
Evolutionary Theory

Mathematical and Conceptual Foundations

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This book is dedicated to the memory of my parents,
Salem J. Rice and Ann R. Rice

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Preface

This is first and foremost a book about evolutionary biology. Though it is filled with equations, it is not an applied mathematics book, nor is it a population genetics text, though that subject dominates half of the chapters. Rather, it is a book about the mechanics of evolution, as illuminated by mathematics, and about the conceptual structure of evolutionary theory. I hope to convey the fact that evolutionary theory is not just a collection of separately constructed models, but is a unified subject in which all of the major results are related to a few basic biological and mathematical principles.

The audience I had in mind while writing the book is made up primarily of graduate students in biology. These students know there is a body of formal evolutionary theory and are familiar with some of its conclusions, but often have never been shown where these conclusions originate from. I also hope that the book will be of interest to researchers in related fields, as well as to biology undergraduates who are frustrated with the fact that they learn calculus and then rarely use it in their courses. In short, my intended audience is composed of readers who know a bit of evolutionary biology and a bit of mathematics. My goal is to take these readers deep into the subject of evolutionary biology, and hopefully expand both their biological and mathematical knowledge in the process.

The single most difficult thing about writing a book that covers this range of material is deciding what to leave out. Most of the topics that I cover have entire books devoted exclusively to them. Giving a comprehensive treatment of each subject would make the book prohibitively long (for both author and readers) and would detract from the goal of uniting different fields and emphasizing the biological insights that they yield.

In deciding what to include and what to leave out, I chose to focus on those results that I feel have the greatest power to influence our thinking about how evolution works. By showing in detail how these central results are derived, I hope to convey some feel for how the different branches of evolutionary theory are constructed and connected.

Because I chose subjects based on their significance to understanding evolution rather than on the kind of mathematics that they require, the level of mathematical sophistication varies throughout the book. Some sections use only basic algebra and a bit of calculus while others, sometimes in the same chapter, use more sophisticated methods. I assume only that the reader is familiar with basic calculus. Beyond this, I strive to explain more advanced mathematical techniques when they arise or in the Appendices.

Acknowledgments

This book is based on a course that I have taught for a number of years. I am grateful to all of the students who, through challenging and insightful questions, lively discussions, and comments on my lecture notes, have not only improved my presentation of the material but have helped me to learn the subject more deeply.

My thinking about this subject has been influenced by many colleagues over the years. Those whose influence I clearly see when I look at what I have written include Jack Cohen, Paul Magwene, Monty Slatkin, Mike Rosenzweig, and Günter Wagner. David Houle and Mark Kirkpatrick read parts of the manuscript and provided helpful input regarding the material and presentation.

I am also grateful to Andy Sinauer and the folks at Sinauer Associates for working hard to keep the book on schedule while dealing with my constant underestimates of how long it would take me to complete each part. In particular I would like to thank Sydney Carroll, who worked overtime to pull the book together.

Most importantly, I would never have completed this book without the continuing encouragement and support of my wife, Melissa. When the project seemed daunting, she reminded me why it was worthwhile and inspired me to continue.

Introduction

All fields of science use mathematical models that allow us to draw accurate conclusions from empirical work as well as to address hypothetical “what if” questions. A few scientific fields go a step further. These sciences possess mathematical theory that is more than just a collection of special case models, it is fundamental to a basic understanding of the subject. In fields built upon this sort of theoretical foundation, discovery is often driven by mathematical arguments, followed by empirical tests. When a particular model fails an empirical test, researchers turn to the mathematical theory to understand why.

Only a few branches of science have this sort of formal mathematical foundation, but it is not surprising that evolutionary biology is one of them. When we look at the roots of evolutionary biology, we can see why this is so. The mechanism of evolution proposed by Darwin and Wallace, though not phrased mathematically, has a feeling of universality to it. The logic of natural selection is so clear and the premises so well founded, that critics—who are unable to find any logical flaws—are reduced to arguing that it has no empirical content. This is of course not true. The fact that offspring resemble their parents is an empirical observation, but the empirical basis of the theory is so well supported that it seems to blend into the logic of the arguments.

In this respect, evolutionary biology is unlike most biological sciences, where fundamental discoveries are usually the result of experiments. Mathematical models, when used at all, are seen more as ways to make numerical predictions than as ways to understand the basic science. In contrast, many of the central ideas in evolutionary biology originate in, or are justified by

purely mathematical analysis. A short list of these central ideas includes: the fact that even seemingly weak selection can drive evolution; the existence of drift and its interplay with selection; the significance of frequency dependent selection for our understanding of adaptation; the importance of population structure in evolution; the role of kinship in the evolution of cooperation; the significance of mate choice as opposed to competition in sexual selection; and the conditions under which it is, or is not, reasonable to think of selection as acting at more than one level of organization. All of these subjects have also been studied experimentally, but none would have gotten far without rigorous mathematical analysis.

Theoretical science begins with what we know and leads us to conclusions that could not have been made without rigorous analysis. How far a theory can take us is determined in large part by how solid the foundation is on which it is built (what we know). This foundation is what allows us to decide when we can or can not apply the results of our theory, how and when these results can be combined, and how to interpret cases in which the theory fails. There are two main types of foundations that underlie successful theories. The first is a set of well-understood empirical rules that apply to a wide range of systems. The second is a set of mathematical theorems derived from unambiguous principles, that apply exactly to a well-defined set of systems. Evolutionary theory provides good examples of both of these foundations.

It is no accident that classical population genetics emerged soon after the rediscovery of Mendel's work in 1900. Mendel's laws have the appropriate combination of precision and generality to form the basis of a body of mathematical theory. The introduction of linkage and recombination fit right into the basic Mendelian framework, and the discovery made in the middle of the 20th century of the chemical basis of genetic transmission only substantiated and explained the basic patterns.

It is interesting to note that other models of inheritance were proposed in the 35 years between Mendel's work (Mendel 1865) and its rediscovery in 1900. One of these models, proposed by Galton (1898), posited that an individual's inherited makeup is a combination of separate contributions from parents, grandparents, and all of the individual's ancestors, each skipping over intervening generations. If this had turned out to be correct, subsequent evolutionary theory would probably not have gone very far, since understanding how a population changes could only be based on a detailed study of its entire history, rather than on its current state and a set of well-established rules.

The first half of this book is concerned with the mathematical analysis of what happens when we combine population level processes, such as selection, with the basic rules of transmission genetics. This kind of theory, focusing on genes and drawing on the mathematics of sampling, was the only well-developed mathematical evolutionary theory for most of the 20th century.

Of course, not all genes behave in a Mendelian fashion. Meiotic drive, in particular, subverts the evenness of transmission that Mendel observed. We will see in Chapter 2, though, that we can still use the formalism of population genetics to model meiotic drive because we understand the basic process that meiotic drive distorts. In analogous ways, classical population genetics has expanded to address a number of subjects, including the evolution of recombination and maternal inheritance, that would have confounded Mendel's experiments.

Some problems, though, never fit well into the framework of population genetics. Though modified Mendelian genetics provides a good foundation for one- and two-locus population genetics theory, it does not give us so solid a footing when we are concerned with phenotypic evolution. Phenotypes, both morphological and behavioral, do not generally exhibit the kinds of simple, regular patterns that we see in the transmission of alleles. The assumptions required to connect morphology to a well-behaved Mendelian process are so extensive and arbitrary that models based on such assumptions cease to have the foundational quality discussed at the beginning of this introduction.

One possible approach would be to search for "laws" of development that could substitute for Mendel's laws as the foundation of a general theory of morphological evolution. This approach appealed to many researchers, and a number of putative developmental or morphological "laws" were proposed. However, though there are many tantalizing generalizations about development which make evolutionary developmental biology an exciting field, there are no empirical rules that are either universal enough or precise enough to form the foundation of a truly general theory of morphological evolution.

Fortunately, there is another route to developing such a theory. As mentioned earlier, a body of theory can be built on a set of purely analytical results as long as those results are derived from unambiguous premises and apply exactly to a well-defined set of systems relevant to our interest. The beginning of such an analytical foundation for evolutionary theory was provided by Price (1970). In one sense, Price's theorem is just a formalization of the basic ideas of Darwin and Wallace. The premise is the same: A population of phenotypically variable organisms (or things of any sort) leave descendants bearing some resemblance to their parents. Add to this the fact that organisms with certain phenotypes leave more descendants than those with other phenotypes and you get evolution. Like Darwin and Wallace, Price assumed a causal connection between phenotype and survival or reproduction and he thus phrased his theory in terms of selection. However, we will see in Chapter 6 that the same mathematics describes drift if we allow the relation between phenotype and reproduction to be random.

Like the ideas of Darwin and Wallace, Price's theorem shifts back and forth between seeming so obvious that it must be universal, and so simple that it

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must be missing something. Simply looking at the theorem does not provide much insight beyond our intuitive understanding of selection. The value of Price's theorem lies not in the fact that it says anything shocking, but in the fact that it is an exact statement of the relationship between differential reproduction, inheritance, and evolution that was intuitive to Wallace and Darwin and to most biologists since. As such, this theorem provides the beginning of an evolutionary algebra; a set of mathematical results that by virtue of their exactness do for general phenotypic evolution what Mendel's work did for population genetics. This is what gives us a foundation from which to derive more elaborate theories and a standard against which we can check our results.

The theory of phenotypic evolution forms most of the second half of this book. In Chapter 6, we will discuss the basic theory and see how it unites the gene based theories that came before with the phenotype based theories that follow in subsequent chapters. In Chapter 8, we will add some further results to the algebra of evolution that are appropriate to the study of development.

Just saying that evolutionary theory has a solid analytical foundation is not the same as saying that the field of evolutionary theory is anywhere near complete. There are many areas within evolutionary biology that still consist largely of loosely connected models with no unifying theoretical framework. Expanding the general theory to include these will likely change how we think about the entire subject, but looking at the history of other sciences that use mathematical theory as a foundation, it seems likely that future developments in evolutionary theory will not discard the theoretical foundations discussed here, but will retain them as special cases and build upon them.

Selection on One Locus

The approach to modeling evolution that arose in the early 20th century in the work of Fisher, Wright, and Haldane involved assigning fitnesses to genotypes and then following evolution as a change in allele frequencies. This is by no means the only informative way to model evolution; we will encounter other approaches briefly in this chapter and in most of the second half of this book. Allele-based models are, however, a very useful way to investigate many evolutionary questions, and they form much of the basis of our understanding of the mechanics of evolution.

Because in this kind of model the things on which selection acts (genotypes) are not the same as the things whose frequency we are following (alleles), we need some way to relate allele frequencies to genotype frequencies. Such a relationship, given a set of assumptions, was provided independently by Hardy (1908) and Weinberg (1908, 1909).

Neither Hardy nor Weinberg was trying to provide a way to model evolution. Hardy was responding to the idea accepted by some biologists that dominance alone could drive evolution. Weinberg was concerned with the genetics of human traits, particularly the tendency to produce twins. He wanted to calculate the frequency of such traits under Mendelian inheritance, but with random mating which he saw as more prevalent in nature than the strict inbreeding used in Mendel's experiments (Weinberg 1908, translated in Boyer 1963).

Hardy and Weinberg independently showed that for an autosomal locus in a large population in the absence of mutation, migration, and selection, one generation of random mating produces a distribution of genotypes that

is a function solely of allele frequencies and does not change over subsequent generations if these conditions (including random mating) continue to hold.

