

NATURAL SELECTION

So far in this book the term "natural selection" has been used in its informal, intuitive sense, the sense used by Darwin over a century ago (1872) in *The Origin of Species*:

Owing to this struggle for life, variations, however slight and from whatever cause proceeding, if they be in any degree profitable to the individuals of a species, in their infinitely complex relations to other organic beings and to their physical conditions of life, will tend to the preservation of such individuals, and will generally be inherited by the offspring. The offspring, also, will thus have a better chance of surviving, for, of the many individuals of any species which are periodically born, but a small number can survive. I have called this principle, by which each slight variation, if useful, is preserved, by the term Natural Selection.

In this section, it is necessary to become more precise, more quantitative. First, it is important to note that natural selection is the driving force of evolution, the process that leads to greater adaptation of organisms to their environment. Subpopulations of a species are bound to live in somewhat different environments. If the environments are substantially different, natural selection, through the effect of increasing the adaptation of each subpopulation to its own environment, will promote genetic divergence of the subpopulations. If the environments are substantially similar, to consider the other extreme, natural selection, again through the effect of increasing adaptation, will tend to prevent genetic divergence of subpopulations. Random genetic drift enhances subpopulation divergence, whereas migration hinders it. Therefore, in any actual species, genetic variation produced by mutation is organized, maintained, eliminated, or dispersed among subpopulations according to the complex balance between natural selection, migration, and random genetic drift.

The Meaning of Fitness

Natural selection acts on phenotypes, not on genotypes, and it acts on the whole phenotype as determined by many genes and countless environmental factors in one of three fundamentally different ways. These are illustrated in Figure 15. When selection favors phenotypes at one extreme of the range, it is called **directional** selection (panel a). Selection favoring intermediate phenotypes is **stabilizing** or **normalizing** selection (panel b). Selection simultaneously favoring phenotypes at both extremes of the range is **disruptive** selection (panel c). Directional and stabilizing selection are discussed in detail

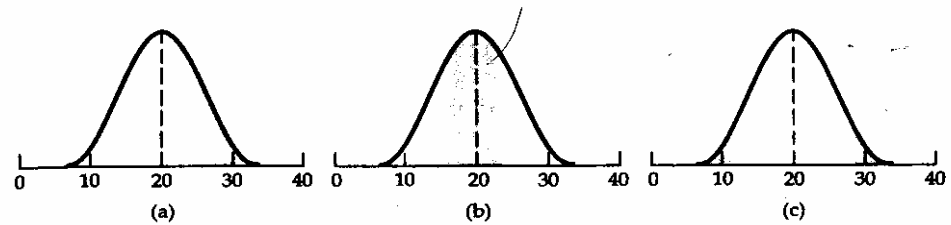


Figure 15. Three fundamentally different modes of selection. The curve represents the distribution of phenotypes in the population. In each case, the shading designates the individuals favored by natural selection. (a) Directional selection. (b) Stabilizing selection. (c) Disruptive selection.

in Chapter 4. Although selection occurs on the phenotype as determined by many genes, for purposes of exploring the consequences of selection, it is easiest to focus on how selection changes the allele frequencies of a single gene.

The simplest way to think about selection is in terms of **viability**, which refers to the probability that an individual survives from fertilization to reproductive age. For example, genotypes *AA*, *Aa*, and *aa* may have probabilities of survival (viabilities) of 0.75, 0.75, and 0.50, respectively. We call 0.75, 0.75, and 0.50 the **absolute viabilities** of the genotypes. However, selection depends only on the relative magnitudes of the viabilities, so it is often convenient to measure the viabilities relative to one another. In the above example, the relative viabilities of *AA*, *Aa*, and *aa* are $(0.75)/(0.75)$, $(0.75)/(0.75)$, and $(0.50)/(0.75)$, or 1.0, 1.0, and 0.67, respectively. Of course, we could just as well write the relative viabilities as $(0.75)/(0.50)$, $(0.75)/(0.50)$, and $(0.50)/(0.50)$, or 1.5, 1.5, and 1.0, respectively, the only difference being in which genotype is regarded as the standard. *Usually, the relative viabilities are calculated so that the largest relative viability equals 1.0.* Relative viabilities (such as the numbers 1.0, 1.0, and 0.67 in the preceding example) are called the **relative fitnesses** of the genotypes if the genotypes are otherwise equally capable of reproduction.

