gamma^j_{i\ell} = -\frac{1}{4}(1 - nx^j). \tag{3.12.8}$$

This vector field vanishes at the center of the simplex, the point with $x^j = \frac{1}{n}$ for all j. At the corner $x^k = 1$, the component $V^k = \frac{n-1}{4}$ is positive, whereas all other components $V^j = -\frac{1}{4}$ are negative. More generally, $V(x)$ always points towards that corner of the simplex closest to x. Thus, we see the difference between Brownian motion and the backward Wright–Fisher process given by the vector field V in geometric terms. Also, while Brownian motion is invariant under all isometries of the sphere, the Wright–Fisher is only invariant under permutation of the alleles and hence has a much smaller symmetry group.

Informally speaking, Brownian motion is a stochastic process whose time derivative is Gaussian white noise. The trajectories represent particles moving randomly on the sphere. In particular, such particles are not confined to the positive sector. The heat equation (3.12.5) involving the Laplace–Beltrami operator describes the evolution of the corresponding probability density on the sphere. In contrast, the elements of the positive sector of the sphere that arise from the continuum limit of the Wright–Fisher-model represent probability distributions on our allele space. With a slightly different interpretation, they stand for relative allele frequencies in an infinite population. Again, we may consider trajectories which then represent random such relative frequency evolutions, where the randomness is governed by the multinomial distribution. For elements of the sphere outside the closed positive sector, no such interpretation is possible, and the random trajectories cannot leave that sector. The densities occurring in the Kolmogorov equations then stand for probability densities on the space of such relative frequencies.

Chapter 4
Continuous Approximations

4.1 The Diffusion Limit

4.1.1 Convergence of Discrete to Continuous Semigroups in the Limit $N \to \infty$

In this section we prove a result about diffusion limits of Markov chains that we shall need in the sequel. This result follows from the general theory of convergence of Markov processes, see [36], but we shall present the proof here in order to keep our treatment self-contained. The proof can be shortened by appealing to general theorems about stochastic processes, but, in order to be self-contained, we do not invoke those results here. A reader not interested in the technical details of the justification of the diffusion limits may directly move on to Sect. 4.2.

Let us start with some remark on the notation. In Chap. 2, and in particular in Sects. 2.2 and 2.3, we had introduced the random variables Y and X. The variable Y expresses the absolute allele numbers with integer time steps, whereas X denotes their relative frequencies, but also with rescaled time. We now need another variable Z which records the relative frequencies, but without rescaling time.

We consider a sequence of homogeneous Markov chains $\{Z_N(m)\}_{m\in\mathbb{N}}$ in the state spaces

$$\overline{\Delta}_n^{(2N)} = \left\{ z = (z^1, \ldots, z^n) : \sum_{i=1}^n z^i \leq 1, z^i = \frac{j^i}{2N} \geq 0 \quad j^i \text{ integer}, i = 1, \ldots, n \right\},$$

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with transition probabilities as in (2.5.7) (note, however, that the Y_m are not normalized, whereas the Z_m are normalized by the factor $(2N)^{-1}$)

$$\begin{aligned} \mathrm{P}_N(z_{m+1}, z_m) &= \mathrm{P}\left(Z_N(m+1) = z_{m+1} \middle| Z_N(m) = z_m\right) \\ &= \binom{2N}{2Nz^0_{m+1} \cdots 2Nz^n_{m+1}} \left(\psi^0(z_m)\right)^{2Nz^0_{m+1}} \cdots \left(\psi^n(z_m)\right)^{2Nz^n_{m+1}} \end{aligned} \tag{4.1.1}$$

where $z_{m+1}, z_m \in \overline{\Delta}_n^{(2N)}$, $z^0_m = 1 - z^1_m - \cdots - z^n_m$, $\psi^0 = 1 - \psi^1 - \cdots - \psi^n$, and $\psi^i(z_m), i = 1, \ldots, n$ are probabilities that may also be influenced by processes of selection and mutation.

We then also have the Chapman–Kolmogorov equation

$$\mathrm{P}_N(z_{m+1}, z_{m-1}) = \sum_z \mathrm{P}_N(z_{m+1}, z)\, \mathrm{P}_N(z, z_{m-1}). \tag{4.1.2}$$

Note that the notation is somewhat ambiguous here, as on the left hand side, we are looking at the transition probabilities for two time steps, from $m-1$ to $m+1$, whereas on the right hand side, single time steps occur. For a more precise version, we refer to (2.3.4). An analogous result will also hold subsequently in the time continuous case.

The following proposition summarizes (2.5.14), (2.5.16) and (2.5.17).

Proposition 4.1.1 *The sequence of homogeneous Markov chains $\{Z_N(m)\}_{m\in\mathbb{N}}$ satisfies*

- $\mathrm{E}\Big(Z^i_N(m+1) - Z^i_N(m) \Big| Z_N(m) = z_N\Big) = b^i(z_N)(2N)^{-1} + o((2N)^{-1})$;
- $\mathrm{E}\Big(\big(Z^i_N(m+1) - Z^i_N(m)\big)\big(Z^j_N(m+1) - Z^j_N(m)\big) \Big| Z_N(m) = z_N\Big) = z^i_N(\delta_{ij} - z^j_N)(2N)^{-1} + o((2N)^{-1})$;
- $\mathrm{E}\Big(\big(Z_N(m+1) - Z_N(m)\big)^{\boldsymbol{\alpha}} \Big| Z_N(m) = z_N\Big) = o((2N)^{-1})$ *with* $\boldsymbol{\alpha} \in \mathbb{N}^n_0 : |\boldsymbol{\alpha}| = \alpha^1 + \ldots + \alpha^n \geq 3$.

Definition 4.1.1 Let E be a metric space. Denote by $D_E[0,\infty)$ the *space of right continuous functions $x : [0,\infty) \to E$ with left limits.*

Then, let $X_N(t) = Z_N([2Nt])$ be the homogeneous Markov process with sample paths in $D_{\overline{\Delta}_n^{(2N)}}[0,\infty)$ embedded in $D_{\overline{\Delta}_n}[0,\infty)$. We shall show that there exists a homogeneous continuous (diffusion) process $\{X(t)\}_{t\geq 0}$ in $\overline{\Delta}_n$ as a limit process of

the X_N when $N \to \infty$. That process will have the following properties.

$$\begin{aligned}
&\mathrm{E}\Big(X^i(t+\delta t) - X^i(t) | X(t) = x\Big) = b^i(x)(\delta t) + o(\delta t);\\
&\mathrm{E}\Big(\big(X^i(t+\delta t) - X^i(t)\big)\big(X^j(t+\delta t) - X^j(t)\big)\Big| X(t) = x\Big) = x^i(\delta_{ij} - x^j)(\delta t) + o(\delta t);\\
&\mathrm{E}\Big(\big(X(t+\delta t) - X(t)\big)^{\boldsymbol{\alpha}}\Big| X(t) = x\Big) = o(\delta t) \text{ with } \boldsymbol{\alpha} \in \mathbb{N}_0^n : |\boldsymbol{\alpha}| = \alpha^1 + \ldots + \alpha^n \geq 3.
\end{aligned} \tag{4.1.3}$$

These conditions are the continuous analogues of those in Proposition 4.1.1, and we shall prove that the process $\{X_N(t)\}_{t\geq 0}$ tends to the continuous process $\{X(t)\}_{t\geq 0}$, in a sense that needs to be specified. A technical point, which is not really conceptually difficult, but requires technical efforts to resolve, is that the discrete processes are defined on discrete spaces with spacing $\frac{1}{2N}$, but the limit space should be defined on the positive real axis. Therefore, the notion of convergence needs some care.

We first recall the basic definitions of semigroup theory, see for instance [36, 58, 72].

Definition 4.1.2 A one-parameter family $\{T(t)\}_{t\geq 0}$ of bounded linear operators on a Banach space $\mathbf{B}$ is called a *semigroup* if $T(0) = I$ and $T(t+s) = T(t)T(s)$ for all $t, s \geq 0$.

In our setting, the semigroup property will arise from the Chapman–Kolmogorov equation.

In order to be analytically tractable, our semigroups need to satisfy some properties that will ensure that they are generated by some infinitesimal generator with controlled behavior; those technical concepts are described in the following definition.

Definition 4.1.3 A semigroup $\{T(t)\}_{t\geq 0}$ on $\mathbf{B}$ is *strongly continuous* if

$$\lim_{t \searrow 0} T(t)f = f, \quad \forall f \in \mathbf{B};$$

it is *contracting* if

$$\|T(t)\| \leq 1, \quad \forall t \geq 0.$$

A (possibly unbounded) *linear operator* A on $\mathbf{B}$ is a linear mapping whose domain $\mathcal{D}(A)$ is a subspace of $\mathbf{B}$ and whose range $\mathcal{R}(A)$ lies in $\mathbf{B}$. The *graph* of A is given by

$$\mathcal{G}(A) = \{(f, Af) : f \in \mathcal{D}(A)\} \subset \mathbf{B} \times \mathbf{B}.$$

A linear operator A on $\mathbf{B}$ is *closed* if $\mathcal{G}(A)$ is a closed subspace of $\mathbf{B} \times \mathbf{B}$.

A linear operator B is a *linear extension* of A if $\mathcal{D}(A) \subset \mathcal{D}(B)$ and $Bf = Af$, $\forall f \in \mathcal{D}(A)$.

A linear operator A on $\mathbf{B}$ is *closable* if it has a closed linear extension.

If A is closable, then the *closure* $\overline{A}$ of A is the minimal closed linear extension of A, more specifically, it is the closed linear operator B whose graph is the closure (in $\mathbf{B} \times \mathbf{B}$) of the graph of A.

The *(infinitesimal) generator of a semigroup* $\{T(t)\}_{t\geq 0}$ on $\mathbf{B}$ is the linear operator A defined by

$$Af = \lim_{t \searrow 0} \frac{T(t)f - f}{t},$$

where the domain $\mathcal{D}(A)$ of A is the subspace of all $f \in \mathbf{B}$ for which this limit exists.

We shall use the abbreviations $\mathbf{B} = C(\overline{\Delta}_n), \mathbf{B}_N = C(\overline{\Delta}_n^{(2N)})$ for the Banach spaces of continuous functions on $\overline{\Delta}_n$, $\overline{\Delta}_n^{(2N)}$ with the sup norm, and we need the projection operator

$$\pi_N : \mathbf{B} \to \mathbf{B}_N, \quad \pi_N(f) = f|_{\overline{\Delta}_n^{(2N)}},$$

which obviously is a contracting linear operator.

Lemma 4.1.1

$$U_N : \mathbf{B}_N \to \mathbf{B}_N,$$

defined by

$$U_N f_N(z_N) = \mathrm{E}\Big(f_N\big(Z_N(1)\big)\Big|Z_N(0) = z_N\Big), \quad \forall f_N \in \mathbf{B}_N, z_N \in \overline{\Delta}_n^{(2N)},$$

is a contracting linear operator U_N *on* $\mathbf{B}_N$.

Proof This follows from the fact that averaging w.r.t. a probability distribution decreases norms. In detail, for $f_N \in \mathbf{B}_N, z_N \in \overline{\Delta}_n^{(2N)}$

$$\begin{aligned} |U_N f_N(z_N)| &= \Big| \sum_{\overline{z}_N \in \overline{\Delta}_n^{(2N)}} f_N(\overline{z}_N)\, \mathrm{P}_N(z_N, \overline{z}_N) \Big| \\ &\leq \sum_{\overline{z}_N \in \overline{\Delta}_n^{(2N)}} \big| f_N(\overline{z}_N) \big|\, \mathrm{P}_N(z_N, \overline{z}_N) \\ &\leq \sum_{\overline{z}_N \in \overline{\Delta}_n^{(2N)}} \Big\| f_N \Big\|_{\mathbf{B}_N} \mathrm{P}_N(z_N, \overline{z}_N) \\ &= \Big\| f_N \Big\|_{\mathbf{B}_N}. \end{aligned} \tag{4.1.4}$$

Thus

$$\left\| U_N f_N \right\|_{\mathbf{B}_N} \leq \left\| f_N \right\|_{\mathbf{B}_N},$$

which is the contraction property. □

Lemma 4.1.2

$$T_N(t) : \mathbf{B}_N \to \mathbf{B}_N,$$

defined by

$$T_N(t) f_N(x_N) = \mathrm{E}\Big(f_N\big(X_N(t)\big) \Big| X_N(0) = x_N \Big), \quad \forall f_N \in \mathbf{B}_N, x_N \in \overline{\Delta}_n^{(2N)},$$

yields a one-parameter family of contracting linear operators $\{T_N(t)\}_{t\geq 0}$ *on* $\mathbf{B}_N$ *with the semigroup property (only) on* $\mathbb{R}^+/2N$.

Proof It follows from the homogeneity and the Chapman–Kolmogorov equation (4.1.2) that

$$\begin{aligned}
T_N(t) f_N(x_N) &= \mathrm{E}\Big(f_N\big(Z_N([2Nt])\big) \Big| Z_N(0) = x_N \Big) \\
&= \mathrm{E}\Big(f_N\big(Z_N(m)\big) \Big| Z_N(0) = x_N \Big) \quad (\text{where } m = [2Nt]) \\
&= \sum_{z_N^m} f_N(z_N^m)\, \mathrm{P}\left(Z_N(m) = z_N^m \Big| Z_N(0) = x_N \right) \\
&= \sum_{z_N^m} f_N(z_N^m) \sum_{z_N^{(m-1)}} \mathrm{P}\left(Z_N(m) = z_N^m \Big| Z_N(m-1) = z_N^{(m-1)} \right) \times \\
&\quad \times \mathrm{P}\left(Z_N(m-1) = z_N^{(m-1)} \Big| Z_N(0) = x_N \right) \quad (\text{by the Chapman Kolmogorov equation}) \\
&= \sum_{z_N^m} f_N(z_N^m) \sum_{z_N^{(1)}, \ldots, z_N^{(m-1)}} \mathrm{P}\left(Z_N(m) = z_N^m \Big| Z_N(m-1) = z_N^{(m-1)} \right) \times \\
&\quad \times \mathrm{P}\left(Z_N(m-1) = z_N^{(m-1)} \Big| Z_N(m-2) = z_N^{(m-2)} \right) \cdots \mathrm{P}\left(Z_N(1) = z_N^{(1)} \Big| Z_N(0) = x_N \right) \\
&= \sum_{z_N^m} f_N(z_N^m) \sum_{z_N^{(1)}, \ldots, z_N^{(m-1)}} \mathrm{P}_N(z_N^{(m-1)}, z_N^m)\, \mathrm{P}_N(z_N^{(m-2)}, z_N^{(m-1)}) \cdots \mathrm{P}_N(x_N, z_N^{(1)}) \\
&\quad (\text{by the homogeneous Markov property}) \\
&= \sum_{z_N^{(1)}, \ldots, z_N^{(m-1)}} \sum_{z_N^m} f_N(z_N^m)\, \mathrm{P}_N(z_N^{(m-1)}, z_N^m)\, \mathrm{P}_N(z_N^{(m-2)}, z_N^{(m-1)}) \cdots \mathrm{P}_N(x_N, z_N^{(1)})
\end{aligned}$$

$$= \sum_{z_N^{(1)},\dots,z_N^{(m-2)}} \sum_{z_N^{(m-1)}} U_N f_N(z_N^{(m-1)})\, \mathrm{P}_N(z_N^{(m-2)}, z_N^{(m-1)}) \cdots \mathrm{P}_N(x_N, z_N^{(1)})$$

$$= \sum_{z_N^{(1)},\dots,z_N^{(m-2)}} (U_N)^2 f_N(z_N^{(m-2)}) \cdots \mathrm{P}_N(x_N, z_N^{(1)})$$

$$= U_N^m f_N(x_N) = U_N^{[2Nt]} f_N(x_N). \tag{4.1.5}$$

Therefore, $T_N(t) = U_N^{[2Nt]}$ is a contracting linear operator for every t. The semigroup property on $\mathbb{R}^+/2N$ is obvious. This completes the proof. □

We shall now prove the analogous result in the continuum limit and identify the generator.

Lemma 4.1.3

$$T(t) : \mathbf{B} \to \mathbf{B},$$

defined by

$$T(t)f(x) = \mathrm{E}\Big(f\big(X(t)\big)\Big|X(0) = x\Big), \quad \forall f \in \mathbf{B}, x \in \overline{\Delta}_n,$$

yields a strongly continuous contracting semigroup $\{T(t)\}_{t\geq 0}$ *on* $\mathbf{B}$ *with generator*

$$Af(x) = \frac{1}{2}\sum_{i,j=1}^{n} x^i(\delta_{ij} - x^j)\frac{\partial^2 f}{\partial x^i \partial x^j}(x) + \sum_{i=1}^{n} b^i(x)\frac{\partial f}{\partial x^i}(x). \tag{4.1.6}$$

We note that when the coefficients b^i vanish, which is the case in the absence of selection or mutation effects, this operator is the same as the operator (3.10.1) for the inverse metric (3.8.7) (except for a factor $\frac{1}{2}$).

Proof We denote the transition density function of the homogeneous diffusion process $\{X(t)\}_{t\geq 0}$ by $p(t, x, z)$. It follows from the Chapman–Kolmogorov equation that

$$T(t+s)f(x) = \mathrm{E}(f(X(t+s))|X(0) = x)$$

$$= \int f(\overline{z})p(t+s, x, \overline{z})d\overline{z}$$

$$= \int f(\overline{z})\Big(\int p(t, x, z)p(s, z, \overline{z})dz\Big)d\overline{z} \quad \text{(by the Chapman–Kolmogorov equation)}$$

$$
\begin{aligned}
&= \int \Big(\int f(\overline{z}) p(s,z,\overline{z}) d\overline{z} \Big) p(t,x,z) dz \\
&= \int T(s) f(z) p(t,x,z) dz \\
&= T(t)T(s)f(x). \qquad (4.1.7)
\end{aligned}
$$

Moreover, $T(0)f(x) = \mathrm{E}(f(X(0))|X(0) = x) = f(x)$, i.e., $T(0) = I$. Therefore $\{T(t)\}_{t\geq 0}$ is a semigroup on $\mathbf{B}$. The strong continuity of this semigroup follows from the continuity of f and $X(t)$. The contraction follows from

$$
\begin{aligned}
|T(t)f(x)| &= \left| \int f(z) p(t,x,z) dz \right| \\
&\leq \int |f(z)| p(t,x,z) dz \qquad (4.1.8) \\
&\leq \int \|f\|_{\mathbf{B}}\, p(t,x,z) dz = \|f\|_{\mathbf{B}}, \quad \forall t \geq 0, f \in \mathbf{B}, x \in \overline{\Delta}_n.
\end{aligned}
$$

It follows that $\|T(t)f\|_{\mathbf{B}} \leq \|f\|_{\mathbf{B}}$ for all $t \geq 0, f \in \mathbf{B}$.

Now, for $f \in C^3(\overline{\Delta}_n)$ we have

$$
\begin{aligned}
T(t)f(x) - f(x) &= \int f(z) p(t,x,z) dz - f(x) \\
&= \int \Big(f(z) - f(x) \Big) p(t,x,z) dz \\
&= \int \Big(\sum_{i=1}^n \frac{\partial f}{\partial x^i}(x)(z^i - x^i) + \frac{1}{2} \sum_{i,j=1}^n \frac{\partial^2 f}{\partial x^i \partial x^j}(x)(z^i - x^i)(z^j - x^j) + \\
&\quad + \frac{1}{6} \sum_{i,j,k=1}^n \frac{\partial^3 f}{\partial x^i \partial x^j \partial x^k}(x^*)(z^i - x^i)(z^j - x^j)(z^k - x^k) \Big) p(t,x,z) dz \\
&\quad \text{(by Taylor expanding } f \text{ at } x, \text{ where } x^* \text{is some point in } \overline{\Delta}_n) \\
&= \sum_{i=1}^n \frac{\partial f}{\partial x^i}(x) \Big(b^i(x)t + o(t) \Big) + \frac{1}{2} \sum_{i,j=1}^n \frac{\partial^2 f}{\partial x^i \partial x^j}(x) \Big(x^i(\delta_{ij} - x^j)t + o(t) \Big) \\
&\quad + \frac{1}{6} \sum_{i,j,k=1}^n \frac{\partial^3 f}{\partial x^i \partial x^j \partial x^k}(x^*) o(t) \quad \text{(due to Eq. (4.1.3))} \\
&= \sum_{i=1}^n \frac{\partial f}{\partial x^i}(x) b^i(x) t + \frac{1}{2} \sum_{i,j=1}^n \frac{\partial^2 f}{\partial x^i \partial x^j}(x) x^i(\delta_{ij} - x^j)t + o(t). \qquad (4.1.9)
\end{aligned}
$$

Therefore, $C^3(\overline{\Delta}_n) \subset \mathcal{D}(A)$[1] and for $f \in C^3(\overline{\Delta}_n)$

$$\begin{aligned} Af(x) &= \lim_{t \searrow 0} \frac{T(t)f(x) - f(x)}{t} \\ &= \sum_{i=1}^{n} b^i(x) \frac{\partial f}{\partial x^i}(x) + \frac{1}{2} \sum_{i,j=1}^{n} x^i(\delta_{ij} - x^j) \frac{\partial^2 f}{\partial x^i \partial x^j}(x). \end{aligned} \tag{4.1.10}$$

This completes the proof. □

Theorem 4.1.1 *The sequence of discrete generators A_N of $\{T_N(t)\}_{t \geq 0}$ given by*

$$A_N = \frac{T_N(\frac{1}{2N}) - I}{\frac{1}{2N}} = 2N(U_N - I)$$

converges to the generator A in the sense that for all $f \in \mathcal{D}(A)$ there exists a sequence $f_N \in \mathbf{B}_N$ such that $f_N \to f$ and $A_N f_N \to Af$ as $N \to \infty$ in the sense that

$$\lim_{N \to \infty} \|f_N - \pi_N f\|_{\mathbf{B}_N} = 0,$$

and

$$\lim_{N \to \infty} \|A_N f_N - \pi_N A f\|_{\mathbf{B}_N} = 0.$$

Proof As $C^3(\overline{\Delta}_n) \subset \mathcal{D}(A)$ is dense in $\mathbf{B}$, we only need to prove the theorem for $f \in C^3(\overline{\Delta}_n)$. In fact, for each $f \in C^3(\overline{\Delta}_n)$, choosing $f_N = \pi_N f$, we have

$$\begin{aligned} A_N f_N(x_N) - \pi_N A f(x_N) &= 2N(U_N - I) f_N(x_N) - \pi_N A f(x_N) \\ &= 2N \sum_{z_N} \Big(f_N(z_N) - f_N(x_N) \Big) p_N(x_N, z_N) - \pi_N A f(x_N) \\ &= \pi_N \left(2N \sum_{z_N} \Big(f(z_N) - f(x_N) \Big) p_N(x_N, z_N) - Af(x_N) \right) \\ &= \pi_N \left(2N \sum_{z_N} \Big(\sum_{i=1}^{n} \frac{\partial f}{\partial x^i}(x)(z_N^i - x_N^i) p_N(x_N, z_N) \right. \end{aligned}$$

[1]The maximal domain of definition $\mathcal{D}(A)$ of A is larger than $C^3(\overline{\Delta}_n)$, but we shall not need that here. It suffices for our purposes that C^3 is dense in $\mathbf{B}$.

$$+\frac{1}{2}\sum_{i,j=1}^{n}\frac{\partial^2 f}{\partial x^i\partial x^j}(x)(z_N^i-x_N^i)(z_N^j-x_N^j)p_N(x_N,z_N)$$

$$+\frac{1}{6}\sum_{i,j,k=1}^{n}\frac{\partial^3 f}{\partial x^i\partial x^j\partial x^k}(x^*)(z_N^i-x_N^i)(z_N^j-x_N^j)(z_N^k-x_N^k)p_N(x_N,z_N)\Big)-Af(x_N)\Bigg)$$

$$=\pi_N\Bigg(\sum_{i=1}^{n}\frac{\partial f}{\partial x^i}(x)\Big(b^i(x)+o(1)\Big)+\frac{1}{2}\sum_{i,j=1}^{n}\frac{\partial^2 f}{\partial x^i\partial x^j}(x)\Big(x^i(\delta_{ij}-x^j)+o(1)\Big)$$

$$+\frac{1}{6}\sum_{i,j,k=1}^{n}\frac{\partial^3 f}{\partial x^i\partial x^j\partial x^k}(x^*)o(1)-Af(x_N)\Bigg)$$

$$=\pi_N(o(1))=o(1). \tag{4.1.11}$$

This implies the proof. □

Theorem 4.1.2 *The sequence of $\{T_N(t)\}_{t\geq 0}$ converges to the semigroup $T(t)_{t\geq 0}$ in the sense that for each $f\in\mathbf{B}$ there exists $f_N\in\mathbf{B}_N$ such that $f_N\to f$ and $T_N(t)f_N\to T(t)f$ uniformly in bounded intervals as $N\to\infty$.*

Proof Choosing $f_N=\pi_N f$, we have

$$\begin{aligned}\|T_N(t))f_N-\pi_N T(t)f\|&\leq\|U_N^{[2Nt]}f_N-e^{[2Nt](U_N-I)}f_N\|+\\&+\|e^{[2Nt](U_N-I)}f_N-e^{2N(U_N-I)t}f_N\|+\|e^{2N(U_N-I)t}f_N-\pi_N T(t)f\|\\&=A_1+A_2+A_3.\end{aligned} \tag{4.1.12}$$

We start by estimating A_1.

Lemma 4.1.4

$$\|U_N^m f_N-e^{m(U_N-I)}f_N\|\leq\sqrt{m}\|(U_N f_N-f_N\|$$

for all $m=0,1,\ldots$.

Proof Fix $m\geq 0$. For $k=0,1,\ldots$, we have due to the contraction of U_N

$$\begin{aligned}\|U_N^m f_N-U_N^k f_N\|&\leq\|U_N^{|k-m|}f_N-f_N\|\\&=\left\|\sum_{i=0}^{|k-m|-1}U_N^i(U_N f_N-f_N)\right\|\\&\leq|k-m|\|U_N f_N-f_N\|.\end{aligned} \tag{4.1.13}$$

Therefore,

$$\begin{aligned}\|U_N^m f_N - e^{m(U_N-I)}f\| &= \left\|U_N^m f_N - e^{-m}\sum_{k=0}^{\infty}\frac{m^k}{k!}B^k f_N\right\| \\ &= e^{-m}\left\|\sum_{k=0}^{\infty}(U_N^m f_N - U_N^k f_N)\frac{m^k}{k!}\right\| \\ &\le e^{-m}\sum_{k=0}^{\infty}|k-m|\frac{m^k}{k!}\|U_N f_N - f_N\| \\ &= \mathrm{E}\Big(|X-\mathrm{E}(X)|\Big)\|U_N f_N - f_N\| \\ &\le \sqrt{\mathrm{E}\Big(X-\mathrm{E}(X)\Big)^2}\,\|U_N f_N - f_N\| \\ &= \sqrt{m}\|U_N f_N - f_N\|,\end{aligned} \tag{4.1.14}$$

where X is a Poisson random variable with parameter m, i.e.

$$\mathrm{P}(X=k) = e^{-m}\frac{m^k}{k!};$$

X has mean and variance m (see (2.7.1)–(2.7.3)). □

Therefore,

$$\begin{aligned}A_1 &= \|U_N^{[2Nt]}f_N - e^{[2Nt](U_N-I)}f_N\| \\ &\le \sqrt{[2Nt]}\|U_N f_N - f_N\| \\ &= \frac{\sqrt{[2Nt]}}{2N}\|A_N f_N\|.\end{aligned} \tag{4.1.15}$$

As $A_N f_N$ converges to Af as $N\to\infty$, so $\|A_N f_N\|$ is bounded, therefore A_1 tends to 0 uniformly in bounded intervals as $N\to\infty$.

To estimate A_2, A_3, put $\overline{T}_N(t) = e^{A_N t} = e^{2N(U_N-I)t}$. We easily see that $\{\overline{T}_N(t)\}_{t\ge 0}$ is a strongly continuous contracting semigroup on $\mathbf{B}_N$ with the generator A_N. In fact, the contraction follows from

$$\begin{aligned}\|\overline{T}_N(t)\| &= \|e^{2N(U_N-I)t}\| \\ &= e^{-2Nt}\|e^{2NtU_N}\| \\ &\le e^{-2Nt}e^{2Nt\|U_N\|} \\ &\le 1.\end{aligned} \tag{4.1.16}$$

Then, we have

$$\begin{aligned} A_2 &= \|e^{[2Nt](U_N-I)}f_N - e^{2N(U_N-I)t}\| \\ &= \|\Big(1-e^{\frac{\{2Nt\}}{2N}}\Big)\overline{T}_N(t)f_N\| \\ &\le \Big(1-e^{\frac{\{2Nt\}}{2N}}\Big)\|f_N\| \\ &\le \Big(1-e^{\frac{\{2Nt\}}{2N}}\Big)\|f\|. \end{aligned} \tag{4.1.17}$$

Therefore, A_2 tends to 0 uniformly on bounded intervals as $N \to \infty$.

We finally estimate A_3.

Lemma 4.1.5 *For $N \in \mathbb{N}$ and $t \ge 0$,*

$$\overline{T}_N(t)\pi_N f - \pi_N T(t)f = \int_0^t \overline{T}_N(t-s)(A_N\pi_N - \pi_N A)T(s)f ds,$$

and therefore

$$\|\overline{T}_N(t)\pi_N f - \pi_N T(t)f\| \le \int_0^t \|(A_N\pi_N - \pi_N A)T(s)f\| ds.$$

Proof It is easy to see that $T(s)f \in \mathcal{D}(A)$ for all $f \in \mathbf{B}$. Set

$$h_N(s) = \overline{T}_N(t-s)\pi_N T(s)f.$$

Then we have

$$\begin{aligned} \frac{d}{ds}h_N(s) &= \Big(\frac{d}{ds}\overline{T}_N\Big)\pi_N T(s)f + \overline{T}_N(t-s)\pi_N \frac{d}{ds}T(s)f \\ &= \overline{T}_N(t-s)(-A_N)\pi_N T(s)f + \overline{T}_N(t-s)\pi_N A T(s)f \\ &= \overline{T}_N(t-s)\Big(\pi_N A - A_N\pi_N\Big)T(s)f. \end{aligned}$$

Thus we obtain

$$\begin{aligned} \overline{T}_N(t)\pi_N f - \pi_N T(t)f &= h_n(0) - h_N(t) \\ &= -\int_0^t \frac{d}{ds}h_N(s)ds \\ &= \int_0^t \overline{T}_N(t-s)\Big(A_N\pi_N - \pi_N A\Big)T(s)f ds. \end{aligned}$$

This completes the proof. □

Therefore, we have

$$\begin{aligned} A_3 &= \|\overline{T}_N(t)f_N - \pi_N T(t)f\| \\ &\le \int_0^t \|(A_N\pi_N - \pi_N A)T(s)f\|ds. \end{aligned} \tag{4.1.18}$$

Hence, A_3 tends to 0 uniformly on bounded intervals as $N \to \infty$.

This completes the proof. □

The following corollary summarizes the results that will be important in our study.

Corollary 4.1.1 *For $f \in \mathbf{B}$, $x \in \overline{\Delta}_n$, $\mathrm{E}(\pi_N f(x_N)|X_N(0) = x)$ converges to*

$$f(x,t) := T(t)f(x) = \mathrm{E}\Big(f\big(X(t)\big)\Big|X(0) = x\Big)$$

which satisfies

$$\frac{\partial}{\partial t}f(x,t) = Af(x,t) = \frac{1}{2}\sum_{i,j=1}^{n} x^i(\delta_{ij} - x^j)\frac{\partial^2 f(x,t)}{\partial x^i \partial x^j} + \sum_{i=1}^{n} b^i(x)\frac{\partial f(x,t)}{\partial x^i}. \tag{4.1.19}$$

Proof The convergence follows from Theorems 4.1.2 and 4.1.1. Equation (4.1.19) has been derived in Lemma 4.1.3. □

The functions f that we shall apply Corollary 4.1.1 to are the moments of our distribution. Thus, we consider the smooth function $f(x,t) = m_{\boldsymbol{\alpha}}(x,t) = \mathrm{E}(X^{\boldsymbol{\alpha}}(t)|x(0) = x)$ on $\overline{\Delta}_n$. Theorem 4.1.2 implies that the $\boldsymbol{\alpha}$th moment of the diffusion random variable $X(t)$ is approximated by the $\boldsymbol{\alpha}$th moment of the Wright–Fisher discrete variable $X_N(t)$ in the sense that, if $x_N \to x$ in $\overline{\Delta}_n$ as $N \to \infty$, then

$$\begin{aligned} &m_{\boldsymbol{\alpha}}(X_N(t)|X_N(0) = x_N) = \mathrm{E}(\pi_N f(x_N)) = T_N(t)f_N(x_N) \\ \to &T(t)f(x) = \mathrm{E}(f(X(t))|X(0) = x) = m_{\boldsymbol{\alpha}}(X(t)|X(0) = x) \quad \text{as } N \to \infty. \end{aligned} \tag{4.1.20}$$

By Corollary 4.1.1, the moments of the diffusion process will satisfy the equation

$$\frac{\partial}{\partial t}m_{\boldsymbol{\alpha}} = \frac{1}{2}\sum_{i,j=1}^{n} x^i(\delta_{ij} - x^j)\frac{\partial^2 m_{\boldsymbol{\alpha}}}{\partial x^i \partial x^j} + \sum_{i=1}^{n} b^i(x)\frac{\partial m_{\boldsymbol{\alpha}}}{\partial x^i}.$$

4.2 The Diffusion Limit of the Wright–Fisher Model

Utilizing the theory developed in the previous section, in this section, we shall consider the diffusion limit of the Wright–Fisher model and state the corresponding Kolmogorov equations. In contrast to the previous section, however, we shall also

incorporate boundary transitions, but for simplicity, we shall concentrate on the case where the b^i vanish.

We recall $P_{2N}(t+\delta t, x_0, x)$ from (2.3.10) and the moment expression (2.3.9). By the general results of the previous section (see Theorems 4.1.1, 4.1.2), the processes P_{2N} converge to a limiting process $p(t, x_0, x)$, and also the corresponding moments converge to the moments of the limiting process by Remark 4.1.20. Considering the special case without selection or mutations, the coefficients b^i of the semigroup generator A of (4.1.6) all vanish. The same technique, however, also works for the case of mutations and selection where we get nontrivial coefficients b^i. This follows from the corresponding moment evolution derived in the next section.

The moments then become

$$m_{\boldsymbol{\alpha}}(t, x_0) = \left[x^{\boldsymbol{\alpha}}, p(t, x_0, x)\right]_n. \tag{4.2.1}$$

Here, we now also include the initial value x_0 in our notation.

Equation (4.2.1) requires some discussion. The moments as defined in (2.3.14) also involve values of the frequencies X where some components are zero. Such values correspond to boundary points of the simplex. Therefore, the moments in the diffusion limit should involve the contributions from the boundary. These are incorporated in the product $[.,.]_n$. Subsequently when we introduce the boundary flux, we shall see that this is the correct product, indeed.

The differential equation (2.3.17) then becomes

$$\dot{m}_{\boldsymbol{\alpha}}(t, x_0) = \left[-\frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1)}{2} x^{\boldsymbol{\alpha}} + \sum_{i=1}^{n} \frac{\alpha_i(\alpha_i-1)}{2} x^{\boldsymbol{\alpha}-e_i}, p(t, x_0, x) \right]_n. \tag{4.2.2}$$

We now recall the generator (4.1.6) of our semigroup. It has polynomial coefficients, and therefore, it maps polynomials to polynomials; in fact, as we assume in this Section that the coefficients b^i vanish, we have

$$Ax^{\boldsymbol{\alpha}} = -\frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1)}{2} x^{\boldsymbol{\alpha}} + \sum_{i=1}^{n} \frac{\alpha_i(\alpha_i-1)}{2} x^{\boldsymbol{\alpha}-e_i}. \tag{4.2.3}$$

Hence, we can rewrite (4.2.2) as

$$\dot{m}_{\boldsymbol{\alpha}}(t, x_0) = [Ax^{\boldsymbol{\alpha}}, p(t, x_0, x)]_n. \tag{4.2.4}$$

On the other hand, differentiating (4.2.1) w.r.t. t yields

$$\dot{m}_{\boldsymbol{\alpha}}(t, x_0) = \left[x^{\boldsymbol{\alpha}}, \frac{\partial}{\partial t} p(t, x_0, x)\right]_n. \tag{4.2.5}$$

Equating (4.2.4) and (4.2.5) therefore yields

$$\left[x^{\boldsymbol{\alpha}}, \frac{\partial}{\partial t}p(t,x_0,x)\right]_n = [Ax^{\boldsymbol{\alpha}}, p(t,x_0,x)]_n \tag{4.2.6}$$

for all $x^{\boldsymbol{\alpha}}$ and by linearity then for all polynomials. Since the polynomials are dense in the space of all smooth functions, we conclude that for any smooth function φ, we must have for the expectation value $\varphi(t,x_0) := \mathrm{E}_{p(t,x_0,\cdot)}(\varphi) := [\varphi(x), p(t,x_0,x)]_n$ (where again the identification of the convolution with $p(t,x_0,\cdot)$ via the scalar product $[.,.]_n$ with the expectation value will be justified below) that

$$\frac{\partial}{\partial t}\varphi(t,x_0) = \frac{\partial}{\partial t}\mathrm{E}_{p(t,x_0,.)}(\varphi) = [A\varphi(x), p(t,x_0,x)]_n. \tag{4.2.7}$$

Also,

$$\frac{\partial}{\partial t}\mathrm{E}_{p(t,x_0,.)}(\varphi) = \frac{d}{dt}[\varphi(x), p(t,x_0,x)]_n = \left[\varphi(x), \frac{\partial}{\partial t}p(t,x_0,x)\right]_n. \tag{4.2.8}$$

An important point in all our considerations will be to investigate the formula resulting from integrating (4.2.7) by parts. In general, this formula will involve boundary terms, and they will be identified in Chap. 8, Eq. (8.1.11). In any case, for smooth test functions φ vanishing at the boundary, integrating (4.2.7) by parts yields

$$\frac{\partial}{\partial t}\varphi(t,x_0) = \int \varphi(x)A_x^* p(t,x_0,x)d\boldsymbol{\lambda} \tag{4.2.9}$$

with the adjoint A^*, where the subscript x indicates that A^* operates w.r.t. the variable x. Since this holds for all smooth functions φ vanishing at the boundary, we conclude that the density $p(t,x_0,x)$ satisfies the differential equation

$$\frac{\partial}{\partial t}p(t,x_0,x) = A_x^* p(t,x_0,x). \tag{4.2.10}$$

Altogether, we generally have (there is an alternative proof in [113], Proposition 3.5; see also the original derivation of Kolmogorov in [82] on $\mathbb{R}^n$ instead of on the simplex as here):

Theorem 4.2.1 *The diffusion approximation of an n-allelic Wright–Fisher model may be described by the Kolmogorov equations for its transition probability density* $u\colon (\Delta_n)_\infty \longrightarrow \mathbb{R}^+$ *of its gametic configuration* $x = (x^1,\ldots,x^n) \in \Delta_n$*:*

$$L_n u(x,t) \equiv A^* u(x,t) = \frac{1}{2}\sum_{i,j=1}^{n}\frac{\partial^2}{\partial x^i \partial x^j}\left(a^{ij}(x)u(x,t)\right) - \sum_{i=1}^{n}\frac{\partial}{\partial x^i}\left(b^i(x)u(x,t)\right) \tag{4.2.11}$$

is the forward operator, and the Kolmogorov forward equation then is

$$\frac{\partial}{\partial t}u(x,t) = L_n u(x,t) \quad \text{in } (\Delta_n)_\infty = \Delta_n \times (0,\infty) \tag{4.2.12}$$

for $u(\cdot\,,t) \in C^2(\Delta_n)$ *for each fixed* $t \in (0,\infty)$ *and* $u(x,\cdot) \in C^1((0,\infty))$ *for each fixed* $x \in \Delta_n$.

Moreover, when we consider the dependency on the initial data x_0, s *of* u*, i.e., consider a conditional probability density* $u(x,t|x_0,s)$*, then for any Borel measurable subset* B *in* $\overline{\Delta}_n$*, the probability*

$$v(s,x_0) = \int_B u(t,x|s,x_0)\mathbb{1}_n(dx)$$

satisfies the Kolmogorov backward equation

$$\frac{\partial}{\partial s}v(x_0,s) = L_n^* v(x_0,s) \quad \text{in } (\overline{\Delta}_n)_\infty = \overline{\Delta}_n \times (0,\infty) \tag{4.2.13}$$

for $v(\cdot,s) \in C^2(\overline{\Delta}_n)$ *for each fixed* $s \in (0,\infty)$ *and* $v(x_0,\cdot) \in C^1((0,\infty))$ *for each fixed* $x_0 \in \overline{\Delta}_n$*, where*

$$L_n^* v \equiv Av = \frac{1}{2}\sum_{i,j=1}^n a^{ij}(x_0)\frac{\partial^2}{\partial x_0^i \partial x_0^j}v(x_0,s) + \sum_{i=1}^n b^i(x_0)\frac{\partial}{\partial x_0^i}v(x_0,s) \tag{4.2.14}$$

is the backward operator.

4.3 Moment Evolution

In this section, we write down the moment evolution equations in detail, from the simplest case of the 2-allele model without selection and mutation to the most general case. We hope that this section can be a useful reference for various applications. A reader only interested in the general theory may wish to skip this section.

We recall the moments of our continuous Markov process $(X_t)_{t\geq 0}$; they satisfy

$$\begin{aligned} \mathrm{E}(\delta X_t^i | X_t) &= b^i(X_t)\delta t + o(\delta t), \\ \mathrm{E}(\delta X_t^i X_t^j | X_t) &= a^{ij}(X_t)\delta t + o(\delta t), \\ \mathrm{E}(\delta X^{\boldsymbol{\alpha}} t | X_t) &= o(\delta t), \text{ for } |\boldsymbol{\alpha}| \geq 3. \end{aligned} \tag{4.3.1}$$

Note that the factor $\frac{1}{2N}$ from (2.5.15)–(2.5.17) is incorporated in the time step δt here.

We now generalize (2.3.16) and (2.3.17) to also include selection and mutation effects:

$$\begin{aligned} m_{\boldsymbol{\alpha}}(t+\delta t) &:= \mathrm{E}(X_{t+\delta t}^{\boldsymbol{\alpha}}) \\ &= \sum_{\boldsymbol{\beta}\le\boldsymbol{\alpha}} \binom{\boldsymbol{\alpha}}{\boldsymbol{\beta}} \mathrm{E}\Big(\mathrm{E}\big((\delta X_t)^{\boldsymbol{\beta}}|X_t\big)X_t^{\boldsymbol{\alpha}-\boldsymbol{\beta}}\Big) \\ &= m_{\boldsymbol{\alpha}}(t) + \sum_{i=1}^{n} \alpha_i \mathrm{E}\Big(b^i(X_t)(\delta t)X_t^{\boldsymbol{\alpha}-e_i}\Big) + \sum_{i\ne j} \alpha_i\alpha_j \mathrm{E}\Big(a^{ij}(X_t)(\delta t)(X_t)^{\boldsymbol{\alpha}-e_i-e_j}\Big) \\ &\quad + \sum_{i=1}^{n} \frac{\alpha_i(\alpha_i-1)}{2} \mathrm{E}\Big(a^{ii}(X_t)(\delta t)X_t^{\boldsymbol{\alpha}-2e_i}\Big) + o(\delta t). \end{aligned} \tag{4.3.2}$$

Subtracting $m_{\boldsymbol{\alpha}}(t)$ from both sides, dividing by δt and letting δt tend to 0, we obtain

$$\begin{aligned} \dot{m}_{\boldsymbol{\alpha}}(t) &= \sum_{i=1}^{n} \alpha_i \mathrm{E}\Big(b^i(X_t)X_t^{\boldsymbol{\alpha}-e_i}\Big) + \sum_{i\ne j} \alpha_i\alpha_j \mathrm{E}\Big(a^{ij}(X_t)X_t^{\boldsymbol{\alpha}-e_i-e_j}\Big) \\ &\quad + \sum_{i=1}^{n} \frac{\alpha_i(\alpha_i-1)}{2} \mathrm{E}\Big(a^{ii}(X_t)X_t^{\boldsymbol{\alpha}-2e_i}\Big). \end{aligned} \tag{4.3.3}$$

We shall now display these equations for various choices of the coefficients a^{ij} and b^i as derived in Sect. 2.5. In all cases, the $a^{ij}(X_t)$ and $b^i(X_t)$ are polynomials in X_t.

1. For the basic Wright–Fisher model with two alleles, $b(x) = 0, a(x) = x(1-x)$, and the moment evolution equation is

$$\begin{aligned} \dot{m}_k(t) &= \frac{k(k-1)}{2} \mathrm{E}\Big(X_t(1-X_t)X^{k-2}\Big) \\ &= \frac{k(k-1)}{2} m_{k-1}(t) - \frac{k(k-1)}{2} m_k(t). \end{aligned} \tag{4.3.4}$$

2. For the Wright–Fisher model with two alleles with mutation, by (2.6.5), $b(x) = \frac{\nu}{2} - \frac{\mu+\nu}{2}x, a(x) = x(1-x)$, and the moment evolution equation is

$$\begin{aligned} \dot{m}_k(t) &= k\mathrm{E}\Big(\big(\frac{1}{2}\nu - \frac{1}{2}(\mu+\nu)X_t\big)X_t^{k-1}\Big) + \frac{k(k-1)}{2}\mathrm{E}\Big(X_t(1-X_t)X^{k-2}\Big) \\ &= k\frac{\nu}{2}m_{k-1}(t) - k\frac{\mu+\nu}{2}m_k(t) + \frac{k(k-1)}{2}(m_{k-1}(t) - m_k(t)) \\ &= \frac{k(k-1+\nu)}{2}m_{k-1}(t) - \frac{k(k-1+\mu+\nu)}{2}m_k(t). \end{aligned} \tag{4.3.5}$$

3. For the Wright–Fisher model with two alleles with selection, by (2.6.6), $b(x) = x(1-x)(h-1+x-2hx)s$, $a(x) = x(1-x)$, and the moment evolution equation is

$$\begin{aligned}\dot{m}_k(t) &= k\mathrm{E}\Big(\big(s(h-1)X_t(1-X_t) + s(1-2h)X_t^2(1-X_t)\big)X_t^{k-1}\Big) \\ &\quad + \frac{k(k-1)}{2}\mathrm{E}\Big(X_t(1-X_t)X^{k-2}\Big) \\ &= ks(h-1)m_k(t) + ks(2-3h)m_{k+1}(t) + ks(2h-1)m_{k+2}(t) \\ &\quad + \frac{k(k-1)}{2}(m_{k-1}(t) - m_k(t)) \\ &= \frac{k(k-1)}{2}m_{k-1}(t) - \frac{k(k-1+s)}{2}m_k(t) + \frac{ks}{2}m_{k+1}(t), \\ &\qquad \Big(\text{in the special case } h = \frac{1}{2}\Big) \\ &= -\frac{ks}{2}(m_k(t) - m_{k+1}(t)) + \frac{k(k-1)}{2}(m_{k-1}(t) - m_k(t)), \\ &\qquad \Big(\text{in the special case } h = \frac{1}{2}\Big).\end{aligned} \tag{4.3.6}$$

4. For the Wright–Fisher model with two alleles with mutation and selection, by (2.6.7), $b(x) = \frac{\nu}{2} - \frac{\mu+\nu}{2}x + x(1-x)(h-1+x-2hx)s$, $a(x) = x(1-x)$, and the moment evolution equation is

$$\begin{aligned}\dot{m}_k(t) &= k\mathrm{E}\Big(\big(\frac{1}{2}\nu - \frac{1}{2}(\mu+\nu)X_t + s(h-1)X_t(1-X_t) \\ &\quad + s(1-2h)X_t^2(1-X_t)\big)X_t^{k-1}\Big) + \frac{k(k-1)}{2}\mathrm{E}\Big(X_t(1-X_t)X^{k-2}\Big) \\ &= k\frac{\nu}{2}m_{k-1}(t) - k\frac{\mu+\nu}{2}m_k(t) + ks(h-1)m_k(t) + ks(2-3h)m_{k+1}(t) \\ &\quad + ks(2h-1)m_{k+2}(t) + \frac{k(k-1)}{2}(m_{k-1}(t) - m_k(t)) \\ &= \frac{k(k-1+\nu)}{2}m_{k-1}(t) - \frac{k(k-1+s+\mu+\nu)}{2}m_k(t) + \frac{ks}{2}m_{k+1}(t) \\ &\qquad \Big(\text{in the special case } h = \frac{1}{2}\Big).\end{aligned} \tag{4.3.7}$$

5. We now turn to the Wright–Fisher model with $(n+1)$ alleles. If there is neither selection nor mutation, then by (2.3.11), (2.3.12), $b^i(x) = 0$, $a^{ij}(x) = x^i(\delta_{ij} - x^j)$,

and the moment evolution equation is

$$\begin{aligned}\dot{m}_{\boldsymbol{\alpha}}(t) &= \sum_{i\neq j}\alpha_i\alpha_j \mathrm{E}\Big(-X_t^iX_t^jX_t^{\boldsymbol{\alpha}-e_i-e_j}\Big)\\ &\quad+\sum_{i=1}^n\frac{\alpha_i(\alpha_i-1)}{2}\mathrm{E}\Big(X_t^i(1-X_t^i)X^{\boldsymbol{\alpha}-2e_i}\Big)\\ &=-\frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1)}{2}m_{\boldsymbol{\alpha}}(t)+\sum_{i=1}^n\frac{\alpha_i(\alpha_i-1)}{2}m_{\boldsymbol{\alpha}-e_i}(t).\end{aligned}\tag{4.3.8}$$

6. For the Wright–Fisher model with $(n+1)$ alleles with general mutation rates, by (2.5.15),

$$b^i(x)=-\Big(\sum_{j=0}^n\frac{\theta_{ij}}{2}\Big)x^i+\sum_{j=0}^n\frac{\theta_{ji}}{2}x^j,$$

where θ_{ii} is arbitrary and can be fixed as 0, and $a^{ij}(x)=x^i(\delta_{ij}-x^j)$, and the moment evolution equation is

$$\begin{aligned}\dot{m}_{\boldsymbol{\alpha}}(t) &= \sum_{i=1}^n\alpha_i\mathrm{E}\Bigg(\Big(-\sum_{j=0}^n\frac{\theta_{ij}}{2}X_t^i+\frac{\theta_{0i}}{2}+\sum_{j=1}^n\frac{\theta_{ji}-\theta_{0i}}{2}X_t^j\Big)X_t^{\boldsymbol{\alpha}-e_i}\Bigg)\\ &\quad+\sum_{i\neq j}\alpha_i\alpha_j\mathrm{E}\Big(-X_t^iX_t^jX_t^{\boldsymbol{\alpha}-e_i-e_j}\Big)+\sum_{i=1}^n\frac{\alpha_i(\alpha_i-1)}{2}\mathrm{E}\Big(X_t^i(1-X_t^i)X^{\boldsymbol{\alpha}-2e_i}\Big)\\ &=\sum_{i=1}^n-\frac{\alpha_i\vartheta_i}{2}m_{\boldsymbol{\alpha}}(t)+\sum_{i=1}^n\frac{\alpha_i\theta_{0i}}{2}m_{\boldsymbol{\alpha}-e_i}(t)+\sum_{i=1}^n\sum_{j=1}^n\frac{\alpha_i(\theta_{ji}-\theta_{0i})}{2}m_{\boldsymbol{\alpha}-e_i+e_j}\\ &\quad-\frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1)}{2}m_{\boldsymbol{\alpha}}(t)+\sum_{i=1}^n\frac{\alpha_i(\alpha_i-1)}{2}m_{\boldsymbol{\alpha}-e_i}(t),\quad\Big(\text{where }\vartheta_i=\sum_{j=0}^n\theta_{ij}\Big)\\ &=\sum_{i=1}^n-\frac{\alpha_i(\vartheta_i+\theta_{0i})}{2}m_{\boldsymbol{\alpha}}(t)+\sum_{i=1}^n\frac{\alpha_i\theta_{0i}}{2}m_{\boldsymbol{\alpha}-e_i}(t)+\sum_{\substack{i,j=1\\i\neq j}}^n\frac{\alpha_i(\theta_{ji}-\theta_{0i})}{2}m_{\boldsymbol{\alpha}-e_i+e_j}\\ &\quad-\frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1)}{2}m_{\boldsymbol{\alpha}}(t)+\sum_{i=1}^n\frac{\alpha_i(\alpha_i-1)}{2}m_{\boldsymbol{\alpha}-e_i}(t)\\ &=-\Big(\frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1)}{2}+\sum_{i=1}^n\frac{\alpha_i(\vartheta_i+\theta_{0i})}{2}\Big)m_{\boldsymbol{\alpha}}(t)+\sum_{i=1}^n\frac{\alpha_i(\alpha_i-1+\theta_{0i})}{2}m_{\boldsymbol{\alpha}-e_i}(t)\\ &\quad+\sum_{i,j=1i\neq j}^n\frac{\alpha_i(\theta_{ji}-\theta_{0i})}{2}m_{\boldsymbol{\alpha}-e_i+e_j}.\end{aligned}\tag{4.3.9}$$

7. For the Wright–Fisher model with $(n+1)$ alleles with uniform mutation (mutation rates depending only on the target genes), by (2.5.4), (2.5.15), $b^i(x) = \frac{\theta_i}{2} - \frac{|\boldsymbol{\theta}|}{2}x^i$, $a^{ij}(x) = x^i(\delta_{ij} - x^j)$, the preceding moment evolution equation (4.3.9) simplifies as

$$\begin{aligned}\dot{m}_{\boldsymbol{\alpha}}(t) &= \sum_{i=1}^{n}\alpha_i \mathrm{E}\left(\left(\frac{1}{2}\theta_i - \frac{1}{2}|\boldsymbol{\theta}|X_t^i\right)X_t^{\boldsymbol{\alpha}-e_i}\right) + \sum_{i\neq j}\alpha_i\alpha_j \mathrm{E}\left(-X_t^iX_t^jX_t^{\boldsymbol{\alpha}-e_i-e_j}\right)\\ &\quad + \sum_{i=1}^{n}\frac{\alpha_i(\alpha_i-1)}{2}\mathrm{E}\left(X_t^i(1-X_t^i)X^{\boldsymbol{\alpha}-2e_i}\right)\\ &= -\frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1+|\boldsymbol{\theta}|)}{2}m_{\boldsymbol{\alpha}}(t) + \sum_{i=1}^{n}\frac{\alpha_i(\alpha_i-1+\theta_i)}{2}m_{\boldsymbol{\alpha}-e_i}(t).\end{aligned} \tag{4.3.10}$$

In fact, if $\theta_{ij} = \theta_j$ for all $i \neq j$, then for all $i \in \{1,\dots,n\}$ we have

$$\theta_i + \theta_{0i} = \sum_{j=0}^{n}\theta_{ij} + \theta_{0i} = \sum_{\substack{j=0\\ j\neq i}}^{n}\theta_{ij} + \theta_{0i} = \sum_{\substack{j=0\\ j\neq i}}^{n}\theta_j + \theta_i = |\boldsymbol{\theta}|,$$

therefore

$$\sum_{i=1}^{n}\frac{\alpha_i(\vartheta_i+\theta_{0i})}{2} = \sum_{i=1}^{n}\frac{\alpha_i|\boldsymbol{\theta}|}{2} = \frac{|\boldsymbol{\alpha}||\boldsymbol{\theta}|}{2}.$$

Thus, the first term in (4.3.9) becomes

$$-\frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1+|\boldsymbol{\theta}|)}{2}m_{\boldsymbol{\alpha}}(t).$$

For the second term, because of $\theta_{0i} = \theta_i$, for all $i \in \{1,\dots,n\}$ we obtain

$$\sum_{i=1}^{n}\frac{\alpha_i(\alpha_i-1+\theta_i)}{2}m_{\boldsymbol{\alpha}-e_i}(t).$$

Finally, because of $\frac{\alpha_i(\theta_{ji}-\theta_{0i})}{2} = 0$ for all $i,j \in \{1,\dots,n\}$ with $j \neq i$, the third term is zero. Thus, for uniform mutation, (4.3.9) becomes (4.3.10), indeed.

8. For the Wright–Fisher model with $(n+1)$ alleles with special selection coefficients $s_{ij} = \frac{s_i+s_j}{2}$, (2.5.15) yields

$$b^i(x) = x^i\left(\sum_{j=0}^{n}\frac{s_i+s_j}{2}x^j - \sum_{k,l=0}^{n}\frac{s_k+s_l}{2}x^kx^l\right) = \frac{s_i}{2}x^i - \sum_{j=0}^{n}\frac{s_j}{2}x^ix^j,$$

and $a^{ij}(x) = x^i(\delta_{ij} - x^j)$, and the moment evolution equation is

$$\begin{aligned}
\dot{m}_{\boldsymbol{\alpha}}(t) &= \sum_{i=1}^{n} \alpha_i \mathrm{E}\left(\left(\frac{s_i}{2} X_t^i - \sum_{j=0}^{n} \frac{s_j}{2} X_t^i X_t^j \right) X_t^{\boldsymbol{\alpha} - e_i} \right) \\
&\quad + \sum_{i \neq j} \alpha_i \alpha_j \mathrm{E}\left(- X_t^i X_t^j X_t^{\boldsymbol{\alpha} - e_i - e_j} \right) + \sum_{i=1}^{n} \frac{\alpha_i(\alpha_i - 1)}{2} \mathrm{E}\left(X_t^i (1 - X_t^i) X^{\boldsymbol{\alpha} - 2e_i} \right) \\
&= \sum_{i=1}^{n} \alpha_i \mathrm{E}\left(\left(\frac{s_i - s_0}{2} - \sum_{j=1}^{n} \frac{s_j - s_0}{2} X_t^j \right) X_t^{\boldsymbol{\alpha}} \right) \\
&\quad - \frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}| - 1)}{2} m_{\boldsymbol{\alpha}}(t) + \sum_{i=1}^{n} \frac{\alpha_i(\alpha_i - 1)}{2} m_{\boldsymbol{\alpha} - e_i}(t) \\
&= \sum_{i=1}^{n} \frac{\alpha_i(s_i - s_0)}{2} m_{\boldsymbol{\alpha}}(t) - \sum_{i,j=1}^{n} \frac{\alpha_i(s_j - s_0)}{2} m_{\boldsymbol{\alpha} + e_j}(t) \\
&\quad - \frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}| - 1)}{2} m_{\boldsymbol{\alpha}}(t) + \sum_{i=1}^{n} \frac{\alpha_i(\alpha_i - 1)}{2} m_{\boldsymbol{\alpha} - e_i}(t) \\
&= -\left(\frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}| - 1)}{2} - \sum_{i=1}^{n} \frac{\alpha_i(s_i - s_0)}{2} \right) m_{\boldsymbol{\alpha}}(t) + \sum_{i=1}^{n} \frac{\alpha_i(\alpha_i - 1)}{2} m_{\boldsymbol{\alpha} - e_i}(t) \\
&\quad - \sum_{i,j=1}^{n} \frac{\alpha_i(s_j - s_0)}{2} m_{\boldsymbol{\alpha} + e_j}.
\end{aligned} \tag{4.3.11}$$

9. For the Wright–Fisher model with $(n+1)$ alleles with general selection, by (2.5.15)

$$\begin{aligned}
b^i(x) &= x^i \left(\sum_{j=0}^{n} s_{ij} x^j - \sum_{k,l=0}^{n} s_{kl} x^k x^l \right) \\
&= x^i \left(s_{i0} + \sum_{j=1}^{n} (s_{ij} - s_{i0}) x^j - \Big(\sum_{k,l=1}^{n} \big(s_{kl} + s_{00} - s_{k0} - s_{l0} \big) x^k x^l \right. \\
&\qquad \left. + 2 \sum_{l=1}^{n} (s_{l0} - s_{00}) x^l + s_{00} \Big) \right)
\end{aligned}$$

$$= x^i\Bigg(-\sum_{k,l=1}^{n} \big(s_{kl} + s_{00} - s_{k0} - s_{l0}\big)x^k x^l + \sum_{j=1}^{n}(s_{ij} - s_{i0} - 2s_{j0} + 2s_{00})x^j + s_{i0} - s_{00}\Bigg)$$

$$= x^i\Bigg(-\sum_{k,l=1}^{n} \tilde{s}_{kl}x^k x^l + \sum_{j=1}^{n}(\tilde{s}_{ij} - \tilde{s}_j)x^j + \tilde{s}_i\Bigg), \tag{4.3.12}$$

where $\tilde{s}_{kl} = s_{kl} + s_{00} - s_{k0} - s_{l0}$, $\tilde{s}_j = s_{j0} - s_{00}$, and $a^{ij}(x) = x^i(\delta_{ij} - x^j)$, and the moment evolution equation is

$$\begin{aligned}
\dot{m}_{\boldsymbol{\alpha}}(t) &= \sum_{i=1}^{n}\alpha_i \mathrm{E}\Bigg(\Big(-\sum_{k,l=1}^{n}\tilde{s}_{kl}X_t^k X_t^l + \sum_{j=1}^{n}(\tilde{s}_{ij} - \tilde{s}_j)X_t^j + \tilde{s}_i\Big)X_t^{\boldsymbol{\alpha}}\Bigg) \\
&\quad + \sum_{i\neq j}\alpha_i\alpha_j \mathrm{E}\Big(-X_t^i X_t^j X_t^{\boldsymbol{\alpha}-e_i-e_j}\Big) + \sum_{i=1}^{n}\frac{\alpha_i(\alpha_i-1)}{2}\mathrm{E}\Big(X_t^i(1-X_t^i)X^{\boldsymbol{\alpha}-2e_i}\Big) \\
&= \sum_{i=1}^{n}\alpha_i\Bigg(-\sum_{k,l=1}^{n}\tilde{s}_{kl}m_{\boldsymbol{\alpha}+e_k+e_l}(t) + \sum_{j=1}^{n}(\tilde{s}_{ij} - \tilde{s}_j)m_{\boldsymbol{\alpha}+e_j}(t) + \tilde{s}_i m_{\boldsymbol{\alpha}}(t)\Bigg) \\
&\quad - \frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1)}{2}m_{\boldsymbol{\alpha}}(t) + \sum_{i=1}^{n}\frac{\alpha_i(\alpha_i-1)}{2}m_{\boldsymbol{\alpha}-e_i}(t) \\
&= -\sum_{k,l=1}^{n}|\boldsymbol{\alpha}|\tilde{s}_{kl}m_{\boldsymbol{\alpha}+e_k+e_l}(t) + \sum_{i=1}^{n}\sum_{j=1}^{n}\alpha_i(\tilde{s}_{ij} - \tilde{s}_j)m_{\boldsymbol{\alpha}+e_j}(t) \\
&\quad - \Big(\frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1)}{2} - \sum_{i=1}^{n}\alpha_i\tilde{s}_i\Big)m_{\boldsymbol{\alpha}}(t) + \sum_{i=1}^{n}\frac{\alpha_i(\alpha_i-1)}{2}m_{\boldsymbol{\alpha}-e_i}(t).
\end{aligned} \tag{4.3.13}$$

10. Finally, for the most general case considered here, that is, the Wright–Fisher model with $(n+1)$ alleles with general mutation and selection, by (2.5.15)

$$b^i(x) = -\Big(\sum_{j=0}^{n}\frac{\theta_{ij}}{2}\Big)x^i + \sum_{j=0}^{n}\frac{\theta_{ji}}{2}x^j + x^i\Bigg(\sum_{j=0}^{n}s_{ij}x^j - \sum_{k,l=0}^{n}s_{kl}x^k x^l\Bigg),$$

and $a^{ij}(x) = x^i(\delta_{ij} - x^j)$, and the moment evolution equation is

$$\begin{aligned}\dot{m}_{\boldsymbol{\alpha}}(t) = &-\sum_{k,l=1}^{n} |\boldsymbol{\alpha}|\tilde{s}_{kl} m_{\boldsymbol{\alpha}+e_k+e_l}(t) + \sum_{i=1}^{n}\sum_{j=1}^{n} \alpha_i(\tilde{s}_{ij} - \tilde{s}_j) m_{\boldsymbol{\alpha}+e_j}(t) \\ &- \left(\frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1)}{2} + \sum_{i=1}^{n} \frac{\alpha_i(\vartheta_i + \theta_{0i} - 2\tilde{s}_i)}{2} \right) m_{\boldsymbol{\alpha}}(t) \\ &+ \sum_{i=1}^{n} \frac{\alpha_i(\alpha_i - 1 + \theta_{0i})}{2} m_{\boldsymbol{\alpha}-e_i}(t).\end{aligned} \tag{4.3.14}$$

11. For the Wright–Fisher model with two loci with two alleles each with recombination,

$$b^i(x) = \epsilon_i r D(x) = \epsilon_i r\big(x^1(1 - x^1 - x^2 - x^3) - x^2 x^3\big),$$

where $\epsilon_1 = -\epsilon_2 = -\epsilon_3 = -1, r = 2NR$ and $a^{ij}(x) = x^i(\delta_{ij} - x^j)$ for $i, j = 1, 2, 3$, then the moment evolution equation is

$$\begin{aligned}\dot{m}_{\boldsymbol{\alpha}}(t) &= \sum_{i=1}^{3} \alpha_i \mathrm{E}\Big(\epsilon_i r D(X_t)(X_t)^{\boldsymbol{\alpha}-e_i}\Big) + \sum_{i=1}^{3} \frac{\alpha_i(\alpha_i-1)}{2} m_{\boldsymbol{\alpha}-e_i}(t) - \frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1)}{2} m_{\boldsymbol{\alpha}}(t) \\ &= \sum_{i=1}^{3} \alpha_i \epsilon_i r\Big(m_{\boldsymbol{\alpha}-e_i+e_1}(t) - m_{\boldsymbol{\alpha}-e_i+2e_1}(t) - m_{\boldsymbol{\alpha}-e_i+e_1+e_2}(t) - m_{\boldsymbol{\alpha}-e_i+e_1+e_3}(t) \\ &\quad - m_{\boldsymbol{\alpha}-e_i+e_2+e_3}(t)\Big) + \sum_{i=1}^{3} \frac{\alpha_i(\alpha_i-1)}{2} m_{\boldsymbol{\alpha}-e_i}(t) - \frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1)}{2} m_{\boldsymbol{\alpha}}(t).\end{aligned} \tag{4.3.15}$$

If we start at a linkage equilibrium, i.e. $D(X(0)) = 0$, we obtain

$$D(X(t)) = \Big(1 - \frac{r}{2N}\Big)^t D(X(0)) = 0$$

for all t. At linkage equilibrium, the genotype frequencies at one locus are independent of the genotype frequencies at the other locus. In this case, it suffices to consider the variables $\big(X^1(t), X^2(t)\big) \in \overline{\Delta}_2$, as they determine the other two via

$$X^3(t) = \frac{X^1(t)}{X^1(t) + X^2(t)}\big(1 - X^1(t) - X^2(t)\big),$$

$$X^4(t) = \frac{X^2(t)}{X^1(t) + X^2(t)}\big(1 - X^1(t) - X^2(t)\big).$$

The problem thus becomes equivalent to the case of a single locus with three alleles.

12. For the Wright–Fisher model with two loci with two alleles each with mutation, selection and recombination,

$$b^i(x) = \epsilon_i r D(x) - \Big(\sum_{j=0}^{3} \frac{\theta_{ij}}{2}\Big)x^i + \sum_{j=0}^{3} \frac{\theta_{ji}}{2} x^j + x^i \Bigg(\sum_{j=0}^{3} s_{ij} x^j - \sum_{k,l=0}^{3} s_{kl} x^k x^l\Bigg),$$

and $a^{ij}(x) = x^i(\delta_{ij} - x^j)$ for $i, j = 1, 2, 3$, and the moment evolution equation is

$$\begin{aligned}
\dot{m}_{\boldsymbol{\alpha}}(t) &= \sum_{i=1}^{3} \alpha_i \mathrm{E}\Big(\epsilon_i r D(X_t)(X_t)^{\boldsymbol{\alpha}-e_i}\Big) + \sum_{i=1}^{3} \frac{\alpha_i(\alpha_i-1)}{2} m_{\boldsymbol{\alpha}-e_i}(t) - \frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1)}{2} m_{\boldsymbol{\alpha}}(t) \\
&\quad - \sum_{k,l=1}^{3} |\boldsymbol{\alpha}| \tilde{s}_{kl} m_{\boldsymbol{\alpha}+e_k+e_l}(t) + \sum_{i=1}^{3}\sum_{j=1}^{3} \alpha_i(\tilde{s}_{ij} - \tilde{s}_j) m_{\boldsymbol{\alpha}+e_j}(t) \\
&= \sum_{i=1}^{3} \alpha_i \epsilon_i r \Big(m_{\boldsymbol{\alpha}-e_i+e_1}(t) - m_{\boldsymbol{\alpha}-e_i+2e_1}(t) - m_{\boldsymbol{\alpha}-e_i+e_1+e_2}(t) - m_{\boldsymbol{\alpha}-e_i+e_1+e_3}(t) \\
&\quad - m_{\boldsymbol{\alpha}-e_i+e_2+e_3}(t)\Big) + \sum_{i=1}^{3} \frac{\alpha_i(\alpha_i-1)}{2} m_{\boldsymbol{\alpha}-e_i}(t) - \frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1)}{2} m_{\boldsymbol{\alpha}}(t) \\
&\quad - \sum_{k,l=1}^{3} |\boldsymbol{\alpha}| \tilde{s}_{kl} m_{\boldsymbol{\alpha}+e_k+e_l}(t) + \sum_{i=1}^{3}\sum_{j=1}^{3} \alpha_i(\tilde{s}_{ij} - \tilde{s}_j) m_{\boldsymbol{\alpha}+e_j}(t) \\
&= \sum_{\boldsymbol{\beta}} A_{\boldsymbol{\alpha},\boldsymbol{\beta}} m_{\boldsymbol{\beta}}(t),
\end{aligned} \tag{4.3.16}$$

where $A = \Big(A_{\boldsymbol{\alpha},\boldsymbol{\beta}}\Big)_{\boldsymbol{\alpha},\boldsymbol{\beta}}$ is an (infinite dimensional) sparse matrix whose entries depend on r, s_{ij}, θ_{ij}.

4.4 Moment Duality

As we have noted in Sect. 4.2, the evolution of the moments determines the entire Wright–Fisher process. In other words, it suffices to solve the moment evolution equations. This also implies that if we find some other model with the same moment evolution equations, then we could also use that model to derive properties of the Wright–Fisher process. And if that other model turns out to be simpler, then this scheme may be used to great advantage. This is indeed possible. There exists a simple death process with the same moment evolution. Actually, that process can also find a biological interpretation in terms of the Wright–Fisher model. That is the Kingman coalescent [81]. We shall make use of the exposition in [26].

Although, in this book, we shall not make systematic use of this relation, we nevertheless would like to use this opportunity to explain it. We shall do so, however, only for the simplest case, the 2-allele model without selection or mutation.

We thus recall Eq. (2.6.4) for the evolution of the moments $m_k(t,y) = \mathrm{E}(Y_t)^k|Y_0 - y)$ in the diffusion limit,

$$\dot{m}_k(t,y) = \binom{k}{2}(m_{k-1}(t,y) - m_k(t,y)). \tag{4.4.1}$$

We then look at the death process $D = (D_t)$ on $\mathbb{N}$ where the transition from k to $k-1$ occurs at the rate $\binom{k}{2}$. That is, in a population of size k, the death of an individual happens at that rate. The expectation value

$$n_k(t,y) := \mathrm{E}(y^{D_t}|D_0 = k) \tag{4.4.2}$$

then satisfies

$$n_k(t+\delta t,y) - n_k(t,y) = \binom{k}{2}(n_{k-1}(t,y) - n_k(t,y)), \tag{4.4.3}$$

and for $\delta t \to 0$, we get

$$\dot{n}_k(t,y) = \binom{k}{2}(n_{k-1}(t,y) - n_k(t,y)), \tag{4.4.4}$$

that is, the same as (4.4.1). (Note that for $\delta t > 0$, $m_k(t,y)$ does not satisfy (4.4.3) exactly, but only up to some error terms of order $o(\delta t)$. Thus, the moment evolutions of the two processes only become identical in the diffusion limit.)

Anyway, this then implies

$$m_k(t,y) = n_k(t,y), \tag{4.4.5}$$

or spelled out,

$$\mathrm{E}(Y_t)^k|Y_0 - y) = \mathrm{E}(y^{D_t}|D_0 = k). \tag{4.4.6}$$

Such a relation is called *moment duality*, and this can be developed in a general and abstract manner, see [68]. Here, however, we do not explicate that theory, but only point out the interpretation in terms of the Kingman coalescent.

But before doing that, we should first point out that since the process D_t is much simpler than the Wright–Fisher process, we can use the relation (4.4.6) to derive some results about the latter in a simpler manner. For instance, (2.8.2) directly

follows from

$$\mathrm{E}(Y_\tau | Y_0 = y) = \mathrm{E}(y^{D_\tau} | D_0 = 1) = y. \tag{4.4.7}$$

Now, the Kingman coalescent model considers the process where we ask about the probabilities that two individuals in the current generation had the same ancestor ℓ generations back in the past (note that time is running backwards here, and therefore, we call the generation ℓ instead of m). Obviously, we should then look at the transitions from some generation ℓ back in the past containing the k ancestors of the current generation of size $2N$ (as always) to generation $\ell + 1$ back in the past and ask how many members of that population created the current one. That is, in each generation in the past, we neglect all individuals that don't have any descendent left in the current generation. Again, we scale the process and look at time steps of size δs (again, time s is running back into the past). The process is scaled such that the probability for two individuals at time s had the same ancestor at time $s + \delta s$ back from the present is δs, up to terms of order $o(\delta s)$ which we neglect. Therefore, if at time s, there were k ancestors, then there are $\binom{k}{2}$ pairs of them each of which could have the same ancestor. Thus, the number of ancestors is expected to reduce by $\binom{k}{2}\delta s$ when we go δs back in time. But this is precisely the same as the above death process D_s with rescaled time step δs. Therefore, the moment duality that we have described above finds its natural explanation in the Kingman coalescent that yields a process that traces the ancestry of individuals resulted from Wright–Fisher sampling back in time.

Chapter 5
Recombination

5.1 Recombination and Linkage

Gametes consist of several loci, each of them occupied by an allele from a set of alleles that is specific for the locus in question. The sites are assumed to be linearly ordered. The number of loci, as well as the set of possible alleles for each, are the same for all gametes within the population under consideration. When two gametes are paired, they form an offspring gamete that at some of its sites gets the alleles from the first parent, and at the other sites those of the second parent. This is recombination, and a recombination scheme may restrict the possibilities for the combinations.

We observe that by such a recombination scheme, half of the alleles of the pair of recombined gametes are wasted. In principle, instead of simply creating one gamete from a pair of gametes by recombination, one could also create the complementary gamete which precisely gets its alleles at those loci from the first (second) parent where the other one received its alleles from the second (first) parent. We would then have to sample only half as many gametes. For the models that we shall consider, this will make no difference for the dynamics of the probabilities of the allele frequencies.

First, we consider the special case of two loci with two alleles each. Recalling the conventions of Sect. 2.11.1, the set of possible alleles at the first locus contains A^0, A^1, and for the second locus B^0, B^1. We thus have the gametes, i.e., allele combinations

$$G^0 = (A^0, B^0), G^1 = (A^0, B^1), G^2 = (A^1, B^0), G^3 = (A^1, B^1).$$

The corresponding relative frequencies are $X^\ell = X^{ij}$ when $G^\ell = (A^i, B^j)$. With $i' = 0(1)$ if $i = 1(0)$,

$$D^{ij} = X^{ij}X^{i'j'} - X^{ij'}X^{i'j}, \text{ and } D^\ell = D^{ij} \text{ when } G^\ell = (A^i, B^j).$$

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When $D^{ij} = 0$, then the relative frequency of (A^i, B^j) equals the product of the relative frequencies of A^i and B^j. This is called linkage equilibrium.

Let R be the recombination rate. This means that when the gamete (A^i, B^j) is mated with the gamete (A^ℓ, B^h), then the gametes (A^i, B^j) and (A^ℓ, B^h) are produced with probability $\frac{1}{2}(1-R)$ each, whereas the combinations (A^i, B^h) and (A^ℓ, B^j) occur with probability $\frac{1}{2}R$ each. The factor $\frac{1}{2}$ here comes up because we assume that the mating and recombination of two gametes produces a single offspring in place of two.

In more detail, recombination can have

- no effect on a relative frequency, for instance when (A^0, B^0) is paired with (A^0, B^1), then (A^0, B^0) is produced with probability $\frac{1}{2}$ independently of R
- a negative effect on a relative frequency, for instance when (A^0, B^0) is paired with (A^1, B^1), then (A^0, B^0) is produced with probability $\frac{1}{2}(1-R)$ only
- a positive effect on a relative frequency, for instance when (A^0, B^1) is paired with (A^1, B^0), then (A^0, B^0) is produced with probability $\frac{1}{2}R$, even though neither parent was of this type.

We now present a preliminary discussion of the effects of these recombination rules where we leave out the multinomial sampling step; as we shall see below the relative order of recombination and sampling does matter, and so, we shall need to address that issue. The relative frequency of G^0 then changes between the generations according to

$$\mathrm{E}(X^0_{m+1}|x_m) = (x^0)^2 + 2x^0x^1\frac{1}{2} + 2x^0x^2\frac{1}{2} + 2x^0x^3\frac{1}{2}(1-R) + 2x^1x^2\frac{1}{2}R = x^0 - RD^0, \tag{5.1.1}$$

since $x^0 + x^1 + x^2 + x^3 = 1$; the factor 2 occurs for symmetry reasons, because the order of the two gametes does not matter. And in general

$$\mathrm{E}(X^\ell_{m+1}|x_m) = x^\ell - RD^\ell. \tag{5.1.2}$$

It is important for the interpretation that R is a probability. $R = 0$ means that no recombination occurs, whereas $R = \frac{1}{2}$ means that the two loci behave independently. The reader will readily check that R and $1-R$ lead to mathematically (but not biologically, of course) equivalent models. Therefore, we may restrict ourselves to the range $0 \le R \le \frac{1}{2}$.

For later purposes, we also write (5.1.2) as

$$\mathrm{E}(X^\ell_{m+1}|x_m) = \sum_{r,s} a^\ell_{rs} x^{r,s}_m, \tag{5.1.3}$$

with the coefficients a_{rs}^{ℓ}, which again represent probabilities. For $\ell = 0$, they are displayed in (5.1.1), and for general ℓ, they are given by the following table

a_{rs}^{ℓ}	$\ell = 0$	$\ell = 1$	$\ell = 2$	$\ell = 3$
$(r,s) = (0,0)$	1	0	0	0
$(0,1)$	$\frac{1}{2}$	$\frac{1}{2}$	0	0
$(0,2)$	$\frac{1}{2}$	0	$\frac{1}{2}$	0
$(0,3)$	$\frac{1}{2}(1-R)$	$\frac{1}{2}R$	$\frac{1}{2}R$	$\frac{1}{2}(1-R)$
$(1,1)$	0	1	0	0
$(1,2)$	$\frac{1}{2}R$	$\frac{1}{2}(1-R)$	$\frac{1}{2}(1-R)$	$\frac{1}{2}R$
$(1,3)$	0	$\frac{1}{2}$	0	$\frac{1}{2}$
$(2,2)$	0	0	1	0
$(2,3)$	0	0	$\frac{1}{2}$	$\frac{1}{2}$
$(3,3)$	0	0	0	1

(5.1.4)

with the symmetry

$$a_{rs}^{\ell} = a_{sr}^{\ell} \text{ for all } r, s, \ell. \tag{5.1.5}$$

Here, we assume that the two partners in a pair are independently chosen for their random union, which is indicated by the i,j-notation as upper index, that is,

$$X^{r,s} = X^r X^s \quad \text{and } x^{r,s} = x^r x^s. \tag{5.1.6}$$

As before, we consider a population of N individuals. In the present context, this means that we have $2N$ gametes in each generation. In distinction to the single locus case, we now have two operations, sampling and recombination. Their order matters, and there are two different possible schemes which we shall now describe.

Perhaps the following general remark concerning randomness will be useful, as the same type of reasoning will appear repeatedly. As long as there are no correlations, it does not matter for the stochastics of sampling (always with replacement) whether we sample individual gametes or pairs of gametes, or according to which scheme we pairwise mate randomly sampled gametes, as long as this scheme does not depend on their identity.

5.2 Random Union of Gametes

In the random union of gametes model (as proposed by Karlin and McGregor in [76]), abbreviated as **RUG**, $2N$, or N pairs of gametes, are randomly sampled from the population, and then pairwise recombined in a mating step to produce the next generation of $2N$ gametes. Thus, for the formal model, we do not need to speak about individuals at all, as in the basic Wright–Fisher model with a single

locus. Of course, for the biological picture, one might want to ask how individuals fit into it. Well, a diploid individual possesses two gametes. Instead of sampling $2N$ gametes, we might then sample N individuals and mate them pairwise and recombine the first gametes of such a pair to form the first gamete of the offspring, and likewise produce the second gamete of the offspring from the second pair of parental gametes. We note that this sampling of pairs of parents each carrying two gametes is different from the simple sampling of pairs of gametes. If, however, there are no correlations between the frequencies of the two gametes an individual carries, then this recombination process will not introduce such correlations either, and therefore, the probabilities for the gamete frequencies are not affected by this different sampling scheme. We should point out, however, that this might change when selection effects are included. The reason is that selective differences might introduce correlations between the gametes within individuals, as certain combinations of two gametes might be fitter than others.

So, anyway, we shall sample from a population of $2N$ gametes to create the next generation by pairwise recombination.

We can easily derive the moments of the RUG process. In fact, the first moment has already been given in (5.1.2). For the sequel, we write

$$\xi^\ell := x^\ell - RD^\ell. \tag{5.2.1}$$

The higher moments can now easily be derived from the fact that the RUG model consists in random multinomial sampling from the frequencies given by ξ^ℓ. Thus, recalling (2.11.9)–(2.11.11), we have

$$\mathrm{E}(X^\ell_{m+1}|x_m) = \xi^\ell \text{ which is (5.1.2)} \tag{5.2.2}$$

$$\begin{aligned}\mathrm{E}(X^\ell_{m+1}X^h_{m+1}|x_m) &= (1-\frac{1}{2N})\xi^\ell\xi^h + \frac{1}{2N}\xi^\ell\delta_{\ell h} \\ &= (1-\frac{1}{2N})(x^\ell - RD^\ell)(x^h - RD^h) + \frac{1}{2N}(x^\ell - RD^\ell)\delta_{\ell h}\end{aligned} \tag{5.2.3}$$

$$\begin{aligned}\mathrm{E}(X^\ell_{m+1}X^h_{m+1}X^k_{m+1}|x_m) &= (1-\frac{1}{2N})(1-\frac{2}{2N})\xi^\ell\xi^h\xi^k + \frac{1}{(2N)^2}\xi^\ell\delta_{\ell h}\delta_{hk} \\ &\quad + \frac{1}{2N}(1-\frac{1}{2N})(\xi^\ell\xi^h\delta_{\ell k} + \xi^\ell\xi^k\delta_{\ell h} + \xi^h\xi^k\delta_{\ell k}),\end{aligned} \tag{5.2.4}$$

and so on. In particular, we get for the coefficient of linkage disequilibrium from (5.2.3)

$$\mathrm{E}(D^{ij}_{m+1}|x_m) = (1-\frac{1}{2N})(1-R)D^{ij}_m = (1-\frac{1}{2N})(\xi^{ij}\xi^{i'j'} - \xi^{ij'}\xi^{i'j}). \tag{5.2.5}$$

Thus, the corresponding coefficient of linkage disequilibrium for the ξ^ℓ gets decreased by a factor of $(1-\frac{1}{2N})$, and the latter is decreased by a factor of $(1-R)$ compared to the coefficient for the x^ℓ_m.