Denoting allele i by A_i and its frequency by p_i , the Hardy-Weinberg (H-W) frequencies of genotypes are just the binomial frequencies:

$$\begin{aligned}\text{Freq}(A_i A_i) &= p_i^2 \\ \text{Freq}(A_i A_j) &= 2p_i p_j \quad (\text{for } j \neq i)\end{aligned}$$

Since this distribution of genotype frequencies is independent of dominance, it follows that dominance alone can not change genotype (and therefore phenotype) frequencies (this was Hardy's point). With random mating and allele frequencies equal in males and females, the H-W frequencies of genotypes are reached in one generation. (Note that two generations are required if males and females have different allele frequencies, and the H-W frequencies are approached gradually in the case of overlapping generations or with sex linkage.)

The significance of this work goes well beyond simply clearing up a misunderstanding about the role of dominance. By defining the relationship between allele frequencies and genotype frequencies, Hardy and Weinberg laid the foundation for a way of modeling evolution by tracking allele frequencies, rather than genotype frequencies, across generations. In this chapter, we focus on the most commonly used selection model in classical population genetics: selection acting on genotypes at one locus with two alleles. At the end of the chapter, we consider some extensions of this theory, including cases in which we cannot model evolution in terms of allele frequencies. We begin by considering the basic equations for change in allele frequency given selection on genotypes. In the following section, we will assume that we are dealing only with viability selection. This means that different genotypes have different probabilities of surviving from the zygote stage to the age of reproduction, and that these survival probabilities are causally determined by each genotype's corresponding phenotype (we will consider fertility selection later in this chapter).

Fitness

There is some variation in the literature in the use of the term **fitness**. Some authors treat it as a property of an individual; others, as a property of a genotype or an allele. We will see in later chapters that the most general and exact mathematical descriptions of evolution focus on the actual contribution of individuals to population growth. Accordingly, fitness (designated by capital W) will be defined as the reproductive contribution of an individual to the next generation. (In Chapter 10, where we consider selection acting at differ-

ent levels of organization, we will define fitness in an analogous way.) In population genetics, it is common to use genotypic fitness, which is the average fitness of all individuals in a population who have the same genotype. The genotypic fitness of genotype A_iA_j is represented with a lower case w_{ij} , understanding that this is simply the average value of W over all individuals with genotype A_iA_j .

In classical population genetics, it is assumed that selection acts on individuals based on their phenotype and that these phenotypes are determined by the individual's genotype. For this reason, the distinction between fitness as a property of individuals and fitness as a property of genotypes is rarely an issue. There is yet another kind of fitness, though, that we need to note. Since in this chapter we will study evolution by following allele frequencies over time, it will be useful to define the effective fitness, or **marginal fitness** of an allele. The marginal fitness of an allele A_i , designated w_i^* , is the average genotypic fitness over all the genotypes that contain allele A_i , weighted by the probability that a random A_i allele finds itself in that genotype (this idea will be clearer when we actually calculate marginal fitness values). We always identify marginal fitness values with an asterisk to remind us that these are average values assigned to a level of organization that is not the level at which selection is acting. (In Chapters 2 and 10 we encounter cases in which selection is acting directly at the level of alleles, in which case we drop the asterisk.)

Fitness and Population Growth

Genotypic fitness may be measured in absolute or relative terms. **Absolute fitness** is the expected number of surviving offspring produced by a parent with a particular genotype (alternately, the expected number of successful gametes). **Relative fitness** values are simply absolute fitness values scaled in some way. For example, dividing each by the largest absolute fitness value so that the most fit genotype has a relative fitness of 1. When studying evolutionary dynamics, we may use either absolute or relative fitness, for reasons discussed shortly. However, absolute fitness will make the results more biologically meaningful because it connects evolutionary theory with the ecological theory of population growth.

Consider growth of the population over one generation. Letting N_t denote population size at time t and assuming H-W frequencies among zygotes, there are p^2N_t individuals with genotype A_1A_1 , $2p(1-p)N_t$ with genotype A_1A_2 , and $(1-p)^2N_t$ individuals with genotype A_2A_2 . Given the absolute fitnesses of the different genotypes, we can write the population size in the next generation as:

$$N_{t+1} = p^2N_t w_{11} + 2p(1-p)N_t w_{12} + (1-p)^2N_t w_{22}$$

We can rewrite this as:

$$N_{t+1} = \bar{w}N_t$$

where:

$$\bar{w} = p^2w_{11} + 2p(1-p)w_{12} + (1-p)^2w_{22} \quad (1.1)$$

The term \bar{w} in Equation 1.1 is termed **mean population fitness**, since it is the sum of the genotypic fitnesses weighted by their corresponding genotype frequency. Equation 1.1 shows that \bar{w} also represents population growth over one generation in a discrete time model; this would not be the case if we used relative fitness values.

While the population dynamics equation presented above is a discrete time model, we also sometimes use continuous time models in which population growth is represented by per capita instantaneous growth rate, or $\bar{m} = 1/N dN/dt$ (\bar{m} is often denoted by “ r ” in the exponential population growth equation). Discrete time models may show very different kinds of behavior than continuous time models, especially if the per generation growth rate is large. If the growth rate is relatively small, though, continuous and discrete time models may be approximately equivalent, and we can find a relationship between discrete time growth rate, \bar{w} , and continuous time growth rate, \bar{m} , by equating the models for growth over a single generation:

$$N_{t+1} = N_t\bar{w} \approx N_t e^{\bar{m}} \Rightarrow \bar{m} \approx \ln(\bar{w})$$

So the per capita population growth rate used in most ecological theory (e.g., in the Lotka–Volterra equations) is the natural log of mean population fitness, as used in population genetics.

Since we have an ecological interpretation of \bar{w} , we wish to know how it changes with allele frequency. Differentiating Equation 1.1 with respect to p yields:

$$\begin{aligned} \frac{d\bar{w}}{dp} &= 2pw_{11} + 2w_{12} - 4pw_{12} - 2w_{22} + 2pw_{22} \\ &= 2[pw_{11} + (1-p)w_{12}] - 2[pw_{12} + (1-p)w_{22}] \end{aligned} \quad (1.2)$$

In this equation, we tacitly assumed that the w_{ij} values are not themselves functions of p . (If they were, we would have to differentiate them as well.) We are thus assuming that genotypic fitness is **frequency-independent**. If the fitnesses were functions of allele frequency, then we would say that fitness is **frequency-dependent**. We briefly consider the results of frequency-dependent selection later in this chapter and more extensively in Chapter 9.

Two Alleles with Viability Selection

In the simplest models, we assume a population with discrete, nonoverlapping generations. In these models, fitness measures contribution to the next generation. However, implicit in our model is the assumption that all differences in this contribution to the next generation involve differences in survivorship of individuals with different genotypes; we are thus studying the effects of **viability selection**. Differences in fitness may also result from differences in mating success among those individuals that survive to reproductive age (**sexual selection**) and differential offspring production given survival and mating (**fertility selection**). Later in this chapter, we learn that fertility selection requires a different modeling approach and can produce different evolutionary outcomes. Sexual selection is discussed in Chapters 2 and 7.

Consider a locus, A , with two alleles, A_1 and A_2 , in a large, randomly mating population in which Hardy-Weinberg frequencies apply among zygotes (though not among adults, due to selection). Let p represent the frequency of the A_1 allele in the population. The frequency of A_2 is then $1 - p$. In order to model selection, we assign fitness values to each of the three resulting genotypes, thus:

Genotype	Fitness	Frequency
A_1A_1	w_{11}	p^2
A_1A_2	w_{12}	$2p(1 - p)$
A_2A_2	w_{22}	$(1 - p)^2$

Now consider the change in frequency of the A_1 allele (i.e., the change in p over a generation). Though selection is acting on genotypes, we can use the assumption of random mating to calculate the **marginal fitness** of an allele by summing the fitnesses that it has in different genotypes, weighted by the probability that it would be found in those genotypes. Let w_1^* denote the marginal fitness of the A_1 allele. This is the average fitness of A_1 alleles. Using the notation $P(X)$ to mean "the probability of X ," we calculate marginal fitness as:

$$w_1^* = P(\text{paired with another } A_1)w_{11} + P(\text{paired with an } A_2)w_{12}$$

$$w_2^* = P(\text{paired with an } A_1)w_{12} + P(\text{paired with another } A_2)w_{22}$$

If we assume random mating, the probability of being paired with another allele of a particular type is simply the frequency of that type of allele, so we find:

$$w_1^* = pw_{11} + (1 - p)w_{12}$$

$$w_2^* = pw_{12} + (1 - p)w_{22} \tag{1.3}$$

We can now write mean population fitness in terms of marginal fitnesses as:

$$\bar{w} = pw_1^* + (1-p)w_2^* \quad (1.4)$$

From Equation 1.2 and Equation 1.3 we get:

$$\frac{d\bar{w}}{dp} = 2(w_1^* - w_2^*) \quad (1.5)$$

The term w_1^* is the expected number of descendants of an A_1 allele. We define n_1 as the actual number of A_1 alleles in generation t , n_2 as the number of A_2 alleles, and $n_T = n_1 + n_2$ as the total number of alleles in the population. The frequency of the A_1 allele is then $p = n_1/n_T$. In the next generation, the expected number of A_1 alleles will be $n_1w_1^*$, and the total number of all alleles will be $n_T\bar{w}$. We thus find the value of p in the next generation as:

$$p_{t+1} = \frac{n_1w_1^*}{n_T\bar{w}} = \frac{p_t w_1^*}{\bar{w}} \quad (1.6)$$

Equation 1.6 illustrates why we can scale fitness values any way we want; any scaling factor applied to all fitness values appears in both the numerator and the denominator of Equation 1.6 and will thus cancel out. To get the change in allele frequency over a generation we calculate $\Delta p = p_{t+1} - p_t$:

$$p_{t+1} - p_t = \frac{p_t w_1^*}{\bar{w}} - \frac{p_t \bar{w}}{\bar{w}} \Rightarrow \Delta p = \frac{p(w_1^* - \bar{w})}{\bar{w}} \quad (1.7)$$

Equations 1.6 and 1.7 are very general; they hold even when the population is not at H-W equilibrium, when there are more than two alleles present, and regardless of whether fitness is frequency-dependent or -independent. They follow as long as we define w_1^* as the expected number of descendant alleles from a given A_1 allele and \bar{w} as the weighted mean of these fitness values for all alleles. Note, though, that without H-W equilibrium we could not use Equation 1.3 to calculate w_1^* .

Returning to the case of two alleles, substituting Equation 1.4 into the numerator of Equation 1.7 gives:

$$\begin{aligned} \Delta p &= \frac{p(w_1^* - pw_1^* - (1-p)w_2^*)}{\bar{w}} \\ &= \frac{p(1-p)(w_1^* - w_2^*)}{\bar{w}} \end{aligned} \quad (1.8)$$

Frequency-Independent Selection

These results apply whether fitness is frequency-dependent or -independent, though they assume H-W frequencies among zygotes. Assuming that fitness is frequency-independent, we can combine Equation 1.5 and Equation 1.8 to get:

$$\Delta p = \frac{p(1-p)}{2\bar{w}} \frac{d\bar{w}}{dp} = \frac{p(1-p)}{2} \frac{d \ln(\bar{w})}{dp} \quad (1.9)$$

This is Wright's (1937) equation for an **adaptive landscape**. A number of important results are apparent simply from inspecting Equation 1.9. First, since $p(1-p)$ is always positive or zero, the direction of evolution (meaning whether p increases or decreases) is determined by the slope of the plot of \bar{w} [or $\ln(\bar{w})$] as a function of p . Recall that $\ln(\bar{w}) = \bar{m}$ is the instantaneous per capita growth rate of the population. We can thus think of a population as "climbing" a slope defined by population growth rate.