In certain instances, an approach to selection based on individual genotypes, analogous to viability differences, can also be used for fertility differences. However, this approach requires that the overall fertility of any mating pair be equal to the product of the fertilities of the individual genotypes in the mating pair. When this multiplication rule does not hold, models of selection with fertility differences become rather complex (see Ewens 1979; Clark and Feldman 1986).

Selection in Haploids

Selection in its simplest form occurs in haploid organisms such as bacteria. Consider two competing bacterial genotypes A and a with relative viabilities w_1 and w_2 , respectively. Suppose that in generation t the frequencies of A and a are p_t and q_t , respectively, with $p_t + q_t = 1$. In the absence of selection, the frequencies remain the same through time, so we have $p_t/q_t = p_{t-1}/q_{t-1} = p_0/q_0$ for any value of t . With selection, a proportion w_1 of the A genotypes survive, and a proportion w_2 of the a genotypes survive, so $p_1/q_1 = p_0 w_1 / q_0 w_2 = (p_0/q_0)(w_1/w_2)$. The relation between p_2/q_2 and p_1/q_1 is the same as that between p_1/q_1 and p_0/q_0 , so $p_2/q_2 = (p_1/q_1)(w_1/w_2) = (p_0/q_0)(w_1/w_2)^2$. Continuing by generations in this manner, we have

$$p_t/q_t = (p_0/q_0)(w_1/w_2)^t \quad (2.22)$$

or

$$\ln(p_t/q_t) = \ln(p_0/q_0) + t \ln(w_1/w_2) \quad (2.23)$$

Problem 18 gives an example of the use of Equation 2.23.

PROBLEM 18

The *gnd* gene in *E. coli* codes for the enzyme 6-phosphogluconate dehydrogenase (6PGD), which is used in the metabolism of gluconate but not ribose. When otherwise genetically identical strains containing the naturally occurring alleles *gnd*(RM77C) and *gnd*(RM43A) were placed in competition in chemostats for gluconate or ribose, the data below were obtained, in which p denotes the frequency of the strain containing *gnd*(RM43A) (Dykhuizen and Hartl 1980; Hartl and Dykhuizen 1981). Estimate the fitness of the strain containing *gnd*(RM77C) relative to that containing *gnd*(RM43A) under the two growth conditions.

Genotype of strains	Medium	p_0	p_{35}
<i>gnd</i> (RM43A) versus <i>gnd</i> (RM77C)	gluconate	0.455	0.898
<i>gnd</i> (RM43A) versus <i>gnd</i> (RM77C)	ribose	0.594	0.587

ANSWER In gluconate medium, $\ln(0.898/0.102) = \ln(0.455/0.545) + [\ln(w_1/w_2)](35)$, so $\ln(w_1/w_2) = -0.0673$ and $w_1/w_2 = 1.0696$. Setting $w_1 = 1$ gives $\langle w_2 \rangle = 0.935$ as the estimated relative fitness of the *gnd*(RM77C) strain. In ribose medium, $\langle w_2 \rangle = 1.001$, which is not significantly different from 1.0.

Selection in Diploids

In diploids, the consequences of selection are most conveniently explored using the simple Hardy-Weinberg model in Chapter 1, but incorporating selection by permitting the fitnesses of the genotypes to differ. Selection is assumed to occur on the diploid genotypes, not on the gametes, and segre-

gation is assumed to be Mendelian. For the relative fitnesses of AA , Aa , and aa , we use the conventional symbols w_{11} , w_{12} , and w_{22} , respectively. As noted earlier, the relative fitnesses are most easily interpreted in terms of viability, but, in certain cases, they can also be interpreted in terms of fertility.