From (5.2.2)–(5.2.4), we also get

$$\mathrm{E}(\delta X^\ell|x_m) = \mathrm{E}(X^\ell_{m+1} - X^\ell_m|x_m) = -RD^\ell \tag{5.2.6}$$

$$\begin{aligned}\mathrm{E}(\delta X^\ell \delta X^h|x_m) &= \mathrm{E}(X^\ell X^h|x_m) + \mathrm{E}(\delta X^\ell|x_m)\mathrm{E}(\delta X^h|x_m)\\ &\quad - \mathrm{E}(X^\ell|x_m)\mathrm{E}(X^h|x_m)\\ &= \frac{1}{2N}\xi^\ell(\delta_{\ell h} - \xi^h) + R^2 D^\ell D^h \end{aligned}\tag{5.2.7}$$

$$\begin{aligned}\mathrm{E}(\delta X^\ell \delta X^h \delta X^j|x_m) &= \mathrm{E}(X^\ell X^h X^j|x_m) - x^\ell_m x^h_m x^j_m \\ &\quad - \mathrm{E}(X^\ell X^h|x_m)x^j_m + \mathrm{E}(X^j|x_m)x^\ell_m x^h_m\\ &\quad - \mathrm{E}(X^\ell X^j|x_m)x^h_m + \mathrm{E}(X^h|x_m)x^\ell_m x^j_m\\ &\quad - \mathrm{E}(X^h X^j|x_m)x^\ell_m + \mathrm{E}(X^\ell|x_m)x^h_m x^j_m \end{aligned}\tag{5.2.8}$$

$$\begin{aligned}&= -R^3 D^\ell D^h D^j - \frac{1}{2N}\big(\xi^\ell\xi^h(1-\delta_{\ell h})D^j + \xi^\ell\xi^j(1-\delta_{\ell j})D^h + \xi^h\xi^j(1-\delta_{hj})D^\ell\big)\\ &\quad + \frac{1}{4N^2}\big(2\xi^\ell\xi^h\xi^j - \xi^\ell\xi^j\delta_{\ell h} - \xi^\ell\xi^h\delta_{hj} - \xi^h\xi^j\delta_{j\ell} + \xi^\ell\delta_{\ell h}\delta_{hj}\big)\end{aligned}\tag{5.2.9}$$

5.3 Random Union of Zygotes

In the random union of zygotes model, abbreviated as **RUZ**, which has been developed in [123], we represent an individual by a pair of gametes, called a zygote. From each zygote, that is, pair of gametes, we form a single gamete by recombination. The model then consists in sampling $2N$ zygotes, from which we form $2N$ gametes which are then pairwise mated into N individuals, i.e., zygotes. (Since the zygotes are sampled randomly, the precise mating scheme then does not matter, as long as it does not depend on the identity of the gametes, and will effectively constitute random mating.) Thus, here the paternal and the maternal gamete are not recombined when forming an individual, but only when that individual produces offspring itself. In other words, recombination is shifted here by one generation compared to the RUG model.

Again, when there are no correlations between the two gametes constituting a zygote in the initial population, then the model will not introduce any such correlations. Therefore, we can consider the two gametes in a zygote as being statistically independent. Again, we point out that this need not remain valid when selection is introduced.

We consider a discrete time m, sometimes indicated by a corresponding subscript. Let $Y^{r,s}$ and $X^{r,s}$ be the absolute and relative frequencies of a zygote of type

(G^i, G^j). When the random variable $X^{r,s}$ assumes the value $x^{r,s}$, the probability that recombination then produces a gamete of G^ℓ is

$$\mathrm{E}(X^\ell_{m+1}|x^{\cdot\cdot}_m) = \sum_{r,s} a^\ell_{rs} x^{r,s} \tag{5.3.1}$$

where $x^{\cdot\cdot}$ stands for the collection $x^{r,s}, r, s = 0, 1, 2, 3$ and the a^ℓ_{rs} are the coefficients of the recombination scheme. Here, importantly, since the two gametes in a zygote are statistically independent, the corresponding random variables satisfy (analogously to the RUG case)

$$X^{r,s} = X^r X^s. \tag{5.3.2}$$

Therefore, we can equivalently write

$$\mathrm{E}(X^\ell_{m+1}|x_m) = \mathrm{E}(\sum_{r,s} a^\ell_{rs} X^{r,s}_{m+1}|x_m) = \sum_{r,s} a^\ell_{rs} x^r_m x^s_m. \tag{5.3.3}$$

This then is the transition rule for the random variables X^ℓ in the RUZ model. Applying (2.11.5) therefore yields the formula of [123]

$$\mathrm{E}(e^{\sum_\ell s_\ell X^\ell_{m+1}}|x_m) = \mathrm{E}(e^{\sum_\ell s_\ell \sum_{r,s} a^\ell_{rs} X^r_{m+1} X^s_{m+1}}|x_m) = (\sum_{r,s} x^r_m x^s_m e^{\sum_\ell s_\ell a^\ell_{rs}})^N \tag{5.3.4}$$

where we have used the formula (2.11.8) for the moment generating function of the multinomial distribution and the fact that we are now multinomially sampling pairs instead of individual gametes.

This formula then has eliminated the zygote frequencies; only the gamete frequencies remain. We should keep in mind, however, that the coefficients a^ℓ_{rs} here represent probabilities.

From (5.3.4) and the considerations in Sect. 2.11.2, we obtain the moments

$$\mathrm{E}(X^\ell_{m+1}|x_m) = \sum_{i,j} a^\ell_{ij} x^i_m x^j_m \text{ which is (5.3.3)} \tag{5.3.5}$$

$$\mathrm{E}(X^\ell_{m+1} X^h_{m+1}|x_m) = \sum_{i,j} \sum_{r,s} ((1 - \frac{1}{N}) x^i_m x^j_m x^r_m x^s_m + \frac{1}{N} x^i_m x^j_m \delta_{ir}\delta_{js}) a^\ell_{ij} a^h_{rs}$$

$$\mathrm{E}(X^\ell_{m+1} X^h_{m+1} X^k_{m+1}|x_m) = \left(1 - \frac{3}{N} + \frac{2}{N^2}\right) \sum_{i,j} x^i_m x^j_m a^\ell_{ij} \sum_{p,q} x^p_m x^q_m a^h_{pq} \sum_{r,s} x^r_m x^s_m a^k_{rs} \tag{5.3.6}$$

$$+ \left(\frac{1}{N} - \frac{1}{N^2}\right) \times \left(\sum_{i,j} x^i_m x^j_m a^\ell_{ij} a^h_{ij} \sum_{r,s} x^r_m x^s_m a^k_{rs} \right.$$

$$+\sum_{p,q} x_m^p x_m^q a_{pq}^\ell a_{pq}^h \sum_{i,j} x_m^i x_m^j a_{ij}^\ell + \sum_{r,s} x_m^r x_m^s a_{rs}^\ell a_{rs}^h$$
$$\times \sum_{p,q} x_m^p x_m^q a_{pq}^h \Big) + \frac{1}{N^2} \sum_{i,j} x_m^i x_m^j a_{ij}^\ell a_{ij}^h a_{ij}^k. \tag{5.3.7}$$

From (5.1.1), (5.1.3), we have

$$\sum_{h,k} a_{hk}^\ell x_m^h x_m^k = x^\ell - RD^\ell. \tag{5.3.8}$$

Therefore, the moments of the RUZ model behave essentially like those of the RUG model, that is, they coincide in the diffusion limit (or in case of absence of recombination). The differences in the formulae for the second and for the higher moments only result from technicalities (that is, sampling with $2N$ trials (RUG) vs. N trials (RUZ)) and as such diminish with increasing N.

5.4 Diffusion Approximation

As in Sect. 4.2, we now pass to the diffusion approximation, that is, we let the population size $N \to \infty$ and rescale time with $\delta t = \frac{1}{2N}$. The expectation values then need to be multiplied by $2N$. We obtain the coefficients of the drift term

$$b_\ell(x) = \lim_{N\to\infty} 2N\mathrm{E}(\delta X_t^\ell) = \lim_{N\to\infty} (-2NRD^\ell). \tag{5.4.1}$$

This can only remain finite if

$$R = R(N) = O(\frac{1}{N}), \tag{5.4.2}$$

that is, if the recombination rate goes to 0 like $\frac{1}{N}$. We henceforth assume (5.4.2). But then

$$\begin{aligned} a_{\ell h}(x) &= \lim_{N\to\infty} 2N\mathrm{E}(\delta X_t^\ell \delta X_t^h) \\ &= \lim_{N\to\infty} 2N(\frac{1}{N} x^\ell(\delta_{\ell h} - x^h) + (RD^\ell)(RD^h)) \\ &= 2x^\ell(\delta_{\ell h} - x^h), \end{aligned} \tag{5.4.3}$$

because of (5.4.2). Thus, with this assumption that was needed to keep the first moments finite, the diffusion coefficients $a_{\ell h}$ are independent of recombination. Since in this situation the third and higher moments behave like $o(\frac{1}{N})$, we can

pass to the diffusion limit as in Theorem 4.2.1 to obtain the forward and backward Kolmogorov operators, that is,

$$L_3^{\mathrm{rec}}: \quad H_3 \to H_3,\ L_3^{\mathrm{rec}}u(x) = \tfrac{1}{2}\sum_{\ell,h=1}^{3}\frac{\partial^2(x^\ell(\delta_{\ell h}-x^h)u(x))}{\partial x^\ell \partial x^h} - \sum_\ell \frac{\partial}{\partial x^\ell}(b_\ell(x)u(x)), \tag{5.4.4}$$

and its adjoint

$$L_3^{*,\mathrm{rec}}:\ H_3 \to H_3,\ (L_3)^{*,\mathrm{rec}}u(p) = \tfrac{1}{2}\sum_{\ell,h=1}^{3} p^\ell(\delta_{\ell h}-p^h)\frac{\partial^2 u(p)}{\partial p^\ell \partial p^h} + \sum_\ell b_\ell(p)\frac{\partial u(p)}{\partial p^\ell}. \tag{5.4.5}$$

5.5 Compositionality

In addition to the hierarchy that we have already discussed for the single locus case, we also have a compositionality in the following sense. In the two-locus case, we could, for instance, ignore the dynamics at the second locus and only consider the dynamics at the first locus. An inspection of the model shows that in the absence of selective effects (which we have assumed so far), the frequencies at the first locus are not affected by those at the second locus. Recombination only affects the correlations between the probabilities at the two loci, but not the marginals. Thus, for the frequencies of A^i, which are given as the sums of the frequencies of the pairs (A^i, B^0) and (A^i, B^1), we have a standard Wright–Fisher dynamics. When X^i now denotes the frequency of A^i and X^{ij} that of the pair (A^i, B^j), we have

$$X^i = \sum_j X^{ij}. \tag{5.5.1}$$

This matches with the coefficients of the Kolmogorov operators, as we have

$$\sum_{j=0}^{1} b_{(ij)} = 0 \tag{5.5.2}$$

$$\sum_{j,s=0}^{1} a_{(ij)(rs)} = \sum_{j,s=0}^{1} \frac{1}{2}x^{(ij)}(\delta_{(ij)(rs)} - x^{(rs)}) = \frac{1}{2}x^i(\delta_{ir} - x^r), \tag{5.5.3}$$

where in (5.4.1), (5.4.2), we let the index ℓ for an allele pair correspond to the pair of indices (ij).

Analogously, we can consider the dynamics of the frequencies at the second locus only. Thus, by taking marginals, the frequency dynamics governed by the Kolmogorov operators (5.4.4), (5.4.5) lead to two frequency dynamics governed by the operators L_1, L_1^*. Geometrically, we thus have a dynamical process on the positive hyperoctant of the three-dimensional sphere that projects to a process on the product of two one-dimensional spheres. The projected processes do not feel effects of recombination.

Obviously, this picture generalize to more than two loci with more than two alleles at each of them. This naturally leads into the field of algebraic statistics, see for instance [95], but this will not be explored here.

5.6 The Geometry of Recombination

In this section we will consider the geometry of the state space of recombination. We shall see that the geometric perspective that we have developed in Chap. 3 can substantially clarify the underlying mathematical structure. We start with the formula of Ohta and Kimura as presented in [93]

$$\begin{aligned}\frac{\partial f}{\partial t} &= \frac{1}{4}p(1-p)\frac{\partial^2 f}{(\partial p)^2} + \frac{1}{4}q(1-q)\frac{\partial^2 f}{(\partial q)^2} + \frac{1}{2}D\frac{\partial^2 f}{\partial p \partial q} + \frac{1}{2}D(1-2p)\frac{\partial^2 f}{\partial p \partial D} \\ &+ \frac{1}{2}D(1-2q)\frac{\partial^2 f}{\partial q \partial D} + \frac{1}{4}\{pq(1-p)(1-q) + D(1-2p)(1-2q) - D^2\}\frac{\partial^2 f}{(\partial D)^2} \\ &- \frac{1}{2}D(1+2NR)\frac{\partial f}{\partial D}\end{aligned} \tag{5.6.4}$$

for $f(\cdot, t) \in C^2(\Omega_{(p,q,D)})$ for every $t > 0$ and $f(p, q, D, \cdot) \in C^1((0, \infty))$ for $(p, q, D) \in \Omega_{(p,q,D)}$ and with

$$\begin{aligned}&\Omega_{(p,q,D)} := \\ &\left\{(p, q, D) \in \mathbb{R}^3 \middle| 0 < p, q < 1, \max(p + q - 1, 0) - pq < D < \min(p, q) - pq\right\}.\end{aligned} \tag{5.6.5}$$

Thus, the coefficient matrix of the 2nd order derivatives equals

$$\begin{aligned}&\left(a^{ij}(p, q, D)\right) \\ &:= \frac{1}{4}\begin{pmatrix} p(1-p) & D & D(1-2p) \\ D & q(1-q) & D(1-2q) \\ D(1-2p) & D(1-2q) & pq(1-p)(1-q) + D(1-2p)(1-2q) - D^2 \end{pmatrix}.\end{aligned} \tag{5.6.6}$$

In fact, we will show that for Eq. (5.6.4) (a^{ij}) coincides with (the inverse of) a Fisher metric on $\Omega_{(p,q,D)}$.

Here, $\Omega_{(p,q,D)} \subset \mathbb{R}^3$ clearly is a differentiable manifold, and it may be checked that $g = (g_{ij})$ given by $(g^{ij}) = (a^{ij})$ defines a scalar product (i.e. (g_{ij}) is symmetric and positive definite in $\Omega_{(p,q,D)}$) with its coefficients depending continuously on the base point. However, inverting (g^{ij}) yields a quite lengthy expression, which we state here only for completeness:

$$(g_{i1})_{(p,q,D)} = 4\det(g^{ij})^{-1}\begin{pmatrix} -(p-1)p(q-1)^2q^2-(2p-1)(q-1)q(2q-1)D+(-1-3(q-1)q)D^2 \\ -(p-1)p(q-1)qD+D^3 \\ D(q(-1-2p(q-1)+q-2D)+D) \end{pmatrix}, \tag{5.6.7}$$

$$(g_{i2})_{(p,q,D)} = 4\det(g^{ij})^{-1}\begin{pmatrix} -(p-1)p(q-1)qD+D^3 \\ -(p-1)^2p^2(q-1)q-(p-1)p(2p-1)(2q-1)D+(-1-3(p-1)p)D^2 \\ D(p(-1+p+2q-2pq-2D)+D) \end{pmatrix}, \tag{5.6.8}$$

$$(g_{i3})_{(p,q,D)} = 4\det(g^{ij})^{-1}\begin{pmatrix} D(q(-1-2p(q-1)+q-2D)+D) \\ D(p(-1+p+2q-2pq-2D)+D) \\ (p-1)p(q-1)q-D^2 \end{pmatrix}. \tag{5.6.9}$$

This is too complicated, and therefore, we shall introduce new coordinates so that we can identify the metric. We begin with simplex coordinates.

Lemma 5.6.1 *Under a change of coordinates* $(p,q,D) \longmapsto x = (x^1,x^2,x^3)$ *with*

$$x^1 := pq + D, \quad x^2 := p(1-q) - D, \quad x^3 := q(1-p) - D, \tag{5.6.10}$$

the domain $\Omega_{(p,q,D)}$ *is mapped onto* Δ_3*, while the coefficient matrix* $(a^{ij}(p,q,D))$ *of the 2nd order derivatives in Eq.* (5.6.4) *transforms into*

$$(\overline{a}^{ij}(x)) = \frac{1}{4}\begin{pmatrix} x^1(1-x^1) & -x^1x^2 & -x^1x^3 \\ -x^1x^2 & x^2(1-x^2) & -x^2x^3 \\ -x^1x^3 & -x^2x^3 & x^3(1-x^3) \end{pmatrix}, \quad x \in \Delta_3 \tag{5.6.11}$$

and

$$(\overline{a}_{ij}(x)) = 4\begin{pmatrix} (x^1)^{-1}+(x^0)^{-1} & (x^0)^{-1} & (x^0)^{-1} \\ (x^0)^{-1} & (x^2)^{-1}+(x^0)^{-1} & (x^0)^{-1} \\ (x^0)^{-1} & (x^0)^{-1} & (x^3)^{-1}+(x^0)^{-1} \end{pmatrix}, \quad x \in \Delta_3 \tag{5.6.12}$$

with $x^0 := 1 - \sum_{i=1}^3 x^i$.

Proof The assertion on $\Omega_{(p,q,D)}$ is straightforward to check. Furthermore, we have

$$\left(\frac{\partial x^i}{\partial p}, \frac{\partial x^i}{\partial q}, \frac{\partial x^i}{\partial D}\right)_{i=1,2,3} = \begin{pmatrix} q & p & 1 \\ 1-q & -p & -1 \\ -q & 1-p & -1 \end{pmatrix}. \tag{5.6.13}$$

Applying the transformation formula for $\overline{a}^{ij}$ of Lemma 3.10.1 yields the desired result. □

We next apply the natural bijection $\Delta_3 \longrightarrow S^3_+$ to transform the simplicial into spherical coordinates by $y^i := \sqrt{x^i}$ for $i = 1, 2, 3$, see (3.8.9).

This transformation satisfies $\frac{\partial y^i}{\partial x^j} = \frac{1}{2\sqrt{x^j}}\delta^i_j$, from which we obtain the formulae (3.8.11), (3.8.10), that is,

$$(\hat{a}^{ij}(y)) = \frac{1}{16}\begin{pmatrix} 1-(y^1)^2 & -y^1y^2 & -y^1y^3 \\ -y^1y^2 & 1-(y^2)^2 & -y^2y^3 \\ -y^1y^3 & -y^2y^3 & 1-(y^3)^3 \end{pmatrix}, \quad y \in S^3_+ \tag{5.6.14}$$

and

$$(\hat{a}_{ij}(y)) = 16\begin{pmatrix} 1+\frac{(y^1)^2}{(y^0)^2} & \frac{y^1y^2}{(y^0)^2} & \frac{y^1y^3}{(y^0)^2} \\ \frac{y^1y^2}{(y^0)^2} & 1+\frac{(y^2)^2}{(y^0)^2} & \frac{y^2y^3}{(y^0)^2} \\ \frac{y^1y^3}{(y^0)^2} & \frac{y^2y^3}{(y^0)^2} & 1+\frac{(y^3)^2}{(y^0)^2} \end{pmatrix}, \quad y \in S^3_+ \tag{5.6.15}$$

with $y^0 := \sqrt{1-\sum_{i=1}^3 (y^i)^2}$.

Thus, $(\hat{a}_{ij})$ resp. $(\bar{a}_{ij})$ coincide (up to the prefactor 16) with (the inverse of) the standard metric g^3 of the 3-sphere $S^3_+ \subset \mathbb{R}^4$. Lemma 3.8.1 (cf. also Lemma 3.4.1) therefore yields

Proposition 5.6.1 *$\Omega_{(p,q,D)}$ equipped with the Fisher metric of the multinomial distribution carries the geometrical structure of a manifold of constant positive curvature $\equiv \frac{1}{16}$.*

In particular, $\bar{a}^{ij}(x)$ is (up to scaling and the missing prefactor N) the covariance matrix of the multinomial distribution $\mathcal{M}(N; p^0, p^1, \ldots, p^3)$ with parameters $p^i = x^i$, $i = 1, 2, 3$; $p^0 = 1 - \sum_{i=1}^3 x^i$. Therefore, it also coincides with the Fisher metric of the multinomial distribution on Δ_3. We state this result as

Lemma 5.6.2 *The coefficients of the 2nd order derivatives of the Ohta–Kimura formula (5.6.4) equal (up to a constant factor) the components of the inverse of the Fisher metric of the multinomial distribution on $\Omega_{(p,q,D)}$.*

5.7 The Geometry of Linkage Equilibrium States

If $D = 0$, a population is said to be in *linkage equilibrium*. This means that the product of the gross frequencies of the alleles A^0 and B^0 equals the frequency of the gamete A^0B^0, and likewise for all other combinations of alleles at different loci, e.g. A^1 and B^1. In the following, we will analyze the geometry of such linkage equilibrium states utilizing the concepts introduced in Sect. 3.2.

Returning to the Ohta–Kimura formula (5.6.4), $D = 0$ yields

$$(a^{ij}(p,q,0)) = \frac{1}{4}\begin{pmatrix} p(1-p) & 0 & 0 \\ 0 & q(1-q) & 0 \\ 0 & 0 & p(p-1)q(q-1) \end{pmatrix} \tag{5.7.16}$$

with $(p,q,0) \in \Omega_{(p,q,0)} = \{(p,q,0) \in \mathbb{R}^2 \times \{0\} \big| 0 < p,q < 1\}$ as coefficient matrix of the second order derivatives and

$$(a_{ij}(p,q,0)) = 4\begin{pmatrix} \frac{1}{p(1-p)} & 0 & 0 \\ 0 & \frac{1}{q(1-q)} & 0 \\ 0 & 0 & \frac{1}{p(p-1)q(q-1)} \end{pmatrix} \tag{5.7.17}$$

for its inverse (cf. Eq. (5.6.7)f.). Interpreting $(a_{ij}(p,q,D))$ as the Fisher metric of the multinomial distribution on $\Omega_{(p,q,D)}$, we thus have that dropping the third coordinate $D = 0$, $(a_{ij}(p,q,0))$ yields a product metric (cf. Lemma 3.2.1) on $\Delta_1 \times \Delta_1$, in which each factor Δ_1 is equipped with the (inverse) metric $g(x) = \frac{1}{4}x(1-x)$, $x \in \Delta_1$—corresponding (up to the prefactor) to the standard metric of the 1-dimensional sphere $S^1_+ \subset \mathbb{R}^2_+$. Hence, the state space $\Omega_{(p,q,0)}$ resp. a corresponding restriction of Δ_3 of the diffusion approximation of the two-loci two-allelic recombinational Wright–Fisher model in linkage equilibrium equipped with the Fisher metric of the multinomial distribution (cf. Lemma 5.6.2) carries (independently of the chosen coordinate representation) the geometrical structure of

$$S^1_+ \times S^1_+ \subset S^3_+, \tag{5.7.18}$$

which is known as the *Clifford torus* (after William K. Clifford, who in [23] first described $S^1 \times S^1$ as a closed, (locally) Euclidean surface embedded in an elliptic 3-space (cf. [103, p. 373])).

We wish to extend this observation to more general Wright–Fisher models as presented previously in this book.

5.7.1 Linkage Equilibria in Two-Loci Multi-Allelic Models

In order to generalize the above observations, we first extend the notion of linkage equilibrium to models with more than two possible alleles at a locus. Generally, 'linkage' between certain loci (or sets of loci) relates to the fact that the allelic configuration at the one locus resp. loci set affects/determines the allelic configuration at the other locus resp. loci set, i.e. in the two-loci 2-allelic model, each allele at the one locus is 'linked' with both other alleles at the other locus. However, as the allele frequencies at each locus actually form a 1-dimensional space, for a given allele only one parameter suffices to describe the degree of linkage disequilibrium with respect to both other alleles at the other locus as well as both relations for the other allele at the same locus. Hence, only one parameter is sufficient to describe $2 \cdot 2$ linkage relations.

With $n+1 \geq 3$ alleles and two loci, we have $(n+1) \cdot (n+1)$ linkage relations, which—as the allele frequencies at each locus form an n-dimensional space—effectively reduces to n^2 linkage relations, which are expressed by n^2 coefficients of linkage disequilibrium D^{ij}, $i,j = 1,\ldots,n$ defined by

$$D_{ij}(c) := \sum_{k\neq i, l\neq j} (c_{il}c_{kj} - c_{ij}c_{kl}). \tag{5.7.19}$$

If all these coefficients vanish, the population is defined to be in *linkage equilibrium*. In that case, each allele at one locus is in linkage equilibrium with all other alleles at the other locus and conversely.

To determine the geometrical structure of the two-loci model in linkage equilibrium, the corresponding state space $\Delta_{(n+1)^2-1}$ needs to be transformed appropriately, so that all D^{ij} become coordinates. This may be achieved by a transformation into the alternative coordinates $(x^\bullet, D) = (x^\bullet, D)_{i,j=1,\ldots,n}$ comprising $2n$ allele frequencies $x^{i\bullet}$ and $x^{\bullet j}$ and all coefficients of linkage disequilibrium D^{ij}. This implies

$$\frac{\partial x^{i\bullet}}{\partial x^{kl}} = \delta^i_k, \quad \frac{\partial x^{\bullet j}}{\partial x^{kl}} = \delta^j_l, \quad \frac{\partial D^{ij}}{\partial x^{kl}} = -\delta^i_k\delta^i_l + \delta^i_k x^{\bullet j} + x^{i\bullet}\delta^j_l \tag{5.7.20}$$

for $i,j \neq 0$ and $(k,l) \neq (0,0)$, and transforming the (inverse) metric given by the coefficients of the second order derivatives of the corresponding Kolmogorov equation, i.e. $(a^{ij,kl}(x)) = \left(x^{ij}(\delta^{ij}_{kl} - x^{kl})\right)$, accordingly yields

$$\begin{aligned} a^{x^{i\bullet},x^{\bullet l}}(x^\bullet, D) &= \sum_{p,q}\sum_{r,s} x^{pq}(\delta^{pq}_{rs} - x^{rs})\frac{\partial x^{i\bullet}}{\partial x^{pq}}\frac{\partial x^{\bullet l}}{\partial x^{rs}} \\ &= \sum_{q}\sum_{r} x^{iq}(\delta^{iq}_{rl} - x^{rl}) \\ &= x^{il} - x^{i\bullet}x^{\bullet l} = D^{il} \\ &\equiv a^{x^{\bullet l},x^{i\bullet}}(x^\bullet, D) \quad \text{for } i,l = 1,\ldots,n \end{aligned} \tag{5.7.21}$$

(with the last equality being due to the undirectedness of linkage) and similarly

$$a^{x^{i\bullet},x^{k\bullet}}(x^\bullet,D) = x^{i\bullet}(\delta^i_k - x^{k\bullet}) \quad \text{for } i,k = 1,\dots,n, \tag{5.7.22}$$

$$a^{x^{\bullet j},x^{\bullet l}}(x^\bullet,D) = x^{\bullet j}(\delta^j_l - x^{\bullet l}) \quad \text{for } j,l = 1,\dots,n. \tag{5.7.23}$$

For the other components of the metric, we have

$$\begin{aligned} a^{x^{i\bullet},D^{kl}}(x^\bullet,D) &= \sum_{p,q}\sum_{r,s} x^{pq}(\delta^{pq}_{rs} - x^{rs})\frac{\partial x^{i\bullet}}{\partial x^{pq}}\frac{\partial D^{kl}}{\partial x^{rs}} \\ &= \sum_q x^{iq}\Big(-(\delta^{iq}_{kl} - x^{kl}) + \sum_r (\delta^{iq}_{rl} - x^{rl})x^{k\bullet} + \sum_s (\delta^{iq}_{ks} - x^{ks})x^{\bullet l}\Big) \\ &= -\delta^i_k D^{kl} + x^{i\bullet}D^{kl} + x^{k\bullet}D^{il} \qquad (5.7.24) \\ &\equiv a^{D^{kl},x^{i\bullet}}(x^\bullet,D) \quad \text{for } i,k,l = 1,\dots,q \end{aligned}$$

and analogously

$$a^{x^{\bullet j},D^{kl}}(x^\bullet,D) \equiv a^{D^{kl},x^{\bullet j}}(x^\bullet,D) = -\delta^j_l D^{kl} + x^{\bullet j}D^{kl} + x^{\bullet l}D^{kj} \quad \text{for } j,k,l = 1,\dots,n. \tag{5.7.25}$$

Thus, these entries also vanish in linkage equilibrium. This means that the corresponding coordinate representation of the inverse metric in linkage equilibrium becomes a block matrix, i.e.

$$(a^{(x^\bullet,D)}) = \begin{pmatrix} (a^{x^{i\bullet},x^{k\bullet}}) & 0^{n,n} & 0^{n,n^2} \\ 0^{n,n} & (a^{x^{\bullet j},x^{\bullet l}}) & 0^{n,n^2} \\ 0^{n^2,n} & 0^{n^2,n} & (a^{D^{ij},D^{kl}}) \end{pmatrix}, \tag{5.7.26}$$

with the remaining entries being

$$a^{D^{ij},D^{kl}}(x^\bullet,D) = (x^{i\bullet} - \delta^i_k)x^{k\bullet}(x^{\bullet j} - \delta^j_l)x^{\bullet l} \quad \text{for } i,j,k,l = 1,\dots,n. \tag{5.7.27}$$

This yields the generalization of the metric representation corresponding to the Ohta–Kimura formula in linkage equilibrium (cf. Eq. (5.7.16)) to an arbitrary number of alleles.

Moreover, $(a^{(x^\bullet,D)}(x^\bullet,D))$ may be inverted in accordance with Eq. (3.2.16), exhibiting the product structure of $(a_{(x^\bullet,D)}(x^\bullet,D))$. We thus have:

Lemma 5.7.1 *In linkage equilibrium, for all* $n + 1 \geq 2$ *the corresponding restriction of the state space* $\Delta_{(n+1)^2-1}$ *of the diffusion approximation of a two-loci* $(n + 1)$*-allelic Wright–Fisher model equipped with the Fisher metric of the multinomial distribution is a* $2n$*-dimensional manifold and carries the geometric structure of*

$$S_+^n \times S_+^n \subset S_+^{2n+1}. \tag{5.7.28}$$

5.7.2 Linkage Equilibria in Three-Loci Multi-Allelic Models

When there are more than two loci, the situation gets significantly more complicated as now linkage does not only need to be considered between pairs of loci, but also in higher order relations. In particular, we need to clarify the term 'linkage equilibrium' in this extended setting. To keep the calculative effort manageable, we first analyze a three-loci model; in doing so, we will give a definition of linkage equilibrium in the current setting plus an adaptation of Lemma 5.7.1.

When wishing to analyze the geometry of the corresponding state space $\Delta_{(n+1)^3-1}$ restricted to the—yet to be determined—linkage equilibrium states, again we need to transform the state space appropriately, for which in turn suitable coordinates are required: This may be done somewhat tentatively by first adapting the coordinate scheme of the two-loci model as far as applicable and subsequently extending it to also fit the three-loci model.

Hence, analogous to the two-loci model, the configuration at each locus will be assessed by the corresponding allele frequencies $x^{i_1\bullet\bullet}, x^{\bullet i_2\bullet}, x^{\bullet\bullet i_3}$ with $i_1, i_2, i_3 = 1, \ldots, n$, yielding n^3 coordinates; the coefficients of linkage disequilibrium D^{ij} are transferred into $3n^2$ *coefficients of generalized 2-linkage disequilibrium* $D_2^{i_1 i_2\bullet}, D_2^{i_1\bullet i_3}, D_2^{\bullet i_2 i_3}$, $i_1, i_2, i_3 = 1, \ldots, n$ with

$$\begin{aligned} D_2^{i_1 i_2\bullet}(x) &:= x^{i_1\bullet\bullet}x^{\bullet i_2\bullet} - x^{i_1 i_2\bullet}, \\ D_2^{i_1\bullet i_3}(x) &:= x^{i_1\bullet\bullet}x^{\bullet\bullet i_3} - x^{i_1\bullet i_3}, \\ D_2^{\bullet i_2 i_3}(x) &:= x^{\bullet i_2\bullet}x^{\bullet\bullet i_3} - x^{\bullet i_2 i_3}, \end{aligned} \tag{5.7.29}$$

measuring the linkage disequilibrium with respect to any pair of loci (the corresponding twofold interactions are structurally analogous to those of the two-loci model, giving rise to the notion of 'generalized 2-linkage').

However, $(x^{\bullet\bullet}, D_2)$ does not yet form a full set of coordinates nor is linkage between more than two loci (threefold interactions) taken into account. For this reason, we introduce the *coefficients of generalized 3-linkage disequilibrium* by extending the structure (5.7.29) into

$$D_3^{i_1 i_2 i_3}(x) := x^{i_1\bullet\bullet}x^{\bullet i_2\bullet}x^{\bullet\bullet i_3} - x^{i_1 i_2 i_3} \quad \text{for } i_1, i_2, i_3 = 1, \ldots, n, \tag{5.7.30}$$

now taking into account all three loci and hence employing the product of all corresponding allele frequencies. By adding these n^3 coefficients as coordinates, $(x^{\bullet\bullet}, D_2, D_3)$ now forms a complete set of $(n+1)^3-1$ coordinates, which will yield a suitable description of the linkage equilibrium.

Thus, the *linkage equilibrium with respect to all three loci* is defined to be a state where all coefficients of generalized 2-linkage and generalized 3-linkage disequilibrium vanish, i.e. both all twofold and all threefold linkage interactions between the loci are in equilibrium. Consequently, we then have for the coordinate representation of the inverse metric

$$(a^{(x^{\bullet\bullet},D_2,D_3)}) = \begin{pmatrix} (a^{x^{\bullet\bullet},x^{\bullet\bullet}}) & 0^{n,n^2} & 0^{n,n^3} \\ 0^{n^2,n} & (a^{D_2,D_2}) & (a^{D_2,D_3}) \\ 0^{n^3,n} & (a^{D_3,D_2}) & (a^{D_3,D_3}) \end{pmatrix} \tag{5.7.31}$$

with $(a^{x^{\bullet\bullet},x^{\bullet\bullet}})$ being a block matrix itself, i.e.

$$(a^{x^{\bullet\bullet},x^{\bullet\bullet}}) = \begin{pmatrix} (a^{x^{j_1\bullet\bullet},x^{j_1\bullet\bullet}}) & 0^{n,n} & 0^{n,n} \\ 0^{n,n} & (a^{x^{\bullet i_2\bullet},x^{\bullet j_2\bullet}}) & 0^{n,n} \\ 0^{n,n} & 0^{n,n} & (a^{x^{\bullet\bullet i_3},x^{\bullet\bullet j_3}}) \end{pmatrix}, \tag{5.7.32}$$

and the remaining entries (a^{D_2,D_2}) equaling

$$\begin{aligned} a^{D_2^{i_1i_2\bullet},D_2^{j_1j_2\bullet}}(x^{\bullet\bullet},D_2,D_3) &= (x^{i_1\bullet\bullet}-\delta^{i_1}_{j_1})x^{j_1\bullet\bullet}(x^{\bullet i_2\bullet}-\delta^{i_2}_{j_2})x^{\bullet j_2\bullet}, \\ a^{D_2^{i_1\bullet i_3},D_2^{j_1\bullet j_3}}(x^{\bullet\bullet},D_2,D_3) &= (x^{i_1\bullet\bullet}-\delta^{i_1}_{j_1})x^{j_1\bullet\bullet}(x^{\bullet\bullet i_3}-\delta^{i_3}_{j_3})x^{\bullet\bullet j_3}, \\ a^{D_2^{\bullet i_2i_3},D_2^{\bullet j_2j_3}}(x^{\bullet\bullet},D_2,D_3) &= (x^{\bullet i_2\bullet}-\delta^{i_2}_{j_2})x^{\bullet j_2\bullet}(x^{\bullet\bullet i_3}-\delta^{i_3}_{j_3})x^{\bullet\bullet j_3} \end{aligned} \tag{5.7.33}$$

as well as

$$\begin{aligned} a^{D_2^{i_1i_2\bullet},D_2^{j_1\bullet j_3}}(x^{\bullet\bullet},D_2,D_3) &\equiv a^{D_2^{j_1\bullet j_3},D_2^{i_1i_2\bullet}}(x^{\bullet\bullet},D_2,D_3) \\ &= -\delta^{i_1}_{j_1}D_3^{i_1i_2i_3}+x^{i_1\bullet\bullet}D_3^{j_1i_2j_3}+x^{j_1\bullet\bullet}D_3^{i_1i_2j_3}, \end{aligned} \tag{5.7.34}$$

$$\begin{aligned} a^{D_2^{i_1i_2\bullet},D_2^{\bullet j_2j_3}}(x^{\bullet\bullet},D_2,D_3) &\equiv a^{D_2^{\bullet j_2j_3},D_2^{i_1i_2\bullet}}(x^{\bullet\bullet},D_2,D_3) \\ &= -\delta^{i_2}_{j_2}D_3^{i_1i_2i_3}+x^{\bullet i_2\bullet}D_3^{i_1j_2j_3}+x^{\bullet j_2\bullet}D_3^{i_1i_2i_3}, \end{aligned} \tag{5.7.35}$$

$$\begin{aligned} a^{D_2^{i_1\bullet i_3},D_2^{\bullet j_2j_3}}(x^{\bullet\bullet},D_2,D_3) &\equiv a^{D_2^{\bullet j_2j_3},D_2^{i_1\bullet i_3}}(x^{\bullet\bullet},D_2,D_3) \\ &= -\delta^{i_3}_{j_3}D_3^{i_1i_2i_3}+x^{\bullet\bullet i_3}D_3^{i_1i_2j_3}+x^{\bullet\bullet j_3}D_3^{i_1i_2i_3} \end{aligned} \tag{5.7.36}$$

and (a^{D_3,D_2}) resp. (a^{D_2,D_3}) being

$$\begin{aligned} a^{D_3^{i_1i_2i_3},D_2^{\bullet j_2j_3}}(x^{\bullet\bullet},D_2,D_3) &\equiv a^{D_2^{\bullet j_2j_3},D_3^{i_1i_2i_3}}(x^{\bullet\bullet},D_2,D_3)\\ &= x^{i_1\bullet\bullet}(x^{\bullet i_2\bullet}-\delta^{i_2}_{j_2})x^{\bullet j_2\bullet}(x^{\bullet\bullet i_3}-\delta^{i_3}_{j_3})x^{\bullet\bullet j_3}, \end{aligned} \tag{5.7.37}$$

$$\begin{aligned} a^{D_3^{i_1i_2i_3},D_2^{j_1\bullet j_3}}(x^{\bullet\bullet},D_2,D_3) &\equiv a^{D_2^{j_1\bullet j_3},D_3^{i_1i_2i_3}}(x^{\bullet\bullet},D_2,D_3)\\ &= (x^{i_1\bullet\bullet}-\delta^{i_1}_{j_1})x^{j_1\bullet\bullet}x^{\bullet i_2\bullet}(x^{\bullet\bullet i_3}-\delta^{i_3}_{j_3})x^{\bullet\bullet j_3}, \end{aligned} \tag{5.7.38}$$

$$\begin{aligned} a^{D_3^{i_1i_2i_3},D_2^{j_1j_2\bullet}}(x^{\bullet\bullet},D_2,D_3) &\equiv a^{D_2^{j_1j_2\bullet},D_3^{i_1i_2i_3}}(x^{\bullet\bullet},D_2,D_3)\\ &= (x^{i_1\bullet\bullet}-\delta^{i_1}_{j_1})x^{j_1\bullet\bullet}(x^{\bullet i_2\bullet}-\delta^{i_2}_{j_2})x^{\bullet j_2\bullet}x^{\bullet\bullet i_3} \end{aligned} \tag{5.7.39}$$

and eventually (a^{D_3,D_3}) equaling

$$a^{D_3^{i_1i_2i_3},D_3^{j_1j_2j_3}}(x^{\bullet\bullet},D_2,D_3)$$

$$= \begin{cases} x^{i_1\bullet\bullet}x^{j_1\bullet\bullet}x^{\bullet i_2\bullet}x^{\bullet j_2\bullet}x^{\bullet\bullet i_3}x^{\bullet\bullet j_3}\\ x^{i_1\bullet\bullet}x^{j_1\bullet\bullet}x^{\bullet i_2\bullet}x^{\bullet j_2\bullet}x^{\bullet\bullet i_3}x^{\bullet\bullet j_3}\Big(2-\frac{1}{\delta^{i_1}_{j_1}x^{j_1\bullet\bullet}+\delta^{i_2}_{j_2}x^{\bullet j_2\bullet}+\delta^{i_3}_{j_3}x^{\bullet\bullet j_3}}\Big)\\ x^{i_1\bullet\bullet}x^{j_1\bullet\bullet}x^{\bullet i_2\bullet}x^{\bullet j_2\bullet}x^{\bullet\bullet i_3}x^{\bullet\bullet j_3}\Big(2-\dfrac{x^{i_1\bullet\bullet}+x^{\bullet i_2\bullet}}{x^{i_1\bullet\bullet}x^{\bullet i_2\bullet}}\delta^{i_1i_2}_{j_1j_2}\\ \qquad\qquad -\dfrac{x^{i_1\bullet\bullet}+x^{\bullet\bullet i_3}}{x^{i_1\bullet\bullet}x^{\bullet\bullet i_3}}\delta^{i_1i_3}_{j_1j_3}-\dfrac{x^{\bullet i_2\bullet}+x^{\bullet\bullet i_3}}{x^{\bullet i_2\bullet}x^{\bullet\bullet i_3}}\delta^{i_2i_3}_{j_2j_3}\Big) \end{cases} \tag{5.7.40}$$

if either none, one or two of the indices i_1, i_2, i_3 and j_1, j_2, j_3 coincide resp.

$$\begin{aligned} &a^{D_3^{i_1i_2i_3},D_3^{i_1i_2i_3}}(x^{\bullet\bullet},D_2,D_3)\\ &\quad = x^{i_1\bullet\bullet}x^{\bullet i_2\bullet}x^{\bullet\bullet i_3}(1-x^{i_1\bullet\bullet}x^{\bullet i_2\bullet}-x^{\bullet i_2\bullet}x^{\bullet\bullet i_3}-x^{i_1\bullet\bullet}x^{\bullet\bullet i_3}+2x^{i_1\bullet\bullet}x^{\bullet i_2\bullet}x^{\bullet\bullet i_3}) \end{aligned} \tag{5.7.41}$$

if all three indices coincide.

Thus, the block matrix $(a^{(x^{\bullet\bullet},D_2,D_3)})$ may be inverted in accordance with Eq. (3.2.16), demonstrating the product structure of $(a_{(x^{\bullet\bullet},D_2,D_3)})$, and we consequently obtain for the three-loci model transferring the assertion of Lemma 5.7.1:

Lemma 5.7.2 *In linkage equilibrium, for all $n+1 \geq 2$ the corresponding restriction of the state space $\Delta_{(n+1)^3-1}$ of the diffusion approximation of a 3-loci $(n+1)$-allelic Wright–Fisher model equipped with the Fisher metric of the multinomial distribution is a $3n$-dimensional manifold and carries the geometric structure of*

$$S^n_+ \times S^n_+ \times S^n_+ \subset S^{3n+2}_+. \tag{5.7.42}$$

5.7.3 The General Case

From these constructions, we naturally expect that also general models with an arbitrary number of loci and alleles feature a product structure in linkage equilibrium when equipped with their Fisher metric. Clearly, the definition of linkage equilibrium for three loci (cf. p. 118) may be extended to any number of loci by defining suitable coefficients of linkage disequilibrium with respect to any tuple of loci. This may be achieved by generalizing (5.7.29) and (5.7.30): For a model with $k \geq 2$ loci and $n+1 \geq 2$ alleles resp. arbitrary number of alleles at each locus (then put n as the maximum number of alleles at a locus), we introduce the *coefficients of generalized l-linkage disequilibrium* for $2 \leq l \leq k$ by putting

$$D_l^{\langle i_{j_1},\ldots,i_{j_l},\bullet\rangle}(x) := \prod_{m=1}^{l} x^{\langle i_{j_m},\bullet\rangle} - x^{\langle i_{j_1},\ldots,i_{j_l},\bullet\rangle} \tag{5.7.43}$$

for $i_{j_1},\ldots,i_{j_l} = 1,\ldots,n$ and every subset $\{j_1,\ldots,j_l\} \subset \{1\ldots,k\}$ with $j_r \neq j_s$ for $r \neq s$, measuring the l-fold linkage interactions for every subset of l loci.

Taking the $\binom{k}{l} n^l$ coefficients of generalized l-linkage disequilibrium, $l = 2,\ldots,k$ plus the kn allele frequencies as coordinates yields a full alternative description of the $\big((n+1)^k - 1\big)$-dimensional model as we have

$$\sum_{l=1}^{k} \binom{k}{l} n^l = (n+1)^k - 1. \tag{5.7.44}$$

We may also formulate coefficients of generalized 1-linkage disequilibrium

$$D_l^{\langle i_{j_1},\bullet\rangle}(x) := \prod_{m=1}^{1} x^{\langle i_{j_m},\bullet\rangle} - x^{\langle i_{j_1},\bullet\rangle} \equiv 0 \quad \text{for all } i_{j_1} = 1,\ldots,n \text{ with } j_1 \in \{1,\ldots,k\}, \tag{5.7.45}$$

which, however, provide no information about the state of the model as each locus is trivially in (full) linkage equilibrium with itself. Instead, the allele frequencies are used as non-interaction coordinates.

As in the three-loci case, we may then define the model to be in linkage equilibrium if for all l the coefficients of generalized l-linkage disequilibrium vanish. It may then be shown as an application of information geometry that the corresponding restriction of the state space $\Delta_{(n+1)^k-1}$ when equipped with the Fisher metric of the multinomial distribution carries the geometrical structure of

$$\underbrace{S_+^n \times \ldots \times S_+^n}_{k} \subset S_+^{k(n+1)-1}. \tag{5.7.46}$$

To prove this, we first consider the allele frequencies $x^{i_1\bullet\cdots\bullet}$, $i_1 = 1,\ldots,n$. They serve as a parameter set of the multinomial distribution $\mathcal{M}$, hence we may consider the corresponding Fisher metric $g^{\cdot\bullet\cdots\bullet}$ on Δ_n (cf. also Sect. 3.5). However, due to their frequency property, i.e., $\sum_{i_1} x^{i_1\bullet\cdots\bullet} = 1$, $(x^{i_1\bullet\cdots\bullet})_{i_1}$ may itself be interpreted as a discrete probability distribution in Δ_n (the last coordinate may be suppressed). We thus consider the corresponding (proper) Fisher metric $\tilde{g}^{\cdot\bullet\cdots\bullet}$ on Δ_n given by

$$\tilde{g}_{ij}^{\cdot\bullet\cdots\bullet}(x^{\cdot\bullet\cdots\bullet}) := \frac{1}{x^{i\bullet\cdots\bullet}}\delta_j^i + \frac{1}{x^{0\bullet\cdots\bullet}} \tag{5.7.47}$$

However, from Eq. (3.7.7), we directly observe that both metrics coincide, except for the factor N (for $N = 1$, the multinomial distribution with parameter $p \in \Delta_n$ agrees with p, which immediately confirms the identity of both metrics). Hence, we may ignore the factor N (which also does not appear in the coefficient matrix of the Kolmogorov equations due to the chosen scaling) and just write g. Analogous considerations hold for $x^{\bullet i_2\bullet\cdots\bullet},\ldots,x^{\bullet\cdots\bullet i_k}$, $i_j = 1,\ldots,n$.

Next, we consider the product

$$(\Delta_n, g^{\cdot\bullet\cdots\bullet}) \times (\Delta_n, g^{\bullet\cdot\bullet\cdots\bullet}) \times \ldots \times (\Delta_n, g^{\bullet\cdots\bullet\cdot}) \longrightarrow (\Delta_{(n+1)^k-1}, g) \tag{5.7.48}$$

$$(x^{i_1\bullet\cdots\bullet}, x^{\bullet i_2\bullet\cdots\bullet}, \ldots, x^{\bullet\cdots\bullet i_k}) \longmapsto x^{i_1 i_2\ldots i_k} \tag{5.7.49}$$

As known from information geometry, the image of the product, i.e. the corresponding restriction of the Fisher metric, has a product structure itself, if the following independence relations are satisfied:

$$x^{i_1\bullet\cdots\bullet} \cdot x^{\bullet i_2\bullet\cdots\bullet} \cdots x^{\bullet\cdots\bullet i_k} = x^{i_1 i_2\ldots i_k}, \quad i_1, i_2, \ldots, i_k = 1,\ldots,n \tag{5.7.50}$$

By suppression of the respective n-th coordinate indices, it may directly be seen that this corresponds to the vanishing of all coefficients of linkage disequilibrium $D_l^{\langle i_{j_1},\ldots,i_{j_l},\bullet\rangle}(x)$ for $i_{j_1},\ldots,i_{j_l} = 1,\ldots,n$ and every subset $\{j_1,\ldots,j_l\} \subset \{1\ldots,k\}$ with $j_r \neq j_s$ for $r \neq s$ and $l = 2,\ldots,k$. This implies

Proposition 5.7.1 *In linkage equilibrium, for all $n+1 \geq 2$ and $k \geq 2$ the corresponding restriction of the state space $\Delta_{(n+1)^k-1}$ of the diffusion approximation of a k-loci $(n+1)$-allelic Wright–Fisher model equipped with the Fisher metric of the multinomial distribution is a kn-dimensional manifold and carries the geometric structure of*

$$\underbrace{S_+^n \times \ldots \times S_+^n}_{k} \subset S_+^{k(n+1)-1}. \tag{5.7.51}$$

Other interesting observations in this context include the following: All considerations with respect to linkage equilibria actually do not take into account the recombinational structure of the model (if present at all) as the calculations only

relate to the diffusion coefficients of the corresponding Kolmogorov equations of the diffusion approximation of the model—which are independent of recombination, see (5.4.4), (5.4.5). Without recombination, however, the assignment of alleles to loci becomes moot as a k-loci $(n+1)$-allelic model and a (1-locus) $(n+1)k$-allelic model may be identified.

In contrast, as soon as any loci structure comes in, the concept of linkage between different loci or subsets of loci leads to the question of linkage equilibria, which themselves directly relate to the concept of recombination via the common structure of coefficients of linkage disequilibrium.

Chapter 6
Moment Generating and Free Energy Functionals

6.1 Moment Generating Functions

In this section, we will construct the moment generating function for the Wright–Fisher model and derive a partial differential equation that it satisfies. This differential equation encodes all the moment evolution equations from the Sect. 4.3. We shall then solve that differential equation and use this to obtain information about the model. moment generating functions are a standard tool in stochastic processes, see for instance [73, Chap. 3]. Master equations for probability distributions have first been applied to the Moran model of population genetics in [65].

Definition 6.1.1

1. For the 2-allele case, let X be a random variable with discrete values with probability distribution function $p(x) = \mathrm{P}\big[X = x\big]$. The (exponential) *moment generating function* of the random variable X is

$$H(s) := \mathrm{E}\big[e^{sX}\big] = \sum_x e^{xs} p(x)$$

   (defined for those values of $s \in \mathbb{R}$ for which the sum converges).
2. In the general case, let $X = (X^1, \cdots, X^n)$ be a tuple of random variables with the joint probability distribution function $p(x^1, \ldots, x^n) = \mathrm{P}\Big[X^1 = x^1, \ldots, X^n = x^n\Big]$. The (exponential) *moment generating function* of X then is

$$H(s_1, \ldots, s_n) := \mathrm{E}\left[e^{\sum_{i=1}^{n} s_i X^i}\right] = \sum_{x^1, \ldots, x^n} e^{\sum_i s_i x^i} p(x^1, \ldots, x^n) = \sum_x e^{s \cdot x} p(x)$$

   (defined for those values of $s \in \mathbb{R}^n$ for which the sum converges).

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When we have the moment generating function $H(s)$, the moments of X can directly be computed from its derivatives at $s = 0$,

$$\mathrm{E}\Big[X^{\alpha}\Big] = \frac{\partial^{\alpha} H(s)}{\partial s^{\alpha}}\Big|_{s=0}.$$

We shall now derive the (second order) partial differential equation for the (exponential) moment generating functions of our Markov process X_t.

6.1.1 Two Alleles

In this case, the exponential moment generating function is

$$\begin{aligned} H(t;s) &= \mathrm{E}[e^{sX_t}] \\ &= \sum_{l\geq 0} \frac{s^l}{l!}\mathrm{E}[(X_t)^l] \\ &= \sum_{l\geq 0} \frac{s^l}{l!} m_l(t), \end{aligned} \tag{6.1.1}$$

where $m_l(t)$ is the lth moment of X_t.

From the moment equation (4.3.4)

$$\dot{m}_l(t) = -\frac{l(l-1)}{2} m_l(t) + \frac{l(l-1)}{2} m_{l-1}(t),$$

we obtain

$$\begin{aligned} \frac{\partial H(t;s)}{\partial t} &= \sum_{l\geq 0} \dot{m}_l(t)\frac{s^l}{l!} \\ &= \sum_{l\geq 0} \left[-\frac{l(l-1)}{2} m_l(t) + \frac{l(l-1)}{2} m_{l-1}(t) \right] \frac{s^l}{l!} \\ &= \sum_{l\geq 2} -\frac{1}{2} m_l(t) \frac{s^l}{(l-2)!} + \sum_{l\geq 2} \frac{1}{2} m_{l-1}(t) \frac{s^l}{(l-2)!} \\ &= -\frac{s^2}{2} \sum_{l\geq 0} m_{l+2}(t) \frac{s^l}{l!} + \frac{s^2}{2} \sum_{l\geq 0} m_{l+1}(t) \frac{s^l}{l!} \\ &= -\frac{s^2}{2} \frac{\partial^2}{\partial s^2} H(t;s) + \frac{s^2}{2} \frac{\partial}{\partial s} H(t;s). \end{aligned} \tag{6.1.2}$$

We now consider solutions of such equations. First, we solve Eq. (6.1.2) by separation of variables. With $H(t;s) = T(t)S(s)$, the equation becomes

$$\frac{T'(t)}{T(t)} = \frac{-s^2S''(s) + s^2S'(s)}{2S} = -\lambda.$$

It follows that $T(t) = Ce^{-\lambda t}$ and that $S(s)$ satisfies the ODE

$$-x^2y_{xx} + x^2y_x = -2\lambda y. \tag{6.1.3}$$

By putting $y(x) = \sum_{n\geq 0} a_n x^n$ and equating coefficients in the ODE (6.1.3), we obtain:

1. If $\lambda \notin \Lambda := \left\{\mu_l = \frac{l(l-1)}{2}, n \in \mathbb{N}\right\}$, then the ODE (6.1.3) has a unique solution $y(x) = 0$.
2. If $\lambda = \mu_0$, then $y_0(x) = a_0^{(0)} := 1$.
3. If $\lambda = \mu_l$ for some $l \geq 1$, then the solution is of the form

$$y_l(x) = \sum_{i\geq 0} a_i^{(l)} x^i \tag{6.1.4}$$

where

$$a_i^{(l)} = \begin{cases} 0, & \text{if } i < l, \\ 1, & \text{if } i = l, \\ \frac{i-1}{2(\mu_i-\mu_l)} \cdots \frac{l}{2(\mu_{l+1}-\mu_l)}, & \text{if } i \geq l+1. \end{cases} \tag{6.1.5}$$

Therefore, the solution of (6.1.2) is

$$\begin{aligned} H(t;s) &= \sum_{l\geq 0} c_l y_l(s) e^{-\mu_l t} \\ &= \sum_{l\geq 0} c_l \left(\sum_{i\geq l} a_i^{(l)} s^i \right) e^{-\mu_l t} \\ &= \sum_{i\geq 0} \left(i! \sum_{l=0}^{i} c_l a_i^{(l)} e^{-\mu_l t} \right) \frac{s^i}{i!}. \end{aligned} \tag{6.1.6}$$

This yields the moment formula

$$m_i(t) = i! \sum_{l=0}^{i} c_l a_i^{(l)} e^{-\mu_l t} = \sum_{l=0}^{i} c_l A_i^{(l)} e^{-\mu_l t}.$$

The coefficients c_l can be calculated from the initial condition

$$\left(\frac{i}{2N}\right)^j := p^j = m_j(0) = \sum_{l=0}^{j} c_l A_j^{(l)}, \quad \forall j \geq 0.$$

In fact, by representing these equalities in matrix form

$$\begin{bmatrix} 1 & 0 & \cdots & 0 & 0 \\ A_1^{(0)} & 1 & \cdots & 0 & 0 \\ \vdots & \vdots & \ddots & \vdots & \\ A_{j-1}^{(0)} & A_{j-1}^{(1)} & \cdots & (j-1)! & 0 \\ A_j^{(0)} & A_j^{(1)} & \cdots & A_j^{(j-1)} & j! \end{bmatrix} \begin{bmatrix} c_0 \\ c_1 \\ \vdots \\ c_{j-1} \\ c_j \end{bmatrix} = \begin{bmatrix} 1 \\ p \\ \vdots \\ p^{j-1} \\ p^j \end{bmatrix}, \tag{6.1.7}$$

it follows that

$$\begin{bmatrix} c_0 \\ c_1 \\ \vdots \\ c_{j-1} \\ c_j \end{bmatrix} = \begin{bmatrix} 1 & 0 & \cdots & 0 & 0 \\ A_1^{(0)} & 1 & \cdots & 0 & 0 \\ \vdots & \vdots & \ddots & \vdots & \\ A_{j-1}^{(0)} & A_{j-1}^{(1)} & \cdots & (j-1)! & 0 \\ A_j^{(0)} & A_j^{(1)} & \cdots & A_j^{(j-1)} & j! \end{bmatrix}^{-1} \begin{bmatrix} 1 \\ p \\ \vdots \\ p^{j-1} \\ p^j \end{bmatrix}. \tag{6.1.8}$$

Remark We can easily check some instances: Because of $c_0 = 1$, $c_1 = p$, $c_2 = \frac{p^2-p}{2}$, $c_3 = \frac{p^3-3/2p^2+1/2p}{6}$, then $m_0(t) = 1$, $m_1(t) = p, m_2(t) = p + (p^2 - p)e^{-t}$, $m_3(t) = p + 3/2(p^2 - p)e^{-t} + (p^3 - 3/2p^2 + 1/2p)e^{-3t}$.

We shall employ a notation analogous to that in (2.3.4); that is, $P(t, i, j)$ denotes the probability that a process starting with i alleles of type A^1 at time 0 has j alleles of that type at time t.

We then obtain the fixation probability at time t as

$$\begin{aligned} P(t, i, 2N) &= \lim_{j\to\infty} m_j(t) \\ &= \lim_{j\to\infty} \sum_{l=0}^{j} c_l A_j^{(l)} e^{-\mu_l t} \\ &= p + \lim_{j\to\infty} \sum_{l=2}^{j} c_l A_j^{(l)} e^{-\mu_l t} := f(p, t) \end{aligned} \tag{6.1.9}$$

and the eventual fixation probability

$$\begin{aligned} P(\infty, i, 2N) &= \lim_{t\to\infty}\left(p + \lim_{j\to\infty}\sum_{l=2}^{j} c_l A_j^{(l)} e^{-\mu_l t}\right) \\ &= p + \lim_{j\to\infty}\lim_{t\to\infty}\sum_{l=2}^{j} c_l A_j^{(l)} e^{-\mu_l t} \\ &= p. \end{aligned} \tag{6.1.10}$$

This is the same as (2.8.2), where a somewhat different notation had been employed.

Denote by $T_2^1(p) = \inf\{t > 0 : X_t \in \{0, 1\} | X_0 = p\}$ the absorption time. Then we have

$$\mathrm{P}(T_2^1(p) \le t) = P(t, i, 0) + P(t, i, 2N).$$

Therefore, the expectation of the absorption time is

$$\begin{aligned} \mathrm{E}(T_2^1(p)) &= \int_0^\infty t\frac{\partial}{\partial t}\Big(P(t, i, 0) + P(t, i, 2N)\Big)dt \\ &= -\lim_{j\to\infty}\sum_{l=2}^{j} c_l (A_j + A_j')^{(l)}\frac{1}{\mu_l}. \end{aligned}$$

Moreover, we have

$$\sum_{j=0}^{2N}\left(\frac{j}{2N}\right)^l P(\infty, i, j) = \lim_{t\to\infty} m_l(t) = \begin{cases} p, & \text{for } l \ge 1, \\ 1, & \text{for } l = 0. \end{cases} \tag{6.1.11}$$

Hence, we obtain the eventual probability

$$P(\infty, i, j) = p\delta_{2N,j} + (1 - p)\delta_{0,j},$$

which is, of course, 0 unless $j = 0$ or $2N$.

The probability of heterogeneity is

$$\begin{aligned} H_t :&= 2\sum_{j=0}^{2N}\frac{j}{2N}\Big(1 - \frac{j}{2N}\Big)P(t, i, j) \\ &= 2(m_1(t) - m_2(t)) \\ &= 2\left(p - \Big(p + c_2 A_2^{(2)} e^{-t}\Big)\right) \\ &= 2p(1 - p)e^{-t}. \end{aligned} \tag{6.1.12}$$

6.1.2 Two Alleles with Mutation

We start with the moment evolution equation (4.3.5)

$$\dot{m}_l(t) = \left(\frac{\nu}{2}l + \frac{l(l-1)}{2}\right)m_{l-1}(t) - \left(\frac{\nu+\mu}{2}l + \frac{l(l-1)}{2}\right)m_l(t). \tag{6.1.13}$$

As before, we can obtain the differential equation for the moment generating function. Let

$$H(t,s) := \sum_{l\geq 0} m_l(t)\frac{s^l}{l!},$$

then we have

$$\begin{aligned}
\frac{\partial H(t;s)}{\partial t} &= \sum_{l\geq 0}\dot{m}_l(t)\frac{s^l}{l!} \\
&= \sum_{l\geq 0}\left[\left(\frac{\nu}{2}l + \frac{l(l-1)}{2}\right)m_{l-1}(t) - \left(\frac{\nu+\mu}{2}l + \frac{l(l-1)}{2}\right)m_l(t)\right]\frac{s^l}{l!} \\
&= \frac{\nu}{2}\sum_{l\geq 1} m_{l-1}(t)\frac{s^l}{(l-1)!} + \frac{1}{2}\sum_{l\geq 2} m_{l-1}(t)\frac{s^l}{(l-2)!} \\
&\quad - \frac{\nu+\mu}{2}\sum_{l\geq 1} m_l(t)\frac{s^l}{(l-1)!} - \frac{1}{2}\sum_{l\geq 2} m_l(t)\frac{s^l}{(l-2)!} \\
&= \frac{\nu}{2}sH(t,s) + \frac{s^2}{2}\frac{\partial}{\partial s}H(t;s) - \frac{\nu+\mu}{2}s\frac{\partial}{\partial s}H(t;s) - \frac{s^2}{2}\frac{\partial^2}{\partial s^2}H(t;s) \\
&= -\frac{s^2}{2}\frac{\partial^2}{\partial s^2}H(t;s) + \left(\frac{s^2}{2} - \frac{\nu+\mu}{2}s\right)\frac{\partial}{\partial s}H(t;s) + \frac{\nu}{2}sH(t,s).
\end{aligned} \tag{6.1.14}$$

We can likewise solve this equation by separation of variables and equating coefficients.

Proposition 6.1.1 *The operator*

$$Ly(x) := -\frac{x^2}{2}y''(x) + \frac{x^2 - (\nu+\mu)x}{2}y'(x) + \frac{\nu x}{2}y(x) \tag{6.1.15}$$

has the set of eigenvalues

$$\Lambda := \left\{\nu_l = \frac{l(l-1) + (\nu+\mu)l}{2}, l \in \mathbb{N}\right\} \tag{6.1.16}$$

and corresponding eigensolutions

$$y_l(x) = \sum_{j\geq 0} a_j^{(l)} x^j \tag{6.1.17}$$

where

$$a_j^{(l)} = \begin{cases} 0, & \text{if } j < l \\ 1, & \text{if } j = l \\ \frac{\mu_j}{\nu_j - \nu_l} \cdots \frac{\mu_{l+1}}{\nu_{l+1} - \nu_l}, & \text{if } j \geq l+1. \end{cases} \tag{6.1.18}$$

where $\mu_n = \frac{n+\nu-1}{2}$

Proof Similar to the case without mutations, by putting $y(x) = \sum_{j\geq 0} a_j x^j$ and equating coefficients in the ODE (6.1.15), we obtain:

1. If $\lambda \notin \Lambda := \left\{\nu_l = \frac{l(l-1+\nu+\mu)}{2}, l \in \mathbb{N}\right\}$, then the ODE (6.1.15) has a unique solution $y(x) = 0$.
2. If $\lambda = \nu_0$, then $y_0(x) = a_0^{(0)} := 1$.
3. If $\lambda = \nu_l$ for some $l \geq 1$, then the solution is of the form

$$y_l(x) = \sum_{j\geq 0} a_j^{(l)} x^j \tag{6.1.19}$$

where $a_j^{(l)}$ as in (6.1.18). □

Therefore, the solution of (6.1.14) is

$$\begin{aligned} H(t;s) &= \sum_{l\geq 0} c_l y_l(s) e^{-\nu_l t} \\ &= \sum_{l\geq 0} c_l \left(\sum_{j\geq l} a_j^{(l)} s^j \right) e^{-\nu_l t} \\ &= \sum_{j\geq 0} \left(j! \sum_{l=0}^{j} c_l a_j^{(l)} e^{-\nu_l t} \right) \frac{s^j}{j!}. \end{aligned} \tag{6.1.20}$$

This yields the moment formula

$$m_j(t) = j! \sum_{l=0}^{j} c_l a_j^{(l)} e^{-\nu_l t} = \sum_{l=0}^{j} c_l A_j^{(l)} e^{-\nu_l t}.$$

The coefficients c_l can be calculated from the initial condition

$$\left(\frac{i}{2N}\right)^j := p^j = m_j(0) = \sum_{l=0}^{j} c_l A_j^{(l)}, \quad \forall j \geq 0.$$

In fact, by representing these equalities in matrix form

$$\begin{bmatrix} 1 & 0 & \cdots & 0 & 0 \\ A_1^{(0)} & 1 & \cdots & 0 & 0 \\ \vdots & \vdots & \ddots & \vdots & \\ A_{j-1}^{(0)} & A_{j-1}^{(1)} & \cdots & (j-1)! & 0 \\ A_j^{(0)} & A_j^{(1)} & \cdots & A_j^{(j-1)} & j! \end{bmatrix} \begin{bmatrix} c_0 \\ c_1 \\ \vdots \\ c_{j-1} \\ c_j \end{bmatrix} = \begin{bmatrix} 1 \\ p \\ \vdots \\ p^{j-1} \\ p^j \end{bmatrix}, \tag{6.1.21}$$

it follows that

$$\begin{bmatrix} c_0 \\ c_1 \\ \vdots \\ c_{j-1} \\ c_j \end{bmatrix} = \begin{bmatrix} 1 & 0 & \cdots & 0 & 0 \\ A_1^{(0)} & 1 & \cdots & 0 & 0 \\ \vdots & \vdots & \ddots & \vdots & \\ A_{j-1}^{(0)} & A_{j-1}^{(1)} & \cdots & (j-1)! & 0 \\ A_j^{(0)} & A_j^{(1)} & \cdots & A_j^{(j-1)} & j! \end{bmatrix}^{-1} \begin{bmatrix} 1 \\ p \\ \vdots \\ p^{j-1} \\ p^j \end{bmatrix}. \tag{6.1.22}$$

6.1.3 Two Alleles with Selection

We use the moment evolution equation (4.3.6)

$$\dot{m}_l(t) = \frac{l(l-1)}{2}\Big(m_{l-1}(t) - m_l(t)\Big) + \frac{sl}{2}\Big(m_l(t) - m_{l+1}(t)\Big)$$

to get the differential equation for the exponential moment generating functions:

$$\begin{aligned} \frac{\partial H(t;x)}{\partial t} &= \sum_{l\geq 0} \dot{m}_l(t)\frac{x^l}{l!} \\ &= -\frac{x^2+sx}{4N}\frac{\partial^2}{\partial x^2}H(t;x) + \frac{x^2+sx}{4N}\frac{\partial}{\partial x}H(t;x). \end{aligned} \tag{6.1.23}$$

Then, we need to solve the eigen-problem

$$-(x^2+sx)y_{xx} + (x^2+sx)y_x = -2\lambda y.$$

By putting $y(x) = \sum_{l\geq 1} a_l x^l$ (note that $a_0 = 0$ follows from the above equation), we are lead to the difference equation

$$s(l+1)la_{l+1} + l(l-1-s)a_l - (l-1)a_{l-1} = 2\lambda a_l, \quad l \geq 1. \tag{6.1.24}$$

This equation is difficult to solve explicitly. However, we can apply a perturbation technique used in [107] to get an approximate solution as follows:

We first rewrite the difference equation (6.1.24) in the (infinite-dimensional) matrix form

$$\begin{pmatrix} -s & 2s & 0 & 0 & 0 & \cdots \\ -1 & 2(1-s) & 6s & 0 & 0 & \cdots \\ 0 & -2 & 3(2-s) & 12s & 0 & \cdots \\ 0 & 0 & -3 & 4(3-s) & 20s & \cdots \\ \vdots & \vdots & \ddots & \ddots & \ddots & \vdots \\ \vdots & \vdots & \ddots & \ddots & \ddots & \vdots \end{pmatrix} \begin{pmatrix} a_1^{(l)} \\ a_2^{(l)} \\ a_3^{(l)} \\ a_4^{(l)} \\ \vdots \\ \vdots \end{pmatrix} = 2\lambda_l \begin{pmatrix} a_1^{(l)} \\ a_2^{(l)} \\ a_3^{(l)} \\ a_4^{(l)} \\ \vdots \\ \vdots \end{pmatrix}, \tag{6.1.25}$$

where λ_l are the eigenvalues which satisfy

$$0 \leq \lambda_0 < \lambda_1 \cdots < \lambda_n \to \infty.$$

We approximate the moment generating function by suppressing the eigen-solutions corresponding to large eigenvalues and solving for the eigenvalues $\lambda_l^{(N)}$ and the corresponding eigen-vectors $\{a_1^{(l)}, \cdots, a_N^{(l)}\}$ of the truncated matrix

$$M_N = \begin{pmatrix} -s & 2s & 0 & 0 & 0 & \cdots & 0 \\ -1 & 2(1-s) & 6s & 0 & 0 & \cdots & 0 \\ 0 & -2 & 3(2-s) & 12s & 0 & \cdots & 0 \\ \vdots & \vdots & \ddots & \ddots & \ddots & \vdots & \vdots \\ 0 & 0 & 0 & \cdots & -(N-1) & N(N-1-s) & N(N+1)s \end{pmatrix}. \tag{6.1.26}$$

Thus, we have the approximate eigen-solution

$$y_l^{(N)}(x) = \sum_{j=1}^{N} a_j^{(l)} x^j.$$

6.1.4 $n+1$ Alleles

We can apply the same scheme for any n. The exponential generating function now is

$$H(t;s_1,\dots,s_n)=\sum_{\boldsymbol{\alpha}} m_{\boldsymbol{\alpha}}(t)\frac{s^{\boldsymbol{\alpha}}}{\boldsymbol{\alpha}!},$$

where $m_{\boldsymbol{\alpha}}(t)$ is the $\boldsymbol{\alpha}$th moment of X_t around 0.

From the moment evolution equation (4.3.8)

$$\dot{m}_{\boldsymbol{\alpha}}(t)=-\frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1)}{2}m_{\boldsymbol{\alpha}}(t)+\sum_{i=1}^{n}\frac{\alpha_i(\alpha_i-1)}{2}m_{\boldsymbol{\alpha}-e_i}(t), \tag{6.1.27}$$

we obtain

$$\begin{aligned}
\frac{\partial H(t;s)}{\partial t}&=\sum_{\boldsymbol{\alpha}}\dot{m}_{\boldsymbol{\alpha}}(t)\frac{s^{\boldsymbol{\alpha}}}{\boldsymbol{\alpha}!}\\
&=\sum_{\boldsymbol{\alpha}}\left[-\frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1)}{2}m_{\boldsymbol{\alpha}}(t)+\sum_{i=1}^{n}\frac{\alpha_i(\alpha_i-1)}{2}m_{\boldsymbol{\alpha}-e_i}(t)\right]\frac{s^{\boldsymbol{\alpha}}}{\boldsymbol{\alpha}!}\\
&=\sum_{\boldsymbol{\alpha}}\left(-\frac{\sum_{i\neq j}\alpha_i\alpha_j}{2}-\frac{\sum_i\alpha_i(\alpha_i-1)}{2}\right)m_{\boldsymbol{\alpha}}(t)\frac{s^{\boldsymbol{\alpha}}}{\boldsymbol{\alpha}!}\\
&+\sum_{\boldsymbol{\alpha}}\sum_{i=1}^{n}\frac{\alpha_i(\alpha_i-1)}{2}m_{\boldsymbol{\alpha}-e_i}(t)\frac{s^{\boldsymbol{\alpha}}}{\boldsymbol{\alpha}!}\\
&=-\frac{1}{2}\sum_{i\neq j}s_is_j\frac{\partial^2H(t,s)}{\partial s_i\partial s_j}-\frac{1}{2}\sum_i s_i^2\frac{\partial^2H(t,s)}{\partial s_i^2}+\sum_{i=1}^{n}\frac{1}{2}\sum_i s_i^2\frac{\partial H(t,s)}{\partial s_i}\\
&=-\frac{1}{2}\sum_{i,j=1}^{n}s_is_j\frac{\partial^2}{\partial s_i\partial s_j}H(t;s)+\sum_{i=1}^{n}\frac{s_i^2}{2}\frac{\partial}{\partial s_i}H(t;s).
\end{aligned} \tag{6.1.28}$$

Separating variables as above, $T(t)=Ce^{-\lambda t}$ and $S(s)$ satisfies the PDE

$$-\frac{1}{2}\sum_{i,j=1}^{n}s_is_j\frac{\partial^2}{\partial s_i\partial s_j}y(s)+\sum_{i=1}^{n}\frac{s_i^2}{2}\frac{\partial}{\partial s_i}y(s)=-\lambda y(s). \tag{6.1.29}$$

By putting $y(s) = \sum_{\alpha} a_{\alpha} s^{\alpha}$ and equating coefficients in the PDE (6.1.29), we obtain:

1. If $\lambda \notin \Lambda := \left\{\mu_l = \frac{l(l-1)}{2}, l \in \mathbb{N}\right\}$, then the PDE (6.1.29) has a unique solution $y(s) = 0$.
2. If $\lambda = \mu_0$, then $y_0(x) = a_0^{(0)} := 1$.
3. If $\lambda = \mu_l$ for some $l \geq 1$, then there are $\binom{l}{2}$ independent solutions of the form

$$y_{l,\alpha}(s) = \sum_{\beta} a_{\alpha,\beta}^{(l)} s^{\beta}, \quad \forall |\alpha| = l \tag{6.1.30}$$

where

$$a_{\alpha,\beta}^{(l)} = \begin{cases} 0, & \text{if } |\beta| < l \\ \delta_{\beta}^{\alpha}, & \text{if } |\beta| = l \\ \text{inductively defined by (6.1.32) below}, & \text{if } |\beta| \geq l+1 \end{cases} \tag{6.1.31}$$

$$a_{\alpha,\beta}^{(l)} = \frac{\sum_{i=1}^{n} (\beta_i - 1) a_{\alpha,\beta-e_i}^{(l)}}{|\beta|(|\beta|-1) - l(l-1)}. \tag{6.1.32}$$

Therefore, the solution of Eq. (6.1.29) is

$$\begin{aligned} H(t;s) &= \sum_{l \geq 0} \sum_{|\alpha|=l} c_{l,\alpha} y_{l,\alpha}(s) e^{-\mu_l t} \\ &= \sum_{l \geq 0} \sum_{|\alpha|=l} c_{l,\alpha} \left(\sum_{\beta} a_{\alpha,\beta}^{(l)} s^{\beta} \right) e^{-\mu_l t} \\ &= \sum_{\beta} \left(\sum_{l=0}^{|\beta|} \sum_{|\alpha|=l} c_{l,\alpha} a_{\alpha,\beta}^{(l)} e^{-\mu_l t} \right) s^{\beta} \\ &= \sum_{\beta} \beta! \left(\sum_{|\alpha| \leq |\beta|} c_{|\alpha|,\alpha} a_{\alpha,\beta}^{(|\alpha|)} e^{-\mu_{|\alpha|} t} \right) \frac{s^{\beta}}{\beta!}. \end{aligned} \tag{6.1.33}$$

This yields the moment formula

$$m_{\beta}(t) = \beta! \sum_{|\alpha| \leq |\beta|} c_{|\alpha|,\alpha} a_{\alpha,\beta}^{(|\alpha|)} e^{-\mu_{|\alpha|} t} = \sum_{|\alpha| \leq |\beta|} c_{|\alpha|,\alpha} A_{\alpha,\beta}^{(|\alpha|)} e^{-\mu_{|\alpha|} t}$$

where the coefficients $c_{|\boldsymbol{\alpha}|,\boldsymbol{\alpha}}$ can be computed from the initial condition

$$p^{\boldsymbol{\beta}} = m_{\boldsymbol{\beta}}(0) = \sum_{|\boldsymbol{\alpha}|\leq|\boldsymbol{\beta}|} c_{|\boldsymbol{\alpha}|,\boldsymbol{\alpha}} A^{(|\boldsymbol{\alpha}|)}_{\boldsymbol{\alpha},\boldsymbol{\beta}}, \quad \forall \boldsymbol{\beta}.$$

Similarly to the two alleles case, we immediately obtain some interesting quantities:

The fixation probabilities at time t is ($l = \overline{0,n}$ with $e_0 = (0,\ldots,0)$ and $p_0 = 1 - p_1 - \cdots - p_n$)

$$\begin{aligned} P(t,i,2Ne_l) &= \lim_{n\to\infty} m_{ne_l}(t) \\ &= \lim_{n\to\infty} \sum_{|\boldsymbol{\alpha}|=0}^{n} c_{|\boldsymbol{\alpha}|,\boldsymbol{\alpha}} A^{(|\boldsymbol{\alpha}|)}_{\boldsymbol{\alpha},ne_l} e^{-\mu_{|\boldsymbol{\alpha}|}t} \\ &= p_l + \lim_{n\to\infty} \sum_{|\boldsymbol{\alpha}|=2}^{n} c_{|\boldsymbol{\alpha}|,\boldsymbol{\alpha}} A^{(|\boldsymbol{\alpha}|)}_{\boldsymbol{\alpha},ne_l} e^{-\mu_{|\boldsymbol{\alpha}|}t} \end{aligned} \tag{6.1.34}$$

and the eventual fixation probability

$$\begin{aligned} P(\infty,i,2Ne_l) &= \lim_{t\to\infty} \left(p_l + \lim_{n\to\infty} \sum_{|\boldsymbol{\alpha}|=2}^{n} c_{|\boldsymbol{\alpha}|,\boldsymbol{\alpha}} A^{(|\boldsymbol{\alpha}|)}_{\boldsymbol{\alpha},ne_l} e^{-\mu_{|\boldsymbol{\alpha}|}t} \right) \\ &= p_l. \end{aligned} \tag{6.1.35}$$

The moments of the sojourn and absorption times were derived by Nagylaki [92] for two alleles, and by Lessard and Lahaie [84] in the multi-allele case. We denote by $T^{k+1}_{n+1}(p) = \inf\left\{t > 0 : X_t \in \overline{\partial_k \Delta_n} | X_0 = p\right\}$ the first time when the population has (at most) $k+1$ alleles. $T^{k+1}_{n+1}(p)$ is a continuous random variable valued in $[0,\infty)$ and we denote by $\varphi(t,p)$ its probability density function. It is easy to see that $\overline{\partial_k \Delta_n}$ is invariant under the process $(X_t)_{t\geq 0}$, i.e. if $X_s \in \overline{\partial_k \Delta_n}$ then $X_t \in \overline{\partial_k \Delta_n}$ for all $t \geq s$ (once an allele is lost from the population, it can never be recovered). We have the equality

$$\mathrm{P}(T^1_{n+1}(p) \leq t) = \sum_{l=0}^{n} P(t,i,2Ne_l). \tag{6.1.36}$$

Therefore, the expectation of the absorption time is

$$\begin{aligned} \mathrm{E}(T^1_{n+1}(p)) &= \int_0^\infty t \frac{\partial}{\partial t} \Big(\sum_{l=0}^{n} P(t,i,2Ne_l) \Big) dt \\ &= -\lim_{n\to\infty} \sum_{|\boldsymbol{\alpha}|=2}^{n} c_{|\boldsymbol{\alpha}|,\boldsymbol{\alpha}} \sum_{l=0}^{n} A^{(|\boldsymbol{\alpha}|)}_{\boldsymbol{\alpha},ne_l} \frac{1}{\mu_{|\boldsymbol{\alpha}|}}. \end{aligned}$$

Moreover, by using the same technique as in [85] (see also [39, Chap. 5]) we obtain

$$\mathrm{E}(T_{n+1}^{k+1}(p)) = \sum_{s=1}^{k+1}(-1)^s \binom{n-s}{k+1-s} \sum \int_0^\infty t \frac{\partial}{\partial t} f(p^{j_1} + \cdots + p^{j_s}, t)dt,$$

where the second sum runs over all possible ordered s-tuples $j_1 < \ldots < j_s$ in $\{1, \ldots, n+1\}$ and $f(p,t)$ is defined from (6.1.9). The probability of heterogeneity is (see [118])

$$\begin{aligned} H_t =& (n+1)! \sum_{j \in \Omega_n^{2N}} \left(\frac{j_1}{2N}\right) \cdots \left(\frac{j_n}{2N}\right) \left(1 - \left(\frac{j_1}{2N}\right) - \cdots - \left(\frac{j_n}{2N}\right)\right) P(t,i,j) \\ =& (n+1)! \left(m_{\mathbf{1}}(t) - \sum_{l=1}^{n} m_{\mathbf{1}+e_l}(t)\right) \\ & (\text{where} \quad \mathbf{1} = (1, \cdots, 1),\ e_l = (0, \cdots, 1, \cdots, 0)). \end{aligned}$$

We have from the moment equation

$$\begin{cases} \dot{m}_{\mathbf{1}}(t) & = -\frac{n(n-1)}{2} m_{\mathbf{1}}(t) \\ m_{\mathbf{1}}(0) & = p_1 \ldots p_n, \end{cases}$$

which yields $m_{\mathbf{1}}(t) = p_1 \ldots p_n e^{-\frac{n(n-1)}{2}t}$.