All stable equilibria are local maxima of \bar{w} and $\ln(\bar{w})$. Thus if stable equilibria exist (as we'll discuss soon), then frequency-independent selection on a single locus with two alleles and Hardy-Weinberg conditions tends to maximize population growth rate. This provides one rigorous formulation of the intuitive idea of **adaptation**: organisms evolve traits that maximize the ability of a population of those organisms to increase in size in its particular environment.

Figure 1.1 shows plots of mean population fitness for three different fitness regimes and above these are plots of p_{t+1} as a function of p_t for the same fitness regimes. Plotting p_{t+1} versus p_t is a standard way of determining the dynamic behavior of a one-dimensional discrete dynamical system. One can visually follow the dynamics from a given point by going vertically to the p_{t+1} line from that point, then horizontally to the diagonal (where $p_{t+1} = p_t$), and repeating the process. A point where the p_{t+1} curve touches the diagonal is an equilibrium, the stability of which is determined by the slope of the p_{t+1} line at the point of intersection. Just by inspecting Figure 1.1, it is clear that an equilibrium is unstable if $dp_{t+1}/dp_t > 1$ at the intersection point (see Figure 1.1C). In the next section, we will see that an equilibrium is also unstable if $dp_{t+1}/dp_t < -1$. Between these values, where $-1 < dp_{t+1}/dp_t < 1$, the equilibrium is stable. For frequency-independent selection on one locus with two alleles, there is always at least one stable point.

We can further understand Equation 1.9 by looking into what $p(1-p)/2$ represents. Consider a binomial sampling process, in which we draw N things (marbles for example) from a very large set of things ($\gg N$, so that we do not need to recalculate the frequencies after each draw) in which a proportion p has some property (p is the frequency of green marbles). If we repeated this exercise many times, the average frequency of green marbles in our sample would be p . The exact frequency in any one experiment, though, would vary.

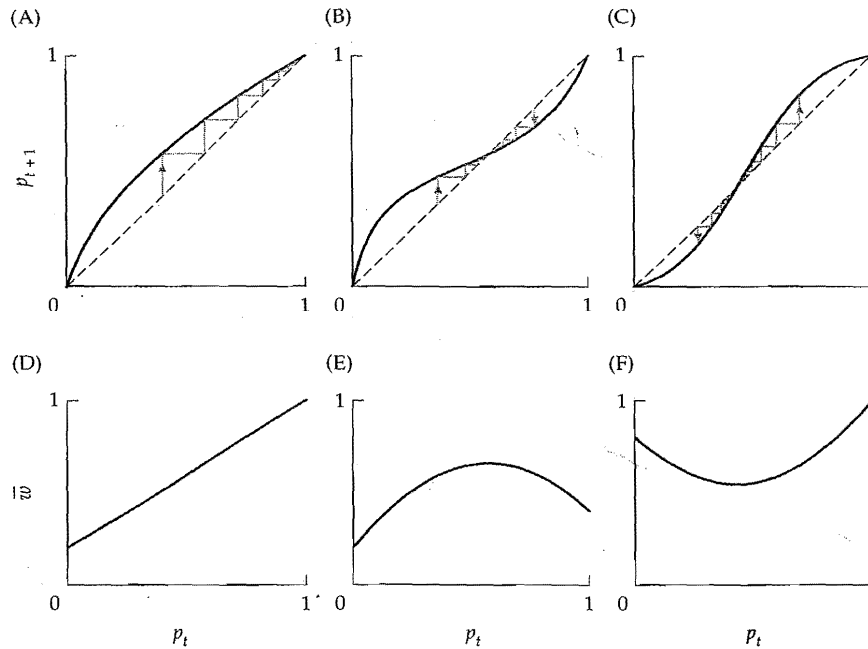


Figure 1.1 Change in allele frequencies and mean population fitness under frequency-independent selection. (A), (B), and (C) plot p_{t+1} against p_t . Points where this curve intersects the diagonal line (on which $p_{t+1} = p_t$) are equilibria, the stability of which is determined by the slope of p_{t+1} at the intersection point. The thin gray lines show trajectories approaching equilibrium in (A) and (B), and diverging from an unstable equilibrium in (C). The genotypic fitness functions corresponding to (A), (B), and (C) are shown in (D), (E), and (F), respectively.

It is a standard result from probability theory that the variance in the frequency of green marbles in our samples of N marbles, if we repeated the experiment many times, would be $p(1-p)/N$. In our biological model by assuming random mating, we are saying that producing an offspring genotype involves picking a sample of two alleles from a very large source (the entire gamete pool, which is much larger than the population size). The frequency of A_1 within a genotype can have one of three values: 0, for A_2A_2 genotypes; $1/2$, for A_1A_2 ; and 1, for A_1A_1 . The variance in these values (frequencies of A_1 within genotypes) is then $p(1-p)/2$.

We now see that Equation 1.9 says that the change in allele frequency is simply the variance in genotypes (the things that selection is acting on) multiplied by the slope of a fitness function and divided by mean population fitness. We will see later on that this basic format is very general, with Equation 1.9 being one special case.

Other biological results also follow from the form of the equations just given. We can see that both alleles will be maintained in the population only if the function \bar{w} has an internal peak (i.e., some local maximum of \bar{w} lies between zero and one). Now note that for the case of frequency-independent selection, \bar{w} is a quadratic function (see Equation 1.1), meaning that it contains terms involving p^2 but no higher powers of p . Quadratic functions can have at most one maximum or minimum. We thus know without any further calculations that there can be at most one equilibrium at which both alleles are maintained. We can also deduce the conditions under which such an equilibrium exists. From Equation 1.5 we know that $d\bar{w}/dp = 0$ only if $w_1^* = w_2^*$. This means that at any internal equilibrium it must be that:

$$\begin{aligned} pw_{11} + (1-p)w_{12} &= pw_{12} + (1-p)w_{22} \\ \Downarrow \\ p(w_{11} - w_{12}) &= (1-p)(w_{22} - w_{12}) \end{aligned}$$

Since both p and $1-p$ are positive, the bottom line of the above equation can only be true if either $w_{12} > (w_{11}, w_{22})$ or $w_{12} < (w_{11}, w_{22})$, meaning that the heterozygote is either more fit than both homozygotes or less fit than both of them. If the heterozygote is more fit than both homozygotes, then the interior equilibrium will be stable, maintaining both alleles in the population. If the heterozygote is the least fit genotype, then the interior equilibrium is unstable, and the outcome of evolution will depend on which side of this unstable equilibrium we start at.

Frequency-Dependent Selection

Before continuing with our analysis of Equation 1.9, it is worthwhile to consider what would happen if fitness were frequency-dependent. The most common sort of frequency-dependence occurs when an individual's fitness is determined in part by its interactions with other individuals; in such a case, the fitness of a genotype is dependent on the frequencies of that and other genotypes in the population. Recall that the assumption of frequency-independence first appeared in Equation 1.2 and became important in going from Equation 1.8 to Equation 1.9. With frequency-dependence, Equation 1.2 must be rewritten as:

$$\begin{aligned} \frac{d\bar{w}}{dp} &= 2pw_{11} + 2w_{12} - 4pw_{12} - 2w_{22} + 2pw_{22} \\ &\quad + p^2 \frac{dw_{11}}{dp} + 2p(1-p) \frac{dw_{12}}{dp} + (1-p)^2 \frac{dw_{22}}{dp} \end{aligned} \quad (1.10)$$

The new terms in Equation 1.10 are simply the derivatives of each genotypic fitness value with respect to p (which would be zero with frequency-independence) multiplied by the frequencies of the corresponding genotype. The sum of these is the average value of the derivative of genotypic fitness with respect to allele frequency, which we can write as $E(dw/dp)$, where $E()$ denotes expected value. We can thus rewrite Equation 1.10 (using Equation 1.3) as:

$$\frac{d\bar{w}}{dp} = 2(w_1^* - w_2^*) + E\left(\frac{dw}{dp}\right) \quad (1.11)$$

Combining this with Equation 1.8 gives:

$$\Delta p = \frac{p(1-p)}{2\bar{w}} \left[\frac{d\bar{w}}{dp} - E\left(\frac{dw}{dp}\right) \right] \quad (1.12)$$

Note that the term in brackets is the derivative of mean genotypic fitness minus the mean derivative of fitness.

Equation 1.12 allows us to draw an important conclusion concerning frequency-dependent selection. Since the mean derivative of genotypic fitness across all genotypes is not likely to be zero at exactly the same point where the derivative of mean population fitness is zero, we see that mean population fitness is no longer necessarily maximized once we have frequency-dependent selection. Thus, our appealing interpretation of “adaptation” as a trait that increases overall population growth rate need not increase over evolutionary time if the fitness of a genotype depends on the frequencies of other genotypes. Selection could, in principle, lead to a reduction in \bar{w} , even to the extent that the population goes extinct (this is sometimes called **Darwinian extinction**).

Figure 1.2 illustrates the fact that frequency-dependent selection need not maximize mean fitness, and further illustrates that there may not be any stable equilibria in a frequency-dependent system. In the example shown in Figure 1.2, changing a single parameter changes a stable equilibrium (see Figure 1.2A) into a limit cycle (see Figure 1.2B) and ultimately into a chaotic attractor (see Figure 1.2C). Note that in this case, how the population evolves is unrelated to the shape of the fitness landscape. The fluctuations in the cases of $s = 1$ and $s = 2$ take place in fitness valleys, and the points of maximum mean fitness are unstable.