If we assume that the allele frequencies of A and a are p_t and q_t , respectively, in generation t , then it is straightforward to derive expressions for p_{t+1} and q_{t+1} , which are the corresponding allele frequencies in the next generation. The subscripts t and $t+1$ are cumbersome to carry along in equations, so we will use the symbols p and q for p_t and q_t , and the symbols p' and q' for p_{t+1} and q_{t+1} .

In terms of p and q , the genotype frequencies of AA , Aa , and aa among newly fertilized eggs in generation t are given by p^2 , $2pq$, and q^2 , respectively. By definition, newly fertilized eggs survive in the ratio $w_{11}:w_{12}:w_{22}$ for AA , Aa , and aa , so the ratio of $AA:Aa:aa$ among adults is

$$p^2 w_{11} : 2pq w_{12} : q^2 w_{22}$$

The ratio of $A:a$ in gametes of the next generation is therefore

$$p^2 w_{11} + 1/2(2pq w_{12}) : 1/2(2pq w_{12}) + q^2 w_{22}$$

(The $1/2$ s enter the ratio because Aa heterozygotes produce $1/2 A$ and $1/2 a$ gametes from Mendelian segregation.) The ratio of $A:a$ in gametes readily simplifies to

$$p(pw_{11} + qw_{12}) : q(pw_{12} + qw_{22})$$

To obtain the gametic frequencies from the gametic ratio, one must divide each value in the ratio by the overall sum, conventionally denoted \bar{w} , which equals

$$\bar{w} = p^2 w_{11} + 2pq w_{12} + q^2 w_{22} \quad (2.24)$$

Biologically speaking, the quantity \bar{w} is simply the average fitness of the individuals in the population. Dividing the gametic ratio by \bar{w} gives the gametic frequencies in generation $t+1$, namely

$$p' = \frac{p(pw_{11} + qw_{12})}{\bar{w}} \quad (2.25)$$

$$q' = \frac{q(pw_{12} + qw_{22})}{\bar{w}}$$

It is often useful to know $p' - p$, usually symbolized Δp , which is the difference in allele frequency which results from one generation of selection. In this case,

$$\Delta p = \frac{pq[p(w_{11} - w_{12}) + q(w_{12} - w_{22})]}{\bar{w}} \quad (2.26)$$

At this point, an example of the use of these equations is in order. We will use data of Teissier (1942) on the change in the frequency of the *Cy* (*Curly wings*) allele in a laboratory population of *Drosophila melanogaster*, which are plotted in Figure 16. The *Cy* allele is lethal when homozygous, so $w_{11} = 0$. The data in Figure 16 pertain to the frequency of *Cy* heterozygotes, but because *Cy/Cy* genotypes do not survive, the allele frequency p of *Cy* equals one-half the frequency of *Cy/+* adults. The points in Figure 16 are each separated by one generation, and the initial generation has a frequency of *Cy/+* adults of 0.67, so $p = 0.335$ and thus $q = 0.665$. Wright (1977) has studied these data and concluded that $w_{12} = 0.5$ for *Cy/+* genotypes, relative to a value of $w_{22} = 1.0$ for *+/+* genotypes. Substituting these values for p , q , w_{11} , w_{12} , and w_{22} into Equation 2.25 for p' yields