Moreover,

$$\begin{cases} \dot{m}_{\mathbf{1}+e_l}(t) & = -\frac{(n+1)n}{2} m_{\mathbf{1}+e_l}(t) + m_{\mathbf{1}}(t) \\ m_{\mathbf{1}+e_l}(0) & = p_1 \ldots p_n \times p_l, \end{cases}$$

which yields $m_{\mathbf{1}+e_l}(t) = e^{-\frac{(n+1)n}{2}t} p_1 \ldots p_n \left(p_l + \frac{e^n - 1}{n}\right)$.

Therefore, the probability of heterogeneity is

$$\begin{aligned} H_t =& (n+1)! \left(m_{\mathbf{1}}(t) - \sum_{l=1}^{n} m_{\mathbf{1}+e_l}(t)\right), \\ =& (n+1)! \left(p_1 \ldots p_n e^{-\frac{n(n-1)}{2}t} - \sum_{l=1}^{n} e^{-\frac{(n+1)n}{2}t} p_1 \ldots p_n \left(p_l + \frac{e^n - 1}{n}\right)\right) \\ =& (n+1)!\, p_1 \ldots p_n (1 - p_1 - \cdots - p_n) e^{-\frac{(n+1)n}{2}t} \\ =& H_0 e^{-\frac{(n+1)n}{2}t}. \end{aligned}$$

6.1.5 $n+1$ *Alleles with Mutation*

We use the moment evolution equation (4.3.9)

$$\dot{m}_{\boldsymbol{\alpha}}(t) = -\left(\frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1)}{2} + \frac{|\theta||\boldsymbol{\alpha}|}{2}\right) m_{\boldsymbol{\alpha}}(t) + \sum_{i=1}^{n}\left(\frac{\alpha_i(\alpha_i-1)}{2} + \frac{\theta_i\alpha_i}{2}\right) m_{\boldsymbol{\alpha}-e_i}(t). \tag{6.1.37}$$

We again want to obtain the differential equation for the moment generating function. With

$$H(t; s_1, \ldots, s_n) = \sum_{\boldsymbol{\alpha}} m_{\boldsymbol{\alpha}}(t)\frac{s^{\boldsymbol{\alpha}}}{\boldsymbol{\alpha}!},$$

we have

$$\begin{aligned}
\frac{\partial}{\partial t}H(t;s) &= \sum_{\boldsymbol{\alpha}} \dot{m}_{\boldsymbol{\alpha}}(t)\frac{s^{\boldsymbol{\alpha}}}{\boldsymbol{\alpha}!} \\
&= \sum_{\boldsymbol{\alpha}}\Bigg[-\left(\frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1)}{2} + \frac{|\theta||\boldsymbol{\alpha}|}{2}\right) m_{\boldsymbol{\alpha}}(t) \\
&\quad + \sum_{i=1}^{n}\left(\frac{\alpha_i(\alpha_i-1)}{2} + \frac{\theta_i\alpha_i}{2}\right) m_{\boldsymbol{\alpha}-e_i}(t)\Bigg]\frac{s^{\boldsymbol{\alpha}}}{\boldsymbol{\alpha}!} \\
&= \sum_{\boldsymbol{\alpha}}\left(-\sum_{i\neq j}\frac{\alpha_i\alpha_j}{2} - \frac{\sum_i \alpha_i(\alpha_i-1)}{2} - \frac{|\theta|}{2}\sum_i \alpha_i\right) m_{\boldsymbol{\alpha}}(t)\frac{s^{\boldsymbol{\alpha}}}{\boldsymbol{\alpha}!} \\
&\quad + \sum_{\boldsymbol{\alpha}}\sum_i\left(\frac{\alpha_i(\alpha_i-1)}{2} + \frac{\theta_i}{2}\alpha_i\right) m_{\boldsymbol{\alpha}-e_i}(t)\frac{s^{\boldsymbol{\alpha}}}{\boldsymbol{\alpha}!} \\
&= -\frac{1}{2}\sum_{i\neq j} s_i s_j \frac{\partial^2 H(t,s)}{\partial s_i \partial s_j} - \frac{1}{2}\sum_i s_i^2 \frac{\partial^2 H(t,s)}{\partial s_i^2} - \frac{|\theta|}{2}\sum_i s_i \frac{\partial}{\partial s_i}H(t;s) \\
&\quad + \frac{1}{2}\sum_i s_i^2 \frac{\partial H(t,s)}{\partial s_i} + \sum_i \frac{\theta_i}{2} s_i H(t,s) \\
&= -\frac{1}{2}\sum_{i,j=1}^{n} s_i s_j \frac{\partial^2}{\partial s_i \partial s_j}H(t;s) + \sum_{i=1}^{n}\left(\frac{s_i^2}{2} - \frac{s_i|\theta|}{2}\right)\frac{\partial}{\partial s_i}H(t;s) + \sum_{i=1}^{n}\frac{\theta_i s_i}{2}H(t,s).
\end{aligned} \tag{6.1.38}$$

We can also solve this equation by separation of variables and equating coefficients as in [118] to obtain:

Proposition 6.1.2 *The operator*

$$L_n\, y(x) := -\frac{1}{2}\sum_{i,j=1}^{n} x^i x^j \frac{\partial^2}{\partial x^i \partial x^j} y(x) + \sum_{i=1}^{n} \left(\frac{(x^i)^2}{2} - \frac{x^i|\theta|}{2}\right)\frac{\partial}{\partial x^i} y(x) + \sum_{i=1}^{n} \frac{x^i \theta_i}{2} y(x) \tag{6.1.39}$$

has the set of eigenvalues

$$\Lambda := \left\{ \nu_l = \frac{l(l-1) + |\theta| l}{2}, l \in \mathbb{N} \right\}, \tag{6.1.40}$$

and the corresponding eigenspaces of dimension $\binom{n+l-1}{n-1}$ *with independent eigensolutions*

$$y_{l,\boldsymbol{\alpha}}(x) = \sum_{\boldsymbol{\beta}} a^{(l)}_{\boldsymbol{\alpha},\boldsymbol{\beta}} x^{\boldsymbol{\beta}}, \quad \forall |\boldsymbol{\alpha}| = l \tag{6.1.41}$$

where

$$a^{(l)}_{\boldsymbol{\alpha},\boldsymbol{\beta}} = \begin{cases} 0, & \text{if } |\boldsymbol{\beta}| < l, \\ \delta^{\boldsymbol{\alpha}}_{\boldsymbol{\beta}}, & \text{if } |\boldsymbol{\beta}| = l, \\ \text{inductively defined by (6.1.43) below}, & \text{if } |\boldsymbol{\beta}| \geq l+1, \end{cases} \tag{6.1.42}$$

$$a^{(l)}_{\boldsymbol{\alpha},\boldsymbol{\beta}} = \frac{\sum_{i=1}^{n} (\beta_i + \theta_i - 1) a^{(l)}_{\boldsymbol{\alpha},\boldsymbol{\beta}-e_i}}{\nu_{|\boldsymbol{\beta}|} - \nu_l}. \tag{6.1.43}$$

Therefore, the solution of Eq. (6.1.38) is

$$\begin{aligned} H(t;s) &= \sum_{l\geq 0} \sum_{|\boldsymbol{\alpha}|=l} c_{l,\boldsymbol{\alpha}} y_{l,\boldsymbol{\alpha}}(s) e^{-\nu_l t} \\ &= \sum_{l\geq 0} \sum_{|\boldsymbol{\alpha}|=l} c_{l,\boldsymbol{\alpha}} \left(\sum_{\boldsymbol{\beta}} a^{(l)}_{\boldsymbol{\alpha},\boldsymbol{\beta}} s^{\boldsymbol{\beta}} \right) e^{-\nu_l t} \\ &= \sum_{\boldsymbol{\beta}} \left(\sum_{l=0}^{|\boldsymbol{\beta}|} \sum_{|\boldsymbol{\alpha}|=l} c_{l,\boldsymbol{\alpha}} a^{(l)}_{\boldsymbol{\alpha},\boldsymbol{\beta}} e^{-\nu_l t} \right) s^{\boldsymbol{\beta}} \\ &= \sum_{\boldsymbol{\beta}} \boldsymbol{\beta}! \left(\sum_{|\boldsymbol{\alpha}|\leq|\boldsymbol{\beta}|} c_{|\boldsymbol{\alpha}|,\boldsymbol{\alpha}} a^{(|\boldsymbol{\alpha}|)}_{\boldsymbol{\alpha},\boldsymbol{\beta}} e^{-\nu_{|\boldsymbol{\alpha}|} t} \right) \frac{s^{\boldsymbol{\beta}}}{\boldsymbol{\beta}!}. \end{aligned} \tag{6.1.44}$$

This yields the moment formula

$$m_{\boldsymbol{\beta}}(t) = \boldsymbol{\beta}! \sum_{|\boldsymbol{\alpha}|\le|\boldsymbol{\beta}|} c_{|\boldsymbol{\alpha}|,\boldsymbol{\alpha}} a^{(|\boldsymbol{\alpha}|)}_{\boldsymbol{\alpha},\boldsymbol{\beta}} e^{-\nu_{|\boldsymbol{\alpha}|}t} = \sum_{|\boldsymbol{\alpha}|\le|\boldsymbol{\beta}|} c_{|\boldsymbol{\alpha}|,\boldsymbol{\alpha}} A^{(|\boldsymbol{\alpha}|)}_{\boldsymbol{\alpha},\boldsymbol{\beta}} e^{-\nu_{|\boldsymbol{\alpha}|}t},$$

where the coefficients $c_{|\boldsymbol{\alpha}|,\boldsymbol{\alpha}}$ can be computed from the initial condition

$$p^{\boldsymbol{\beta}} = m_{\boldsymbol{\beta}}(0) = \sum_{|\boldsymbol{\alpha}|\le|\boldsymbol{\beta}|} c_{|\boldsymbol{\alpha}|,\boldsymbol{\alpha}} A^{(|\boldsymbol{\alpha}|)}_{\boldsymbol{\alpha},\boldsymbol{\beta}}, \quad \forall \boldsymbol{\beta}.$$

6.1.6 Exponential Families

As in (3.6.1), we consider an n-dimensional exponential family of (Gibbs) probability densities of the form

$$p(x;\nu) = e^{\gamma(x)+\sum_{i=1}^{n} f_i(x)\nu^i - F(\nu)} = \frac{1}{Z(\nu)} e^{\gamma(x)+\sum_{i=1}^{n} f_i(x)\nu^i}, \tag{6.1.45}$$

where the f^i are observables and the ν^i are the family parameters. $Z(\nu)$ is the partition function

$$Z(\nu) = e^{F(\nu)} = \int e^{\gamma(x)+\sum_{i=1}^{n} f_i(x)\nu^i} dx \tag{6.1.46}$$

and $F(\nu)$ is a convex function (the free energy).

Now let X_ν be an (n-dimensional) family of random variables with probability densities $p(x;\nu)$ and $Y_\nu = f(X_\nu)$. Then we obtain the expectations (3.6.4)

$$\bar{Y}^i_\nu = \mathrm{E}_{p(\cdot,\nu)} f_i(X_\nu) = \int f_i(x) p(x;\nu) dx = D_i F(\nu),$$

and moreover from (3.6.4) and (3.6.10),

$$\begin{aligned} \mathrm{E}_{p(\cdot,\nu)}\left(Y_\nu - \bar{Y}_\nu\right)^{\boldsymbol{\alpha}} &= \int \left(f(x) - \bar{f}\right)^{\boldsymbol{\alpha}} p(x;\nu) dx \\ &= \begin{cases} 1, & \text{if } |\boldsymbol{\alpha}| = 0, \\ 0, & \text{if } |\boldsymbol{\alpha}| = 1, \\ D_{\boldsymbol{\alpha}} F(\nu), & \text{if } |\boldsymbol{\alpha}| \ge 2. \end{cases} \end{aligned}$$

Hence, we obtain the moment generating function for Y_ν as

$$\begin{aligned} H(\nu; s) &= \mathrm{E}_{p(\cdot,\nu)} e^{Y_\nu \cdot s} \\ &= e^{\bar{Y}_\nu \cdot s} \mathrm{E}_{p(\cdot,\nu)} e^{(Y_\nu - \bar{Y}_\nu)\cdot s} \\ &= e^{DF(\nu)\cdot s} \sum_{|\boldsymbol{\alpha}|\geq 0} \mathrm{E}_{p(\cdot,\nu)} \left(Y_\nu - \bar{Y}_\nu\right)^{\boldsymbol{\alpha}} \frac{s^{\boldsymbol{\alpha}}}{\boldsymbol{\alpha}!} \\ &= e^{Df(\nu)\cdot s} \left(1 + \sum_{|\boldsymbol{\alpha}|\geq 2} D_{\boldsymbol{\alpha}} F(\nu) \frac{s^{\boldsymbol{\alpha}}}{\boldsymbol{\alpha}!}\right) \\ &= e^{DF(\nu)\cdot s} \Big(1 + F(\nu + s) - F(\nu) - DF(\nu) \cdot s\Big). \end{aligned}$$

6.2 The Free Energy Functional

Free energy functionals have already been introduced in Sect. 3.5. In this section, we shall systematically construct free energy functionals for our Kolmogorov forward equations. We shall then use them to construct a necessary and sufficient condition for our diffusion processes to have a unique stationary, reversible, or ergodic probability measure. When this condition is satisfied, we show that the flow of probability measures (densities) converges to the stationary one under various notions of convergence (exponential, total variation, entropy distances, etc.) Connections to information geometry and large deviation theory will also be mentioned. A free energy functional has already been considered in [67], but here we can draw upon a richer theory to draw more precise conclusions about the asymptotics of the Wright–Fisher process.

6.2.1 General Definitions

We begin with some general concepts in order to introduce the theoretical context; a good reference is [13].

In this section, for simplicity, we just write dx instead of $d\boldsymbol{\lambda}(x)$ for the Lebesgue measure on Δ_n and leave out the dimension index as no confusion is to be feared.

Definition 6.2.1 Let $\{X_t\}_{t\geq 0}$ be a Markov diffusion process on Ω. Denote by $(T_t)_{t\geq 0}$ the corresponding strongly continuous semigroup, by $\mathcal{L}$ its generator, and by $u(x, t|x_0)$ the conditional transition probability density with respect to the Lebesgue

measure dx.

(i) A measure μ on Ω is called *stationary (invariant)* if

$$\int_\Omega T_t f(x) d\mu(x) = \int_\Omega f(x) d\mu(x), \quad \forall t \geq 0, f \in C_0^\infty(\Omega) \tag{6.2.1}$$

or if equivalently (following [49, Theorem 2.3])

$$\int_\Omega \mathcal{L} f(x) d\mu(x) = 0, \quad \forall f \in C_0^\infty(\Omega). \tag{6.2.2}$$

If $\mu(x)$ has a density $p(x)$ with respect to dx, then (6.2.1) is equivalent to

$$p(x) = \int_\Omega p(x_0) u(x, t|x_0) dx_0, \quad \forall x, x_0 \in \Omega, t > 0. \tag{6.2.3}$$

(ii) It is called *reversible* if

$$\int_\Omega g(x) T_t f(x) d\mu(x) = \int_\Omega f(x) T_t g(x) d\mu(x), \quad \forall t \geq 0, f, g \in C_0^\infty(\Omega) \tag{6.2.4}$$

or equivalently

$$\int_\Omega g(x) \mathcal{L} f(x) d\mu(x) = \int_\Omega f(x) \mathcal{L} g(x) d\mu(x), \quad \forall f, g \in C_0^\infty(\Omega). \tag{6.2.5}$$

If again $\mu(x)$ has a density $p(x)$ with respect to dx, then (6.2.4) is equivalent to

$$u(x, t|x_0) p(x_0) = u(x_0, t|x) p(x), \quad \forall x, x_0 \in \Omega, t > 0. \tag{6.2.6}$$

(iii) It is called *ergodic* if

$$\lim_{t \to \infty} T_t f(x) = \int_\Omega f(y) \mu(dy), \quad \mu - \text{a.e. } x \in \Omega, \forall f \in C_0^\infty(\Omega). \tag{6.2.7}$$

Definition 6.2.2 For a nonnegative functional $f(x)$ defined on a σ-finite measure space (Ω, μ), we define its (negative) entropy functional by

$$S_\mu(f) := \int_\Omega f \log f d\mu - \Big(\int_\Omega f d\mu \Big) \log \Big(\int_\Omega f d\mu \Big). \tag{6.2.8}$$

If $f(x)$ is a density with respect to μ, i.e. $\int_\Omega f d\mu = 1$, then this reduces to the standard negative entropy functional,

$$S_\mu(f) = \int_\Omega f \log f d\mu. \tag{6.2.9}$$

Definition 6.2.3 We say that the family of densities $\{u(\cdot,t)\}_{t\geq 0}$ on a σ-finite measure space (Ω,μ) *satisfies the condition* $I(A,\psi)$ if it solves a diffusion equation of the form

$$\begin{aligned}\partial_t u(x,t) &= \partial_i\Big(A^{ij}(x)\partial_j u(x,t) + A^{ij}(x)u(x,t)\partial_j\psi(x)\Big)\\ &= \nabla_x\cdot(A(x)\nabla_x u(x,t) + A(x)u(x,t)\nabla\psi(x))\\ &= \nabla_x\cdot\Big(A(x)u(x,t)\nabla_x\big(\log u(x,t)+\psi(x)\big)\Big),\end{aligned} \tag{6.2.10}$$

where

$$A^{ij}(x) = A^{ji}(x),$$

and that it *satisfies the condition* $II(A,\psi)$ if, in addition to $I(A,\psi)$, we also have

$$\int_\Omega e^{-\psi(x)}d\mu(x) < \infty.$$

Definition 6.2.4 For a family of densities $\{u(\cdot,t)\}_{t\geq 0}$ on a σ-finite measure space (Ω,μ) with condition $I(A,\psi)$, we define the *potential energy functional* by

$$\Psi(u(\cdot,t)) := \int_\Omega u(x,t)\psi(x)d\mu(x) \tag{6.2.11}$$

and the *free energy functional* by

$$\begin{aligned}F(u(\cdot,t)) &:= \int_\Omega u(x,t)\Big(\log u(x,t)+\psi(x)\Big)d\mu(x)\\ &= S_\mu(u(\cdot,t)) + \Psi(u(\cdot,t)).\end{aligned} \tag{6.2.12}$$

(See [16, 69], for instance.)
We can extend this functional to the space of all densities $\mathcal{D}$ as

$$F_\psi(q) := \int_\Omega q(x)\Big(\log q(x)+\psi(x)\Big)d\mu(x). \tag{6.2.13}$$

We therefore say that the family of densities $\{u(\cdot,t)\}_{t\geq 0}$

(i) has a free energy functional on (Ω,μ) if it satisfies the condition $I(A,\psi)$ as in Eq. (6.2.10);
(ii) has a good free energy functional on (Ω,μ) if it satisfies the condition $II(A,\psi)$ as in Eq. (6.2.10).

Remark In the important paper [69], the relation between a Fokker–Planck equation and the associated free energy functional was systematically explored. In particular, it was demonstrated that a Fokker–Planck equation with gradient drift term may be interpreted as a gradient flux, or a steepest descent, of a free energy functional with respect to a certain (i.e. Wasserstein) metric. This result was originally developed for Fokker–Planck equations on $\mathbb{R}^n$ for which the second order operator is the standard Laplacian. This result has been extended in various ways, for example on Riemannian/Finsler manifolds, but the results usually assume that the operator is uniformly elliptic, which is not satisfied in our context, as the operator becomes singular on the boundary. This problem will be discussed elsewhere in more general terms.

Definition 6.2.5 Let f_1, f_2 be densities on a σ-finite measure space (Ω, μ). The relative entropy *relative entropy* (*Kullback–Leibler divergence*) of f_1 with respect to f_2 is

$$D_{\mathrm{KL}}(f_1 \| f_2) := \begin{cases} \int_\Omega f_1(x) \log \frac{f_1(x)}{f_2(x)} d\mu(x) & \text{if } \operatorname{supp}(f_1) \subset \operatorname{supp}(f_2), \\ \infty & \text{otherwise.} \end{cases}$$

Theorem 6.2.1 *Let $\{u(\cdot, t|x_0)\}_{t\geq 0}$ be a family of conditional densities on the simplex Δ_n endowed with the Lebesgue measure $\boldsymbol{\lambda}(x)$ satisfying the Kolmogorov equations*

$$\partial_t u(x,t|x_0) = \nabla_i^{(x)} \nabla_j^{(x)} \Big(A^{ij}(x) u(x,t|x_0) \Big) - \nabla_i^{(x)} \Big(b^i(x) u(x,t|x_0) \Big) =: L_x u(x,t|x_0), \tag{6.2.14}$$

$$\partial_t u(x,t|x_0) = A^{ij}(x_0) \nabla_i^{(x_0)} \nabla_j^{(x_0)} u(x,t|x_0) + b^i(x_0) \nabla_i^{(x_0)} u(x,t|x_0) =: L_{x_0}^* u(x,t|x_0), \tag{6.2.15}$$

where $A^{ij}(x) = x^i(\delta_{ij} - x^j)$, $b^i(x)$ are smooth functions on Δ_n and $\nabla_i^{(x)} = \frac{\partial}{\partial x^i}$, $\nabla_i^{(x_0)} = \frac{\partial}{\partial x_0^i}$. Then the family $\{u(\cdot, t|x_0)\}_{t\geq 0}$ has a good free energy functional if and only if there exists a unique absolutely continuous probability measure on Δ_n which is reversible with respect to the infinitesimal generator

$$L_x^* = A^{ij}(x) \nabla_i^{(x)} \nabla_j^{(x)} + b^i(x) \nabla_i^{(x)}.$$

Proof ($\Rightarrow$): We assume that $\{u(\cdot, t|x_0)\}_{t\geq 0}$ satisfies the condition $II(A, \psi)$, i.e. $\partial_t u = L_x u$ with

$$L_x u = \nabla^{(x)} \cdot (A(x) \nabla^{(x)} u) + \nabla^{(x)} \cdot (A(x) u \nabla^{(x)} \psi(x)),$$

where $\psi(x) \in C^1(\Delta_n)$ satisfies

$$\int_{\Delta_n} e^{-\psi(x)} dx < \infty. \tag{6.2.16}$$

Then the generator L_x^* is of the form

$$L_x^* f = \nabla^{(x)} \cdot (A(x)\nabla^{(x)} f) - A(x)\nabla^{(x)}\psi(x) \cdot \nabla^{(x)} f. \tag{6.2.17}$$

By (6.2.16), $d\mu_\infty(x) = \frac{e^{-\psi(x)}}{Z}dx$ is well-defined. By Lemma 6.2.3 below, $d\mu_\infty(x) = \frac{e^{-\psi(x)}}{Z}dx$ is reversible with respect to L^*. (Also note that in this case $d\mu_\infty(x) = \frac{e^{-\psi(x)}}{Z}dx$ is also stationary with respect to L^*, by applying the reversibility condition, which we have just observed, with an arbitrary f and $g = 1$ and using $L^*1 = 0$.)

We now want to show that $d\mu_\infty(x) = \frac{e^{-\psi(x)}}{Z}dx$ is the unique absolutely continuous probability measure on Δ_n which is reversible with respect to L^*. Indeed, assume that ν is an absolutely continuous probability measure on Δ_n which is reversible with respect to L^*. Then $d\nu(x) = k(x)d\mu_\infty(x)$ for some positive function k and of course we also have $d\mu_\infty(x) = k(x)^{-1}d\nu(x)$. Therefore,

$$\begin{aligned} 0 &= \int_{\Delta_n} L^* f d\nu \\ &= \int_{\Delta_n} L^* f k d\mu_\infty \\ &= \int_{\Delta_n} f L^* k d\mu_\infty \quad \text{due to the symmetry of } \mu_\infty. \end{aligned} \tag{6.2.18}$$

This implies that $L^*k = 0$. Similarly, because of the symmetry of ν, we also have $L^*(k^{-1}) = 0$. Thus

$$\begin{aligned} 0 &= L^*(1) - kL^*(k^{-1}) - k^{-1}L^*k \\ &= A^{ij}(x)\nabla_i^{(x)} k \nabla_j^{(x)} k^{-1} \\ &= -\frac{A^{ij}(x)\nabla_i^{(x)} k \nabla_j^{(x)} k}{k^2}, \end{aligned} \tag{6.2.19}$$

which implies that k is constant. Because ν and μ_∞ are probability measures, $k = 1$. This means that $\nu = \mu_\infty$, which is the desired uniqueness.

($\Leftarrow$): Assume that $d\nu(x) = v(x)dx$ is an absolute continuous stationary probability measure that is reversible with respect to L^*. This implies that v is the unique positive solution of $Lv = 0$ in Δ_n with $\int_{\Delta_n} v(x)dx = 1$. Following the technique in [83], we rewrite Eq. (6.2.14) in the canonical form

$$Lv(x_0) = \Delta_{g(x_0)} v(x_0) - \nabla_i^{(x_0)}\Big(\alpha^i(x_0)v(x_0)\Big) = 0, \tag{6.2.20}$$

where Δ_g is the Laplace–Beltrami operator with respect to the metric depending only on the state $(g_{ij}(x_0)) = (A_{ij}(x_0)) = (A^{ij}(x_0))^{-1}$ and $\alpha^i(x_0) = b^i(x_0) - \Gamma_{ik}^k(x_0)$, where $\Gamma_{ik}^k(x_0)$ is the Christoffel symbol corresponding to metric $g_{ij}(x_0)$. Rescaling

by volume density $\sqrt{g(x)} = \sqrt{\det(A_{ij}(x))}$

$$u(x,t|x_0) = \sqrt{g(x)}\varphi(x,t|x_0) \quad \text{and } v(x_0) = \sqrt{g(x_0)}\pi(x_0), \tag{6.2.21}$$

we obtain equations for φ and π as follows:

$$\partial_t\varphi(x,t|x_0) = \Delta_{g(x_0)}\varphi(x,t|x_0) + \alpha^i(x_0)\nabla_i^{(x_0)}\varphi(x,t|x_0), \tag{6.2.22}$$

$$\partial_t\varphi(x,t|x_0) = \Delta_{g(x)}\varphi(x,t|x_0) - \nabla_i^{(x)}\Big(\alpha^i(x)\varphi(x,t|x_0)\Big), \tag{6.2.23}$$

$$\Delta_{g(x_0)}\pi(x_0) - \nabla_i^{(x_0)}\Big(\alpha^i(x_0)\pi(x_0)\Big) = 0. \tag{6.2.24}$$

Moreover, the reversibility of ν means also that

$$u(x,t|x_0)v(x_0) = u(x_0,t|x)v(x), \quad \forall t > 0, x, x_0 \in \Delta_n. \tag{6.2.25}$$

This is equivalent to

$$\varphi(x,t|x_0)\pi(x_0) = \varphi(x_0,t|x)\pi(x), \quad \forall t > 0, x, x_0 \in \Delta_n. \tag{6.2.26}$$

It implies that

$$\begin{aligned}\partial_t(\varphi(x,t|x_0)\pi(x_0)) &= \partial_t(\varphi(x_0,t|x)\pi(x)) \\ &= \Delta_{g(x_0)}(\varphi(x,t|x_0)\pi(x_0)) - \nabla_i^{(x_0)}\Big(\alpha^i(x_0)\varphi(x,t|x_0)\pi(x_0)\Big).\end{aligned} \tag{6.2.27}$$

Combining (6.2.22), (6.2.24), and (6.2.27) we obtain

$$\nabla_i^{(x_0)}\varphi(x,t|x_0)\Big(-\alpha^i(x_0)\pi(x_0) + \nabla^{i,(x_0)}\pi(x_0)\Big) = 0.$$

Since $\nabla_i^{(x_0)}\varphi(x,t|x_0)$ does not vanish identically in Δ_n, we have in Δ_n

$$b^j(x) - \nabla_i^{(x)}g^{ij}(x) - \frac{\nabla_i^{(x)}g(x)}{2g(x)}g^{ij}(x) = \alpha^j(x) = g^{ij}(x)\frac{\nabla_i^{(x)}\pi(x)}{\pi(x)},$$

which implies that

$$b^j(x) - \nabla_i^{(x)}g^{ij}(x) = g^{ij}(x)\nabla_i^{(x)}\ln\Big(\pi(x)\sqrt{g(x)}\Big),$$

i.e.

$$-Z^i(x) = \nabla_i^{(x)}\ln\Big(\pi(x)\sqrt{g(x)}\Big) = \nabla_i^{(x)}\ln v(x),$$

where the vector Z is

$$Z(x) = \begin{pmatrix} A^{11}(x) & \cdots & A^{1n}(x) \\ \vdots & \ddots & \vdots \\ A^{n1}(x) & \cdots & A^{nn}(x) \end{pmatrix}^{-1} \begin{pmatrix} \partial_1 A^{11}(x) + \cdots + \partial_n A^{1n}(x) - b^1(x) \\ \vdots \\ \partial_1 A^{n1}(x) + \cdots + \partial_n A^{nn}(x) - b^n(x) \end{pmatrix}.$$

Thus, Z is of the form $\nabla\psi$, which implies $v = Ce^{-\psi}$ for some $\psi \in C^1(\Delta_n)$. Because of $\int_{\Delta_n} v dx = 1$, we obtain $C = \frac{1}{Z} < \infty$, which means that $\{u(\cdot, t)_{t\geq 0}\}$ satisfies the condition $II(A, \psi)$. This completes the proof. □

Remark The necessary condition in the two alleles case was proved by Ethier and Kurtz [36, p. 417].

6.2.2 The Free Energy of Wright–Fisher Models

Two Alleles with Mutation

We start with a diploid Wright Fisher population of N individuals with two alleles A^0 and A^1. Assume that there are mutations from A^1 to A^0 with rate $\frac{\beta}{4N}$ and from A^0 to A^1 with rate $\frac{\alpha}{4N}$ (the time unit is $2N$ generations). Then the frequency X_t of allele A^1 at generation $2Nt$ satisfies (2.6.9), which we recall here as

$$\begin{aligned} \mathrm{E}(\delta X_t | X_t) &= \Big(\frac{\nu}{2} - \frac{\nu+\mu}{2} X_t\Big)(\delta t) + o(\delta t), \\ \mathrm{E}((\delta X_t)^2 | X_t) &= X_t(1 - X_t)(\delta t) + o(\delta t), \\ \mathrm{E}((\delta X_t)^\alpha | X_t) &= o(\delta t), \quad \text{for } \alpha \geq 3. \end{aligned} \tag{6.2.28}$$

The Kolmogorov forward equation (4.2.12) for the family of density functions $\{u(\cdot, t)\}_{t\geq 0}$ on the probability measure space $([0, 1], dx)$ thus becomes

$$\partial_t u(x, t) = \frac{1}{2} \frac{\partial^2}{\partial x^2} \Big(x(1 - x)u(x, t)\Big) - \frac{\partial}{\partial x} \Big(b(x)u(x, t)\Big) \tag{6.2.29}$$

with drift coefficient $b(x) = \frac{\nu}{2} - \frac{\nu+\mu}{2} x$.

To construct a free energy functional for this equation, we will rewrite it in the following form

$$\begin{aligned}\partial_t u(x,t) &= \frac{\partial}{\partial x}\left(\frac{x(1-x)}{2}\frac{\partial}{\partial x}u(x,t)\right) + \frac{\partial}{\partial x}\left(\Big(\frac{1-2x}{2} - b(x)\Big)u(x,t)\right)\\ &= \frac{\partial}{\partial x}\left(\frac{x(1-x)}{2}\frac{\partial}{\partial x}u(x,t)\right) + \frac{\partial}{\partial x}\left(\frac{x(1-x)}{2}u(x,t)\Big(\frac{1-\nu}{x} - \frac{1-\mu}{1-x}\Big)\right)\\ &= \nabla\cdot(A(x)\nabla u(x,t)) + \nabla\cdot(A(x)u(x,t)\nabla\psi(x))\\ &= \nabla\cdot\Big(A(x)u(x,t)\nabla\big(\log u(x,t) + \psi(x)\big)\Big),\end{aligned} \tag{6.2.30}$$

where

$$\nabla = \frac{\partial}{\partial x}, \quad A(x) = \frac{x(1-x)}{2},$$

and

$$\psi(x) = (1-\nu)\log x + (1-\mu)\log(1-x). \tag{6.2.31}$$

We see that the normalizing coefficient

$$Z(\nu,\mu) := \int_0^1 e^{-\psi(x)}dx = \int_0^1 x^{\nu-1}(1-x)^{\mu-1}dx = B(\nu,\mu)$$

is finite if and only if both ν and μ are positive.

Therefore, this family of densities always satisfies the condition $I(A,\psi)$ and satisfies the condition $II(A,\psi)$ if and only if $\nu,\mu > 0$. Thus, we need positive mutation rates for $II(A,\psi)$.

In the finite case, the unique minimizer of the free energy functional is the Gibbs density

$$u_\infty(x) := \frac{e^{-\psi(x)}}{Z(\nu,\mu)} = \frac{x^{\nu-1}(1-x)^{\mu-1}}{B(\nu,\mu)}. \tag{6.2.32}$$

This is seen by solving the stationary density equation

$$0 = \nabla\cdot\Big(A(x)u_\infty(x)\nabla\big(\log u_\infty(x) + \psi(x)\big)\Big). \tag{6.2.33}$$

The minimum of F is

$$F_\infty = \int_0^1 f_\infty(x)(\log f_\infty(x) + \psi(x))dx = -\log Z(\nu,\mu) = -\log B(\nu,\mu).$$

Two Alleles with Mutation and Selection

We next consider the case where in addition to mutation as in Sect. 6.2.2, there are also selection effects. Let the fitness of an individual of type A^1A^1, A^1A^0, A^0A^0 be $1, 1+\frac{sh}{2N}, 1+\frac{s}{2N}$, resp. We recall (2.6.9) for the frequency X_t of allele A^1 at generation $2Nt$:

$$\begin{aligned}
\mathrm{E}(\delta X_t|X_t) &= \Big(\frac{\nu}{2} - \frac{\nu+\mu}{2}X_t + sX_t(1-X_t)\big(1-h+(1-2h)X_t\big)\Big)(\delta t) + o(\delta t),\\
\mathrm{E}((\delta X_t)^2|X_t) &= X_t(1-X_t)(\delta t) + o(\delta t),\\
\mathrm{E}((\delta X_t)^\alpha|X_t) &= o(\delta t), \quad \text{for } \alpha \geq 3.
\end{aligned} \tag{6.2.34}$$

For the family of density functions $\{u(\cdot,t)\}_{t\geq 0}$ on the probability measure space $([0,1], dx)$, we have the Kolmogorov forward equation (4.2.12)

$$\partial_t u(x,t) = \frac{1}{2}\frac{\partial^2}{\partial x^2}\Big(x(1-x)u(x,t)\Big) - \frac{\partial}{\partial x}\Big(b(x)u(x,t)\Big) \tag{6.2.35}$$

with drift coefficient $b(x) = \frac{\nu}{2} - \frac{\nu+\mu}{2}x + sx(1-x)\big(1-h+(1-2h)x\big)$.

To construct a free energy functional for this equation, we rewrite it as

$$\begin{aligned}
\partial_t u(x,t) &= \frac{\partial}{\partial x}\left(\frac{x(1-x)}{2}\frac{\partial}{\partial x}u(x,t)\right) + \frac{\partial}{\partial x}\left(\Big(\frac{1-2x}{2} - b(x)\Big)u(x,t)\right)\\
&= \frac{\partial}{\partial x}\left(\frac{x(1-x)}{2}\frac{\partial}{\partial x}u(x,t)\right) + \frac{\partial}{\partial x}\left(\frac{x(1-x)}{2}u(x,t)\Big(\frac{1-\nu}{x} - \frac{1-\mu}{1-x} -\right.\\
&\qquad \left.2s\big(1-h+(1-2h)x\big)\Big)\right)\\
&= \nabla\cdot(A(x)\nabla u(x,t)) + \nabla\cdot(A(x)u(x,t)\nabla\psi(x))\\
&= \nabla\cdot\Big(A(x)u(x,t)\nabla\big(\log u(x,t) + \psi(x)\big)\Big),
\end{aligned} \tag{6.2.36}$$

where

$$\nabla = \frac{\partial}{\partial x}, \quad A(x) = \frac{x(1-x)}{2},$$

and

$$\psi(x) = (1-\nu)\log x + (1-\mu)\log(1-x) - 2s\Big((1-h)x + \frac{1}{2}(1-2h)x^2\Big).$$

Again, the partition function

$$Z(\nu,\mu,s,h) := \int_0^1 e^{-\psi(x)}dx = \int_0^1 x^{\nu-1}(1-x)^{\mu-1}e^{2s\left((1-h)x+\frac{1}{2}(1-2h)x^2\right)}dx$$

is finite if and only if both ν and μ are positive.

Therefore, this family of densities always satisfies the condition $I(A,\psi)$ and satisfies the condition $II(A,\psi)$ if and only if $\nu,\mu > 0$.

The free energy functional is

$$F(u(\cdot,t)) := \int_0^1 \psi(x)u(x,t)dx + \int_0^1 u(x,t)\log u(x,t)dx, \tag{6.2.37}$$

which is finite if and only if $\nu,\mu > 0$.

In the finite case, the unique minimizer of the free energy functional is the Gibbs density

$$u_\infty(x) := \frac{e^{-\psi(x)}}{Z(\nu,\mu,s,h)} = \frac{x^{\nu-1}(1-x)^{\mu-1}e^{2s\left((1-h)x+\frac{1}{2}(1-2h)x^2\right)}}{Z(\nu,\mu,s,h)} \tag{6.2.38}$$

obtained by solving the stationary density equation

$$0 = \nabla\cdot\Big(A(x)u_\infty(x)\nabla\big(\log u_\infty(x)+\psi(x)\big)\Big). \tag{6.2.39}$$

The minimum of F is

$$F_\infty = \int_0^1 f_\infty(x)(\log f_\infty(x)+\psi(x))dx = -\log Z(\nu,\mu,s,h).$$

We shall see that our flow of density functions exponentially converges to this Gibbs density function and the free energy functional plays the role of the Lyapunov functional.

$n+1$ Alleles with Mutation

For a diploid Wright Fisher population of N individuals with $n+1$ alleles $A^0,\dots,A^n$ undergoing mutations from A^i to A^j with rates $\frac{\theta_{ij}}{4N} \in \mathbb{R}$ for all $i \neq j \in \{0,1,\cdots,n\}$, the relative frequencies $X_t = (X_t^1,\dots,X_t^n)$ of alleles $(A^1,\dots,A^n)$ and $X_t^0 = 1-X_t^1-\cdots-X_t^n$ for allele A^0 at generation $2Nt$ satisfy (2.5.15)–(2.5.17), recalled

here as

$$\begin{aligned} \mathrm{E}(\delta X_t^i|X_t) &= b^i(X_t)(\delta t) + o(\delta t); \\ \mathrm{E}(\delta X_t^i \delta X_t^j|X_t) &= a^{ij}(X_t)(\delta t) + o(\delta t), \quad \forall i,j = 1,\ldots,n; \\ \mathrm{E}((\delta X_t)^{\boldsymbol{\alpha}}|X_t) &= o(\delta t), \quad \text{for } |\boldsymbol{\alpha}| \geq 3 \end{aligned} \tag{6.2.40}$$

with the drift term

$$b^i(x) = -\Big(\sum_{j=0}^n \frac{1}{2}\theta_{ij}\Big)x^i + \sum_{j=0}^n \frac{1}{2}\theta_{ji}x^j, \quad i = 1,\ldots,n$$

and the diffusion term

$$a^{ij}(x) = x^i(\delta_{ij} - x^j) \quad i,j = 1,\ldots,n.$$

Remark Putting

$$b^0(x) = -\frac{1}{2}\Big(\sum_{j=0}^n \theta_{0j}\Big)x^0 + \frac{1}{2}\sum_{j=0}^n \theta_{j0}x^j,$$

we have

$$\sum_{i=0}^n b^i(x) = 0.$$

We shall prove:

Theorem 6.2.2 *In a diploid Wright–Fisher model of N individuals with $n+1$ alleles with general mutation rates, a necessary and sufficiency condition to have a unique stationary distribution is*

$$\theta_{ij} = \theta_j > 0 \quad \textit{for all } i \neq j, \quad i,j = 0,\ldots,n. \tag{6.2.41}$$

The stationary distribution in this case is of the form

$$d\mu_\infty^m(x) = f_\infty^m(x)dx = \frac{e^{-\psi(x)}}{Z(\theta)}dx = \frac{\Pi_{i=0}^n (x^i)^{\theta_i - 1}}{Z(\theta)}dx. \tag{6.2.42}$$

Proof Again, we consider the Kolmogorov forward equation for the density function $u(x,t)$

$$\partial_t u(x,t) = \sum_{i,j=1}^n \frac{\partial^2}{\partial x^i \partial x^j}\Big(\frac{a^{ij}(x)}{2}u(x,t)\Big) - \sum_{i=1}^n \frac{\partial}{\partial x^i}\Big(b^i(x)u(x,t)\Big). \tag{6.2.43}$$

To use the free energy method, we rewrite this equation in divergence form:

$$\begin{aligned}\partial_t u(x,t) &= \sum_{i=1}^n \frac{\partial}{\partial x^i}\left(\sum_{j=1}^n \frac{\partial}{\partial x^j}\Big(\frac{a^{ij}(x)}{2}u(x,t)\Big)\right) - \sum_{i=1}^n \frac{\partial}{\partial x^i}\Big(b^i(x)u(x,t)\Big)\\ &= \sum_{i=1}^n \frac{\partial}{\partial x^i}\left(\sum_{j=1}^n \Big(A^{ij}(x)\frac{\partial}{\partial x^j}u(x,t)\Big)\right) + \sum_{i=1}^n \frac{\partial}{\partial x^i}\left(\Big(\sum_{j=1}^n \frac{\partial}{\partial x^j}A^{ij}(x) - b^i(x)\Big)u(x,t)\right)\\ &= \sum_{i=1}^n \frac{\partial}{\partial x^i}\left(\sum_{j=1}^n \Big(A^{ij}(x)\frac{\partial}{\partial x^j}u(x,t)\Big)\right) + \sum_{i=1}^n \frac{\partial}{\partial x^i}\left(\Big(\frac{1-(n+1)x^i}{2} - b^i(x)\Big)u(x,t)\right)\\ &= \nabla\cdot(A(x)\nabla u(x,t)) + \nabla\cdot(A(x)u(x,t)\nabla\psi(x)),\end{aligned} \tag{6.2.44}$$

with the gradient

$$\nabla = \Big(\frac{\partial}{\partial x^1},\dots,\frac{\partial}{\partial x^n}\Big)$$

and the diffusion coefficients

$$A(x) = \Big(A^{ij}(x)\Big)_{i,j=1}^n = \frac{1}{2}\Big(a^{ij}(x)\Big)_{i,j=1}^n.$$

ψ then has to satisfy

$$\Big(A(x)\nabla\psi(x)\Big)_i = \frac{1-(n+1)x^i}{2} - b^i(x)$$

and hence

$$\begin{aligned}\partial_i\psi(x) &= \sum_{j=1}^n 2\left(\frac{\delta_{ij}}{x^j} + \frac{1}{x^0}\right)\left(\frac{1-(n+1)x^j}{2} - b^j(x)\right)\\ &= \frac{1-2b^i(x)}{x^i} - \frac{1-2b^0(x)}{x^0}\\ &= f_i(x) - f_0(x).\end{aligned} \tag{6.2.45}$$

We are looking for conditions for the rates θ_{ij} so that there is a potential function. Such a ψ exists if and only if (see [59, p. 253])

$$\partial_j\Big(f_i(x) - f_0(x)\Big) = \partial_i\Big(f_j(x) - f_0(x)\Big).$$

This is equivalent to

$$-\frac{\theta_{ji}}{x^i}+\frac{\theta_{0,i}}{x^i}+\frac{\theta_{j,0}}{x^0}=-\frac{\theta_{ij}}{x^j}+\frac{\theta_{0,j}}{x^j}+\frac{\theta_{i,0}}{x^0},\quad \forall i\neq j, x\in int\Delta_n.$$

Letting $x^i\to 0$ while keeping x^j, x^0 fixed, we conclude that $\theta_{ji}=\theta_{0,i}$ for all $j\neq i$. Similarly, we obtain $\theta_{ij}=\theta_{0,j}$ and $\theta_{j,0}=\theta_{i,0}$. It follows that

$$\theta_{ij}=\theta_j \quad \text{for all } i\neq j,\quad i,j=0,\ldots,n. \tag{6.2.46}$$

From (6.2.45), we then get

$$\psi(x)=\sum_{i=0}^{n}(1-\theta_i)\log(x^i).$$

Moreover, ψ then satisfies

$$\int_{\Delta_n} e^{-\psi(x)}dx<\infty$$

if and only if $\theta_i>0$ for all i. □

For a diploid Wright–Fisher population with uniform mutation rates $\frac{\theta_j}{4N}\in\mathbb{R}$ for all $i\neq j\in\{0,1,\cdots,n\}$, the free energy functional then is

$$\underbrace{F(q)}_{\text{free energy}}:=\underbrace{\int_{\Delta_n}\psi(x)q(x)dx}_{\text{potential energy}}+\underbrace{\int_{\Delta_n}q(x)\log q(x)dx}_{\text{negative entropy}} \tag{6.2.47}$$

for a density function q on Δ_n.

As we assume $\theta_i>0$ for all i, the partition function

$$\begin{aligned}Z(\theta):&=\int_{\Delta_n}e^{-\psi(y)}dy=\int_{\Delta_n}(y^1)^{\theta_1-1}(y^2)^{\theta_2-1}\cdots(y^n)^{\theta_n-1}(1-y^1-\cdots-y^n)^{\theta_0-1}dy\\&=B(\theta)\end{aligned} \tag{6.2.48}$$

is finite, and the minimizer of the free energy is the Gibbs density

$$q_\infty(x):=\frac{e^{-\psi(x)}}{Z(\theta)}. \tag{6.2.49}$$

Below, we shall consider the evolution of the free energy functional along the flow of densities

$$F(p(\cdot,t)) := \int_{\Delta_n} \psi(x)u(x,t)dx + \int_{\Delta_n} u(x,t)\log u(x,t)dx \tag{6.2.50}$$

$n+1$ Alleles with Mutation and Selection

We return to the case of general mutation rates $\frac{\theta_{ij}}{4N} \in \mathbb{R}$ for $i \neq j \in \{0,1,\cdots,n\}$. In addition, we now also include selection and assume that the genotype A^iA^j has fitness $1+\frac{s_{ij}}{2N}$. Equations (2.5.15)–(2.5.17) then become

$$\begin{aligned} \mathrm{E}(\delta X_t^i|X_t) &= b^i(X_t)(\delta t) + o(\delta t), \\ \mathrm{E}(\delta X_t^i \delta X_t^j|X_t) &= a^{ij}(X_t)(\delta t) + o(\delta t), \quad \forall i,j = 1,\ldots,n, \\ \mathrm{E}((\delta X_t)^{\boldsymbol{\alpha}}|X_t) &= o(\delta t), \quad \text{for } |\boldsymbol{\alpha}| \geq 3, \end{aligned} \tag{6.2.51}$$

with the drift term

$$b^i(x) = -\Big(\sum_{j=0}^n \frac{1}{2}\theta_{ij}\Big)x^i + \sum_{j=0}^n \frac{1}{2}\theta_{ji}x^j + s_i(x)x^i - s(x)x^i, \quad i = 1,\ldots,n \tag{6.2.52}$$

with

$$s_i(x) = \sum_{j=0}^n s_{ij}x^j \tag{6.2.53}$$

and

$$s(x) = \sum_{i=0}^n s_i(x)x^i \tag{6.2.54}$$

and the diffusion term

$$a^{ij}(x) = x^i(\delta_{ij} - x^j), \quad i,j = 1,\ldots,n.$$

We then have the following extension of Theorem 6.2.2.

Theorem 6.2.3 *In a diploid Wright–Fisher model of N individuals of $n+1$-alleles with mutation and selection, a necessary and sufficient condition for having a unique stationary distribution is*

$$\theta_{ij} = \theta_j > 0 \quad \textit{for all } i \neq j, \quad i,j = 0,\ldots,n \tag{6.2.55}$$

and

$$s_{ij} = s_{ji} \text{ for all } i, j. \tag{6.2.56}$$

The stationary distribution in this case is of the form

$$d\mu_\infty^{m,s}(x) = f_\infty^{m,s}(x)dx = \frac{e^{-\psi(x)}}{Z(\theta,s)}dx = \frac{\Pi_{i=0}^n (x^i)^{\theta_i - 1} e^{s(x)}}{Z(\theta,s)}dx \tag{6.2.57}$$

with the partition function

$$Z(\theta,s) = \int_{\Delta_n} \Pi_{i=0}^n (x^i)^{\theta_i - 1} e^{s(x)} dx$$

Proof As in the proof of Theorem 6.2.2, ψ exists if and only if for all $i \neq k$

$$\partial_k \Big(f_i(x) - f_0(x) \Big) = \partial_i \Big(f_k(x) - f_0(x) \Big), \tag{6.2.58}$$

where

$$f_i(x) = \frac{1 - 2b^i(x)}{x^i}. \tag{6.2.59}$$

Since we have already handled the mutation terms in (6.2.58) and shown that for them (6.2.41) is necessary and sufficient, we only need to look at the contributions from selection. From (6.2.52), (6.2.53), this contribution is

$$\begin{aligned} &\frac{\partial}{\partial x^k}(s_i(x) - s(x) - s_0(x) - s(x)) - \frac{\partial}{\partial x^i}(s_k(x) - s(x) - s_0(x) - s(x)) \\ &\quad = \frac{\partial s_i(x)}{\partial x^k} - \frac{\partial s_0(x)}{\partial x^k} - \frac{\partial s_k(x)}{\partial x^i} + \frac{\partial s_0(x)}{\partial x^i} \\ &\quad = s_{ik} - s_{0k} - s_{i0} + s_{00} - s_{ki} + s_{0i} + s_{k0} - s_{00}, \end{aligned}$$

which vanishes if and only if the symmetry condition (6.2.56) holds for all indices.

In the case of uniform mutation rates, then

$$b_i(x) = \frac{\theta_i}{2} - \frac{|\theta|}{2}x^i + s_i(x)x^i - s(x)x^i.$$

Therefore we can easily calculate the potential energy function as

$$\psi(x) = \sum_{i=0}^{n} (1-\theta_i)\log(x^i) - s(x), \tag{6.2.60}$$

which follows from

$$\begin{aligned}\partial_i \psi(x) &= \frac{1-2b_i(x)}{x^i} - \frac{1-2b_0}{x^0} \\ &= \left(\frac{1-\theta_i}{x^i} + |\theta| - 2(s_i(x) - s(x))\right) - \left(\frac{1-\theta_0}{x^0} + |\theta| - 2(s_0(x) - s(x))\right) \\ &= \frac{1-\theta_i}{x^i} - \frac{1-\theta_0}{x^0} - 2(s_i(x) - s_0(x)).\end{aligned} \tag{6.2.61}$$

□

We now assume that the selection coefficients are of the form

$$s_{ij} = \frac{s_i + s_j}{2}. \tag{6.2.62}$$

In that case, (6.2.53), (6.2.54) become

$$s(x) = \sum_{j,k} \frac{s_j + s_k}{2} x^j x^k = \sum_j s_j x^j \tag{6.2.63}$$

since $\sum_k x^k = 1$. Therefore, (6.2.60) becomes

$$\psi(x) = \sum_{i=0}^{n} (1-\theta_i)\log(x^i) - \sum_{i=0}^{n} s_i x^i, \quad \text{where } x^0 = 1 - x^1 - \cdots - x^n.$$

In this case, the partition function for the free energy becomes

$$Z(\theta, s) := \int_{\Delta_n} e^{-\psi(y)} dy = \int_{\Delta_n} (y^1)^{\theta_1 - 1} (y^2)^{\theta_2 - 1} \cdots (y^n)^{\theta_n - 1} (1 - y^1 - \cdots - y^n)^{\theta_0 - 1} e^{\sum_{i=0}^{n} s_i y^i} dy, \tag{6.2.64}$$

and Z is finite if and only if $\theta_i > 0$ for all $i = 0, \ldots, n$. In that case again, the minimizer of the free energy is the Gibbs density

$$q_\infty(x) := \frac{e^{-\psi(x)}}{Z(\theta, s)}. \tag{6.2.65}$$

6.2.3 The Evolution of the Free Energy

Now we consider the evolution of the free energy functional along the flow of densities

$$F(p(\cdot,t)) := \int_\Omega \psi(x)u(x,t)dx + \int_\Omega u(x,t)\log u(x,t)dx. \tag{6.2.66}$$

We shall see that our flow of density functions exponentially converges to the Gibbs density function (6.2.65) and the free energy functional plays the role of the Lyapunov functional.

We know from the last subsection that in order to have a unique stationary reversible density we need to assume uniform positive mutation rates. So, in this subsection we shall assume that.

Lemma 6.2.1 *$F(p(\cdot,t))$ decreases along the flow of densities.*

Proof Using the divergence form of the flow (6.2.44), we have

$$\begin{aligned}
\frac{\partial}{\partial t}F(p(\cdot,t)) &= \int_\Omega \psi(x)\frac{\partial}{\partial t}u(x,t)dx + \int_\Omega \log u(x,t)\frac{\partial}{\partial t}u(x,t)dx + \underbrace{\int_\Omega \frac{\partial}{\partial t}u(x,t)dx}_{=0} \\
&= \int_\Omega \psi(x)\nabla\cdot(A(x)\nabla u(x,t))dx + \psi(x)\nabla\cdot(A(x)u(x,t)\nabla\psi(x))dx \\
&\quad + \int_\Omega \log u(x,t)\nabla\cdot(A(x)\nabla u(x,t))dx + \log u(x,t)\nabla\cdot(A(x)u(x,t)\nabla\psi(x))dx \\
&= -\int_\Omega \nabla\psi(x)\cdot(A(x)\nabla u(x,t))dx - \nabla\psi(x)\cdot(A(x)u(x,t)\nabla\psi(x))dx \\
&\quad - \int_\Omega \nabla\log u(x,t)\cdot(A(x)\nabla u(x,t))dx - \nabla\log u(x,t)\cdot(A(x)u(x,t)\nabla\psi(x))dx \\
&\quad \text{(integrating by parts as in [114], Proposition 2.4)} \\
&= -\int_\Omega \nabla\psi(x)\cdot(A(x)\nabla u(x,t))dx - \nabla\psi(x)\cdot(A(x)u(x,t)\nabla\psi(x))dx \\
&\quad - \int_\Omega \frac{\nabla u(x,t)\cdot(A(x)\nabla u(x,t))}{u(x,t)}dx - \nabla u(x,t)\cdot A(x)\nabla\psi(x)dx \\
&= -\int_\Omega I(x,t)dx.
\end{aligned} \tag{6.2.67}$$

where

$$\begin{aligned} I(x,t) &= u(x,t)\nabla\psi(x)\cdot(A(x)\nabla\psi(x)) + \frac{1}{u(x,t)}\nabla u(x,t)\cdot(A(x)\nabla u(x,t)) \\ &\quad + 2\nabla\psi(x)\cdot(A(x)\nabla u(x,t)) \\ &= p < \nabla\psi, \nabla\psi >_D + \frac{1}{p} < \nabla p, \nabla p >_D + 2 < \nabla\psi, \nabla p >_D \\ &\geq 0. \end{aligned} \tag{6.2.68}$$

This completes the proof. □

Remark We note that in our case $A(x)$ does not satisfy a uniform ellipticity condition as in [16]. In fact, when x goes to the boundary $\partial\Omega$, the Fisher information metric goes to infinity, and therefore $A(x)$ goes to 0.

We assume that there exists a unique stationary distribution $d\mu_\infty(x) = u_\infty(x)dx$. We focus on the rate of the convergence of u to u_∞. Putting

$$h := \frac{u}{u_\infty},$$

we shall investigate the rate of the convergence of h to 1.

The stationary density is the Gibbs density function

$$u_\infty(x) = \frac{e^{-\psi(x)}}{Z},$$

which is an exponential family (3.6.1). Thus

$$\log u_\infty + \psi = -\log Z.$$

Since Z is independent of x, this implies

$$\partial_j(\log u + \psi) = \partial_j\Big(\log\frac{u}{u_\infty}\Big) + \partial_j(\log u_\infty + \psi) = \partial_j(\log h).$$

We now derive a partial differential equation for h from that of u.

Lemma 6.2.2

$$\partial_t h = \nabla\cdot(A(x)\nabla h) - \nabla\psi\cdot A(x)\nabla h = L^* h.$$

Proof We have

$$\begin{aligned}
\partial_t h &= u_\infty^{-1}\partial_t u \\
&= u_\infty^{-1}\partial_i\Big(A^{ij}u\partial_j\big(\log u+\psi\big)\Big) \\
&= u_\infty^{-1}\partial_i\Big(A^{ij}u_\infty h\partial_j\big(\log h\big)\Big) \\
&= \partial_i\Big(A^{ij}h\partial_j\big(\log h\big)\Big)+u_\infty^{-1}\partial_i(u_\infty)\Big(A^{ij}h\partial_j\big(\log h\big)\Big) \\
&= \partial_i\Big(A^{ij}\partial_j h\Big)+\partial_i(\log u_\infty)\partial_i\Big(A^{ij}\partial_j h\Big) \\
&= \nabla\cdot(A(x)\nabla h)-\nabla\psi\cdot A(x)\nabla h
\end{aligned} \tag{6.2.69}$$

This completes the proof. □

Then, we can easily see that

$$d\mu_\infty(x)=u_\infty(x)dx=\frac{e^{-\psi(x)}}{Z}dx$$

is reversible with respect to L^*.

Lemma 6.2.3

$$\int_{\Delta_n} fL^*g\,d\mu_\infty=\int_{\Delta_n} gL^*f\,d\mu_\infty,\quad \forall f,g\in C^2(\Delta_n).$$

Proof

$$\begin{aligned}
\int_{\Delta_n} fL^*g\,d\mu_\infty &= \int_{\Delta_n} f\Big(\nabla\cdot(A(x)\nabla g)\Big)u_\infty(x)dx-\int_{\Delta_n} f\Big(\nabla\psi\cdot A(x)\nabla g\Big)u_\infty(x)dx \\
&= -\int_{\Delta_n} A(x)\nabla g\cdot\nabla\Big(f\frac{e^{-\psi(x)}}{Z}\Big)dx-\int_{\Delta_n}\Big(\nabla\psi\cdot A(x)\nabla g\Big)fu_\infty(x)dx \\
&= -\int_{\Delta_n} A(x)\nabla g\cdot\Big(\nabla f-f\nabla\psi(x)\Big)\frac{e^{-\psi(x)}}{Z}dx \\
&\quad -\int_{\Delta_n}\Big(\nabla\psi\cdot A(x)\nabla g\Big)fu_\infty(x)dx \\
&= -\int_{\Delta_n} A(x)\nabla g\cdot\nabla f\frac{e^{-\psi(x)}}{Z}dx \\
&= -\int_{\Delta_n} A(x)\nabla g\cdot\nabla f\,d\mu_\infty(x),
\end{aligned} \tag{6.2.70}$$

which is symmetric between f and g. This yields the proof. □

We can now compute the decay rate of the free energy functional towards its asymptotic limit along the evolution of the probability density function u. For simplicity, we shall write $F(t)$ in place of $F(p(\cdot, t))$.

Lemma 6.2.4

$$F(t,\theta) - F_\infty(\theta) = D_{\mathrm{KL}}(u\|u_\infty) = S_{\mu_\infty}(h) \geq 0.$$

Proof We have

$$\begin{aligned} F(t,\theta) &= \int_{\Delta_n} u(\log u + \psi)dx \\ &= \int_{\Delta_n} u(\log u_\infty + \psi)dx + \int_{\Delta_n} u(\log u - \log u_\infty)dx \\ &= \int_{\Delta_n} u(-\log Z)dx + \int_{\Delta_n} u \log \frac{u}{u_\infty} dx \\ &= -\log Z + \int_{\Delta_n} u \log \frac{u}{u_\infty} dx \\ &= -\log Z + \int_{\Delta_n} h \log h d\mu_\infty \end{aligned} \tag{6.2.71}$$

and

$$F_\infty(\theta) = F(u_\infty) = \int_{\Delta_n} u_\infty(\log u_\infty + \psi) = -\log Z.$$

This implies the proof. □

Lemma 6.2.5

$$\frac{d}{dt} S_{\mu_\infty}(h) = \partial_t F(t,\theta) = -J_{\mu_\infty}(h) := -\int_{\Delta_n} \frac{A(x)\nabla h \cdot \nabla h}{h} d\mu_\infty.$$

Proof We have

$$\begin{aligned}\partial_t F(t,\theta) &= \int_{\Delta_n} \partial_t u(\log u + \psi)dx + \int_{\Delta_n} u\partial_t(\log u + \psi)dx \\ &= \int_{\Delta_n} \partial_i\Big(A^{ij}u\partial_j\big(\log u + \psi\big)\Big)(\log u + \psi)dx + \int_{\Delta_n} \partial_t u dx \\ &\quad \text{(because } \partial_t\psi = 0\text{)} \\ &= -\int_{\Delta_n} \Big(A^{ij}u\partial_j\big(\log u + \psi\big)\Big)\partial_i(\log u + \psi)dx + \partial_t\Big(\int_{\Delta_n} u dx\Big) \\ &\quad \text{(integrating by parts)} \\ &= -\int_{\Delta_n} A^{ij}u\partial_j(\log h)\partial_i(\log h)dx \\ &= -\int_{\Delta_n} \frac{A^{ij}\partial_j h\partial_i h}{h}u_\infty dx.\end{aligned} \tag{6.2.72}$$

Since $F(u_\infty)$ is independent of t, this implies the proof. □

6.2.4 Curvature-Dimension Conditions and Asymptotic Behavior

We start with some general notions, see [13] again.

We consider an operator $(L, D(L))$ defined on a measure space (Ω, μ) of the form

$$Lf = a^{ij}(x)\partial_i\partial_j f + b^i(x)\partial_i f, \forall f \in \mathcal{A} = L^2(\Omega, \mu) \cap D(L).$$

Definition 6.2.6 The *carré du champ operator* of L is defined by

$$\Gamma(f,g) = \frac{1}{2}\Big(L(fg) - fLg - gLf\Big), \quad \forall f, g \in \mathcal{A} \tag{6.2.73}$$

and the *iterated carré du champ operator* of L is defined by

$$\Gamma_2(f,g) = \frac{1}{2}\Big(L\Gamma(f,g) - \Gamma(f,Lg) - \Gamma(g,Lf)\Big), \quad \forall f, g \in \mathcal{A}. \tag{6.2.74}$$

We will also denote $\Gamma(f,f) = \Gamma(f)$ and $\Gamma_2(f,f) = \Gamma_2(f)$ for short.

Definition 6.2.7 The measure μ satisfies the *logarithmic Sobolev inequality LSI*(ρ) (see [55]) if for all densities f we have

$$\int_\Omega f \log f d\mu \leq \frac{1}{\rho}\int_\Omega \frac{1}{2f}|\nabla f|^2 d\mu.$$

Definition 6.2.8 The measure μ satisfies the *spectral gap condition SG*(ρ) if for all functions h with $\int_\Omega h(x)d\mu(x) = 0$, we have

$$\int_\Omega h^2 d\mu \leq \frac{1}{\rho}\int_\Omega |\nabla h|^2 d\mu.$$

Definition 6.2.9 A family of densities $\{u(\cdot,t)\}_{t\geq 0}$ on a σ-finite measure space (Ω, μ) is called *hypercontractive* with respect to μ if for all p_t satisfying

$$p_t - 1 = e^{2\rho t}(p_0 - 1),$$

we have

$$\left(\int_\Omega |u(x,t)|^{p_t} d\mu(x)\right)^{\frac{1}{p_t}} \leq \left(\int_\Omega |u(x,0)|^{p_0} d\mu(x)\right)^{\frac{1}{p_0}}.$$

Definition 6.2.10 We say that L satisfies the *curvature-dimension condition* $CD(\rho, n)$ for $\rho > 0$ and $n \in [1, \infty]$ if for all $f \in \mathcal{A}$

$$\Gamma_2(f) \geq \rho\Gamma(f) + \frac{1}{n}(Lf)^2, \quad \mu\text{-a.e.} \tag{6.2.75}$$

We recall some background results:

Proposition 6.2.1 (Bochner–Lichnerowicz Formula) *For a Riemannian manifold* (Ω, g)*, the Laplacian and the Ricci curvature are related via*

$$\frac{1}{2}\Delta_g\Big(|\nabla f|^2\Big) = \nabla f \cdot \nabla\Big(\Delta_g f\Big) + |\nabla\nabla f|^2 + Ric_g(\nabla f, \nabla f) \tag{6.2.76}$$

for all smooth functions $f\colon \Omega \to \mathbb{R}$.

Proof See [71], for instance. □

Proposition 6.2.2 (Hessian Formula) *For a Riemannian manifold* (Ω, g)*, we have the Hessian formula*

$$\nabla\nabla f(\nabla g, \nabla h) = \frac{1}{2}\Big(\Gamma(g, \Gamma(f,h)) + \Gamma(h, \Gamma(f,g)) - \Gamma(f, \Gamma(g,h))\Big) \tag{6.2.77}$$

for all smooth functions $f, g, h : \Omega \to \mathbb{R}$.

Proof See [13], for instance. □

Proposition 6.2.3 *Consider an n-dimensional Riemannian manifold* (Ω, g) *with Riemannian measure* μ_g. *Let* $m \geq n$, *then* $L = \Delta_g + Z$ *satisfies* $CD(\rho, m)$, *i.e.*

$$\Gamma_2(f) \geq \rho\Gamma(f) + \frac{(Lf)^2}{m}, \forall f \in \mathcal{A} \quad \mu_g\text{-a.e.},$$

if and only if

$$Ric(L) := Ric_g - \nabla_S Z \geq \rho g + \frac{1}{m-n} Z \otimes Z,$$

where

$$(\nabla_S Z)_{ij} := \frac{1}{2}\Big(\partial_i Z^j + \partial_j Z^i\Big), \quad i, j = 1, \cdots, n$$

is the symmetric covariant derivative of the vector field Z in the metric g. $Ric(L)$ *is often called the generalized Ricci tensor.*

Remark

1. The case $m = n$ can only occur when $Z = 0$;
2. The case $m = \infty$, $L \in CD(\rho, \infty)$, i.e. $\Gamma_2(f) \geq \rho\Gamma(f)$, occurs if and only if $Ric(L) \geq \rho g$.
3. If $Z = -\nabla W \cdot \nabla$, then $Ric(L) = Ric_g + \nabla\nabla W$. Therefore, $L \in CD(\rho, \infty)$ if and only if $Ric_g + \nabla\nabla W \geq \rho g$, which is a general result of Bakry and Émery [12] in the Riemannian setting. Moreover, by denoting $w_1^{m-n} = e^{-W}$, we have the more general criterion $L \in CD(\rho, m)$ if and only if $Ric_m(L) := Ric_g - \frac{m-n}{w_1}\nabla\nabla w_1 \geq \rho g$.

Proof This follows from the Bochner–Lichnerowicz and Hessian formulas. □

We note that for the above operator L, we always have

$$\Gamma(f, g) = a^{ij}\partial_i f \partial_j g.$$

We now consider the Kolmogorov backward operator on $\Omega = \Delta_n$ with $\mathcal{A} = C^2(\Delta_n)$:

$$L^* h = A^{ij}(x)\partial_i\partial_j h + b^i(x)\partial_i h,$$

where

$$A^{ij} = \frac{1}{2}\Big(x^i(\delta_{ij} - x^j\Big)$$

and

$$b^i = \frac{\theta_i}{2} - \frac{|\boldsymbol{\theta}|}{2}.$$

We have $g_{ij} = 2(\frac{\delta_{ij}}{x^i} + \frac{1}{x^0})$ as our Riemannian metric on Δ_n, which is the inverse of $A^{ij}(x)$. We note that this metric is twice the metric in Chap. 3, but since the Ricci curvature tensor R_{ij} does not change when we multiply the metric by a constant λ (although the sectional curvature will change by λ), by the relation $R_{ij} = \rho g_{ij}$ (which holds since we have a constant curvature metric), the Ricci curvature ρ becomes $\frac{n-1}{8}$.

With this Riemannian metric, we can write our Kolmogorov backward operator in the form

$$L^* = \Delta_g - \nabla W \cdot \nabla,$$

where e^{-W} is the density of the reversible measure μ with respect to the Riemannian measure $d\mu_g(x) = |\det(A(x))|^{-\frac{1}{2}} dx$. We know that the only reversible measure in this case is μ_∞. Therefore we can obtain $W(x), w_1(x)$ by

$$e^{-W(x)} = \frac{\Gamma(\theta_0)\ldots\Gamma(\theta_n)}{2^{\frac{n}{2}}\Gamma(|\theta|)} \prod_{i=0}^{n} (x^i)^{\theta_i - \frac{1}{2}} = w_1^{m-n}(x).$$

We have

$$\Gamma(w_1, f) = A^{ij}(x)\partial_i w_1 \partial_j f = \frac{w_1}{2(m-n)} Zf, \tag{6.2.78}$$

where

$$Zf := \sum_{i=1}^{n} (c_i - |c|x^i)\partial_i f$$

is a vector field on Δ_n with $c_i = \theta_i - \frac{1}{2}$, $|c| = \sum_{i=0}^{n} c_i = |\theta| - \frac{n+1}{2}$. Therefore

$$\begin{aligned}
Ric_m(L)(\nabla f, \nabla f) &= Ric_g(\nabla f, \nabla f) - \frac{m-n}{w_1} \nabla\nabla w_1(\nabla f, \nabla f) \\
&= \frac{n-1}{8}(\nabla f, \nabla f) - \frac{1}{2}\Big(2\Gamma(f, \Gamma(w_1, f)) - \Gamma(w_1, \Gamma(f, f))\Big) \\
&\quad \text{by the Hessian formula (6.2.77)} \\
&= \frac{n-1}{8}(\nabla f, \nabla f) - \Big(\frac{1}{4(m-n)}(Zf)^2 + \frac{1}{2}A^{ij}(x)\partial_i f \partial_j (Zf) \\
&\quad - \frac{1}{2} Z(A^{ij}(x)\partial_i f \partial_j f)\Big) \text{ by (6.2.78)} \\
&= \frac{n-1+2|c|}{8}\Gamma(f) + \frac{1}{8}[c_i(\partial_i f - x^i \partial_i f)^2 + c_0(x^i \partial_i f)^2] - \frac{(Zf)^2}{4(m-n)}
\end{aligned} \tag{6.2.79}$$

Hence, if $c_i \geq 0$ for all $i = 0, \ldots, n$ i.e. $\theta_i \geq \frac{1}{2}$ for all $i = 0, \ldots n$, then for $m \to \infty$ we have

$$Ric_\infty(L^*) \geq \frac{n-1+2|c|}{8} g = \rho_n g.$$

Thus, $L^* \in CD(\rho_n, \infty)$.

Remark For $\theta_i = \frac{1}{2}$, i.e. $c_i = 0$, then $Zf = 0$ and $L^* = \Delta_g$ is the Laplacian; moreover,

$$Ric_m(L) = Ric_g = \frac{n-1}{8} g$$

for all $m \geq n$. Therefore in this case, L^* satisfies $CD(\frac{n-1}{8}, n)$.

We can also directly calculate

$$\begin{aligned} \Gamma_2(f) &= |\nabla\nabla f|^2 + Ric(L^*)(\nabla f, \nabla f) \\ &= |\nabla\nabla f|^2 + Ric_g(\nabla f, \nabla f) + \nabla\nabla W(\nabla f, \nabla f). \end{aligned} \tag{6.2.80}$$

We now apply the Hessian formula (6.2.77) to calculate $\nabla\nabla W$. We have

$$W(x) = -\log \frac{2^{-\frac{n}{2}}}{Z} + \sum_{i=0}^{n} (\frac{1}{2} - \theta_i) \log x^i = -\log c + \sum_{i=0} d_i \log x^i$$

where

$$d_i = \frac{1}{2} - \theta_i, \quad |d| = \sum_{i=0}^{n} d_i = \frac{n+1}{2} - |\theta|.$$

Then

$$\partial_j W = \frac{d_j}{x^j} - \frac{d_0}{x^0}$$

and

$$A^{ij}\partial_j W = \frac{1}{2}(x^i \delta_{ij} - x^i x^j)(\frac{d_j}{x^j} - \frac{d_0}{x^0}) = \frac{1}{2}(d_i - |d| x^i).$$

This implies that

$$\Gamma(W, f) = A^{ij}\partial_i W \partial_j f = \frac{1}{2}(d_j - |d| x^j)\partial_j f.$$

Therefore,

$$\begin{aligned}
\nabla\nabla W(\nabla f,\nabla f) &= \Gamma(f,\Gamma(W,f)) - \frac{1}{2}\Gamma(W,\Gamma(f,f)) \\
&= \frac{1}{2}A^{ij}\partial_i f\partial_j((d_k-|d|)\partial_k f) - \frac{1}{4}(d_k-|d|x^k)\partial_k\Big(A^{ij}\partial_i f\partial_j f\Big) \\
&= \frac{1}{2}A^{ij}\partial_i f\Big(-|d|\partial_j f\Big) - \frac{1}{4}(d_k-|d|x^k)\partial_k A^{ij}\partial_i f\partial_j f \\
&= -\frac{|d|}{2}|\nabla f|^2 - \frac{1}{8}(d_k-|d|x^k)(\delta_{ik}\delta_{ij}-\delta_{ik}x^j-\delta_{jk}x^i)\partial_i f\partial_j f \\
&= -\frac{|d|}{2}|\nabla f|^2 - \frac{1}{8}\Big(d_i(\partial_i f)^2 - |d|x^i(\partial_i f)^2 \\
&\quad - 2d_i\partial_i f x^j\partial_j f + 2|d|(x^i)^2(\partial_i f)^2\Big) \\
&= -\frac{|d|}{2}|\nabla f|^2 - \frac{1}{8}\Bigg(\Big(d_i(\partial_i f)^2 - 2d_i\partial_i f x^j\partial_j f \\
&\quad + |d|(x^i)^2(\partial_i f)^2\Big) - 2|d||\nabla f|^2\Bigg) \\
&= -\frac{|d|}{4}|\nabla f|^2 - \frac{1}{8}\Big(d_i(\partial_i f - Z_1 f)^2 + d_0(Z_1 f)^2\Big), \\
&= \frac{|c|}{4}|\nabla f|^2 + \frac{1}{8}\Big(c_i(\partial_i f - Z_1 f)^2 + c_0(Z_1 f)^2\Big)
\end{aligned} \tag{6.2.81}$$

with the vector field

$$Z_1 f = x^i\partial_i f.$$

This implies that

$$\Gamma_2(f) = |\nabla\nabla f|^2 + Ric_g(\nabla f,\nabla f) + \frac{|c|}{4}|\nabla f|^2 + \frac{1}{8}\big(c_i(\partial_i f - Z_1 f)^2 + c_0(Z_1 f)^2\big).$$

If $c_i \geq 0$ for all $i = 0,\dots n$, i.e. $\theta_i \geq \frac{1}{2}$ for all $i = 0,\dots n$, then we obtain

$$\Gamma_2(f) \geq \frac{n-1+2|c|}{8}\Gamma(f) = \rho_n\Gamma(f). \tag{6.2.82}$$

This means that we have the curvature-dimension condition $CD(\rho_n,\infty)$ and that μ_∞ satisfies the $LSI(\rho_n,\infty)$.

Note that

$$\rho_n = \frac{n-1+2|c|}{8}$$

is not optimal as we have used the rather coarse estimate

$$c_i(\partial_i f - Z_1 f)^2 + c_0(Z_1 f)^2 \geq 0.$$

So, let us try to find the optimal value for the case of two alleles ($n = 1$). In this case, the Ricci curvature $\frac{n-1}{8}$ vanishes. We have

$$W(x) = -\log \frac{\Gamma(\theta_1)\Gamma(\theta_0)}{\sqrt{2}\Gamma(\theta_1+\theta_0)} + (\frac{1}{2} - \theta_1)\log x + (\frac{1}{2} - \theta_0)\log(1-x).$$

With the Riemannian metric $g(x) = \frac{2}{x(1-x)}$ on $\Delta_1 = (0,1)$, we have $\Gamma(f) = |\nabla f|^2 = \frac{1}{2}x(1-x)(\partial_x f)^2$ and the Hessian of W

$$\nabla\nabla W(\nabla f, \nabla f) = \frac{c_1+c_0}{4}|\nabla f|^2 + \frac{1}{8}\Big(c_1(1-x)^2 + c_0 x^2\Big)(\partial_x f)^2, \tag{6.2.83}$$

where $c_1 = \theta_1 - \frac{1}{2}$ and $c_0 = \theta_0 - \frac{1}{2}$.

When $\theta_1, \theta_0 \geq \frac{1}{2}$, i.e. $c_0, c_1 \geq 0$, the smallest eigenvalue of the Hessian of W is

$$\rho_1 = \Big(\frac{\sqrt{c_1} + \sqrt{c_0}}{2}\Big)^2$$

by the Cauchy inequality.

Therefore, we have

Lemma 6.2.6 *If $\theta_1, \theta_0 > \frac{1}{2}$, then L^* satisfies $CD(\rho_1, \infty)$ with*

$$\rho_1 = \left(\frac{\sqrt{\theta_1 - \frac{1}{2}} + \sqrt{\theta_0 - \frac{1}{2}}}{2}\right)^2.$$

Proposition 6.2.4 *If L is symmetric with respect to the stationary measure μ and satisfies the $CD(\rho, \infty)$ condition, then μ satisfies $LSI(\rho, \infty)$.*

Proof See for example [13]. □

These results will allow us to reach very precise conclusions. For instance, we have:

Theorem 6.2.4 *For the Wright–Fisher model with $n+1$ alleles and positive uniform mutation rates satisfying $\theta_i > \frac{1}{2}$ for all $i = 0, \ldots, n$, the stationary distribution $f_\infty dx$*

satisfies the LSI(ρ_n, ∞) *with*

$$\rho_n = \frac{n-1+|c|}{4} = \frac{n-3+2|\theta|}{8}.$$

Proof Applying the results of (6.2.82) and (6.2.4). □

Theorem 6.2.4 immediately implies some corollaries (see for example [13] for further details):

Corollary 6.2.1 *Under the above assumptions, the family of densities* $\{u(\cdot,t)\}_{t\geq 0}$ *is hypercontractive with respect to* μ_∞*, i.e., for all* p_t *satisfying*

$$p_t - 1 = e^{2\rho t}(p_0 - 1),$$

we have

$$\left(\int_\Omega |u(x,t)|^{p_t} d\mu_\infty(x)\right)^{\frac{1}{p_t}} \leq \left(\int_\Omega |u(x,0)|^{p_0} d\mu_\infty(x)\right)^{\frac{1}{p_0}}.$$

Corollary 6.2.2 *Under the above assumptions, the measure* μ_∞ *has the spectral gap* $SG(\rho)$.

We now recall some known transport inequalities, which will be helpful for our entropy estimates.

Proposition 6.2.5 (Csiszár–Kullback–Pinsker Inequality) *If* μ *and* ν *are two probability distributions, then*

$$\|\mu - \nu\|_{TV} \leq \sqrt{\frac{1}{2} D_{\mathrm{KL}}(\mu\|\nu)}, \tag{6.2.84}$$

where

$$\|\mu - \nu\|_{TV} = \sup\left\{|\mu(A) - \nu(A)| : A \text{ is an event to which probabilities are assigned.}\right\}$$

is the total variation distance (or statistical distance) between μ *and* ν.

Proof See for example [19]. □

Proposition 6.2.6 *If* μ *and* ν *are two probability distributions with Radon–Nikodym derivatives* f *and* g *with respect to* ρ*, then*

$$\|f - g\|_{L^1(\rho)} \leq \sqrt{2 D_{\mathrm{KL}}(\mu\|\nu)}. \tag{6.2.85}$$

Proof It follows from (6.2.84) and the equality

$$\|\nu - \mu\|_{TV} = \frac{1}{2}\|f - g\|_{L^1(\rho)}.\square$$

Corollary 6.2.3 *Under the above assumptions, the rate of convergence of the relative entropy* $D_{\mathrm{KL}}(u\|u_\infty)$ *is*

$$D_{\mathrm{KL}}(u(t)\|u_\infty) \le e^{-2\rho t} D_{\mathrm{KL}}(u(0)\|u_\infty).$$

Combining this with (6.2.84) and (6.2.85) implies that

(i) $u(t)dx$ *exponentially converges to* $u_\infty dx$ *with respect to the total variation distance;*
(ii) $u(t)dx$ *exponentially converges to* $u_\infty dx$ *with respect to the* L^1*-norm.*

Chapter 7
Large Deviation Theory

This chapter applies Wentzell's theory of large deviations to the Wright–Fisher model, using the approach of Papangelou [96–98, 100]. For a different approach to the large deviation principle for exit times in population genetics, we refer the reader to [90, 91]. As customary, we shall abbreviate Large Deviation Principle as LDP.

7.1 LDP for a Sequence of Measures on Different State Spaces

In this section, we develop the definition of LDP for a sequence of probability measures on different state spaces. This will be illustrated by some standard examples.

Definition 7.1.1 Let $\{\Omega_r\}_r$ be a sequence of discrete state spaces, μ_r a probability measure on Ω_r and $\{a_r\}_r$ a sequence of positive real numbers such that $\lim_{r\to\infty} a_r = \infty$. We consider a functional $I : \mathcal{D}(I) := \overline{\cup_r \Omega_r} \to \mathbb{R}$. We say that the sequence $\{\mu_r\}_r$ satisfies a *large deviation principle with speed* $\{a_r\}_r$ and rate I, denoted by $\{\mu_r\} \in LD(I, \{a_r\})$, if for every $x \in \mathcal{D}(I)$, there exists a sequence $\{x_r\}_r$ such that $x_r \in \Omega_r$ and $x_r \to x$ as $r \to \infty$ and

$$\lim_{r\to\infty} a_r^{-1} \ln \mu_r(x_r) = -I(x).$$

When $a_r = r$, we simply write $\{\mu_r\} \in LD(I)$.