Continuous Time

The derivation above is based on the idea that the population has discrete, nonoverlapping generations, so we can model evolution with a difference equation. This is the most common approach in population genetics, but

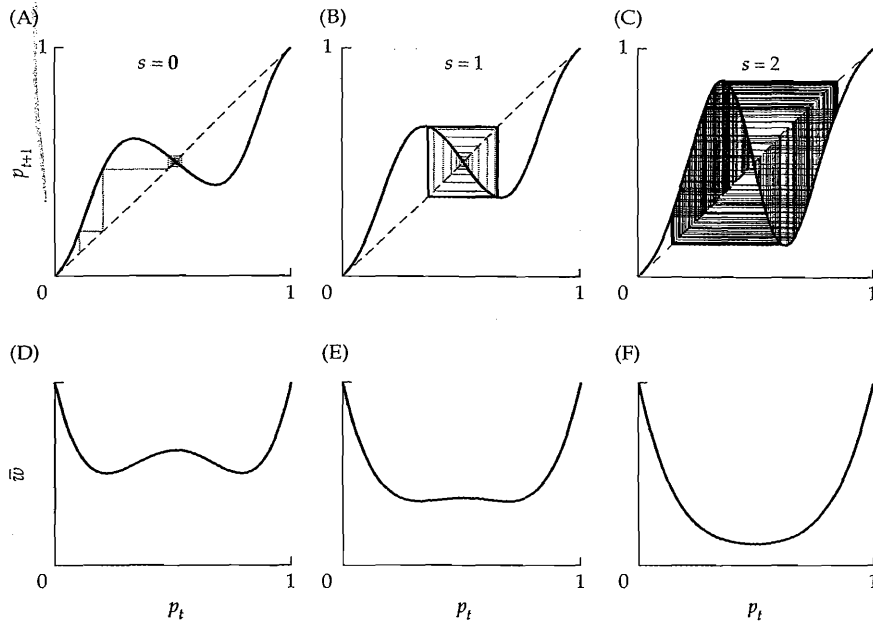


Figure 1.2 Evolution under frequency-dependent selection. Denoting the frequency of genotype $A_i A_j$ by γ_{ij} , the fitness functions shown are all of the form: $w_{11} = 1 - 3\gamma_{12} + 3\gamma_{22}$, $w_{12} = 1 - s\gamma_{12}$, $w_{22} = 1 - 3\gamma_{12} + 3\gamma_{11}$, for different values of the parameter s . In (A) and (B) the gray lines show the first 200 iterations from the starting point, with the following 200 iterations shown in black. The black lines thus show the asymptotic behavior of the system. (A) For $s = 0$, there is a stable point; (B) for $s = 1$, the system settles into a limit cycle; (C) for $s = 2$, the system shows chaotic fluctuations, which are aperiodic and would eventually fill in a region of the graph. (D), (E), and (F) show mean population fitness as a function of p for the systems shown in (A), (B), and (C), respectively.

sometimes it is more appropriate to use a continuous time model. It is important to note that the choice of a discrete or continuous time model can influence the results we get. For example, the nonequilibrium dynamics shown in Figure 1.2B and C are impossible in a one-dimensional continuous time model (dynamical systems theory states that a one-dimensional continuous dynamical system can exhibit only stable and unstable point equilibria, not limit cycles or chaos, as seen in Figure 1.2). Discrete and continuous time models are approximately equivalent only when the per generation rate of change is small.

In devising a continuous time model, we are implicitly assuming that generations overlap and that reproduction is always occurring. For some organisms, this is more realistic than the assumption of discrete, nonoverlapping generations, but it carries a cost for modeling; we can no longer assume that

genotype frequencies are in Hardy-Weinberg equilibrium. The following derivation thus makes no reference to genotype frequencies. We are also assuming that the population is not age structured (though a similar model can be used if the population is in stable age distribution).

Define n_i as the number of A_i alleles in the population and $n_T = \sum n_i$ as the total number of alleles of all types. The frequency of the i allele is just $p_i = n_i/n_T$. Instead of using the number of descendants to capture fitness, we focus on the rate of change in the numbers of each allele type in the population. More specifically, we are concerned with the per capita rate of change, which is just the rate of change divided by the actual number of alleles. This term is traditionally designated by m (after Malthus) and is defined for each allele as:

$$m_i = \frac{1}{n_i} \frac{dn_i}{dt} \quad (1.13)$$

If m_i remains constant over time, then the population of A_i alleles would grow or decline exponentially. We are concerned with looking over a very short time interval, dt , so it is reasonable to assume that m_i is constant over this interval, thus:

$$n_{i,t+dt} = n_{i,t} e^{m_i dt} \quad (1.14)$$

As with \bar{w} in the discrete time case, we define $\bar{m} = \sum p_i m_i$ as the mean per capita rate of increase. The following line of reasoning shows that \bar{m} is also the per capita rate of change of the entire population of alleles:

$$\frac{1}{n_T} \frac{dn_T}{dt} = \frac{1}{n_T} \sum_i \frac{dn_i}{dt} = \sum_i \frac{n_i}{n_T} m_i = \sum_i p_i m_i = \bar{m}$$

Thus, over a short interval, we can write $n_{T,t+1} = n_{T,t} e^{\bar{m} dt}$.

To get the rate of change in the frequency of a particular allele, we look over the very short time interval dt , in which the frequency of allele A_i changes from p_i to $(p_i + dp_i)$. We will treat dt and dp_i as differentials, and arrange them into a derivative. Using Equation 1.14, we can now write:

$$p_i + dp_i = \frac{n_i e^{m_i dt}}{n_T e^{\bar{m} dt}} = p_i \frac{e^{m_i dt}}{e^{\bar{m} dt}} = p_i e^{(m_i - \bar{m}) dt} \quad (1.15)$$

Dividing both sides by p_i and taking the natural log of both sides yields:

$$\ln \left(1 + \frac{dp_i}{p_i} \right) = (m_i - \bar{m}) dt \quad (1.16)$$

A useful fact is that if x is very small, $\ln(1+x) \approx x$. Since we are doing calculus and are thus interested in the limit as dp approaches zero, we can rewrite Equation 1.16 as:

$$\frac{dp_i}{p_i} = (m_i - \bar{m})dt \Rightarrow \frac{dp_i}{dt} = p_i(m_i - \bar{m}) \quad (1.17)$$

Note the similarity between Equation 1.17 and Equation 1.7 for the discrete time case. In fact, theorists often choose to use Equation 1.7 or Equation 1.17 based on whether it is most mathematically convenient to use a discrete time model or a continuous time model. As previously noted, this is only appropriate when the change across a discrete generation is small. For the remainder of this chapter, we will go back to using discrete time models, but continuous models will appear again in the discussion of two-locus theory.

Introducing Mutation

So far we have assumed that allelic variation is simply *there*, ignoring where it comes from. We now wish to introduce mutation into the model in order to address an important question: What happens when selection opposes an allele that keeps reappearing due to mutation? Or, more specifically: How much variation can be maintained by the balance between mutation and selection? Answering this last question involves more than just including mutation in our equations for Δp , it also involves studying the long-term interaction of selection and mutation.

The **mutation–selection equilibrium** is the expected frequency of an allele that is selected against but repeatedly reappears due to mutation. This equilibrium is a critical part of evolutionary theory because this balance of forces is one of the most important factors maintaining genetic variation within populations. In Chapter 7, we consider this equilibrium for many loci influencing a character. For now, we will derive the one-locus case, which is useful because it gives us some notion of the expected frequency of deleterious alleles.

Finding the mutation–selection equilibrium is an exercise in approximation and simplification of equations. In this case, it is traditional and convenient to describe fitness in terms of a selection coefficient, s , and a measure of dominance, h . We can then write relative genotypic fitnesses as:

Genotype	Fitness
A_1A_1	$1 - s$
A_1A_2	$1 - hs$
A_2A_2	1

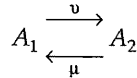
Given these fitness values and using the fact that $p^2 + 2p(1-p) + (1-p)^2 = 1$, we get:

$$\begin{aligned} \bar{w} &= 1 - sp^2 - 2hsp(1-p) \\ w_1^* &= 1 - sp - hs(1-p) \end{aligned} \quad (1.18)$$

The degree to which the presence of the deleterious allele reduces mean fitness below the maximum possible value is sometimes referred to as the **genetic load** on the population. When fitness is scaled so that the highest fitness is 1 (as we are doing in this case), the genetic load is $1 - \bar{w}$ or, in this case, $sp^2 + 2hsp(1-p)$:

$$\begin{aligned} \text{Genetic Load} &= 1 - \bar{w} \\ &= sp^2 + 2hsp(1-p) \end{aligned} \quad (1.19)$$

We introduce mutation by specifying the rate at which each allele mutates to the other:



The rate at which new A_1 alleles appear by mutation from A_2 is $\mu(1-p)$, and the rate at which they disappear due to mutation is νp . We find the frequency of A_1 in the next generation by combining these mutation rates with the fact that $p_{t+1} = p_t w_1^* / \bar{w}$ (see Equation 1.6) to get:

$$p_{t+1} = \frac{p(1-sp-hs+hsp)}{1-sp^2-2hsp(1-p)} + \mu(1-p) - \nu p \quad (1.20)$$

In order to simplify the subsequent calculations, we use the fact that we are solving for the equilibrium frequency of a deleterious allele, so the values of p that interest us are quite small. When we see a sum of two numbers with one number much smaller than the other, we can often ignore the smaller number without introducing much error into our calculations. (Note that this does not mean that we can ignore small terms elsewhere in our equations, such as when they multiply other terms.) In this case, since the equilibrium frequency for the allele is expected to be quite small, we can set $\bar{w} = 1$ without introducing much error. Using this approximation, we find the equilibrium frequency of the deleterious allele, \hat{p} , by setting $\hat{p}_{t+1} = \hat{p}_t$ to get:

$$\mu(1-\hat{p}) \approx s\hat{p}^2 + h\hat{p}(1-\hat{p}) \quad (1.21)$$

If s and \hat{p} are small and h is not too close to zero, then $h\hat{p}(1-\hat{p}) \gg s\hat{p}^2$. In this case we have $\mu \approx h\hat{p}$, so for the case in which A_1 is dominant ($h = 1$) or in which the heterozygote fitness is intermediate but not too close to that of the A_2A_2 homozygote, we find the mutation-selection equilibrium to be:

$$\hat{p} \approx \frac{\mu}{hs} \quad (1.22)$$

This approximation is obviously not valid if $h = 0$, so for a completely recessive allele, we use the fact that $\mu p \ll \mu$ and solve $\mu = sp^2$ to get:

$$\hat{p} \approx \sqrt{\frac{\mu}{s}} \tag{1.23}$$

We can check the accuracy of the approximations in Equations 1.22 and 1.23 against the numerical solution to Equation 1.21 (Figure 1.3). It turns out that Equation 1.23 is only accurate when there is complete dominance ($h = 0$). Otherwise, even if h is quite small, Equation 1.22 is the best approximation. Figure 1.3 also shows that reducing the amount of dominance (i.e., moving h away from 0) rapidly reduces the allele frequency at mutation-selection equilibrium. We thus expect most of the genetic variation maintained by mutation-selection equilibrium to involve recessive alleles.

For truly recessive mutations, given $s = 0.1$ (moderate selection) and a reasonable allelic mutation rate of 10^{-5} , Equation 1.23 gives an allele frequency at mutation-selection equilibrium of $\hat{p} = 0.01$; so we expect to find a fair number of such alleles segregating at a population of a few thousand individuals.

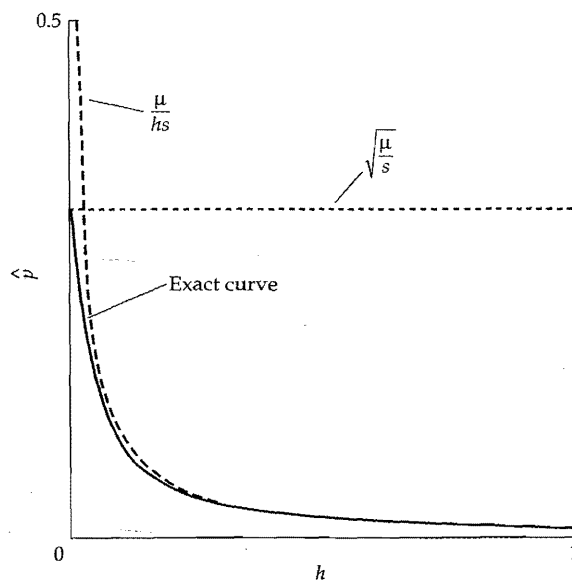


Figure 1.3 The solid curve shows the mutation-selection equilibrium for different values of h with $s = 0.001$. The dashed lines show the approximations based on Equations 1.22 and 1.23.