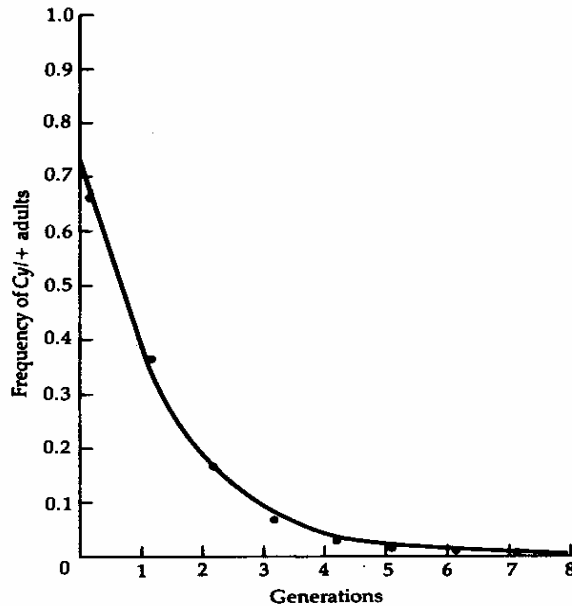


Figure 16. Change in frequency of adult *Drosophila melanogaster* heterozygous for the dominant mutation *Cy* (*Curly wings*) in an experimental population. *Cy/Cy* homozygotes are inviable, and the curve represents the theoretical change in frequency when the ratio of viabilities of *Cy/+* to *+/+* is 0.5:1. (Data from Teissier 1942. The fitness value of 0.5 was estimated by Wright 1977.)

$$p' = \frac{(0.335)[(0.335)(0) + (0.665)(0.5)]}{(0.335)^2(0) + 2(0.335)(0.665)(0.5) + (0.665)^2(1.0)} = 0.168$$

Thus, the predicted frequency of *Cy/+* adults in generation 1 is $2p' = 0.336$, which is reasonably close to the observed value of 0.368.

Assuming a value of $p = 0.168$ for the frequency of the *Cy* allele in generation 1 in the population in Figure 16, calculate the expected frequency of *Cy/+* heterozygotes in generation 2.

PROBLEM
19

ANSWER In this example, $p' = (0.168)[(0.168)(0) + (0.832)(0.5)] / [(0.168)^2(0) + 2(0.168)(0.832)(0.5) + (0.832)^2(1.0)] = 0.084$, so the expected frequency of *Cy/+* adults is $2p' = 0.168$. This is very close to the observed value of 0.165. The theoretical curve in Figure 16 was calculated using this generation-by-generation procedure.

We may be excused a slight digression to point out that it is sometimes convenient to think in terms of the **marginal fitnesses** of the *A* and *a* alleles, which equals the average fitness of all genotypes containing *A* or *a*, respectively, weighed by their relative frequency and the number of *A* or *a* alleles they contain. For example, *A* alleles occur in *AA* and *Aa* genotypes with relative probabilities p and q , and therefore the marginal fitness \bar{w}_1 of *A*-containing genotypes equals $pw_{11} + qw_{12}$. Similarly, the marginal fitness of *a*-containing genotypes is $\bar{w}_2 = pw_{12} + qw_{22}$. Equation 2.25 for p' therefore becomes $p' = p\bar{w}_1/\bar{w}$, and Equation 2.26 becomes $\Delta p = p(\bar{w}_1 - \bar{w})/\bar{w}$. This expression makes it clear that any allele increases in frequency if the marginal fitness of genotypes containing the allele (\bar{w}_i) is greater than the average fitness of the population (\bar{w}). This approach also generalizes nicely to multiple alleles: for an allele with frequency p_i and marginal fitness \bar{w}_i , the change in frequency in one generation equals $\Delta p_i = p_i(\bar{w}_i - \bar{w})/\bar{w}$.

Time Required for Changes in Gene Frequency

Having derived Equation 2.25 for p_{t+1} in terms of p_t (i.e., p' in terms of p), it is an appropriate next step to express p_t in terms of p_0 , as we did earlier in this chapter for the analogous equations involving mutation and migration. Unfortunately, in the case of selection, a simple formula for p_t in terms of p_0 does not exist. However, if w_{11} , w_{12} , and w_{22} are not too different, then \bar{w} is close to 1.0, and the expression for Δp can be used to derive approximations. Obtaining the approximations requires calculus (the idea is to treat Δp as the derivative (dp/dt) and then to integrate), but for our purposes, only the final

answers are of interest. The answers are most easily presented if we change the symbolism somewhat. For this purpose, we rewrite the fitnesses of the genotypes as follows:

$$\begin{aligned} w_{11} &= 1 \\ w_{12} &= 1 - hs \\ w_{22} &= 1 - s \end{aligned} \quad (2.27)$$