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In this setting, Varadhan's examples [121] become

Example 7.1.1 Consider tossing a coin: The probability of k heads in r tosses of a fair coin is

$$P(r,k) = \binom{r}{k} 2^{-r}.$$

A corresponding sequence of state spaces is $\Omega_r = \{0, \frac{1}{r}, \ldots, 1\}$, and we put

$$\mu_r\left(\frac{k}{r}\right) = P(r,k)$$

as a probability measure on Ω_r. As $\bigcup_r \Omega_r$ is dense in $\Omega = [0,1]$, there exists a sequence $x_r = \frac{k_r}{r} \in \Omega_r$ with $x_r \to x$ as $r \to \infty$ for every $x \in [0,1]$.

Using the Stirling approximation

$$\lim_{r\to\infty} \frac{r!}{\sqrt{2\pi r}\left(\frac{r}{e}\right)^r} = 1,$$

we easily get

$$\begin{aligned}\lim_{r\to\infty} \frac{1}{r} \ln \mu_r(x_r) = \lim_{r\to\infty} \frac{1}{r} \ln P(r,k_r) &= -\Big(x\ln x + (1-x)\ln(1-x) + \ln 2\Big) \\ &= -\left(x \ln \frac{x}{1/2} + (1-x)\ln\frac{1-x}{1/2}\right).\end{aligned}$$

Therefore $\{\mu_r\} \in LD(I)$ with the rate functional $I\colon [0,1] \to \mathbb{R}_+$ given by

$$I(x) = x\ln\frac{x}{1/2} + (1-x)\ln\frac{1-x}{1/2}.$$

Similarly, we can see that the sequence of probability measures on Ω_r

$$\mu_{r,p}\left(\frac{k}{r}\right) := \binom{r}{k} p^k (1-p)^{r-k}$$

satisfies $\{\mu_{r,p}\} \in LD(I_p)$ with the rate functional $I_p\colon [0,1] \to \mathbb{R}_+$ defined by

$$I_p(x) = x\ln\frac{x}{p} + (1-x)\ln\frac{1-x}{1-p}.$$

Remark We can also interpret this example in the following manner (see [104]):

Let X be a Bernoulli distributed random variable with a parameter p in the state space $\{0,1\}$, i.e. $\mathrm{P}(X=1) = p$ and $\mathrm{P}(X=0) = 1-p$, denoted by

$X \sim Bernoulli(p)$. Assume that we have a sequence of i.i.d. random variables $X_1, X_2, \ldots$ with the same distribution as X and put $S_r = X_1 + \cdots + X_r$. Then $\{\frac{S_r}{r}\} \in LD(I_p)$, i.e.

$$\lim_{r\to\infty} \frac{1}{r} \ln \mathrm{P}\left(\frac{S_r}{r} = \frac{[rx]}{r}\right) = -I_p(x).$$

We see that at $x = p$ we have $I_p(p) = 0$ therefore $\lim_{r\to\infty} \mathrm{P}\left(\frac{S_r}{r} = \frac{[rp]}{r}\right) = 1$ which is the law of large number; at $x \neq p$ we have $I_p(x) > 0$ and thus obtain a large deviation. We note that the rate function I_p can be represented by $I_p(x) = D_{KL}(Bernoulli(x) \| Bernoulli(p))$ which is Sanov's version of the LDP (see 7.2.5).

Example 7.1.2 Consider a sequence of n-dimensional normalized discrete simplexes

$$\Omega^{(2N)} := \left\{ \frac{i}{2N} = \left(\frac{i^1}{2N}, \ldots, \frac{i^n}{2N}\right) : i^1 \in \mathbb{N}_0, \ldots, i^n \in \mathbb{N}_0 \text{ and } \sum_{k=1}^{n} i^k \leq 2N \right\},$$

and multinomial distributions with parameter p, denoted by $\mu_{2N,p} \sim Multinom$ $(2N, p)$, i.e.

$$\mu_{2N,p}\left(\frac{i}{2N}\right) = \frac{2N!}{i^0! \ldots i^n!} (p^0)^{i^0} \ldots (p^n)^{i^n}, \quad \frac{i}{2N} \in \Omega^{(2N)}$$

with $p \in \overline{\Delta}_n := \{x = (x^1, \ldots, x^n) : x^i \geq 0 \text{ for } i = 1, \ldots, n \text{ and } x^1 + \ldots + x^n \leq 1\}$, $p^0 = 1 - p^1 - \ldots - p^n$ and $i^0 = 2N - i^1 - \ldots - i^n$.

Similarly, we have for each $p \in \Delta_n$, $\{\mu_{2N,p}\} \in LD(I_p)$ where the rate functional $I_p \colon \overline{\Delta}_n \to \mathbb{R}_+$ is defined by

$$I_p(x) = \sum_{i=0}^{n} x^i \ln \frac{x^i}{p^i} = D_{KL}(x \| p), \quad x \in \overline{\Delta}_n.$$

7.2 LDP for a Sequence of Stochastic Processes

7.2.1 Preliminaries

For consistency of notation and definitions, we shall adapt the concepts of Papangelou for LDP in continuous state space to our setting.

Definition 7.2.1 Let (Ω, τ_Ω) be a Polish space, i.e. a separable completely metrizable topological space, $\{a_r\}_r$ be a sequence of positive real numbers such that $\lim_{r\to\infty} a_r = \infty$, and let $I \colon \Omega \to [0, \infty]$ be a lower semicontinuous functional which

is proper (also called "good" in the literature), i.e. every level set $\{x \in \Omega : I(x) \leq c\}$ is compact in Ω for all $c \geq 0$. Furthermore, let μ_r be a sequence of probabilities on Ω.

We then say that the sequence $\{\mu_r\}_r$

1. satisfies an *upper large deviation principlewith speed* $\{a_r\}_r$ *and rate* I, denoted by $\{\mu_r\} \in LD_u(I, \{a_r\})$, if for all closed subsets C in (Ω, τ_Ω)

$$\limsup_{r\to\infty} a_r^{-1} \log \mu_r(C) \leq -\inf_{x\in C} I(x);$$

2. satisfies a *lower large deviation principle with speed* $\{a_r\}_r$ *and rate* I, denoted by $\{\mu_r\} \in LD_l(I, \{a_r\})$, if for all open subsets A in (Ω, τ_Ω)

$$\liminf_{r\to\infty} a_r^{-1} \log \mu_r(A) \geq -\inf_{x\in A} I(x);$$

3. satisfies a *large deviation principle with speed* $\{a_r\}_r$ *and rate* I, denoted by $\{\mu_r\} \in LD(I, \{a_r\})$, if it satisfies both the upper and the lower large deviation principle with speed $\{a_r\}_r$ and rate I;
4. satisfies a *G-lower large deviation principle with speed* $\{a_r\}_r$ *and rate* I, denoted by $\{\mu_r\} \in LD_{l,G}(I, \{a_r\})$, if for all open subsets A in (G, τ_G) of a given subset $G \subseteq \Omega$

$$\liminf_{r\to\infty} a_r^{-1} \log \mu_r(A) \geq -\inf_{x\in A} I(x).$$

If $a_r = r$, we will drop the expression $\{a_r\}$ in $LD(I, \{a_r\})$, and simply write $LD(I)$.

Definition 7.2.2 Let Ω be a Polish space, $\{a_r\}_r$ be a sequence of positive real numbers such that $\lim_{r\to\infty} a_r = \infty$. Let $\{X_{(\cdot)}^{(r)}\}_{r\in\mathbb{N}_0}$ be a sequence of Markov processes in the state space Ω starting at some given $p \in \Omega$. Let K be a compact subset of Ω and fix some $T > 0$. We say that the sequence $\{X_T^{(r)}\}_r$ satisfies the *large deviation principle with speed* $\{a_r\}_r$ *and rate* $J_{p,T}$ *uniformly on* K, denoted by $\{X_T^{(r)}\} \in LD(J_{p,T}, \{a_r\}, K)$ if

1. a lower bound condition holds uniformly on K, i.e.

$$\limsup_{r\to\infty} a_r^{-1} \log \sup_{p\in K} \mathrm{P}_p(X_T^{(r)} \in C) \leq -\inf_{p\in K} \inf_{q\in C} J_{p,T}(q)$$

   for all closed subsets C,
2. an upper bound conditions holds uniformly on K, i.e.

$$\limsup_{r\to\infty} a_r^{-1} \log \sup_{p\in K} \mathrm{P}_p(X_T^{(r)} \in A) \leq -\sup_{p\in K} \inf_{q\in A} J_{p,T}(q)$$

   for all open subsets A.

7.2.2 Basic Properties

We now list some basic properties of the large deviation principle (see, for example, [104, 120]):

Proposition 7.2.1 *If $\mu_r \in LD(I)$ and $F \in BC(\Omega, \mathbb{R})$, then*

$$\lim_{r\to\infty} \frac{1}{r} \log \int_\Omega e^{rF(x)} \mu_r(dx) = \sup_{x\in\Omega} \{F(x) - I(x)\}.$$

Proposition 7.2.2 *Let be given a sequence $\{F_r\}_r$ of nonnegative functions and a lower semicontinuous nonnegative function F satisfying*

$$\liminf_{r\to\infty} F_r(x_r) \geq F(x) \quad \text{for all } x \in \Omega \text{ and } x_r \to x \text{ as } r \to \infty.$$

Then, if $\mu_r \in LD(I)$, we have

$$\limsup_{r\to\infty} \frac{1}{r} \log \int_\Omega e^{-rF_r(x)} \mu_r(dx) \leq - \inf_{x\in\Omega} \{F(x) + I(x)\}.$$

Proposition 7.2.3 *Let Ω' also be a Polish space and $F \in C(\Omega, \Omega')$. If $\mu_r \in LD(I)$, then $F_\sharp \mu_n := \mu_r \circ F^{-1} \in LD(I')$ with*

$$I'(y) = \inf_{x\in F^{-1}(y)} I(x).$$

Proposition 7.2.4 *Let Ω' also be a Polish space and $F_r \in C(\Omega, \Omega')$ a sequence converging locally uniformly to F. If $\mu_r \in LD(I)$, then $\mu_r \circ F_r^{-1} \in LD(I')$ with*

$$I'(y) = \inf_{x\in F^{-1}(y)} I(x).$$

Proposition 7.2.5 (Sanov's Theorem) *Assume that $X_1, X_2, \ldots$ are i.i.d. random variables with values in a Polish space E and probability distribution $\mu \in \mathcal{P}(E)$. Denote by d_{W_2} the 2-Wasserstein metric in $\mathcal{P}(E)$. It is well known that $(\mathcal{P}(E), d_{W_2})$ is also a Polish space (see [122, Theorem 6.18, p. 104]).We consider a sequence of probability measures $\mu_r = \frac{1}{r} \sum_{j=1}^{r} \delta_{X_j} \in \mathcal{P}(\mathcal{P}(E))$. Then $\{\mu_r\} \in LD(I)$ with the rate function $I(\cdot) : \mathcal{P}(E) \to [0, \infty]$ defined by*

$$I(\nu) = \begin{cases} D_{KL}(\nu \| \mu), & \text{if } \nu \ll \mu \\ \infty, & \text{else.} \end{cases}$$

Proposition 7.2.6 (Cramér's Theorem) *Assume that $X_1, X_2, \ldots$ are i.i.d. random variables with common distribution ν. Let μ_r be the distribution of the sample mean*

$Y_r = \frac{X_1+\ldots+X_r}{r}$. *Denote by* $\Lambda(\lambda) := \log \mathrm{E}(e^{\lambda X_1})$ *the logarithmic moment generating function associated with* ν *and* $\Lambda^*(x) = \sup_{\lambda\in\mathbb{R}} \{\lambda x - \Lambda(\lambda)\}$ *the Legendre–Fenchel transform of* $\Lambda(\lambda)$. *Then,* $\{\mu_n\} \in LD(\Lambda^*)$.

Example 7.2.1 Here are some illustrative examples for Cramér's and Sanov's theorems (see [101, pp. 144–147]):

1. If the i.i.d. sequence of random variables $\{X_i\}$ are normally distributed with mean μ and variance σ^2, i.e. $X_i \sim \mathbb{N}(\mu, \sigma^2)$, then

$$\Lambda(\lambda) = \mu\lambda + \frac{1}{2}\sigma^2\lambda^2, \quad (\lambda \in \mathbb{R})$$

and

$$\Lambda^*(x) = \frac{(x-\mu)^2}{2\sigma^2}, \quad (x \in \mathbb{R}).$$

It is easy to see that

$$D_{KL}(\mathbb{N}(x,\sigma^2)\|\mathbb{N}(\mu,\sigma^2)) = \int_{\mathbb{R}} \left(\frac{1}{\sqrt{2\pi}\sigma} e^{-\frac{(y-x)^2}{2\sigma^2}}\right) \log \frac{\left(\frac{1}{\sqrt{2\pi}\sigma} e^{-\frac{(y-x)^2}{2\sigma^2}}\right)}{\left(\frac{1}{\sqrt{2\pi}\sigma} e^{-\frac{(y-\mu)^2}{2\sigma^2}}\right)} dy \tag{7.2.1}$$

$$= \int_{\mathbb{R}} \left(\frac{1}{\sqrt{2\pi}\sigma} e^{-\frac{(y-x)^2}{2\sigma^2}}\right) \left(\frac{(y-\mu)^2}{2\sigma^2} - \frac{(y-x)^2}{2\sigma^2}\right) dy \tag{7.2.2}$$

$$= \Lambda^*(x). \tag{7.2.3}$$

2. If the i.i.d. sequence of random variables $\{X_i\}$ are Poisson distributed with parameter $\theta > 0$, i.e. $X_i \sim Poisson(\theta)$, then

$$\Lambda(\lambda) = \theta(e^\lambda - 1), \quad (\lambda \in \mathbb{R})$$

and

$$\Lambda^*(x) = \begin{cases} \theta - x + x\log(\frac{x}{\theta}) & \text{if } x \geq 0, \\ \infty & \text{else.} \end{cases}$$

It is easily seen that

$$D_{KL}(Poisson(x)\|Poisson(\theta)) = \begin{cases} \sum_{k=0}^{\infty} e^{-x}\frac{x^k}{k!}\log\frac{e^{-x}\frac{x^k}{k!}}{e^{-\theta}\frac{\theta^k}{k!}}, & \text{if } x \geq 0 \\ \infty, & \text{else} \end{cases} \tag{7.2.4}$$

$$= \Lambda^*(x). \tag{7.2.5}$$

3. If the i.i.d. sequence of random variables $\{X_i\}$ is Bernoulli distributed with parameter $p \in (0,1)$, i.e. $X_i \sim Bernoulli(p)$, then

$$\Lambda(\lambda) = \log(pe^{\lambda} + 1 - p), \quad (\lambda \in \mathbb{R}),$$

and

$$\Lambda^*(x) = \begin{cases} x\log(\frac{x}{p}) + (1-x)\log(\frac{1-x}{1-p}) & \text{if } x \in [0,1], \\ \infty & \text{else.} \end{cases}$$

It is easy to see that

$$\Lambda^*(x) = D_{KL}(Bernoulli(x)\|Bernoulli(p)).$$

7.3 LDP for a Sequence of τ-Scaled Wright–Fisher Processes

In this section we first show that τ-scaled Wright–Fisher processes are τ-processes, in the terminology of Wentzell [124, p. 20]. We then recall Wentzell's theory for finding an action functional for a sequence of such processes, which immediately yields the rate functional as well as the speed function for the large deviation principle of the sequence. We also briefly mention the techniques of Papangelou in treating the singularity problem on the boundary. Finally we systematically reconstruct minimizers for action functionals for the various Wright–Fisher models.

7.3.1 τ-Processes

We consider here a diploid Wright–Fisher population of N individuals with $n+1$ types of alleles $\{A_0, \ldots, A_n\}$ with mutation and selection. Let the mutation rate from A_i to A_j be γ_{ij} and the fitness for genotype A_iA_j be $1 + \sigma_{ij}$. We denote by Z_m^i the relative frequency of allele A_i at generation m for $i = 0, \ldots, n$ and also write

$\mathbf{Z}_m = (Z_m^1, \ldots, Z_m^n)$. We then have a Markov chain $\{\mathbf{Z}_m\}_{m\in\mathbb{N}_0}$ with the state space

$$\overline{\Delta}_n^{(2N)} := \left\{ (z_1, \ldots, z_n) = \left(\frac{i^1}{2N}, \ldots, \frac{i^n}{2N} \right) : i^1 \in \mathbb{N}_0, \ldots, i^n \in \mathbb{N}_0 \text{ and } \sum_{k=1}^{n} i^k \le 2N \right\},$$

and the transition probability given by

$$\mathrm{P}\left(\mathbf{Z}_{m+1} = \tilde{z} \middle| \mathbf{Z}_m = z \right) = \frac{(2N)!}{(2N\tilde{z}_0)! \ldots (2N\tilde{z}_n)!} \prod_{k=0}^{n} \left(\psi_k^{(ms)}(z) \right)^{j_k}, \quad (z, \tilde{z} \in \overline{\Delta}_n^{(2N)}, m \in \mathbb{N}_0),$$

where $\tilde{z}_0 = 1 - \sum_{k=1}^{n} \tilde{z}_k$ and $\psi_0^{(ms)}(z) = 1 - \sum_{k=1}^{n} \psi_k^{(ms)}(z)$ with

$$\psi_k^{(ms)}(z) = \frac{\psi_k^{(m)}(z) \sum_{l=0}^{n} (1 + \sigma_{kl}) \psi_l^{(m)}(z)}{\sum_{i,j=0}^{n} (1 + \sigma_{ij}) \psi_i^{(m)}(z) \psi_j^{(m)}(z)}, \quad k = 1, \ldots, n \tag{7.3.6}$$

and

$$\psi_k^{(m)}(z) = z_k \left(1 - \sum_{l \neq k} \gamma_{kl} \right) + \sum_{l \neq k} z_l \gamma_{lk}, \quad k = 1, \ldots, n. \tag{7.3.7}$$

Remark This model implies that we allow mutations, and then selection before random sampling with replacements in each generation takes places.

Now, for each $r = 1, 2, \ldots,$ following the method of Papangelou, see for example, [97], we consider its $\frac{1}{r}$-scaled chain, i.e. a time continuous Markov chain $\{X_t^{(r)}\}_{t\ge 0}$ with $X_t^{(r)} = \mathbf{Z}_{[rt]}$. Assume further that mutations and selection are small with order of $\frac{1}{r}$, i.e.

$$\gamma_{ij} = \frac{\theta_{ij}}{r}, \quad \text{and } \sigma_{ij} = \frac{s_{ij}}{r}.$$

Then the transition probability at jumps is

$$P_{x,y} = \mathrm{P}\left(X_{t+\frac{1}{r}} = y \middle| X_t = x \right) = \frac{(2N)!}{(2Ny_0)! \ldots (2Ny_n)!} \prod_{k=0}^{n} \left(\psi_k^{(ms)}(x) \right)^{2Ny_k},$$

$$(x, y \in \overline{\Delta}_n^{(2N)}, t \ge 0)$$

with

$$\psi_i^{(ms)}(x) = x^i + \frac{b^i(x)}{r} + o\left(\frac{1}{r}\right), \tag{7.3.8}$$

where

$$b^i(x) = -\Big(\sum_{j=0}^{n} \theta_{ij}\Big)x^i + \sum_{j=0}^{n} \theta_{ji}x^j + x^i\left(\sum_{j=0}^{n} s_{ij}x^j - \sum_{k,l=0}^{n} s_{kl}x^k x^l\right).$$

This implies that $X_t^{(r)}$ is piecewise constant in $\overline{\Delta}_n^{(2N)}$ with jumps at times $t = \frac{k}{r}$, $k \in \mathbb{N}_0$ and each unit time of the chain $\{X_t^{(r)}\}_t$ is equivalent to r generations in the chain $\{\mathbf{Z}_m\}_m$. These processes $\{X_t^{(r)}\}_t$ are called τ-processes (see [124, p. 20]).

Remark In case of $r = 2N$, it is well known that for $\frac{k_N}{2N} \to t$ as $N \to \infty$, the sequence of discrete Wright–Fisher processes $\left\{X^{(2N)}_{\frac{k_N}{2N}}\right\}$ converges to a Wright–Fisher diffusion process $\{X_t\}_t$ on every bounded set of times as $N \to \infty$.

7.3.2 *Wentzell Theory for τ-Processes*

In this subsection, we fix $T > 0$ and look for the large deviation principle for a sequence of τ-processes $\{X^{(r)}\}_{r\in\mathbf{N}_0}$ with sample paths in $\Lambda([0,T];\Delta_n)$. We recall Wentzell theory (see [124, Chap. 3]) for finding the action functional in the setting of variational problems and derive then the rate functional on the basis of the following remark:

Remark That $a_r S_{0,T}(\cdot) : \Lambda([0,T];\Delta_n) \to [0,\infty]$ is the action functional (see [124, pp. 4–5]) for $\{X^{(r)}\}_{r\in\mathbf{N}_0}$ as $r \to \infty$ is equivalent to $\{X^{(r)}\}_{r\in\mathbf{N}_0}$ satisfying the large deviation principle with a good rate functional $S_{0,T}$ and speed a_r, i.e. $\{X^{(r)}\} \in LD(S_{0,T}, \{a_r\})$.

We start with notation.

$$\Lambda([0,T];\Delta_n) := \{\varphi\colon [0,T] \to \Delta_n \text{ is càdlàg, i.e. paths are right continuous and have left limits}\},$$

$$\Lambda_{p,q}([0,T];\Delta_n) := \{\varphi \in \Lambda([0,T];\Delta_n) : \varphi(0) = p, \varphi(T) = q\},$$

$$\Lambda^{AC}([0,T];\Delta_n) := \{\varphi\colon [0,T] \to \Delta_n : \text{ absolutely continuous}\},$$

$$\Lambda^{AC}_{p,q}([0,T];\Delta_n) := \{\varphi \in \Lambda^{AC}([0,T];\Delta_n) : \varphi(0) = p, \varphi(T) = q\}.$$

From [124, p. 27], we have the definition of the cumulant generating function of a Markov chain:

Definition 7.3.1 For a sequence of Markov chains $\{X_t^{(r)}\}_{t\geq 0}$ in the state spaces

$$\overline{\Delta}_n := \left\{ x = (x^1, \ldots, x^n) \in \mathbb{R}^n_{\geq 0} : \sum_{k=1}^{n} x^k \leq 1 \right\},$$

the *cumulant generating function* is

$$G^r(x, z) = r \log \mathrm{E}_x \left\{ \exp\left[z \cdot \left(X^{(r)}_{\frac{1}{r}} - x \right) \right] \right\}, \quad (x \in \overline{\Delta}_n, z \in \mathbb{R}^n).$$

Therefore,

$$\begin{aligned}
\lim_{r\to\infty} (a_r)^{-1} G^r(x, a_r z) &= \lim_{r\to\infty} (a_r)^{-1} r \log \mathrm{E}_x \left\{ \exp\left[a_r z \cdot \left(X^{(r)}_{\frac{1}{r}} - x \right) \right] \right\} \\
&= \lim_{r\to\infty} \left\{ -rx \cdot z + (a_r)^{-1} r \log \left[\sum_{y \in \overline{\Delta}_n^{(2N)}} \exp\left[a_r z \cdot y \right] P_{x,y} \right] \right\} \\
&= \lim_{r\to\infty} \left\{ -rx \cdot z + (a_r)^{-1} r \log \left[\sum_{y \in \overline{\Delta}_n^{(2N)}} \frac{(2N)!}{(2Ny_0)! \ldots (2Ny_n)!} \left(\psi_0^{(ms)}(x) \right)^{2Ny_0} \right. \right. \\
&\quad \left. \left. \times \prod_{k=1}^{n} \left(e^{\frac{z_k}{r}} \psi_k^{(ms)}(x) \right)^{2Ny_k} \right] \right\} \\
&= \lim_{r\to\infty} \left\{ -rx \cdot z + (a_r)^{-1} r \log \left[\left(\psi_0^{(ms)}(x) + \sum_{k=1}^{n} e^{\frac{z_k}{r}} \psi_k^{(ms)}(x) \right)^{2N} \right] \right\} \\
&= \lim_{r\to\infty} \left\{ -rx \cdot z + r^2 \log \left[1 + \sum_{k=1}^{n} \left(e^{\frac{z_k}{r}} - 1 \right) \psi_k^{(ms)}(x) \right] \right\} \\
&= \frac{1}{2} z \cdot A(x) z + b(x) \cdot z =: G(x, z),
\end{aligned}$$

where

$$A(x) = \left(a^{ij}(x) \right)_{i,j=1}^{n} = \left(x^i (\delta_{ij} - x^j) \right)_{i,j=1}^{n}.$$

The Legendre–Fenchel transform of $G(x, z)$ is

$$H(x,u) = \sup_z [z \cdot u - G(x,z)] = \frac{1}{2}(u - b(x)) \cdot A^{-1}(x)(u - b(x)), \quad (x \in \overline{\Delta}_n, u \in \mathbb{R}^n) \tag{7.3.9}$$

$$= \frac{1}{2}\|u - b(x))\|_g^2, \tag{7.3.10}$$

where we consider the Riemannian manifold (Δ_n, g) with the Fisher information metric

$$g_{ij}(x) = \frac{\delta_{ij}}{x^i} + \frac{1}{x^0}, \quad \text{for } i, j = 1, \ldots d.$$

Then, from the results of Wentzell for τ-processes [124, Theorem 3.2.3', p. 68] as well as techniques of Papangelou for treating the singularity at the boundary (see, e.g., [96]), we obtain the main proposition:

Proposition 7.3.1 *Assume that $a_r = \frac{N}{r} \to \infty$ as $r \to \infty$. Then $a_r S_{0,T}$ is the action functional for $\{X^{(r)}\}_{r \in \mathbf{N}_0}$ as $r \to \infty$, where the normalized action functional $S_{0,T}$ is defined by*

$$\begin{aligned} S_{0,T}(x) &:= \begin{cases} \int_0^T H(x(t), \dot{x}(t))dt & \text{if } x \in \Lambda^{AC}([0,T]; \Delta_n), \\ \infty & \text{otherwise} \end{cases} \\ &= \begin{cases} \frac{1}{2}\int_0^T \|\dot{x}(t) - b(x(t))\|_g^2 dt & \text{if } x \in \Lambda^{AC}([0,T]; \Delta_n), \\ \infty & \text{otherwise.} \end{cases} \end{aligned} \tag{7.3.11}$$

In other words, we have

$$S_{0,T}(x) = -\lim_{\delta \to 0} \lim_{r \to \infty} \frac{r}{N} \log \mathrm{P}\left(|X_t^{(r)} - x(t)| < \delta \text{ for all } t \in [0,T]\right). \tag{7.3.12}$$

Remark

1. Assume that $S_{0,T}$ vanishes at $\hat{x}(\cdot)$, (this also means that $\hat{x}(\cdot)$ is the minimum of $S_{0,T}$) then Eq. (7.3.12) implies that the process $\{X^{(r)}\}$ will asymptotically follow the path $\hat{x}(\cdot)$. This may be considered as *the law of large numbers for paths*.
2. In case $b(x) = 0$, i.e. if there is only random genetic drift, the minimizers of $S_{0,T}$ are precisely the Fisher metric geodesics with constant speed.
3. In case $b(x) = 0$, if we fix endpoints, i.e. sample paths of $\{X^{(r)}\}$ in $\Lambda_{p,q}([0,T]; \Delta_n)$, then, asymptotically, when the path $X^{(r)}(t)$ starts at p and ends at q, then with overwhelming probability, it has followed the shortest geodesic w.r.t. the Fisher metric betweens its start and end point.
4. In case $b(x) = 0$, if we fix the start point at p, we have the following results of Papangelou [99, 100] about the large deviation theory for $\{X_T^{(r)}\}_r$.

Proposition 7.3.2 (Theorem 1 in [100]) *Let K be a closed subset of Δ_n, F a closed subset of $\overline{\Delta}_n$ and G a subset of $\overline{\Delta}_n$ open in the relative topology of $\overline{\Delta}_n$. Then, for any $T > 0$, we obtain $\{X_T^{(r)}\} \in LD(S_{p,T}, \{a_r\}, K)$ with*

$$S_{p,T}(q) = \frac{2}{T}\left[\arccos\left(\sum_{k=0}^{n}\sqrt{p^k q^k}\right)\right]^2.$$

Moreover, when $\lim_{r\to\infty}\frac{a_r}{r} = \infty$, we have the lower estimate for the large deviation on the boundary (see Theorem 8.2.2 in [99]):

Proposition 7.3.3 *Let $T > 0$. If $\lim_{r\to\infty}\frac{a_r}{r} = \infty$, then for every subset $G \subseteq \partial\overline{\Delta}_n$ which is open in $\tau_{\partial\overline{\Delta}_n}$, we have $\{X_T^{(r)}\} \in LD_{l,G}(S_{p,T}, \{a_r\})$.*

7.3.3 Minimum of the Action Functional $S_{p,q}(\cdot)$

In this subsection, we consider $\{X^{(r)}\}_r$ with sample paths $\Lambda_{p,q}([0,T];\Delta_n)$ and would like to find minima for the action functionals $S_{p,q}(\cdot)$ for the various Wright–Fisher models. In general, from the Euler–Lagrange equation, we conclude that if x is an extremal curve, then

$$\begin{aligned} x^k H_{x^k} - H &= g_{ij}(x)\left(\delta_{ik}\dot{x}^i(\dot{x}^j - b^j(x)) + \delta_{jk}\dot{x}^k(\dot{x}^i - b^i(x)) - (\dot{x}^i - b^i(x))(\dot{x}^j - b^j(x))\right) \\ &= g_{ij}(x)(\dot{x}^i\dot{x}^j - b^i(x)b^j(x)) \\ &= \|\dot{x}\|_g^2 - \|b(x)\|_g^2 \\ &= c \quad \text{for some constant } c. \end{aligned} \tag{7.3.13}$$

Remark The geometric idea behind finding the extremal curve is the following. In case of $b(x) = 0$, the extremal curve is simply the geodesic curve with respect to the Fisher information metric. When $b(x)$ does not vanish, the extremal curve is a perturbation of that geodesic curve. More precisely, it is the solution of a *non-homogeneous geodesic equation* in which the non-homogeneous part comes from the evolutionary forces $b(x)$. In one dimension, the variational problem is

$$\begin{cases} \int_0^T H(x(t),\dot{x}(t))dt \to \min & \text{for } x(\cdot) \in \Lambda_{p,q}([0,T];(0,1)), \\ x(0) = p, \quad x(T) = q, \end{cases}$$

where the Lagrangian is

$$H(x,\dot{x}) = \frac{1}{2}g(x)(\dot{x} - b(x))^2$$

with $g(x) = \frac{1}{x(1-x)}$.

The Euler–Lagrange equation can be rewritten in the form

$$2g(x)\Big(\ddot{x} + \Gamma_{11}^1(g(x))\dot{x}^2\Big) = 2b(x)b'(x)g(x) + b^2(x)g'(x), \tag{7.3.14}$$

where $\Gamma_{11}^1(g(x)) = \frac{g'(x)}{2g(x)}$ is the Christoffel force (see Sect. 3.11), the symbol $\cdot$ means a derivative with respect to time t whereas $'$ stands for a derivative with respect to the coordinate x.)

This implies that

$$\begin{aligned}\frac{d}{dt}\Big(\dot{x}^2 g(x)\Big) &= 2\dot{x}\ddot{x}g(x) + \dot{x}^2 g'(x)\dot{x} = 2g(x)\Big(\ddot{x} + \Gamma_{11}^1(g(x))\dot{x}^2\Big)\dot{x} \\ &= \Big(2b(x)b'(x)g(x) + b^2(x)g'(x)\Big)\dot{x} = \frac{d}{dt}\Big(b^2(x)g(x)\Big),\end{aligned}$$

which implies that $\dot{x}^2 g(x) - b^2(x)g(x) = c$ as in Eq. (7.3.13). On the other hand, Eq. (7.3.14) is

$$\ddot{x} + \Gamma_{11}^1(g(x))\dot{x}^2 = b(x)b'(x) + b^2(x)\frac{2x-1}{2x(1-x)} := F(x), \tag{7.3.15}$$

a *non-homogeneous geodesic equation*. It becomes a geodesic equation if $F(x) = 0$, i.e., $b(x) = 0$ or $b(x) = c + \frac{1}{2}\ln x(1-x)$ (the latter case does not occur in population genetics where $b(x)$ should be a polynomial). By the transformation $y = 2\arcsin\sqrt{x}$ (Fisher's angular transformation, see [5]), i.e., $dy = \sqrt{g(x)}dx$ is the Riemannian volume measure with the Fisher information metric, Eq. (7.3.15) is transformed into the simpler form $\ddot{y} = \sqrt{\tilde{g}(y)}\tilde{F}(y) := G(y)$ with $\tilde{g}(y) = g(x)$ and $\tilde{F}(y) = F(x)$.

Two Alleles Case Without Mutations and Selection

In this case we have $n = 1$, $b(x) = 0$ and

$$g(x) = \frac{1}{x} + \frac{1}{1-x} = \frac{1}{x(1-x)}.$$

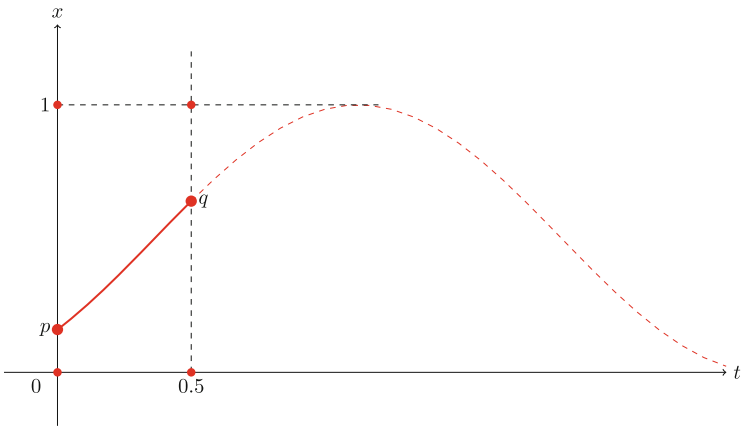

Fig. 7.1 $T = 0.5,\ p = 0.16,\ q = 0.64, x(t) = \sin^2\left((1-2t)\arcsin\sqrt{0.16} + 2t\arcsin\sqrt{0.64}\right)$

It follows from (7.3.13) that each extremal x of $S_{0,T}(x)$ satisfies

$$\frac{\dot{x}(t)^2}{x(t)(1-x(t))} \equiv c, \quad t \in [0,T] \quad \text{(for some constant } c\text{)}.$$

Therefore, by taking the square root on both sides and integrating from 0 to t, we obtain

$$2\arcsin\sqrt{x(s)}\Big|_0^t = \sqrt{c}t.$$

Combining this with the boundary condition $x(0) = p,\ x(T) = q$, we obtain (see Fig. 7.1)

$$x(t) = \sin^2\left(\frac{T-t}{T}\arcsin\sqrt{p} + \frac{t}{T}\arcsin\sqrt{q}\right).$$

Two Alleles Case with One-Way Mutation

In this case we have $n = 1$, $b(x) = -\theta_0 x := \gamma x$, $(\theta_1 = 0)$ and

$$g(x) = \frac{1}{x} + \frac{1}{1-x} = \frac{1}{x(1-x)}.$$

It follows from (7.3.13) that each extremal x of $S_{0,T}(x)$ satisfies

$$\frac{\dot{x}(t)^2 - \gamma^2 x(t)^2}{x(t)(1-x(t))} \equiv c, \quad t \in [0,T] \quad \text{(for some constant } c\text{)}.$$

This implies that

$$\dot{x}(t)^2 = (\gamma^2 - c)x(t)^2 + cx(t) \quad \text{for } t \in [0, T].$$

Now put $g(c, x) = (\gamma^2 - c)x^2 + cx = \gamma^2 x^2 + cx(1-x)$ and, without loss of generality, assume that $p \leq q$. Then, we see that c should be found such that $g(c, x) \geq 0$ for all $x \in [p, q]$. It is easy to see that $c \geq c_0 := \frac{\gamma^2 q}{q-1}$ and $g(c, x) \nearrow \infty$ as $c \to \infty$. Put

$$G(c, x) = \int_p^x \frac{du}{\sqrt{g(c, u)}}.$$

We note that the quantity

$$T = T(p, q, c) = \int_p^q \frac{du}{\sqrt{g(c, u)}} \tag{7.3.16}$$

has nontrivial derivative with respect to c, i.e.

$$\partial_c T = -\frac{1}{2} \int_p^q \frac{u(1-u)du}{g(c, u)^{3/2}} \neq 0.$$

Therefore, there is a unique $\bar{c} = \bar{c}(p, q, T)$ which solves Eq. (7.3.16). For this $\bar{c}$, we define

$$H_{\bar{c}}(x) = \int^x \frac{du}{\sqrt{g(\bar{c}, u)}}.$$

Then we have $t = H_{\bar{c}}(x(t)) - H_{\bar{c}}(p)$ and $T = H_{\bar{c}}(q) - H_{\bar{c}}(p)$, which implies that

$$H_{\bar{c}}(x(t)) = \frac{T-t}{T} H_{\bar{c}}(p) + \frac{t}{T} H_{\bar{c}}(q).$$

Since $\partial_x H_{\bar{c}}(x) = \frac{1}{\sqrt{g(\bar{c}, x)}} > 0$, then $H_{\bar{c}}$ is invertible and we immediately obtain the minimum

$$x(t) = H_{\bar{c}}^{-1}\Big(\frac{T-t}{T} H_{\bar{c}}(p) + \frac{t}{T} H_{\bar{c}}(q)\Big).$$

Remark In the case of two alleles without mutations or selection, $H_{\bar{c}}(x) = 2\arcsin\sqrt{x}$ and $H_{\bar{c}}^{-1}(y) = \sin^2\frac{y}{2}$. Then the minimum curve is

$$\begin{aligned} x(t) &= H_{\bar{c}}^{-1}\Big(\frac{T-t}{T}H_{\bar{c}}(p) + \frac{t}{T}H_{\bar{c}}(q)\Big) \\ &= H_{\bar{c}}^{-1}\Big(\frac{T-t}{T}2\arcsin\sqrt{p} + \frac{t}{T}2\arcsin\sqrt{q}\Big) \\ &= \sin^2\Big(\frac{T-t}{T}\arcsin\sqrt{p} + \frac{t}{T}\arcsin\sqrt{q}\Big). \end{aligned} \tag{7.3.17}$$

Remark The behavior of $x(t)$ will depend on $\bar{c} = \bar{c}(p, q, T)$.

1. If $\bar{c} = \gamma^2$, then the minimum curve is of parabolic type. In this case, the equality (7.3.16) becomes

$$T = \int_p^q \frac{du}{\gamma\sqrt{u}} = \frac{2}{\gamma}(\sqrt{q} - \sqrt{p}). \tag{7.3.18}$$

   This means that if p, q, T satisfy the above relation (7.3.18), then we have $\bar{c} = \gamma^2$ and we easily obtain $H_{\bar{c}}(x) = \frac{2}{\gamma}\sqrt{x}$ and $H_{\bar{c}}^{-1}(y) = \frac{\gamma^2}{4}y^2$.

   This yields the minimum curve

$$\begin{aligned} x(t) &= H_{\bar{c}}^{-1}\Big(\frac{T-t}{T}H_{\bar{c}}(p) + \frac{t}{T}H_{\bar{c}}(q)\Big) \\ &= H_{\bar{c}}^{-1}\Big(\frac{T-t}{T}\frac{2}{\gamma}\sqrt{p} + \frac{t}{T}\frac{2}{\gamma}\sqrt{q}\Big) \\ &= \Big(\frac{T-t}{T}\sqrt{p} + \frac{t}{T}\sqrt{q}\Big)^2, \end{aligned} \tag{7.3.19}$$

   which is of parabolic type (see Fig. 7.2).

2. If $\bar{c} > \gamma^2$, then the minimum curve is of trigonometric (co)sine type. In this case, the equality (7.3.16) becomes

$$\begin{aligned} T &= \int_p^q \frac{du}{\sqrt{-(\bar{c}-\gamma^2)u^2 + \bar{c}u}} \\ &= \frac{1}{\sqrt{\bar{c}-\gamma^2}}\left(\arcsin\Big(\frac{2(\bar{c}-\gamma^2)q}{\bar{c}} - 1\Big) - \arcsin\Big(\frac{2(\bar{c}-\gamma^2)p}{\bar{c}} - 1\Big)\right). \end{aligned} \tag{7.3.20}$$

   Then, we easily obtain

$$H_{\bar{c}}(x) = \frac{1}{\sqrt{\bar{c}-\gamma^2}}\arcsin\left(\frac{2(\bar{c}-\gamma^2)x}{\bar{c}} - 1\right)$$

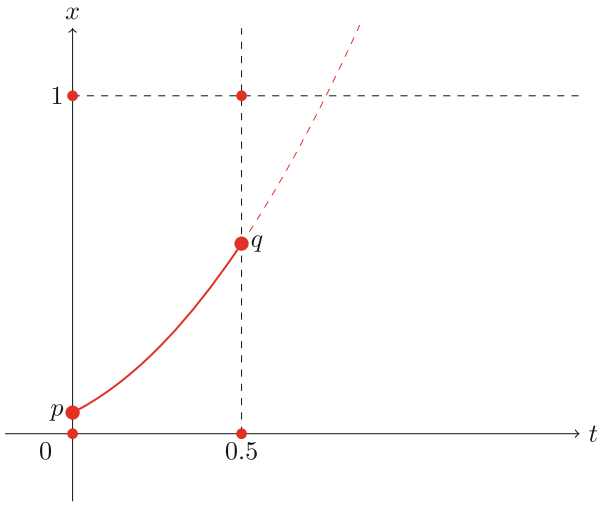

Fig. 7.2 $T = 0.5$, $\gamma = 2$, $\bar{c} = 4 = \gamma^2$, $p = \frac{1}{16}$, $q = \frac{9}{16}$, $x(t) = \left((1-2t)\frac{1}{4} + (2t)\frac{3}{4}\right)^2 = (\frac{1}{4} - t)^2$

and

$$H_{\bar{c}}^{-1}(y) = \frac{\bar{c}}{2(\bar{c}-\gamma^2)}\left(\sin\left(\sqrt{\bar{c}-\gamma^2}y\right) + 1\right)$$

This implies the minimum curve

$$\begin{aligned} x(t) &= H_{\bar{c}}^{-1}\left(\frac{T-t}{T}H_{\bar{c}}(p) + \frac{t}{T}H_{\bar{c}}(q)\right) \\ &= H_{\bar{c}}^{-1}\left(\frac{T-t}{T}\frac{1}{\sqrt{\bar{c}-\gamma^2}}\arcsin\left(\frac{2(\bar{c}-\gamma^2)p}{\bar{c}} - 1\right)\right. \\ &\left. + \frac{t}{T}\frac{1}{\sqrt{\bar{c}-\gamma^2}}\arcsin\left(\frac{2(\bar{c}-\gamma^2)q}{\bar{c}} - 1\right)\right) \\ &= \frac{\bar{c}}{2(\bar{c}-\gamma^2)}\left[1 + \sin\left(\frac{T-t}{T}\arcsin\left(\frac{2(\bar{c}-\gamma^2)p}{\bar{c}} - 1\right)\right.\right. \\ &\left.\left. + \frac{t}{T}\arcsin\left(\frac{2(\bar{c}-\gamma^2)q}{\bar{c}} - 1\right)\right)\right], \end{aligned} \tag{7.3.21}$$

which is of trigonometric (co)sine type (see Fig. 7.3).

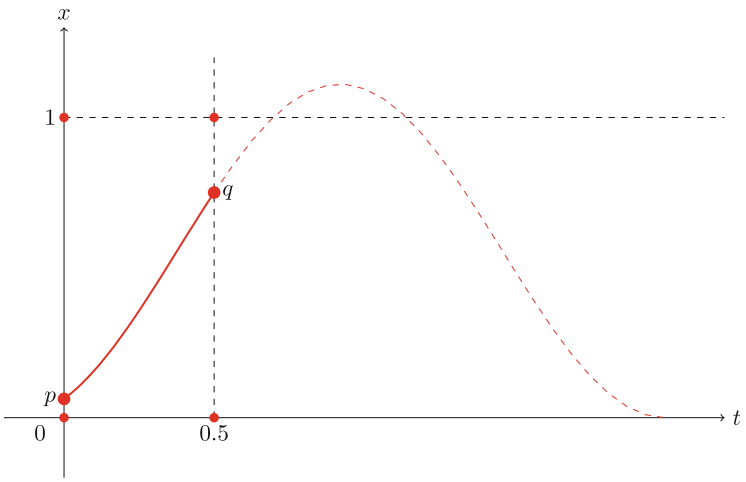

Fig. 7.3 $T = 0.5,\ \gamma = 1,\ \bar{c} = 10 > \gamma^2,\ p = \frac{1}{16},\ q = \frac{3}{4},\ x(t) = \frac{5}{9}\left[1 + \sin\left((1-2t)\arcsin\left(-\frac{71}{80}\right) + 2t\arcsin\left(\frac{7}{20}\right)\right)\right]$

3. If $\bar{c} < \gamma^2$, then the minimum curve is of hyperbolic cosine type. In this case, the equality (7.3.16) becomes

$$\begin{aligned} T &= \int_p^q \frac{du}{\sqrt{(\gamma^2-\bar{c})u^2 + \bar{c}u}} \\ &= \frac{1}{\sqrt{\gamma^2-\bar{c}}}\left(\ln\left(\sqrt{\gamma^2-\bar{c}}q + \frac{\bar{c}}{2\sqrt{\gamma^2-\bar{c}}} + \sqrt{(\gamma^2-\bar{c})q^2 + \bar{c}q}\right)\right. \\ &\quad \left. - \ln\left(\sqrt{\gamma^2-\bar{c}}p + \frac{\bar{c}}{2\sqrt{\gamma^2-\bar{c}}} + \sqrt{(\gamma^2-\bar{c})p^2 + \bar{c}p}\right)\right). \end{aligned} \tag{7.3.22}$$

Then we easily obtain

$$H_{\bar{c}}(x) = \frac{1}{\sqrt{\gamma^2-\bar{c}}}\ln\left(\sqrt{\gamma^2-\bar{c}}x + \frac{\bar{c}}{2\sqrt{\gamma^2-\bar{c}}} + \sqrt{(\gamma^2-\bar{c})x^2 + \bar{c}x}\right)$$

and

$$H_{\bar{c}}^{-1}(y) = \frac{\bar{c}}{2(\gamma^2-\bar{c})}\left(\cosh\left(\sqrt{\gamma^2-\bar{c}}y - \alpha\right) - 1\right),$$

where

$$\alpha = \ln\Big(\frac{\bar{c}}{2\sqrt{\gamma^2-\bar{c}}}\Big).$$

This implies the minimum curve

$$\begin{aligned} x(t) &= H_{\bar{c}}^{-1}\Big(\frac{T-t}{T}H_{\bar{c}}(p) + \frac{t}{T}H_{\bar{c}}(q)\Big) \\ &= H_{\bar{c}}^{-1}\Bigg[\frac{T-t}{T}\frac{1}{\sqrt{\gamma^2-\bar{c}}}\ln\Bigg(\sqrt{\gamma^2-\bar{c}}p + \frac{\bar{c}}{2\sqrt{\gamma^2-\bar{c}}} + \sqrt{(\gamma^2-\bar{c})p^2+\bar{c}p}\Bigg) \\ &\quad + \frac{t}{T}\frac{1}{\sqrt{\gamma^2-\bar{c}}}\ln\Bigg(\sqrt{\gamma^2-\bar{c}}q + \frac{\bar{c}}{2\sqrt{\gamma^2-\bar{c}}} + \sqrt{(\gamma^2-\bar{c})q^2+\bar{c}q}\Bigg)\Bigg] \\ &= \frac{\bar{c}}{2(\gamma^2-\bar{c})}\Bigg[\cosh\Bigg(\frac{T-t}{T}\ln\Big(\sqrt{\gamma^2-\bar{c}}p + \frac{\bar{c}}{2\sqrt{\gamma^2-\bar{c}}} + \sqrt{(\gamma^2-\bar{c})p^2+\bar{c}p}\Big) \\ &\quad + \frac{t}{T}\ln\Big(\sqrt{\gamma^2-\bar{c}}q + \frac{\bar{c}}{2\sqrt{\gamma^2-\bar{c}}} + \sqrt{(\gamma^2-\bar{c})q^2+\bar{c}q}\Big) - \alpha\Bigg) - 1\Bigg], \end{aligned} \tag{7.3.23}$$

which is of hyperbolic cosine type (see Fig. 7.4).

Two Alleles Case with Two-Way Mutation

In this case we have $n = 1$, $b(x) = \theta_1 - (\theta_0+\theta_1)x$ and

$$g(x) = \frac{1}{x} + \frac{1}{1-x} = \frac{1}{x(1-x)}.$$

It follows from (7.3.13) that each extremal x of $S_{0,T}(x)$ satisfies

$$\frac{\dot{x}(t)^2 - \Big(\theta_1 - (\theta_0+\theta_1)x(t)\Big)^2}{x(t)(1-x(t))} \equiv c, \quad t \in [0,T] \quad \text{(for some constant } c\text{)}.$$

It implies that for all $t \in [0,T]$

$$\dot{x}(t)^2 = (\theta_1-(\theta_0+\theta_1)x(t))^2 + cx(t)(1-x(t)) = \big((\theta_0+\theta_1)^2-c\big)x^2 + \big(c-2\theta_1(\theta_0+\theta_1)\big)x + \theta_1^2.$$

Put $g(c,x) = \big((\theta_0+\theta_1)^2-c\big)x^2 + \big(c-2\theta_1(\theta_0+\theta_1)\big)x + \theta_1^2$. Without loss of generality, we assume that $p \le q$. Then, we see that c should be found such that

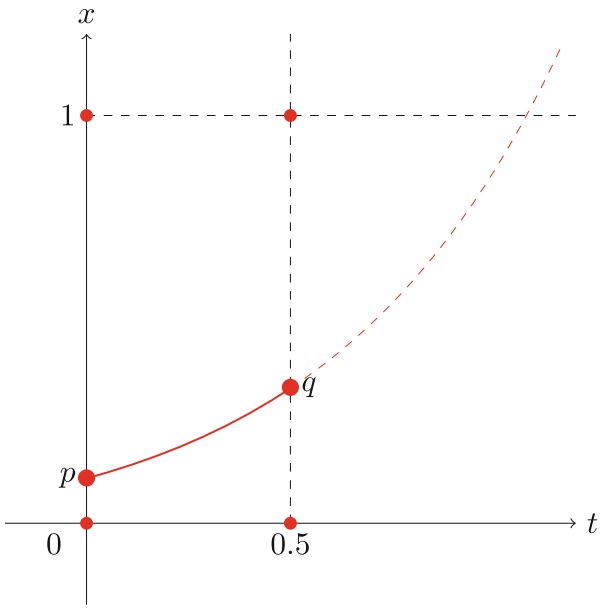

Fig. 7.4 $T = 0.5$, $\gamma = \sqrt{10}$, $\bar{c} = 1 < \gamma^2$, $p = \frac{1}{9}$, $q = \frac{1}{3}$, $x(t) = \frac{1}{18}\left[\cosh\left((1-2t)\ln(\frac{1}{2} + \sqrt{\frac{2}{9}}) + 2t\ln(\frac{7}{6} + \sqrt{\frac{4}{3}}) - \ln\frac{1}{6}\right) - 1\right]$

$g(c,x) \geq 0$ for all $x \in [p,q]$. It is easy to see that $c \geq c_0 := \left(-\frac{(\theta_1-(\theta_0+\theta_1)p)^2}{p(1-p)}\right) \vee \left(-\frac{(\theta_1-(\theta_0+\theta_1)q)^2}{q(1-q)}\right)$ and $g(c,x) \nearrow \infty$ as $c \to \infty$. Put

$$G(c,x) = \int_p^x \frac{du}{\sqrt{g(c,u)}}$$

We note that the quantity

$$T = T(p,q,c) = \int_p^q \frac{du}{\sqrt{g(c,u)}} \tag{7.3.24}$$

has nontrivial derivative with respect to c, i.e.

$$\partial_c T = -\frac{1}{2}\int_p^q \frac{u(1-u)du}{g(c,u)^{3/2}} \neq 0.$$

Therefore there is a unique $\bar{c} = \bar{c}(p, q, T)$ which solves Eq. (7.3.24). For this $\bar{c}$, we define

$$H_{\bar{c}}(x) = \int^{x} \frac{du}{\sqrt{g(\bar{c}, u)}}.$$

Then we have $t = H_{\bar{c}}(x(t)) - H_{\bar{c}}(p)$ and $T = H_{\bar{c}}(q) - H_{\bar{c}}(p)$, which implies that

$$H_{\bar{c}}(x(t)) = \frac{T-t}{T} H_{\bar{c}}(p) + \frac{t}{T} H_{\bar{c}}(q).$$

Because $\partial_x H_{\bar{c}}(x) = \frac{1}{\sqrt{g(\bar{c},x)}} > 0$ then $H_{\bar{c}}$ is invertible and we immediately obtain the minimum

$$x(t) = H_{\bar{c}}^{-1}\Big(\frac{T-t}{T} H_{\bar{c}}(p) + \frac{t}{T} H_{\bar{c}}(q)\Big).$$

Then, the behavior of $x(t)$ will depend on $\bar{c} = \bar{c}(p, q, T)$ and similar to the one-way mutation case, we easily obtain

1. If $\bar{c} = (\theta_0+\theta_1)^2$, then the minimum curve is of linear or parabolic type depending on whether θ_0 is equal to θ_1 or not. In this case, the equality (7.3.24) becomes

$$\begin{aligned} T &= \int_p^q \frac{du}{\sqrt{(\theta_0^2 - \theta_1^2)x + \theta_1^2}} \\ &= \begin{cases} \frac{q-p}{\theta_1}, & \text{if } \theta_0 = \theta_1 \\ \frac{2}{\theta_0^2-\theta_1^2}\Big(\sqrt{(\theta_0^2 - \theta_1^2)q + \theta_1^2} - \sqrt{(\theta_0^2 - \theta_1^2)p + \theta_1^2}\Big), & \text{otherwise} \end{cases} \end{aligned} \tag{7.3.25}$$

Thus, if p, q, T satisfy the above relation (7.3.25), then we have $\bar{c} = (\theta_0+\theta_1)^2$ and we obtain

$$H_{\bar{c}}(x) = \begin{cases} \frac{x}{\theta_1}, & \text{if } \theta_1 = \theta_0 \\ \frac{2}{\theta_0^2-\theta_1^2}\sqrt{(\theta_0^2 - \theta_1^2)x + \theta_1^2}, & \text{otherwise} \end{cases}$$

and

$$H_{\bar{c}}^{-1}(y) = \begin{cases} \theta_1 y, & \text{if } \theta_1 = \theta_0 \\ \frac{\theta_0^2-\theta_1^2}{4} y^2 - \frac{\theta_1^2}{\theta_0^2-\theta_1^2}, & \text{otherwise.} \end{cases}$$

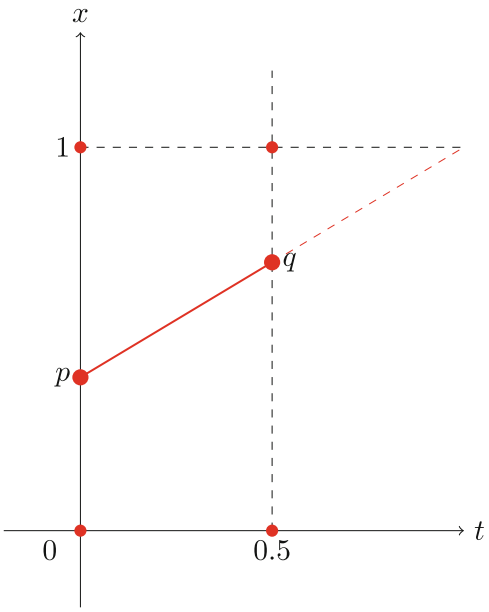

Fig. 7.5 $T = 0.5$, $\theta_0 = \theta_1 = 0.6$, $\bar{c} = 1.44 = (\theta_0 + \theta_1)^2$, $p = 0.4$, $q = 0.7$ [i.e. (p, q, T) satisfy (7.3.25)], $x(t) = (1-2t)0.4 + (2t)0.7 = 0.4 + 0.6t$

It implies the minimum curve

$$x(t) = H_{\bar{c}}^{-1}\Big(\frac{T-t}{T}H_{\bar{c}}(p) + \frac{t}{T}H_{\bar{c}}(q)\Big)$$
$$= \begin{cases} \frac{T-t}{T}p + \frac{t}{T}q, & \text{if } \theta_1 = \theta_0 \\ \frac{1}{\theta_0^2-\theta_1^2}\Big(\frac{T-t}{T}\sqrt{(\theta_0^2-\theta_1^2)p+\theta_1^2} + \frac{t}{T}\sqrt{(\theta_0^2-\theta_1^2)q+\theta_1^2}\Big)^2 - \frac{\theta_1^2}{\theta_0^2-\theta_1^2}, & \text{otherwise} \end{cases} \tag{7.3.26}$$

which is of linear or parabolic type (see Figs. 7.5 and 7.6).

2. If $\bar{c} > (\theta_0 + \theta_1)^2$, then the minimum curve is of trigonometric (co)sine type. In this case, the equality (7.3.24) becomes

$$T = \int_p^q \frac{du}{\sqrt{g(\bar{c}, u)}}$$
$$= \frac{1}{k}\left(\arcsin\frac{kq - \frac{b}{k}}{\sqrt{\frac{b^2}{k^2} + \theta_1^2}} - \arcsin\frac{kp - \frac{b}{k}}{\sqrt{\frac{b^2}{k^2} + \theta_1^2}}\right), \tag{7.3.27}$$

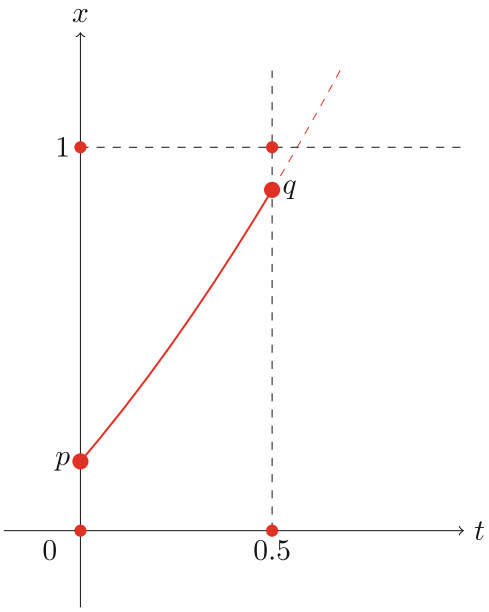

Fig. 7.6 $T = 0.5$, $\theta_1 = 1$, $\theta_0 = \sqrt{3}$, $\bar{c} = (1+\sqrt{3})^2$, $p = \frac{13}{72}$, $q = \frac{8}{9}$ [i.e. (p, q, T) satisfy (7.3.25)], $x(t) = \frac{1}{2}(\frac{7}{6} + t)^2 - \frac{1}{2}$

where

$$k^2 = \bar{c} - (\theta_0 + \theta_1)^2, \quad b = \frac{\bar{c}}{2} - \theta_1(\theta_0 + \theta_1).$$

Then, we easily obtain

$$H_{\bar{c}}(x) = \frac{1}{k} \arcsin \frac{kx - \frac{b}{k}}{\sqrt{\frac{b^2}{k^2} + \theta_1^2}}$$

and

$$H_{\bar{c}}^{-1}(y) = \frac{\sqrt{\frac{b^2}{k^2} + \theta_1^2}}{k} \sin ky + \frac{b}{k^2}.$$

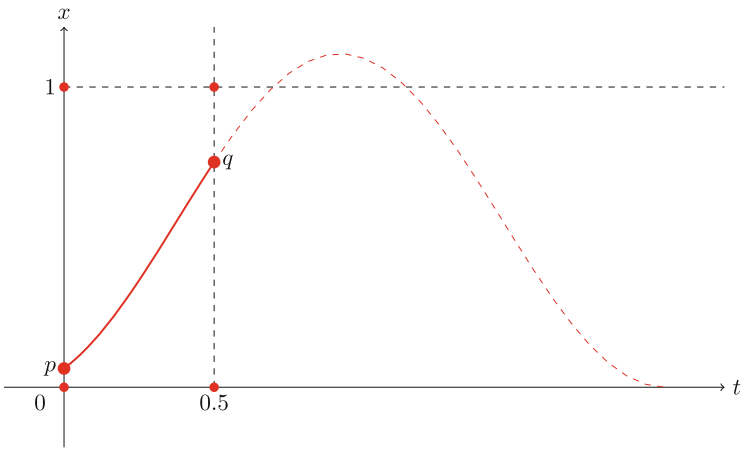

Fig. 7.7 $T = 0.5,\ \gamma = 1,\ \bar{c} = 10 > \gamma^2,\ p = \frac{1}{16},\ q = \frac{3}{4},\ x(t) = \frac{5}{9}\left[1 + \sin\left((1-2t)\arcsin\left(-\frac{71}{80}\right) + 2t\arcsin\left(\frac{7}{20}\right)\right)\right]$

This implies the minimum curve

$$\begin{aligned} x(t) &= H_{\bar{c}}^{-1}\Big(\frac{T-t}{T}H_{\bar{c}}(p) + \frac{t}{T}H_{\bar{c}}(q)\Big) \\ &= H_{\bar{c}}^{-1}\left(\frac{T-t}{T}\frac{1}{k}\arcsin\frac{kp-\frac{b}{k}}{\sqrt{\frac{b^2}{k^2}+\theta_1^2}} + \frac{t}{T}\frac{1}{k}\arcsin\frac{kq-\frac{b}{k}}{\sqrt{\frac{b^2}{k^2}+\theta_1^2}}\right) \\ &= \frac{\sqrt{\frac{b^2}{k^2}+\theta_1^2}}{k}\sin\left(\frac{T-t}{T}\arcsin\frac{kp-\frac{b}{k}}{\sqrt{\frac{b^2}{k^2}+\theta_1^2}} + \frac{t}{T}\arcsin\frac{kq-\frac{b}{k}}{\sqrt{\frac{b^2}{k^2}+\theta_1^2}}\right) + \frac{b}{k^2}, \end{aligned} \tag{7.3.28}$$

which is of trigonometric (co)sine type (see Fig. 7.7).

3. If $\bar{c} < (\theta_0 + \theta_1)^2$, then the minimum curve is of hyperbolic cosine or hyperbolic sine or exponential type depending on $\bar{c}(4\theta_0\theta_1 - c) < 0,\ > 0$ or $= 0$, respectively.

In this case, the equality (7.3.24) becomes

$$\begin{aligned} T &= \int_p^q \frac{du}{\sqrt{g(\bar{c},u)}} \\ &= \frac{1}{k}\Bigg[\ln\left(kq+\frac{b}{k}+\sqrt{\left(kq+\frac{b}{k}\right)^2+\theta_1^2-\frac{b^2}{k^2}}\right) \\ &\quad -\ln\left(kp+\frac{b}{k}+\sqrt{\left(kp+\frac{b}{k}\right)^2+\theta_1^2-\frac{b^2}{k^2}}\right)\Bigg] \end{aligned} \tag{7.3.29}$$

where

$$k^2=(\theta_0+\theta_1)^2-\bar{c},\quad b=\frac{\bar{c}}{2}-\theta_1(\theta_0+\theta_1).$$

Then we easily obtain

$$H_{\bar{c}}(x)=\frac{1}{k}\ln\left(kx+\frac{b}{k}+\sqrt{\left(kx+\frac{b}{k}\right)^2+\theta_1^2-\frac{b^2}{k^2}}\right)$$

and

$$H_{\bar{c}}^{-1}(y)=\begin{cases}\frac{1}{k}\left(e^{\alpha}\cosh(ky-\alpha)-\frac{b}{k}\right) & \text{if } c(\theta_0\theta_1-c)<0,\\ \frac{1}{k}\left(e^{\alpha}\sinh(ky-\alpha)-\frac{b}{k}\right) & \text{if } c(\theta_0\theta_1-c)>0,\\ \frac{1}{2k}e^{ky}-\frac{b}{k^2} & \text{if } c(\theta_0\theta_1-c)=0,\end{cases}$$

where

$$\alpha=\begin{cases}\frac{1}{2}\ln\left(\frac{b^2}{k^2}-\theta_1^2\right) & \text{if } c(\theta_0\theta_1-c)<0,\\ \frac{1}{2}\ln\left(-\frac{b^2}{k^2}+\theta_1^2\right) & \text{if } c(\theta_0\theta_1-c)>0.\end{cases}$$

This implies the minimum curve

$$x(t)=H_{\bar{c}}^{-1}\Big(\frac{T-t}{T}H_{\bar{c}}(p)+\frac{t}{T}H_{\bar{c}}(q)\Big), \tag{7.3.30}$$

which is of hyperbolic cosine type (see Fig. 7.8).

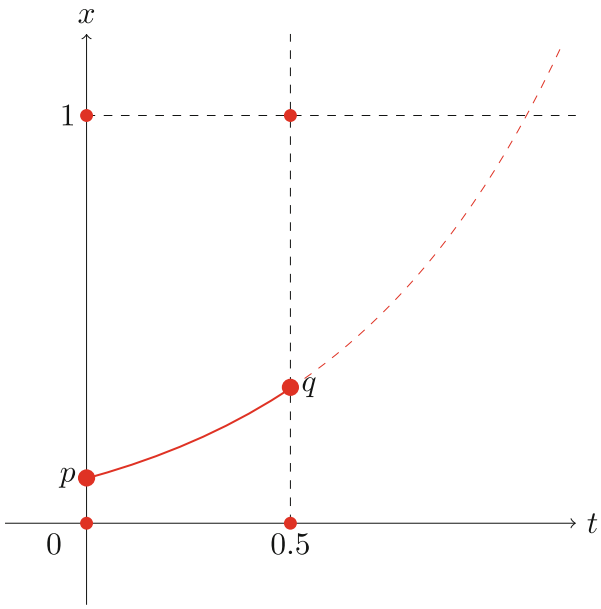

Fig. 7.8 $T = 0.5,\ \gamma = \sqrt{10},\ \bar{c} = 1 < \gamma^2,\ p = \frac{1}{9},\ q = \frac{1}{3},\ x(t) = \frac{1}{18}\left[\cosh\left((1-2t)\ln(\frac{1}{2} + \sqrt{\frac{2}{9}}) + 2t\ln(\frac{7}{6} + \sqrt{\frac{4}{3}}) - \ln\frac{1}{6}\right) - 1\right]$

Chapter 8
The Forward Equation

In this chapter, we treat the Kolmogorov forward equation for the diffusion approximation of the $(n+1)$-allelic 1-locus Wright–Fisher model, without mutation and selection. We recall the basic definitions.

$$L_n u(x,t) := \frac{1}{2}\sum_{i,j=1}^{n} \frac{\partial^2}{\partial x^i \partial x^j}\left(x^i(\delta_j^i - x^j)u(x,t)\right) \tag{8.0.1}$$

is the forward operator (cf. also Sect. 2.9). The Kolmogorov forward equation then is

$$\begin{cases} \frac{\partial}{\partial t}u(x,t) = L_n u(x,t) & \text{in } (\Delta_n)_\infty = \Delta_n \times (0,\infty) \\ u(x,0) = f(x) & \text{in } \Delta_n, f \in L^2(\Delta_n) \end{cases} \tag{8.0.2}$$

for $u(\cdot\,,t) \in C^2(\Delta_n)$ for each fixed $t \in (0,\infty)$ and $u(x,\cdot\,) \in C^1((0,\infty))$ for each fixed $x \in \Delta_n$. Also, we have the backward operator

$$L_n^* u(x,t) \equiv Au(x,t) = \frac{1}{2}\sum_{i,j=1}^{n} a^{ij}(x)\frac{\partial^2}{\partial x^i \partial x^j}u(x,t) + \sum_{i=1}^{n} b^i(x)\frac{\partial}{\partial x^i}u(x,t). \tag{8.0.3}$$

Furthermore, we shall need

$$\omega_k(x) := \prod_{i=0}^{k} x^i = x^1 x^2 \cdots x^k \left(1 - \sum_{j=1}^{k} x^j\right).$$

J. Hofrichter et al., *Information Geometry and Population Genetics*,
Understanding Complex Systems, DOI 10.1007/978-3-319-52045-2_8

8.1 Eigenvalues and Eigenfunctions

We shall start our solution scheme with expansions in terms of the eigenvalues and eigenfunctions of the forward and backward Kolmogorov operators, i.e., of L and L^*. In this section, we shall therefore determine these eigenvalues and eigenfunctions.

For later purposes, we shall present these results not only for the top-dimensional simplex Δ_n, but also for all simplices Δ_k, as these results are the same in all dimensions. In particular, the subsequent formulae will then apply to the various boundary strata $\partial_k \Delta_n$. The corresponding index scheme will be used throughout: n refers to the top-dimensional component (corresponding to $n+1$ alleles in the Wright–Fisher model), whereas for any (specific) boundary stratum of dimension smaller than n, we usually use k.

We shall construct solutions of the forward and backward Kolmogorov equations by the method of separation of variables. That is, we first consider a solution of (4.2.10),

$$u_t = L_k u \quad \text{in } \Delta_k \tag{8.1.1}$$

of the form

$$u(x,t) = X(x)T(t). \tag{8.1.2}$$

This entails

$$\frac{T_t}{T} = \frac{L_k X}{X} = -\lambda\,. \tag{8.1.3}$$

λ then is a constant[1] which is independent of T, X. From Proposition (8.1.4) below, we shall then obtain the local[2] solution of Eq. (8.1.1) as a linear combination

$$u_k(x,t) = \sum_{m=0}^{\infty} \sum_{|\boldsymbol{\alpha}|=m} c_{m,\boldsymbol{\alpha}} X_{m,\boldsymbol{\alpha}}(x) e^{-\lambda_m t},$$

where

$$\lambda_m = \frac{(k+m)(k+m+1)}{2}$$

[1] The convention with the minus sign is used to make the eigenvalues nonnegative, as L_k is a nonpositive operator.

[2] "Local" here means that the boundary conditions are not yet included.

is the eigenvalue of L_k and

$$X_{m,\boldsymbol{\alpha}}(x), \quad |\boldsymbol{\alpha}| = m$$

are the corresponding eigenvectors of L_k. We now enter the details. The reader should be alerted to the fact that the same construction will in fact work on every face of our simplex Δ_k. Later, on each such face, we shall have to compare the process inherited from Δ_k with the corresponding intrinsic process on that face with fewer alleles. We shall subsequently utilize this principle for building up a global solution from the local solutions on Δ_k and on all its faces.

Proposition 8.1.1 *For each multi-index $\boldsymbol{\alpha} = (\alpha^1, \ldots, \alpha^k)$ with $|\boldsymbol{\alpha}| = \alpha^1 + \cdots + \alpha^k = m$, the polynomial of degree m in k variables $x = (x^1, \ldots, x^k)$ in Δ_k*

$$X_{m,\boldsymbol{\alpha}}(x) = x^{\boldsymbol{\alpha}} + \sum_{|\boldsymbol{\beta}|<m} a_{m,\boldsymbol{\beta}} x^{\boldsymbol{\beta}}, \tag{8.1.4}$$

where the $a_{m,\boldsymbol{\beta}}$ are inductively defined by

$$a_{m,\boldsymbol{\alpha}} = 1, \quad a_{m,\boldsymbol{\beta}} = 0, \quad \forall \boldsymbol{\beta} \neq \boldsymbol{\alpha} \text{ with } |\boldsymbol{\beta}| = m,$$

$$a_{m,\boldsymbol{\beta}} = -\frac{\sum_{i=1}^{k} (\beta^i + 2)(\beta^i + 1) a_{m,\boldsymbol{\beta}+e_i}}{(m - |\boldsymbol{\beta}|)(m + |\boldsymbol{\beta}| + 2k + 1)}, \quad \forall |\boldsymbol{\beta}| < m,$$

is an eigenvector of L_k for the eigenvalue $\lambda_m = \frac{(m+k)(m+k+1)}{2}$.

Proof We have

$$\begin{aligned}
LX_{m,\boldsymbol{\alpha}}(x) &= \frac{1}{2} \sum_i \frac{\partial^2}{(\partial x^i)^2} \left[x^i (1 - x^i) \Big(x^{\boldsymbol{\alpha}} + \sum_{|\boldsymbol{\beta}|<m} a_{m,\boldsymbol{\beta}} x^{\boldsymbol{\beta}} \Big) \right] \\
&\quad - \sum_{i \neq j} \frac{\partial^2}{\partial x^i \partial x^j} \left[x^i x^j \Big(x^{\boldsymbol{\alpha}} + \sum_{|\boldsymbol{\beta}|<m} a_{m,\boldsymbol{\beta}} x^{\boldsymbol{\beta}} \Big) \right] \\
&= \frac{1}{2} \sum_i \frac{\partial^2}{(\partial x^i)^2} \left[x^{\boldsymbol{\alpha}+e_i} - x^{\boldsymbol{\alpha}+2e_i} + \sum_{|\boldsymbol{\beta}|<m} a_{m,\boldsymbol{\beta}} x^{\boldsymbol{\beta}+e_i} \right. \\
&\quad \left. - \sum_{|\boldsymbol{\beta}|<m} a_{m,\boldsymbol{\beta}} x^{\boldsymbol{\beta}+2e_i} \right] \\
&\quad - \sum_{i \neq j} \frac{\partial^2}{\partial x^i \partial x^j} \left[x^{\boldsymbol{\alpha}+e_i+e_j} + \sum_{|\boldsymbol{\beta}|<m} a_{m,\boldsymbol{\beta}} x^{\boldsymbol{\beta}+e_i+e_j} \right]
\end{aligned}$$

$$
\begin{aligned}
&= \frac{1}{2}\sum_i \Bigg[(\alpha^i+1)\alpha^i x^{\boldsymbol{\alpha}-e_i} - (\alpha^i+2)(\alpha^i+1)x^{\boldsymbol{\alpha}} \\
&\qquad + \sum_{|\boldsymbol{\beta}|<m} (\beta^i+1)\beta^i a_{m,\boldsymbol{\beta}} x^{\boldsymbol{\beta}-e_i} - \sum_{|\boldsymbol{\beta}|<m} (\beta^i+2)(\beta^i+1)a_{m,\boldsymbol{\beta}}x^{\boldsymbol{\beta}} \Bigg] \\
&\quad - \sum_{i\neq j} \Bigg[(\alpha^i+1)(\alpha^j+1)x^{\boldsymbol{\alpha}} + \sum_{|\boldsymbol{\beta}|<m} (\beta^i+1)(\beta^j+1)a_{m,\boldsymbol{\beta}}x^{\boldsymbol{\beta}} \Bigg] \\
&= \Bigg[-\frac{1}{2}\sum_i (\alpha^i+2)(\alpha^i+1) - \sum_{i\neq j}(\alpha^i+1)(\alpha^j+1) \Bigg] x^{\boldsymbol{\alpha}} \\
&\quad + \frac{1}{2}\sum_i (\alpha^i+1)\alpha^i x^{\boldsymbol{\alpha}-e_i} + \frac{1}{2}\sum_i \sum_{|\boldsymbol{\beta}|<m} (\beta^i+1)\beta^i a_{m,\boldsymbol{\beta}} x^{\boldsymbol{\beta}-e_i} \\
&+ \sum_{|\boldsymbol{\beta}|<m} \Bigg[-\frac{1}{2}\sum_i (\beta^i+2)(\beta^i+1) - \sum_{i\neq j}(\beta^i+1)(\beta^j+1) \Bigg] a_{m,\boldsymbol{\beta}} x^{\boldsymbol{\beta}} \\
&= \Bigg[-\frac{1}{2}\Big(\sum_i \alpha^i + k\Big)\Big(\sum_i \alpha^i + k + 1\Big) \Bigg] x^{\boldsymbol{\alpha}} \\
&\quad + \frac{1}{2}\sum_{|\boldsymbol{\gamma}|<m+1} \sum_i (\gamma^i+1)\gamma^i a_{m,\boldsymbol{\gamma}} x^{\boldsymbol{\gamma}-e_i} \quad (\text{ here } a_{m,\boldsymbol{\gamma}} = 0 \text{ for } |\boldsymbol{\gamma}| = m \text{ and } \boldsymbol{\gamma} \neq \boldsymbol{\alpha}) \\
&+ \sum_{|\boldsymbol{\beta}|<m} \Bigg[-\frac{1}{2}\Big(\sum_i \beta^i + k\Big)\Big(\sum_i \beta^i + k + 1\Big) \Bigg] a_{m,\boldsymbol{\beta}} x^{\boldsymbol{\beta}} \\
&= -\frac{(m+k)(m+k+1)}{2} x^{\boldsymbol{\alpha}} \\
&\quad + \frac{1}{2}\sum_{|\boldsymbol{\beta}|<m} \sum_i (\beta^i+2)(\beta^i+1)a_{m,\boldsymbol{\beta}+e_i} x^{\boldsymbol{\beta}} \\
&- \sum_{|\boldsymbol{\beta}|<m} \frac{(|\boldsymbol{\beta}|+k)(|\boldsymbol{\beta}|+k+1)}{2} a_{m,\boldsymbol{\beta}} x^{\boldsymbol{\beta}}
\end{aligned}
$$

By equating coefficients we obtain the eigenvalue

$$\lambda_m = \frac{(m+k)(m+k+1)}{2}$$

and

$$a_{m,\boldsymbol{\beta}} = -\frac{\sum_{i=1}^{k}(\beta^i+2)(\beta^i+1)a_{m,\boldsymbol{\beta}+e_i}}{(m-|\boldsymbol{\beta}|)(m+|\boldsymbol{\beta}|+2k+1)}, \quad \forall |\boldsymbol{\beta}| < m.$$

This completes the proof. □

Remark For $k = 1$, $X_{m,m}(x^1)$ is the mth Gegenbauer polynomial (up to a constant). Thus, the polynomials $X_{m,\boldsymbol{\alpha}}(x^1, \ldots, x^k)$ can be considered as generalizations of the Gegenbauer polynomials to higher dimensions.

The following propositions describe the relations between the two operators.

Proposition 8.1.2 *If $X \in C^\infty(\Delta_k)$ is an eigenvector of L_k corresponding to λ then $\omega_k X$ is an eigenvector of L_k^* for the same eigenvalue λ.*

Proof Looking for a function ω_k with $L_k^*(\omega_k u) = \omega_k L_k(u)$ (and hence for L_k-eigenfunctions φ consequently $L_k^*(\omega_k \varphi) = \omega_k L_k(\varphi) = \lambda \omega_k \varphi$), we have on the one hand

$$L_k u = -\frac{k(k+1)}{2}u + \sum_i (1-(k+1)x^i)\frac{\partial}{\partial x^i}u + \frac{1}{2}\sum_{i,j} x^i(\delta_j^i - x^j)\frac{\partial}{\partial x^i}\frac{\partial}{\partial x^j}u \tag{8.1.5}$$

and

$$L_k^*(\omega_k u) = \frac{1}{2}\sum_{i,j} x^i(\delta_j^i - x^j)\frac{\partial}{\partial x^i}\frac{\partial}{\partial x^j}u \tag{8.1.6}$$

$$= \frac{1}{2}\sum_{i,j} x^i(\delta_j^i - x^j)\Big(\Big(\frac{\partial}{\partial x^i}\frac{\partial}{\partial x^j}\omega_k\Big)u + 2\frac{\partial}{\partial x^j}\omega_k\frac{\partial}{\partial x^i}u + \omega_k\frac{\partial}{\partial x^i}\frac{\partial}{\partial x^j}u\Big) \tag{8.1.7}$$

on the other hand. Thus, it is sufficient if such a function ω_k satisfies

$$\begin{cases} \sum_{i,j} x^i(\delta_j^i - x^j)\frac{\partial}{\partial x^i}\frac{\partial}{\partial x^j}\omega_k = -k(k+1)\omega_k \\ \sum_j x^i(\delta_j^i - x^j)\frac{\partial}{\partial x^j}\omega_k = (1-(k+1)x^i)\omega_k \quad \text{for all } i, \end{cases} \tag{8.1.8}$$

which is the case for ω_k as can easily be verified by direct computation. □

Proposition 8.1.3 *Let ν be the exterior unit normal vector of the domain Δ_k. Then we have*

$$\sum_j a^{ij}\nu^j = 0 \tag{8.1.9}$$

for each i on the corresponding boundary simplex.