Mutational Load

Genetic load is the degree to which deleterious alleles cause mean population fitness to be reduced below its maximum value. This is the same as the degree to which population growth rate is reduced by the presence of a deleterious allele. Considering completely recessive alleles ($h = 0$) we can calculate the equilibrium **mutational load** (genetic load resulting from mutation to deleterious alleles) from Equation 1.19 (with $h = 0$) and Equation 1.23 as:

$$\text{Equilibrium load} = s\hat{p}^2 = s\left(\sqrt{\frac{\mu}{s}}\right)^2 = \mu \quad (1.24)$$

Thus, the load resulting from mutation to deleterious recessive alleles is simply the mutation rate to those alleles. This is surprising since s , the degree to which having two copies of the mutant allele reduces fitness, does not influence the degree to which having those alleles in the population reduces population growth rate. The reason for this is that the degree of selection against the mutant, s , influences both the load equation and the equilibrium allele frequency, and these influences are exactly complimentary. If we increase the damage done to an individual by the mutant allele, the mutation-selection equilibrium frequency of the deleterious allele decreases, so that the total loss to the population is unchanged.

The idea of genetic load appears repeatedly in evolutionary theory as a way to capture the degree to which some process reduces equilibrium fitness relative to what it would be if that process were not acting. Mutation is not the only process that does this. For example, consider a case in which $w_{11} = 1 - s$, $w_{12} = 1$, and $w_{22} = 1 - s$, so that the most fit possible population would consist of all heterozygotes. Mendelian segregation insures that, at equilibrium, each generation starts out with half homozygotes, so in reality $\bar{w} = 1 - s/2$. In this case, mean fitness is reduced by a factor of $s/2$, which is referred to as the **segregation load**. Segregation load plays an important role in some models for the evolution of sex (Feldman et al. 1997).

It is important to keep in mind that Equation 1.24 describes the mutational load *at equilibrium*. Unlike the Hardy-Weinberg frequencies with discrete generations, this equilibrium is not attained in one generation, but rather is approached more slowly. The next example shows that the interplay of selection with this gradual approach to equilibrium can produce a type of directionality in evolution.

The Evolution of Outcrossing

An interesting application of the idea of genetic load is the evolution of outcrossing versus selfing (Bernstein et al. 1985). All of the theory we have studied so far concerns randomly mating populations that are large. In other words, almost all reproduction involves outcrossing. In order to study selfing,

we need to recalculate the mutation–selection equilibrium and from this, the equilibrium genetic load.

First, we must find the mutation–selection equilibrium for a selfing population with the same fitness values that we used previously for an outcrossing population. In a population of selfing individuals Hardy-Weinberg frequencies do not apply. Instead, almost all individuals are homozygous and the frequency of the A_1A_1 genotype is the same as the frequency of the A_1 allele. Considering only recessive mutations (which make up the majority of deleterious alleles in a population, as indicated by Figure 1.3), we thus have:

Genotype	Frequency	Fitness
A_1A_1	p	$1 - s$
A_1A_2	0	1
A_2A_2	$1 - p$	1

From this we see that:

$$\begin{aligned} \bar{w} &= 1 - sp \\ \text{Load} &= sp \\ w_1^* &= 1 - s \end{aligned}$$

From Equation 1.6 and the mutation process described above, the value of p after a generation of selection and mutation is:

$$p_{t+1} = \frac{p_t(1-s)}{1-sp} + \mu(1-p) \tag{1.25}$$

At equilibrium, $p_{t+1} = p_t = \hat{p}$. Assuming that $sp \ll 1$, we have:

$$\hat{p} \approx \hat{p} - s\hat{p} + \mu - \mu\hat{p} \Rightarrow \hat{p} \approx \frac{\mu}{s + \mu} \tag{1.26}$$

If $s \gg \mu$ (which is reasonable, since μ is on the order of 10^{-6}), then the mutation–selection equilibrium for a selfing population is:

$$\hat{p} \approx \frac{\mu}{s} \tag{1.27}$$

Note that this is a much smaller number than the equilibrium for an outcrossing population (see Equation 1.23; recall that a small number squared is a much smaller number). We can now calculate the equilibrium genetic load for a selfing population as:

$$\text{Load} = s\hat{p} = \mu \tag{1.28}$$

Thus the equilibrium genetic load (the number of individuals lost in each generation due to the presence of deleterious mutations) is exactly the same for a selfing population as for an outcrossing one. The allele frequencies that underlie this load are different for the two reproductive systems though, so something has to change when a population switches between outcrossing and selfing.

First, consider a population of selfing individuals and the fitness of a rare outcrosser. The initial frequency of deleterious alleles is μ/s and the mean population fitness is $\bar{w} = 1 - \mu$. Rare outcrossers will get a fitness advantage from the masking of any deleterious alleles they may carry, since the odds are low that another individual would carry the same alleles. Thus, outcrossing increases in frequency (Figure 1.4B). At the same time, the frequency of dele-

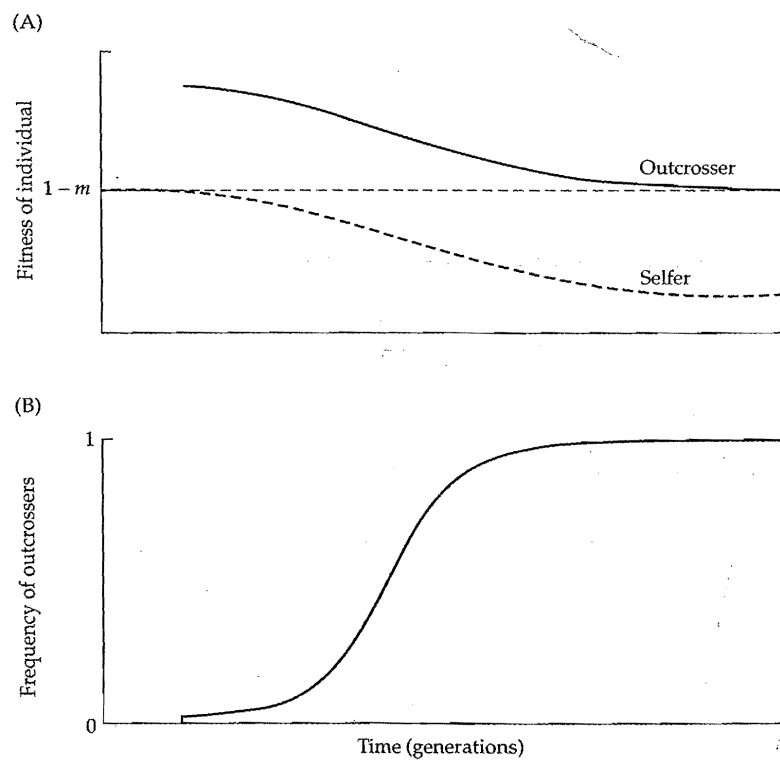


Figure 1.4 (A) Fitness of an individual that outcrosses (solid line) and an individual that self-fertilizes (dashed line) over time in a population that is initially all selfing until some outcrossers are introduced. (B) Frequency of outcrossers once introduced. Note that the fitness of outcrossers may continue to drop even after they have gone to fixation in the population.

terious alleles increases, since more and more of them are masked, and they approach the new mutation–selection equilibrium. At this new equilibrium, the mean fitness of outcrossers is exactly the same as was the mean fitness of selfers before the switch (see Figure 1.4A).

Now consider a rare selfer in a population of outcrossers. There will be an initial decrease in the fitness of any individual who does not outcross, since they will be expressing a relatively large number of deleterious alleles. If we forced the entire population to switch, there would be an initial reduction in \bar{w} , after which it would return to the same equilibrium value that it had before the switch.

All else held equal, it is therefore always easier to switch from selfing to outcrossing than the reverse, even though the equilibrium genetic loads are the same. Of course, all else is never held equal; there are advantages to selfing, such as not having to worry about finding a mate, that may outweigh the initial reduction in fitness. This will be particularly likely if there is little genetic variation to begin with. Nonetheless, the example provides a good illustration of the fact that it is sometimes easier to evolve in one direction than in another. It also shows that we may miss interesting evolutionary phenomena if we always assume that populations are at equilibrium.

Multiple Alleles

All of the discussion so far has assumed that there are only two alleles at a locus. Obviously, there can be (and usually are) more than two alleles of a particular gene in a population. When there are more than two alleles involved, we assign a different symbol for the frequency of each allele. We will use p_i to denote the frequency of allele A_i , keeping in mind that $\sum p_i = 1$. In the following derivation we consider only the frequency-independent case.

As before, the mean population fitness is the sum of genotypic fitnesses, weighted by the genotypic frequencies. With random union of gametes, this is just:

$$\bar{w} = \sum_i \sum_j p_i p_j w_{ij} \tag{1.29}$$

As in the two-allele case, the marginal fitness of allele A_i is found by summing over the fitnesses that it would have in each possible genotype, weighted by the probability that a given A_i allele will find itself in that genotype:

$$w_i^* = \sum_j p_j w_{ij} \quad \text{so} \quad \bar{w} = \sum_i p_i w_i^* \tag{1.30}$$

In a population of N diploid individuals, there are a total of $2Np_i$ alleles of type A_i , so $2Np_i w_i^*$ is the expected number of descendants of A_i alleles and

$2N\bar{w}$ is the expected total number of alleles in the next generation. From this we see that Equation 1.6 is unchanged; the value of p_i after one generation is:

$$p_{i,t+1} = \frac{p_{i,t}w_i^*}{\bar{w}} \quad (1.31)$$

In the two-allele case, we found that $d\bar{w}/dp$ determined the direction of evolution. With more alleles, \bar{w} is now a multivariate function, so we are concerned with the partial derivatives. If selection is frequency-independent, then differentiating Equation 1.29 and invoking Equation 1.30 yields:

$$\frac{\partial \bar{w}}{\partial p_i} = 2 \sum_j p_j w_{ij} = 2w_i^* \quad (1.32)$$

Note that what we are doing here is taking the derivative of \bar{w} with respect to p_i , holding all other allele frequencies constant (this is the definition of a partial derivative). Substituting Equation 1.32 into Equation 1.31 gives:

$$p_{i,t+1} = \frac{p_{i,t}w_i^*}{\bar{w}} = \frac{p_i}{2\bar{w}} \frac{\partial \bar{w}}{\partial p_i} \quad (1.33)$$

The change in the frequency of allele A_i is $p_{i,t+1} - p_{i,t}$ so:

$$\Delta p_i = \frac{p_i}{2\bar{w}} \frac{\partial \bar{w}}{\partial p_i} - \frac{p_i \bar{w}}{\bar{w}} \quad (1.34)$$

Using Equations 1.30 and 1.32, we can rewrite \bar{w} as:

$$\bar{w} = \sum_j \frac{p_j}{2} \frac{\partial \bar{w}}{\partial p_j} \quad (1.35)$$

Substituting this into the far right term in Equation 1.34 and rearranging yields:

$$\Delta p_i = \frac{p_i}{2\bar{w}} \left(\frac{\partial \bar{w}}{\partial p_i} - \sum_j p_j \frac{\partial \bar{w}}{\partial p_j} \right) \quad (1.36)$$

Equation 1.36 gives the change over a generation in the frequency of a particular allele. This equation is somewhat different than the equation presented in many texts, which follows Wright (1942) and involves a nonstandard interpretation of the partial derivative (Edwards 2000). The single allele equation has led to confusion (Edwards 2000) and seems inappropriate for an inherently multivariate problem. We thus focus on the vector of frequencies of all alleles, \vec{p} . When we write out Equation 1.36 for each allele, we find that the

resulting set of equations can be rewritten as a single equation involving vectors and matrices. For the three-allele case, we can write the vector of allele frequency changes as:

$$\Delta \vec{p} = \Delta \begin{bmatrix} p_1 \\ p_2 \\ p_3 \end{bmatrix} = \frac{1}{2\bar{w}} \begin{bmatrix} p_1(1-p_1) & -p_1p_2 & -p_1p_3 \\ -p_2p_1 & p_2(1-p_2) & -p_2p_3 \\ -p_3p_1 & -p_3p_2 & p_3(1-p_3) \end{bmatrix} \begin{bmatrix} \frac{\partial \bar{w}}{\partial p_1} \\ \frac{\partial \bar{w}}{\partial p_2} \\ \frac{\partial \bar{w}}{\partial p_3} \end{bmatrix} \quad (1.37)$$

The vector at the far right of Equation 1.37 is the gradient of mean fitness, written $\nabla \bar{w}$. The gradient vector has a straightforward geometric interpretation; it points in the direction of maximum increase of the function (in this case \bar{w}), and its length is the slope of the function in that direction.