Use of the h and s symbols for the fitnesses in Equation 2.27 has the advantage of making the gene effects and dominance explicit. If s is positive and h is nonnegative, the type of selection is directional selection, and A is the favored allele. In this context, s is called the **selection coefficient** against the aa genotype, and h is called the **degree of dominance** of the a allele. For example, when $h = 0$, the fitnesses of AA , Aa , and aa are 1, 1, and $1 - s$, respectively, and a is recessive to A . Alternatively, when $h = 1$, the fitnesses are 1, $1 - s$, and 1, respectively, and a is dominant to A . In terms of the selection coefficient and the degree of dominance, an approximate expression for Δp can be derived from Equation 2.26 as

$$\Delta p = pqs[ph + q(1 - h)] \quad (2.28)$$

where the approximation in Equation 2.28 assumes that s and hs are sufficiently small that \bar{w} is close to 1.0.

The following equations give p_t in terms of p_0 in three cases of importance (for methods of derivation, see Hartl 1980):

1. A is a favored dominant. In this case, $h = 0$, so $\Delta p = pq^2s$, and

$$\ln(p_t/q_t) + 1/q_t = [\ln(p_0/q_0) + 1/q_0] + st \quad (2.29)$$

2. A is favored and the alleles are additive in their effects on fitness. Additive effects on fitness means that the fitness of the heterozygote is exactly intermediate between the fitnesses of the homozygotes, so in the additive case, $h = 1/2$. (Some authors refer to the additive case as *semidominance*, others use the term *genic selection*.) When $h = 1/2$, then $\Delta p = pqs/2$, and

$$\ln(p_t/q_t) = \ln(p_0/q_0) + (s/2)t \quad (2.30)$$

Note that Equation 2.30 for additive alleles is similar in form to Equation 2.23 for haploid selection, when $w_1 = 1$ and $w_2 = 1 - (s/2)$ and s is small.

3. A is a favored recessive. In this case, $h = 1$, so $\Delta p = p^2qs$, and

$$\ln(p_t/q_t) - 1/p_t = [\ln(p_0/q_0) - 1/p_0] + st \quad (2.31)$$

Some of the implications of these equations are explored in Problems 20 through 22. One implication should be spelled out immediately, however. The case of interest pertains to rare, harmful recessives, so the favored allele is dominant and, from Equation 2.28, $\Delta p = pq^2s$. Because the harmful allele

is assumed to be rare, q is close to 0, and q^2 is therefore extremely small. Consequently, an increase in s from a value of, say, 0.5 to a value of, say, 1, has a trivial effect on the change in allele frequency because, with q^2 so small, the actual value of s matters little. The change in allele frequency of a rare harmful recessive is slow whatever the value of s . For this reason, an increase in selection against rare homozygous recessive genotypes has almost no effect in changing the allele frequency. The implication for human population genetics is that the forced sterilization of rare homozygous recessive individuals—a procedure advocated in a number of naive eugenic programs to “improve” the “genetic quality” of human beings—is not only morally and ethically questionable, it is genetically unsound.

Changes in allele frequency for Equations 2.29 through 2.31 are shown in Figure 17. Note that the change in frequency of a favored dominant allele is slow when the allele is common, which implies that the change in frequency of a harmful recessive is slow when the recessive is rare. Conversely, a favored recessive allele changes in frequency most slowly when rare, which implies that a harmful dominant allele changes most slowly in frequency when common. In general, *recessive alleles change slowly in frequency when they are rare, dominant alleles change slowly in frequency when they are common*. With a favorable additive allele, the initial increase in frequency is slower than that of a favored dominant, but the additive allele eventually overtakes and goes to fixation faster because selection continues to distinguish between the homozygous and heterozygous genotypes.