Proof In fact, on the surface $(x^s = 0)$, for some $s \in \{1, \ldots, k\}$ we have $\nu = -e_s$, and hence $\sum_j a^{ij}\nu^j = -a_{is} = -x^s(\delta_{si} - x^i) = 0$. On the surface $(x^0 = 0)$ we have $\nu = \frac{1}{\sqrt{k}}(e_1 + \ldots + e_k)$, hence $\sum_j a^{ij}\nu^j = \frac{1}{\sqrt{k}}\sum_j a^{ij} = \frac{1}{\sqrt{k}}x^i x^0 = 0$. This completes the proof. □

Proposition 8.1.4 *L_k and L_k^* are (formal) adjoints in the sense that*

$$(L_k X, Z) = (X, L_k^* Z) \quad \text{for all } X \in H_k, Z \in H_k^0.$$

Proof We put $F_i(x) := \sum_j \frac{\partial(a^{ij}(x)X(x))}{\partial x^j}$. Since Z vanishes on the boundary of our simplex, we can use the second Green formula and Proposition 8.1.3 to obtain

$$\begin{aligned}
(L_k X, Z) &= \frac{1}{2}\sum_{i,j}\int_{\partial_k\Delta_n} \frac{\partial^2(a^{ij}(x)X(x))}{\partial x^i \partial x^j} Z(x) d\boldsymbol{\lambda}_k(x) \\
&= \frac{1}{2}\sum_i \int_{\partial_k\Delta_n} \frac{\partial F_i(x)}{\partial x^i} Z(x) d\boldsymbol{\lambda}_k(x) \\
&= \frac{1}{2}\sum_i \int_{\partial(\partial_k\Delta_n)} F_i(x)\nu_i Z(x) d\boldsymbol{\lambda}_{k-1}(x) - \frac{1}{2}\sum_i \int_{\partial_k\Delta_n} F_i(x)\frac{\partial Z(x)}{\partial x^i} d\boldsymbol{\lambda}_k(x) \\
&= -\frac{1}{2}\sum_i \int_{\partial_k\Delta_n} F_i(x)\frac{\partial Z(x)}{\partial x^i} d\boldsymbol{\lambda}_k(x) \\
&= -\frac{1}{2}\sum_{i,j} \int_{\partial_k\Delta_n} \frac{\partial(a^{ij}(x)X(x))}{\partial x^j}\frac{\partial Z(x)}{\partial x^i} d\boldsymbol{\lambda}_k(x) \\
&= -\frac{1}{2}\sum_{i,j} \int_{\partial(\partial_k\Delta_n)} a^{ij}(x)\nu_j X(x)\frac{\partial Z(x)}{\partial x^i} d\boldsymbol{\lambda}_{k-1}(x) + \left(X, L_k^* Z\right) \\
&= \left(X, L_k^* Z\right).
\end{aligned} \tag{8.1.10}$$

□

More generally, from the preceding proof, in particular (8.1.10), we obtain

Proposition 8.1.5

$$(L_k X, Y) = (X, L_k^* Y) + \frac{1}{2}\int_{\partial(\partial_k \Delta_n)} YF \cdot \nu d\lambda_{k-1} \quad \text{for all } X, Y \in H_k. \tag{8.1.11}$$

Proposition 8.1.6 *$\{X_{m,\alpha}\}_{m\geq 0,|\alpha|=m}$ is a basis of $L^2(\Delta_k)$ for which the members corresponding to different eigenvalues are orthogonal with respect to the weight ω_k, i.e.,*

$$\left(X_{m,\alpha}, \omega_k X_{j,\beta}\right) = 0, \quad \forall j \neq m, |\alpha| = m, |\beta| = j.$$

Proof The proof is standard. $\{X_{m,\alpha}\}_{m\geq 0,|\alpha|=m}$ is a basis of $L^2(\Delta_k)$ because $\{x^\alpha\}_\alpha$ is a basis of this space. To prove the orthogonality we apply the Propositions 8.1.1, 8.1.2, 8.1.4 (noting that ω_k vanishes on the boundary of Δ_k) as follows

$$\begin{aligned} -\lambda_m \left(X_{m,\alpha}, \omega_k X_{j,\beta}\right) &= \left(L_k X_{m,\alpha}, \omega_k X_{j,\beta}\right) \\ &= \left(X_{m,\alpha}, L_k^*(\omega_k X_{j,\beta})\right) \\ &= -\lambda_j \left(X_{m,\alpha}, \omega_k X_{j,\beta}\right) \end{aligned}$$

Because $\lambda_m \neq \lambda_j$, this finishes the proof. □

Proposition 8.1.7 *The spectra of the operators L_k and L_k^*, where in the latter case we require vanishing boundary values, are*

$$Spec(L_k) = Spec(L_k^*) = \bigcup_{m\geq 0} \left\{ \lambda_m = \frac{(m+k)(m+k+1)}{2} \right\} =: \Lambda_k$$

and the eigenvectors of L_k corresponding to λ_m are linear combinations of the $X_{m,\alpha}$, and those of L_k^* are linear combinations of the $\omega_k X_{m,\alpha}$. Hence, the eigenspace corresponding to λ_m is of dimension $\binom{k+m-1}{k-1}$. In addition, L_k^* possesses the eigenvalue 0 with eigenfunctions 1 and p^i, $i = 1, \ldots, k$.

Proof For L_k, this follows from Proposition 8.1.1 and the fact that the $X_{m,\alpha}$ constitute a basis by Proposition 8.1.3. For L_k^*, this then follows from Proposition 8.1.4. □

From the $\{X_{m,\alpha}\}$, we can then construct a basis $\{Y_{m,\alpha}\}$ of $L^2(\Delta_k)$ of eigenfunctions of L_k for the eigenvalues λ_m with

$$\left(Y_{m,\alpha}, \omega_k Y_{j,\beta}\right) = \begin{cases} 1 & \text{if } m = j, \alpha = \beta, \\ 0 & \text{else.} \end{cases} \tag{8.1.12}$$

Let us summarize the findings of this section. We have obtained all the eigenvalues and eigenvectors of L_k and L_k^*. The idea of the method was quite simple. Since we are taking the partial derivatives w.r.t. x^i and x^j of a function multiplied by $-x^i x^j$, we should expect the eigenfunctions to be polynomials. Moreover, by this simple algebraic observation, we should be able to have any monomial x^α as the leading term. For the lower terms, we then can determine the appropriate coefficients recursively. In particular, since the monomials x^α constitute an L^2-basis of our function space, so then should these eigenfunctions. Thus, we can be sure to find all of them by this method. Moreover, since the problem is invariant under permutations of the alleles, the eigenspaces should be representation spaces for this permutation group. In particular, this yields the multiplicities of the eigenspaces. More simply, the multiplicity of the eigenvalue λ_m can also be obtained by counting how many different monomials there are for degree m in k variables.

Finally, we have observed that the operators L_k and L_k^* are formal adjoints. In fact, in the proof of Proposition 8.1.4, one of the boundary terms arising from integration by parts vanishes because suitable coefficients a^{ij} vanish on the boundary, whereas the other boundary term vanished by assumption. Below, we shall investigate the relationship between these operators for arbitrary boundary values.

As a consequence of our results about the eigenvalues and eigenfunctions of the operators L_k and L_k^*, we can write down local solutions for the forward and backward Kolmogorov equations as expansions in terms of the eigenfunctions. We shall now move on to the construction of global solutions by combining the local solutions in the interior of the simplex Δ_k and on all of its boundary simplices.

8.2 A Local Solution for the Kolmogorov Forward Equation

Knowing the eigenfunctions as constructed in Proposition 8.1.1, it is straightforward to reconstruct the local solution of [14, 80] (for details cf. [113, 118]).

Proposition 8.2.1 *For $n \in \mathbb{N}$ and any initial condition $f \in L^2(\Delta_n)$, the Kolmogorov forward equation corresponding to the diffusion approximation of the n-dimensional Wright–Fisher model (8.0.2) always allows a unique solution u: $(\Delta_n)_\infty \longrightarrow \mathbb{R}$ with $u \in C^\infty(\Delta_n \times (0,\infty))$. Furthermore, this solution (and all its spatial derivatives) may be extended continuously to the boundary $\partial\Delta_n$.*

The regularity, which follows from the regularity of the generalized Gegenbauer polynomials (see the discussion in Sect. A.1, in particular Proposition A.1.1), of course agrees with standard PDE theory (cf. e.g. [72]).

Thus, we know the existence (and uniqueness) of a solution in the interior Δ_n. The more difficult question is the behavior of the process near the boundary. After all, the appropriate inclusion of the boundary in terms of a probability density describing the entire evolution of the process is crucial for a complete account of the model. Thus, we will establish a solution scheme which includes the behavior of the process on the boundary. For this purpose, we have to extend the solution to

the boundary in a regular manner. More precisely, we want an extension of at least class C^2 with respect to the spatial variables. In the interior, we have the regularity result of Proposition 8.2.1. In order to start the investigation of the regularity at the boundary, we observe that by the proposition, the solution and its spatial derivatives extend continuously to $\partial\Delta_n$.

8.3 Moments and the Weak Formulation of the Kolmogorov Forward Equation

The solution of Eq. (8.0.2) in Δ_n lacks conservation properties: As the smallest eigenvalue of L_n is $\lambda_0^{(n)} = \frac{n(n+1)}{2} > 0$, a solution vanishes everywhere in Δ_n for $t \to \infty$, which in particular implies that the total mass and other moments are not preserved. However, again these properties are an important aspect of the validity of the model, and what disappears in the interior of the simplex should accumulate in its boundary. After all, the process should continue after the loss of one or several alleles. We shall therefore introduce a suitable extended solution on the entire $\overline{\Delta}_n$. This solution will be derived from the conservation of the moments of the process.

The moments of the n-dimensional process as obtained as limits of those from the underlying discrete model satisfy the *moment evolution equation*s (2.3.17)

$$\frac{\partial}{\partial t} m_{\boldsymbol{\alpha}}(t) = -\frac{|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1)}{2} m_{\boldsymbol{\alpha}}(t) + \sum_{i=1}^{n} \frac{\alpha_i(\alpha_i-1)}{2} m_{\boldsymbol{\alpha}-e_i}(t), \tag{8.3.13}$$

for $\boldsymbol{\alpha} = (\alpha_1, \ldots, \alpha_n)$, $|\boldsymbol{\alpha}| \geq 1$, whereas $\frac{\partial}{\partial t} m_0(t) = 0$ (with e_i denoting the multi-index $(0, \ldots, 0, 1, 0, \ldots, 0)$ with 1 appearing at the i-th position). These moments can be defined as

$$m_{\boldsymbol{\alpha}}(t) := \left[U, x^{\boldsymbol{\alpha}}\right]_n \equiv \sum_{k=0}^{n} \int_{\partial_k \Delta_n} U(x,t) x^{\boldsymbol{\alpha}} \lambda_k(dx), \tag{8.3.14}$$

for $t \geq 0$, $\boldsymbol{\alpha} = (\alpha_1, \ldots, \alpha_n)$. Here, we utilize the hierarchical product as introduced in Eq. (2.11.21). This now involves an integration over $\overline{\Delta}_n$, that is, including the boundary $\partial\Delta_n$ of the state space, which corresponds to configurations of the model where some allele frequencies may be zero. Correspondingly, the capitalized $U\colon (\overline{\Delta}_n)_\infty \longrightarrow \mathbb{R}$ is introduced as an extended solution which is assumed to be the probability density function of the diffusion approximation of the n-dimensional Wright–Fisher process on the entire $\overline{\Delta}_n$ (thus in particular $U|_{\Delta_n}$ is a solution of the Kolmogorov forward equation (8.0.2) in Δ_n).

We shall now discuss the consistency between the moment evolution equation (8.3.13) and the Kolmogorov backward operator L^* in $\overline{\Delta}_n$ as defined in Eq. (8.0.3); however, the following considerations also hold for a generic product

$[\cdot,\cdot]$: Since L^* has polynomial coefficients, it maps polynomials to polynomials, and we have

$$\begin{aligned} L^*x^{\boldsymbol{\alpha}} &= \frac{1}{2}\sum_{i,j=1}^{n}\left(x^i(\delta_j^i - x^j)\right)\frac{\partial^2}{\partial x^i \partial x^j}x^{\boldsymbol{\alpha}} \\ &= \frac{1}{2}\sum_{i=1}^{n}\alpha_i(\alpha_i-1)(x^{\boldsymbol{\alpha}-e_i}-x^{\boldsymbol{\alpha}}) - \frac{1}{2}\sum_{i\neq j}\alpha_i\alpha_j x^{\boldsymbol{\alpha}} \\ &= \frac{1}{2}\sum_{i=1}^{n}\alpha_i(\alpha_i-1)x^{\boldsymbol{\alpha}-e_i} - \frac{1}{2}|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1)x^{\boldsymbol{\alpha}} \qquad \text{for } x\in\overline{\Delta}_n, \end{aligned} \tag{8.3.15}$$

which yields, using the notation of Eq. (8.3.14),

$$\left[U(t), L_n^* x^{\boldsymbol{\alpha}}\right]_n = \frac{1}{2}\sum_{i=1}^{n}\alpha_i(\alpha_i-1)m_{\boldsymbol{\alpha}-e_i}(t) - \frac{1}{2}|\boldsymbol{\alpha}|(|\boldsymbol{\alpha}|-1)m^{\boldsymbol{\alpha}}(t) \tag{8.3.16}$$

with the right-hand side being equal to that of Eq. (8.3.13). Thus, if the moments equation is satisfied for some probability density function U, we may equivalently write

$$\frac{\partial}{\partial t}m_{\boldsymbol{\alpha}}(t) = \left[\frac{\partial}{\partial t}U(t), x^{\boldsymbol{\alpha}}\right]_n = \left[U(t), L_n^* x^{\boldsymbol{\alpha}}\right]_n \quad \text{for } t\in(0,\infty). \tag{8.3.17}$$

Since the $x^{\boldsymbol{\alpha}}$ generate the space of all polynomials and since the polynomials are dense in C^∞, we therefore also have such relations for arbitrary test functions φ,

$$\left[\frac{\partial}{\partial t}U(t), \varphi\right]_n = \left[U(t), L_n^*\varphi\right]_n \quad \text{for } \varphi\in C^\infty(\overline{\Delta}_n) \text{ and all } t\in(0,\infty). \tag{8.3.18}$$

This is our *weak formulation* of the Kolmogorov forward equation (8.0.2). We may also write the initial condition[3] weakly as

$$\left[U(\cdot,0),\varphi\right]_n = \left[f,\varphi\right]_n \quad \text{for all } \varphi\in C^\infty(\overline{\Delta}_n), \tag{8.3.19}$$

which requires no explicit regularity towards the boundary (yet, we will need that its restriction to interior strata is continuously extendable to the corresponding

[3] As the integration is over $\overline{\Delta}_n$, f may now also be formulated as an extended initial condition on the entire $\overline{\Delta}_n$. Then, $f|_{\partial\Delta_n}\neq 0$ would correspond to the process (partially) already starting on certain boundary strata. However, since there can be flux into the boundary, but not from the boundary into the interior (alleles can get lost, but then cannot reappear), these boundary contributions will not affect our considerations. For this reason, we will usually assume $f|_{\partial\Delta_n}\equiv 0$ or that f is extended that way if it is only given on Δ_n.

boundary). Only, an integrability condition applies, which is $U(\cdot,t), \frac{\partial}{\partial t}U(\cdot,t), f \in L^2\big(\bigcup_{k=0}^n \partial_k \Delta_n\big)$ for $t \geq 0$.

Summarizing our findings, we have:

Lemma 8.3.1 *A function* $U\colon \big(\overline{\Delta}_n\big)_\infty \longrightarrow \mathbb{R}$, $U(\cdot,t), \frac{\partial}{\partial t}U(\cdot,t) \in L^2\big(\bigcup_{k=0}^n \partial_k \Delta_n\big)$ *for* $t \geq 0$ *with corresponding moments* $m_{\boldsymbol{\alpha}}(t) = [U(t), x^{\boldsymbol{\alpha}}]_n$, $\boldsymbol{\alpha} = (\alpha_1, \ldots, \alpha_n)$, $t \geq 0$ *satisfying the moment evolution equation* (8.3.13) *also solves the weak formulation of the Kolmogorov forward equation* (8.3.18) *and conversely.*

8.4 The Hierarchical Solution

The operator L_n^*, if restricted to subsimplices $\Delta_k^{(l)} \cong \Delta_k$ of $\overline{\Delta}_n$ of any dimension k, coincides with the corresponding differential operator L_k^* for that simplex:

Lemma 8.4.1 L_n^* *satisfies*

$$L_n^*\big|_{\Delta_k} = L_k^*. \tag{8.4.1}$$

Proof We consider
$\Delta_k = \Delta_k^{(i_0,\ldots,i_k)} = \{(x^1,\ldots,x^n)\big| x^i > 0 \text{ for } i = i_0,\ldots,i_k,\ x^i = 0 \text{ else};\ \sum_{i=0}^n x^i = 1\}$.

$$\begin{aligned} L_n^*\big|_{\Delta_k} &= \frac{1}{2}\sum_{i,j=1}^n \big(x^i(\delta_j^i - x^j)\big)\frac{\partial^2}{\partial x^i \partial x^j}\Big|_{\Delta_k} \\ &= \frac{1}{2}\sum_{i,j=i_0,\ldots,i_k} \big(x^i(\delta_j^i - x^j)\big)\frac{\partial^2}{\partial x^i \partial x^j} \equiv L_k^* \end{aligned} \tag{8.4.2}$$

□

We may therefore omit the index k in L_k^* whenever convenient.

In contrast, the operator L_n does not satisfy such a restriction property: If restricted to some $\Delta_k = \Delta_k^{(i_0,\ldots,i_k)}$, it does not correspond to L_k, which describes a $(k+1)$-allelic process in Δ_k. We rather have

$$L_n u(x,t) = -\frac{n(n+1)}{2}u(x,t) + \sum_{i=1}^n (1-(n+1)x^i)\frac{\partial}{\partial x^i}u(x,t) + L_n^* u(x,t) \tag{8.4.3}$$

This expanded equation may be interpreted as follows. In order to obtain the boundary relations for L_n, we need to go through the adjoint operator L_N^* which differs from L_n by a first and zero order term. The second order derivatives ($= L_n^*$) then represent the contribution of diffusion, while the first order derivatives may be

interpreted as (directed) drift from the center $\left(\frac{1}{n+1},\dots,\frac{1}{n+1}\right)$ of Δ_n to the boundary. The reaction term $-\frac{n(n+1)}{2}u$ expresses the total loss of mass due to the flux into the boundary (see Proposition 8.1.5). Now restricting Eq. (8.4.3) to some Δ_{n-1} by putting $x^k = 0$ for some k and subtracting the corresponding equation for L_{n-1} on Δ_{n-1}, we obtain

$$(L_n - L_{n-1})u(x,t)\big|_{\Delta_{n-1}} = -nu(x,t) + \sum_{i\neq k}(-x^i)\frac{\partial}{\partial x^i}u(x,t) + \frac{\partial}{\partial x^k}u(x,t). \tag{8.4.4}$$

Thus, a distribution on Δ_{n-1} inherited from the process on the higher-dimensional simplex Δ_n satisfies a different differential equation. On one hand, we see additional first order derivatives, which may be interpreted as the flux from the interior of Δ_n into its boundary part Δ_{n-1}. On the other hand, we have an additional reaction term with the factor $-n$, which arises from the larger number of possibilities to lose an allele in the higher-dimensional solution.

We now wish to construct a global solution by piecing together the local solutions on the various open simplices, from the top-dimensional simplex Δ_n, to the trivial solution at the corners $\Delta_0^{(j)}, j = 0,\dots,n$. We shall utilize the results of Sect. 8.1.

On the basis of (8.3.18), we now explicitly formulate the definition of our solution

Definition 8.4.1 $u \in H$ is a solution of the forward Kolmogorov (or Fokker–Planck) equation associated with the Wright–Fisher model if

$$u_t = L_n u \text{ in } \Delta_n \times (0,\infty), \tag{8.4.5}$$

$$u(x,0) = \delta_{x_0}(x) \text{ in } \Delta_n; \tag{8.4.6}$$

$$[u_t,\varphi]_n = [u, L_n^*\varphi]_n,\ \forall \varphi \in H_n. \tag{8.4.7}$$

In fact, this definition is somewhat redundant, as (8.4.7), the weak formulation (8.3.18) introduced above, already implies (8.4.5). Nevertheless, it might be helpful for understanding the meaning of the definition to include the latter equation explicitly.

We shall make the fundamental ansatz of representing a solution as a superposition of solutions of the form (8.1.3). We can then use the eigenvalues λ and the corresponding eigenfunctions, the generalized Gegenbauer polynomials, determined in Sect. 8.1.

Step 1: We start with the general local solution, i.e., the solution of (8.4.5), on the open simplex Δ_n which by Proposition 8.1.4 [recalling (8.1.12)] is of the form

$$u_n(x,t) = \sum_{m=0}^{\infty}\sum_{|\boldsymbol{\alpha}|=m} c_{m,\boldsymbol{\alpha}}^{(n)} Y_{m,\boldsymbol{\alpha}}^{(n)}(x) e^{-\lambda_m^{(n)} t},$$

with coefficients $c^{(n)}_{m,\boldsymbol{\alpha}}$, where

$$\lambda^{(n)}_m = \frac{(n+m)(n+m+1)}{2}$$

is an eigenvalue of L_n and

$$Y^{(n)}_{m,\boldsymbol{\alpha}}(x), \quad |\boldsymbol{\alpha}| = m$$

are the corresponding eigenvectors of L_n.

For $m \geq 0$, $|\boldsymbol{\beta}| = m$, we conclude from Proposition 8.1.2 that

$$L^*_n\left(\omega_n Y^{(n)}_{m,\boldsymbol{\beta}}\right) = -\lambda^{(n)}_m \omega_n Y^{(n)}_{m,\boldsymbol{\beta}}.$$

It follows that the moment condition

$$[u_t, \omega_n Y^{(n)}_{m,\boldsymbol{\beta}}]_n = \left[u, L^*_n\left(\omega_n Y^{(n)}_{m,\boldsymbol{\beta}}\right)\right]_n$$

is satisfied for the $\omega_n Y^{(n)}_{m,\boldsymbol{\beta}}$, hence for all smooth functions vanishing on the boundary of Δ_n. Therefore, because ω_n vanishes on the boundary,

$$\begin{aligned}(u_n, \omega_n Y^{(n)}_{m,\boldsymbol{\beta}})_n &= (u_n(\cdot,0), \omega_n Y^{(n)}_{m,\boldsymbol{\beta}})_n e^{-\lambda^{(n)}_m t} \\ &= \omega_n(x_0) Y^{(n)}_{m,\boldsymbol{\beta}}(x_0) e^{-\lambda^{(n)}_m t}.\end{aligned}$$

We can thus determine the coefficients by the initial condition. In fact,

$$\begin{aligned}\omega_n(x_0) Y^{(n)}_{m,\boldsymbol{\beta}}(x_0) e^{-\lambda^{(n)}_m t} &= (u_n, \omega_n Y^{(n)}_{m,\boldsymbol{\beta}})_n \\ &= \sum_{|\boldsymbol{\alpha}|=m} c^{(n)}_{m,\boldsymbol{\alpha}} (Y^{(n)}_{m,\boldsymbol{\alpha}}, \omega_n Y^{(n)}_{m,\boldsymbol{\beta}})_n e^{-\lambda^{(n)}_m t},\end{aligned}$$

and hence with (8.1.12)

$$c^{(n)}_{m,\boldsymbol{\alpha}} = \omega_n(x_0) Y^{(n)}_{m,\boldsymbol{\alpha}}(x_0).$$

*S*tep 2: We now make the ansatz for the global solution $u \in H$, i.e., satisfying all the conditions in Definition 8.4.1, in particular (8.4.7),

$$u(x,t) = \sum_{k=0}^{n} u_k(x,t) \chi_{\partial_k \Delta_n}(x). \tag{8.4.8}$$

Here, $\chi_{\partial_k \Delta_n}$ is the characteristic function of $\partial_k \Delta_n$.

We use the condition (8.4.7) to iteratively obtain the values of u_k, $k = n-1, \ldots, 0$. The solution u_n in the interior of the simplex Δ_n is already known from Step 1. We next turn to u_{n-1}, the solution on the $(n-1)$-dimensional faces. For instance, let us consider $u_{n-1}^{(\{0,\ldots,n-1\})}(x^1, \cdots, x^{n-1}, 0, t)$.

We note that, if we choose

$$\varphi(x) = x^1 \cdots x^n Y_{k,\boldsymbol{\beta}}^{(n-1)}(x^1, \ldots, x^{n-1}), \quad |\boldsymbol{\beta}| = k.$$

then $\varphi(x)$ vanishes on all faces except for the face $\Delta_{n-1}^{(\{0,\ldots,n-1\})}$. Therefore,

$$[u, \varphi]_n = (u_n, \varphi)_n + (u_{n-1}^{(\{0,\ldots,n-1\})}, \varphi)_{n-1}. \tag{8.4.9}$$

The left hand side can be calculated easily by the condition (8.4.7)

$$[u_t, \varphi]_n = [u, L_n^*(\varphi)]_n = -\lambda_k^{(n-1)}[u, \varphi]_n. \tag{8.4.10}$$

It follows that

$$[u, \varphi]_n = \varphi(x_0)e^{-\lambda_k^{(n-1)}t}.$$

Since we have already determined u_n, the first part of the right hand side of (8.4.9) is

$$(u_n, \varphi)_n = \sum_{m,\boldsymbol{\alpha}} c_{m,\boldsymbol{\alpha}}^{(n)} \left(\int_{\Delta_n} Y_{m,\boldsymbol{\alpha}}^{(n)}(x)\varphi(x)dx \right) e^{-\lambda_m^{(n)}t}.$$

Therefore we can then determine the coefficients $c_{m,l,\boldsymbol{\alpha}}^{(n-1)}$ in the expansion of $u_{n-1}^{(\{0,\ldots,n-1\})}(x^1, \cdots, x^{n-1}, 0, t)$.

Similarly we shall obtain u_{n-1} on the other faces. Iteratively, we shall obtain all u_k, $k = n-1, \ldots, 0$. Thus, we obtain the global solution

$$\begin{aligned} u(x,t) &= \sum_{k=0}^{n} u_k \chi_{\partial_k \Delta_n}(x) \\ &= \sum_{k=0}^{n} \sum_{m \geq 0} \sum_{l \geq 0} \sum_{|\boldsymbol{\alpha}|=l} c_{m,l,\boldsymbol{\alpha}}^{(k)} Y_{l,\boldsymbol{\alpha}}^{(k)}(x) e^{-\lambda_m^{(k)}t} \chi_{\partial_k \Delta_n}(x). \end{aligned} \tag{8.4.11}$$

By construction, u is a solution of our Kolmogorov forward (Fokker–Planck) equation.

Step 3: This solution is unique. In fact, if u_1, u_2 are two solutions, then $u = u_1 - u_2$ will satisfy

$$\begin{aligned} u_t &= L_n u \text{ in } \Delta_n \times (0,\infty), \\ u(x,0) &= 0 \text{ in } \overline{\Delta}_n; \\ [u_t,\varphi]_n &= [u, L^*\varphi]_n, \ \forall \varphi \in H_n. \end{aligned}$$

It follows that

$$\begin{aligned} [u_t,1]_n &= [u, L_n^*(1)]_n = 0, \\ [u_t,x^i]_n &= [u, L_n^*(x^i)]_n = 0, \\ [u_t,\omega_k^{(\{i_0,\ldots,i_k\})}Y_{j,\boldsymbol{\alpha}}^{(k)}]_n &= [u, L_n^*(\omega_k^{(\{i_0,\ldots,i_k\})}Y_{j,\boldsymbol{\alpha}}^{(k)})]_n \\ &= [u, L_k^*(\omega_k^{(\{i_0,\ldots,i_k\})}Y_{j,\boldsymbol{\alpha}}^{(k)})]_n \\ &= -\lambda_j^{(k)}[u,\omega_k^{(\{i_0,\ldots,i_k\})}Y_{j,\boldsymbol{\alpha}}^{(k)}]_n. \end{aligned}$$

Therefore

$$\begin{aligned} [u,1]_n &= [u(\cdot,0),1]_n = 0, \\ [u,x^i]_n &= [u(\cdot,0),x^i]_n = 0, \\ [u,\omega_k^{(\{i_0,\ldots,i_k\})}Y_{j,\boldsymbol{\alpha}}^{(k)}\chi_{\Delta_k^{(\{i_0,\ldots,i_k\})}}]_n &= [u(\cdot,0),\omega_k^{(\{i_0,\ldots,i_k\})}Y_{j,\boldsymbol{\alpha}}^{(k)}\chi_{\Delta_k^{(\{i_0,\ldots,i_k\})}}]_n e^{-\lambda_j^{(k)}t} = 0. \end{aligned}$$

Since $\left\{1, \{x^i\}_i, \{\omega_k^{(\{i_0,\ldots,i_k\})}Y_{j,\boldsymbol{\alpha}}^{(k)}\chi_{\Delta_k^{(\{i_0,\ldots,i_k\})}}\}_{1\le k\le n,\{i_0,\ldots,i_k\},j\ge 0,|\boldsymbol{\alpha}|=j}\right\}$ is also a basis of H_n it follows that $u = 0 \in H$.

In conclusion, we have established

Theorem 8.4.1 *The forward Kolmogorov (Fokker Planck) equation associated with the Wright–Fisher model with $n+1$ alleles possesses the unique solution*

$$\begin{aligned} u(x,t) &= \sum_{k=0}^{n} u_k \chi_{\partial_k \Delta_n}(x) \\ &= \sum_{k=0}^{n}\sum_{m\ge 0}\sum_{l\ge 0}\sum_{|\boldsymbol{\alpha}|=l} c_{m,l,\boldsymbol{\alpha}}^{(k)} Y_{l,\boldsymbol{\alpha}}^{(k)}(x) e^{-\lambda_m^{(k)}t}\chi_{\partial_k\Delta_n}(x). \end{aligned} \tag{8.4.12}$$

8.5 The Boundary Flux and a Hierarchical Extension of Solutions

We shall now investigate the flux from the interior into the boundary in more detail. This will also yield an alternative proof of the existence and uniqueness of a global solution of the Kolmogorov forward equation.

In order to construct suitable boundary values as required for an extended solution $U\colon (\overline{\Delta}_n)_\infty \longrightarrow \mathbb{R}$, we shall now introduce the concept of the boundary flux. The investigation of the boundary flux as the basis for a hierarchical solution scheme is the main technical contribution of this chapter.

The flux $G_u\colon (\Delta_n)_\infty \longrightarrow \mathbb{R}^n$ of a solution $u\colon (\Delta_n)_\infty \longrightarrow \mathbb{R}^n$ of Eq. (8.0.2) is given in terms of its components

$$G_u^i(x,t) := -\frac{1}{2}\sum_{j=1}^n \frac{\partial}{\partial x^j}(x^j(\delta_j^i - x^j)u(x,t)) = -\frac{1}{2}\sum_{j=1}^n \frac{\partial}{\partial x^j}(a^{ij}u(x,t)), \quad i = 1,\dots,n. \tag{8.5.13}$$

Again, this concept directly extends to boundary strata of $\overline{\Delta}_n$ if u is extendable to the boundary such that the extension is of class C^2 with respect to the spatial variables (which is the case for a solution as in Proposition 8.2.1).

The boundary flux is related to the Kolmogorov forward operator via

$$\operatorname{div} G_u = \sum_{i=1}^n \frac{\partial}{\partial x^i} G_u^i = -L_n u = -u_t, \tag{8.5.14}$$

and therefore, it shall naturally appear in integration by parts formulae. In particular, we can now extend the adjointness relation for the Kolmogorov operators L_n and L_n^* of Proposition 8.1.4 to the case of non-vanishing boundary terms.

Proposition 8.5.1 *For $n \in \mathbb{N}_+$ and $u, \varphi \in C^2(\overline{\Delta}_n)$, we have*

$$(L_n u, \varphi)_n = -\int\limits_{\partial_{n-1}\Delta_n} \varphi\, G_u \cdot \nu \, d\lambda_{n-1} + (u, L_n^*\varphi)_n \tag{8.5.15}$$

where $(.,.)_n$ is the L^2-product (see (2.11.20)), G_u is the boundary flux of u and ν is the outward unit normal vector to $\partial\Delta_n$.

Proof For a domain Ω with piecewise continuous boundary $\partial\Omega$ and $u, \varphi \in C^1(\overline{\Omega})$, we have the integration by parts formula

$$\int\limits_\Omega \frac{\partial u}{\partial x^i}\varphi \, d\Omega = \int\limits_{\partial\Omega} \varphi u \, \nu^i \, d\partial\Omega - \int\limits_\Omega u\frac{\partial \varphi}{\partial x^i}\, d\Omega, \tag{8.5.16}$$

where ν^i is the i-th component of the outward unit normal vector to $\partial\Omega$. This yields

$$\begin{aligned}(L_n u, \varphi)_n &= -\int_{\Delta_n} \sum_i \frac{\partial}{\partial x^i} G_u^i \varphi \, d\boldsymbol{\lambda}_n \\ &= -\int_{\partial\Delta_n} \sum_i G_u^i \nu^i \varphi \, d\boldsymbol{\lambda}_{n-1} + \int_{\Delta_n} \sum_i G_u^i \frac{\partial}{\partial x^i} \varphi \, d\boldsymbol{\lambda}_n. \end{aligned} \tag{8.5.17}$$

Since $\bigcup_{k=0}^{n-2} \partial_k \Delta_n$ is a null set with respect to $\boldsymbol{\lambda}_{n-1}$, it suffices to evaluate the boundary integral on $\partial_{n-1}\Delta_n$. We then integrate the last term once more by parts (again, with a boundary integral on $\partial_{n-1}\Delta_n$):

$$\begin{aligned}\int_{\Delta_n} \sum_i G_u^i \frac{\partial}{\partial x^i} \varphi \, d\boldsymbol{\lambda}_n = &- \int_{\partial_{n-1}\Delta_n} \frac{1}{2} \sum_{i,j} x^i (\delta_j^i - x^j) u \nu^j \frac{\partial}{\partial x^i} \varphi \, d\boldsymbol{\lambda}_{n-1} \\ &+ \int_{\Delta_n} \frac{1}{2} \sum_{i,j} a^{ij} u \frac{\partial^2}{\partial x^i \partial x^j} \varphi \, d\boldsymbol{\lambda}_n. \end{aligned} \tag{8.5.18}$$

We have $\partial_{n-1}\Delta_n = \bigcup_{l=0}^{n} \Delta_{n-1}^{(I_n \setminus \{l\})}$, and $\nu^j = -\delta_l^j$ on $\Delta_{n-1}^{(I_n \setminus \{l\})}$, $l = 1, \ldots, n$ and $\nu^j = \frac{1}{\sqrt{n}}$ on $\Delta_{n-1}^{(I_n \setminus \{0\})}$, which yields

$$\sum_j x^i (\delta_j^i - x^j) u \nu^j = -x^i (\delta_l^i - x^l) u = 0 \qquad \text{on } \Delta_{n-1}^{(I_n \setminus \{l\})} = \{x^l = 0\} \tag{8.5.19}$$

and

$$\begin{aligned}\sum_j x^i (\delta_j^i - x^j) u \nu^j &= \frac{1}{\sqrt{n}} \sum_j x^i (\delta_j^i - x^j) u \\ &= \frac{1}{\sqrt{n}} x^i \Big(1 - \sum_j x^j\Big) u = 0 \quad \text{on } \Delta_{n-1}^{(I_n \setminus \{0\})} = \Big\{1 - \sum_j x^j = 0\Big\}. \end{aligned} \tag{8.5.20}$$

Thus, the boundary integral in (8.5.18) vanishes. From (8.5.17) and (8.5.18), we therefore obtain

$$(L_n u, \varphi)_n = -\int\limits_{\partial_{n-1}\Delta_n} \sum_i G_u^i \nu^i \varphi \, d\boldsymbol{\lambda}_{n-1} + \int\limits_{\Delta_n} u \frac{1}{2} \sum_{i,j} a^{ij} \frac{\partial^2}{\partial x^i \partial x^j} \varphi \, d\boldsymbol{\lambda}_n \tag{8.5.21}$$

$$= -\int\limits_{\partial_{n-1}\Delta_n} G_u \cdot \nu \varphi \, d\boldsymbol{\lambda}_{n-1} + (u, L_n^* \varphi)_n.$$

□

We now want to integrate (8.5.15) over time. If $\varphi\colon \overline{\Delta}_n \longrightarrow \mathbb{R}$ is a polynomial of degree less than 2, we have $L^*\varphi = 0$. Integrating the flux G_u on $\partial_{n-1}\Delta_n$ over time as boundary values for a solution u of Eq. (8.0.2) (resp. for its continuous extension to $\partial\Delta_n$), Proposition 8.5.1 already yields the behavior for the 0th and the 1st moment which is prescribed by the moment evolution equation (8.3.14). Thus, the total mass and the expectation value of the process are preserved.

This concept of a solution in Δ_n plus accumulated flux on the boundary $\partial_{n-1}\Delta_n$, however, does not yet suffice for our purposes. It does not yield the desired evolution laws for moments of degree 2 or higher, nor does $\partial_{n-1}\Delta_n$ account for the full boundary $\partial\Delta_n$. To resolve this, instead of accumulating the incoming flux on $\partial_{n-1}\Delta_n$ for $n \geq 2$ statically, we assume that it rather evolves as if it were an $(n-1)$-dimensional Wright–Fisher process, i.e. as a subsolution on $\partial_{n-1}\Delta_n$. We therefore consider the boundary flux on the next lower strata, that is, on $\partial_{n-2}\Delta_{n-1}$. We then iterate the construction to go down to lower and lower dimensional strata. This leads us to

Definition 8.5.1 For $\Delta_n^{(I_n)}$ with $I_n = \{0, 1, \ldots, n\}$ and a solution $u\colon \left(\Delta_n^{(I_n)}\right)_\infty \longrightarrow \mathbb{R}$ of the Kolmogorov forward equation (8.0.2) for given $f\colon \Delta_n^{(I_n)} \longrightarrow \mathbb{R}$ as in Proposition 8.2.1, a *hierarchical extension*

$$U\colon \left(\overline{\Delta_n^{(I_n)}}\right)_\infty \longrightarrow \mathbb{R} \quad \text{with} \quad U(x,t) := \sum_{k=0}^{n} U_k(x,t) \chi_{\partial_k \Delta_n^{(I_n)}}(x) \tag{8.5.22}$$

is given by

$$U_k\colon \left(\partial_k \Delta_n^{(I_n)}\right)_\infty \longrightarrow \mathbb{R} \quad \text{with} \quad U_k(x,t) := \begin{cases} u(x,t) & \text{for } x \in \Delta_n^{(I_n)} \equiv \partial_n \Delta_n^{(I_n)} \\ U_{k,I_k}(x,t) & \text{for } x \in \Delta_k^{(I_k)} \subset \partial_k \Delta_n^{(I_n)}, I_k \subset I_n \\ 0 & \text{else} \end{cases} \tag{8.5.23}$$

for all $0 \leq k \leq n$ and

$$U_{k,I_k}\colon \left(\Delta_k^{(I_k)}\right)_\infty \longrightarrow \mathbb{R} \quad \text{with} \quad U_{k,I_k}(x,t) := \int_0^t u_{k,I_k}^\tau(x,t-\tau)\,d\tau \tag{8.5.24}$$

for $0 \leq k \leq n-1$ and for all subsets $I_k \subset I_n$. Here, $u_{k,I_k}^\tau(x,t)\colon \left(\Delta_k^{(I_k)}\right)_\infty \longrightarrow \mathbb{R}$ is a solution of

$$\begin{cases} L_k u(x,t) = \frac{\partial}{\partial t}u(x,t) & (x,t) \in \left(\Delta_k^{(I_k)}\right)_\infty \\ u(x,0) = \sum_{I_{k+1}\supset I_k} G^\perp_{U_{k+1,I_{k+1}}}(x,\tau) & x \in \Delta_k^{(I_k)} \end{cases} \tag{8.5.25}$$

for all $\tau > 0$ as in Proposition 8.2.1 and $G^\perp_{U_{k+1,I_{k+1}}}$ is the normal component of the flux of the continuous extension of $U_{k+1,I_{k+1}}$ to $\overline{\Delta_{k+1}^{(I_{k+1})}}$.

Remark 8.5.1 It is important to realize that for a solution u of Eq. (8.0.2), the induced boundary functions U_k on $\partial_k\Delta_n^{(I_n)}$ for $0 \leq k \leq n-1$ in general do not satisfy the equation $\frac{\partial}{\partial t}U_k = L_k U_k$ in some $\Delta_k^{(I_k)} \subset \partial_k\Delta_n^{(I_n)}$ and therefore are not solutions of the corresponding k-dimensional problem (8.0.2) in $\Delta_k^{(I_k)}$. This equation is an intrinsic equation on $\Delta_k^{(I_k)} \subset \partial_k\Delta_n^{(I_n)}$, but the U_k here contain not only intrinsic contributions of those boundary strata, but also include what flows in from higher dimensional strata.

8.6 An Application of the Hierarchical Scheme

For the hierarchically extended solution and the product $[\cdot,\cdot]_n$, we may now continue the line of reasoning of Propositions 8.1.4 and 8.5.1.

Proposition 8.6.1 *A hierarchical extension* $U\colon \left(\overline{\Delta_n^{(I_n)}}\right)_\infty \longrightarrow \mathbb{R}$ *(cf. Definition 8.5.1) of a solution* u *of the Kolmogorov forward equation* (8.0.2) *in* Δ_n *satisfies the weak formulation (8.3.18), that is,*

$$\left[\frac{\partial}{\partial t}U(t),\varphi\right]_n = \left[U(t),L^*\varphi\right]_n \tag{8.6.26}$$

for $\varphi \in C^\infty\left(\overline{\Delta_n^{(I_n)}}\right)$ *and for all* $t \in (0,\infty)$.

Proof By Proposition 8.5.1 we have for $U_n \equiv u$ and arbitrary $\varphi \in C^\infty\big(\overline{\Delta_n^{(I_n)}}\big)$

$$\left(\frac{\partial}{\partial t}U_n, \varphi\right)_n = \big(L_n U_n, \varphi\big)_n = -\int\limits_{\partial_{n-1}\Delta_n^{(I_n)}} \varphi\, G_{U_n}^{\perp}\, d\boldsymbol{\lambda}_{n-1} + \big(U_n, L_n^*\varphi\big)_n \tag{8.6.27}$$

with $G_{U_n}^{\perp} = G_{U_n} \cdot \nu$ denoting the (normal) flux of the continuous extension of U_n to $\partial_{n-1}\Delta_n^{(I_n)}$. The boundary integral may be expressed in terms of the evolution of the boundary function U_{n-1} that lives on $\partial_{n-1}\Delta_n^{(I_n)}$. As this implies a hierarchical dependence on the particular subprocesses, we directly start our consideration for arbitrary $k \in \{1, \ldots, n\}$. Then we have by Proposition 8.5.1 and for all $I_k \subset I_n$

$$\int\limits_{\Delta_k^{(I_k)}} (L_k U_{k,I_k})\varphi\, d\boldsymbol{\lambda}_k = -\int\limits_{\partial_{k-1}\Delta_k^{(I_k)}} \varphi\, G_{U_{k,I_k}}^{\perp}\, d\boldsymbol{\lambda}_{k-1} + \int\limits_{\Delta_k^{(I_k)}} U_{k,I_k} L_k^*\varphi\, d\boldsymbol{\lambda}_k \tag{8.6.28}$$

where $G_{U_{k,I_k}}$ again denotes the flux of the continuous extension of U_{k,I_k} to $\partial_{k-1}\Delta_k^{(I_k)}$ (not to be confused with the proper boundary function U_{k-1} on $\partial_{k-1}\Delta_n^{(I_n)}$). In order to account for the whole k-dimensional boundary $\partial_k\Delta_n^{(I_n)}$ of $\Delta_n^{(I_n)}$, we simply sum over all $\Delta_k^{(I_k)} \subset \partial_k\Delta_n^{(I_n)}$ resp. all subsets $I_k \subset I_n$. This yields (because of $\bigcup_{I_k \subset I_n} \Delta_k^{(I_k)} = \partial_k\Delta_n^{(I_n)}$ and the definition of U_k)

$$\int\limits_{\partial_k\Delta_n^{(I_n)}} (L_k U_k)\varphi\, d\boldsymbol{\lambda}_k = \sum_{I_k \subset I_n} \int\limits_{\partial_{k-1}\Delta_k^{(I_k)}} \varphi\, G_{U_{k,I_k}}^{\perp}\, d\boldsymbol{\lambda}_{k-1} + \int\limits_{\partial_k\Delta_n^{(I_n)}} U_k L_k^*\varphi\, d\boldsymbol{\lambda}_k. \tag{8.6.29}$$

Transforming the boundary term using $\bigcup_{I_k \subset I_n} \partial_{k-1}\Delta_k^{(I_k)} = \bigcup_{I_{k-1} \subset I_n} \Delta_{k-1}^{(I_{k-1})}$ and employing the product notation, we get

$$\big(L_k U_k, \varphi\big)_k = \sum_{I_{k-1} \subset I_n} \int\limits_{\Delta_{k-1}^{(I_{k-1})}} \varphi \sum_{I_k \supset I_{k-1}} G_{U_{k,I_k}}^{\perp}\, d\boldsymbol{\lambda}_{k-1} + \big(U_k, L_k^*\varphi\big)_k. \tag{8.6.30}$$

Now, the sum of fluxes appearing here may be expressed in terms of the evolution of the associated boundary function $U_{k-1,I_{k-1}}$ on $\Delta_{k-1}^{(I_{k-1})}$ for every $I_{k-1} \subset I_n$. By the

chain rule, we have on $\Delta_{k-1}^{(I_{k-1})}$

$$\begin{aligned}\frac{\partial}{\partial t}U_{k-1,I_{k-1}}(x,t) &= \frac{\partial}{\partial t}\int_0^t u^\tau_{k-1,I_{k-1}}(x,t-\tau)\,d\tau \\ &= u^\tau_{k-1,I_{k-1}}(x,t-\tau)\big|_{\tau=t} + \int_0^t \frac{\partial}{\partial t}u^\tau_{k-1,I_{k-1}}(x,t-\tau)\,d\tau \\ &= u^t_{k-1,I_{k-1}}(x,0) + \int_0^t L_{k-1}u^\tau_{k-1,I_{k-1}}(x,t-\tau) \qquad (8.6.31)\end{aligned}$$

by the solution property of $u^\tau_{k-1,I_{k-1}}$. Interchanging L_{k-1} with the τ-integration and substituting $u^t_{k-1,I_{k-1}}(x,0)$ by the initial values as prescribed altogether yields

$$-\sum_{I_k\supset I_{k-1}} G^\perp_{U_{k,I_k}}(x,t) = -\frac{\partial}{\partial t}U_{k-1,I_{k-1}}(x,t) + L_{k-1}U_{k-1,I_{k-1}}(x,t). \qquad (8.6.32)$$

Multiplying this with φ, integrating over $\Delta_{k-1}^{(I_{k-1})}$ and summing over all $I_{k-1}\subset I_n$ results in

$$\begin{aligned}&-\sum_{I_{k-1}\subset I_n}\int_{\Delta_{k-1}^{(I_{k-1})}} \varphi \sum_{I_k\supset I_{k-1}} G^\perp_{U_{k,I_k}}\,d\boldsymbol{\lambda}_{k-1} \\ =&-\sum_{I_{k-1}\subset I_n}\int_{\Delta_{k-1}^{(I_{k-1})}} \varphi\,\frac{\partial}{\partial t}U_{k-1,I_{k-1}}\,d\boldsymbol{\lambda}_{k-1} + \sum_{I_{k-1}\subset I_n}\int_{\Delta_{k-1}^{(I_{k-1})}} \varphi\,L_{k-1}U_{k-1,I_{k-1}}\,d\boldsymbol{\lambda}_{k-1} \\ =&-\left(\frac{\partial}{\partial t}U_{k-1},\varphi\right)_{k-1} + \left(L_{k-1}U_{k-1},\varphi\right)_{k-1} \qquad (8.6.33)\end{aligned}$$

because of $\bigcup_{I_{k-1}\subset I_n}\Delta_{k-1}^{(I_{k-1})} = \partial_{k-1}\Delta_n^{(I_n)}$. Combining this with Eq. (8.6.30), we get

$$\left(L_kU_k,\varphi\right)_k = -\left(\frac{\partial}{\partial t}U_{k-1},\varphi\right)_{k-1} + \left(L_{k-1}U_{k-1},\varphi\right)_{k-1} + \left(U_k,L_k^*\varphi\right)_k, \qquad (8.6.34)$$

which—by assumption—holds for all $k \in \{1, \dots, n\}$. Hence, this formula may be iterated over k, yielding

$$\begin{aligned} & \left(\frac{\partial}{\partial t} U_n, \varphi\right)_n = \left(L_n U_n, \varphi\right)_n \\ \Leftrightarrow \quad & \left(\frac{\partial}{\partial t} U_n, \varphi\right)_n + \left(\frac{\partial}{\partial t} U_{n-1}, \varphi\right)_{n-1} = \left(U_n, L_n^* \varphi\right)_n + \left(L_{n-1} U_{n-1}, \varphi\right)_{n-1} \\ & \vdots \\ \Leftrightarrow \quad & \sum_{k=0}^{n} \left(\frac{\partial}{\partial t} U_k, \varphi\right)_k = \sum_{k=1}^{n} \left(U_k, L_k^* \varphi\right)_k + \left(L_0 U_0, \varphi\right)_0. \end{aligned} \tag{8.6.35}$$

The last summand on the right-hand side may (formally) be replaced by $\left(U_0, L_0^* \varphi\right)_0$ as they both vanish due to $L_0 = L_0^* = 0$, thus proving the assertion. □

By Lemma 8.3.1 we immediately obtain:

Corollary 8.6.1 *All moments $m_\alpha(t)$, $t \geq 0$ as defined in Eq. (8.3.14) of a hierarchical extension $U\colon \left(\overline{\Delta_n^{(I_n)}}\right)_\infty \longrightarrow \mathbb{R}$ (cf. Definition 8.5.1) of a solution u of the Kolmogorov forward equation (8.0.2) in Δ_n satisfy the moment evolution equation (8.3.13).*

Proof For $\varphi = 1$ and $\varphi = x^i$, we have $L^*(\varphi) = 0$, thus by Eq. (8.6.26)

$$\sum_{k=0}^{n} \left(\frac{\partial}{\partial t} U_k, \varphi\right)_k = 0.$$

□

Thus, the hierarchical extension of a solution of the Kolmogorov forward equation (8.0.2) via the flux of the solution yields the 'right' boundary values on the entire $\partial\Delta_n$ in the sense that all moments of the process defined via the hierarchical product $[\cdot, \cdot]_n$ in Eq. (8.3.14) do behave like the limit of the moments of the original discrete processes. This also justifies our choice of the hierarchical product $[\cdot, \cdot]_n$.

Moreover, we may show that any extension of a solution of the Kolmogorov forward equation (8.0.2) to $\overline{\Delta}_n$ that yields the correct moments already coincides with the hierarchical extension as in Definition 8.5.1. This is due to Lemma 8.3.1 and the following proposition:

Proposition 8.6.2 *For any initial condition $f \in L^2(\Delta_n)$, a solution $U\colon \left(\overline{\Delta}_n\right)_\infty \longrightarrow \mathbb{R}$ of the weak Kolmogorov forward equation (8.3.18) is uniquely defined on $\overline{\Delta}_n$.*

Corollary 8.6.2 *For any initial condition $f \in L^2(\Delta_n)$, a solution $U\colon (\overline{\Delta}_n)_\infty \longrightarrow \mathbb{R}$ of the weak Kolmogorov forward equation (8.3.18) coincides with the hierarchical extension $U\colon (\overline{\Delta}_n)_\infty \longrightarrow \mathbb{R}$ (cf. Definition 8.5.1) of a solution u of the (strong) Kolmogorov forward equation (8.0.2) in Δ_n.*

For the proof of Proposition 8.6.2, we need the following lemma:

Lemma 8.6.1 *The linear span of $\{\omega_n\varphi \in C_0^\infty(\overline{\Delta}_n) \,|\, \varphi$ eigenfunction of $L_n\}$ is dense in $C_c^\infty(\overline{\Delta}_n)$.*

Proof From Proposition 8.1.1 we already see that the linear combinations of the eigenfunctions of L_n are dense in $C^\infty(\overline{\Delta}_n)$. Dividing a function $f \in C_c^\infty(\overline{\Delta}_n)$ by ω_n (cf. Proposition 8.1.2) again yields a function in $C_c^\infty(\overline{\Delta}_n) \subset C_0^\infty(\overline{\Delta}_n)$ as ω_n is in $C_0^\infty(\overline{\Delta}_n)$ itself and positive in the interior Δ_n. □

Proof of Proposition 8.6.2 Assume that $U'\colon (\overline{\Delta}_n)_\infty \longrightarrow \mathbb{R}$ is another solution of Eq. (8.3.18) for a given initial condition f. We need to show that U and U' agree on all $\partial_k\Delta_n \subset \overline{\Delta}_n$ for $k = n, \ldots, 0$. We start with $\partial_n\Delta_n \equiv \Delta_n$. For an eigenfunction $\varphi \in C^\infty(\overline{\Delta}_n)$ of L_n (corresponding to the eigenvalue λ), we obtain by Proposition 8.1.2 that $\psi := \omega_n\varphi$ is an eigenfunction of L_n^* corresponding to the eigenvalue λ and, by the properties of ω_n, that $\psi \in C_0^\infty(\overline{\Delta}_n)$. For such a ψ, the weak Kolmogorov forward equation (8.3.18) then reduces to

$$\left(\frac{\partial}{\partial t}U, \psi\right)_n = (U, L_n^*\psi)_n \equiv -\lambda(U, \psi)_n \tag{8.6.36}$$

and

$$\left(\frac{\partial}{\partial t}U', \psi\right)_n = (U', L_n^*\psi)_n \equiv -\lambda(U', \psi)_n \tag{8.6.37}$$

respectively. Integrating these differential equations yields

$$(U(t), \psi)_n = e^{-\lambda t}(U(0), \psi)_n, \tag{8.6.38}$$

$$(U'(t), \psi)_n = e^{-\lambda t}(U'(0), \psi)_n, \tag{8.6.39}$$

and since $U(0) = U'(0) = f$

$$(U(t), \psi)_n = (U'(t), \psi)_n \quad \text{for } t \geq 0 \tag{8.6.40}$$

and for all eigenfunctions ψ. Since the linear span of these functions is dense in $C_c^\infty(\overline{\Delta}_n)$ (cf. Lemma 8.6.1), U and U' agree in Δ_n, indeed.

Now, we proceed inductively. Assume that we have already shown that U and U' agree on all $\partial_k\Delta_n \subset \overline{\Delta}_n$ with $k > m$. Then for an eigenfunction $\varphi\colon \overline{\Delta}_m \longrightarrow \mathbb{R}$ of L_m (corresponding to the eigenvalue λ), then, see Proposition 8.1.7, $\psi := \omega_m\varphi$ is an eigenfunction of L_m^* corresponding to the same eigenvalue λ and $\psi \in C_0^\infty(\overline{\Delta}_m)$. Given such a $\psi\colon \overline{\Delta}_m \longrightarrow \mathbb{R}$, we may construct a function $\overline{\psi}\colon \overline{\Delta_n^{(I_n)}} \longrightarrow \mathbb{R}$ as follows. We copy ψ to $\Delta_m^{(I_m)} \subset \partial_m\Delta_n$ for all $I_m \subset I_n$ and form convex combinations of the boundary values to extend it to all higher dimensional (boundary) strata, and we put $\overline{\psi} := 0$ on all lower dimensional boundary strata. Of course, $\overline{\psi}$ is in general not an eigenfunction of L^* in $\overline{\Delta}_n$, but we still have $(L^*\overline{\psi})\big|_{\Delta_m^{(I_m)}} = L_m^*\psi = -\lambda\psi$ for all $\Delta_m^{(I_m)} \subset \partial\Delta_n$.

For such a $\overline{\psi}$, the weak Kolmogorov forward equation (8.3.18) is converted into

$$\left(\frac{\partial}{\partial t}U, \overline{\psi}\right)_m = -\big(U, L_n^*\overline{\psi}\big)_m + \sum_{k=m+1}^{n}\left(\left(\frac{\partial}{\partial t}U, \overline{\psi}\right)_k - \big(U, L_k^*\overline{\psi}\big)_k\right) \tag{8.6.41}$$

and

$$\left(\frac{\partial}{\partial t}U', \overline{\psi}\right)_m = -\big(U', L_n^*\overline{\psi}\big)_m + \sum_{k=m+1}^{n}\left(\left(\frac{\partial}{\partial t}U', \overline{\psi}\right)_k - \big(U', L_k^*\overline{\psi}\big)_k\right) \tag{8.6.42}$$

where the sums on the right are the same as $U = U'$ on all $\partial_k\Delta_n$ with $k > m$, hence

$$\left(\frac{\partial}{\partial t}(U - U'), \overline{\psi}\right)_m = \big(U' - U, L_n^*\overline{\psi}\big)_m \equiv \lambda\big(U' - U, \overline{\psi}\big)_m, \tag{8.6.43}$$

which yields—analogously to our considerations above—$U = U'$ in $\partial_m\Delta_n$ on account of the completeness of the $\overline{\psi}$'s and the initial condition. □

Thus, with the additional assumption that the moments of the process coincide with the limits of the moments of the underlying discrete processes, we altogether have an alternative approach to Theorem 8.4.1 with a more precise understanding of the boundary transitions.

Theorem 8.6.1 *For $n \in \mathbb{N}$ and an initial condition $f \in L^2(\Delta_n)$, the Kolmogorov forward equation corresponding to the diffusion approximation of the n-dimensional Wright–Fisher model (8.0.2) always allows a unique extended solution $U\colon \big(\overline{\Delta}_n\big)_\infty \longrightarrow \mathbb{R}$ in the sense that $U|_{\Delta_n}$ is a solution of Eq. (8.0.2) and that its moments $m_\alpha(t) := \big[U(t), x^\alpha\big]_n$, $t \geq 0$ (cf. Eq. (8.3.14)) satisfy the n-dimensional moments evolution equation (8.3.13).*

Chapter 9
The Backward Equation

The backward solution $u(p,t)$ expresses the probability of having started in some $p \in \Delta_n$ at the negative time t conditional upon being in a certain state $u(p,0) = f(p)$ at time $t = 0$, i.e. having reached the corresponding (generalised) target set. It becomes a parabolic equation upon time reversal, that is, replacing t by $-t$. We can then treat $u(p,0) = f(p)$ as the initial condition at time $t = 0$. In view of the biological model behind the Kolmogorov backward equation, however, we shall work with negative time and call $u(p,0) = f(p)$ a *final* condition.

Now, there is an asymmetry between the forward and the backward equation. When we look at how the forward solution evolves from some initial condition supported in the interior of the simplex, then some of the probability will move into the boundary, and asymptotically, nothing will be left in the interior. When, in contrast, we solve the backward equation and look at which probability distribution in the past may have lead to a current final condition, then that past probability distribution has to be contained entirely in the interior of the simplex, as nothing can move into the interior from the boundary. However, that past probability distribution likewise could have moved into the boundary. Therefore, if we only specified a final condition in the interior, but not on the boundary, the flow into the boundary would be undetermined, and therefore, no uniqueness of the solution could be expected. Thus, in order to get uniqueness, we also need to specify a final condition on the boundary. But then, what we see in the boundary at such an final condition, could also have come from the boundary instead of from the interior. In other words, whatever in the past could have lead to a current distribution in the interior of the simplex could also have lead to a distribution in the boundary. Therefore, when we want to follow a current distribution back into the past, we need to look in turn at all distributions in the closure of the simplex to which an ancestral distribution could have lead. Thus for a solution, we also need to take the configuration on the boundary into account in order to properly assess its influence on the interior. Technical issues then arise for the lower dimensional boundary strata, that is, those

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that correspond to the loss of more than one allele. We shall treat this by a blow-up procedure. Also, the issue of the order of allele loss will arise.

This again illustrates the fundamental difference between the forward and the backward equation: For the forward equation, as we have seen in the preceding chapter, it sufficed to specify an initial condition in the interior. The reason for this is that the boundary is independent from the interior in the sense that its configuration has no effect on the interior. However, conversely, the interior influences the configuration on the boundary; this was the major difficulty in constructing the global solution in the preceding chapter.

With the backward equation, the situation is the converse: As hinted in Chap. 1, a backward solution describes ancestral distributions, and those do not interfere, regardless of the numbers of alleles they involve. This indicates that we have some superposition principle, and hence, a solution in the interior extends to the boundary. However, going in the opposite direction, this means that a solution in the interior always is influenced by the boundary. Hence for any solution, the role of the boundary, i.e. its contribution to the interior, needs to be clarified, which also requires the extended final condition. Eventually, this applies to the entire stratified boundary of the domain. Thus, analyzing the contribution of each of the strata of the domain and thereby establishing the uniqueness of a solution is what will occupy us in this chapter.

9.1 Solution Schemes for the Kolmogorov Backward Equation

The Kolmogorov backward equation and of the Kolmogorov forward equation are linked by the adjointness of the Kolmogorov operators L_n and L_n^* proved in Proposition 8.1.4. Therefore, there also exists a relationship between their corresponding solutions, and known solution schemes (cf. [14, 80]) can be applied to either equation. Nevertheless, there is a subtle difference between these two equations caused by the different boundary behavior. This is reflected in the fact that the spectra of L_n and L_n^* don't match (cf. [118]). All eigenfunctions of L_n^* derived from the adjointness with L_n in Proposition 8.1.2 are in $C_0^\infty(\Delta_n)$, but L_n^* in Δ_n possesses additional eigenfunctions (in particular for smaller eigenvalues) that do not correspond to eigenfunctions of L_n. The reason is that all eigenfunctions of L_k^* in Δ_k for some $0 \leq k < n$ also occur as eigenfunctions of L_n^* in Δ_n, e.g. for some eigenfunction φ of L_k^* in Δ_k, simply put $\bar{\varphi}(\bar{p}) := \varphi(p)$ for $\bar{p} := (p, p') \in \Delta_n$, $p \in \Delta_k$ to obtain an eigenfunction $\bar{\varphi}$ of L_n^*. In case Δ_k is a boundary stratum of Δ_n which lacks the 0th-coordinate, i.e. $\Delta_k^0 := \{(p^1, \ldots, p^{k+1}) | \sum_{i=1}^{k+1} p^i = 1\}$ as a face of $\Delta_n = \{(p^1, \ldots, p^n) | \sum_{j=1}^{n} p^j < 1\}$, we have for $\bar{p} \in \Delta_n$ that $p := \frac{(\bar{p}^1, \ldots, \bar{p}^{k+1})}{\sum_{i=1}^{k+1} \bar{p}^i} \in \Delta_k^0$, and hence we may put $\bar{\varphi}(\bar{p}) := \varphi(p)$ as an extension of the eigenfunction φ to Δ_n.

The construction of a solution of Eq. (4.2.13) in Δ_n in terms of the eigenfunctions (e.g. the generalised Gegenbauer polynomials, cf. [113]) is rather straightforward. However, the, when compared with the forward case, larger set of eigenfunctions causes ambiguities when decomposing a final condition, which prevents uniqueness results for the solution. But if we restrict the choice of eigenfunctions to the 'proper' eigenfunctions in the domain,[1] i.e. those in $C_0^\infty(\Delta_n)$, which correspond to eigenfunctions of L_n, the same existence and uniqueness scheme as in the forward case applies. Thus, for such a solution by proper eigenfunctions (which will be called a *proper solution of the Kolmogorov backward equation in* Δ_n), we have the result of e.g. [86]:

Proposition 9.1.1 *For $n \in \mathbb{N}$ and a given final condition $f \in \mathcal{L}^2(\Delta_n)$, the Kolmogorov backward equation corresponding to the diffusion approximation of the n-dimensional Wright–Fisher model (4.2.13) possesses a unique proper solution u: $\left(\Delta_n\right)_{-\infty} \longrightarrow \mathbb{R}$ with $u \in C_0^\infty(\Delta_n \times (-\infty, 0))$*

By construction, such proper solutions do not cover the boundary. In the next section, the non-proper components will be interpreted as originating from (proper) solutions on lower-dimensional boundary strata.

9.2 Inclusion of the Boundary and the Extended Kolmogorov Backward Equation

We shall now include the boundary and its contribution into the model. We enlarge the domain of Eq. (4.2.13) such that it comprises the entire $\overline{\Delta}_n$.

This yields the *extended Kolmogorov backward equation*

$$\begin{cases} -\frac{\partial}{\partial t}U(p,t) = L^*U(p,t) & \text{in } \left(\overline{\Delta}_n\right)_{-\infty} = \overline{\Delta}_n \times (-\infty, 0) \\ U(p,0) = f(p) & \text{in } \overline{\Delta}_n,\ f \in \mathcal{L}^2\left(\bigcup_{k=0}^n \partial_k \Delta_n\right) \end{cases} \tag{9.2.1}$$

for $U(\cdot, t) \in C_p^2\left(\overline{\Delta}_n\right)$ for each fixed $t \in (-\infty, 0)$ and $U(p, \cdot) \in C^1((-\infty, 0))$ for each fixed $p \in \overline{\Delta}_n$. Here, f is the *extended final condition* which is defined on $\overline{\Delta}_n$. Thus, any boundary stratum of the boundary of the simplex may also belong to the target set considered.

Our problem now is different from standard final-boundary value problems. This is because in our case, the configuration on the boundary is no longer static, but

[1] This is also sufficient as their linear span is already dense in $C_c^\infty(\overline{\Delta}_n)$ and consequently also in $\mathcal{L}^2(\Delta_n)$: Linear combinations of the generalised Gegenbauer polynomials as eigenfunctions of L_n (cf. [113]) are dense in $C^\infty(\overline{\Delta}_n)$; dividing a function $f \in C_c^\infty(\overline{\Delta}_n)$ by ω_n (cf. Proposition 8.1.2) again yields a function in $C_c^\infty(\overline{\Delta}_n) \subset C_0^\infty(\overline{\Delta}_n)$ as ω_n is in $C_0^\infty(\overline{\Delta}_n)$ itself and positive in the interior Δ_n.

evolves itself according to the various L_k^* where k is the dimension of a subsimplex of the boundary of our simplex. We have already observed, that such an L_k^* simply is the restriction of L_n^* to the corresponding domain (cf. Lemma 8.4.1). Hence, we may omit the index k and simply write L^* (for dimension 0, we formally put $L^* = L_0^* := 0$). In terms of the underlying Wright–Fisher model, this means that the boundary is subject to the same type of evolution, merely in a different dimension, justifying the choice of Eq. (4.2.13).

The key point now is to connect the different boundary strata, by requiring $U \in C_p^2(\overline{\Delta}_n)$ w. r. t. the spatial variables: Clearly, inside each boundary stratum the solution needs to be sufficiently regular for L^*, but regarding the boundary, we also ask for such regularity for simple boundary transitions, i.e. when the dimension decreases by one. For higher order transitions, however, singularities may occur. This corresponds to the degeneracy behaviour of the operator at the boundary. This leads us to a much wider class of global solutions, which are not artificial, but correspond to natural scenarios in the underlying Wright–Fisher model.

9.3 An Extension Scheme for Solutions of the Kolmogorov Backward Equation

We want to construct the class of global solutions of the Kolmogorov backward equation (4.2.13) by successive backward extension of local solutions in different boundary strata. For this, we first look at single extensions of solutions from a facet in the boundary of our domain to the interior. The extensions are confined by[2]:

Definition 9.3.1 (Extension Constraints) Let I_d be an index set with $|I_d| = d + 1 \geq 2$, $0, s \in I_d$ and $\Delta_d^{(I_d)} = \{(p^i)_{i \in I_d \setminus \{0\}} | p^i > 0 \text{ for } i \in I_d\}$ with $p^0 := 1 - \sum_{i \in I_d \setminus \{0\}} p^i$. For $d \geq 2$ and a solution $u: \left(\Delta_{d-1}^{(I_d \setminus \{s\})}\right)_{-\infty} \longrightarrow \mathbb{R}$ of the Kolmogorov backward equation (4.2.13), i.e. $u(\cdot, t) \in C^\infty\left(\Delta_{d-1}^{(I_d \setminus \{s\})}\right)$ for $t < 0$, $u(p, \cdot) \in C^\infty((-\infty, 0))$ for $p \in \Delta_{d-1}^{(I_d \setminus \{s\})}$ and

$$-\frac{\partial}{\partial t} u = L^* u \quad \text{in } \left(\Delta_{d-1}^{(I_d \setminus \{s\})}\right)_{-\infty}, \tag{9.3.2}$$

a function $\bar{u}: \left(\Delta_d^{(I_d)}\right)_{-\infty} \longrightarrow \mathbb{R}$ with $\bar{u}(\cdot, t) \in C^\infty\left(\Delta_d^{(I_d)}\right)$ for $t < 0$ and $\bar{u}(p, \cdot) \in C^\infty((-\infty, 0))$ for $p \in \Delta_d^{(I_d)}$ is said to be an extension of u satisfying the *extension*

[2]Note the dimension index conventions as in the forward case: n refers to the top-dimensional component (corresponding to $n + 1$ alleles in Wright–Fisher model), whereas k or d denotes the dimension of any (specific) boundary stratum. Specifically, d will be used as running index for iterations over dimension.

constraints if

(i) for $t < 0$ $\bar{u}(\cdot, t)$ is continuously extendable to the boundary $\partial_{d-1}\Delta_d^{(I_d)}$ such that it coincides with $u(\cdot, t)$ in $\Delta_{d-1}^{(I_d\setminus\{s\})}$ resp. vanishes on the remainder of $\partial_{d-1}\Delta_d^{(I_d)}$ and is of class C^∞ with respect to the spatial variables in $\Delta_d^{(I_d)} \cup \partial_{d-1}\Delta_d^{(I_d)}$,

(ii) it is a solution of the corresponding Kolmogorov backward equation in $\left(\Delta_d^{(I_d)}\right)_{-\infty}$, i.e. $-\frac{\partial}{\partial t}\bar{u} = L^*\bar{u}$ in $\left(\Delta_d^{(I_d)}\right)_{-\infty}$.

For $d = 1$, this analogously applies to functions u with $-\frac{\partial}{\partial t}u = 0$ (since $L_0^* \equiv 0$), and consequently the equation in condition (ii) is replaced by $L^*\bar{u} = 0$. An extension that involves multiple extension steps is said to satisfy the extension constraints if this holds for every extension step.

Remark 9.3.1 In case of $d \geq 2$, if u for $t < 0$ extends smoothly to the boundary $\partial_{d-2}\Delta_{d-1}^{(I_d\setminus\{s\})}$ such that this extension vanishes everywhere on $\partial_{d-2}\Delta_{d-1}^{(I_d\setminus\{s\})}$, the above definition means that $(u\chi_{\Delta_{d-1}^{(I_d\setminus\{s\})}} + \bar{u}\chi_{\Delta_d^{(I_d)}}) \in C_{p_0}^\infty(\Delta_{d-1}^{(I_d\setminus\{s\})} \cup \Delta_d^{(I_d)})$ with respect to the spatial variables for $t < 0$ (cf. equality (2.11.24)).

We shall first investigate the existence of such extensions that obey Definition 9.3.1. After that, we shall turn to the issue of their uniqueness. Since our construction is based on a separation ansatz (cf. Proposition 9.1.1), we shall have to construct extensions of the eigenmodes:

Lemma 9.3.1 (Extension of Eigenfunctions) *Let I_d be an index set with $|I_d| = d + 1 \geq 2$, $0, s \in I_d$ and $\Delta_d^{(I_d)} = \{(p^i)_{i\in I_d\setminus\{0\}} | p^i > 0 \text{ for } i \in I_d\}$ with $p^0 := 1 - \sum_{i\in I_d\setminus\{0\}} p^i$. For $d \geq 2$ and an eigenfunction $\psi \in C^\infty\left(\Delta_{d-1}^{(I_d\setminus\{s\})}\right)$ of L_{d-1}^* for the eigenvalue $\kappa \geq 0$, i.e.*

$$L_{d-1}^*\psi = -\kappa\psi \quad \text{in } \Delta_{d-1}^{(I_d\setminus\{s\})} \subset \partial\Delta_d^{(I_d)}, \tag{9.3.3}$$

a linear interpolation $\bar{\psi} = \bar{\psi}^{r,s}\colon \Delta_d^{(I_d)} \longrightarrow \mathbb{R}$ of ψ from $\Delta_{d-1}^{(I_d\setminus\{s\})}$ (source face) towards $\Delta_{d-1}^{(I_d\setminus\{r\})} \subset \partial_{d-1}\Delta_d^{(I_d)}$ for some $r \in I_d \setminus \{s\}$ (target face) is given by

$$\bar{\psi}^{r,s}(p) := \psi(\pi^{r,s}(p)) \cdot \frac{p^r}{p^s + p^r} \quad \text{for } p \in \Delta_d^{(I_d)} \tag{9.3.4}$$

with $\pi^{r,s}(p^1, \ldots, p^d) = (\tilde{p}^1, \ldots, \tilde{p}^d)$ such that $\tilde{p}^s = 0$, $\tilde{p}^r = p^s + p^r$ and $\tilde{p}^i = p^i$ for $i \in I_d \setminus \{s, l\}$.

The regularity of $\bar{\psi}$ corresponds to that of ψ in $\Delta_d^{(I_d)}$ (i.e. it is of class C^∞) and $\bar{\psi}$ satisfies

$$L_d^* \bar{\psi} = -\kappa \bar{\psi} \quad \text{in } \Delta_d^{(I_d)}. \tag{9.3.5}$$

Moreover, $\bar{\psi}$ extends smoothly to $\Delta_{d-1}^{(I_d \setminus \{s\})}$ and $\Delta_{d-1}^{(I_d \setminus \{r\})}$, and there we have

$$\bar{\psi}|_{\Delta_{d-1}^{(I_d \setminus \{s\})}} = \psi, \qquad \bar{\psi}|_{\Delta_{d-1}^{(I_d \setminus \{r\})}} = 0. \tag{9.3.6}$$

If furthermore ψ extends smoothly to $\Delta_{d-2}^{(I_d \setminus \{s,q\})} \subset \partial_{d-2} \Delta_d^{(I_d \setminus \{s\})}$ for some $q \in I_d \setminus \{r, s\}$, then $\bar{\psi}$ likewise extends smoothly to $\Delta_{d-1}^{(I_d \setminus \{q\})}$. In particular, $\bar{\psi}$ satisfies the extension constraint 9.3.1 (i) if ψ extends smoothly to $\partial_{d-2} \Delta_{d-1}^{(I_d \setminus \{s\})} \setminus \Delta_{d-2}^{(I_d \setminus \{r,s\})}$ and vanishes there.

For $d = 1$, the preceding statements analogously hold for arbitrary $\psi \colon \Delta_0^{(I_1 \setminus \{s\})} \longrightarrow \mathbb{R}$ as eigenfunction of $L_0^* \equiv 0$ for the eigenvalue 0; then, $\bar{\psi}$ is of class C^∞ in $\Delta_1^{(I_1)}$, and such an extension always obeys the extension constraint 9.3.1 (i).

Since the eigenfunctions are the building blocks for a solution scheme, the preceding lemma directly extends to solutions of the Kolmogorov backward equation:

Proposition 9.3.1 (Extension of Solutions) *Let I_d be an index set with $|I_d| = d + 1 \geq 2$, $0, s \in I_d$ and $\Delta_d^{(I_d)} = \{(p^i)_{i \in I_d \setminus \{0\}} | p^i > 0 \text{ for } i \in I_d\}$ with $p^0 := 1 - \sum_{i \in I_d \setminus \{0\}} p^i$. For $d \geq 2$, a given final condition $f \in \mathcal{L}^2\big(\Delta_{d-1}^{(I_d \setminus \{s\})}\big)$ and a given extension target face index $r \in I_d \setminus \{s\}$, a solution $u \colon \big(\Delta_{d-1}^{(I_d \setminus \{s\})}\big)_{-\infty} \longrightarrow \mathbb{R}$ of the Kolmogorov backward equation (4.2.13), $u(\cdot, t) \in C^\infty\big(\Delta_{d-1}^{(I_d \setminus \{s\})}\big)$ for $t < 0$ and $u(p, \cdot) \in C^\infty((-\infty, 0))$ for $p \in \Delta_{d-1}^{(I_d \setminus \{s\})}$, may be extended to a function*

$$\bar{u} = \bar{u}^{r,s} \colon \big(\Delta_d^{(I_d)}\big)_{-\infty} \longrightarrow \mathbb{R} \tag{9.3.7}$$

with $\bar{u}(\cdot, t) \in C^\infty\big(\Delta_d^{(I_d)}\big)$ for $t < 0$ and $\bar{u}(p, \cdot) \in C^\infty((-\infty, 0))$ for $p \in \Delta_d^{(I_d)}$ and which satisfies

$$-\frac{\partial}{\partial t} \bar{u} = L^* \bar{u} \quad \text{in } \big(\Delta_d^{(I_d)}\big)_{-\infty}. \tag{9.3.8}$$

Furthermore, for $t < 0$ $\bar{u}(\cdot, t)$ smoothly extends to the boundary in $\Delta_{d-1}^{(I_d \setminus \{s\})}$ with

$$\bar{u}(\cdot, t)|_{\Delta_{d-1}^{(I_d \setminus \{s\})}} = u, \quad \text{in particular} \quad \bar{u}(\cdot, 0)|_{\Delta_{d-1}^{(I_d \setminus \{s\})}} = f|_{\Delta_{d-1}^{(I_d \setminus \{s\})}} \tag{9.3.9}$$

and in $\Delta_{d-1}^{(I_d\setminus\{r\})}$ *with* $\bar{u}(\cdot,t)|_{\Delta_{d-1}^{(I_d\setminus\{r\})}} = 0$. *If furthermore* $u(\cdot,t)$ *for* $q \in I_d \setminus \{r,s\}$ *extends smoothly to* $\Delta_{d-2}^{(I_d\setminus\{q,s\})} \subset \partial_{d-2}\Delta_d^{(I_d\setminus\{s\})}$ *for some* t, *then* $\bar{u}(\cdot,t)$ *likewise extends smoothly to* $\Delta_{d-1}^{(I_d\setminus\{q\})}$. *In particular,* $\bar{u}$ *satisfies the extension constraints 9.3.1 if* $u(\cdot,t)$ *extends smoothly to* $\partial_{d-2}\Delta_{d-1}^{(I_d\setminus\{s\})} \setminus \Delta_{d-2}^{(I_d\setminus\{r,s\})}$ *and vanishes there for* $t < 0$.

For $d = 1$, *the preceding analogously holds for functions* u: $\big(\Delta_0^{(I_1\setminus\{s\})}\big)_{-\infty} \longrightarrow \mathbb{R}$ *with* $u(p,\cdot) \in C^\infty((-\infty,0))$ *and* $\frac{\partial}{\partial t}u = 0$; *then,* $\bar{u}(\cdot,t)$ *is of class* C^∞ *in* $\Delta_1^{(I_1)}$ *for every* t *as well as* $\bar{u}(p,\cdot) \in C^\infty((-\infty,0))$ *for* $p \in \Delta_d^{(I_d)}$ *with* $\frac{\partial}{\partial t}\bar{u} = 0$, *and Eq. (9.3.8) holds correspondingly. Furthermore, this extension always satisfies the extension constraints 9.3.1.*

Remark 9.3.2 The extension of a solution of the Kolmogorov backward equation for a final condition $f \in \mathcal{L}^2\big(\Delta_{d-1}^{(I_d\setminus\{s\})}\big)$ as in Proposition 9.3.1 is also applicable for $t = 0$, yielding an analogously extended final condition $\bar{f} = \bar{f}^{r,s} \in \mathcal{L}^2\big(\Delta_d^{(I_d)}\big)$. We then have $\bar{u}(\cdot,0) \equiv \bar{f}$ in $\Delta_d^{(I_d)}$ by continuous extension as we have $u(\cdot,0) = f$ in $\Delta_{d-1}^{(I_d\setminus\{s\})}$; however, for $d \geq 2$ this extension of f need not be regular at the boundary because f is not necessarily regular (and hence in general, it does not satisfy the extension boundary constraint 9.3.1 (i)).

In addition to the preceding proposition, it should be noted that $\bar{u}$ does not necessarily extend continuously to the entire $\overline{\Delta}_d$, in particular not to the remaining boundary parts of dimension $d-2$ and less. This is due to the fact that on components of $\partial_{d-2}\Delta_d^{(I_d)}$, which are shared boundaries of higher-dimensional faces of the simplex, continuous extensions from each of those faces may exist, but do not necessarily coincide.

Proof of Lemma 9.3.1 The regularity assertion for $\bar{\psi}$ in $\Delta_d^{(I_d)}$ follows from the regularity of π and of the projection and from $\frac{p^r}{p^s+p^r}$ being of class C^∞ on $\Delta_d^{(I_d)}$. The boundary behaviour is similarly straightforward as $\pi^{r,s} = \mathrm{id}$ and $\frac{p^r}{p^s+p^r} = 1$ on $\Delta_{d-1}^{(I_d\setminus\{s\})}$, whereas $\frac{p^r}{p^s+p^r} = 0$ on $\Delta_{d-1}^{(I_d\setminus\{r\})}$. Both boundary extensions are smooth in the sense described, which is again due to the regularity of the projection and of $\frac{p^r}{p^s+p^r}$ when approaching $\Delta_{d-1}^{(I_d\setminus\{s\})}$ resp. $\Delta_{d-1}^{(I_d\setminus\{r\})}$. Analogous considerations yield the assertion for other boundary faces of $\partial_{d-1}\Delta_d^{(I_d)}$: The projection $\pi^{r,s}$ maps $\partial_{d-1}\Delta_d^{(I_d)} \setminus \big(\Delta_{d-1}^{(I_d\setminus\{r\})} \cup \Delta_{d-1}^{(I_d\setminus\{s\})}\big)$ smoothly onto $\partial_{d-2}\Delta_{d-1}^{(I_d\setminus\{s\})}$, which together with $\frac{p^r}{p^s+p^r}$ being of class C^∞ on $\partial_{d-1}\Delta_d^{(I_d)}$ (via $p^s + p^r > 0$) yields the stated regularity; the value of this boundary extension of $\bar{\psi}$ of course coincides with the one of the corresponding extension of ψ.

To prove Eq. (9.3.5), w. l. o. g. let $I_d = \{0, 1, \dots, d\}$; summation indices, however, run from 1 to d unless indicated otherwise. To begin with, we have

$$\begin{aligned} L_d^*\left(\psi(\pi^{r,s}(p)) \cdot \frac{p^r}{p^s + p^r}\right) &= \left(L_d^*\psi(\pi^{r,s}(p))\right)\frac{p^r}{p^s + p^r} \\ &\quad + \sum_{i,j} p^i(\delta_j^i - p^j)\left(\frac{\partial}{\partial p^i}\psi(\pi^{r,s}(p))\right)\left(\frac{\partial}{\partial p^j}\frac{p^r}{p^s + p^r}\right) \\ &\quad + \frac{1}{2}\psi(\pi^{r,s}(p))\sum_{i,j} p^i(\delta_j^i - p^j)\left(\frac{\partial}{\partial p^i}\frac{\partial}{\partial p^j}\frac{p^r}{p^s + p^r}\right). \end{aligned} \tag{9.3.10}$$

Next, we will show that the first summand equals $-\kappa\bar{\psi}$, whereas the two other summands vanish on $\Delta_d^{(I_d)}$.