The matrix on the right-hand side of Equation 1.37 also has a straightforward interpretation. We can name this matrix G , with diagonal elements $G_{ii} = p_i(1-p_i)/2$ and off-diagonal elements given by $G_{ij} = -p_i p_j / 2$, where $j \neq i$ (note that we are including the $1/2$ term in the elements of the matrix). Recall from our discussion of Equation 1.9 that the $p(1-p)/2$ term was the variance in genotypes, given that genotypes were quantified by the frequency of the A_1 allele within them (i.e., the values 1, $1/2$, and 0 correspond to genotypes A_1A_1 , A_1A_2 , and A_2A_2 , respectively). Now that we have more than two alleles, we need more ways to quantify genotypes. We define g_i as the frequency of A_i alleles within a genotype, so that genotype A_1A_2 has the values $g_1 = 1/2$, $g_2 = 1/2$, $g_3 = 0$ (half the alleles in the genotype are A_1 , half are A_2 , and none are A_3), and genotype A_3A_3 has the values $g_1 = 0$, $g_2 = 0$, $g_3 = 1$. Each genotype thus has a value for each of g_1 , g_2 , and g_3 . We know from our discussion of Equation 1.9 that the diagonal elements of G [the $p_i(1-p_i)/2$ terms] are the variances of the different genotypic values, with $G_{ii} = p_i(1-p_i)/2$ being the variance in the values of g_i within the population. We can show from the definition of covariance that the off-diagonal elements of G (the $-p_i p_j / 2$ terms) are the **covariances** between the different genotypic values. These are negative because increasing the frequency of one type of allele within a particular genome tends to reduce the frequencies of the others.

We can now rewrite Equation 1.37 in a form that is both compact and applies to any number of alleles at a locus:

$$\Delta \vec{p} = \frac{G}{\bar{w}} \nabla \bar{w} \quad (1.38)$$

Note that this equation has the same basic form as Equation 1.9, simply substituting the multivariate terms $\Delta \vec{p}$, G , and $\nabla \bar{w}$ for their univariate counterparts Δp , $p(1-p)/2$, and $d\bar{w}/dp$. Equations of the same form as Equation 1.38 will come up repeatedly later in the book, wherever we are concerned with the effects of selection on multiple traits.

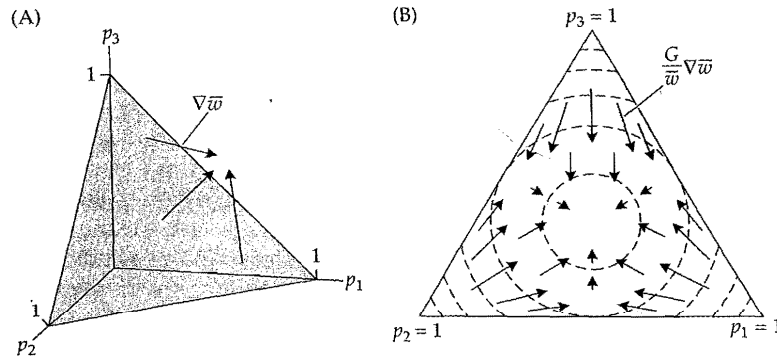


Figure 1.5 The geometry of Equation 1.38 for the case of three alleles. (A) The shaded triangle is the simplex defined by $p_1 + p_2 + p_3 = 1$. The arrows beginning on the simplex and extending off of it are the vectors $\nabla \bar{w}$ for different points on the simplex, given selection favoring heterozygotes ($w_{11} = w_{22} = w_{33} = 0.2$ and $w_{12} = w_{13} = w_{23} = 1$). (B) The simplex head on, with dashed lines showing curves of equal fitness and maximum fitness in the center. The arrows on the right figure are the vectors $\Delta \vec{p}$ defined in Equation 1.38. The labeled $\nabla \bar{w}$ vector is the labeled $\nabla \bar{w}$ vector from (A) multiplied by $G/(\bar{w})$.

If the vector of allele frequency changes were proportional to $\nabla \bar{w}$, then the population would always be moving towards a fitness maximum. This is not the case, however, since $\nabla \bar{w}$ is multiplied by the matrix G . Figure 1.5 illustrates the effect that this has on evolution. Because we are considering frequencies (p_i), populations are restricted to the subset of allele frequency space in which $\sum p_i = 1$. For the three-allele case, this is the triangular region shown in Figure 1.5A, referred to as a **simplex**.

Figure 1.5 shows the geometry of the three-allele case. The vectors $\nabla \bar{w}$ extend outside the simplex, but are projected back into it by $G/(\bar{w})$. A common approach to visualizing the three-allele case is to look only at the simplex, represented head on, as in Figure 1.5B. In this representation, each vertex is the point at which one allele is fixed and the others disappear. For internal points, the frequency of each allele is the distance of the point from the side opposite the vertex at which that allele is fixed. Such a representation of three frequencies is used in many areas of science; in genetics it is called a De Finetti diagram (De Finetti 1926) and was originally used to represent the three genotype frequencies in a two-allele model.

The dashed lines in Figure 1.5B are contours of equal mean fitness for the case in which all heterozygotes have high fitness and all homozygotes have low fitness (specifically, $w_{11} = w_{22} = w_{33} = 0.2$ and $w_{12} = w_{13} = w_{23} = 1$). The arrows are the vectors $\Delta \vec{p}$. Note that these vectors are not at right angles to the fitness contours, meaning that from most starting points, the population does not climb straight up to the point of maximum mean fitness. Thus, even with frequency-independence, a population does not climb straight up the fitness landscape.

Despite the fact that the population does not follow the fastest route uphill, it does end up at some local fitness maximum. The internal equilibria of Equation 1.38 (i.e., those that are not on a boundary of the simplex) are those points at which $\nabla \bar{w}$ points at right angles to the simplex. To see this, note that any vector pointing at right angles to the simplex is of the form (x, x, x) , with all elements of the vector being the same. In such a case, we can use Equation 1.36 to get:

$$\Delta p_i = \frac{1}{2\bar{w}} \left(p_i x - p_i x \sum_j p_j \right) \quad (1.39)$$

but since $\sum p_j = 1$, we get $\Delta p_i = 0$. A classic theorem in calculus derived by Lagrange states that, given a smooth function, f , in n -dimensional space, the maxima and minima of that function on a lower dimensional surface are points at which the vector ∇f is normal to the surface. Thus, points at which the gradient of mean population fitness are normal to the simplex are also points at which fitness is locally maximized or minimized on the simplex; in other words, the equilibria are local maxima or minima of \bar{w} , as in the two-allele case.

It should be noted that the treatment of the multiallelic case just presented is different from what is presented in many texts. Wright (1937, 1960) presented an equation for the multiallelic case that focused on a single allele frequency, p_i . This equation was basically the equation for the two-allele case (see Equation 1.9) with the derivative of mean fitness term, $d\bar{w}/dp$, replaced by a partial derivative, $\partial\bar{w}/\partial p_i$, in which the partial derivative was interpreted as the slope of the \bar{w} function in the direction of the vertex at which $p_i = 1$. This equation has been repeated, along with Wright's interpretation, in a number of texts. Unfortunately, Wright's interpretation of the partial derivative was incorrect; a fact pointed out by Edwards (2000), who derived a corrected version, analogous to our Equation 1.36, which lacks the intuitive clarity of the two-allele case. Our Equation 1.38 evades these problems of interpretation by describing the change in the vector of all allele frequencies rather than just one. Doing this preserves the conceptual form of the two-allele case and illustrates that sometimes taking the seemingly more complicated route—following the vector of all allele frequencies rather than a single frequency—yields a simpler and more intuitive result.

Fertility Selection

The models discussed up to this point assume that selection is manifested as differential survivorship, properly called **viability selection**. As we noted briefly, selection can also act through differential mating success (**sexual selection**) or differential reproductive output (**fertility selection**; sometimes called **fecundity selection**). At first glance, one might expect the evolutionary consequences of viability selection and fertility selection to be the same. After all, what ultimately matters is the number of surviving offspring, which could be thought of as (survivorship) \times (mating success) \times (fertility). In fact, modeling

fertility selection is much more difficult than modeling viability selection. Much of the theoretical work on fertility selection has involved special cases, such as when the reproductive output of a pair of individuals is the product of the contribution of the two. Nagylaki (1992) presents a number of different models involving fertility selection. Rather than go through these different cases, we will illustrate the approach to modeling fertility selection with an example that illustrates how it differs from the viability selection models we have been studying thus far.

What makes fertility selection different is the fact that, in a population of sexually reproducing organisms, an individual does not properly have fertility; a pair of individuals does. Thus, when modeling fertility selection, we assign fitnesses to mated pairs. This means that, for a one-locus two-allele system, we may need as many as nine different fitness values, corresponding to the nine different ordered pairs of genotypes. (We consider ordered pairs because females and males play different roles in reproduction, so an $A_1A_1\text{♀} \times A_2A_2\text{♂}$ cross may have a different fitness than an $A_2A_2\text{♀} \times A_1A_1\text{♂}$ cross.)

Fertility selection is a case of selection acting at a higher level of organization than the individual organism (i.e., a kind of group selection). This is no mere semantic or philosophical point; it means that we need to modify our modeling procedure. To illustrate how different fertility selection is from viability selection, consider a case in which individuals mate at random, so that the frequencies of pairs can be calculated from the frequencies of genotypes. We denote the frequency of the genotype A_iA_j by γ_{ij} and calculate the contribution of each kind of mating to each different genotype in the next generation. In Table 1.1 the numbers on the right are the proportions of offspring from each cross that have a particular genotype. The values under the A_1A_1 column indicate the proportion of offspring from each mating that are A_1A_1 .