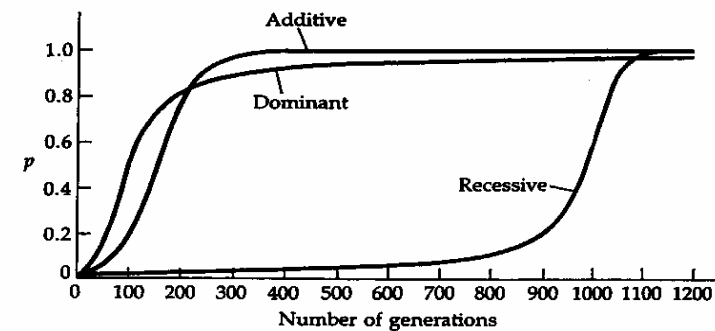


Figure 17. Changes in frequency p of favorable alleles which are dominant, additive, or recessive in their effects on fitness. The frequency of a favored dominant allele changes most slowly when the allele is common, and the frequency of a favored recessive allele changes most slowly when the allele is rare. In all cases the difference in relative fitness between the contrasting homozygous genotypes is assumed to be five percent.

**PROBLEM
20**

In the evolution of industrial melanism (see Problem 9 in Chapter 1), the allele resulting in black body coloration may be considered a favored dominant. In *Biston betularia*, the frequency of melanic individuals increased from 1 percent in 1848 to 95 percent in 1898. This species has one generation per year. Estimate the approximate value of the selection coefficient s against nonmelanics that would be necessary to account for the change in frequency of the melanic forms. How many generations would be required for the same change in frequency of melanic forms in a hypothetical case in which the allele for melanism is recessive, assuming the same value of s against nonmelanics?

ANSWER Let q represent the frequency of the normal (nonmelanic) allele. Then q^2 is the frequency of nonmelanic moths because the normal allele is recessive. Thus $q_0^2 = 1 - 0.01 = 0.99$, or $q_0 = 0.995$ and $p_0 = 0.005$. Also, $q_t^2 = 1 - 0.95 = 0.05$, so $q_t = 0.224$ and $p_t = 0.776$. Since the species has one generation per year, $t = 1898 - 1848 = 50$ generations. Now substitute into Equation 2.29 for a favored dominant: $\ln[(0.776)/(0.224)] + [1/(0.224)] = \ln[(0.005)/(0.995)] + [1/(0.995)] + s(50)$, or $5.707 = -4.288 + 50s$, or $(s) = 0.20$. Thus, the relative fitnesses of melanics and nonmelanics required to account for the change are $1:1 - s$ or $1:0.8$. In the hypothetical case of recessiveness for the melanic allele, $p_0^2 = 0.01$, so $p_0 = 0.1$ ($q_0 = 0.9$); and $p_t^2 = 0.95$, so $p_t = 0.975$ ($q_t = 0.025$); now use Equation 2.31 for a favored recessive with $s = 0.20$, which yields $t = 74.2$ generations. Over the past 20 years, smoke-control programs in industrial areas of England have resulted in a decrease in the frequency of melanic moths consistent with a selection coefficient against melanics in smoke-controlled areas of 0.12 ± 0.02 (Cook et al. 1986).

**PROBLEM
21**

An extensively studied isolated colony of the moth *Paraxia dominula* was cited earlier in this chapter (Problem 7) as an example of fluctuations in population size. This colony also contains a mutant allele affecting color pattern. The frequency of the mutant allele declined steadily over the period 1939 to 1968. Indeed, the corresponding steady increase in the frequency of the normal allele follows Equation 2.30 for additive genes with $s = 0.20$ (see Wright, 1978, for a graph). The species has one generation per year, and in 1965, the estimated frequency of the mutant allele was 0.008 (actually, this value is the average for the 7-year period 1962 to 1968). Estimate the frequency of the mutant allele in 1950 and in 1940.