For the first summand, we use $L_{d-1}^*\psi = -\kappa\psi$ in $\Delta_{d-1}^{(I_d\setminus\{s\})}$, which holds by assumption. To extend this statement to $\Delta_d^{(I_d)}$, the interplay of the operator with the projections $\pi^{r,s}$ needs to be analysed, for which several cases have to be distinguished. That is, for $s \neq 0$, $r = 0$, the projection $\pi^{0,s}$ yields $\tilde{p}^s = 0$ and $\tilde{p}^i = p^i$ for $i \in \{1, \dots, d\} \setminus \{s\}$, hence $\frac{\partial \tilde{p}^m}{\partial p^i} = \delta_i^m(1 - \delta_s^m)$, and we have

$$\begin{aligned} L_d^*\psi(\pi^{0,s}(p)) &= \frac{1}{2}\sum_{i,j} p^i(\delta_j^i - p^j)\frac{\partial}{\partial p^i}\frac{\partial}{\partial p^j}\psi(\pi^{0,s}(p)) \\ &= \frac{1}{2}\sum_{m,n}\sum_{i,j} p^i(\delta_j^i - p^j)\delta_i^m(1 - \delta_s^m)\delta_j^n(1 - \delta_s^n)\frac{\partial}{\partial \tilde{p}^m}\frac{\partial}{\partial \tilde{p}^n}\psi(\tilde{p}) \\ &= \frac{1}{2}\sum_{m,n\neq s} \tilde{p}^m(\delta_n^m - \tilde{p}^n)\frac{\partial}{\partial \tilde{p}^m}\frac{\partial}{\partial \tilde{p}^n}\psi(\tilde{p}) = L_{d-1}^*\psi(\tilde{p}) \equiv -\kappa\psi(\tilde{p}). \end{aligned} \tag{9.3.11}$$

If $s = 0$, $r \neq 0$ and hence $\Delta_{d-1}^{(I_d\setminus\{0\})} = \left\{(\tilde{p}^1, \dots, \tilde{p}^d)\middle|\tilde{p}^i > 0 \text{ for } i = 1, \dots, d, \sum_{i=1}^d \tilde{p}^i = 1\right\}$, we have $\tilde{p}^i = p^i$ for $i \in \{1, \dots, d\} \setminus \{r\}$ and $\tilde{p}^r = p^r + p^0$, thus $\frac{\partial \tilde{p}^m}{\partial p^i} = \delta_i^m - \delta_r^m$. We get:

$$\begin{aligned} L_d^*\psi(\pi^{r,0}(p)) &= \frac{1}{2}\sum_{m,n}\sum_{i,j} p^i(\delta_j^i - p^j)(\delta_i^m - \delta_r^m)(\delta_j^n - \delta_r^n)\frac{\partial}{\partial \tilde{p}^m}\frac{\partial}{\partial \tilde{p}^n}\psi(\tilde{p}) \\ &= \frac{1}{2}\sum_{m,n} p^m(\delta_n^m - p^n)\frac{\partial}{\partial \tilde{p}^m}\frac{\partial}{\partial \tilde{p}^n}\psi(\tilde{p}) - \frac{1}{2}\sum_n\sum_i p^i(\delta_n^i - p^n)\frac{\partial}{\partial \tilde{p}^r}\frac{\partial}{\partial \tilde{p}^n}\psi(\tilde{p}) \\ &\quad - \frac{1}{2}\sum_m\sum_j p^m(\delta_j^m - p^m)\frac{\partial}{\partial \tilde{p}^r}\frac{\partial}{\partial \tilde{p}^n}\psi(\tilde{p}) + \frac{1}{2}\sum_{i,j} p^i(\delta_j^i - p^j)\frac{\partial^2}{(\partial \tilde{p}^r)^2}\psi(\tilde{p}) \end{aligned}$$

$$= \frac{1}{2}\sum_{m,n} p^m(\delta_n^m - p^n)\frac{\partial}{\partial \tilde{p}^m}\frac{\partial}{\partial \tilde{p}^n}\psi(\tilde{p}) - \frac{1}{2}\sum_n p^0 p^n \frac{\partial}{\partial \tilde{p}^r}\frac{\partial}{\partial \tilde{p}^n}\psi(\tilde{p})$$

$$- \frac{1}{2}\sum_m p^m p^0 \frac{\partial}{\partial \tilde{p}^m}\frac{\partial}{\partial \tilde{p}^r}\psi(\tilde{p}) + \frac{1}{2}p^0(1-p^0)\frac{\partial^2}{(\partial \tilde{p}^r)^2}\psi(\tilde{p}). \tag{9.3.12}$$

When replacing the remaining p-coordinates by $\tilde{p}$ (except for p^0, which is missing in $\Delta_{d-1}^{(I_d\setminus\{0\})}$) via $p^i = \tilde{p}^i - p^0\delta_r^i$ for $i = \{1,\ldots,d\}$, the expression transforms into:

$$\begin{aligned} L_d^*\psi(\pi^{r,0}(p)) &= \frac{1}{2}\sum_{m,n\neq r}\tilde{p}^m(\delta_n^m - \tilde{p}^n)\frac{\partial}{\partial \tilde{p}^m}\frac{\partial}{\partial \tilde{p}^n}\psi(\tilde{p}) + \frac{1}{2}\sum_{n\neq r}(-\tilde{p}^r + p^0)\tilde{p}^n\frac{\partial}{\partial \tilde{p}^r}\frac{\partial}{\partial \tilde{p}^n}\psi(\tilde{p}) \\ &+ \frac{1}{2}\sum_{m\neq r}\tilde{p}^m(-\tilde{p}^r + p^0)\frac{\partial}{\partial \tilde{p}^m}\frac{\partial}{\partial \tilde{p}^r}\psi(\tilde{p}) + \frac{1}{2}(\tilde{p}^r - p^0)(1-\tilde{p}^r + p^0)\times \\ &\frac{\partial^2}{(\partial \tilde{p}^r)^2}\psi(\tilde{p}) - \frac{1}{2}\sum_{n\neq r}p^0\tilde{p}^n\frac{\partial}{\partial \tilde{p}^r}\frac{\partial}{\partial \tilde{p}^n}\psi(\tilde{p}) - \frac{1}{2}\sum_{m\neq r}\tilde{p}^m p^0\frac{\partial}{\partial \tilde{p}^m}\frac{\partial}{\partial \tilde{p}^r}\psi(\tilde{p}) \\ &- p^0(\tilde{p}^r - p^0)\frac{\partial^2}{(\partial \tilde{p}^r)^2}\psi(\tilde{p}) + \frac{1}{2}p^0(1-p^0)\frac{\partial^2}{(\partial \tilde{p}^r)^2}\psi(\tilde{p}) \\ &= \frac{1}{2}\sum_{m,n}\tilde{p}^m(\delta_n^m - \tilde{p}^n)\frac{\partial}{\partial \tilde{p}^m}\frac{\partial}{\partial \tilde{p}^n}\psi(\tilde{p}) = L_{d-1}^*\psi(\tilde{p}) \equiv -\kappa\psi(\tilde{p}). \end{aligned} \tag{9.3.13}$$

The next-to-last equality is due to the fact that in $\Delta_{d-1}^{(I_d\setminus\{0\})}$ one coordinate is obsolete and consequently ψ is formulated in $d-1$ coordinates (which may be chosen freely). It is straightforward to show that, independently of the choice of the omitted coordinate r, we have $L_{d-1}^* = \frac{1}{2}\sum_{m,n\neq r}\tilde{p}^m(\delta_n^m - \tilde{p}^n)\frac{\partial}{\partial \tilde{p}^m}\frac{\partial}{\partial \tilde{p}^n}$ on $\Delta_{d-1}^{(I_d\setminus\{0\})}$.

Finally, if $s \neq 0$, $r \neq 0$, the projection $\pi^{r,s}$ yields $\tilde{p}^s = 0$, $\tilde{p}^r = p^s + p^r$ and $\tilde{p}^i = p^i$ for the remaining indices, hence $\frac{\partial \tilde{p}^m}{\partial p^i} = \delta_i^m(1-\delta_s^m) + \delta_r^m\delta_s^i$. Then we have:

$$\begin{aligned} L_d^*\psi(\pi^{r,s}(p)) &= \frac{1}{2}\sum_{i,j}p^i(\delta_j^i - p^j)\frac{\partial}{\partial p^i}\frac{\partial}{\partial p^j}\psi(\pi^{r,s}(p)) \\ &= \frac{1}{2}\sum_{\substack{m,n,\\ i,j}}p^i(\delta_j^i - p^j)(\delta_i^m(1-\delta_s^m) + \delta_r^m\delta_s^i)(\delta_j^n(1-\delta_s^n) + \delta_r^n\delta_s^j)\frac{\partial}{\partial \tilde{p}^m}\frac{\partial}{\partial \tilde{p}^n}\psi(\tilde{p}) \\ &= \frac{1}{2}\sum_{m,n\neq s}p^m(\delta_n^m - p^n)\frac{\partial}{\partial \tilde{p}^m}\frac{\partial}{\partial \tilde{p}^n}\psi(\tilde{p}) - \frac{1}{2}\sum_{n\neq s}p^s p^n\frac{\partial}{\partial \tilde{p}^r}\frac{\partial}{\partial \tilde{p}^n}\psi(\tilde{p}) \\ &- \frac{1}{2}\sum_{m\neq s}p^m p^s\frac{\partial}{\partial \tilde{p}^m}\frac{\partial}{\partial \tilde{p}^r}\psi(\tilde{p}) + \frac{1}{2}p^s(1-p^s)\frac{\partial^2}{(\partial \tilde{p}^r)^2}\psi(\tilde{p}). \end{aligned} \tag{9.3.14}$$

Replacing the p-coordinates works as shown in the preceding case, and thereupon we obtain

$$L_d^*\psi(\pi^{r,s}(p)) = \frac{1}{2}\sum_{m,n\neq s}\tilde{p}^m(\delta_n^m - \tilde{p}^n)\frac{\partial}{\partial\tilde{p}^m}\frac{\partial}{\partial\tilde{p}^n}\psi(\tilde{p}) = L_{d-1}^*\psi(\tilde{p}) \equiv -\kappa\psi(\tilde{p}), \tag{9.3.15}$$

thus in total

$$L_d^*\psi(\pi^{r,s}(p)) = L_{d-1}^*\psi(\tilde{p}) \equiv -\kappa\psi(\tilde{p}) = -\kappa\psi(\pi^{r,s}(p)) \tag{9.3.16}$$

for arbitrary r, s, which is the desired equality result for the first summand.

To show that the two remaining summands vanish, an analogous case-by-case analysis is necessary. If $s = 0$, $r \neq 0$, we have $\frac{p^r}{p^0+p^r} = \frac{p^r}{1-\sum_{l\neq r}p^l}$. Due to (remember $\frac{\partial\tilde{p}^m}{\partial p^i} = \delta_i^m - \delta_r^m$)

$$\frac{\partial}{\partial p^r}\psi(\pi^{r,0}(p)) = \sum_m \frac{\partial\tilde{p}^m}{\partial p^r}\frac{\partial}{\partial\tilde{p}^m}\psi(\tilde{p}) = 0, \tag{9.3.17}$$

the second summand is

$$\sum_{i\neq r} p^i\left(\frac{\partial}{\partial p^i}\psi(\pi^{r,0}(p))\right)\underbrace{\sum_j(\delta_j^i - p^j)\left(\frac{\partial}{\partial p^j}\frac{p^r}{1-\sum_{l\neq r}p^l}\right)} \tag{9.3.18}$$

$$= \left(1-\sum_{j\neq r}p^j\right)\frac{p^r}{\left(1-\sum_{l\neq r}p^l\right)^2} - p^r\frac{1}{1-\sum_{l\neq r}p^l} = 0,$$

and so is the third summand,

$$\frac{1}{2}\psi(\pi^{r,0}(p))\sum_{i\neq r}\left(\sum_{j\neq r}p^i(\delta_j^i - p^j)\left(\frac{\partial}{\partial p^i}\frac{\partial}{\partial p^j}\frac{p^r}{1-\sum_{l\neq r}p^l}\right)\right.$$

$$\left. - 2p^ip^r\left(\frac{\partial}{\partial p^i}\frac{\partial}{\partial p^r}\frac{p^r}{1-\sum_{l\neq r}p^l}\right)\right)$$

$$= \frac{1}{2}\psi(\pi^{r,0}(p))\sum_{i\neq r}\left(p^i\left(1-\sum_{j\neq r}p^j\right)\frac{2p^r}{\left(1-\sum_{l\neq r}p^l\right)^3} - 2p^ip^r\frac{1}{\left(1-\sum_{l\neq r}p^l\right)^2}\right) = 0. \tag{9.3.19}$$

Thus, they both vanish.

Similarly, if $s \neq 0$, $r = 0$, thus $\frac{p^0}{p^s+p^0} = \frac{1-\sum_l p^l}{1-\sum_{l\neq s} p^l}$ and again (with $\frac{\partial \tilde{p}^m}{\partial p^i} = \delta_i^m(1-\delta_s^m)$)

$$\frac{\partial}{\partial p^s}\psi(\pi^{0,s}(p)) = \sum_m \frac{\partial \tilde{p}^m}{\partial p^s}\frac{\partial}{\partial \tilde{p}^m}\psi(\tilde{p}) = 0, \tag{9.3.20}$$

the second summand is

$$\begin{aligned}\sum_{i\neq s} p^i \left(\frac{\partial}{\partial p^i}\psi(\pi^{0,s}(p))\right) \underbrace{\sum_j (\delta_j^i - p^j)\left(\frac{\partial}{\partial p^j}\frac{1-\sum_l p^l}{1-\sum_{l\neq s} p^l}\right)} \\ = \big(1-\sum_j p^j\big)\frac{-1}{1-\sum_{l\neq s} p^l} + \big(1-\sum_{j\neq s} p^j\big)\frac{1-\sum_l p^l}{\big(1-\sum_{l\neq s} p^l\big)^2} = 0,\end{aligned} \tag{9.3.21}$$

and the third summand via

$$\begin{aligned}&\sum_{i,j} p^i(\delta_j^i - p^j)\frac{\partial}{\partial p^i}\frac{\partial}{\partial p^j}\frac{1-\sum_l p^l}{1-\sum_{l\neq s} p^l} \\ &= \sum_{i,j} p^i(\delta_j^i - p^j)\left(\frac{(\delta_s^i-1)+(\delta_s^j-1)}{\big(1-\sum_{l\neq s} p^l\big)^2} + 2(1-\delta_s^i)(1-\delta_s^j)\frac{1-\sum_l p^l}{\big(1-\sum_{l\neq s} p^l\big)^3}\right) \\ &= -2\frac{\big(\sum_{i\neq s} p^i\big)\big(1-\sum_{j\neq s} p^j\big)}{\big(1-\sum_{l\neq s} p^l\big)^2} + 2\Big(\sum_{i\neq s} p^i\Big)\Big(1-\sum_{j\neq s} p^j\Big)\frac{1-\sum_l p^l}{\big(1-\sum_{l\neq s} p^l\big)^3} = 0\end{aligned} \tag{9.3.22}$$

also vanishes.

Ultimately, if $s \neq 0$, $r \neq 0$, we have

$$p^j \frac{\partial}{\partial p^j}\frac{p^r}{p^s+p^r} = \frac{p^s p^r}{(p^s+p^r)^2}(\delta_r^j - \delta_s^j). \tag{9.3.23}$$

Using this property for the second summand, we obtain

$$\begin{aligned}&\sum_{i,j} p^i(\delta_j^i - p^j)\left(\frac{\partial}{\partial p^i}\psi(\pi^{r,s}(p))\right)\left(\frac{\partial}{\partial p^j}\frac{p^r}{p^s+p^r}\right) \\ &= \sum_i \left(\frac{\partial}{\partial p^i}\psi(\pi^{r,s}(p))\right) p^i\left(\sum_j \delta_j^i\left(\frac{\partial}{\partial p^j}\frac{p^r}{p^s+p^r}\right) - \sum_j p^j\left(\frac{\partial}{\partial p^j}\frac{p^r}{p^s+p^r}\right)\right) \\ &= \sum_i \frac{\partial}{\partial p^i}\psi(\pi^{r,s}(p))\frac{p^s p^r}{(p^s+p^r)^2}(\delta_r^i - \delta_s^i) = 0.\end{aligned} \tag{9.3.24}$$

The last equality is due to the fact that the sum over i in the last line vanishes because of the symmetry of π in the coordinates p^s and p^r, i.e. we have $\frac{\partial \tilde{p}^m}{\partial p^i} = \delta_i^m(1-\delta_s^m) + \delta_r^m\delta_s^i$ and consequently

$$\frac{\partial}{\partial p^s}\psi(\pi^{r,s}(p)) = \frac{\partial}{\partial \tilde{p}^r}\psi(\tilde{p}) = \frac{\partial}{\partial p^r}\psi(\pi^{r,s}(p)). \tag{9.3.25}$$

For the third summand, we use

$$\frac{\partial}{\partial p^i}\frac{\partial}{\partial p^j}\frac{p^r}{p^s+p^r} = 2\frac{\delta_j^i(\delta_s^i p^r - \delta_r^i p^s)}{(p^s+p^r)^3} + \frac{\delta_s^i\delta_r^j(1-\delta_j^i)(p^r-p^s)}{(p^s+p^r)^3} \tag{9.3.26}$$

and get

$$\sum_{i,j} p^i(\delta_j^i - p^j)\frac{\partial}{\partial p^i}\frac{\partial}{\partial p^j}\frac{p^r}{p^s+p^r} = \frac{2p^s(1-p^s)p^r - 2p^r(1-p^r)p^s - 2p^sp^r(p^r-p^s)}{(p^s+p^r)^3} = 0. \tag{9.3.27}$$

Altogether, we have

$$L_d^*\bar{\psi} = L_d^*\left(\psi(\pi^{r,s}(p))\cdot\frac{p^r}{p^s+p^r}\right) = -\kappa\psi(\pi^{r,s}(p))\frac{p^r}{p^s+p^r} = -\kappa\bar{\psi} \tag{9.3.28}$$

for arbitrary $r, s \in I_d$, thus proving Eq. (9.3.5). □

9.4 Probabilistic Interpretation of the Extension Scheme

Before proceeding with an iteration of the extension scheme, we should like to discuss the meaning of the extension constraints 9.3.1. A target set on the space of $d-1$ alleles can not only be reached from a constellation of $d-1$ alleles, but also from one of d alleles by allele loss. That is, the ancestral populations might have possessed more alleles than the current one.

Therefore, we need to analyze how such a target set can also attract contributions from the space of d alleles. A natural assumption for such an extension is that the probability density at the transition from the d-allelic domain to the $(d-1)$-allelic domain stays regular, i.e. small alterations of the allelic configuration should only affect the probability in a controlled way. This is formulated in condition (i) and implies the C_p^∞ regularity (cf. equality (2.11.23)) for the corresponding domains. Moreover, a boundary condition enters, as for transitions to domains of a different set of $d-1$ alleles, the corresponding probability should also stay regular with the additional requirement that in the limit it vanishes on those other $(d-1)$-allelic domains; this is also part of condition (i) and correspondingly implies the

$C^{\infty}_{p_0}$ regularity (cf. equality (2.11.24)). We also wish to link the evolution of the original probability density and its extension by requiring that both are subject to the same type of evolution in the corresponding domain, i.e. are governed by the corresponding Kolmogorov backward equation in the relevant formulation, which is condition (ii). The extension Proposition 9.3.1 then states that any (proper) solution of the Kolmogorov backward equation, which describes the evolving attraction of some target set via the final condition f, may be extended to a corresponding solution of the Kolmogorov backward equation in the domain of subsequent higher dimension with both conditions above applying. In the context of a Wright–Fisher model, this loss of the extra allele s is modelled as if it was in competition with just one other allele r dependent on the index chosen *(fibration property)* . Thus, we say that allele s is lost over allele r.

However, as may be observed by Remark 9.3.2, this extension actually yields the solution to a different problem, namely the attraction generated by the target set itself plus an induced (generalised) target set in the bigger domain which are given by f and its corresponding extension $\bar{f}$. If one wishes to return to the original problem, the attraction of the original target set only located in the $(d-1)$-allelic domain, the induced target set needs to be compensated for by a proper solution in (the interior of) the d-allelic domain for a corresponding final condition.

As may also be seen in Proposition 9.3.1, for $d \geq 2$ the given extension scheme involves a potential ambiguity regarding the choice of the extension target face index r. However, in case of iterations, the boundary condition in Definition 9.3.1 (i) limits this to a unique appropriate value as will be demonstrated in the next section; for a simple extension from a 0-dimensional domain or if the starting distribution smoothly vanishes towards all boundaries of subsequent lower dimension (as with proper solutions), an extension is always in accordance with the boundary condition.

9.5 Iterated Extensions

A repeated application of Proposition 9.3.1 yields the existence of iterated extensions (generalising the corresponding result for $n = 2$ in [85] and the (less explicit) result stated in [87] without proof):

Proposition 9.5.1 (Pathwise Extension of Solutions) *Let $k, n \in \mathbb{N}$ with $0 \leq k < n$, $\{i_k, i_{k+1}, \ldots, i_n\} \subset I_n := \{0, 1, \ldots, n\}$ with $i_i \neq i_j$ for $i \neq j$ and $I_k := I_n \setminus \{i_{k+1}, \ldots, i_n\}$, and let u_{I_k} be a proper solution of the Kolmogorov backward equation (9.2.1) in $\Delta_k^{(I_k)}$ for some final condition $f \in \mathcal{L}^2\big(\Delta_k^{(I_k)}\big)$ as in Proposition 9.1.1. For $d = k+1, \ldots, n$ and $I_d := I_k \cup \{i_{k+1}, \ldots i_d\}$, an extension of $\bar{u}_{I_k}^{i_k,\ldots,i_{d-1}}$ in $\big(\Delta_{d-1}^{(I_{d-1})}\big)_{-\infty}$ to $\bar{u}_{I_k}^{i_k,\ldots,i_d} := \big(\bar{u}_{I_k}^{i_k,\ldots,i_{d-1}}\big)^{i_{d-1},i_d}$ in $\big(\Delta_d^{(I_d)}\big)_{-\infty}$ as by Proposition 9.3.1 is compatible with the extension constraints 9.3.1 if (and for $d \geq k+2$ and $[f] \neq 0$ in $L^2\big(\Delta_k^{(I_k)}\big)$ also only if) putting $r(d) = i_{d-1}$ for the extension*

target face index, and we respectively have

$$\bar{u}_{I_k}^{i_k,\dots,i_d}(p,t) = u_{I_k}(\pi^{i_k,\dots,i_d}(p),t)\prod_{j=k}^{d-1}\frac{p^{i_j}}{\sum_{l=j}^{d}p^{i_l}}, \quad (p,t)\in\left(\Delta_d^{(I_d)}\right)_{-\infty} \tag{9.5.29}$$

with $p^0 = 1-\sum_{i\in I_d\setminus\{0\}}p^i$ *and* $\pi^{i_k,\dots,i_d}(p) = (\tilde{p}^1,\dots,\tilde{p}^n)$ *such that* $\tilde{p}^{i_k} = p^{i_k}+\ldots+p^{i_d}$, $\tilde{p}^{i_{k+1}} = \ldots = \tilde{p}^{i_d} = 0$ *and* $\tilde{p}^j = p^j$ *for* $j\in I_d\setminus\{i_k,\dots,i_d\}$.

Thus, the resulting combination of all extensions to a function $\bar{U}_{I_k}^{i_k,\dots,i_n}$ *in* $\left(\bigcup_{k\le d\le n}\Delta_d^{(I_d)}\right)_{-\infty}$ *is obtained by putting*

$$\begin{aligned}\bar{U}_{I_k}^{i_k,\dots,i_n}(p,t) &:= u_{I_k}(p,t)\chi_{\Delta_k^{(I_k)}}(p) + \sum_{k+1\le d\le n}\bar{u}_{I_k}^{i_k,\dots,i_d}(p,t)\chi_{\Delta_d^{(I_d)}}(p)\\ &= u_{I_k}(p,t)\chi_{\Delta_k^{(I_k)}}(p) + \sum_{k+1\le d\le n}u_{I_k}(\pi^{i_k,\dots,i_d}(p),t)\prod_{j=k}^{d-1}\frac{p^{i_j}}{\sum_{l=j}^{d}p^{i_l}}\chi_{\Delta_d^{(I_d)}}(p)\end{aligned} \tag{9.5.30}$$

with $p^0 = 1-\sum_{i\in I_n\setminus\{0\}}p^i$ *is in* $C^\infty_{p_0}\left(\bigcup_{k\le d\le n}\Delta_d^{(I_d)}\right)$ *with respect to the spatial variables for* $t<0$ *as well as in* $C^\infty((-\infty,0))$ *with respect to* t, *and we have*

$$\begin{cases} L^*\bar{U}_{I_k}^{i_k,\dots,i_n} = -\frac{\partial}{\partial t}\bar{U}_{I_k}^{i_k,\dots,i_n} & \text{in } \left(\bigcup_{k\le d\le n}\Delta_d^{(I_d)}\right)_{-\infty}\\ \bar{U}_{I_k}^{i_k,\dots,i_n}(\cdot,0) = \bar{F}_{I_k}^{i_k,\dots,i_n} & \text{in } \bigcup_{k\le d\le n}\Delta_d^{(I_d)}\end{cases} \tag{9.5.31}$$

where $\bar{F}_{I_k}^{i_k,\dots,i_n}\in\mathcal{L}^2\left(\bigcup_{k\le d\le n}\Delta_d^{(I_d)}\right)$ *is an analogous extension of the final condition* $f = f_{I_k}$ *in* $\Delta_k^{(I_k)}$ *as in Remark 9.3.2; in particular, we have* $\bar{U}_{I_k}^{i_k,\dots,i_n}\big|_{\Delta_k^{(I_k)}}(\cdot,0) = f$ *in* $\Delta_k^{(I_k)}$.

Corollary 9.5.1 *For* $n\in\mathbb{N}_+$, $k=0$ *and* $u_{\{i_0\}}\equiv 1$ *in* $\Delta_0^{(\{i_0\})}\subset\partial_0\Delta_n$, *Eq.* (9.5.29) *resp. Equation* (9.5.30) *restricted to* Δ_n *and with the t-coordinate suppressed coincides with Littler's formula in* Δ_n *(cf. [87]):*

$$\bar{U}_{\{i_0\}}^{i_0,i_1\dots,i_n}\big|_{\Delta_n}(p) \equiv \bar{u}_{\{i_0\}}^{i_0,i_1\dots,i_n}(p) = p^{i_0}\cdot\frac{p^{i_1}}{1-p^{i_0}}\cdot\ldots\cdot\frac{p^{i_{n-1}}}{1-\sum_{l=0}^{n-2}p^{i_l}}. \tag{9.5.32}$$

Proof of Proposition 9.5.1 The result is basically an application of Proposition 9.3.1, which yields the regularity and the solution property (cf. Eq. (9.5.31)) in every $\Delta_d^{(I_d)}$. It only remains to show inductively that the boundary behaviour in each extension step respects the extension constraints 9.3.1 as well as the formula (9.5.29).

Clearly, a proper solution u_{I_k} of the Kolmogorov backward equation in $\left(\Delta_k^{(I_k)}\right)_{-\infty}$ as in Proposition 9.1.1 satisfies Eq. (9.5.29) and is of class $C_0^\infty\left(\Delta_k^{(I_k)}\right)$ w. r. t. the spatial variables for $t < 0$ (which in particular implies that it is smoothly extendable to $\partial_{k-1}\Delta_k^{(I_k)}$). Extending u_{I_k} to $\left(\Delta_{k+1}^{(I_{k+1})}\right)_{-\infty}$ via Proposition 9.3.1 with $s(k+1) = i_{k+1}$ and $r(k+1) = i_k$ yields a function $\bar{u}_{I_k}^{i_k,i_{k+1}}$ of type (9.5.29), which for $t < 0$ smoothly extends to all boundary faces $\partial_k\Delta_{k+1}^{(I_{k+1})}$ and vanishes there except for $\Delta_k^{(I_k)}$ (where it coincides with u_{I_k}) by the assumed boundary behaviour of u_{I_k}. We may thus assume that for $k < d-1 < n$ an assembled extension $\bar{U}_{I_k}^{i_k,\dots,i_{d-1}}$ (corresponding to Eq. (9.5.30)) in $C_{p_0}^\infty\left(\bigcup_{k\le m\le d-1}\Delta_m^{(I_m)}\right)$ with respect to the spatial coordinates exists whose top-dimensional component $\bar{U}_{I_k}^{i_k,\dots,i_{d-1}}\big|_{\left(\Delta_{d-1}^{(I_{d-1})}\right)_{-\infty}} =: \bar{u}_{I_k}^{i_k,\dots,i_{d-1}}$ satisfies Eq. (9.5.29).

We may then perform an extension of $\bar{u}_{I_k}^{i_k,\dots,i_{d-1}}$ in $\left(\Delta_{d-1}^{(I_{d-1})}\right)_{-\infty}$ to $\bar{u}_{I_k}^{i_k,\dots,i_d}$ in $\left(\Delta_d^{(I_d)}\right)_{-\infty}$ via Proposition 9.3.1 with $s(d) = i_d$ and $r(d) = i_{d-1}$. By the assumed boundary behaviour of $\bar{u}_{I_k}^{i_k,\dots,i_{d-1}}$ (i.e. $\bar{U}_{I_k}^{i_k,\dots,i_{d-1}}$ being of class $C_{p_0}^\infty$), $\bar{u}_{I_k}^{i_k,\dots,i_d}$ smoothly extends to all boundary faces $\partial_{d-1}\Delta_d^{(I_d)} \setminus \Delta_{d-1}^{(I_d\setminus\{i_{d-1}\})}$ and vanishes there except for $\Delta_{d-1}^{(I_{d-1})}$ (where it coincides with $\bar{u}_{I_k}^{i_k,\dots,i_{d-1}}$) for $t < 0$. By putting $r(d) = i_{d-1}$, this in particular also holds for $\Delta_{d-1}^{(I_d\setminus\{i_{d-1}\})}$, which in turn would otherwise be violated if $f \neq 0$ almost everywhere as may be seen from the proof of Proposition 9.3.1. Then, the boundary behaviour respects the extension constraints 9.3.1, and we correspondingly have $\bar{U}_{I_k}^{i_k,\dots,i_d} := \bar{U}_{I_k}^{i_k,\dots,i_{d-1}} + \bar{u}_{I_k}^{i_k,\dots,i_d}\chi_{\Delta_d^{(I_d)}} \in C_{p_0}^\infty\left(\bigcup_{k\le m\le d}\Delta_m^{(I_m)}\right)$ w. r. t. the spatial variables for $t < 0$.

To show Eq. (9.5.29), we obtain for $\bar{u}_{I_k}^{i_k,\dots,i_d}$ by Eq. (9.3.4) when plugging in the formula (9.5.29) for $\bar{u}_{I_k}^{i_k,\dots,i_{d-1}}$

$$\begin{aligned}
\bar{u}_{I_k}^{i_k,\dots,i_d}(p,t) &= \bar{u}_{I_k}^{i_k,\dots,i_{d-1}}(\pi^{i_{d-1},i_d}(p),t)\frac{p^{i_{d-1}}}{p^{i_{d-1}}+p^{i_d}} \\
&= u_{I_k}(\pi^{i_k,\dots,i_{d-1}}(\pi^{i_{d-1},i_d}(p)),t)\prod_{j=k}^{d-2}\frac{(\pi^{i_{d-1},i_d}(p))^{i_j}}{\sum_{l=j}^{d-1}(\pi^{i_{d-1},i_d}(p))^{i_l}}\frac{p^{i_{d-1}}}{p^{i_{d-1}}+p^{i_d}} \\
&= u_{I_k}(\pi^{i_k,\dots,i_d}(p),t)\prod_{j=k}^{d-1}\frac{p^{i_j}}{\sum_{l=j}^{d}p^{i_l}} \qquad \text{in } \left(\Delta_d^{(I_d)}\right)_{-\infty} \qquad (9.5.33)
\end{aligned}$$

as $(\pi^{i_{d-1},i_d}(p))^{i_j} = p^{i_j}$ for $i_j = i_k,\dots,i_{d-2}$ and $(\pi^{i_{d-1},i_d}(p))^{i_{d-1}} = p^{i_{d-1}} + p^{i_d}$. If some index i_j equals zero (w. l. o. g. $i_0 = 0$) corresponding to $(\pi^{i_{d-1},i_d}(p))^0$, this expression gets replaced by $p^0 \in \Delta_d^{(I_d)}$ as we have $(\pi^{i_{d-1},i_d}(p))^0 = 1 - \sum_{j=1}^{d-1}(\pi^{i_{d-1},i_d}(p))^{i_j} = 1 - \sum_{j=1}^{d}p^{i_j} \equiv p^0$. Furthermore, $\pi^{i_k,\dots,i_{d-1}}(\pi^{i_{d-1},i_d}(p)) = \pi^{i_k,\dots,i_d}(p)$ directly follows from the definitions, thus proving Eq. (9.5.29) for $\bar{u}_{I_k}^{i_k,\dots,i_d}$ in $\left(\bigcup_{k\le m\le d}\Delta_m^{(I_m)}\right)_{-\infty}$. □

Remark 9.5.1 Geometrically, the choice of the extension target face indices $s(d) = i_d$ and $r(d) = i_{d-1}$ signifies that the extension source face $\Delta_{d-1}^{(\{i_0,\dots,i_{d-2},i_{d-1}\})}$ and the target face $\Delta_{d-1}^{(\{i_0,\dots,i_{d-2},i_d\})}$ are adjacent faces to the highest degree, as they share $d-1$ vertices (for $d \geq 2$). Furthermore, their intersection $\Delta_{d-2}^{(\{i_0,\dots,i_{d-2}\})}$ is the extension source face of the previous step.

Sticking to the preceding probabilistic interpretation, $\bar{u}_{I_k}^{i_k,i_{k+1},\dots,i_n}$ depicts the iterated 'attraction' of an (analogously extended) target set in $\Delta_k^{(I_k)}$ along a corresponding *extension path* specified by $i_k,\dots,i_n$ resp. the corresponding index sets $I_k \subset \dots \subset I_n$. Thus, $\bar{u}_{I_k}^{i_k,i_{k+1},\dots,i_n}$ gives the total probability for all paths in $\overline{\Delta}_n$ starting in $\Delta_n^{(I_n)}$, passing through the (sub)simplices

$$\Delta_{n-1}^{(I_{n-1})} \longrightarrow \Delta_{n-2}^{(I_{n-1})} \longrightarrow \dots \longrightarrow \Delta_{k+1}^{(I_{k+1})} \longrightarrow \Delta_k^{(I_k)} \tag{9.5.34}$$

and reaching the eventual target set, which, in the setting of the Wright–Fisher model, corresponds to eventually losing $n-k$ of originally $n+1$ alleles in such a manner that from dimension $n-1$ down to k exactly the allele sets

$$I_n \longrightarrow I_{n-1} \longrightarrow \dots \longrightarrow I_{k+1} \longrightarrow I_k \tag{9.5.35}$$

are present until reaching the eventual target set.

As depicted, these pathwise extensions are a consequence of the boundary condition of the extension constraints 9.3.1: On the one hand, there is only one allele which is lost at a certain time; on the other hand, as this loss is modelled as if it was in competition with just one other allele, the corresponding allele always is the one which is lost next. Thus allele i_d is lost over i_{d-1}; merely in the last step, i.e. the loss of allele i_{k+1}, the index i_k determines which of the alleles in I_k is the one i_{k+1} is lost over. Other extensions which may likewise be constructed by the extension Lemma 9.3.1 will not be considered here.

However, the corresponding extensions in Proposition 9.5.1 lack a global (pathwise) regularity property on the entire $\overline{\Delta}_n$, i.e. are not in C_p^∞ w. r. t. the spatial variables, as this applies only along the corresponding extension path. Outside this path, generally no continuous, and a fortiori no smooth extensions exist. This is caused by the incompatibilities involved by this construction (cf. also Sect. 9.4): For example on $\Delta_{k+1}^{(\tilde{I}_{k+1})}$ with $\tilde{I}_{k+1} := I_k \cup \{\tilde{\imath}_k\}$ and $\tilde{\imath}_k \in I_n \setminus I_{k+1}$, a positive hit probability for the target set in $\Delta_k^{(I_k)}$ by a direct loss of allele $\tilde{\imath}_k$ would exist, yet the considered solution necessarily vanishes on $\Delta_{k+1}^{(\tilde{I}_{k+1})}$ as this is a boundary face of $\Delta_{k+2}^{(I_{k+2})}$ outside the specified path.

This defect is overcome by mounting these extensions into a global solution covering all possible extensions paths, each one of them corresponding to a certain ordering of the indices in $I_n \setminus I_k$. As in the first extension step, the extension target face is not defined for a given extension path and a non-empty target set by the extension boundary condition (i) in Definition 9.3.1 (except for $k = 0$;

cf. Proposition 9.5.1), correspondingly all indices in I_k may serve as target face index. This is taken into account by additionally summing over all possible first stage extensions and normalising, yielding in total:

Proposition 9.5.2 (Global Extension of Solutions) *Let $k, n \in \mathbb{N}$ with $0 \leq k < n$, $I_k \subset I_n := \{0, 1, \ldots, n\}$ with $|I_k| = k + 1$, and let u_{I_k} be a proper solution of the Kolmogorov backward equation (9.2.1) in $\Delta_k^{(I_k)}$ for some final condition $f \in \mathcal{L}^2\big(\Delta_k^{(I_k)}\big)$ as in Proposition 9.1.1. Then we assemble all pathwise extensions of u_{I_k} as by Proposition 9.5.1 into a function $\bar{U}_{I_k} \in \big(\overline{\Delta}_n\big)_{-\infty}$ by putting*[3]

$$\bar{U}_{I_k}(p,t) := u_{I_k}(p,t)\chi_{\Delta_k^{(I_k)}}(p) + \frac{1}{|I_k|}\sum_{i_k \in I_k}\sum_{k+1 \leq d \leq n}\sum_{i_{k+1} \in I_n \setminus I_k} \cdots \sum_{\substack{i_d \in I_n \setminus (I_k \cup \\ \{i_{k+1}, \ldots, i_{d-1}\})}} \bar{u}_{I_k}^{i_k, \ldots, i_d}(p,t)\chi_{\Delta_d^{(I_k \cup \{i_{k+1}, \ldots, i_d\})}}(p) \tag{9.5.36}$$

for $(p,t) \in \big(\bigcup_{I_k \subset I_d \subset I_n} \Delta_d^{(I_d)}\big)_{-\infty}$ and $\bar{U}_{I_k}(p,t) := 0$ in the remainder of $\big(\overline{\Delta}_n\big)_{-\infty}$. Then this function $\bar{U}_{I_k} \in \big(\overline{\Delta}_n\big)_{-\infty}$ is in $C_p^\infty\big(\overline{\Delta}_n\big)$ with respect to the spatial variables for $t < 0$ as well as in $C^\infty((-\infty, 0))$ with respect to t. Furthermore, $\bar{U}_{I_k}$ is a solution of the corresponding Kolmogorov backward equation in $\big(\overline{\Delta}_n\big)_{-\infty}$ and for $t = 0$ matches an analogously assembled extension $\bar{F}_{I_k}$ off $= f_{I_k}$ in $\Delta_k^{(I_k)}$ as final condition in $\overline{\Delta}_n$ (cf. Remark 9.3.2).

Proof The asserted global regularity directly follows from properties of the applied extension scheme as stated in Lemma 9.3.1 and Proposition 9.5.1 and the construction of $\bar{U}_{I_k}$, which is such that potential discontinuities are ruled out by assembling all extensions along arbitrary paths. The solution property and the compliance with the analogously constructed final condition likewise straightforwardly extend from Proposition 9.5.1. □

Returning again to the probabilistic interpretation, $\bar{U}_{I_k}$ now depicts the full iterated 'attraction' of some eventual target set in $\Delta_k^{(I_k)}$ and its (successively) induced target sets in $\Delta_d^{(I_d)} \subset \overline{\Delta}_n$ with $I_d \supset I_k$, which may now be reached along arbitrary paths. Thus, $\bar{U}_{I_k}$ gives the total probability for all paths from $\Delta_n^{(I_n)}$ to eventually $\Delta_k^{(I_k)}$—with no assumptions on possible intermediate stages made. In the setting of the Wright–Fisher model, this corresponds to eventually losing $n - k$ of previously $n + 1$ alleles irrespective of any order of loss.

[3]The last sum actually only comprises a single summand; this notation is used to illustrate the choice of the index i_d, however.

Since $\bar{U}_{I_k}$ represents the most general extension of a given solution u_{I_k} in $\Delta_k^{(I_k)}$ to $\overline{\Delta}_n$, the general solution scheme for solutions of the extended Kolmogorov backward equation (9.2.1) may now be developed.

9.6 Construction of General Solutions via the Extension Scheme

We now consider a general final condition of the form $f = \sum_{d=0}^{n} f_d \chi_{\partial_d \Delta_n} \in \mathcal{L}^2\big(\bigcup_{d=0}^{n} \partial_d \Delta_n\big)$. Our aim is to construct a solution of the extended Kolmogorov backward equation (9.2.1) that captures the full dynamics of the process on the entire $\big(\overline{\Delta}_n\big)_{-\infty}$. This will be achieved by global extensions of a (proper) solution of the Kolmogorov backward equation in every face of the domain as in Proposition 9.5.2; these globally extended solutions then will be superposed in a way that eventually the given final condition is met in the entire $\overline{\Delta}_n$. The probabilistic interpretation of this process was described in Sect. 9.4.

The procedure works as follows. First, Eq. (9.2.1) is solved in each $\big(\Delta_0^{(\{i_0\})}\big)_{-\infty} \subset (\partial_0 \Delta_n)_{-\infty}$ for the final condition f_0, and afterwards, these solutions are iteratively extended to $\big(\overline{\Delta}_n\big)_{-\infty}$ with the help of Proposition 9.5.2, which analogously generates an iteratively extended final condition in $\overline{\Delta}_n$ for $t = 0$.

Subsequently, a (proper) solution in each $\big(\Delta_1^{(I_1)}\big)_{-\infty} \subset (\partial_1 \Delta_n)_{-\infty}$ for the final condition f_1 minus the extension of f_0 is determined, which is then iteratively extended to $\big(\overline{\Delta}_n\big)_{-\infty}$ (again likewise generating an analogously extended final condition). This procedure is repeated until after finding a (proper) solution in $(\Delta_n)_{-\infty}$ an extended solution in the entire $\big(\overline{\Delta}_n\big)_{-\infty}$ is determined.

A solution of the extended Kolmogorov backward equation (9.2.1) restricted to some $\big(\Delta_0^{(\{i_0\})}\big)_{-\infty} \subset (\partial_0 \Delta_n)_{-\infty}$ is—of course—trivial, i.e. $u_{\{i_0\}}(p,t) = f_0(p)$ for $(p,t) \in \big(\Delta_0^{(\{i_0\})}\big)_{-\infty}$, and by Proposition 9.5.2 we obtain $\bar{U}_{\{i_0\}}$ as an extension to $\big(\overline{\Delta}_n\big)_{-\infty}$. Summing over all $\Delta_0^{(\{i_0\})}$ yields

$$\bar{U}_0 := \sum_{\{i_0\} \subset I_n} \bar{U}_{\{i_0\}} \qquad \text{in } \big(\overline{\Delta}_n\big)_{-\infty} \tag{9.6.37}$$

with $\bar{U}_0$ in $C_p^\infty\big(\overline{\Delta}_n\big)$ with respect to the spatial variables as well as in $C^\infty((-\infty,0))$ with respect to t and

$$\begin{cases} L^* \bar{U}_0 = -\frac{\partial}{\partial t} \bar{U}_0 & \text{in } \big(\overline{\Delta}_n\big)_{-\infty} \\ \bar{U}_0(\cdot\,,0) = \bar{F}_0' & \text{in } \overline{\Delta}_n \end{cases} \tag{9.6.38}$$

where $\bar{F}'_0$ is a corresponding superposed global extension of all $f'_0 \equiv f_0$ in $\partial_0\Delta_n$ as described above for the $u_{\{i_0\}}$ (cf. also Remark 9.3.2); in particular, we have $\bar{U}_0|_{\partial_0\Delta_n}(\cdot,0) = f_0$.

For the next step, proper solutions in $(\partial_1\Delta_n)_{-\infty}$ are determined and likewise extended to $\left(\overline{\Delta_n}\right)_{-\infty}$. However, as this extension procedure will be repeated for all d-dimensional faces of $(\Delta_n)_{-\infty}$ for $d = 1,\dots,n$, we directly assume that suitable solutions in $\left(\bigcup_{m=0}^{d-1}\partial_m\Delta_n\right)_{-\infty}$ already have been determined and extended to $\left(\overline{\Delta_n}\right)_{-\infty}$. Thus $\sum_{m=0}^{d-1}\bar{U}_m$ solves the extended Kolmogorov backward equation (9.2.1) in $\left(\overline{\Delta_n}\right)_{-\infty}$ and matches the final condition f for $t = 0$ in $\bigcup_{m=0}^{d-1}\partial_m\Delta_n$ (still, with $\bar{U}_0(\cdot,0),\dots,\bar{U}_{d-1}(\cdot,0)$ in $\overline{\Delta_n}$ respectively matching a corresponding superposed global extension $\bar{F}'_m$ of the final condition f'_m in $\partial_m\Delta_n$ modified as below). Then, a proper solution u_{I_d} by Proposition 9.1.1 in each $\left(\Delta_d^{(I_d)}\right)_{-\infty} \subset (\partial_d\Delta_n)_{-\infty}$, $I_d \subset I_n$ is determined which matches the modified final condition

$$f'_d := f_d - \sum_{m=0}^{d-1}\bar{F}'_m|_{\partial_d\Delta_n} \quad \text{in } \partial_d\Delta_n, \tag{9.6.39}$$

correspondingly restricted to the relevant $\Delta_d^{(I_d)}$. For each I_d, the solution u_{I_d} is then extended to $\left(\overline{\Delta_n}\right)_{-\infty}$ via Proposition 9.5.2 each leading to a function $\bar{U}_{I_d}$. Clearly, these extensions do not interfere with the solutions on lower dimensional faces by definition.

Summing over the extensions of all u_{I_d}, $I_d \subset I_n$, we obtain

$$\bar{U}_d := \sum_{I_d\subset I_n}\bar{U}_{I_d} \quad \text{in } \left(\overline{\Delta_n}\right)_{-\infty} \tag{9.6.40}$$

as the global extension of all (proper) solutions in $(\partial_d\Delta_n)_{-\infty}$. By Proposition 9.5.2 and the linearity of the differential equation, $\bar{U}_d$ is in $C_p^\infty\left(\overline{\Delta_n}\right)$ w. r. t. the spatial variables as well as in $C^\infty((-\infty,0)$ with respect to t and solves the extended Kolmogorov backward equation and for $t = 0$ matches a corresponding superposed global extension $\bar{F}'_d$ of the final condition f'_d in $\partial_d\Delta_n$, thus in particular $\bar{U}_d(\cdot,0)|_{\partial_d\Delta_n} = f'_d$. Consequently, the sum of all solutions that we have extended so far also is in $C_p^\infty\left(\overline{\Delta_n}\right)$ w. r. t. the spatial variables as well as in $C^\infty((-\infty,0)$ with respect to t and satisfies

$$\begin{cases} L^*\left(\sum_{m=0}^d\bar{U}_m\right) = -\frac{\partial}{\partial t}\left(\sum_{m=0}^d\bar{U}_m\right) & \text{in } \left(\overline{\Delta_n}\right)_{-\infty} \\ \left(\sum_{m=0}^d\bar{U}_m\right)|_{\bigcup_{m=0}^d\partial_m\Delta_n}(\cdot,0) = f|_{\bigcup_{m=0}^d\partial_m\Delta_n} & \text{in } \bigcup_{m=0}^d\partial_m\Delta_n. \end{cases} \tag{9.6.41}$$

Iterating the preceding step, we eventually arrive at $\sum_{m=0}^{n-1}\bar{U}_m$. For the remaining $(\Delta_n)_{-\infty}$, finally a (proper) solution $u_{I_n} =: \bar{U}_n$ by Proposition 9.1.1 is determined

matching the modified final condition

$$f_n' := f_n - \sum_{m=0}^{n-1} \bar{F}_m'|_{\Delta_n} \quad \text{in } \Delta_n. \tag{9.6.42}$$

Then the sum of all globally extended (proper) solutions in all strata of the domain

$$\bar{U} := \sum_{j=0}^{n} \bar{U}_j \tag{9.6.43}$$

is in $C_p^\infty\big(\overline{\Delta}_n\big)$ w. r. t. the spatial variables as well as in $C^\infty((-\infty, 0))$ with respect to t and satisfies

$$\begin{cases} L^*\bar{U} = -\frac{\partial}{\partial t}\bar{U} & \text{in } \big(\overline{\Delta}_n\big)_{-\infty} \\ \bar{U}(\cdot\,, 0) = f & \text{in } \overline{\Delta}_n, \end{cases} \tag{9.6.44}$$

and thus is a solution of the extended Kolmogorov backward equation (9.2.1).

Altogether, we have obtained the following existence result.

Theorem 9.6.1 *For a given final condition $f \in \mathcal{L}^2\big(\bigcup_{d=0}^n \partial_d\Delta_n\big)$, the extended Kolmogorov backward equation (4.2.13) corresponding to the n-dimensional Wright–Fisher model in diffusion approximation always has a solution $\bar{U}\colon \big(\overline{\Delta}_n\big)_{-\infty} \longrightarrow \mathbb{R}$ with $\bar{U}(\cdot\,, t) \in C_p^\infty\big(\overline{\Delta}_n\big)$ for each fixed $t \in (-\infty, 0)$ and $\bar{U}(p, \cdot\,) \in C^\infty((-\infty, 0))$ for each fixed $p \in \overline{\Delta}_n$.*

Below, we shall show that for $f \in \mathcal{L}^2\big(\partial_0\Delta_n\big)$—and under some additional regularity assumptions—the solution obtained, i.e. $\bar{U}_0$, also is the unique solution given the described extension scheme. For this, we will employ a regularising blow-up scheme, which will be the subject of the next section.

9.7 A Regularising Blow-Up Scheme for Solutions of the Extended Backward Equation

In the present section, we continue the detailed investigation of the boundary behavior of solutions of the (extended) Kolmogorov backward equation (9.2.1). In analytical terms, the issue is the regularity of solutions at singularities of the boundary, that is, where two or more faces of the simplex Δ_n meet. The particular extension paths from the boundary into the interior of the simplex may result in boundary singularities at certain strata of the boundary the domain. We are interested in the directions in which the singularities of the boundary of the simplex are approached from the interior, because our aim is to resolve these boundary singularities.

What we want to achieve in this section is the global regularity in the closure of the domain by resolving any incompatibilities between different boundary strata. For that purpose, we shall construct an appropriate transformation of the relevant part of the domain (i.e. the simplex Δ_n, cf. below) which transports the whole problem to the corresponding image domain of a product of a simplex and a cube. Through this procedure, the iteratively extended solutions are turned into corresponding solutions of the transformed equation, which are then of sufficient global regularity, in particular, they are globally continuous. For generic iteratively extended solutions this does not yet yield global continuity. It seems, however, that their transformation image may be extended that way as well.

In Sect. 9.8, we shall also apply this to the stationary case. In the stationary case, such regularised solutions are uniquely defined by their values on the vertices of the domain (analogous to a globally continuous solution of the original problem in Δ_n, cf. Sect. 9.8). It just needs to be shown that there is sufficient (unique) boundary data.

9.7.1 Motivation

The current section is the technically most involved one of this book. Therefore, it might be helpful for the reader to have some motivation for our technical constructions. To illustrate the motivation for the regularisation scheme, we use the example of $\bar{U}_{I_k}^{i_k,\dots,i_n}$ in $\overline{\Delta_n^{(I_n)}}$ as in Eq. (9.5.30): When we analyze the geometry of the respective incompatibilities we see that for every $t < 0$ the critical set for the top-dimensional component $\bar{u}_{I_k}^{i_k,\dots,i_n}$ resp. its continuous extension actually only consists of the domain where we have $p^{i_n} + p^{i_{n-1}} = 0$, hence $\overline{\Delta_{n-2}^{(I_{n-2})}}$. On all other boundary strata of arbitrary dimension, $\bar{u}_{I_k}^{i_k,\dots,i_n}$ as in Eq. (9.5.29) is continuously extendable and of class C^∞ with respect to the spatial variables there. Thus, at first there is only one connected component of the boundary gap which needs to be addressed.

However, as will turn out, the full hierarchical solution $\bar{U}_{I_k}^{i_k,\dots,i_n}$ actually comprises a nested incompatibility in $\overline{\Delta_{n-2}^{(I_{n-2})}}$ in the sense that also $\bar{u}_{I_k}^{i_k,\dots,i_{n-1}}$ does not extend continuously to $\overline{\Delta_{n-3}^{(I_{n-3})}}$ and so forth until $\bar{u}_{I_k}^{i_k,i_{k+1},i_{k+2}}$ not extending continuously to $\overline{\Delta_k^{(I_k)}}$. This implies that the desired transformation needs to affect all relevant dimensions, which will be accomplished by an iterative procedure: In each step, one dimension from the simplex is removed and converted into a dimension of the corresponding cube component, i.e. the corresponding coordinate is released from the simplex property $\sum_i p^i \leq 1$. In doing so, the solution gains the required regularity at the corresponding level with each iteration, i.e. eventually each of its components is transformed such that it extends smoothly to the boundary. Thus, after $n - k - 1$ of these steps, the relevant component of $\overline{\Delta_n^{(I_n)}}$ is converted into a cube of dimension $n - k - 1$, and the correspondingly transformed solution is

sufficiently regularised. In particular, we shall show that it smoothly extends to the full boundary.

9.7.2 The Blow-Up Transformation and Its Iteration

We shall now present the details of the blow-up transformation and derive all necessary results. We start with the basic transformation and then proceed to the results for a suitably iterated application of this blow-up transformation (see Fig. 9.1). For the notation, we refer to Sect. 2.11, in particular to Sect. 2.11.4 for the cube notation.

Lemma 9.7.1 (Blow-Up Transformation) *Let $I_d = \{0, 1, \dots, d\}$. A blow-up transformation Φ_s^r with $r, s \in I_d \setminus \{0\}$ mapping*

$$\overline{\Delta_d^{(I_d)}} \setminus \overline{\Delta_{d-2}^{(I_d \setminus \{r,s\})}} = \left\{(p^1, \dots, p^d) \middle| p^i \geq 0 \text{ for } i \in I_d, p^r + p^s > 0\right\} \tag{9.7.45}$$

with $p^0 := 1 - \sum_{i \in I_d \setminus \{0\}} p^i$ C^∞-diffeomorphically onto

$$\left(\overline{\Delta_{d-1}^{(I_d \setminus \{s\})}} \setminus \overline{\Delta_{d-2}^{(I_d \setminus \{r,s\})}}\right) \times \overline{\square_1^{(\{s\})}}$$
$$= \left\{(\tilde{p}^1, \dots, \tilde{p}^d) \middle| \tilde{p}^i \geq 0 \text{ for } i \in I_d \setminus \{s\}, \tilde{p}^r > 0; \tilde{p}^s \in [0, 1]\right\} \tag{9.7.46}$$

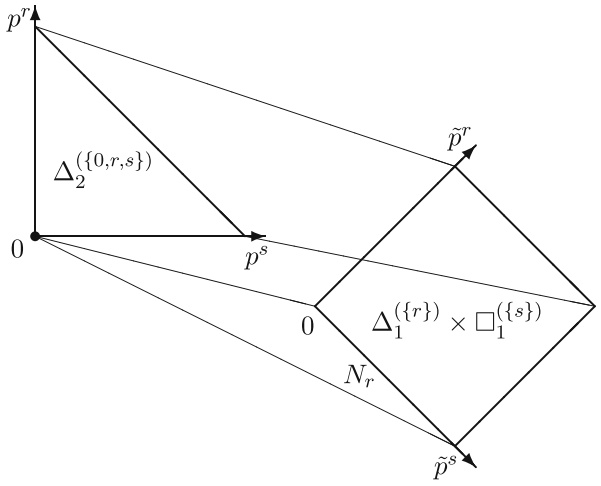

Fig. 9.1 An illustration of the blow-up transformation for $d = 2$

with $\tilde{p}^0 := 1 - \sum_{i \in I_d \setminus \{0,s\}} \tilde{p}^i$ *and altogether*

$$\overline{\Delta_d^{(I_d)}} \longmapsto \left(\overline{\Delta_{d-1}^{(I_d \setminus \{s\})}} \times \overline{\square_1^{(\{s\})}} \right) \setminus N_r \tag{9.7.47}$$

with

$$N_r := \overline{\Delta_{d-2}^{(I_d \setminus \{r,s\})}} \times \{0\}^{(\{r\})} \times \overline{\boxtimes_1^{(\{s\})}}, \tag{9.7.48}$$

appearing as an additional $(d-1)$*-dimensional face of* $\overline{\Delta_{d-1}^{(I_d \setminus \{s\})}} \times \overline{\square_1^{(\{s\})}}$*, is given by*

$$\tilde{p}^i := \quad p^i \qquad \text{for } i \neq r, s, \tag{9.7.49}$$

$$\tilde{p}^r := \quad p^r + p^s, \tag{9.7.50}$$

$$\tilde{p}^s := \begin{cases} \frac{p^s}{p^r + p^s} & \text{for } p^r + p^s > 0 \\ 0 & \text{for } p^r + p^s = 0. \end{cases} \tag{9.7.51}$$

Corollary 9.7.1 *While we obtain* $N_r = \overline{\Delta_{d-2}^{(I_d \setminus \{r,s\})}} \times \overline{\boxtimes_1^{(\{s\})}}$ *as an additional* $(d-1)$*-dimensional face with* Φ_s^r*, the existing* $(d-1)$*-dimensional faces of* $\overline{\Delta_d^{(I_d)}}$ *including their boundaries are mapped as follows:*

$$\overline{\Delta_{d-1}^{(I_d \setminus \{s\})}} \longmapsto \overline{\Delta_{d-1}^{(I_d \setminus \{s\})}} \times \{0\}^{(\{s\})}, \tag{9.7.52}$$

$$\overline{\Delta_{d-1}^{(I_d \setminus \{r\})}} \setminus \overline{\Delta_{d-2}^{(I_d \setminus \{r,s\})}} \longmapsto \left(\overline{\Delta_{d-1}^{(I_d \setminus \{s\})}} \setminus \overline{\Delta_{d-2}^{(I_d \setminus \{r,s\})}} \right) \times \{1\}^{(\{s\})} \tag{9.7.53}$$

and

$$\overline{\Delta_{d-1}^{(I_d \setminus \{i\})}} \setminus \overline{\Delta_{d-3}^{(I_d \setminus \{i,r,s\})}} \longmapsto \left(\overline{\Delta_{d-2}^{(I_d \setminus \{i,s\})}} \setminus \overline{\Delta_{d-3}^{(I_d \setminus \{i,r,s\})}} \right) \times \overline{\square_1^{(\{s\})}} \quad \text{for } i \in I_d \setminus \{r, s\}. \tag{9.7.54}$$

Remark 9.7.1 If the $\tilde{p}^s$ in Lemma 9.7.1 is chosen differently with

$$\tilde{p}^s := \frac{p^r}{p^r + p^s}, \tag{9.7.55}$$

this flips the orientation of the $\tilde{p}^s$-coordinate in $\square_1^{(\{s\})}$ as $\tilde{p}^s$ now need to be replaced by $1 - \tilde{p}^s$ wherever it occurs. This, however, does not affect the statements of Lemma 9.7.1, whereas in Corollary 9.7.1 the images of $\overline{\Delta_{d-1}^{(I_d \setminus \{r\})}} \setminus \overline{\Delta_{d-2}^{(I_d \setminus \{r,s\})}}$ and $\overline{\Delta_{d-1}^{(I_d \setminus \{s\})}} \setminus \overline{\Delta_{d-2}^{(I_d \setminus \{r,s\})}}$ are interchanged. Thus, unless stated otherwise, in the following

we shall always assume that the $\tilde{p}^s$-coordinate is chosen with an orientation as given in Lemma 9.7.1.

Proof of Lemma 9.7.1 The transformation corresponds geometrically to a scaling of the domain into the $\tilde{p}^s$-direction with scaling factor given by $\frac{1}{\tilde{p}^r}$. The assertion about the transformation domains is straightforward since we have $0 \leq \frac{p^s}{p^r+p^s} \leq 1$ on $\overline{\Delta_d^{(I_d)}} \setminus \overline{\Delta_{d-2}^{(I_d \setminus \{r,s\})}}$. Likewise, the C^∞-diffeomorphism property follows from the fact that Φ_s^r is smoothly differentiable as long as $\tilde{p}^r = p^r + p^s > 0$ and the smoothness of the inverse transformation $(\Phi_s^r)^{-1}$, given by

$$p^r = \tilde{p}^r(1 - \tilde{p}^s), \tag{9.7.56}$$

$$p^s = \tilde{p}^r \tilde{p}^s, \tag{9.7.57}$$

$$p^i = \tilde{p}^i \quad \text{for } i \neq r, s. \tag{9.7.58}$$

By this, it also becomes obvious that $(\Phi_s^r)^{-1}$ maps $\left(\overline{\Delta_{d-1}^{(I_d \setminus \{s\})}} \setminus \overline{\Delta_{d-2}^{(I_d \setminus \{r,s\})}}\right) \times \overline{\square_1^{(\{s\})}}$ onto $\overline{\Delta_d^{(I_d)}} \setminus \overline{\Delta_{d-2}^{(I_d \setminus \{r,s\})}}$. □

The next lemma is concerned with the transformation behaviour of the operator L_n^*; all considerations apply to L_n^* in its domain Δ_n as well as, taking the restriction property of L_n^* (cf. Lemma 8.4.1) into account, in the closure $\overline{\Delta_n}$ resp. to the transformed operator $\tilde{L}_n^*$ in the subsequent transformed images of the domain (the domain in question will not be stated explicitly—this will be done in Proposition 9.7.1):

Lemma 9.7.2 *Let $I_n' := \{1, \ldots, n\}$ be an index set with $r, s \in I_n'$ and let $\{i_1, \ldots, i_n\}$ be an ordering of I_n' such that $r, s \in \{i_1, \ldots, i_m\}$ for some $m \leq n$. When changing coordinates $(p^i)_{i \in I_n'} \mapsto (\tilde{p}^i)_{i \in I_n'}$ by Φ_s^r, the operator*

$$L_n^* = \frac{1}{2} \sum_{i,j=1}^{n} a^{ij}(p) \frac{\partial}{\partial p^i} \frac{\partial}{\partial p^j} \tag{9.7.59}$$

with $a^{ij}(p) = p^i(\delta_j^i - p^j)$ for $i, j \in \{i_1, \ldots, i_m\}$, $a^{ij} = 0$ else for $i \neq j$ is transformed into

$$\tilde{L}_n^* = \frac{1}{2} \sum_{k,l=1}^{k} \tilde{a}^{kl}(\tilde{p}) \frac{\partial}{\partial \tilde{p}^k} \frac{\partial}{\partial \tilde{p}^l} \tag{9.7.60}$$

with $\tilde{a}^{kl}(\tilde{p}) = \tilde{p}^k(\delta_l^k - \tilde{p}^l)$ for $k, l \in \{i_1, \ldots, i_m\} \setminus \{s\}$, $\tilde{a}^{ss}(\tilde{p}) = \frac{\tilde{p}^s(1-\tilde{p}^s)}{\tilde{p}^r}$, $\tilde{a}^{sl} = \tilde{a}^{ls} = 0$ for $l \neq s$ and $\tilde{a}^{kl}(\tilde{p}) = a^{kl}(p)$ (with the coordinates yet to be replaced) for all remaining indices. This also holds if the $\tilde{p}^s$-coordinate is chosen with opposite orientation (cf. Remark 9.7.1).

Proof As we have derived in Lemma 3.10.1, under a change of coordinates $(p^i) \mapsto (\tilde{p}^i)$, the coefficients of the 2nd order derivatives a^{ij} transform as

$$\tilde{a}^{kl} = \sum_{i,j} a^{ij} \frac{\partial \tilde{p}^k}{\partial p^i} \frac{\partial \tilde{p}^l}{\partial p^j}, \tag{9.7.61}$$

while we may get additional first order terms with coefficients $\sum_{i,j} a^{ij} \frac{\partial^2 \tilde{p}^k}{\partial p^i \partial p^j}$.

For the transformation at hand, we have (cf. Eqs. (9.7.50) and (9.7.49))

$$\frac{\partial \tilde{p}^k}{\partial p^i} = \delta_i^k + \delta_r^k \delta_i^s \quad \text{for } k \neq s \tag{9.7.62}$$

and (cf. Eq. (9.7.51))

$$\frac{\partial \tilde{p}^s}{\partial p^i} = \frac{p^r}{(p^r + p^s)^2} \delta_i^s - \frac{p^s}{(p^r + p^s)^2} \delta_i^r = \frac{1 - \tilde{p}^s}{\tilde{p}^r} \delta_i^s - \frac{\tilde{p}^s}{\tilde{p}^r} \delta_i^r. \tag{9.7.63}$$

Therefore, (9.7.61) yields

$$\tilde{a}^{kl}(\tilde{p}) = \sum_{i,j} a^{ij}(p)(\delta_i^k + \delta_r^k \delta_i^s)(\delta_j^l + \delta_r^l \delta_j^s) \tag{9.7.64}$$

for $k, l \neq s$, that is,

$$\begin{aligned} \tilde{a}^{kl}(\tilde{p}) &= a^{kl}(p) + a^{ks}(p)\delta_r^l + a^{sl}(p)\delta_r^k + a^{ss}(p)\delta_r^k \delta_r^l \\ &= p^k(\delta_l^k - p^l) - p^k p^s \delta_r^l - p^s p^l \delta_r^k + p^s(1 - p^s)\delta_r^k \delta_r^l \\ &= \tilde{p}^k(\delta_l^k - \tilde{p}^l) \end{aligned} \tag{9.7.65}$$

for $k, l \in \{i_1, \ldots, i_m\} \setminus \{s\}$ using the given form of the a^{ij}, whereas for all other index pairs not containing the index s, we always have

$$a^{ks}(p)\delta_r^l = a^{sl}(p)\delta_r^k = a^{ss}(p)\delta_r^k \delta_r^l = 0 \tag{9.7.66}$$

and hence

$$\tilde{a}^{kl}(\tilde{p}) = \sum_{i,j} a^{ij}(p)\delta_i^k\delta_j^l = a^{kl}(p), \tag{9.7.67}$$

thus proving the last statement. Furthermore, we have for arbitrary $l \neq s$

$$\begin{aligned}
\tilde{a}^{sl}(\tilde{p}) &= \sum_{i,j} a^{ij}(p)\left(\frac{1-\tilde{p}^s}{\tilde{p}^r}\delta_i^s - \frac{\tilde{p}^s}{\tilde{p}^r}\delta_i^r\right)(\delta_j^l + \delta_r^l\delta_j^s) \\
&= \frac{1-\tilde{p}^s}{\tilde{p}^r}(a^{sl}(p) + a^{ss}(p)\delta_r^l) - \frac{\tilde{p}^s}{\tilde{p}^r}(a^{rl}(p) + a^{rs}(p)\delta_r^l) \\
&= \Big(-\frac{1-\tilde{p}^s}{\tilde{p}^r}\tilde{p}^r\tilde{p}^s\tilde{p}^l + \frac{\tilde{p}^s}{\tilde{p}^r}(1-\tilde{p}^s)\tilde{p}^r\tilde{p}^l\Big)\chi_{\{i_1,\ldots,i_m\}}(l) \\
&\quad - \frac{\tilde{p}^s}{\tilde{p}^r}\tilde{p}^r(1-\tilde{p}^s)\delta_r^l + \Big(\frac{1-\tilde{p}^s}{\tilde{p}^r}\tilde{p}^r\tilde{p}^s(1-\tilde{p}^r\tilde{p}^s) + \frac{\tilde{p}^s}{\tilde{p}^r}\tilde{p}^r(1-\tilde{p}^s)\tilde{p}^r\tilde{p}^s\Big)\delta_r^l = 0
\end{aligned} \tag{9.7.68}$$

as well as $\tilde{a}^{ls} = 0$ $(l \neq s)$ by symmetry and finally

$$\begin{aligned}
\tilde{a}^{ss}(\tilde{p}) &= \sum_{i,j} a^{ij}(p)\left(\frac{1-\tilde{p}^s}{\tilde{p}^r}\delta_i^s - \frac{\tilde{p}^s}{\tilde{p}^r}\delta_i^r\right)\left(\frac{1-\tilde{p}^s}{\tilde{p}^r}\delta_j^s - \frac{\tilde{p}^s}{\tilde{p}^r}\delta_j^r\right) \\
&= a^{ss}(p)\left(\frac{1-\tilde{p}^s}{\tilde{p}^r}\right)^2 + a^{rr}(p)\left(\frac{\tilde{p}^s}{\tilde{p}^r}\right)^2 - 2a^{rr}(p)\frac{\tilde{p}^s(1-\tilde{p}^s)}{(\tilde{p}^r)^2} \\
&= \tilde{p}^s(1-\tilde{p}^r\tilde{p}^s)\frac{(1-\tilde{p}^s)^2}{\tilde{p}^r} + (1-\tilde{p}^s)(1-\tilde{p}^r+\tilde{p}^r\tilde{p}^s)\frac{(\tilde{p}^s)^2}{\tilde{p}^r} \\
&\quad - 2\tilde{p}^r\tilde{p}^s(1-\tilde{p}^s)\frac{\tilde{p}^s(1-\tilde{p}^s)}{\tilde{p}^r} = \frac{\tilde{p}^s(1-\tilde{p}^s)}{\tilde{p}^r}.
\end{aligned} \tag{9.7.69}$$

Thus, all $\tilde{a}^{kl}$ have the desired expression.

Possible additional first order terms would have to contain second derivatives of $\tilde{p}$; the only component for which they do not obviously vanish is $\tilde{p}^s$. But we have (cf. Eq. (9.7.63))

$$\frac{\partial}{\partial p^j}\frac{\partial}{\partial p^i}\tilde{p}^s = \frac{2}{(p^r+p^s)^3}(p^s\delta_i^r - p^r\delta_i^s)(\delta_j^r + \delta_j^s) + \frac{1}{(p^r+p^s)^2}(\delta_i^s\delta_j^r - \delta_i^r\delta_j^s) \tag{9.7.70}$$

and subsequently

$$\sum_{i,j} a^{ij} \frac{\partial}{\partial p^i} \frac{\partial}{\partial p^j} \tilde{p}^s = \frac{2}{(p^r + p^s)^3} \big(p^s (a^{rr} + a^{rs}) - p^r (a^{rr} + a^{ss}) \big) + \frac{1}{(p^r + p^s)^2} (a^{rr} - a^{rs})$$
$$= \frac{2}{(p^r + p^s)^3} \big(p^s p^r (1 - p^r - p^s) + p^r p^s (p^r - 1 + p^s) \big) = 0, \tag{9.7.71}$$

for which again the particular expression for the a^{ij} is needed.

If $\tilde{p}^s$ is chosen with different orientation as in Remark 9.7.1, instead of Eq. (9.7.63) we then have

$$\frac{\partial \tilde{p}^s}{\partial p^i} = \frac{\tilde{p}^s}{\tilde{p}^r} \delta_i^s - \frac{1 - \tilde{p}^s}{\tilde{p}^r} \delta_i^r. \tag{9.7.72}$$

This means that in the respective formulae the indices r and s are swapped, which in turn is matched by the corresponding inverse transformation which now yields $p^r = \tilde{p}^r \tilde{p}^s$ and $p^s = \tilde{p}^r (1 - \tilde{p}^s)$. □

Combining the preceding results, we obtain for an iterated application of the blow-up transformation:

Proposition 9.7.1 *Let $k, n \in \mathbb{N}$ with $0 \leq k \leq n-2$, $\{i_k, i_{k+1}, \ldots, i_n\} \subset I_n := \{0, 1, \ldots, n\}$ with $i_i \neq i_j$ for $i \neq j$ and $I_d := I_n \setminus \{i_{d+1}, \ldots, i_n\}$ for $d = k, \ldots, n-1$. A repeated blow-up transformation $\Phi^{r_{n-k-1}}_{s_{n-k-1}} \circ \ldots \circ \Phi^{r_1}_{s_1}$ with $\Phi^{r_m}_{s_m}$ as in Lemma 9.7.1 with $r_m = i_{n-m}$ and $s_m = i_{n-m+1}$ for $m = 1, \ldots, n-k-1$ maps $\overline{\Delta^{(I_{k+1})}_{k+1}}$ onto itself and*

$$\Delta^{(I_d)}_d \longmapsto \Delta^{(I_{k+1})}_{k+1} \times \square^{(I_d \setminus I_{k+1})}_{d-k-1} \quad \text{for } d = k+2, \ldots, n \tag{9.7.73}$$

and altogether

$$\overline{\Delta^{(I_n)}_n} \longmapsto \Big(\overline{\Delta^{(I_{k+1})}_{k+1}} \times \overline{\square^{(I_n \setminus I_{k+1})}_{n-k-1}} \Big) \setminus \bigcup_{j=k+1}^{n-1} N_j. \tag{9.7.74}$$

The $n-k-1$ additional $(n-1)$-dimensional faces $N_{k+1}, \ldots, N_{n-1}$ of $\overline{\Delta^{(I_{k+1})}_{k+1}} \times \overline{\square^{(I_n \setminus I_{k+1})}_{n-k-1}}$ are given by

$$N_{k+1} = \overline{\Delta^{(I_k)}_k} \times \{0\}^{(\{i_{k+1}\})} \times \overline{\boxtimes^{(I_n \setminus I_{k+1})}_{n-k-1}} \tag{9.7.75}$$

and

$$N_j = \overline{\Delta_{k+1}^{(I_{k+1})}} \times \overline{\square_{j-k-2}^{(I_{j-1}\setminus I_{k+1})}} \times \{0\}^{(\{ij\})} \times \overline{\boxtimes_{n-j}^{(I_n\setminus I_j)}} \tag{9.7.76}$$

for $j = k+2, \ldots, n-1$. *At the same time, the operator* $L^* = \sum p^i(\delta_j^i - p^j)\frac{\partial}{\partial p^i}\frac{\partial}{\partial p^j}$ *in* $\overline{\Delta_n^{(I_n)}}$ *is transformed into*[4]

$$\tilde{L}^* = \frac{1}{2}\sum_{j,l=1}^{k+1} \tilde{p}^{i_j}(\delta_l^j - \tilde{p}^{i_l})\frac{\partial}{\partial \tilde{p}^{i_j}}\frac{\partial}{\partial \tilde{p}^{i_l}} + \frac{1}{2}\sum_{j=k+2}^{n} \frac{\tilde{p}^{i_j}(1-\tilde{p}^{i_j})}{\prod_{l=k+1}^{j-1}\tilde{p}^{i_l}}\frac{\partial^2}{(\partial \tilde{p}^{i_j})^2} \tag{9.7.77}$$

in $\left(\overline{\Delta_{k+1}^{(I_{k+1})}} \times \overline{\square_{n-k-1}^{(I_n\setminus I_{k+1})}}\right) \setminus \bigcup_{j=k+1}^{n-1} N_j$.

If in any step the coordinate $\tilde{p}^{s_j}$ *is chosen with opposite orientation (cf. Remark 9.7.1),* $\tilde{p}^{s_j}$, *whenever it appears in the above formulae, is replaced by* $(1-\tilde{p}^{s_j})$.

Thus, the iterated blow-up translates the (extended) Kolmogorov backward equation in $\overline{\Delta}_n$ into a corresponding differential equation in $\left(\overline{\Delta_{k+1}^{(I_{k+1})}} \times \overline{\square_{n-k-1}^{(I_n\setminus I_{k+1})}}\right) \setminus \bigcup_{j=k+1}^{n-1} N_j$. For the iteratively extended solutions of the Kolmogorov backward equation introduced in the preceding chapter, the transformation behaviour is as follows:

Proposition 9.7.2 *Let* $k, n \in \mathbb{N}$ *with* $0 \leq k \leq n-2$, $\{i_k, i_{k+1}, \ldots, i_n\} \subset I_n := \{0, 1, \ldots, n\}$ *with* $i_i \neq i_j$ *for* $i \neq j$ *and* $I_d := I_n \setminus \{i_{d+1}, \ldots, i_n\}$ *for* $d = k, \ldots, n-1$, *and let* u_{I_k} *in* $\left(\Delta_k^{(I_k)}\right)_{-\infty}$ *and* $\bar{U}_{I_k}^{i_k,\ldots,i_n}$ *in* $\left(\bigcup_{k\leq d\leq n}\Delta_d^{(I_d)}\right)_{-\infty}$ *as in Proposition 9.5.1. Then a repeated blow-up transformation* $\Phi_{s_{n-k-1}}^{r_{n-k-1}} \circ \ldots \circ \Phi_{s_1}^{r_1}$ *with* $\Phi_{s_m}^{r_m}$ *as in Lemma 9.7.1 with* $r_m = i_{n-m}$ *and* $s_m = i_{n-m+1}$ *for* $m = 1, \ldots, n-k-1$ *converts*

$$\begin{aligned}\bar{U}_{I_k}^{i_k,\ldots,i_n}(p,t) &:= u_{I_k}(p,t)\chi_{\Delta_k^{(I_k)}}(p) + \sum_{k+1\leq d\leq n} \bar{u}_{I_k}^{i_k,\ldots,i_d}(p,t)\chi_{\Delta_d^{(I_d)}}(p) \\ &= u_{I_k}(p,t)\chi_{\Delta_k^{(I_k)}}(p) + \sum_{k+1\leq d\leq n} u_{I_k}(\pi^{i_k,\ldots,i_d}(p),t)\prod_{j=k}^{d-1}\frac{p^{i_j}}{\sum_{l=j}^{d}p^{i_l}}\chi_{\Delta_d^{(I_d)}}(p)\end{aligned} \tag{9.7.78}$$

[4]Note that on boundary strata of $\square_{n-k-1}^{(I_n\setminus I_{k+1})}$, i.e. $\tilde{p}^{i_l} = 0$ for some $l \in I_n \setminus I_{k+1}$, the corresponding summands are assumed not to appear in the right sum in Eq. (9.7.77), which may be interpreted as a result of a successive restriction. The given domain is the maximal domain for the operator as it is not defined on the exception set $\bigcup_{j=k+1}^{n-1} N_j$ (however, cf. also Lemma 9.8.2 for the stationary case).

on $\left(\bigcup_{k\le d\le n}\Delta_d^{(I_d)}\right)_{-\infty}$ *into*

$$\tilde{U}_{I_k}^{i_k,i_{k+1};i_{k+2},\dots,i_n}(\tilde{p},t) := u_{I_k}(\tilde{p},t)\chi_{\Delta_k^{(I_k)}}(\tilde{p}) + \sum_{k+1\le d\le n}\tilde{u}_{I_k}^{i_k,i_{k+1};i_{k+2},\dots,i_d}(\tilde{p},t)\chi_{\Delta_{k+1}^{(I_{k+1})}\times\square_{d-k-1}^{(I_d\setminus I_{k+1})}}(\tilde{p}) \tag{9.7.79}$$

on $\left(\bigcup_{k\le d\le n}\Delta_{k+1}^{(I_{k+1})}\times\square_{n-k-1}^{(I_n\setminus I_{k+1})}\right)_{-\infty}$ *with*

$$\tilde{u}_{I_k}^{i_k,i_{k+1};i_{k+2},\dots,i_d}(\tilde{p},t) := \bar{u}_{I_k}^{i_k,i_{k+1}}(\tilde{\pi}^{i_{k+1}}(\tilde{p}),t)\prod_{j=k+2}^{d}(1-\tilde{p}^{i_j}) \quad \text{for } d=k+2,\dots,n \tag{9.7.80}$$

with $\tilde{\pi}^{i_{k+1}}(\tilde{p}^{i_j}) := \tilde{p}^{i_j}$ *for* $i_j \in I_{k+1}$, $\tilde{\pi}^{i_{k-1}}(\tilde{p}^{i_j}) := 0$ *else. The transformed functions* $\tilde{u}_{I_k}^{i_k,i_{k+1};i_{k+2},\dots,i_d}$ *smoothly extend to* $\left(\overline{\Delta_{k+1}^{(I_{k+1})}}\times\overline{\square_{d-k-1}^{(I_d\setminus I_{k+1})}}\right)_{-\infty}$ *respectively; consequently also* $\tilde{U}_{I_k}^{i_k,i_{k+1};i_{k+2},\dots,i_n}$ *smoothly extends to* $\left(\overline{\Delta_{k+1}^{(I_{k+1})}}\times\overline{\square_{n-k-1}^{(I_n\setminus I_{k+1})}}\right)_{-\infty}$. *Furthermore, it may be simplified to*

$$\tilde{U}_{I_k}^{i_k,i_{k+1};i_{k+2},\dots,i_n}(\tilde{p},t) \equiv \tilde{u}_{I_k}^{i_k,i_{k+1};i_{k+2},\dots,i_n}(\tilde{p},t) \quad \text{in } \left(\overline{\Delta_{k+1}^{(I_{k+1})}}\times\overline{\square_{n-k-1}^{(I_n\setminus I_{k+1})}}\right)_{-\infty}. \tag{9.7.81}$$

If in any step the coordinate $\tilde{p}^{s_j}$ *is chosen with opposite orientation (cf. Remark 9.7.1),* $\tilde{p}^{s_j}$ *in the above formulae need to be replaced by* $(1-\tilde{p}^{s_j})$.

For the stationary components, we have in particular:

Corollary 9.7.2 *For* $k=0$ *and w. l. o. g.* $i_0=0$, *the transformed function of Proposition 9.7.2 in Eq. (9.7.81) simplifies to*

$$\tilde{U}_{\{i_0\}}^{i_0,i_1;i_2,\dots,i_n}(\tilde{p}) = u_{\{i_0\}}(1)\cdot\prod_{j=1}^{n}(1-\tilde{p}^{i_j}) \quad \text{in } \overline{\square_n^{(I'_n)}}, \tag{9.7.82}$$

while in accordance with Proposition 9.7.1 the domain is mapped

$$\Delta_d^{(I_d)} \longmapsto \square_d^{(I'_d)} \quad \text{for } d=0,\dots,n \tag{9.7.83}$$

and altogether

$$\overline{\Delta_n^{(I_n)}} \longmapsto \overline{\square_n^{(I'_n)}}\setminus\bigcup_{j=1}^{n-1}N_j. \tag{9.7.84}$$

The $n-1$ additional $(n-1)$-dimensional faces $N_1,\dots,N_{n-1}$ of $\partial\square_n^{(I'_n)}$ are given by

$$N_1 = \{0\}^{(\{i_1\})} \times \overline{\boxtimes_{n-1}^{(I'_n\setminus I'_1)}} \tag{9.7.85}$$

and

$$N_j = \overline{\square_{j-1}^{(I'_{j-1})}} \times \{0\}^{(\{i_j\})} \times \overline{\boxtimes_{n-j}^{(I'_n\setminus I'_j)}} \tag{9.7.86}$$

for $j = 2,\dots,n-1$, whereas the operator $L^* = \sum p^i(\delta^i_j - p^j)\frac{\partial}{\partial p^i}\frac{\partial}{\partial p^j}$ in $\overline{\Delta_n^{(I_n)}}$ is transformed into

$$\tilde{L}^* = \frac{1}{2}\sum_{j=1}^{n} \frac{\tilde{p}^{i_j}(1-\tilde{p}^{i_j})}{\prod_{l=1}^{j-1}\tilde{p}^{i_l}} \frac{\partial^2}{(\partial\tilde{p}^{i_j})^2} \quad \text{in } \overline{\square_n^{(I'_n)}} \setminus \bigcup_{j=1}^{n-1} N_j. \tag{9.7.87}$$

Proof of Propositions 9.7.1 and 9.7.2 We prove the assertions of both propositions in parallel: Our aim is to transform $\bar{U}_{I_k}^{i_k,\dots,i_n}$ into a function that does not feature any incompatibilities and hence is of sufficient regularity with respect to the entire closure of the (transformed) domain. For that purpose, we shall show that the full blow-up via a repeated application of the coordinate transformation Φ_s^r of Lemma 9.7.1 with the indices r and s to be picked as shown in each step yields the desired result for $\tilde{U}_{I_k}^{i_k,i_{k+1};i_{k+2},\dots,i_n}$, while the transformation behaviour of the domain and the operator is as stated in Proposition 9.7.1. For notational simplicity, we will usually suppress the t-component in the notation for our domains throughout this proof; for instance, we shall write $\Delta_n^{(I_n)}$ instead of $\left(\Delta_n^{(I_n)}\right)_{-\infty}$.