TABLE 1.1 Table for calculating the contribution of each kind of mated pair to each genotype in the offspring

Cross	Fitness	Frequency	A_1A_1	A_1A_2	A_2A_2
$A_1A_1 \times A_1A_1$	w_{1111}	γ_{11}^2	1		
$A_1A_1 \times A_1A_2$	w_{1112}	$\gamma_{11}\gamma_{12}$	$\frac{1}{2}$	$\frac{1}{2}$	
$A_1A_2 \times A_1A_1$	w_{1211}	$\gamma_{12}\gamma_{11}$	$\frac{1}{2}$	$\frac{1}{2}$	
$A_1A_1 \times A_2A_2$	w_{1122}	$\gamma_{11}\gamma_{22}$		1	
$A_2A_2 \times A_1A_1$	w_{2211}	$\gamma_{22}\gamma_{11}$		1	
$A_1A_2 \times A_1A_2$	w_{1212}	γ_{12}^2	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{1}{4}$
$A_1A_2 \times A_2A_2$	w_{1222}	$\gamma_{12}\gamma_{22}$		$\frac{1}{2}$	$\frac{1}{2}$
$A_2A_2 \times A_1A_2$	w_{2212}	$\gamma_{22}\gamma_{12}$		$\frac{1}{2}$	$\frac{1}{2}$
$A_2A_2 \times A_2A_2$	w_{2222}	γ_{22}^2			1

The frequency values are based on the assumption of random mating. In each cross, the first genotype is the female, and the second is the male.

From this table we can find the genotype frequencies in the next generation as:

$$\begin{aligned}\gamma_{11,t+1} &= \frac{1}{\bar{w}} \left[\gamma_{11}^2 w_{1111} + \frac{1}{2} \gamma_{11} \gamma_{12} (w_{1112} + w_{1211}) + \frac{1}{4} \gamma_{12}^2 w_{1212} \right] \\ \gamma_{22,t+1} &= \frac{1}{\bar{w}} \left[\gamma_{22}^2 w_{2222} + \frac{1}{2} \gamma_{12} \gamma_{22} (w_{1222} + w_{2212}) + \frac{1}{4} \gamma_{12}^2 w_{1212} \right] \\ \gamma_{12,t+1} &= 1 - \gamma_{11,t+1} - \gamma_{22,t+1}\end{aligned}\quad (1.40)$$

Regardless of how alleles are distributed between genotypes, it must be the case that $p = \gamma_{11} + \gamma_{12}/2$, so we can always calculate the allele frequencies in any generation. This does not mean, however, that we can model fertility selection by following allele frequencies, because we cannot necessarily calculate genotype frequencies from allele frequencies. Though we are assigning fitnesses to mated pairs, random mating allows us to calculate the marginal fitness of each genotype, just as we calculated marginal fitnesses for alleles in Equation 1.3.

$$w_{ij}^* = \sum_k \sum_{m \geq k} \gamma_{km} w_{ijkm} \quad (1.41)$$

The marginal fitness of an allele is a bit harder to calculate, since we can not use the Hardy-Weinberg equilibrium to find the probability that an A_i allele is paired with an A_j allele (see Equation 1.3). In the most general case, we seek the conditional probability that a chosen A_i allele is paired with an A_j allele, written $P(A_j|A_i)$ —read “probability of A_j given A_i .” The frequency of the (ordered) $A_i A_j$ genotype is written $P(A_i \cap A_j)$ —read “probability of A_i and A_j .” These terms are related by a standard result from probability theory: $P(A_i \cap A_j) = P(A_j|A_i) \cdot P(A_i)$. Using this relation, and the fact that by definition, $P(A_i) = p$ and $P(A_i \cap A_j) = \gamma_{ij}$, we find the conditional probability that an A_i allele is paired with an A_j allele as:

$$P(A_j|A_i) = \frac{P(A_i \cap A_j)}{P(A_i)} = \frac{\gamma_{ij}}{p_i} \quad (1.42)$$

We can now find the marginal fitness of an allele as:

$$w_i^* = \sum_j \frac{\gamma_{ij}}{p_i} w_{ij}^* \quad (1.43)$$

Equation 1.43 contains both allele frequencies and genotype frequencies, suggesting that the marginal fitness of the allele is no longer just a function of allele frequency. To see some possible consequences of this, consider Figure 1.6, which plots the allele and genotype frequencies for the case in which a cross between the two different homozygotes has high fitness while all other

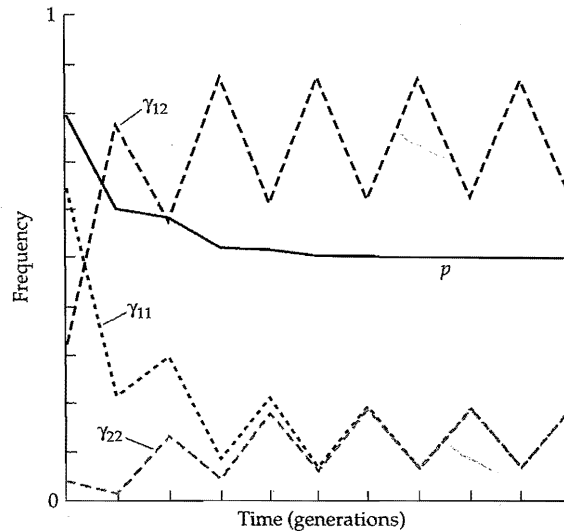


Figure 1.6 Frequencies of the three genotypes (dashed lines) and the A_1 allele (solid line) plotted over time for the case of fertility selection with $w_{1122} = 1$ and all other fitnesses = 0.025. The system starts out with Hardy-Weinberg frequencies and $p_0 = 0.8$.

crosses have very low fitness ($w_{1122} = 1$, all other fitnesses = 0.025). The system begins in H-W equilibrium with $p = 0.8$, $\gamma_{11} = 0.64$, $\gamma_{12} = 0.32$, and $\gamma_{22} = 0.04$.

Figure 1.6 illustrates two important points. First, genotype frequencies continue to fluctuate after the allele frequencies have reached a stable equilibrium. If we calculate the marginal fitnesses of the alleles, we find that at $p = 0.5$, $w_1^* = w_2^*$, so from the “gene’s eye view,” there is no selection going on. There is of course selection in this system—we built it in and it drives the fluctuations in genotype frequencies—but it is selection at a higher level of organization that is not always visible at the allelic level.

The second thing to note from Figure 1.6 is that although the initial genotype frequencies are the expected H-W values, they quickly diverge from this state, despite the fact that we stipulated that individuals randomly mate. This illustrates the difference between *random mating* and *random union of gametes*. In the model illustrated in Figure 1.6, the probability that an individual will mate with another having genotype $A_i A_j$ is just γ_{ij} . This is a reasonable definition of random mating, but it does not insure that the probability that an allele will be successfully paired with an allele of type A_j is p_j . This is because, although individuals randomly pair up, differential fertility makes some combinations of alleles more likely and others less likely than would be expected if alleles combined at random. Thus, fertility selection has the same effect as would nonrandom mating. In fact, we could model the evolutionary effects of assortative mating in a table similar to Table 1.1 simply by modifying the

terms in the "Frequency" column to represent the probabilities of different matings that take place (Crow and Kimura 1970).

Both fertility selection and nonrandom mating illustrate the significance of the assumption of Hardy-Weinberg frequencies described at the beginning of the chapter. Populations that attain Hardy-Weinberg equilibrium in one generation are much easier to model than those that do not. Furthermore, given H-W frequencies at the beginning of each generation, we can model evolution as though selection were acting on alleles, even though genotypes and their corresponding phenotypes are what really determine reproductive success. Note, though, that this is a fragile state of affairs; a slight change in the patterns of mating or a bit of fertility selection may require us to track higher level entities, such as genotypes or even mated pairs (if we combine fertility selection with nonrandom mating). This is not just a modeling issue, it represents the potential for new kinds of evolutionary dynamics.

Regression Interpretation

Though it is traditional to model one-locus dynamics purely in terms of allele frequency, it is also possible to focus on genotype frequencies. Since we started out by assigning fitness to genotypes, it seems reasonable to follow the units on which selection is acting directly. The drawback is that there are always more possible genotypes than alleles, making our calculations a bit more complicated. We shall see, though, that the result is actually simpler than what we derived when focusing on alleles.

First, we need a quantitative measure of genotype. For a two-allele case, we use the proportion of A_1 alleles in the genotype. As mentioned earlier, this quantity can take one of three values: 0 for A_2A_2 , $1/2$ for A_1A_2 , and 1 for A_1A_1 . We can now plot genotypic fitness against genotype. Figure 1.7 plots fitness as a function of genotype for a particular selection regime (in this example, $w_{11} = w_{22} = 0.4$ and $w_{12} = 1$) for different values of p . The size of the dots is proportional to the genotype frequencies, and the lines represent the least squares linear regression for each case (see Appendix A).

In Figure 1.7, the heterozygote is more fit than either homozygote (this is classically referred to as **overdominance**) and the two homozygotes are equally fit. Note that the regression line changes as the genotype frequencies (represented by the size of the dots) change.

In order to see exactly how this representation relates to our earlier results, we calculate the covariance between fitness and genotypic value (see Appendix A). We define genotypic value, g_{ij} , as the proportion of A_1 alleles in the genotype ($g_{11} = 1, g_{12} = g_{21} = 1/2, g_{22} = 0$) and γ_{ij} as the frequency of genotype g_{ij} . The marginal fitness of A_1 , for the two-allele case, is then:

$$w_1^* = \frac{\gamma_{11}}{p} w_{11} + \frac{\gamma_{12}}{p} w_{12} \quad (1.44)$$

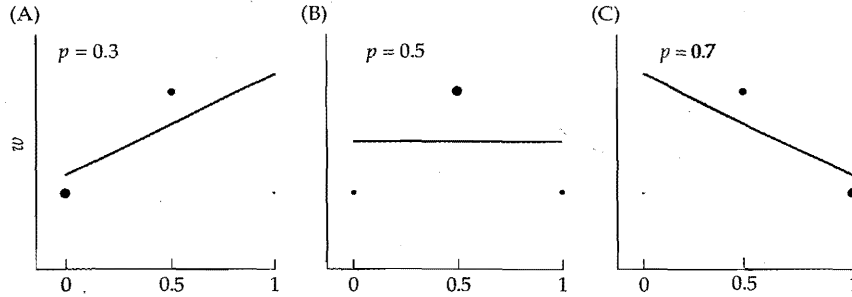


Figure 1.7 Regressions of fitness on genotype for the case of $w_{12} = 1$ and $w_{11} = w_{22} = 0.4$, given different allele frequencies (A, $p = 0.3$; B, $p = 0.5$; C, $p = 0.7$). The size of the dots indicates the relative frequencies of the three genotypes.