ANSWER Here we are given (q_t) and want to use Equation 2.30 "backward" to estimate (q_0) . Between 1950 and 1965, there were $t = 1965 - 1950 = 15$ generations. We are given $(q_t) = 0.008$, so $p_t = 0.992$, and $\ln(0.992/0.008) = 4.820$. Thus, $4.820 = \ln(p_0/q_0) + (0.20/2)(15)$, or $\ln(p_0/q_0) = 3.32$. Then $p_0/q_0 = e^{3.32} = 27.660$, or $(p_0) = 0.965$ and $(q_0) = 0.035$. For the year 1940, $t = 1965 - 1940 = 25$ generations, from which $(p_0) = 0.911$ and $(q_0) = 0.089$. (Based on actual observations made at the time, the estimates of (q) were 0.037 in 1950 and 0.111 in 1940.)

Some of the most dramatic examples of evolution in action result from the natural selection for chemical pesticide resistance in natural populations of insects and other agricultural pests. In the 1940s, when chemical pesticides were first applied on a large scale, an estimated 7 percent of the agricultural crops in the United States were lost to insects. Initial successes in chemical pest management were followed by gradual loss of effectiveness. Today, more than 400 pest species have evolved significant resistance to one or more pesticides, and 13 percent of the agricultural crops in the United States are lost to insects (May 1985).

In many cases, significant pesticide resistance has evolved in 5–50 generations irrespective of the insect species, geographical region, pesticide, frequency and method of application, and other seemingly important variables (May 1985). Equations 2.29 through 2.31 help to understand this apparent paradox, since many of the resistant phenotypes result from single mutant genes. The resistant genes are often partially or completely dominant, so Equations 2.29 and 2.30 are applicable. Prior to application of the pesticide, the allele frequency p_0 of the resistant mutant is generally close to 0. Application of the pesticide increases the allele frequency, sometimes by many orders of magnitude, but significant resistance is noticed in the pest population even before the allele frequency p_t increases above a few percent. Thus, as rough approximations, we may assume that q_0 and q_t are both close enough to 1 that $\ln(p_0/q_0) \approx \ln(p_0)$ and $\ln(p_t/q_t) \approx \ln(p_t)$. Using these approximations, Equation 2.30 implies that $t \approx (2/s)\ln(p_t/p_0)$ [additive case] and Equation 2.29 implies that $t \approx (1/s)\ln(p_t/p_0)$ [dominant case]. In many cases, the ratio p_t/p_0 may range from 1×10^2 to perhaps 1×10^7 , and s may typically be 0.5 or greater. Over this wide range of parameter values, the time t is effectively limited to 5–50 generations for the appearance of a significant degree of pesticide resistance. Details in actual cases will depend on such factors as effective population number and extent of genetic isolation between local populations, and the evolution of polygenic resistance may be expected to take somewhat longer than single-gene resistance.

Evaluate the adequacy of the approximations for t with additive and dominant genes, as compared with values calculated from Equations 2.29 and 2.30, in the following cases:

**PROBLEM
22**

Case	p_0	p_t	s
1	1×10^{-4}	0.01	0.5
2	1×10^{-4}	0.10	0.5
3	1×10^{-4}	0.50	0.5
4	1×10^{-7}	0.10	0.5
5	1×10^{-4}	0.10	0.20

ANSWER In the following, $ADDAPX = (2/s)\ln(p_0/p_0)$, $DOMAPX = (1/s)\ln(p_0/p_0)$, $ADD =$ Value from Equation 2.30, and $DOM =$ Value from Equation 2.29.

Case	ADDAPX	ADD	DOMAPX	DOM
1	18.4	18.5	9.2	9.3
2	27.6	28.1	13.8	14.2
3	34.1	36.8	17.0	20.4
4	55.3	55.7	27.6	28.1
5	69.1	70.1	34.5	35.6

In all cases the approximations are acceptable.