Starting with the top-dimensional component of $\bar{U}_{I_k}^{i_k,\dots,i_n}$, which is

$$\begin{aligned}\bar{u}_{I_k}^{i_k,\dots,i_n}(p,t) &= \bar{u}_{I_k}^{i_k,\dots,i_{n-1}}(\pi^{i_{n-1},i_n}(p),t)\cdot\frac{p^{i_{n-1}}}{p^{i_{n-1}}+p^{i_n}}\\ &= u_{I_k}(\pi^{i_k,\dots,i_{n-1}}(\pi^{i_{n-1},i_n}(p)),t)\prod_{j=k}^{n-2}\frac{p^{i_j}}{\sum_{l=j}^{n}p^{i_l}}\cdot\frac{p^{i_{n-1}}}{p^{i_{n-1}}+p^{i_n}} \quad \text{in } \Delta_n^{(I_n)}\end{aligned} \tag{9.7.88}$$

with $p^{i_0} \equiv p^0 = 1-\sum_{j=1}^n p^{i_j}$ (if $i_0 \neq 0$, one may change the coordinates, i.e. permute the vertices correspondingly), we initially put[5] $r_1 := i_{n-1}$ and $s_1 := i_n$. Changing coordinates $(p^i) \mapsto (\tilde{p}^i)$ by $\Phi_{s_1}^{r_1}$ maps $\Delta_n^{(I_n)}$ onto $\Delta_{n-1}^{(I_{n-1})} \times \square_1^{(\{i_n\})}$ and

[5] Alternatively, one could also put $r_1 := i_n$ and $s_1 := i_{n-1}$, which would correspond to inverting the orientation of the $\tilde{p}^{s_1}$-coordinate as in Remark 9.7.1 (cf. also below) plus subsequently swapping the coordinate indices i_n and i_{n-1}, thus $\tilde{p}^{i_n}$ would get replaced by $1-\tilde{p}^{i_{n-1}}$ and $\tilde{p}^{i_{n-1}}$ with $\tilde{p}^{i_n}$.

$\overline{\Delta_{n-1}^{(I_{n-1})}}$ onto $\overline{\Delta_{n-1}^{(I_{n-1})}} \times \{0\}^{(\{i_n\})}$, whereas the entire domain $\overline{\Delta_n^{(I_n)}}$ is transformed into $\left(\overline{\Delta_{n-1}^{(I_{n-1})}} \times \overline{\square_1^{(\{i_n\})}}\right) \setminus N_{n-1}$ with

$$N_{n-1} := \overline{\Delta_{n-2}^{(I_{n-2})}} \times \{0\}^{(\{i_{n-1}\})} \times \overline{\boxtimes_1^{(\{i_n\})}} \tag{9.7.89}$$

being an additional $(n-1)$-dimensional face of $\overline{\Delta_{n-1}^{(I_{n-1})}} \times \overline{\square_1^{(\{i_n\})}}$ (cf. Lemma 9.7.1). At the same time, the $(n-2)$-dimensional incompatibility at $\overline{\Delta_{n-2}^{(I_{n-2})}}$ of the continuous extension of $\bar{u}_{I_k}^{i_k,\dots,i_n}$ to $\partial_{n-1}\Delta_n^{(I_n)}$ is removed as the transformation yields

$$\begin{aligned}\tilde{u}_{I_k}^{i_k,\dots,i_{n-1};i_n}(\tilde{p},t) &:= \bar{u}_{I_k}^{i_k,\dots,i_{n-1}}(\tilde{\pi}^{i_{n-1}}(\tilde{p}),t)\cdot(1-\tilde{p}^{i_n}) \\ &= u_{I_k}(\pi^{i_k,\dots,i_{n-1}}(\tilde{\pi}^{i_{n-1}}(\tilde{p})),t)\prod_{j=k}^{n-2}\frac{\tilde{p}^{i_j}}{\sum_{l=j}^n \tilde{p}^{i_l}}\cdot(1-\tilde{p}^{i_n}) \\ &\qquad\qquad \text{in } \Delta_{n-1}^{(I_{n-1})}\times\square_1^{(\{i_n\})}\end{aligned} \tag{9.7.90}$$

by Eq. (9.7.56) et seq. (note $\tilde{\pi}^{i_{n-1}}(\tilde{p}) = \pi^{i_{n-1},i_n}(p)$). Hence, the complete function $\bar{U}_{I_k}^{i_k,\dots,i_n}$ is transformed into

$$\begin{aligned}\tilde{U}_{I_k}^{i_k,\dots,i_{n-1};i_n}(p,t) &:= \sum_{k\le d\le n-1}\bar{u}_{I_k}^{i_k,\dots,i_d}(p,t)\chi_{\Delta_d^{(I_d)}}(p) \\ &\quad + \tilde{u}_{I_k}^{i_k,\dots,i_{n-1};i_n}(p,t)\chi_{\Delta_{n-1}^{(I_{n-1})}\times\square_1^{(I_n\setminus I_{n-1})}}(p)\end{aligned} \tag{9.7.91}$$

with the transformed top-dimensional component $\tilde{u}_{I_k}^{i_k,\dots,i_{n-1};i_n}(\tilde{p},t)$ smoothly extending to $\Delta_{n-1}^{(I_{n-1})}\times\overline{\square_1^{(\{i_n\})}}$ with

$$\tilde{u}_{I_k}^{i_k,\dots,i_{n-1};i_n}(\tilde{p},t)\big|_{\Delta_{n-1}^{(I_{n-1})}\times\{0\}^{(\{i_n\})}} \equiv \bar{u}_{I_k}^{i_k,\dots,i_{n-1}}(\tilde{p},t) \quad \text{in } \Delta_{n-1}^{(I_{n-1})}\times\{0\}^{(\{i_n\})}. \tag{9.7.92}$$

As $\bar{u}_{I_k}^{i_k,\dots,i_{n-1}}$ itself smoothly extends to $\partial_{n-2}\Delta_{n-1}^{(I_{n-1})}$, thus $\tilde{u}_{I_k}^{i_k,\dots,i_{n-1};i_n}$ now smoothly extends to the entire $(\partial_{n-2}\Delta_{n-1}^{(I_{n-1})})\times\overline{\square_1^{(\{i_n\})}}$, in particular to $\Delta_{n-2}^{(I_{n-2})}\times\overline{\square_1^{(\{i_n\})}}\subset\overline{N}_{n-1}$ (however, $\bar{u}_{I_k}^{i_k,\dots,i_{n-1}}$ resp. its continuous extension to $\partial_{n-2}\Delta_{n-1}^{(I_{n-1})}$ still has an incompatibility at $\overline{\Delta_{n-3}^{(I_{n-3})}}$).

The operator $L^* = \frac{1}{2}\sum_{i,j=1}^n p^i(\delta_j^i - p^j)\frac{\partial}{\partial p^i}\frac{\partial}{\partial p^j}$ in $\overline{\Delta_n^{(I_n)}}$ transforms into (cf. Lemma 9.7.2)

$$\tilde{L}^* = \frac{1}{2}\sum_{j,l\neq n}\tilde{p}^{i_j}(\delta_l^j - \tilde{p}^{i_l})\frac{\partial}{\partial\tilde{p}^{i_j}}\frac{\partial}{\partial\tilde{p}^{i_l}} + \frac{1}{2}\frac{\tilde{p}^{i_n}(1-\tilde{p}^{i_n})}{\tilde{p}^{i_{n-1}}}\frac{\partial}{\partial\tilde{p}^{i_n}}\frac{\partial}{\partial\tilde{p}^{i_n}} \tag{9.7.93}$$

on $\left(\overline{\Delta_{n-1}^{(I_{n-1})}} \times \overline{\square_1^{(\{i_n\})}}\right) \setminus N_{n-1}$ since we have $\tilde{a}^{kl}(\tilde{p}) = p^k(\delta_l^k - p^l) = \tilde{p}^k(\delta_l^k - \tilde{p}^l)$ for $k, l \neq i_{n-1}, i_n$. If $\tilde{p}^{i_n}$ is chosen with opposite orientation (cf. Remark 9.7.1), then $\tilde{p}^{i_n}$ needs to be replaced by $(1 - \tilde{p}^{i_n})$ everywhere.

As already indicated, the transformed solution is still not smoothly extendable to the full boundary of the transformed domain: Its $(n-2)$-dimensional incompatibility is resolved, but its lower-dimensional incompatibilities persist. Thus, the highest-dimensional incompatibility now is of dimension $n-3$, and hence the situation is ready for another application of the blow-up transformation.

Thus, we need an iterative procedure to resolve all incompatibilities. For this purpose, we assume that after the m-th step ($m = 1, \ldots, n-k-2$) an already transformed function $\tilde{U}_{I_k}^{i_k,\ldots,i_{n-m};i_{n-m+1},\ldots,i_n}$ with (note that we again associate coordinates p resp. $\tilde{p}$ etc. to the domain before/after the $(m+1)$-th transition; furthermore, we will use the convention $\bar{u}_{I_k}^{i_k} \equiv u_{I_k}$ to simplify the notation)

$$\begin{aligned}\tilde{U}_{I_k}^{i_k,\ldots,i_{n-m};i_{n-m+1},\ldots,i_n}(p,t) &= \sum_{k\le d\le n-m} \bar{u}_{I_k}^{i_k,\ldots,i_d}(p,t)\chi_{\Delta_d^{(I_d)}}(p) \\ &+ \sum_{n-m+1\le d\le n} \tilde{u}_{I_k}^{i_k,\ldots,i_{n-m};i_{n-m+1},\ldots,i_d}(p,t)\chi_{\Delta_{n-m}^{(I_{n-m})}\times\square_{d-n+m}^{(I_d\setminus I_{n-m})}}(p) \end{aligned} \tag{9.7.94}$$

with

$$\tilde{u}_{I_k}^{i_k,\ldots,i_{n-m};i_{n-m+1},\ldots,i_d}(p,t) = \bar{u}_{I_k}^{i_k,\ldots,i_{n-m}}(\tilde{\pi}^{i_{n-m}}(p),t) \prod_{j=n-m+1}^{d}(1-p^{i_j}) \tag{9.7.95}$$

for $d = n-m+1, \ldots, n$ and

$$\begin{aligned}\bar{u}_{I_k}^{i_k,\ldots,i_{n-m}}(p,t) &= \bar{u}_{I_k}^{i_k,\ldots,i_{n-m-1}}(\pi^{i_{n-m-1},i_{n-m}}(p),t)\cdot\frac{p^{i_{n-m-1}}}{p^{i_{n-m-1}}+p^{i_{n-m}}} \\ &= u_{I_k}(\pi^{i_k,\ldots,i_{n-m-1}}(\pi^{i_{n-m-1},i_{n-m}}(p)),t)\prod_{j=k}^{n-m-2}\frac{p^{i_j}}{\sum_{l=j}^n p^{i_l}}\cdot\frac{p^{i_{n-m-1}}}{p^{i_{n-m-1}}+p^{i_{n-m}}}\end{aligned} \tag{9.7.96}$$

in $\Delta_{n-m}^{(I_{n-m})}$. The corresponding total domain as an image of $\overline{\Delta_n^{(I_n)}}$ is given by

$$\left(\overline{\Delta_{n-m}^{(I_{n-m})}} \times \overline{\square_m^{(I_n\setminus I_{n-m})}}\right) \setminus \bigcup_{j=n-m}^{n-1} N_j \tag{9.7.97}$$

with additional $(n-1)$-dimensional faces from previous steps

$$N_{n-m} = \overline{\Delta_{n-m-1}^{(I_{n-m-1})}} \times \{0\}^{(\{i_{n-m}\})} \times \overline{\boxtimes_m^{(I_n \setminus I_{n-m})}} \tag{9.7.98}$$

and

$$N_j = \overline{\Delta_{n-m}^{(I_{n-m})}} \times \overline{\square_{j-n+m-1}^{(I_{j-1} \setminus I_{n-m})}} \times \{0\}^{(\{i_j\})} \times \overline{\boxtimes_{n-j}^{(I_n \setminus I_j)}} \tag{9.7.99}$$

for $j = n-m+1, \ldots, n-1$.

The functions $\tilde{u}_{I_k}^{i_k,\ldots,i_{n-m};i_{n-m+1},\ldots,i_d}$ smoothly extend each to $\Delta_{n-m}^{(I_{n-m})} \times \overline{\square_{d-n+m}^{(I_d \setminus I_{n-m})}}$, and we have

$$\tilde{u}_{I_k}^{i_k,\ldots,i_{n-m};i_{n-m+1},\ldots,i_d}|_{\Delta_{n-m}^{(I_{n-m})} \times \square_m^{(I_{d-1} \setminus I_{n-m})}} = \tilde{u}_{I_k}^{i_k,\ldots,i_{n-m};i_{n-m+1},\ldots,i_{d-1}} \tag{9.7.100}$$

for $d = n-m+2, \ldots, n$ and

$$\tilde{u}_{I_k}^{i_k,\ldots,i_{n-m};i_{n-m+1}}|_{\Delta_{n-m}^{(I_{n-m})}} = \bar{u}_{I_k}^{i_k,\ldots,i_{n-m}}. \tag{9.7.101}$$

With $\bar{u}_{I_k}^{i_k,\ldots,i_{n-m}}$ being smoothly extendable to $\partial_{n-m-1}\Delta_{n-m}^{(I_{n-m})}$, also the functions $\tilde{u}_{I_k}^{i_k,\ldots,i_{n-m};i_{n-m+1},\ldots,i_d}$ smoothly extend to $\left(\partial_{n-m-1}\Delta_{n-m}^{(I_{n-m})}\right) \times \overline{\square_{d-n+m}^{(I_d \setminus I_{n-m})}}$, in particular all additional faces are covered.

Furthermore, we assume that the operator L^* has the corresponding form

$$L^* = \frac{1}{2}\sum_{j,l=1}^{n-m} p^{i_j}(\delta_l^j - p^{i_l})\frac{\partial}{\partial p^{i_j}}\frac{\partial}{\partial p^{i_l}} + \frac{1}{2}\sum_{j=n-m+1}^{n} \frac{p^{i_j}(1-p^{i_j})}{\prod_{l=n-m}^{j-1} p^{i_l}}\frac{\partial^2}{(\partial p^{i_j})^2} \tag{9.7.102}$$

on $\left(\overline{\Delta_{n-m}^{(I_{n-m})}} \times \overline{\square_m^{(I_n \setminus I_{n-m})}}\right) \setminus \bigcup_{j=n-m}^{n-1} N_j$.

For the $(m+1)$-th blow-up step, we first notice that $\bar{u}_{I_k}^{i_k,\ldots,i_{n-m}}$ resp. its continuous extension to $\partial_{n-m-1}\Delta_{n-m}^{(I_{n-m})}$ still has an incompatibility at $\overline{\Delta_{n-m-2}^{(I_{n-m-2})}} \subset \Delta_{n-m}^{(I_{n-m})}$, corresponding to $p^{i_{n-m}} + p^{i_{n-m-1}} = 0$. Consequently, this may be resolved by a blow-up transformation $\Phi_{s_{m+1}}^{r_{m+1}}$ with $r_{m+1} = i_{n-m-1}$ and $s_{m+1} = i_{n-m}$ (note that, due to the stipulation $i_0 = 0$, we always have $r_{m+1}, s_{m+1} \neq 0$), mapping the simplex part of the domain (cf. Lemma 9.7.1)

$$\Delta_{n-m}^{(I_{n-m})} \longmapsto \Delta_{n-m-1}^{(I_{n-m-1})} \times \square_1^{(\{i_{n-m}\})} \tag{9.7.103}$$

resp.

$$\overline{\Delta_{n-m-1}^{(I_{n-m-1})}} \longmapsto \overline{\Delta_{n-m-1}^{(I_{n-m-1})}} \times \{0\}^{(\{i_{n-m}\})} \tag{9.7.104}$$

and altogether

$$\overline{\Delta_{n-m}^{(I_{n-m})}} \longmapsto \overline{\Delta_{n-m-1}^{(I_{n-m-1})}} \times \overline{\square_1^{(\{i_{n-m}\})}} \setminus N_{n-m-1} \tag{9.7.105}$$

with

$$N_{n-m-1} := \overline{\Delta_{n-m-2}^{(I_{n-m-2})}} \times \{0\}^{(\{i_{n-m-1}\})} \times \overline{\boxtimes_1^{(\{i_{n-m}\})}} \tag{9.7.106}$$

being an additional $(n-m-1)$-dimensional face of $\overline{\Delta_{n-m-1}^{(I_{n-m-1})}} \times \overline{\square_1^{(\{i_{n-m}\})}}$.

From this, when gradually adding the cube part $\square_m^{(I_n \setminus I_{n-m})}$ with coordinates $p^{i_{n-m+1}}, \ldots, p^{i_n}$, Eq. (9.7.103) turns into

$$\Delta_{n-m}^{(I_{n-m})} \times \square_{d-n+m}^{(I_d \setminus I_{n-m})} \longmapsto \Delta_{n-m-1}^{(I_{n-m-1})} \times \square_{d-n+m+1}^{(I_d \setminus I_{n-m-1})} \quad \text{for } d \geq n-m, \tag{9.7.107}$$

and by applying Eq. (9.7.105) to the previous image of the initial domain $\overline{\Delta_n^{(I_n)}}$ in Eq. (9.7.97), we obtain for the transformed total domain

$$\Big(\overline{\Delta_{n-m-1}^{(I_{n-m-1})}} \times \overline{\square_{m+1}^{(I_n \setminus I_{n-m-1})}}\Big) \setminus \bigcup_{j=n-m-1}^{n-1} \tilde{N}_j \tag{9.7.108}$$

with $\tilde{N}_{n-m}, \ldots, \tilde{N}_{n-1}$ being the images of the previous additional faces: The faces $N_{n-m+1}, \ldots, N_{n-1}$ are only affected indirectly as they contain the full $\overline{\Delta_{n-m}^{(I_{n-m})}}$ as a factor, and hence only the i_{n-m}-th coordinate is moved from the simplex to the cube, thus

$$\tilde{N}_j = \overline{\Delta_{n-m-1}^{(I_{n-m-1})}} \times \overline{\square_{j-n+m}^{(I_{j-1} \setminus I_{n-m-1})}} \times \{0\}^{(\{i_j\})} \times \overline{\boxtimes_{n-j}^{(I_n \setminus I_j)}} \tag{9.7.109}$$

for $j = n-m+1, \ldots, n-1$, whereas $N_{n-m} \equiv \tilde{N}_{n-m}$ is virtually not affected as only $p^{i_{n-m}} = 0$ is transformed into $\tilde{p}^{i_{n-m}} = 0$. For the 'new' additional $(n-1)$-dimensional face $\tilde{N}_{n-m-1}$ (resulting from N_{n-m-1}), we may—having added the remaining dimensions—relax the condition $\tilde{p}^{i_{n-m}} > 0$ in Eq. (9.7.106). This ensures $N_{n-m-1} \neq \overline{\Delta_{n-m-2}^{(I_{n-m-2})}}$, into $\sum_{j=n-m}^{n} \tilde{p}^{i_j} > 0$. Hence, we obtain

$$\tilde{N}_{n-m-1} := \overline{\Delta_{n-m-2}^{(I_{n-m-2})}} \times \{0\}^{(\{i_{n-m-1}\})} \times \overline{\boxtimes_{m+1}^{(I_n \setminus I_{n-m-1})}}. \tag{9.7.110}$$

At the same time, $\bar{u}_{I_k}^{i_k,\ldots,i_{n-m}}$ and $\tilde{u}_{I_k}^{i_k,\ldots,i_{n-m};i_{n-m+1},\ldots,i_d}$, $d = n-m+1, \ldots, n$ get transformed into

$$\tilde{u}_{I_k}^{i_k,\ldots,i_{n-m-1};i_{n-m},\ldots,i_d}(\tilde{p},t) = \bar{u}_{I_k}^{i_k,\ldots,i_{n-m-1}}(\tilde{\pi}^{i_{n-m-1}}(\tilde{p}),t) \prod_{j=n-m}^{d} (1-\tilde{p}^{i_j}) \tag{9.7.111}$$

in $\Delta_{n-m-1}^{(I_{n-m-1})} \times \square_{d-n+m+1}^{(I_d \setminus I_{n-m-1})}$ for $d \geq n-m$, and hence

$$\tilde{U}_{I_k}^{i_k,\dots,i_{n-m-1};i_{n-m},\dots,i_n}(p,t) := \sum_{k \leq d \leq n-m-1} \bar{u}_{I_k}^{i_k,\dots,i_d}(p,t)\chi_{\Delta_d^{(I_d)}}(p) + \sum_{n-m \leq d \leq n} \tilde{u}_{I_k}^{i_k,\dots,i_{n-m-1};i_{n-m},\dots,i_d}(p,t)\chi_{\Delta_{n-m-1}^{(I_{n-m-1})} \times \square_{d-n+m+1}^{(I_d \setminus I_{n-m-1})}}(p). \tag{9.7.112}$$

The transformed functions $\tilde{u}_{I_k}^{i_k,\dots,i_{n-m-1};i_{n-m},\dots,i_d}$ then each smoothly extend to $\Delta_{n-m-1}^{(I_{n-m-1})} \times \overline{\square_{d-n+m+1}^{(I_d \setminus I_{n-m-1})}}$, and we have

$$\tilde{u}_{I_k}^{i_k,\dots,i_{n-m-1};i_{n-m},\dots,i_d}\big|_{\Delta_{n-m-1}^{(I_{n-m-1})} \times \square_{m+1}^{(I_{d-1} \setminus I_{n-m-1})}} = \tilde{u}_{I_k}^{i_k,\dots,i_{n-m-1};i_{n-m},\dots,i_{d-1}} \tag{9.7.113}$$

for $d = n-m+1,\dots,n$ and

$$\tilde{u}_{I_k}^{i_k,\dots,i_{n-m-1};i_{n-m}}\big|_{\Delta_{n-m-1}^{(I_{n-m-1})}} = \bar{u}_{I_k}^{i_k,\dots,i_{n-m-1}}. \tag{9.7.114}$$

With $\bar{u}_{I_k}^{i_k,\dots,i_{n-m-1}}$ being smoothly extendable to $\partial_{n-m-2}\Delta_{n-m-1}^{(I_{n-m-1})}$, the functions $\tilde{u}_{I_k}^{i_k,\dots,i_{n-m-1};i_{n-m},\dots,i_d}$ also smoothly extend to $\left(\partial_{n-m-2}\Delta_{n-m-1}^{(I_{n-m-1})}\right) \times \overline{\square_{d-n+m+1}^{(I_d \setminus I_{n-m-1})}}$, by which all additional faces are covered; in particular, $\tilde{u}_{I_k}^{i_k,\dots,i_{n-m-1};i_{n-m}}$ smoothly extends to N_{n-m-1} resp. eventually $\tilde{u}_{I_k}^{i_k,\dots,i_{n-m-1};i_{n-m},\dots,i_n}$ extends to $\tilde{N}_{n-m-1}$ (however, $\bar{u}_{I_k}^{i_k,\dots,i_{n-m-1}}$ resp. its continuous extension to $\partial_{n-m-2}\Delta_{n-m-1}^{(I_{n-m-1})}$ still has an incompatibility at $\overline{\Delta_{n-m-3}^{(I_{n-m-3})}}$).

To analyse the transformation behaviour of the operator, we first note that the requirements of Lemma 9.7.2 on a^{ij} are met as for $i,j \in \{i_1,\dots,i_{n-m}\}$ we have $a^{ij}(p) = p^i(\delta_j^i - p^j)$ by Eq. (9.7.102), while all other non-diagonal coefficients vanish. Hence, by the lemma, we have for $i,j \in \{i_1,\dots,i_{n-m}\}$

$$\tilde{a}^{ij}(\tilde{p}) = \tilde{p}^i(\delta_j^i - \tilde{p}^j), \tag{9.7.115}$$

while for $\tilde{a}^{i_j i_j}$ with $j = n-m+1,\dots,n$ we obtain

$$\tilde{a}^{i_j i_j}(\tilde{p}) = a^{i_j i_j}(p) = \frac{p^{i_j}(1-p^{i_j})}{\prod_{l=n-m}^{j-1} p^{i_l}} = \frac{\tilde{p}^{i_j}(1-\tilde{p}^{i_j})}{\prod_{l=n-m-1}^{j-1} \tilde{p}^{i_l}}. \tag{9.7.116}$$

Likewise, $\tilde{a}^{i_{n-m} i_{n-m}}$ takes the form

$$\tilde{a}^{i_{n-m} i_{n-m}}(\tilde{p}) = \frac{\tilde{p}^{i_{n-m}}(1-\tilde{p}^{i_{n-m}})}{\tilde{p}^{i_{n-m-1}}}, \tag{9.7.117}$$

whereas all other coefficients vanish. Altogether, this yields

$$\tilde{L}^* = \frac{1}{2}\sum_{j,l=1}^{n-m-1} \tilde{p}^{i_j}(\delta_l^j - \tilde{p}^{i_l})\frac{\partial}{\partial \tilde{p}^{i_j}}\frac{\partial}{\partial \tilde{p}^{i_l}} + \frac{1}{2}\sum_{j=n-m}^{n} \frac{\tilde{p}^{i_j}(1-\tilde{p}^{i_j})}{\prod_{l=n-m-1}^{j-1}\tilde{p}^{i_l}}\frac{\partial^2}{(\partial \tilde{p}^{i_j})^2} \tag{9.7.118}$$

on $\left(\overline{\Delta_{n-m-1}^{(I_{n-m-1})}} \times \overline{\square_{m+1}^{(I_n \setminus I_{n-m-1})}}\right) \setminus \bigcup_{j=n-m-1}^{n-1} N_j$. If $\tilde{p}^{i_{n-m}}$ is chosen with opposite orientation (cf. Remark 9.7.1), then $\tilde{p}^{i_{n-m}}$ needs to be replaced by $(1-\tilde{p}^{i_{n-m}})$ everywhere.

Thus, after the $(m+1)$-st blow-up step, domain, solution and operator are of analogous form as before, just with the index m replaced by $m+1$. Eventually, after $n-k-1$ blow-up steps domain, solution and operator have attained the asserted form of the corresponding statements. In particular, the remaining u_{I_k} as a proper solution smoothly extends to the entire boundary of $\Delta_k^{(I_k)}$, and hence so does $\bar{u}_{I_k}^{i_k,i_{k+1}}$ in $\Delta_{k+1}^{(I_k)}$, implying that each $\tilde{u}_{I_k}^{i_k,i_{k+1};i_{k+2},\ldots,i_d}$ smoothly extends to $\overline{\Delta_{k+1}^{(I_{k+1})}} \times \overline{\square_{d-k-1}^{(I_d \setminus I_{k+1})}}$, and eventually $\tilde{U}_{I_k}^{i_k,i_{k+1};i_{k+2},\ldots,i_n}$ smoothly extends to $\overline{\Delta_{k+1}^{(I_{k+1})}} \times \overline{\square_{n-k-1}^{(I_n \setminus I_{k+1})}}$. Moreover, the restriction property in Eqs. (9.7.113) and (9.7.114) yields Eq. (9.7.81). □

Proof of Corollary 9.7.2 In the given setting, we have $\bar{u}_{\{i_0\}}^{i_0,i_1}(\tilde{p}) = u_{\{i_0\}}(\tilde{p}^{i_0} + \tilde{p}^{i_1})\frac{\tilde{p}^{i_0}}{\tilde{p}^{i_0}+\tilde{p}^{i_1}} = u_{\{i_0\}}(1)(1-\tilde{p}^{i_1})$ in $\overline{\Delta_1^{(\{i_0,i_1\})}} = \overline{\square_1^{(\{i_1\})}}$ (and $\overline{\Delta_0^{(\{i_0\})}} = \{0\}^{(\{i_0\})}$), which proves the asserted form of the (simplified) solution, the domain and the additional faces. □

However, the global smoothness of the transformed solution of Proposition 9.5.1 observed in the preceding corollary does not necessarily hold for other functions in question, i.e. arbitrary iteratively extended solutions U satisfying the extension constraints 9.3.1 (this corresponds to U particularly being of class $C_{p_0}^\infty$). However, we still have a weaker global regularity assertion for the transformed function $\tilde{U}$ on the entire image of the simplex (only formulated for the stationary component corresponding to the setting of Corollary 9.7.2):

Lemma 9.7.3 *Let $n \geq 2$, $I_d := \{i_0, i_1, \ldots, i_d\} \subset \{0,1,\ldots,n\}$ for $d = 0,\ldots,n$ with $i_i \neq i_j$ for $i \neq j$ and $u_{\{i_0\}}\colon \Delta_0^{(\{i_0\})} \longrightarrow \mathbb{R}$. Then an iterated extension $U = \sum_{d=0}^n u_d \in C_{p_0}^\infty\left(\bigcup_{d=0}^n \Delta_d^{(I_d)}\right)$ of $u_{\{i_0\}}$ obeying the extension constraints 9.3.1 is transformed by a successive blow-up transformation $\Phi_{s_{n-1}}^{r_{n-1}} \circ \ldots \circ \Phi_{s_1}^{r_1}$ as in Proposition 9.7.1 into a function $\tilde{U} = \sum_{d=0}^n \tilde{u}_d\colon \bigcup_{d=0}^n \square_d^{(I'_d)} \longrightarrow \mathbb{R}$ with extension to all faces $\{\tilde{p}^{i_1} = 1\},\ldots,\{\tilde{p}^{i_n} = 1\}$ (which can be considered as boundary strata of any $\square_d^{(I'_d)} \subset \overline{\square_n^{(I'_n)}}$) which is of class C_p^∞ and vanishes on the mentioned faces.*

For the proof, we trace the extendability of $\tilde{U}$ towards the additional faces back to that of U in $\overline{\Delta_n^{(I_n)}}$ for approaching the incompatibilities—which will be accomplished by the next lemma. Note that in the following we will use a disjoint

formulation of the additional faces by putting

$$N_j = \square_{j-1}^{(I'_{j-1})} \times \{0\}^{(\{i_j\})} \times \overline{\boxtimes_{n-j}^{(I'_n \setminus I'_j)}}. \tag{9.7.119}$$

Lemma 9.7.4 *In the setting of a full blow-up transformation as in Proposition 9.7.1, for $d = 1, \ldots, n$ the additional face $N_d = \square_{d-1}^{(I'_{d-1})} \times \{0\}^{(\{i_d\})} \times \overline{\boxtimes_{n-d}^{(I'_n \setminus I'_d)}} \subset \overline{\square_n^{(I'_n)}}$ corresponds to $\Delta_{d-1}^{(I_{d-1})} \subset \overline{\Delta_n^{(I_n)}}$ with additional values existing for $\frac{p^{i_d+1}+\ldots+p^{i_n}}{p^{i_d}+p^{i_d+1}+\ldots+p^{i_n}}, \ldots, \frac{p^{i_n}}{p^{i_n-1}+p^{i_n}}$ (which can be considered as limits of corresponding sequences). Furthermore, for $j = 1, \ldots, d-1$ the face $\{\tilde{p}^{i_j} = 1\} \subset \overline{\square_{d-1}^{(I'_{d-1})}}$ corresponds to $p^{i_{j-1}} = 0$ in $\overline{\Delta_{d-1}^{(I_{d-1})}}$, in particular its interior corresponds to $\Delta_{d-2}^{(I_{d-1} \setminus \{i_{j-1}\})}$.*

Proof To take account of the 'additional' faces N_m of $\overline{\square_n^{(I'_n)}}$ produced during the blow-up transformations, we carry out the full blow-up transformation of Proposition 9.7.1. This yields

$$\tilde{p}^{i_1} := p^{i_1} + \ldots + p^{i_n}, \tag{9.7.120}$$

$$\tilde{p}^{i_2} := \begin{cases} \frac{p^{i_2}+\ldots+p^{i_n}}{p^{i_1}+p^{i_2}+\ldots+p^{i_n}} & \text{for } p^{i_1} + \ldots + p^{i_n} > 0 \\ 0 & \text{for } p^{i_1} + \ldots + p^{i_n} = 0, \end{cases} \tag{9.7.121}$$

$$\vdots$$

$$\tilde{p}^{i_j} := \begin{cases} \frac{p^{i_j}+\ldots+p^{i_n}}{p^{i_j-1}+p^{i_j}+\ldots+p^{i_n}} & \text{for } p^{i_j-1} + \ldots + p^{i_n} > 0 \\ 0 & \text{for } p^{i_j-1} + \ldots + p^{i_n} = 0, \end{cases} \tag{9.7.122}$$

$$\vdots$$

$$\tilde{p}^{i_n} := \begin{cases} \frac{p^{i_n}}{p^{i_n-1}+p^{i_n}} & \text{for } p^{i_n-1} + p^{i_n} > 0 \\ 0 & \text{for } p^{i_n-1} + p^{i_n} = 0 \end{cases} \tag{9.7.123}$$

for $p \in \bigcup_{d=0}^{n} \Delta_d^{(I_d)}$ and conversely

$$p^{i_1} = \tilde{p}^{i_1}(1 - \tilde{p}^{i_2}), \tag{9.7.124}$$

$$\vdots$$

$$p^{i_j} = \tilde{p}^{i_1} \cdots \tilde{p}^{i_j}(1 - \tilde{p}^{i_{j+1}}), \tag{9.7.125}$$

$$\vdots$$

$$p^{i_{n-1}} = \tilde{p}^{i_1} \cdots \tilde{p}^{i_{n-1}}(1 - \tilde{p}^{i_n}), \tag{9.7.126}$$

$$p^{i_n} = \tilde{p}^{i_1} \cdots \tilde{p}^{i_n} \tag{9.7.127}$$

for $\tilde{p} \in \bigcup_{d=0}^{n} \square_d^{(I'_d)}$ (note that we also have $p^{i_0} = 1 - \tilde{p}^{i_1}$); however, the given equations also smoothly extend to the entire $\overline{\square_n^{(I'_n)}}$. We can therefore also transform the $N_d \subset \overline{\square}_n$ back to $\overline{\Delta}_n$, i.e. $\tilde{p}^{i_d} = 0$ implies $p^{i_d}, \ldots, p^{i_n} = 0$, whereas $0 < \tilde{p}^{i_1}, \ldots, \tilde{p}^{i_{d-1}} < 1$ leads to $p^{i_1}, \ldots, p^{i_{d-1}} > 0$. Keeping the values of $\tilde{p}^{i_{d+1}}, \ldots, \tilde{p}^{i_n}$ yields the pivotal allele (limit) ratios $\frac{p^{i_d+1}+\ldots+p^{i_n}}{p^{i_d}+p^{i_d+1}+\ldots+p^{i_n}}, \ldots, \frac{p^{i_n}}{p^{i_n-1}+p^{i_n}}$. If however $\tilde{p}^{i_j} = 1$, this corresponds to $p^{i_{j-1}} = 0$ (and $p^{i_1}, \ldots, p^{i_{j-1}}, p^{i_{j+1}} \ldots, p^{i_d} > 0$ if $0 < \tilde{p}^{i_1}, \ldots, \tilde{p}^{i_{j-1}}, \tilde{p}^{i_{j+1}}, \ldots, \tilde{p}^{i_d} < 1$ and $\tilde{p}^{i_{d+1}} = 0$). □

Proof of Lemma 9.7.3 By Lemma 9.7.1 and Proposition 9.7.1 and Corollary 9.7.2, the full blow-up transformation respectively maps

$$\bigcup_{d=0}^{n} \Delta_d^{(I_d)} \longmapsto \bigcup_{d=0}^{n} \square_d^{(I'_d)} \tag{9.7.128}$$

C^∞-diffeomorphically (cf. Eq. (9.7.83)). By the $C^\infty_{p_0}$-regularity of U, u_n in $\Delta_n^{(I_n)}$ smoothly connects with u_{n-1} in $\Delta_{n-1}^{(I_{n-1})}$, and consequently so does $\tilde{u}_n$ in $\square_n^{(I'_n)}$ with $\tilde{u}_{n-1}$ in $\square_{n-1}^{(I'_{n-1})}$; an analogous statement holds for all lower dimensions. Thus it remains to show that $\tilde{U}$ extends those faces of $\overline{\square_n^{(I'_n)}}$ given by $\{\tilde{p}^{i_j} = 1\}$ for $j = 1, \ldots, n$ such that the extension is of class C^∞_p.

By Lemma 9.7.4, the interior of $\{\tilde{p}^{i_j} = 1\} \subset \overline{\square_n^{(I'_n)}}$ corresponds to $p^{i_{j-1}} = 0$ and $p^{i_l} > 0$ for $l \neq j-1$ in $\overline{\Delta_n^{(I_n)}}$, thus to $\Delta_{n-1}^{(I_n \setminus \{i_{j-1}\})}$, which is a boundary face of $\Delta_n^{(I_n)}$ outside the assumed extension path defined by the (ordered) I_n. Hence by the $C^\infty_{p_0}$-regularity, the relevant continuous extension of U needs to be zero there, and this is attained smoothly when coming from the interior $\Delta_n^{(I_n)}$. Because of the diffeomorphism properties of the transformation, this also applies to the cube.

An analogous observation holds for subcubes $\square_{d-1}^{(I'_{d-1})} \subset \overline{\square}_n$, $d = 1, \ldots, n$: The interior of its face $\{\tilde{p}^{i_j} = 1\}$ corresponds to $\Delta_{d'-1}^{(I_{d-1} \setminus \{i_{j-1}\})} \subset \overline{\Delta_{d-1}^{(I_{d-1})}}$ when transformed back to the simplex (cf. Eq. (9.7.128) and Lemma 9.7.4). This is again outside the assumed extension path, in particular if starting in $\Delta_{d-1}^{(I_{d-1})}$, and hence the corresponding boundary extension of u_{d-1} needs to smoothly attain zero there by the $C^\infty_{p_0}$-regularity, which likewise applies analogously to the cube. □

9.8 The Stationary Kolmogorov Backward Equation and Uniqueness

When we ask for the long-term behaviour of the process, i.e. which alleles are eventually lost and in which order, we are lead to the stationary Kolmogorov backward equation. Solutions of this equation have already appeared implicitly in the preceding section as extensions of solutions in $\partial_0\Delta_n$ since the corresponding operator L_0^* has 0 as its only eigenvalue.

Although we have already developed the extended setting presented in Sect. 9.2, we start by considering some interior simplex Δ_n, (resp. the corresponding restriction of an extended solution). Then, for a solution in Δ_n, we may argue again that all eigenmodes of the solution corresponding to a positive eigenvalue vanish for $t \to -\infty$, while those corresponding to the eigenvalue zero are preserved. This implies that a solution of the Kolmogorov backward equation (4.2.13) in Δ_n converges uniformly to a solution of the corresponding *homogeneous* or *stationary Kolmogorov backward equation*

$$\begin{cases} L^*u(p) = 0 & \text{in } \Delta_n \\ u(p) = f(p) & \text{in } \partial\Delta_n \end{cases} \tag{9.8.129}$$

for $u \in C^2(\Delta_n)$ and with boundary condition f (which needs to be attained smoothly in a suitable sense).

At first sight, this appears as a boundary value problem (for some suitably chosen boundary function f, assuring the uniqueness of a solution). However, as may be expected from the previous considerations, the role of the boundary here is different from usual boundary value problems and again requires some extra care: On the one hand, a proper solution in Δ_n always converges to the trivial stationary solution ($\equiv 0$), whose (continuous) extension to the boundary also vanishes at all negative times. On the other hand, any solution which extends to $\partial\Delta_n$ is already strongly constrained by the degeneracy behaviour of the differential operator if suitable regularity assumptions on the solution in $\overline{\Delta}_n$ (cf. also equality (2.11.23)) apply:

Lemma 9.8.1 (Stem Lemma) *For a solution $u \in C^\infty(\Delta_n)$ of Eq. (9.8.129) with extension $U \in C_p^\infty(\overline{\Delta}_n)$, we have*

$$L^*U = 0 \qquad \text{in } \overline{\Delta}_n. \tag{9.8.130}$$

Proof We shall proceed iteratively: Assuming that $L_k^*U = 0$ for all $\Delta_k^{(I_k)} \subset \partial_k\Delta_n$, we show that this property extends to each $\Delta_{k-1}^{(I_{k-1})} \subset \partial_{k-1}\Delta_k^{(I_k)}$ for every $\Delta_k^{(I_k)}$, and hence we obtain $L_{k-1}^*U = 0$ on $\partial_{k-1}\Delta_n$. A repeated application then yields Eq. (9.8.130).

W. l. o. g. let $\Delta_k^{(I_k)}$ and $\Delta_{k-1}^{(I_{k-1})} \subset \partial_{k-1}\Delta_k^{(I_k)}$ with $I_k \setminus I_{k-1} = \{i_k\}$. Then for the operator L_k^* in $\Delta_k^{(I_k)}$, we have

$$L_k^* = L_{k-1}^* + p^{i_k}\Big(\sum_{i_j \in I_k \setminus \{0\}} (\delta_{i_k}^{i_j} - p^{i_j})\frac{\partial}{\partial p^{i_j}}\frac{\partial}{\partial p^{i_k}}\Big) \tag{9.8.131}$$

with L_{k-1}^* being the restriction of L_k^* to $\Delta_{k-1}^{(I_{k-1})}$.

We take some $p \in \Delta_{k-1}^{(I_{k-1})}$ and choose a sequence $(p_l)_{l\in\mathbb{N}}$ in $\Delta_k^{(I_k)}$ with $p_l \to p$ and apply this operator to U at $p_l \in \Delta_k^{(I_k)}$. The resulting expression in the big bracket is controlled by $p_l^{i_k} \to 0$ while approaching p and—with the derivatives of U inside being bounded on a closed neighbourhood of p because of the regularity of U—is continuous up to p. Likewise, all derivatives of U within $\Delta_{k-1}^{(I_{k-1})}$ are continuously matched by the corresponding ones in $\Delta_k^{(I_k)}$, thus $L_{k-1}^*(U(p_l))$ is also continuous up to the boundary in p (as the corresponding coefficients are, too). Hence, the whole expression is continuous up to the boundary in p with $L_{k-1}^*U(p) \equiv L_k^*U(p) = 0$, and since p was arbitrary, this applies to all of $\Delta_{k-1}^{(I_{k-1})}$. □

Assuming the stated pathwise regularity, this confines the boundary values of U resp. f on $\partial\Delta_n = \bigcup_{k=0}^{n-1}\partial_k\Delta_n$ and consequently, Eq. (9.8.129) is rather restated as an *extended homogeneous* or *extended stationary Kolmogorov backward equation*[6]

$$\begin{cases} L^*U(p) = 0 & \text{in } \overline{\Delta}_n \setminus \partial_0\Delta_n \\ U(p) = f(p) & \text{in } \partial_0\Delta_n \end{cases} \tag{9.8.132}$$

for $U \in C_p^2\big(\overline{\Delta}_n\big)$ with the only 'free' boundary values remaining the ones at the vertices $\partial_0\Delta_n$. If we also assume global continuity of the solution, the values on $\partial_0\Delta_n$, however, suffice as boundary information determining a solution uniquely because we can extend the solution iteratively to strata of increasing dimension. In such a case, a stationary solution and the stationary component of a global extension as in the preceding section also coincide:

Proposition 9.8.1 *A solution $U \in C_p^\infty\big(\overline{\Delta}_n\big) \cap C^0\big(\overline{\Delta}_n\big)$ of the extended stationary Kolmogorov backward equation (9.8.132) for some boundary condition $f_0\colon \partial_0\Delta_n \longrightarrow \mathbb{R}$ is uniquely defined and coincides with (the projection of) a solution of the extended Kolmogorov backward equation (9.2.1) in $\big(\overline{\Delta}_n\big)_{-\infty}$ to $\overline{\Delta}_n$ for a final condition $f \in \mathcal{L}^2\big(\bigcup_{d=0}^n \partial_d\Delta_n\big)$ with $f \equiv f_0\chi_{\partial_0\Delta_n}$ as by Theorem 9.6.1. Furthermore, the space of solutions is spanned by $p^1, \ldots, p^n$ and 1.*

[6] As already stated, it is without effect whether $\partial_0\Delta_n$ is added to the domain of definition of the differential equation or not. Although $\partial_0\Delta_n$ has been included in Eq. (9.8.130), this is not done here for formal reasons.

Proof The first assertion may be shown by an iterative application of the maximum principle: On every face $\Delta_k^{(I_k)} \subset \partial_k \Delta_n$ for all $1 \leq k \leq n$, the operator L^* is locally uniformly elliptic, and hence, $U|_{\Delta_k^{(I_k)}}$ is uniquely defined by its values on $\partial \Delta_k^{(I_k)}$ by virtue of the maximum principle. Applying this consideration iteratively for $\partial_0 \Delta_n, \ldots, \partial_n \Delta_n = \Delta_n$ yields the desired global uniqueness.

Next, we will show that a final condition $f = \chi_{\Delta_0^{(\{i_0\})}}$ for some $i_0 \in I_n$ gives rise to an extended solution $\bar{U}(p,t) = \bar{U}(p) = p^{i_0}$ in $\left(\overline{\Delta}_n\right)_{-\infty}$ resp. $\overline{\Delta}_n$ proving the second assertion. With f as described, the extended solution (cf. Theorem 9.6.1) is solely given by $\bar{U} \equiv \bar{U}_{i_0}$, i.e.

$$\begin{aligned}\bar{U}_{\{i_0\}}(p,t) &= u_{\{i_0\}}(p,t)\chi_{\Delta_0^{(\{i_0\})}}(p) \\ &\quad + \sum_{1 \leq d \leq n} \sum_{i_1 \in I_n \setminus \{i_0\}} \cdots \sum_{i_d \in I_n \setminus \{i_0,\ldots,i_{d-1}\}} U_{\{i_0\}}^{i_0,\ldots,i_d}(p,t)\chi_{\Delta_d^{(\{i_0,\ldots,i_d\})}}(p)\end{aligned} \tag{9.8.133}$$

(cf. Eq. (9.5.36)). Considering an arbitrary $\Delta_d^{(I_d)} \subset \overline{\Delta}_n$, $I_d \subset I_n$, we obtain for the restriction of $\bar{U}_{i_0}$ to $\Delta_d^{(I_d)}$ using Eq. (9.5.30)

$$\begin{aligned}\bar{U}_{\{i_0\}}(p,t)|_{\Delta_d^{(I_d)}} &= \sum_{i_1 \in I_d \setminus \{i_0\}} \cdots \sum_{\substack{i_d \in \\ I_d \setminus \{i_0,\ldots,i_{d-1}\}}} U_{\{i_0\}}^{i_0,\ldots,i_d}(p,t) \\ &= \sum_{i_1 \in I_d \setminus \{i_0\}} \cdots \sum_{\substack{i_d \in \\ I_d \setminus \{i_0,\ldots,i_{d-1}\}}} u_{\{i_0\}}(\pi^{i_0,\ldots,i_d}(p),t) \prod_{j=0}^{d-1} \frac{p^{i_j}}{\sum_{l=j}^{d} p^{i_l}}\end{aligned} \tag{9.8.134}$$

with $u_{\{i_0\}}(\pi^{i_0,\ldots,i_d}(p),t) \equiv 1$ as $\pi^{i_0,\ldots,i_d}(p) \in \Delta_0^{(\{i_0\})}$ for all $p \in \Delta_d^{(I_d)}$ and $u_{\{i_0\}} = f = 1$ in $\left(\Delta_0^{(\{i_0\})}\right)_{-\infty}$ by assumption. Since we have $\sum_{l=0}^{d} p^{i_l} = 1$ in $\Delta_d^{(I_d)}$, we may replace the expression $\sum_{l=j}^{d} p^{i_l}$ by $1 - \sum_{l=0}^{j-1} p^{i_l}$ and rearrange the sum (by also suppressing the last sum as the index i_d does no longer occur), which yields altogether

$$\begin{aligned}&\bar{U}_{\{i_0\}}(p,t)|_{\Delta_d^{(I_d)}} = \\ &p^{i_0}\left(\sum_{\substack{i_1 \in \\ I_d \setminus \{i_0\}}} \frac{p^{i_1}}{1-p^{i_0}} \cdots \left(\sum_{\substack{i_j \in \\ I_d \setminus \{i_0,\ldots,i_{j-1}\}}} \frac{p^{i_j}}{1-\sum_{l=0}^{j-1} p^{i_l}} \cdots \left(\sum_{\substack{i_{d-1} \in \\ I_d \setminus \{i_0,\ldots,i_{d-2}\}}} \frac{p^{i_{d-1}}}{1-\sum_{l=0}^{d-2} p^{i_l}}\right)\right)\right).\end{aligned} \tag{9.8.135}$$

As we have $\frac{p^{ij}+\ldots+p^{id}}{1-\sum_{l=0}^{j-1}p^{il}} = 1$ for $j = d-1,\ldots,1$, the whole expression reduces to $\bar{U}_{\{i_0\}}(p,t)|_{\Delta_d^{(I_d)}} = p^{i_0}$. Since $\Delta_d^{(I_d)}$ was arbitrary, we obtain $\bar{U}_{\{i_0\}}(p,t) \equiv \bar{U}_{\{i_0\}}(p) = p^{i_0}$ in the entire $\overline{\Delta}_n$. □

In terms of the probabilistic interpretation, the extended setting (9.8.132) also matches the considerations of Sect. 9.2 as Eq. (9.8.132) may be viewed as the limit equation for $t \to -\infty$ of the extended Kolmogorov backward equation (9.2.1) (which may be shown as previously). This is also reflected in Proposition 9.8.1: For $t \to -\infty$ and any solution, the only target sets with persisting attraction are of course the vertices (which correspond to configurations of the model where all but one allele are extinct), and hence the stationary solutions match the stationary components of the global extensions as in Theorem 9.6.1, which in turn result from a non-vanishing final condition in $\partial_0\Delta_n$. Then, every $\Delta_0^{(\{i\})} \subset \partial_0\Delta_n$ may give rise to a solution (component) p^i—in particular yielding a positive target hit probability on the entire Δ_n for all times. However, even the stationary component of solutions as in Theorem 9.6.1 may in principle be perceived as time-dependent and also describing the transitional attraction of target sets in the entire $\overline{\Delta}_n$ induced by a given ultimate target set in $\partial_0\Delta_n$.

Altogether, Proposition 9.8.1 under the given restrictions thus already yields a full description of the stationary model in the entire $\overline{\Delta}_n$. However, dropping the global continuity assumption, a much wider class of (stationary) solutions, i.e. iteratively extended solutions of the Kolmogorov backward equation obeying the extension constraints 9.3.1, may be obtained as described in the preceding section. To establish the uniqueness also for this bigger class, we may apply the blow-up scheme of Sect. 9.7 and demonstrate the uniqueness of solutions of the correspondingly transformed stationary Kolmogorov backward equation on the cube (which is basically analogous to the simplex, cf. the preceding considerations). The eventual result will be obtained by applying the uniqueness result for the cube to the transformed iteratively extended solutions (assuming sufficient regularity if necessary). Again, this is limited to the stationary components.

Regarding the uniqueness of stationary solutions on the cube with the transformed Kolmogorov backward operator given by Eq. (9.7.87), we have the cube version of the simplex result of Lemma 9.8.1.

Lemma 9.8.2 (Stem Lemma, Cube Version) *For a solution $u \in C^\infty(\square_n)$ of the stationary Kolmogorov backward equation $\tilde{L}_n^* u = 0$ in $\square_n$ with*

$$\tilde{L}_n^* := \frac{1}{2}\sum_{i=1}^{n} \frac{\tilde{p}^i(1-\tilde{p}^i)}{\prod_{j=1}^{i-1}\tilde{p}^j} \frac{\partial^2}{(\partial\tilde{p}^i)^2} \tag{9.8.136}$$

and with extension $U \in C_p^\infty(\overline{\square}_n)$, we have

$$\tilde{L}^* U = 0 \quad \text{in } \overline{\square}_n, \tag{9.8.137}$$

i.e.

$$\tilde{L}_d^* U = 0 \quad \textit{with} \quad \tilde{L}_d^* := \frac{1}{2} \sum_{\substack{i=\hat{\imath}(d)+1 \\ i \neq i_m}}^{n} \frac{\tilde{p}^i(1-\tilde{p}^i)}{\prod\limits_{\substack{j=\hat{\imath}(d)+1 \\ j \neq i_m}}^{i-1} \tilde{p}^j} \frac{\partial^2}{(\partial \tilde{p}^i)^2} \tag{9.8.138}$$

in $\square_d = \left\{\tilde{p}^{i_1} = b_{i_1}, \ldots, \tilde{p}^{i_{n-d}} = b_{i_{n-d}}\right\} \subset \partial_d \square_n$ *for all* $1 \leq d \leq n-1$ *and all* $i_1, \ldots, i_{n-d} \in \{1, \ldots, n\}$, $i_k \neq i_l$ *for* $k \neq l$ *with* $\hat{\imath} = \hat{\imath}(d) := \arg\max\limits_{i_1, \ldots, i_{n-d}} \{b_{i_m} = 0\}$ *resp.* $\hat{\imath}(d) := 0$ *if* $b_{i_m} = 1$ *for all* i_m.

Proof The statement is proven iteratively: Assuming that Eq. (9.8.138) holds in some (arbitrary) domain $\square_{d+1} \subset \partial_{d+1} \square_n$, we show that a corresponding formula also holds for any $\square_d \subset \partial_d \square_{d+1} \subset \partial_d \square_n$. A repeated application of the argument then yields the assertion.

Let $\square_{d+1} = \left\{\tilde{p}^{i_1} = b_1, \ldots, \tilde{p}^{i_{n-d-1}} = b_{n-d-1}\right\}$ and $\square_d = \left\{\tilde{p}^{i_1} = b_1, \ldots, \tilde{p}^{i_{n-d}} = b_{n-d}\right\}$ with $i_{n-d} \neq i_1, \ldots, i_{n-d-1}$ and $b_{n-d} \in \{0, 1\}$. If we have $i_{n-d} < \hat{\imath}(d+1)$, then as $\tilde{p}^{i_{n-d}} \to 0$ resp. $\tilde{p}^{i_{n-d}} \to 1$, the value of the operator in Eq. (9.8.138) applied to U—with the occurring derivatives and the coefficients being continuous—depends continuously on $\tilde{p}$ up to the boundary, thus Eq. (9.8.138), which already has the corresponding form for $\square_d$ (note $\hat{\imath}(d) \equiv \hat{\imath}(d+1)$), also holds on $\square_d$.

If we rather have $i_{n-d} > \hat{\imath}(d+1)$ and $b_{n-d} = 1$, then, when choosing some $\tilde{p} \in \square_d$ and a sequence $(\tilde{p}_l)_{l \in \mathbb{N}}$ in $\square_{d+1}$ with $\tilde{p}_l \to \tilde{p}$, the expression

$$\frac{1}{2} \frac{\tilde{p}_l^{i_{n-d}}(1-\tilde{p}_l^{i_{n-d}})}{\prod_{\substack{j=\hat{\imath}(d)+1 \\ j \neq i_m}}^{i_{n-d}-1} \tilde{p}_l^j} \frac{\partial^2}{(\partial \tilde{p}_l^{i_{n-d}})^2} U(\tilde{p}_l) \tag{9.8.139}$$

is controlled by $(1-\tilde{p}_l^{i_{n-d}})$ while approaching $\tilde{p}$ and—with the derivatives of U being bounded on a closed neighbourhood of $\tilde{p}$ because of the regularity of U—is continuous up to $\tilde{p}$. Analogous to the previous case, all other summands of the operator in Eq. (9.8.138) are also continuous on the boundary, thus proving that the corresponding form of Eq. (9.8.138) (with the i_{n-d}-th summand deleted) holds in $\square_d$ (again $\hat{\imath}(d) \equiv \hat{\imath}(d+1)$).

If instead $i_{n-d} > \hat{\imath}(d+1)$ and $b_{n-d} = 0$, then we may multiply the whole Eq. (9.8.138) by $\tilde{p}^{i_{n-d}}$. If now $\tilde{p}^{i_{n-d}} \to 0$, then by a similar argument as above all derivatives of the operator that do not contain $\tilde{p}^{i_{n-d}}$ in the denominator of their coefficient continuously vanish, whereas the values of all other summands are also continuous up to the boundary. Thus, Eq. (9.8.138) holds on $\square_d$ with the index $\hat{\imath}(d+1)$ replaced by $\hat{\imath}(d) = i_{n-d}$. □

The obtained Eq. (9.8.137) may again be perceived as an extended version of the stationary Kolmogorov backward equation on the cube (cf. also Eq. (9.8.132), although the domains do not fully correspond), and we have (cf. Proposition 9.8.1):

Proposition 9.8.2 *A solution* $U \in C_p^\infty(\overline{\square}_n) \cap C^0\big(\overline{\square}_n\big)$ *of the extended stationary Kolmogorov backward equation*

$$\tilde{L}^* U = 0 \quad \text{in } \overline{\square}_n \tag{9.8.140}$$

with $\tilde{L}^*$ *as in Eq.* (9.8.138) *is uniquely determined by its values on* $\partial_0 \square_n$.

Proof The uniqueness may be shown by a successive application of the maximum principle: In every stratum of the domain $\square_d \subset \partial_d \square_n$ for all $1 \leq d \leq n$, the solution $U|_{\square_d}$ is uniquely defined by its values on $\partial \square_d$: If Eq. (9.8.138) comprises d derivative terms, this follows directly from Hopf's maximum principle (see e.g. [72]) as the operator is locally uniformly elliptic on $\square_d$; if it only comprises $d' < d$ derivative terms, analogous considerations apply for each d'-dimensional fibre of $\square_d$ (with corresponding boundary part), thus giving the uniqueness of a solution on every fibre first and after assembling also on all $\square_d$. Applying this consideration successively for $\partial_0 \square_n, \ldots, \partial_n \square_n = \square_n$ yields the desired global uniqueness. □

With the blow-up scheme of Sect. 9.7 at hand, the preceding uniqueness result may also be conveyed to the simplex $\overline{\Delta}_n$, assuming some additional regularity. We finally arrive at

Theorem 9.8.1 *Let* $n \in \mathbb{N}_+$, $I_d := \{i_0, i_1, \ldots, i_d\} \subset \{0, 1, \ldots, n\}$ *for* $d = 0, \ldots, n$ *with* $i_i \neq i_j$ *for* $i \neq j$ *and* $u_{\{i_0\}} \colon \Delta_0^{(\{i_0\})} \longrightarrow \mathbb{R}$ *be given. Then an extension* $\bar{U}_{\{i_0\}}^{i_0,\ldots,i_n} \colon \bigcup_{0 \leq d \leq n} \Delta_d^{(I_d)} \longrightarrow \mathbb{R}$ *as in Proposition 9.5.1 is unique within the class of extensions* $\bar{U}$ *which satisfy the extension constraints 9.3.1, i.e.*

(i) are of class $C_{p_0}^\infty\big(\bigcup_{0 \leq d \leq n} \Delta_d^{(I_d)}\big)$ *with* $U|_{\Delta_0^{(\{i_0\})}} = u_{\{i_0\}}$ *and*

(ii) solve the stationary Kolmogorov backward equation (9.8.132) *in* $\bigcup_{0 \leq d \leq n} \Delta_d^{(I_d)}$, *as well as, in case* $n \geq 2$, *whose*

(iii) transformation image $\tilde{U} \colon \bigcup_{d=0}^n \square_d^{(I'_d)} \longrightarrow \mathbb{R}$ *by a successive blow-up transformation* $\Phi_{s_{n-1}}^{r_{n-1}} \circ \ldots \circ \Phi_{s_1}^{r_1}$ *as in Proposition 9.7.1 has an extension to the entire boundary* $\partial \square_n^{(I'_n)}$ *which is of class* $C_p^\infty\big(\overline{\square_n^{(I'_n)}}\big) \cap C^0\big(\overline{\square_n^{(I'_n)}}\big)$.

Consequently, also the global extension $\bar{U}_{\{i_0\}}$ *as in Proposition 9.5.2 resp. also in Theorem 9.6.1 is unique.*

Proof The assertion for the trivial case $n = 1$ directly follows, as $\bar{U}_{\{i_0\}}^{i_0,i_1}$ is already sufficiently regular in $\overline{\Delta_1^{(I_1)}} \equiv \overline{\square_1^{(I'_1)}}$ for an application of the maximum principle, in particular globally continuous. For $n \geq 2$, any function U which is a solution of the stationary Kolmogorov backward equation (9.8.132) in $\overline{\Delta_n^{(I_n)}}$ by a full blow-up transformation of the domain transforms into a function $\tilde{U}$, which solves the stationary Kolmogorov backward equation (9.7.77) in $\bigcup_{d=0}^n \square_d^{(I'_d)}$ (cf. Proposition 9.7.1 and Corollary 9.7.2 and Lemma 9.7.3). Furthermore, with the assumed regularity after a full blow-up, it has an extension to $\overline{\square_n^{(I'_n)}}$ which is pathwise

smooth as well as globally continuous and by Lemma 9.8.2 solves the stationary Kolmogorov backward equation $\tilde{L}^*\tilde{\bar{U}} = 0$ in $\overline{\square_n^{(I_n')}}$ with $\tilde{L}^*$ as in Eq. (9.8.138). Hence, the uniqueness result of Proposition 9.8.2 applies and proves the uniqueness of the transformed function (and, in view of the injectivity of the blow-up, also the uniqueness of U)—for specified boundary data on the entire $\partial_0\square_n^{(I_n')}$. Thus, we only need to show that these boundary data are uniquely determined by the assumptions.

This is straightforward: In accordance with Lemma 9.7.3, $\tilde{U}$ or its corresponding continuous extension vanishes on $\{\tilde{p}^{ij} = 1\} \subset \partial\square_n^{(I_n')}$, $j = 1, \ldots, n$. As by assumption (iii) the continuous extendability applies to the entire $\overline{\square_n^{(I_n')}}$, $\tilde{U}$ or its extension even vanishes on

$$\overline{\{\tilde{p}^{i_1} = 1\}}, \ldots, \overline{\{\tilde{p}^{i_n} = 1\}}. \tag{9.8.141}$$

In particular, this means that $\tilde{U}$ or its extension vanishes on any vertex $\square_0 \subset \partial_0\square_n^{(I_n')}$—which may always be written as

$$\square_0 = \{\tilde{p}^{ij} = b_j \quad \text{for } j = 1, \ldots, n\} \quad \text{with correspondingly } b_j \in \{0, 1\} - \tag{9.8.142}$$

except for the vertex $\square_0^{(\varnothing)} = \{(0, \ldots, 0)\}$, where it attains the value $u_{\{i_0\}}$ as stated previously. Thus, the (transformed) boundary data given on all vertices are the same for any extension in question, and since $\bar{U}_{\{i_0\}}^{i_0,\ldots,i_n} : \bigcup_{0\le d\le n} \Delta_d^{(I_d)} \longrightarrow \mathbb{R}$ as in Proposition 9.5.1 satisfies the extension constraints and has an extension to the entire boundary $\partial\square_n^{(I_n')}$ which is in $C_p^\infty(\overline{\square_n^{(I_n')}}) \cap C^0\big(\overline{\square_n^{(I_n')}}\big)$ (this may be seen directly from Eq. (9.7.82)), it also is the unique extension. □

9.9 The Backward Equation and Exit Times

In this section, we shall consider the Kolmogorov backward equation and its stationary solutions. We shall utilize this to derive the general formula for the absorption times of the Wright–Fisher model, that is, the expected times for loosing one or several alleles. The relevant differential operator is

$$L_n^* = \frac{1}{2}\sum_{i,j=1}^n p^i(\delta_{ij} - p^j)\frac{\partial^2}{\partial p^i \partial p^j}. \tag{9.9.1}$$

As we have seen in Sect. 9.8 (see Proposition 9.8.1), the Dirichlet problem for this operator,

$$\begin{aligned} L_n^* u(p) &= 0 \text{ in } \Delta_n \\ u(p) &= \psi(p) \text{ on } \partial_0 \Delta_n \end{aligned} \tag{9.9.2}$$

is solvable, in contrast to that for L_n, where, instead of boundary values, we had to impose the moment condition.

We now turn to the *inhomogeneous* stationary Kolmogorov backward equation, because from this, the expected first time τ_{Δ_n} can be obtained. τ_{Δ_n} is the expected time when one allele gets lost from the population. This expected first exit time is given by the solution of

$$\begin{aligned} L_n^* u(p) &= -1 \text{ in } \Delta_n \\ u(p) &= 0 \text{ on } \partial\Delta_n = \bigcup_{k=0}^{n-1} \partial_k \Delta_n. \end{aligned} \tag{9.9.3}$$

From the restriction Lemma 8.4.1, we can then also formulate the equation for the expected time for losing m alleles,

$$\begin{aligned} L_k^* u(p) &= -1 \text{ in } \bigcup_{k=n-m+1}^{n} \partial_k \Delta_n \\ u(p) &= 0 \text{ on } \bigcup_{k=0}^{n-m} \partial_k \Delta_n. \end{aligned} \tag{9.9.4}$$

From Lemma 3.10.1, we now recall that we can construct such solutions from the potential of the affine structure. In fact, for the function

$$\varphi(p) = \sum_{i=i_0,\ldots,i_k} p_i \log p_i \tag{9.9.5}$$

of (3.6.14), we have

$$L_k^* \varphi = \frac{k}{2} \text{ in } \Delta_k^{(\{i_0,\ldots,i_k\})} \tag{9.9.6}$$

(note the factor $\frac{1}{2}$ in the definition of L_k^* in contrast to the operator A in Lemma 3.10.1).

In order to realize the boundary condition $u(p) = 0$, we start with $m = n$, that is, with the case where n alleles get lost and thus only a single one remains. From the

preceding, we observe that

$$u_1(p) := -2\sum_{i=1}^{n+1}(1-p_i)\log(1-p_i) \tag{9.9.7}$$

satisfies (9.9.4) for $m = n$. Therefore, $u_1(p)$ is the expected time for losing n of the $n+1$ alleles in the population when starting at time 0 with allele frequencies given by p.

Next,

$$u_2(p) := -2\Big(\sum_{1\le i_1<i_2\le n+1}(1-p_{i_1}-p_{i_2})\log(1-p_{i_1}-p_{i_2}) - (n-1)\sum_{i=1}^{n+1}p_i\log p_i\Big) \tag{9.9.8}$$

satisfies (9.9.4) for $m = n-1$. To see this, we note that $L_k^*(\sum_{1\le i_1<i_2\le n+1}(1-p_{i_1}-p_{i_2})\log(1-p_{i_1}-p_{i_2})) = \frac{n}{2}, L_k^*(\sum_i(1-p_i)\log(1-p_i)) = \frac{1}{2}$ for all $k = 2,\dots,n$ and also check the boundary condition. $u_2(p)$ then yields the expected time for having only two alleles left, that is, for having lost $n-1$ of the $n+1$ ones.

Iterating this process, we obtain Littler's formula [85]

$$u_m(p) = -2\left(\sum_{j=1}^{m}(-1)^{m-j}\binom{n-j}{m-j}\left(\sum_{1\le i_1<i_2<\cdots<i_j\le n+1}(1-\sum_\nu p_{i_\nu})\log(1-\sum_\nu p_{i_\nu})\right)\right). \tag{9.9.9}$$

In particular, this shows that $u_n(p)(p) = \mathrm{E}^p(\tau_{\Delta_n})$, the expected time for the process X_t to leave Δ_n, is finite. More generally, we can also solve hierarchical Dirichlet problems on $\Delta_n \cup \partial_{n-1}\Delta_n \cup \cdots \cup \partial_m\Delta_n$ for $0 < m < n$.

We can also treat the fixation probabilities, that certain alleles die out and others remain in the population. The probability $\pi(p_1,\dots,p_n)$ of the fixation event given in terms of a boundary condition solves the time independent Kolmogorov backward equation

$$L_n^*\pi = \frac{1}{2}\sum_{i,j=1}^{n}p^i(\delta_{ij}-p^j)\frac{\partial^2\pi}{\partial p^i\partial p^j} = 0. \tag{9.9.10}$$

The boundary condition specifies that π is 1 on some part of the boundary and 0 on the rest. This simply means that ultimately the process leaves Δ_n on that part of its boundary where $\pi = 1$. For instance, for the probability that eventually allele A^j

becomes fixed, we have the boundary condition

$$\pi(p_1,\dots,p_n) = \begin{cases} 1 & \text{if } p_j = 1 \\ 0 & \text{if } \sum_{i\neq j} p_i = 1 \end{cases} \tag{9.9.11}$$

and impose the PDEs $L_k^*\pi = 0$ on the remaining parts of the simplex Δ_n and its boundary. The solution with the boundary condition (9.9.11) is simply given by

$$\pi = p_j, \tag{9.9.12}$$

that is, the probability that allele $A^j, j \in \{1,\dots,n+1\}$, gets fixed is equal to its initial relative frequency p_j. This can, in fact, also be seen by the following intuitive argument of Ewens [39]. At any time, any allele in the population is derived from some ancestral allele at time 0, and the probability for any such allele A^j in the ancestral population (i.e., that at time 0) to be the ancestor of some given allele whose identity is not known is equal to its relative frequency p_j. This then also applies to the asymptotic state when only one allele survives. Without knowing its identity, the probability of it being derived from A^j then is again p_j. Turning this around then yields the probability that A^j is that allele that eventually becomes fixated is p_j.

Moving on, the probability that A^j and A^ℓ, $j,\ell \in \{1,\dots,n+1\}, j \neq \ell$, are the last two surviving alleles leads to the boundary condition

$$\pi(p_1,\dots,p_n) = \begin{cases} 1 & \text{if } p_j + p_\ell = 1 \\ 0 & \text{if } \sum_{i\neq j,\ell} p_i = 1. \end{cases} \tag{9.9.13}$$

The solution of (9.9.10) with the boundary condition (9.9.13) is (cf. [87, p. 216], or [39])

$$\pi = p_j p_\ell \left(\frac{1}{1-p_j} + \frac{1}{1-p_\ell}\right). \tag{9.9.14}$$

The general scheme is as follows. Let $T_k(p) = v_k$ be the expected time for the process starting at p to have only k alleles left. Let π_k be the function of k variables defined inductively by

$$\begin{aligned} \pi_1(p^1) &= p^1; \\ \pi_2(p^1,p^2) &= \frac{p^1}{1-p^2}\pi_1(p^2) + \frac{p^2}{1-p^1}\pi_1(p^1); \\ \pi_{k+1}(p^1,\dots,p^{k+1}) &= \sum_{i=1}^{k+1} \frac{p^i}{1-\sum_{j\neq i} p^j}\pi_k(p^1,\dots,p^{i-1},p^{i+1},\dots,p^{k+1}) \end{aligned}$$

Then

Theorem 9.9.1

$$\mathrm{P}\left(X_{T_{k+1}(p)} \in \overline{\Delta_k^{(\{i_0,\ldots,i_k\})}}\right) = \pi_{k+1}(p^{i_0},\ldots,p^{i_k}).$$

Proof Method 1: By observing that

$$\mathrm{P}\left(X_{T_{k+1}(p)} \in \overline{\Delta_k^{(\{i_0,\ldots,i_k\})}} | X_{T_k(p)} \in \overline{\Delta_k - 1^{(\{i_1,\ldots,i_k\})}}\right) = \frac{p^{i_0}}{1-p^{i_1}-\ldots-p^{i_k}}.$$

and elementary combinatorial arguments, see [87].

Method 2: By proving that it is the unique solution of the Dirichlet problem

$$\begin{cases} L_m^* u(p) & = 0 \text{ in } \bigcup_{m=k+1}^n \partial_m \Delta_n \\ \lim\limits_{p\to q} u(p) & = 1, q \in \Delta_k^{(\{i_0,\ldots,i_k\})}, \\ \lim\limits_{p\to q} u(p) & = 0, q \in \partial_k \Delta_n \backslash \Delta_k^{(\{i_0,\ldots,i_k\})} \cup \bigcup_{m=0}^{k-1} \partial_m \Delta_n. \end{cases}$$

□

Chapter 10
Applications

In this chapter, we derive explicit formulae for various quantities of interest in population genetics that have been introduced in Sect. 2.8. In particular, we shall calculate the expectation and the second moment of the absorption time, fixation probabilities, the probability of coexistence, αth moments, and the probability of heterozygosity of the process $(X_t)_{t\geq 0}$.

We shall use two different methods. On one hand, we use the geometric constructions of Chap. 3; these will give explicit expressions involving in particular entropy like terms. On the other hand, we shall use the expansions of Chap. 8, which will yield formulas involving series in terms of the coefficients derived in the Appendix.

10.1 The Case of Two Alleles

As in previous sections, we begin with the simplest case, that of two alleles A^0, A^1 and let X_t be the relative frequency of allele A^1 at time t.

10.1.1 The Absorption Time

The moments of the sojourn and absorption times were first derived by Nagylaki [92] for the case of two alleles. Let $\partial_0\Delta_1 = \{0, 1\}$ be the domain representing a population of 1 allele. Here, 1 corresponds to the loss of A^0, that is, the fixation of A^1, and 0 corresponds to the opposite situation. Either of these irreversible events is called an absorption.

We denote by $T_2^1(p) = \inf\{t > 0 : X_t \in \partial_0\Delta_1 | X_0 = p\}$ the first time when the population has only 1 allele left, that is, when absorption occurs. $T_2^1(p)$ is

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a continuous random variable valued in $[0,\infty)$ with probability density function denoted by $\varphi(t,p)$. $\partial_0\Delta_1$ is invariant (absorption set) under the process X_t, i.e. if $X_s \in \partial_0\Delta_1$ then $X_t \in \partial_0\Delta_1$ for all $t \geq s$. We have

$$\mathrm{P}(T_2^1(p) \leq t) = \mathrm{P}(X_t \in \partial_0\Delta_1 | X_0 = p)$$

It follows that

$$\varphi(t,p) = \int_{\partial_0\Delta_1} \frac{\partial}{\partial t} u(x,p,t) \boldsymbol{\lambda}_1(dx).$$

Therefore the expectation of the absorption time for having only 1 allele is (see also [114]):

$$\begin{aligned}
\mathrm{E}(T_2^1(p)) &= \int_0^\infty t\varphi(t,p)dt \\
&= \int_{\partial_0\Delta_1} \left(\int_0^\infty t \frac{\partial}{\partial t} u(x,t)dt \right) \boldsymbol{\lambda}_1(dx) \\
&= \sum_{r=0}^\infty \int_{\partial_0\Delta_1} \left(\int_0^\infty te^{-\lambda_r t}dt \right) (-\lambda_r) c_r \left(X_r(x)\chi_{(0,1)}(dx) \right. \\
&\quad \left. + a_{r,0}\delta_{e_0}(dx) + a_{r,1}\delta_{e_1}(dx) \right) \\
&= -\sum_{r=0}^\infty \frac{1}{\lambda_r} c_r \left(a_{r,0} + a_{r,1} \right) \\
&= \sum_{r=0}^\infty \frac{1}{\lambda_{2r}} c_{2r} \\
&= \sum_{r=0}^\infty \frac{16p(1-p)(2r+3/2)X_{2r}(p)}{(2r+1)^2(2r+2)^2},
\end{aligned} \tag{10.1.1}$$

and its second moment is

$$\begin{aligned}
\mathrm{E}(T_2^1(p))^2 &= \int_0^\infty t^2 \varphi(t,p)dt \\
&= \int_{\partial_0\Delta_1} \int_0^\infty t^2 \frac{\partial}{\partial t} u(x,p,t)dt \boldsymbol{\lambda}_1(dx) \\
&= \sum_{r=0}^\infty \int_{\partial_0\Delta_1} \left(\int_0^\infty t^2 e^{-\lambda_r t} dt \right) (-\lambda_r) c_r \left(X_r(x)\chi_{(0,1)}(dx) \right. \\
&\quad \left. + a_{r,0}\delta_{e_0}(dx) + a_{r,1}\delta_{e_1}(dx) \right) \\
&= -\sum_{r=0}^\infty \frac{2}{\lambda_r^2} c_r \left(a_{r,0} + a_{r,1} \right) \\
&= \sum_{r=0}^\infty \frac{2}{\lambda_{2r}^2} c_{2r} \\
&= \sum_{r=0}^\infty \frac{64p(1-p)(2r+3/2)X_{2r}(p)}{(2r+1)^3(2r+2)^3},
\end{aligned} \tag{10.1.2}$$

where $X_r(p)$ is a Gegenbauer polynomial $X_r(p) = C_{2r}^{\frac{3}{2}}(1-2p)$ and

$$\begin{aligned}
\lambda_r &= \frac{(r+1)(r+2)}{2}, \\
a_{r,0} &= -\int_{\Omega_1} (1-x)X_r(x)dx = -\frac{1}{2}, \\
a_{r,1} &= -\int_{\Omega_1} xX_r(x)dx = (-1)^{r+1}\frac{1}{2}, \\
c_r &= \frac{w(p)X_r(p)}{(X_r, wX_r)} = \frac{8w(p)X_r(p)(r+3/2)}{(r+1)(r+2)}.
\end{aligned} \tag{10.1.3}$$

Remark We already know from Sect. 9.9, see (9.9.7) that

$$\mathrm{E}(T_2^1(p)) = -2\{p\ln(p) + (1-p)\ln(1-p)\}$$

is the unique solution of the one-dimensional boundary value problem (also see in [39, p. 140])

$$\begin{cases} L^*v &= -1, \text{ in } (0,1) \\ v(0) &= v(1) = 0. \end{cases}$$

It can be checked that this agrees with (10.1.1), of course.

10.1.2 Fixation Probabilities and Probability of Coexistence of Two Alleles

The fixation probability for A^1 is

$$\begin{aligned}\mathrm{P}(X_t = 1|X_0 = p) &= \int_{\{1\}} u(x,t)\boldsymbol{\lambda}_1(dx)\\ &= p + \sum_{r=0}^{\infty} c_r a_{r,1} e^{-\lambda_r t}\\ &= p - \frac{1}{2}\sum_{r=0}^{\infty}(-1)^r \frac{8w(p)X_r(p)(r+3/2)}{(r+1)(r+2)} e^{-\lambda_r t}.\end{aligned}$$

In particular, for $t \to \infty$, we obtain (2.8.2).

Analogously, the fixation probability of A^0 (loss of A^1) is

$$\begin{aligned}\mathrm{P}(X_t = 0|X_0 = p) &= \int_{\{0\}} u(x,t)\boldsymbol{\lambda}_1(dx)\\ &= 1 - p + \sum_{r=0}^{\infty} c_r a_{r,0} e^{-\lambda_r t}\\ &= 1 - p - \frac{1}{2}\sum_{r=0}^{\infty} \frac{8w(p)X_r(p)(r+3/2)}{(r+1)(r+2)} e^{-\lambda_r t}.\end{aligned}$$

The probability of coexistence of the two alleles A^0, A^1 therefore is

$$\begin{aligned}\mathrm{P}(X_t \in (0,1)|X_0 = p) &= \int_{(0,1)} u(x,t)\boldsymbol{\lambda}_1(dx)\\ &= \sum_{r=0}^{\infty} c_r \int_{(0,1)} X_r(x)dx e^{-\lambda_r t}\\ &= \sum_{r=0}^{\infty} c_{2r} e^{-\lambda_{2r} t}\\ &= \sum_{r=0}^{\infty} \frac{8w(p)X_{2r}(p)(2r+3/2)}{(2r+1)(2r+2)} e^{-\lambda_{2r} t}.\end{aligned}$$

These three probabilities sum to 1, as they should.

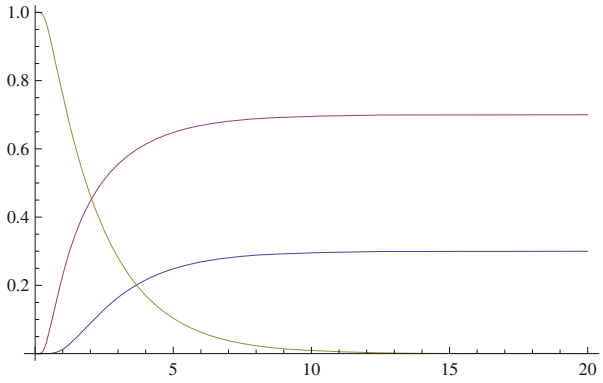

Fig. 10.1 $p = 0.3$

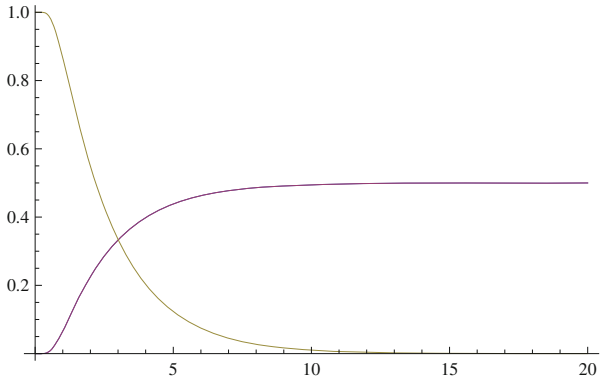

Fig. 10.2 $p = 0.5$

We consider their behaviour for $p = 0.3$ and $p = 0.5$ (see Figs. 10.1 and 10.2):

Remark

(i) $\mathrm{P}(X_t \in [0,1] | X_0 = p) = \mathrm{P}(X_t = 0 | X_0 = p) + \mathrm{P}(X_t = 1 | X_0 = p) + \mathrm{P}(X_t \in (0,1) | X_0 = p) = 1$;

(ii) $\mathrm{P}(X_t = 0 | X_0 = p)$ and $\mathrm{P}(X_t = 1 | X_0 = p)$ increase quickly in $t \in (0,5)$ ($10N$ generations) from 0 and then tends slowly to $1 - p$ and p, resp.;

10.1.3 The αth Moments

By induction, it is easy to prove that

$$\int_{(0,1)} x^\alpha X_{r-1}(x)dx = (-1)^r \frac{1}{2}\left\{\frac{(\alpha-1)\dots(\alpha-r)}{(\alpha+1)\dots(\alpha+r)} - 1\right\},$$

where again $X_{r-1}(x)$ is a Gegenbauer polynomial $X_{r-1}(x) = C^{\frac{3}{2}}_{2r-2}(1-2x)$. Therefore, the αth moment is

$$\begin{aligned} m_\alpha(t) &= [u, x^\alpha]_1 \\ &= \sum_{r=0}^{\infty} c_r \left(\int_{(0,1)} x^\alpha X_r(x)dx\right) e^{-\lambda_r t} + \left(p + \sum_{r=0}^{\infty} c_r a_{r,1} e^{-\lambda_r t}\right) \\ &= p + \sum_{r=1}^{\infty} c_{r-1}\left(\int_{[0,1]} x^\alpha X_{r-1}(x)dx + a_{r-1,1}\right) e^{-\lambda_{r-1} t} \\ &= p + \sum_{r=1}^{\infty} \frac{2(2r+1)}{r(r+1)} p(1-p)(-1)^r X_{r-1}(p) \frac{(\alpha-1)\dots(\alpha-r)}{(\alpha+1)\dots(\alpha+r)} e^{-\frac{r(r+1)}{2}t}. \end{aligned}$$

This formula for the αth moment was first derived by Kimura in [79].