We can now write the covariance between fitness and genotype in terms of the same parameters that we used in the first part of the chapter. Keeping in mind that $\bar{g} = p$ and that $\sum \sum \gamma_{ij} w_{ij} = \bar{w}$, we find:

$$\begin{aligned}
 \text{cov}(w, g) &= \sum_i \sum_j \gamma_{ij} (g_{ij} - \bar{g})(w_{ij} - \bar{w}) \\
 &= \sum_i \sum_j \gamma_{ij} g_{ij} w_{ij} - \bar{g} \sum_i \sum_j \gamma_{ij} w_{ij} - \bar{w} \sum_i \sum_j \gamma_{ij} g_{ij} + \bar{g} \bar{w} \sum_i \sum_j \gamma_{ij} \\
 &= \sum_i \sum_j \gamma_{ij} g_{ij} w_{ij} - \bar{g} \bar{w} \\
 &= \gamma_{11} w_{11} + \gamma_{12} w_{12} - \bar{g} \bar{w} \\
 &= p(w_1^* - \bar{w})
 \end{aligned} \tag{1.45}$$

Substituting Equation 1.45 into Equation 1.7 and keeping in mind that $\bar{g} = p$ yields:

$$\Delta p = \Delta \bar{g} = \frac{1}{\bar{w}} \text{cov}(w, g) \tag{1.46}$$

Thus, the change in the mean genotype (or the change in p) over a generation is just the covariance between genotypic fitness and genotypic value, divided by mean population fitness. Equation 1.46, which makes no assumptions about frequency-dependence or about how alleles are arranged into genotypes, is a special case of the Price equation (Price 1970), (discussed in Chapter 6) and is even more general than is hinted at by the derivation presented here.

The same derivation can be applied to the continuous case, where we use the **Malthusian parameter**, m , rather than w . The exact same derivation as in Equation 1.45 yields $\text{cov}(m, g) = p(m^* - \bar{m})$, which when substituted into Equation 1.17 immediately yields the continuous time equation:

$$\frac{dp}{dt} = \frac{d\bar{g}}{dt} = \text{cov}(w, g) \quad (1.47)$$

We can also write Equation 1.46 in terms of the slope of the least squares linear regression of fitness on genotype β_{wg} by using the fact that $\text{cov}(x, y) = \beta_{yx} \text{var}(x) = \beta_{xy} \text{var}(y)$ and recalling that $\text{var}(\bar{g}) = p(1-p)/2$, we get:

$$\begin{aligned} \Delta p &= \Delta \bar{g} = \frac{1}{\bar{w}} \text{var}(g) \beta_{wg} \\ &= \frac{p(1-p)}{2\bar{w}} \beta_{wg} \end{aligned} \quad (1.48)$$

Note that because we are making no assumptions about frequency-dependence, Equation 1.48 generalizes both Equations 1.9 and 1.12. This illustrates that modeling evolution in terms of genotypes rather than alleles can actually lead to a simpler and more general result, though a result not better for all purposes. The insights concerning the effects of selection on population growth rate that were clear from Equations 1.9 and 1.12 are not obvious in Equation 1.46.

Additive Genetic Variance

The regression of fitness on genotype β_{wg} is related to another historically important idea, that of **additive genetic variance**. Additive genetic variance properly estimates the covariance between parents and their offspring, and can be defined for any measurable quantity, including a phenotypic trait or fitness. We will consider the general concept of additive genetic variance in Chapter 7. For the one-locus case, additive genetic variance in fitness, $V_A(w)$, measures the variance in the fitnesses predicted from a linear (additive) regression of fitness on genotype, as shown in Figure 1.8. Since variance measures squared deviations from the mean, we get this by multiplying the variance in genotypes by the squared slope of the regression line:

$$V_A = \frac{p(1-p)}{2} \beta_{w,g}^2 \quad (1.49)$$

Figure 1.8 shows what we are doing when we calculate additive genetic variance for a one-locus, two-allele system. $V_A(w)$ is the variance in fitness that

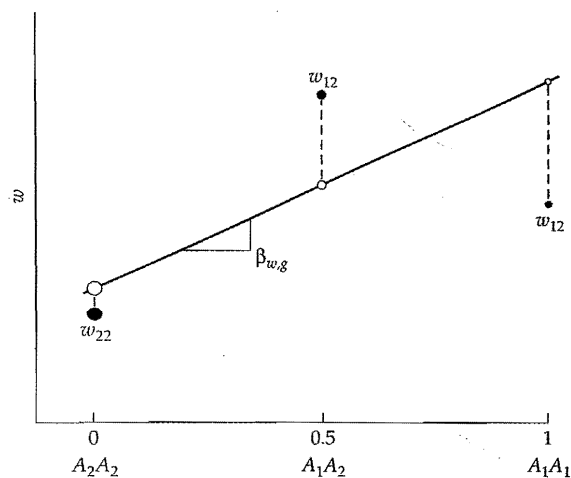


Figure 1.8 Calculation of additive genetic variance. The solid dots represent the actual genotypic fitnesses, and the line is the least squares linear regression through them. The open circles represent the estimates of genotypic fitnesses based only on the regression through them. $V_A(w)$ is the variance in these estimates.

we would have if the actual fitness values (solid dots) lay along the least squares linear regression line (open circles). $V_A(w)$ is clearly less than the actual variance in fitness, since the variance in the distribution of open circles [what $V_A(w)$ measures] is less than the variance in the distribution of filled circles (the actual variance in fitness). In this case, with one locus and no environmental effects, the residual variation is generally referred to as **dominance variance**.

We could also calculate the regression of fitness on the number of A_1 alleles in a genotype (0, 1, or 2) rather than their frequency (0, $1/2$, or 1). If we designate the regression of fitness on number of A_1 alleles by γ_{wa} , then $\beta_{wg} = 2\gamma_{wa}$ since we are just rescaling the abscissa by a factor of 2. The variance in the number of A_1 alleles in a genotype is $2p(1-p)$, so we could write the additive genetic variance as $V_A(w) = 2p(1-p)\gamma_{wa}^2$. This is the form found in many textbooks, it is equivalent to Equation 1.49 since $\beta_{wg}^2 = 4\gamma_{wa}^2$.

If $V_A(w)$ is equal to zero, then selection cannot change the allele frequency and thus there is no directional selection effect. An example of this is seen in Figure 1.7B, where the regression slope is zero. Note that in this case there is variance in fitness, and this fitness variation corresponds to genetic variation, but selection nonetheless does not alter allele frequencies.

It is important to understand that contrary to some statements in textbooks, having zero additive genetic variance does *not* mean that there is no selection acting. Nor does it mean that selection does not influence evolution. Zero additive genetic variance in fitness means only that directional selection

produces no change in the population mean. The example shown in Figure 1.7B is in fact a classic example of stabilizing (or balancing) selection. Stabilizing selection is an important evolutionary process, influencing such phenomena as the maintenance of genetic variation (see Chapters 5 and 7) and the evolution of developmental interactions (see Chapter 8).

Equations 1.48 and 1.49 are composed of many of the same parts as Equation 1.12, suggesting a relationship between $V_A(w)$ and Δp . Combining these equations, we find:

$$V_A(w) = \bar{w} \cdot \Delta p \cdot \beta_{wg} = \bar{w} \Delta p \left[\frac{d\bar{w}}{dp} - E\left(\frac{dw}{dp}\right) \right] \quad (1.50)$$

If Δp is small (or if $d\bar{w}/dp$ is approximately linear over the range Δp), then to a good approximation $\Delta p \cdot d\bar{w}/dp = \Delta\bar{w}$. Similarly, we can write $\Delta p \cdot E(dw/dp) = E(\delta w)$, where $E(\delta w)$ is the average change in genotypic fitness due to the effects of frequency-dependence. Using these new terms, we can rewrite Equation 1.50 as:

$$V_A(w) = \bar{w} \Delta\bar{w} - \bar{w} E(\delta w) \quad (1.51)$$

Rearranging Equation 1.51 yields:

$$\Delta\bar{w} = \frac{V_A(w)}{\bar{w}} + E(\delta w) \quad (1.52)$$

Equation 1.52 is one form of the **fundamental theorem of natural selection** derived by R. A. Fisher (1930), who thought this equation had great significance for our understanding of the process of evolution. In a sense, this equation partitions the change in mean fitness into two parts. The first part, $V_A(w)/\bar{w}$, can be thought of as the change resulting just from the effects of selection favoring the most fit individuals, holding all aspects of the environment (including allele frequencies) constant. The second part, $E(\delta w)$, is the change in fitness due to the fact that with frequency-dependence, genotypic fitnesses change as allele frequencies change. If selection is frequency-independent, then $E(\delta w) = 0$ and we need only consider the first term. Since $V_A(w)/\bar{w}$ is never negative (variance is never negative), we conclude that with frequency-independent selection on one locus with a constant environment, mean population fitness is never decreasing. Many textbooks consider only the first term on the right side of Equation 1.52.

Fisher referred to the second term on the right side of Equation 1.52 [$E(\delta w)$ in our notation] as the "deterioration of the environment." In the most general case, he saw this deterioration as resulting not only from frequency-dependence but also from coevolution of competitors and predators and from changes in the physical environment. (See Crow and Kimura 1970 for a derivation that focuses on factors other than frequency-dependence, but yields a result similar to Equation 1.52.)

Fitness Maximization, Optimization, and Potential Functions

Both Wright and Fisher knew that selection need not maximize mean population fitness. Nonetheless, both seemed concerned with phrasing their results in terms of something being maximized whenever possible. Wright was inspired by the possibility that Equation 1.9 suggested that evolution could be described in terms of a **potential function**. A potential function is a function that is minimized or maximized at equilibria and has the property that the rate of change of the system is proportional to the derivative of the function. According to Equation 1.9, given the assumptions of frequency-independence, random mating, etc., mean population fitness meets one of these criteria [though the $p(1-p)$ term prevents it from meeting the other]. Wright was attracted to the idea that evolution could be described in terms of such a function and tried to generalize Equation 1.9 by invoking a **fitness function** that is maximized even under frequency-dependent selection. Wright noted, however, that this fitness function which he defined by an integral equation, does not always exist. Even when Wright's fitness function does exist, it does not guarantee a stable equilibrium in discrete time models because of the overshoot effect that produces the unstable dynamics shown in Figure 1.2.

Fisher's fundamental theorem represents a different approach; it essentially identifies the component of evolution that involves fitness maximization and treats this separately from everything else (the deterioration of the environment). This particular way of decomposing the evolutionary process has not been widely used for modeling purposes (though Frank and Slatkin [1992] find an application), but Fisher considered it to be very significant for our understanding of the nature of evolution. In particular, he emphasized the similarities between the fundamental theorem and the second law of thermodynamics, which also involves an aggregate property of a system that increases with time in the absence of outside influences (entropy) (Fisher 1958, page 44). The problem with this comparison is that there is no evolutionary analog of a "closed system" in thermodynamics (which allows no energy exchange with the outside and within which entropy is nondecreasing). If the only things that could prevent the steady increase in \bar{w} were environmental changes external to the population itself, then we could (in principle) hold the external environment constant and have a system in which \bar{w} is nondecreasing. However, the fact that the "deterioration of the environment" includes changes in allele frequencies brought about by the selection process within a population implies that there is no evolutionary analog of a thermodynamic closed system.

In fact, there is no general potential function underlying evolution. All that we need to do in order to demonstrate this is find a case in which, under selection alone, the allele frequencies in a population do not settle down to a stable point, but rather continue changing forever. We have already seen an

example of this in Figure 1.2. The fact that selection can result in limit cycles (see Figure 1.2B), in which the population repeatedly revisits the same states in alternate generations, shows that we can not model all evolution in terms of some function that increases every generation. Note that this is not a contradiction of the fundamental theorem, since the frequency-dependence that drives the fluctuations is part of the $E(\delta w)$ term in Equation 1.52. Though evolutionary theory is not built on the idea that any quantity is necessarily maximized, the idea that there is such a quantity remains one of the most widely held popular misconceptions about evolution.