10.1.4 The Probability of Heterozygosity

The probability of heterozygosity again was first derived by Kimura (see [79, p. 6], note our rescaling of time by $2N$)

$$\begin{aligned} H_t &= \int_{[0,1]} 2x(1-x)u(x,t)\boldsymbol{\lambda}_1(dx) \\ &= 2(u, wX_0) \\ &= 2(c_0 X_0, wX_0)e^{-\lambda_0 t} \\ &= 2w(p)X_0(p)e^{-t} \\ &= H_0 e^{-t}. \end{aligned}$$

Of course, this goes to 0 for $t \to \infty$, as it should.

10.2 The Case of $n+1$ Alleles

In this section, we consider the case where we initially have $n+1$ alleles. We compute the expectation and the second moment of the absorption time, the probability distribution of the absorption time for having $k+1$ alleles, the probability of having exactly $k+1$ alleles, the $\boldsymbol{\alpha}$th moments, the probability of heterozygosity, and the rate of loss of one allele in a population having $k+1$ alleles. Several of our formulas are known from other methods, see [39, 78–80, 85, 87], but we emphasize here the general and unifying approach.

10.2.1 The Absorption Time for Having $k+1$ Alleles

The moments of the sojourn and absorption times were derived by Lessard and Lahaie [84] in the multi-allele case. We denote by $T_{n+1}^{k+1}(p) = \inf\{t > 0 : X_t \in \overline{\partial_k \Delta_n} | X_0 = p\}$ the first time when the population has (at most) $k+1$ alleles. $T_{n+1}^{k+1}(p)$ is a continuous random variable valued in $[0,\infty)$ and we denote by $\varphi(t,p)$ its probability density function. $\overline{\partial_k \Delta_n}$ is invariant under the process $(X_t)_{t\geq 0}$, i.e. if $X_s \in \overline{\partial_k \Delta_n}$ then $X_t \in \overline{\partial_k \Delta_n}$ for all $t \geq s$ (once an allele is lost from the population, it can never again be recovered). We have the equality

$$\mathrm{P}(T_{n+1}^{k+1}(p) \leq t) = \mathrm{P}(X_t \in \overline{\partial_k \Delta_n} | X_0 = p) = \int_{\overline{\partial_k \Delta_n}} u(x,p,t) d\mu(x).$$

It follows that

$$\varphi(t,p) = \int_{\overline{\partial_k \Delta_n}} \frac{\partial}{\partial t} u(x,p,t) d\mu(x)$$

Therefore the expectation for the absorption time of having $k+1$ alleles is (see also [118])

$$\begin{aligned}
\mathrm{E}(T_{n+1}^{k+1}(p)) &= \int_0^\infty t\varphi(t,p)dt \\
&= \int_{\overline{\partial_k \Delta_n}} \int_0^\infty t \frac{\partial}{\partial t} u(x,p,t) dt d\mu(x) \\
&= \sum_{j=1}^{k} \sum_{(i_0,\ldots,i_j)\in I_j} \sum_{m\geq 0} \sum_{|\alpha|=m} c_{m,\alpha}^{(j)} \int_{\Delta_j^{(\{i_0,\ldots,i_j\})}} X_{m,\alpha}^{(j)}(x) \left(\int_0^\infty t \frac{\partial}{\partial t} e^{-\lambda_m^{(j)} t} dt \right) d\mu_j^{(i_0,\ldots,i_j)}(x)
\end{aligned}$$

$$+\sum_{i=0}^{n}\sum_{k=1}^{n}\sum_{m\geq 0}\sum_{|\alpha|=m} c_{m,\alpha}^{(k)} a_{m,\alpha,i}^{(k)} \left(\int_0^\infty t\frac{\partial}{\partial t}e^{-\lambda_m^{(k)}t}dt\right),$$

$$=\sum_{j=1}^{k}\sum_{(i_0,\dots,i_j)\in I_j}\sum_{m\geq 0}\sum_{|\alpha|=m} c_{m,\alpha}^{(j)} \int_{\Delta_j^{(\{i_0,\dots,i_j\})}} X_{m,\alpha}^{(j)}(x)\left(-\frac{1}{\lambda_m^{(j)}}\right) d\mu_j^{(i_0,\dots,i_j)}(x)$$

$$+\sum_{i=0}^{n}\sum_{k=1}^{n}\sum_{m\geq 0}\sum_{|\alpha|=m} c_{m,\alpha}^{(k)} a_{m,\alpha,i}^{(k)} \left(-\frac{1}{\lambda_m^{(k)}}\right).$$

and the second moment of this absorption time is

$$\begin{aligned}
\mathrm{E}(T_{n+1}^{k+1}(p))^2 &= \int_0^\infty t^2\varphi(t,p)dt \\
&= \int_{\overline{\partial_k\Delta_n}}\int_0^\infty t^2\frac{\partial}{\partial t}u(x,p,t)dtd\mu(x) \\
&= \sum_{j=1}^{k}\sum_{(i_0,\dots,i_j)\in I_j}\sum_{m\geq 0}\sum_{|\alpha|=m} c_{m,\alpha}^{(j)} \int_{\Delta_j^{(\{i_0,\dots,i_j\})}} X_{m,\alpha}^{(j)}(x)\left(\int_0^\infty t^2\frac{\partial}{\partial t}e^{-\lambda_m^{(j)}t}dt\right) d\mu_j^{(i_0,\dots,i_j)}(x) \\
&\quad +\sum_{i=0}^{n}\sum_{k=1}^{n}\sum_{m\geq 0}\sum_{|\alpha|=m} c_{m,\alpha}^{(k)} a_{m,\alpha,i}^{(k)} \left(\int_0^\infty t^2\frac{\partial}{\partial t}e^{-\lambda_m^{(k)}t}dt\right), \\
&= \sum_{j=1}^{k}\sum_{(i_0,\dots,i_j)\in I_j}\sum_{m\geq 0}\sum_{|\alpha|=m} c_{m,\alpha}^{(j)} \int_{\Delta_j^{(\{i_0,\dots,i_j\})}} X_{m,\alpha}^{(j)}(x)\left(-\frac{2}{(\lambda_m^{(j)})^2}\right) d\mu_j^{(i_0,\dots,i_j)}(x) \\
&\quad +\sum_{i=0}^{n}\sum_{k=1}^{n}\sum_{m\geq 0}\sum_{|\alpha|=m} c_{m,\alpha}^{(k)} a_{m,\alpha,i}^{(k)} \left(-\frac{2}{(\lambda_m^{(k)})^2}\right).
\end{aligned}$$

In order to see what this means, we consider the case of three alleles ($n = 2$). First, we construct the global solution:

$$\begin{aligned}
u(x^1,x^2;t) =& u_2(x^1,x^2;t)\chi_{\Delta_2} + u_1^{0,1}(x^1,0;t)\chi_{\Delta_1^{(\{0,1\})}} + u_1^{0,2}(0,x^2;t)\chi_{\Delta_1^{(\{0,2\})}} \\
&+ u_1^{0,0}(x^1,1-x^1;t)\chi_{\Delta_1^{(\{0,0\})}} + u_0^1(t)\delta_{\Delta_0^{(\{1\})}} + u_0^2(t)\delta_{\Delta_0^{(\{2\})}} + u_0^0(t)\delta_{\Delta_0^{(\{0\})}}.
\end{aligned}$$

Thus,

$$\begin{aligned}
[u,\varphi]_2 &= (u_2,\varphi)_2 + (u_1^{0,1},\varphi(\cdot,0))_1 + (u_1^{0,2},\varphi(0,\cdot))_1 + (u_1^{0,1},\varphi(\cdot,1-\cdot))_1 \\
&\quad + u_0^1(1,0;t)\varphi(1,0) + u_0^2(0,1;t)\varphi(0,1) + u_0^0(0,0;t)\varphi(0,0) \\
&= \int_{\Delta_2} u_2(x^1,x^2;t)\varphi(x^1,x^2)dx^1dx^2 + \int_0^1 u_1^{0,1}(x^1,0;t)\varphi(x^1,0)dx^1
\end{aligned}$$

$$+\int_0^1 u_1^{0,2}(0,x^2;t)\varphi(0,x^2)dx^2$$
$$+\frac{1}{\sqrt{2}}\int_0^1 u_1^{1,2}(x^1,1-x^1;t)\varphi(x^1,1-x^1)dx^1$$
$$+u_0^1(1,0;t)\varphi(1,0)+u_0^2(0,1;t)\varphi(0,1)+u_0^0(0,0;t)\varphi(0,0).$$

By expansion of eigenvectors, we have

$$u_2(x;p;t)=\sum_{m\geq 0}\sum_{|\alpha|=m} c_{m,\alpha}^{(2)}(p)X_{m,\alpha}^{(2)}(x)e^{-\lambda_m^{(2)}t}.$$

where $c_{m,\alpha}^{(2)}(p)$ is uniquely defined. We represent $u_1(x;t)$ by

$$u_1^{0,1}(x^1,0;t)=\sum_{m\geq 0} a_m^{0,1}(x^1)e^{-\lambda_m^{(1)}t}; \tag{10.2.4}$$

$$u_1^{0,2}(0,x^2;t)=\sum_{m\geq 0} a_m^{0,2}(x^2)e^{-\lambda_m^{(1)}t}; \tag{10.2.5}$$

$$u_1^{1,2}(x^1,1-x^1;t)=\sum_{m\geq 0} a_m^{1,2}(x^1)e^{-\lambda_m^{(1)}t}, \tag{10.2.6}$$

where the coefficients $a_m^{\cdot,\cdot}(x^1)$ are defined as follows: First, putting

$$\psi_n(x^1):=x^1(1-x^1)X_n^{(1)}(x^1).$$

we note that $\psi_n(0)=\psi_n(1)=0$ and

$$L_2^*\psi_n(x^1)=-\lambda_n^{(1)}\psi_n(x^1).$$

It follows that

$$\begin{aligned}\Big[u_t,\psi_n(x^1)\Big]_2&=\Big[u,L_2^*(\psi_n(x^1))\Big]_2\\&=-\lambda_n^{(1)}\Big[u,\psi_n(x^1)\Big]_2\end{aligned}$$

Therefore

$$\begin{aligned}
\psi_n(p^1)e^{-\lambda_n^{(1)}t} &= \Big[u(0), \psi_n(x^1)\Big]_2 e^{-\lambda_n^{(1)}t} = \Big[u, \psi_n(x^1)\Big]_2 \\
&= \Big(u_2, \psi_n(x^1)\Big)_2 + \Big(u_1, \psi_n(x^1)\Big)_1 + (u_0, \psi_n(x^1))_0 \\
&= \sum_{m\geq 0}\sum_{|\alpha|=m} c_{m,\alpha}^{(2)}\Big(X_{m,\alpha}^{(2)}, \psi_n(x^1)\Big)_2 e^{-\lambda_m^{(2)}t} + \sum_{m\geq 0}\Big(a_m(x^1), \psi_n(x^1)\Big)_1 e^{-\lambda_m^{(1)}t} \\
&\text{where } a_m(x^1) := a_m^{0,1}(x^1) + a_m^{1,2}(x^1) \text{ and } \psi_n(0) = \psi_n(1) = 0 \\
&= \Big(a_0(x^1), \psi_n(x^1)\Big)_1 e^{-\lambda_0^{(1)}t} \\
&+ \sum_{m\geq 1}\left\{\Big(a_m(x^1), \psi_n(x^1)\Big)_1 + \sum_{|\alpha|=m-1} c_{m-1,\alpha}^{(2)}\Big(X_{m-1,\alpha}^{(2)}, \psi_n(x^1)\Big)_2\right\} e^{-\lambda_m^{(1)}t} \\
&\quad \text{(because of } \lambda_m^{(1)} = \lambda_{m-1}^{(2)}\text{)}
\end{aligned}$$

We obtain by equating the coefficients in terms of $e^{-\lambda t}$

$$\begin{aligned}
\Big(a_0(x^1), \psi_n(x^1)\Big)_1 &= \delta_{0,n}\psi_n(p^1) \\
\Big(a_m(x^1), \psi_n(x^1)\Big)_1 &= \delta_{m,n}\psi_n(p^1) - \sum_{|\alpha|=m-1} c_{m-1,\alpha}^{(2)}\Big(X_{m-1,\alpha}^{(2)}, \psi_n(x^1)\Big)_2, \text{ if } m \geq 1.
\end{aligned} \tag{10.2.7}$$

This implies that we have the formula for $a_m(x) = a_m^{0,1}(x) + a_m^{1,2}(x)$. Similarly, putting

$$\psi_n(x^2) := x^2(1-x^2)X_n^{(1)}(x^2) \quad \text{and} \quad \psi_n(x^0) := x^0(1-x^0)X_n^{(1)}(x^0)$$

we also have the formula for $a_m'(x) = a_m^{0,2}(x) + a_m^{1,2}(x)$ and $a_m''(x) = a_m^{0,1}(x) + a_m^{0,2}(x)$. These formulae imply the formula for each $a_m^{\cdot,\cdot}(x)$.

Remark The coefficients of u_2 occur in the representation of the coefficients of u_1 because of the probability flux.

Similarly because of

$$L_2^*(x^1) = 0,$$

$$\Big[u_t, x^1\Big]_2 = \Big[u, L_2^*(x^1)\Big]_2 = 0.$$

We have

$$\begin{aligned} p^1 &= \left[u(0), x^1\right]_2 = \left[u, x^1\right]_2 \\ &= \left(u_2, x^1\right)_2 + \left(u_1, x^1\right)_1 + (u_0, x^1)_0 \end{aligned}$$

Thus,

$$\begin{aligned} u_0^1(p;t) &= p^1 - \sum_{m\geq 0}\sum_{|\alpha|=m} c_{m,\alpha}^{(2)}(p)\left(X_{m,\alpha}^{(2)}, x^1\right)_2 e^{-\lambda_m^{(2)}t} \\ &\quad - \sum_{m\geq 0}\left(a_m^{0,1}, x^1\right)_1 e^{-\lambda_m^{(1)}t} \\ &\quad - \sum_{m\geq 0}\left(a_m^{1,2}, x^1\right) e^{-\lambda_m^{(1)}t} \\ &= p^1 - \left(a_0(x^1), x^1\right)_1 e^{-\lambda_0^{(1)}t} \\ &\quad - \sum_{m\geq 1}\left\{\left(a_m(x^1), x^1\right)_1 + \sum_{|\alpha|=m-1} c_{m-1,\alpha}^{(2)}\left(X_{m-1,\alpha}^{(2)}, x^1\right)_2\right\} e^{-\lambda_m^{(1)}t}. \end{aligned}$$

Thus, we obtain the explicit global solution, and it easily yields the expectation and the second moment of the absorption time $T_3^1(p)$.

There is an alternative way [118] for calculating the expectation for the absorption time of having only 1 allele; this works as follows

$$\begin{aligned} \mathrm{E}(T_3^1(p)) &= \int_0^\infty t\varphi(t,p)dt \\ &= \int_0^\infty t\frac{\partial}{\partial t}\left(u_0^1(p;t) + u_0^2(p;t) + u_0^0(p;t)\right)dt. \end{aligned}$$

We first calculate the first term; the other terms will be obtained similarly. To do this, we expand x^1 by $\psi_n(x^1)$

$$x^1 = \sum_{n\geq 0} d_n\psi_n(x^1).$$

We construct a sequence of entropy functions on $[0, 1]$ as follows

- $E_0(x) = -x$
- $E_r(x)$ is the unique solution of the boundary value problem

$$\begin{cases} L_1^*(E_r(x)) & = -rE_{r-1}(x) \\ E_r(0) & = E_r(1) = 0 \end{cases}$$

By some simple calculations, we obtain the first entropy functions

$$\begin{aligned}
E_0(x) &= -x \\
E_1(x) &= -2(1-x)\log(1-x) \\
E_2(x) &= -8xz(x) + 8(1-x)\log(1-x) \\
E_3(x) &= 48(1-x)u(x) + 96[xz(x) - (1-x)\log(1-x)]
\end{aligned}$$

where

$$z(x) = \int_x^1 \frac{ln(1-y)}{y}dy, \quad u(x) = \int_x^1 \frac{z(y)}{1-y}dy$$

Lemma 10.2.1 *The entropy functions satisfy*

$$\begin{aligned}
\frac{\left(X_m^{(1)}, x^1\right)_1}{\lambda_m^{(1)}} &= \left(E_1(x^1), X_m^{(1)}\right)_1, \\
\frac{2\left(X_m^{(1)}, x^1\right)_1}{\left(\lambda_m^{(1)}\right)^2} &= \left(E_2(x^1), X_m^{(1)}\right)_1,
\end{aligned}$$

and more generally,

$$\frac{r!\left(X_m^{(1)}, x^1\right)_1}{\left(\lambda_m^{(1)}\right)^r} = \left(E_r(x^1), X_m^{(1)}\right)_1, \quad r \geq 2.$$

Proof We have

$$\begin{aligned}
\lambda_m^{(1)}\left(E_1(x^1), X_m^{(1)}\right)_1 &= \left(E_1(x^1), \lambda_m^{(1)} X_m^{(1)}\right)_1 \\
&= \left(E_1(x^1), -L_1\left(X_m^{(1)}\right)\right)_1 \\
&= \left(-L_1^*\left(E_1(x^1)\right), X_m^{(1)}\right)_1, \quad \text{because of } E_1(0) = E_1(1) = 0 \\
&= \left(-L_1^*\left(E_1(x^1)\right), X_m^{(1)}\right)_1 \\
&= \left(x^1, X_m^{(1)}\right)_1.
\end{aligned}$$

Similarly we have

$$\begin{aligned}
\left(\lambda_m^{(1)}\right)^2\left(E_2(x^1), X_m^{(1)}\right)_1 =& \lambda_m^{(1)}\left(E_2(x^1), \lambda_m^{(1)} X_{m,\alpha}^{(1)}\right)_1 \\
=& \lambda_m^{(1)}\left(E_2(x^1), -L_1\left(X_{m,\alpha}^{(1)}\right)\right)_1 \\
=& \lambda_m^{(1)}\left(-L_1^*\left(E_2(x^1)\right), X_m^{(1)}\right)_1, \quad \text{because of } E_2(0) = E_2(1) = 0 \\
=& \lambda_m^{(1)}\left(-L_1^*\left(E_2(x^1)\right), X_m^{(1)}\right)_1 \\
=& \lambda_m^{(1)}\left(2E_1(x^1), X_m^{(1)}\right)_1 \\
=& \left(2x^1, X_m^{(1)}\right)_1, \quad \text{because of the above calculation.}
\end{aligned}$$

The proof for all r is similar. □

From the Lemma, we have the expansion of $E_1(x^1)$

$$E_1(x^1) = \sum_{n\geq 0} \frac{d_n}{\lambda_n^{(1)}} \psi_n(x^1).$$

Therefore we have

$$\begin{aligned}
&\int_0^\infty t \frac{\partial u_0^1(p;t)}{\partial t} dt \\
&= \left(a_0(x^1), x^1\right)_1 \int_0^\infty t\lambda_0^{(1)} e^{-\lambda_0^{(1)} t} dt \\
&+ \sum_{m\geq 1} \left\{ \left(a_m(x^1), x^1\right)_1 + \sum_{|\alpha|=m-1} c_{m-1,\alpha}^{(2)} \left(X_{m-1,\alpha}^{(2)}, x^1\right)_2 \right\} \int_0^\infty t\lambda_m^{(1)} e^{-\lambda_m^{(1)} t} dt \\
&= \frac{\left(a_0(x^1), x^1\right)_1}{\lambda_0^{(1)}} + \sum_{m\geq 1} \frac{\left(a_m(x^1), x^1\right)_1 + \sum_{|\alpha|=m-1} c_{m-1,\alpha}^{(2)} \left(X_{m-1,\alpha}^{(2)}, x^1\right)_2}{\lambda_m^{(1)}} \\
&= \sum_{n\geq 0} d_n \left\{ \frac{\left(a_0(x^1), \psi_n(x^1)\right)_1}{\lambda_0^{(1)}} \right. \\
&\quad \left. + \sum_{m\geq 1} \frac{\left(a_m(x^1), \psi_n(x^1)\right)_1 + \sum_{|\alpha|=m-1} c_{m-1,\alpha}^{(2)} \left(X_{m-1,\alpha}^{(2)}, \psi_n(x^1)\right)_2}{\lambda_m^{(1)}} \right\}
\end{aligned}$$

$$= \sum_{n\geq 0} d_n \left\{ \frac{\delta_{0,n}\psi_n(p^1)}{\lambda_0^{(1)}} + \sum_{m\geq 1} \frac{\delta_{m,n}\psi_n(p^1)}{\lambda_m^{(1)}} \right\}, \quad \text{because of (10.2.7)}$$

$$= \sum_{m\geq 0} \frac{d_m}{\lambda_m^{(1)}} \psi_m(p^1)$$

$$= E_1(p^1).$$

Thus, we have

$$\mathrm{E}(T_3^1(p)) = E_1(p^1) + E_1(p^2) + E_1(p^3).$$

Remark We can obtain the r-th moments of this absorption time by the same method, i.e.

$$\mathrm{E}(T_3^1(p))^r = E_r(p^1) + E_r(p^2) + E_r(p^3).$$

Remark We can generalize the preceding to the case of $n+1$ alleles by the inclusion-exclusion technique of Feller [44, p. 109]

$$\mathrm{E}(T_{n+1}^{k+1}(p))^r = \sum_{s=1}^{k+1} (-1)^{k+1-s} \binom{n-s}{k+1-s} \sum_{1\leq i_1<\ldots<i_s\leq n+1} E_r(p^{i_1} + \cdots + p^{i_s}).$$

For the case of $r = 1$, such formulas were derived by Littler and Good [87, p. 217]; see also [39, p. 194].

10.2.2 The Probability Distribution of the Absorption Time for Having $k+1$ Alleles

We note that $X_{T_{n+1}^{k+1}(p)}$ is a random variable valued in $\overline{\partial_k \Delta_n}$. We consider the probability that this random variable takes its value in $\Delta_k^{(\{i_0,\ldots,i_k\})}$, i.e., the probability of the population at the first time having at most $k+1$ alleles to consist precisely of the $k+1$ alleles $\{A_{i_0}, \ldots, A_{i_k}\}$. Let g_k be a function of k variables defined inductively by

$$g_1(p^1) = p^1;$$

$$g_2(p^1, p^2) = \frac{p^1}{1-p^2} g_1(p^2) + \frac{p^2}{1-p^1} g_1(p^1);$$

$$g_{k+1}(p^1, \ldots, p^{k+1}) = \sum_{i=1}^{k+1} \frac{p^i}{1-\sum_{j\neq i} p^j} g_k(p^1, \ldots, p^{i-1}, p^{i+1}, \ldots, p^{k+1})$$

Then we have

Theorem 10.2.1

$$\mathrm{P}\left(X_{T_{n+1}^{k+1}(p)} \in \overline{\Delta_k^{(\{i_0,\ldots,i_k\})}}\right) = g_{k+1}(p^{i_0},\ldots,p^{i_k}).$$

Proof Method 1: By proving that

$$\mathrm{P}\left(X_{T_{n+1}^{k+1}(p)} \in \overline{\Delta_k^{(\{i_0,\ldots,i_k\})}} | X_{T_{n+1}^{k}(p)} \in \overline{\Delta_k^{(\{i_1,\ldots,i_k\})}}\right) = \frac{p^{i_0}}{1-p^{i_1}-\ldots-p^{i_k}}.$$

and elementary combinatorial arguments, we immediately obtain the result (see [85])

Method 2: We check that $g_{k+1}(p^{i_0},\ldots,p^{i_k})$ solves the classical Dirichlet problem

$$\begin{cases} L_k^* v(p) & = 0 \text{ in } \overline{\partial_k \overline{\Delta_n}} \\ \lim\limits_{p\to q} v(p) & = 1, q \in \Delta_k^{(\{i_0,\ldots,i_k\})}, \\ \lim\limits_{p\to q} v(p) & = 0, q \in \partial_k \Delta_n \setminus \Delta_k^{(\{i_0,\ldots,i_k\})}. \end{cases}$$

This can be seen as a generalization of Lemma 3.10.1. By the results of Sect. 9.8, it is the unique solution. □

10.2.3 The Probability of Having Exactly $k+1$ Alleles

The probability of having only the particular allele A_i is (see [51])

$$\begin{aligned} \mathrm{P}(X_t \in \Delta_0^{(\{i\})} | X_0 = p) &= \int\limits_{\Delta_0^{(\{i\})}} u_0^{(i)}(x,t) d\mu_0^{(i)}(x) \\ &= u_0^{(i)}(e_i,t) \\ &= p^i - \sum_{k=1}^{n} \sum_{m^{(k)}\geq 0} \sum_{l^{(k)}\geq 0} \sum_{|\alpha^{(k)}|=l^{(k)}} c^{(k)}_{m^{(k)},l^{(k)},\alpha^{(k)}} \left(x^j, X^{(k)}_{l^{(k)},\alpha^{(k)}}\right)_k e^{-\lambda^{(k)}_{m^{(k)}} t}. \end{aligned}$$

The probability of having exactly the $(k+1)$ alleles $\{A_0, \ldots, A_k\}$ (the coexistence probability of alleles $\{A_0, \ldots, A_k\}$) is (see [78, 87])

$$\begin{aligned}\mathrm{P}(X_t \in \Delta_k^{(\{i_0,\ldots,i_k\})} | X_0 = p) &= \int\limits_{\Delta_k^{(\{i_0,\ldots,i_k\})}} u_k^{(i_0,\ldots,i_k)}(x,t) d\mu_k^{(i_0,\ldots,i_k)}(x) \\ &= \sum_{m\geq 0} \sum_{l\geq 0} \sum_{|\alpha|=l} c_{m,l,\alpha}^{(k)} \left(\int\limits_{\Delta_k^{(\{i_0,\ldots,i_k\})}} X_{m,\alpha}^{(k)}(x) d\mu_k^{(i_0,\ldots,i_k)}(x) \right) e^{-\lambda_m^{(k)} t}.\end{aligned}$$

10.2.4 The αth Moments

The $\boldsymbol{\alpha}$th-moments are (see [78–80])

$$\begin{aligned}m_{\boldsymbol{\alpha}}(t) &= [u, x^{\boldsymbol{\alpha}}]_n \\ &= \int\limits_{\Delta_n} x^{\boldsymbol{\alpha}} u(x,t) d\mu(x) \\ &= \sum_{k=0}^{n} \sum_{(i_0,\ldots,i_k)\in I_k} \int\limits_{\Delta_k^{(\{i_0,\ldots,i_k\})}} x^{\boldsymbol{\alpha}} u_k^{(i_0,\ldots,i_k)}(x,t) d\mu_k^{(i_0,\ldots,i_k)}(x).\end{aligned}$$

10.2.5 The Probability of Heterozygosity

The probability of heterozygosity is defined in [78] as

$$H_t = \mathrm{E}\Big(2 \sum_{j>i} X^j(t) X^i(t)\Big).$$

By applying the moment evolution equation (4.3.8) for $\boldsymbol{\alpha} = e_i + e_j$ for $i \neq j$ we have

$$\dot{m}_{e_i+e_j}(t) = -m_{e_i+e_j}(t).$$

This implies

$$H_t = 2 \sum_{j>i} m_{e_i+e_j}(t) = 2 \sum_{j>i} m_{e_i+e_j}(0) e^{-t} = H_0 e^{-t}.$$

10.2.6 The Rate of Loss of One Allele in a Population Having $k+1$ Alleles

We have the solution of the form

$$u = \sum_{k=0}^{n} u_k(x,t)\chi_{\partial_k \Delta_n}(x)$$

The rate of loss of one allele in a population with (k+1) alleles equals the rate of decrease of

$$u_k(x,t) = \sum_{m\geq 0}\sum_{l\geq 0}\sum_{|\alpha|=l} c^{(k)}_{m,l,\alpha} X^{(k)}_{l,\alpha}(x)\chi_{\partial_k \Delta_n}(x) e^{-\lambda^{(k)}_m t} = O(e^{-\lambda^{(k)}_0 t}).$$

This mean that this rate is $\lambda^{(k)}_0 = \frac{k(k+1)}{2}$. This implies that the rate of loss of alleles in the population decreases as k gets smaller in the course of the process (see [45, 52, 78]).

10.3 Applications of the Hierarchical Solution

In this section, we shall use the hierarchical solution to compute other quantities of biological interest. To make the computations more transparent, we shall spell out the details for three alleles.

10.3.1 The Rate of Loss of One Allele in a Population Having Three Alleles

We have the hierarchically extended solution of Definition 8.5.1

$$\begin{aligned}
U(x,t) &:= \sum_{k=0}^{2} U_k(x,t)\chi_{\partial_k \Delta_2^{(I_2)}}(x) \\
&= \sum_{k=0}^{2}\sum_{I_k \subset I_2} U_{k,I_k}(x,t)\chi_{\Delta_k^{(I_k)}}(x) \\
&= U_2(x,t) + U_{1,\{0,1\}}(x,t)\chi_{\Delta_1^{(\{0,1\})}}(x) + U_{1,\{0,2\}}(x,t)\chi_{\Delta_1^{(\{0,2\})}}(x) \\
&\quad + U_{1,\{1,2\}}(x,t)\chi_{\Delta_1^{(\{1,2\})}}(x) \\
&\quad + U_{0,\{1\}}(x,t)\delta_{e_1}(x) + U_{0,\{2\}}(x,t)\delta_{e_2}(x) + U_{0,\{0\}}(x,t)\delta_{e_0}(x)
\end{aligned}$$

where the local solution $U_2(x,t)$ has the form

$$U_2(x,t) = \sum_{m\geq 0} c_m^{(2)} X_m^{(2)}(x) e^{-\lambda_m^{(2)} t}, \tag{10.3.8}$$

the boundary solutions U_{1,I_1} are given by, for example,

$$U_{1,\{0,1\}}(x,t)\chi_{\Delta_1^{(\{0,1\})}}(x) := \int_0^t u^{\tau}_{1,\{0,1\}}(x^1,0,t-\tau)\,d\tau \tag{10.3.9}$$

and the vertex solutions U_{0,I_0} can be calculated similarly.

It is easy to see from (10.3.8) that the rate of loss of one allele in a population of three alleles is $\lambda_0^{(2)}$.

To calculate the rate of loss of one allele in a remaining population of two alleles, we consider boundary solutions.

Because of $u^{\tau}_{1,\{0,1\}}(x^1,0,t)$: $\left(\Delta_1^{\{0,1\}}\right)_\infty \longrightarrow \mathbb{R}$ is the solution of

$$\begin{cases} L_1 u(x,t) = \frac{\partial}{\partial t} u(x,t) & (x,t) \in \left(\Delta_1^{\{0,1\}}\right)_\infty \\ u(x,0) = G^{\perp}_{U_2}(x,\tau) & x \in \Delta_1^{\{0,1\}} \end{cases} \tag{10.3.10}$$

for all $\tau > 0$ as in Proposition 8.2.1 and $G^{\perp}_{U_{k+1,I_{k+1}}}$ is the normal component of the flux of the continuous extension of $U_{k+1,I_{k+1}}$ to $\overline{\Delta_{k+1}^{(I_{k+1})}}$,

Note that in this case,

$$\begin{aligned} G^2_{U_2}(x^1,0,\tau) &= \frac{1}{2}\frac{\partial}{\partial x^1}\Big(a^{21}(x)U_2(x,\tau)\Big)\Big|_{x=(x^1,0)} + \frac{1}{2}\frac{\partial}{\partial x^2}\Big(a^{22}(x)U_2(x,\tau)\Big)\Big|_{x=(x^1,0)} \\ &= -\frac{1}{2}U_2(x^1,0,\tau) \end{aligned}$$

The normal unit vector at $\chi_{\Delta_1^{(\{0,1\})}}$ is

$$\nu = (0,-1).$$

It implies that

$$G^{\perp}_{U_2}(x,\tau) = \frac{1}{2}U_2(x^1,0,\tau).$$

We represent $X_m^{(2)}(x^1,0)$ in terms of the basis of $X_k^{(1)}(x^1)$ as

$$X_m^{(2)}(x^1,0) = \sum_{k=0}^{m} a_{mk} X_k^{(1)}(x^1).$$

This implies

$$\begin{aligned}
u^{\tau}_{1,\{0,1\}}(x^1,0,0) &= \frac{1}{2}U_2(x^1,0,\tau) = \sum_{m\geq 0}\frac{c_m^{(2)}}{2}X_m^{(2)}(x^1,0)e^{-\lambda_m^{(2)}\tau} \\
&= \sum_{m\geq 0}\frac{c_m^{(2)}}{2}e^{-\lambda_m^{(2)}\tau}\sum_{k=0}^{m}a_{mk}X_k^{(1)}(x^1) \\
&= \sum_{k\geq 0}\underbrace{\left(\sum_{m\geq k}\frac{c_m^{(2)}}{2}e^{-\lambda_m^{(2)}\tau}a_{mk}\right)}_{d_k(\tau)}X_k^{(1)}(x^1) \\
&= \sum_{k\geq 0} d_k(\tau)X_k^{(1)}(x^1).
\end{aligned}$$

Therefore

$$\begin{aligned}
U_{1,\{0,1\}}(x,t)\chi_{\Delta_1^{(\{0,1\})}}(x) &= \int_0^t u^{\tau}_{1,\{0,1\}}(x^1,0,t-\tau)\,d\tau \\
&= \int_0^t \sum_{k\geq 0} d_k(\tau)X_k^{(1)}(x^1)e^{-\lambda_k^{(1)}(t-\tau)}\,d\tau \\
&= \sum_{k\geq 0}X_k^{(1)}(x^1)\int_0^t\sum_{m\geq 0}\frac{c_m^{(2)}}{2}a_{mk}e^{-\lambda_m^{(2)}\tau-\lambda_k^{(1)}(t-\tau)}\,d\tau \\
&= \sum_{k\geq 0}X_k^{(1)}(x^1)\sum_{m\geq k}\frac{c_m^{(2)}}{2}a_{mk}e^{-\lambda_k^{(1)}t}\left(\frac{e^{\left(\lambda_k^{(1)}-\lambda_m(2)\right)t}-1}{\lambda_k^{(1)}-\lambda_m^{(2)}}\right) \\
&= -\sum_{k\geq 0}X_k^{(1)}(x^1)\sum_{m\geq k}\frac{c_m^{(2)}}{2}\frac{a_{mk}}{\lambda_m^{(2)}-\lambda_k^{(1)}}e^{-\lambda_m^{(2)}t} \\
&\quad + \sum_{k\geq 0}X_k^{(1)}(x^1)\sum_{m\geq k}\frac{c_m^{(2)}}{2}\frac{a_{mk}}{\lambda_m^{(2)}-\lambda_k^{(1)}}e^{-\lambda_k^{(1)}t} \\
&= O\left(e^{-\lambda_0^{(1)}t}\right).
\end{aligned}$$

This means that the rate of loss of one allele in a population of two alleles is λ_0^1. More generally, we can prove that the rate of loss of one allele in a population of $k+1$ alleles is $\lambda_0^k = \frac{k(k+1)}{2}$. In particular, the rate of loss of alleles in the population decreases as k gets smaller.

Appendix A
Hypergeometric Functions and Their Generalizations

In this appendix, we list the basic properties of the hypergeometric functions used for the 2-allele case and their generalizations used for the multi-allele case in Chaps. 8 and 9. These functions are useful tools for solving singular linear second order ODEs. We refer readers to [1, 108, 111] for hypergeometric functions and to [6–8, 32, 40, 86] for generalized hypergeometric functions for further details.

A.1 Gegenbauer Polynomials

Definition A.1.1 Gegenbauer polynomials or ultraspherical polynomials (named after Leopold Gegenbauer [50]) $C_n^\alpha(x)$ are defined in terms of their generating function [108, § IV.2]:

$$\frac{1}{(1-2xt+t^2)^\alpha} = \sum_{n\geq 0} C_n^\alpha(x) t^n.$$

They generalize the Legendre polynomials and the Chebyshev polynomials, and are special cases of the Jacobi polynomials.

Proposition A.1.1 (Suetin '01 [111])

- *The Gegenbauer polynomials satisfy the recurrence relation*

$$C_0^\alpha(x) = 1 \tag{A.1.1}$$

$$C_1^\alpha(x) = 2\alpha x \tag{A.1.2}$$

$$C_n^\alpha(x) = \frac{1}{n}[2x(n+\alpha-1)C_{n-1}^\alpha(x) - (n+2\alpha-2)C_{n-2}^\alpha(x)]. \tag{A.1.3}$$

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- *The Gegenbauer polynomials solve the Gegenbauer differential equation*

$$(1-x^2)y'' - (2\alpha+1)xy' + n(n+2\alpha)y = 0. \tag{A.1.4}$$

- *The Gegenbauer polynomials are special cases of the Jacobi polynomials*

$$C_n^{(\alpha)}(x) = \frac{(2\alpha)_n}{(\alpha+\frac{1}{2})_n} P_n^{(\alpha-1/2,\alpha-1/2)}(x).$$

In particular, we see from the recurrence relations that $C_n^{\alpha}(x)$ is a polynomial of degree n, hence in particular smooth. We shall apply these polynomials in the range $-1 < x < 1$ where (A.1.4) is nondegenerate and where therefore any solution of this equation is smooth. The behavior at the boundary points $x = \pm 1$ then is an important issue.

Proposition A.1.2 *For a fixed α, the Gegenbauer polynomials are orthogonal polynomials on the interval $[-1,1]$ with respect to the weight function $(1-x^2)^{\alpha-\frac{1}{2}}$:*

$$\int_{-1}^{1} (1-x^2)^{\alpha-\frac{1}{2}} \left[C_n^{(\alpha)}(x)\right]\left[C_m^{(\alpha)}(x)\right] dx = \delta_{nm} \frac{\pi 2^{1-2\alpha}\Gamma(n+2\alpha)}{n!(n+\alpha)[\Gamma(\alpha)]^2}. \tag{A.1.5}$$

For a detail *proof*, see [28]. Also see [1, p. 774] for the first formula setting.

A.2 Jacobi Polynomials

Definition A.2.1 The Jacobi polynomials are defined as

$$P_n^{(\alpha,\beta)}(z) = \frac{\Gamma(\alpha+n+1)}{n!\,\Gamma(\alpha+\beta+n+1)} \sum_{m=0}^{n} \binom{n}{m} \frac{\Gamma(\alpha+\beta+n+m+1)}{\Gamma(\alpha+m+1)} \left(\frac{z-1}{2}\right)^m, \tag{A.2.6}$$

for $n \in \mathbb{N}, \alpha, \beta > -1, z \in [-1,1]$.

Proposition A.2.1

- *The Jacobi polynomials satisfy the symmetry relation*

$$P_n^{(\alpha,\beta)}(-z) = (-1)^n P_n^{(\beta,\alpha)}(z);$$

- *The kth derivative of (A.2.6) is*

$$\frac{\mathrm{d}^k}{\mathrm{d}z^k} P_n^{(\alpha,\beta)}(z) = \frac{\Gamma(\alpha+\beta+n+1+k)}{2^k\Gamma(\alpha+\beta+n+1)} P_{n-k}^{(\alpha+k,\beta+k)}(z);$$

- *The Jacobi polynomial $P_n^{(\alpha,\beta)}$ is a solution of the second order linear homogeneous differential equation*

$$(1-x^2)y'' + (\beta - \alpha - (\alpha+\beta+2)x)y' + n(n+\alpha+\beta+1)y = 0; \quad \text{(A.2.7)}$$

- *The Jacobi polynomials are special cases of the hypergeometric polynomials*

$$P_n^{(\alpha,\beta)}(z) = \frac{(\alpha+1)_n}{n!}\, {}_2F_1\left(-n, 1+\alpha+\beta+n; \alpha+1; \frac{1-z}{2}\right).$$

Proposition A.2.2 *For fixed $\alpha > -1$ and $\beta > -1$, the Jacobi polynomials are orthogonal polynomials on the interval $[-1,1]$ with respect to the weight function $(1-x)^\alpha(1+x)^\beta$:*

$$\int_{-1}^{1} (1-x)^\alpha (1+x)^\beta P_m^{(\alpha,\beta)}(x) P_n^{(\alpha,\beta)}(x)\, dx = \frac{2^{\alpha+\beta+1}}{2n+\alpha+\beta+1} \frac{\Gamma(n+\alpha+1)\Gamma(n+\beta+1)}{\Gamma(n+\alpha+\beta+1)n!} \delta_{nm}$$

A.3 Hypergeometric Functions

Definition A.3.1 The Gaussian or ordinary hypergeometric function ${}_2F_1(a,b;c;z)$ is a special function represented by the hypergeometric series,

$${}_2F_1(a,b;c;z) = \sum_{n=0}^{\infty} \frac{(a)_n (b)_n}{(c)_n} \frac{z^n}{n!} \quad \text{(A.3.8)}$$

provided c is not $0, -1, -2, \ldots$, where the Pochhammer symbol is given by

$$(a)_n = a(a+1)(a+2)\cdots(a+n-1) = \frac{\Gamma(a+n)}{\Gamma(a)},\ (a)_0 = 1. \quad \text{(A.3.9)}$$

For complex values of z it can be analytically continued along any path that avoids the branch points 0 and 1.

Proposition A.3.1 *The hypergeometric function is a solution of Euler's hypergeometric differential equation*

$$z(1-z)\frac{d^2w}{dz^2} + [c-(a+b+1)z]\frac{dw}{dz} - abw = 0. \quad \text{(A.3.10)}$$

which has three regular singular points: $0, 1$ *and* ∞*. The generalization of this equation to three arbitrary regular singular points is given by Riemann's differential equation. Any second order differential equation with three regular singular points can be converted to the hypergeometric differential equation by a change of variables.*

Proposition A.3.2

- *The Jacobi polynomials* $P_n^{(\alpha,\beta)}$ *and their special cases the Legendre polynomials, the Chebyshev polynomials, the Gegenbauer polynomials can be written in terms of hypergeometric functions using the following*

$$ {}_2F_1(-n, \alpha + 1 + \beta + n; \alpha + 1; x) = \frac{n!}{(\alpha + 1)_n} P_n^{(\alpha,\beta)}(1 - 2x) $$

- *The Gegenbauer polynomials are given as finite Gaussian hypergeometric series*

$$ C_n^{(\alpha)}(z) = \frac{(2\alpha)_n}{n!} {}_2F_1\left(-n, 2\alpha + n; \alpha + \frac{1}{2}; \frac{1 - z}{2}\right). $$

A.4 Appell's Generalized Hypergeometric Functions

In 1880, Appell [6, 7] introduced the concept of a generalized hypergeometric function.

Definition A.4.1

$$ {}_2F_2(a, b, b'; c, c'; x, y) = \sum_{j=0}^{\infty} \sum_{k=0}^{\infty} (a)_{j+k} \frac{(b)_j (b')_k}{(c)_j (c')_k} \frac{x^j y^k}{j!k!} $$

Proposition A.4.1

(i) ${}_2F_2(a, b, b'; c, c'; x, y)$ *is a solution of the equation*

$$ x(1 - x)z_{xx} - xyz_{xy} + (c - (a + b + 1)x)z_x - byz_y - abz = 0; $$

(ii) ${}_2F_2(a, b, b'; c, c'; x, y)$ *is a solution of the equation*

$$ y(1 - y)z_{yy} - xyz_{xy} + (c' - (a + b' + 1)x)z_y - b'xz_x - ab'z = 0; $$

(iii) ${}_2F_2(a, b, b'; c, c'; x, y)$ *is a solution of the equation*

$$ \begin{aligned} x(1 - x)z_{xx} - 2xyz_{xy} + y(1 - y)z_{yy} + (c - (a + b + b' + 1)x)z_x \\ + (c' - (a + b + b' + 1)y)z_y - a(b + b')z = 0. \end{aligned} $$

Proof Firstly, note that we need only to prove the first assertion. The second follows immediately by interchanging x and y, b and b', c and c' respectively, and the last assertion is obtained when we add the first two assertions.

We shall prove the first assertion by equating coefficients. We denote by $[v][j,k]$ the coefficient of $x^j y^k$ in the Taylor expansion at $(0,0)$ of v. Then for

$$v = \sum_{j=0}^{\infty}\sum_{k=0}^{\infty}(a)_{j+k}\frac{(b)_j(b')_k}{(c)_j(c')_k}\frac{x^j y^k}{j!k!},$$

we have

- $[v][j,k] = \dfrac{(a)_{j+k}(b)_j(b')_k}{(c)_j(c')_k j!k!}$;
- $[v_x][j,k] = \dfrac{(a)_{j+k+1}(b)_{j+1}(b')_k}{(c)_{j+1}(c')_k j!k!}$;
- $[v_y][j,k] = \dfrac{(a)_{j+k+1}(b)_j(b')_{k+1}}{(c)_{j+1}(c')_{k+1} j!k!}$;
- $[v_{xx}][j,k] = \dfrac{(a)_{j+k+2}(b)_{j+2}(b')_k}{(c)_{j+2}(c')_k j!k!}$;
- $[v_{xy}][j,k] = \dfrac{(a)_{j+k+2}(b)_{j+1}(b')_{k+1}}{(c)_{j+1}(c')_{k+1} j!k!}$;
- $[xv_x][j,k] = \dfrac{(a)_{j+k}(b)_j(b')_k}{(c)_j(c')_k (j-1)!k!}$;
- $[yv_y][j,k] = \dfrac{(a)_{j+k}(b)_j(b')_k}{(c)_j(c')_k j!(k-1)!}$;
- $[xv_{xx}][j,k] = \dfrac{(a)_{j+k+1}(b)_{j+1}(b')_k}{(c)_{j+1}(c')_k (j-1)!k!}$;
- $[x^2 v_{xx}][j,k] = \dfrac{(a)_{j+k}(b)_j(b')_k}{(c)_j(c')_k (j-2)!k!}$;

Therefore,

$$\begin{aligned}
&[x(1-x)v_{xx} - xyv_{xy} + (c-(a+b+1)x)v_x - byv_y - abv][j,k] \\
&\quad = [xv_{xx}][j,k] - [xv_{xx}][j,k] - [xyv_{xy}][j,k] \\
&\quad + c[v_x][j,k] - (a+b+1)[xv_x][j,k] - b[yv_y][j,k] - ab[v][j,k] \\
&\quad = \frac{(a)_{j+k}(b)_j(b')_k}{(c)_j(c')_k j!k!}\left\{\frac{(a+j+k)(b+j)}{c+j}j - j(j-1) - jk\right. \\
&\quad \left. + c\frac{(a+j+k)(b+j)}{c+j} - (a+b+1)j - bk - ab\right\} \\
&\quad = 0.
\end{aligned} \tag{A.4.11}$$

This holds for all $j, k \geq 0$, thus

$$x(1-x)v_{xx} - xyv_{xy} + (c - (a+b+1)x)v_x - byv_y - abv = 0;$$

i.e. v is the solution of the first equation. This completes the proof. □

A.5 Lauricella's Generalized Hypergeometric Functions

Definition A.5.1

$${}_2F_n(a, b_1, \ldots, b_n; c_1, \ldots c_n; x^1, \ldots, x^n)$$
$$\sum_{m_1,\ldots,m_n=0}^{\infty} \frac{(a)_{m_1+\ldots+m_n}(b_1)_{m_1}\ldots(b_n)_{m_n}}{(c_1)_{m_1}\ldots(c_n)_{m_n}} \frac{(x^1)^{m_1}}{m_1!} \cdots \frac{(x^n)^{m_n}}{m_n!}$$

Proposition A.5.1

(i) ${}_2F_n(a, b_1, \ldots, b_n; c_1, \ldots c_n; x^1, \ldots, x^n)$ *is a solution of the equation*

$$\mathcal{A}_i z = \sum_{j=1}^{n} x^i(\delta_{ij} - x^j) z_{x^i x^j} + \Big(c_i - (a+1)x^i\Big) z_{x^i} - b_i \sum_{j=1}^{n} x^j z_{x^j} - ab_i z = 0;\ \forall i = \overline{1,n}$$

(ii) ${}_2F_n(a, b_1, \ldots, b_n; c_1, \ldots c_n; x^1, \ldots, x^n)$ *is a solution of the equation*

$$\sum_{i,j=1}^{n} x^i(\delta_{ij} - x^j) z_{x^i x^j} + \sum_{i=1}^{n} \Big(c_i - (a + b_1 + \cdots + b_n + 1)x^i\Big) z_{x^i} - a(b_1 + \ldots + b_n)z = 0.$$

Proof It is easy to see that the second assertion follows by adding the equalities in the first assertion for varying i. So we need only show the first assertion.

Similar to the case of two variables, for any given $(m_1, \ldots, m_n)$, we denote by $[v] = [v][m_1, \ldots, m_n]$ the coefficient of $(x^1)^{m_1} \ldots (x^n)^{m_n}$ in the Taylor expansion at $(\underbrace{0, \ldots, 0}_{n})$. Then we have

- $[v] = \dfrac{(a)_{m_1+\ldots m_n}(b_1)_{m_1}\ldots(b_n)_{m_n}}{(c_1)_{m_1}\ldots(c_n)_{m_n} m_1!\ldots m_n!}$;
- $[v_{x^i}] = \dfrac{(a)_{m_1+\ldots m_n+1}(b_1)_{m_1}\ldots(b_i)_{m_i+1}\ldots(b_n)_{m_n}}{(c_1)_{m_1}\ldots(c_i)_{m_i+1}\ldots(c_n)_{m_n} m_1!\ldots(m_i-1)!\ldots m_n!}$;
- $[v_{x^i x^j}] = \dfrac{(a)_{m_1+\ldots m_n+2}(b_1)_{m_1}\ldots(b_i)_{m_i+1}\ldots(b_j)_{m_j+1}\ldots(b_n)_{m_n}}{(c_1)_{m_1}\ldots(c_i)_{m_i+1}\ldots(c_j)_{m_j+1}\ldots(c_n)_{m_n} m_1!\ldots(m_i-1)!\ldots(m_j-1)!\ldots m_n!}$; for $i \neq j$
- $[v_{x^i x^i}] = \dfrac{(a)_{m_1+\ldots m_n+2}(b_1)_{m_1}\ldots(b_i)_{m_i+2}\ldots(b_n)_{m_n}}{(c_1)_{m_1}\ldots(c_i)_{m_i+1}\ldots(c_n)_{m_n} m_1!\ldots(m_i-2)!\ldots m_n!}$;

- $[x^i v_{x^i x^i}] = \dfrac{(a)_{m_1,\ldots,m_n+1}(b_1)_{m_1}\ldots(b_i)_{m_i+1}\ldots(b_n)_{m_n}}{(c_1)_{m_1}\ldots(c_i)_{m_i+1}\ldots(c_n)_{m_n}m_1!\ldots(m_i-1)!\ldots m_n!}$;
- $[(x^i)^2 v_{x^i x^i}] = \dfrac{(a)_{m_1,\ldots,m_n}(b_1)_{m_1}\ldots(b_n)_{m_n}}{(c_1)_{m_1}\ldots(c_n)_{m_n}m_1!\ldots(m_i-2)!\ldots m_n!}$;
- $[x^i x^j v_{x^i x^j}] = \dfrac{(a)_{m_1,\ldots,m_n}(b_1)_{m_1}\ldots(b_n)_{m_n}}{(c_1)_{m_1}\ldots(c_n)_{m_n}m_1!\ldots(m_i-1)!\ldots(m_j-1)!\ldots m_n!}$; for $i \neq j$
- $[x^i v_{x^i}] = \dfrac{(a)_{m_1,\ldots,m_n+1}(b_1)_{m_1}\ldots(b_i)_{m_i+1}\ldots(b_n)_{m_n}}{(c_1)_{m_1}\ldots(c_i)_{m_i+1}\ldots(c_n)_{m_n}m_1!\ldots m_n!}$;

Therefore

$$\begin{aligned}
\mathcal{A}_i vt &= [x^i v_{x^i x^i}] - [(x^i)^2 v_{x^i x^i}] - \sum_{j\neq i}[x^i x^j v_{x^i x^j}] + c_i[v_{x^i}] \\
&\quad - (a+1)[x^i v_{x^i}] - b_i \sum_{j=1}^{n}[x^j v_{x^j}] - ab_i[v] \\
&= K\left\{ \frac{(a+m_1,\ldots,m_n)(b_i+m_i)}{c_i+m_i} m_i - m_i(m_i-1) - \sum_{j\neq i} m_i m_j \right. \\
&\quad \left. + c_i \frac{(a+m_1,\ldots,m_n)(b_i+m_i)}{c_i+m_i} - (a+1)m_i - b_i \sum_{j=1}^{n} m_j - ab_i \right\} \\
&= 0
\end{aligned}$$

This holds for all $(m_1,\ldots,m_n)$ so

$$\mathcal{A}_i v = 0,$$

i.e. v is the solution of the first equation. This completes the proof. □

A.6 Biorthogonal Systems

In 1881, Appell [8] introduced the polynomials

$$F_{m,n}(\alpha,\gamma,\gamma';x,y) = \frac{[w(x,y)]^{-1}}{(\gamma)_m(\gamma')_n}\frac{\partial^{m+n}}{\partial x^m \partial y^n}\left(w(x,y)x^m y^n (1-x-y)^{m+n} \right)$$

in connection with the analysis of polynomials that are orthogonal with respect to the weight function

$$w(x,y) = x^{\gamma-1}y^{\gamma'-1}(1-x-y)^{\alpha-\gamma-\gamma'}$$

in the triangle $T = \overline{\Delta_2}$.

In 1882, he also proved that in the special case $\alpha = \gamma + \gamma'$, the two families

$$F_{m,n}(\gamma,\gamma';x,y) = \frac{[t(x,y)]^{-1}}{(\gamma)_m(\gamma')_n}\frac{\partial^{m+n}}{\partial x^m \partial y^n}\left(t(x,y)x^m y^n(1-x-y)^{m+n}\right)$$

and

$$E_{m,n}(\gamma,\gamma';x,y) = {}_2F_2(\gamma+\gamma'+m+n,-m,-n;\gamma,\gamma';x,y)$$

form a biorthogonal system with the weight function

$$t(x,y) = x^{\gamma-1}y^{\gamma'-1},$$

i.e.

$$\iint\limits_T t(x,y)F_{m,n}(\gamma,\gamma';x,y)E_{k,l}(\gamma,\gamma';x,y)dxdy$$

$$= \frac{\delta_{mk}\delta_{nl}\Gamma(\gamma)\Gamma(\gamma')m!n!(m+n)!}{(\gamma+\gamma'+2m+2n)\Gamma(\gamma+\gamma'+m+n)(\gamma)_m(\gamma')_n}$$

Definition A.6.1 In n dimensions, we call

$$w(x^1,\ldots,x^n) = (x^1)^{\gamma_1-1}\ldots(x^n)^{\gamma_n-1}(1-x^1-\ldots-x^n)^{\alpha-\gamma_1-\ldots-\gamma_n}$$

the weight function on Δ_n and

$$\mathcal{E}_{m_1,\ldots,m_n}(\alpha,\gamma_1,\ldots,\gamma_n;x^1,\ldots,x^n)$$

$$= {}_2F_n(\alpha+m_1+\ldots+m_n,-m_1,\ldots,-m_n;\gamma_1,\ldots\gamma_n;x^1,\ldots,x^n)$$

and

$$\mathcal{F}_{m_1,\ldots,m_n}(\alpha,\gamma_1,\ldots,\gamma_n;x^1,\ldots,x^n) = \frac{[w(x^1,\ldots,x^n)]^{-1}}{(\gamma_1)_{m_1}\ldots(\gamma_n)_{m_n}}\left\{\frac{\partial^{m_1+\ldots+m_n}}{\partial(x^1)^{m_1}\ldots\partial(x^n)^{m_n}}\right.$$

$$\left.\left(w(x^1,\ldots,x^n)(x^1)^{m_1}\ldots(x^n)^{m_n}(1-x^1-\ldots-x^n)^{m_1+\ldots+m_n}\right)\right\}$$

the corresponding biorthogonal systems.

These two families of hypergeometric functions satisfy

Proposition A.6.1 *Each*

$$\mathcal{F}_{m_1,\ldots,m_n}(\alpha,\gamma_1,\ldots,\gamma_n;x^1,\ldots,x^n)$$

and

$$\mathcal{E}_{m_1,\ldots,m_n}(\alpha,\gamma_1,\ldots,\gamma_n;x^1,\ldots,x^n)$$

is a solution of the equation

$$\sum_{i,j=1}^{n} x^i(\delta_{ij}-x^j)z_{x^ix^j}+\sum_{i=1}^{n}\Big(\gamma_i-(\alpha+1)x^i\Big)z_{x^i}+\Big(m_1+\ldots+m_n\Big)\Big(\alpha+m_1+\ldots+m_n\Big)z=0.$$

Proof From Proposition A.5.1, it is easy to see that

$$\mathcal{E}_{m_1,\ldots,m_n}(\alpha,\gamma_1,\ldots,\gamma_n;x^1,\ldots,x^n)$$

is the solution to the equation

$$\sum_{i,j=1}^{n} x^i(\delta_{ij}-x^j)z_{x^ix^j}+\sum_{i=1}^{n}\Big(\gamma_i-(\alpha+1)x^i\Big)z_{x^i}+\Big(m_1+\ldots+m_n\Big)\Big(\alpha+m_1+\ldots+m_n\Big)z=0.$$

To prove the other assertion we proceed as follows. First, note that by Taylor expansion at $\underbrace{(0,\ldots,0)}_{n}$ we have

$$(1-x_1-\ldots-x_n)^a=\sum_{i_1,\ldots,i_n=0}^{\infty}(-a)_{i_1+\ldots+i_n}\frac{(x^1)^{i_1}\ldots(x^n)^{i_n}}{i_1!\ldots i_n!}$$

Therefore

$$\begin{aligned}&\mathcal{F}_{m_1,\ldots,m_n}(\alpha,\gamma_1,\ldots,\gamma_n;x^1,\ldots,x^n)\\&=\frac{[w(x^1,\ldots,x^n)]^{-1}}{(\gamma_1)_{m_1}\ldots(\gamma_n)_{m_n}}\left\{\frac{\partial^{m_1+\ldots+m_n}}{\partial(x^1)^{m_1}\ldots\partial(x^n)^{m_n}}\right.\\&\qquad\left.\Big(w(x^1,\ldots,x^n)(x^1)^{m_1}\ldots(x^n)^{m_n}(1-x^1-\ldots-x^n)^{m_1+\ldots+m_n}\Big)\right\}\end{aligned}$$

$$= \frac{[w(x^1,\dots,x^n)]^{-1}}{(\gamma_1)_{m_1}\dots(\gamma_n)_{m_n}}\left\{\frac{\partial^{m_1+\dots+m_n}}{\partial(x^1)^{m_1}\dots\partial(x^n)^{m_n}}\right.$$

$$\left.\left((x^1)^{m_1+\gamma_1-1}\dots(x^n)^{m_n+\gamma_n-1}(1-x^1-\dots-x^n)^{m_1+\dots+m_n+\alpha-\gamma_1-\dots-\gamma_n}\right)\right\}$$

$$= \frac{[w(x^1,\dots,x^n)]^{-1}}{(\gamma_1)_{m_1}\dots(\gamma_n)_{m_n}}\left\{\frac{\partial^{m_1+\dots+m_n}}{\partial(x^1)^{m_1}\dots\partial(x^n)^{m_n}}\right.$$

$$\left(\sum_{i_1,\dots,i_n=0}^{\infty}(\gamma_1+\dots+\gamma_n-m_1-\dots-m_n-\alpha)_{i_1+\dots+i_n}\right.$$

$$\left.\left.\times\frac{(x^1)^{m_1+\gamma_1-1+i_1}\dots(x^n)^{m_n+\gamma_n-1+i_n}}{i_1!\dots i_n!}\right)\right\}$$

$$= \frac{[w(x^1,\dots,x^n)]^{-1}}{(\gamma_1)_{m_1}\dots(\gamma_n)_{m_n}}\left(\sum_{i_1,\dots,i_n=0}^{\infty}(\gamma_1+\dots+\gamma_n-m_1-\dots-m_n-\alpha)_{i_1+\dots+i_n}\right.$$

$$\left.\times(\gamma_1+i_1)_{m_1}\dots(\gamma_n+i_n)_{m_n}\frac{(x^1)^{\gamma_1-1+i_1}\dots(x^n)^{\gamma_n-1+i_n}}{i_1!\dots i_n!}\right)$$

$$= \sum_{i_1,\dots,i_n=0}^{\infty}(\gamma_1+\dots+\gamma_n-m_1-\dots-m_n-\alpha)_{i_1+\dots+i_n}$$

$$\times\frac{(\gamma_1+i_1)_{m_1}\dots(\gamma_n+i_n)_{m_n}}{(\gamma_1)_{m_1}\dots(\gamma_n)_{m_n}}\frac{(x^1)^{i_1}\dots(x^n)^{i_n}}{i_1!\dots i_n!}(1-x_1-\dots-x_n)^{\gamma_1+\dots+\gamma_n-\alpha}$$

$$= \sum_{i_1,\dots,i_n=0}^{\infty}(\gamma_1+\dots+\gamma_n-m_1-\dots-m_n-\alpha)_{i_1+\dots+i_n}$$

$$\times\frac{(\gamma_1+m_1)_{i_1}\dots(\gamma_n+m_n)_{i_n}}{(\gamma_1)_{i_1}\dots(\gamma_n)_{i_n}}\frac{(x^1)^{i_1}\dots(x^n)^{i_n}}{i_1!\dots i_n!}(1-x_1-\dots-x_n)^{\gamma_1+\dots+\gamma_n-\alpha}$$

$$= (1-x_1-\dots-x_n)^{\gamma_1+\dots+\gamma_n-\alpha}\,{}_2F_n\Big(\gamma_1+\dots+\gamma_n-m_1-\dots-m_n-\alpha,$$

$$\gamma_1+m_1,\dots,\gamma_n+m_n;\gamma_1,\dots\gamma_n;x^1,\dots,x^n\Big).$$

To simplify the notations, we put

$$f(x) = \mathcal{F}_{m_1,\dots,m_n}(\alpha,\gamma_1,\dots,\gamma_n;x^1,\dots,x^n),$$

$$g(x) = {}_2F_n(\gamma_1+\dots+\gamma_n-m_1-\dots-m_n-\alpha,\gamma_1+m_1,\dots,\gamma_n$$

$$+m_n;\gamma_1,\dots\gamma_n;x^1,\dots,x^n),$$

and

$$\varphi(x) = (1 - x_1 - \ldots - x_n)^{\gamma_1 + \ldots + \gamma_n - \alpha}.$$

Then we have

$$f(x) = \varphi(x) g(x).$$

It follows that

$$\begin{aligned}
&\sum_{i,j=1}^{n} x^i(\delta_{ij} - x^j) f_{x^i x^j} + \sum_{i=1}^{n} \Big(\gamma_i - (\alpha+1)x^i\Big) f_{x^i} + \Big(m_1 + \ldots + m_n\Big)\Big(\alpha + m_1 + \ldots + m_n\Big) f \\
&\quad = \sum_{i,j=1}^{n} x^i(\delta_{ij} - x^j)\Big(\varphi g_{x^i x^j} + \varphi_{x^i} g_{x^j} + \varphi_{x^j} g_{x^i} + \varphi_{x^i x^j} g\Big) \\
&\quad + \sum_{i=1}^{n} \Big(\gamma_i - (\alpha+1)x^i\Big)\Big(\varphi g_{x^i} + \varphi_{x^i} g\Big) + \Big(m_1 + \ldots + m_n\Big)\Big(\alpha + m_1 + \ldots + m_n\Big)(\varphi g) \\
&\quad = \sum_{i,j=1}^{n} x^i(\delta_{ij} - x^j)\varphi g_{x^i x^j} + \sum_{i=1}^{n} \Big((\gamma_i - (\alpha+1)x^i)\varphi + 2\sum_{j=1}^{n} x^i(\delta_{ij} - x^j)\varphi_{x^j}\Big) g_{x^i} \\
&\quad + \Bigg(\sum_{i,j=1}^{n} x^i(\delta_{ij} - x^j)\varphi_{x^i x^j} + \sum_{i=1}^{n} \Big((\gamma_i - (\alpha+1)x^i)\varphi_{x^i} \\
&\quad + \Big(m_1 + \ldots + m_n\Big)\Big(\alpha + m_1 + \ldots + m_n\Big)\varphi \Bigg) g \\
&\quad = \varphi \Bigg(\sum_{i,j=1}^{n} x^i(\delta_{ij} - x^j) g_{x^i x^j} + \sum_{i=1}^{n} \Big(\gamma_i - \big(2\gamma_1 + \ldots + 2\gamma_n - \alpha + 1\big)x^i\Big) g_{x^i} \\
&\quad - \Big(\gamma_1 + \ldots + \gamma_n - m_1 - \ldots - m_n - \alpha\Big)\Big(\gamma_1 + \ldots + \gamma_n + m_1 + \ldots + m_n\Big) g \Bigg) \\
&\quad = 0 \quad \text{by Proposition A.5.1}
\end{aligned}$$

This completes the proof. □

Proposition A.6.2 *The generalized hypergeometric function*

$$\mathcal{E}_{m'_1, \ldots, m'_n}(\alpha, \gamma_1, \ldots, \gamma_n; x^1, \ldots, x^n)$$

is the sum of a monomial of degree $m_1' + \ldots + m_n'$

$$(-1)^{m_1'+\ldots+m_n'} \frac{(\alpha + m_1' + \ldots + m_n')_{m_1'+\ldots+m_n'}}{(\gamma_1)_{m_1'} \ldots (\gamma_n)_{m_n'}} (x^1)^{m_1'} \ldots (x^n)^{m_n'} + \left\{ \textit{polynomial of degree } < m_1' + \ldots + m_n' \right\}.$$

Proof In fact, from the definition of $\mathcal{E}$ we have

$$\begin{aligned}
&\mathcal{E}_{m_1',\ldots,m_n'}(\alpha, \gamma_1, \ldots, \gamma_n; x^1, \ldots, x^n) \\
&= \quad {}_2F_n(\alpha + m_1' + \ldots + m_n', -m_1', \ldots, -m_n'; \gamma_1, \ldots \gamma_n; x^1, \ldots, x^n) \\
&= \sum_{i_1,\ldots,i_n=0}^{\infty} (\alpha + m_1' + \ldots + m_n')_{i_1+\ldots+i_n} \frac{(-m_1')_{i_1} \ldots (-m_n')_{i_n}}{(\gamma_1)_{i_1} \ldots (\gamma_n)_{i_n} i_1! \ldots i_n!} (x^1)^{i_1} \ldots (x^n)^{i_n} \\
&= \sum_{i_1=0}^{m_1'} \ldots \sum_{i_n=0}^{m_n'} (\alpha + m_1' + \ldots + m_n')_{i_1+\ldots+i_n} \frac{(-m_1')_{i_1} \ldots (-m_n')_{i_n}}{(\gamma_1)_{i_1} \ldots (\gamma_n)_{i_n} i_1! \ldots i_n!} (x^1)^{i_1} \ldots (x^n)^{i_n}. \\
&\quad \Big(\text{because if } i_k > m_k' \text{ then } (-m_k')_{i_k} = 0\Big) \\
&= (\alpha + m_1' + \ldots + m_n')_{m_1'+\ldots+m_n'} \frac{(-m_1')_{m_1'} \ldots (-m_n')_{m_n'}}{(\gamma_1)_{m_1'} \ldots (\gamma_n)_{m_n'} m_1'! \ldots m_n'!} (x^1)^{m_1'} \ldots (x^n)^{m_n'} \\
&+ \left\{ \text{polynomial of degree } < m_1' + \ldots + m_n' \right\} \\
&= (-1)^{m_1'+\ldots+m_n'} \frac{(\alpha + m_1' + \ldots + m_n')_{m_1'+\ldots+m_n'}}{(\gamma_1)_{m_1'} \ldots (\gamma_n)_{m_n'}} (x^1)^{m_1'} \ldots (x^n)^{m_n'} \\
&+ \left\{ \text{polynomial of degree } < m_1' + \ldots + m_n' \right\}.
\end{aligned}$$

This completes the proof. □

Lemma A.6.1 *With* $a_1, \ldots, a_{n+1}$ *given positive numbers, we have*

$$\int_{\Delta_n} (x^1)^{a_1-1} \ldots (x^n)^{a_n-1} (1 - x_1 - \ldots - x_n)^{a_{n+1}-1} dx = \frac{\Gamma(a_1) \ldots \Gamma(a_{n+1})}{\Gamma(a_1 + \ldots + a_{n+1})}.$$

Proof Obviously, when $a, b > 0$

$$\int_0^r x^{a-1}(r-x)^{b-1}dx = \int_0^1 (ry)^{a-1}[r(1-y)]^{b-1}rdy = r^{a+b-1}\frac{\Gamma(a)\Gamma(b)}{\Gamma(a+b)}.$$

So we have

$$\begin{aligned}
&\int_{\Delta_n} (x^1)^{a_1-1}\dots(x^n)^{a_n-1}(1-x^1-\dots-x^n)^{a_{n+1}-1}dx \\
&= \int_0^1 (x^1)^{a_1-1}\Bigg\{\int_0^{1-x^1}(x^2)^{a_2-1} \\
&\dots\left(\int_0^{1-x^1-\dots-x^{n-1}}(x^n)^{a_n-1}\left(1-x^1-\dots-x^{n-1}-x^n\right)^{a_{n+1}-1}dx^n\right)\dots dx^2\Bigg\}dx^1 \\
&= \int_0^1 (x^1)^{a_1-1}\Bigg\{\int_0^{1-x^1}(x^2)^{a_2-1} \\
&\dots\left(\left(1-x^1-\dots-x^{n-1}\right)^{a_n+a_{n+1}-1}\frac{\Gamma(a_n)\Gamma(a_{n+1})}{\Gamma(a_n+a_{n+1})}\right)\dots dx^2\Bigg\}dx^1 \\
&= \cdots \\
&= \int_0^1 (x^1)^{a_1-1}\Bigg\{\int_0^{1-x^1}(x^2)^{a_2-1}(1-x^1-x^2)^{a_3+\dots+a_{n+1}-1}\frac{\Gamma(a_3)\dots\Gamma(a_{n+1})}{\Gamma(a_3+\dots+a_{n+1})}dx^2\Bigg\}dx^1 \\
&= \int_0^1 (x^1)^{a_1-1}(1-x^1)^{a_2+\dots+a_{n+1}-1}\frac{\Gamma(a_2)\Gamma(a_3+\dots+a_{n+1})}{\Gamma(a_2+\dots+a_{n+1})}\frac{\Gamma(a_3)\dots\Gamma(a_{n+1})}{\Gamma(a_3+\dots+a_{n+1})}dx^1 \\
&= \int_0^1 (x^1)^{a_1-1}(1-x^1)^{a_2+\dots+a_{n+1}-1}\frac{\Gamma(a_2)\dots\Gamma(a_{n+1})}{\Gamma(a_2+\dots+a_{n+1})}dx^1 \\
&= \frac{\Gamma(a_1)\Gamma(a_2+\dots+a_{n+1})}{\Gamma(a_1+\dots+a_{n+1})}\frac{\Gamma(a_2)\dots\Gamma(a_{n+1})}{\Gamma(a_2+\dots+a_{n+1})} \\
&= \frac{\Gamma(a_1)\dots\Gamma(a_{n+1})}{\Gamma(a_1+\dots+a_{n+1})}.
\end{aligned}$$

This completes the proof. □

Proposition A.6.3 *The system of*

$$\mathcal{F}_{m_1,\dots,m_n}(\alpha,\gamma_1,\dots,\gamma_n;x^1,\dots x^n)$$

and

$$\mathcal{E}_{m_1,\dots,m_n}(\alpha,\gamma_1,\dots,\gamma_n;x^1,\dots x^n)$$

is a biorthogonal system with the weight function w, i.e.

$$\int\limits_{\Delta_n} w(x^1,\dots,x^n)\mathcal{F}_{m_1,\dots,m_n}\mathcal{E}_{m'_1,\dots,m'_n}dx^1\dots dx^n = K_{m_1,\dots,m_n}\delta_{m_1,m'_1}\dots\delta_{m_n,m'_n}.$$

where

$$K_{m_1,\dots m_n} = \frac{(\alpha+m_1+\dots+m_n)_{m_1+\dots+m_n}m_1!\dots m_n!}{[(\gamma_1)_{m_1}]^2\dots[(\gamma_n)_{m_n}]^2}$$
$$\times\frac{\Gamma(m_1+\gamma_1)\dots\Gamma(m_n+\gamma_n)\Gamma(m_1+\dots+m_n+\alpha-\gamma_1-\dots-\gamma_n+1)}{\Gamma(2m_1+\dots+2m_n+\alpha+1)}.$$

Proof From Proposition A.6.1 we have

$$\sum_{i,j=1}^{n} x^i(\delta_{ij}-x^j)u_{x^ix^j}+\sum_{i=1}^{n}\Big(\gamma_i-(\alpha+1)x^i\Big)u_{x^i}$$
$$+\Big(m_1+\dots+m_n\Big)\Big(\alpha+m_1+\dots+m_n\Big)u=0. \qquad \text{(A.6.12)}$$

where

$$u=\mathcal{F}_{m_1,\dots,m_n}(\alpha,\gamma_1,\dots,\gamma_n;x^1,\dots,x^n)$$

and

$$\sum_{i,j=1}^{n} x^i(\delta_{ij}-x^j)v_{x^ix^j}+\sum_{i=1}^{n}\Big(\gamma_i-(\alpha+1)x^i\Big)v_{x^i}$$
$$+\Big(m'_1+\dots+m'_n\Big)\Big(\alpha+m'_1+\dots+m'_n\Big)v=0. \qquad \text{(A.6.13)}$$

where

$$v=\mathcal{E}_{m'_1,\dots,m'_n}(\alpha,\gamma_1,\dots,\gamma_n;x^1,\dots,x^n)$$

Multiplying Eq. (A.6.13) by u and subtracting Eq. (A.6.12) multiplied by v, we obtain

$$\sum_{i,j=1}^{n} x^i(\delta_{ij} - x^j)\Big(uv_{x^ix^j} - u_{x^ix^j}v\Big) + \sum_{i=1}^{n}\Big(\gamma_i - (\alpha+1)x^i\Big)\Big(uv_{x^i} - u_{x^i}v\Big)$$
$$= \Big(\alpha + m_1 + \ldots + m_n + m_1' + \ldots + m_n'\Big)\Big(m_1 + \ldots + m_n - m_1' - \ldots - m_n'\Big)uv.$$

Multiplying both sides of this equation by w and integrating over Δ_n we obtain

$$\int_{\Delta_n} \big(\alpha + m_1 + \ldots + m_n + m_1' + \ldots + m_n'\big)\big(m_1 + \ldots + m_n - m_1' - \ldots - m_n'\big)wuvdx$$
$$= \int_{\Delta_n} \Big(\sum_{i,j=1}^{n} x^i(\delta_{ij} - x^j)\big(wuv_{x^ix^j} - wu_{x^ix^j}v\big) + \sum_{i=1}^{n}\big(\gamma_i - (\alpha+1)x^i\big)\big(wuv_{x^i} - wu_{x^i}v\big)\Big)dx$$
$$= \int_{\Delta_n} \sum_{j=1}^{n} \frac{\partial}{\partial x^j}\left(\sum_{i=1}^{n} x^i(\delta_{ij} - x^j)w(uv_{x^i} - u_{x^i}v)\right)dx$$
$$= \int_{\Delta_n} \operatorname{div} F\, dx, \qquad \text{where } F^j = \sum_{i=1}^{n} x^i\Big(\delta_{ij} - x^j\Big)w\Big(uv_{x^i} - u_{x^i}v\Big)$$
$$= \int_{\partial\Delta_n} F \cdot \nu\, do(\sigma)$$
$$= 0, \qquad \text{since } F_{|\partial\Delta_n} = 0 \quad \text{follows from } w_{|\partial\Delta_n} = 0.$$

It follows that if

$$m_1 + \ldots + m_n \neq m_1' + \ldots + m_n'$$

then

$$\int_{\Delta_n} wuvdx = 0.$$

Now we consider the case $m_1+\ldots+m_n = m'_1+\ldots+m'_n$. Applying the integration by parts to the Proposition A.6.2 and Lemma A.6.1, we obtain

$$\begin{aligned}
&\int_{\Delta_n} wuvdx \\
&= \int_{\Delta_n} w\frac{w^{-1}}{(\gamma_1)_{m_1}\ldots(\gamma_n)_{m_n}}\left\{\frac{\partial^{m_1+\ldots+m_n}}{\partial(x^1)^{m_1}\ldots\partial(x^n)^{m_n}}\left((x^1)^{m_1+\gamma_1-1}\ldots(x^n)^{m_n+\gamma_n-1}\right.\right. \\
&\quad\left.\left.\times(1-x^1-\ldots-x^n)^{m_1+\ldots+m_n+\alpha-\gamma_1-\ldots-\gamma_n}\right)\right\}vdx \\
&= \frac{(-1)^{m_1+\ldots+m_n}}{(\gamma_1)_{m_1}\ldots(\gamma_n)_{m_n}}\int_{\Delta_n}\left((x^1)^{m_1+\gamma_1-1}\ldots(x^n)^{m_n+\gamma_n-1}\right. \\
&\quad\left.\times(1-x^1-\ldots-x^n)^{m_1+\ldots+m_n+\alpha-\gamma_1-\ldots-\gamma_n}\right)\frac{\partial^{m_1+\ldots+m_n}v}{\partial(x^1)^{m_1}\ldots\partial(x^n)^{m_n}}dx \\
&= \frac{(-1)^{m_1+\ldots+m_n}}{(\gamma_1)_{m_1}\ldots(\gamma_n)_{m_n}}\int_{\Delta_n}\left((x^1)^{m_1+\gamma_1-1}\ldots(x^n)^{m_n+\gamma_n-1}\right. \\
&\quad\left.\times(1-x^1-\ldots-x^n)^{m_1+\ldots+m_n+\alpha-\gamma_1-\ldots-\gamma_n}\right) \\
&\delta_{m_1,m'_1}\ldots\delta_{m_n,m'_n}\frac{(-1)^{m_1+\ldots+m_n}(\alpha+m_1+\ldots+m_n)_{m_1+\ldots+m_n}m_1!\ldots m_n!}{(\gamma_1)_{m_1}\ldots(\gamma_n)_{m_n}}dx \\
&= \delta_{m_1,m'_1}\ldots\delta_{m_n,m'_n}\frac{(\alpha+m_1+\ldots+m_n)_{m_1+\ldots+m_n}m_1!\ldots m_n!}{[(\gamma_1)_{m_1}]^2\ldots[(\gamma_n)_{m_n}]^2} \\
&\quad\times\frac{\Gamma(m_1+\gamma_1)\ldots\Gamma(m_n+\gamma_n)\Gamma(m_1+\ldots+m_n+\alpha-\gamma_1-\ldots-\gamma_n+1)}{\Gamma(2m_1+\ldots+2m_n+\alpha+1)}.
\end{aligned}$$

This completes the proof. □

When $\alpha = 2n+1, \gamma_1 = \ldots = \gamma_n = 2$ we have the result of Littler and Fackerell [86].

Corollary A.6.1

$$\begin{aligned}
K_{m_1,\ldots,m_n} &= \frac{(2n+1+m_1+\ldots+m_n)_{m_1+\ldots+m_n}m_1!\ldots m_n!}{[(2)_{m_1}]^2\ldots[(2)_{m_n}]^2} \\
&\quad\times\frac{\Gamma(m_1+2)\ldots\Gamma(m_n+2)\Gamma(m_1+\ldots+m_n+2)}{\Gamma(2m_1+\ldots+2m_n+2n+2)}.
\end{aligned}$$

$$
\begin{aligned}
&= \frac{(2n+1+m_1+\ldots+m_n)_{m_1+\ldots+m_n} m_1! \ldots m_n!}{[(m_1+1)!]^2 \ldots [(m_n+1)!]^2} \\
&\quad \times \frac{(m_1+1)! \ldots (m_n+1)!(m_1+\ldots+m_n+1)!}{(2m_1+\ldots+2m_n+2n+1)!} \\
&= \frac{1}{(m_1+1)\ldots(m_n+1)} \\
&\quad \times \frac{(2n+1+m_1+\ldots+m_n)_{m_1+\ldots+m_n}(m_1+\ldots+m_n+1)!}{(2m_1+\ldots+2m_n+2n+1)!} \\
&= \frac{1}{(m_1+1)\ldots(m_n+1)} \\
&\quad \times \frac{1}{(m_1+\ldots+m_n+2)\ldots(m_1+\ldots+m_n+2n)(2m_1+\ldots+2m_n+2n+1)} \\
&= \frac{1}{(m_1+1)\ldots(m_n+1)(m_1+\ldots+m_n+2)_{2n-1}(2m_1+\ldots+2m_n+2n+1)}.
\end{aligned}
$$

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Index of Notation

$\langle .,. \rangle$, 48
$(f,g)_n$, 40
$[f,g]_n$, 40
$f(p,s,x,t)$, 32
${}_2F_1(a,b;c;z)$, 291

A, 70, 80, 82
α, 4
$\boldsymbol{\alpha}$, 19, 35
A^*, 90
A^i, 18
$a^{ij}(x,t)$, 27, 32
$A_\mu^{i_\mu}$, 35
a_{rs}^{ℓ}, 105
A_N, 84

$\mathbf{B}$, 79
$b^i(x,t)$, 26, 32
$\mathbf{B}_N$, 80

$C_n^\alpha(x)$, 289
$C_p^l(\overline{\square}_n)$, 43
$C_p^l(\overline{\Delta}_n)$, 41
$C_{p_0}^l\left(\bigcup_{d=k}^n \Delta_d^{(I_d)}\right)$, 41
$C_{\xi\eta\zeta}(\mu)$, 6

D, 51
$D_2^{i_1 i_2 \bullet}(x)$, 117
$D_E[0,\infty)$, 78
$d\varphi$, 50

$\Delta_g\varphi$, 50
D^{ij}, 36
$D_{ij}(c)$, 115
$\operatorname{div} Z$, 50
$\partial_k \Delta_n$, 39
$\Delta_k^{(I_k)}$, 39
$D_{\mathrm{KL}}(f_1\ f_2)$142
$\partial_k \square_n$, 42
$D_l^{\langle i_{j_1},\ldots,i_{j_l},\bullet\rangle}$, 120
Δ_n, 38
$\overline{\Delta}_n^{(2N)}$, 77
$(\Delta_n)_\infty$, 38
$d(\xi,\eta)$, 5

e_i, 41

f, 221
$f(p,s,x,t)$, 7
$F(p(\cdot,t))$, 155
Φ_s^r, 240
$\bar{f}^{r,s}$, 225
$F(\theta)$, 58
$F(u(\cdot,t))$, 141

$g = \det(g_{ij})$, 48
$g(.,.)$, 48
$\mathcal{G}(A)$, 79
$\Gamma_2(f,g)$, 159
$\Gamma(f,g)$, 159
G^i, 36
$G = (g_{ij})_{i,j}$, 47
$G^{-1} = (g^{ij})_{i,j}$, 47

J. Hofrichter et al., *Information Geometry and Population Genetics*,
Understanding Complex Systems, DOI 10.1007/978-3-319-52045-2

Index

J. Hofrichter et al., *Information Geometry and Population Genetics*,
Understanding Complex Systems, DOI 10.1007/978-3-319-52045-2