Equilibria with Selection

An **equilibrium** value of p is a value for which $\Delta p = 0$. That is, when the allele frequency is at an equilibrium value, the allele frequency remains at that value generation after generation. There are, however, several types of equilibria depending on what happens to allele frequency when the allele frequency does *not* equal the equilibrium value. Consider first the case when the initial allele frequency is near (but not equal to) the equilibrium: if the allele frequency moves progressively farther away from the equilibrium in subsequent generations, the equilibrium is said to be **unstable**; if the allele frequency moves progressively closer to the equilibrium in subsequent generations, the equilibrium is said to be **locally stable**. A locally stable equilibrium might also be **globally stable**, which means that, whatever the initial allele frequency may be, it always moves progressively closer to the equilibrium. In cases such as those exemplified by the Hardy-Weinberg equilibrium, in which every allele frequency represents an equilibrium because, whatever the value, allele frequency does not change, the equilibria are said to be **semistable** or **neutrally stable**.

These concepts of stability can be applied to the case of directional selection for the A allele governed by Equation 2.26. In the case of directional selection for A , there are only two equilibria, namely $p = 0$ and $p = 1$. If p is close to 0, p increases in subsequent generations, so the equilibrium at $p = 0$ is unstable. On the other hand, if p is near 1, it moves still closer to 1 in subsequent generations, so the equilibrium at $p = 1$ is locally stable. Indeed, because p eventually goes to 1 whatever its initial value, the equilibrium at $p = 1$ is globally stable.

The various types of stability are important in discussing two further cases that can occur when selection involves two alleles of a single gene.

Overdominance or **heterozygote superiority** occurs when the heterozygote has a greater fitness than both homozygotes—that is, when w_{12} is greater than both w_{11} and w_{22} . When overdominance occurs, there is a third equilib-

rium in addition to $p = 0$ and $p = 1$ because $p(w_{11} - w_{12}) + q(w_{12} - w_{22})$ can equal 0. The third equilibrium, \hat{p} , can be found by solving $\hat{p}(w_{11} - w_{12}) + (1 - \hat{p})(w_{12} - w_{22}) = 0$, from which a little algebra gives

$$\hat{p} = \frac{w_{12} - w_{22}}{2w_{12} - w_{11} - w_{22}} \quad (2.32)$$

The equilibrium in Equation 2.32 is globally stable, whereas those at $p = 0$ and $p = 1$ are now unstable, as indicated in Figure 18(a) where the arrows show the direction of change in allele frequency. Figure 18(b) shows the course of change in \bar{w} with overdominance, and it is of interest that the average fitness of the population is maximal when $p = \hat{p}$. Maximization of average fitness is a frequent outcome of selection in random-mating populations with constant fitnesses, but there are many exceptions to the rule when random mating does not occur, when fitnesses are not constant, or when more than one gene is involved (Ewens 1979; Curtsinger 1984).

Although overdominance might seem to be a potent force for maintaining polymorphisms in natural populations, overdominance has been documented in only a few cases. The best known case involves two alleles which code for the β chain of human hemoglobin, $Hb\beta^+$, the normal allele, and $Hb\beta^s$, the mutant allele with an amino acid substitution that causes sickle-

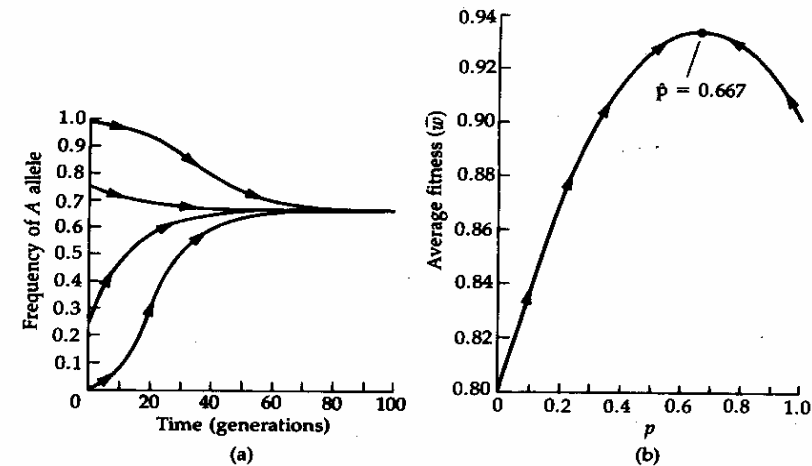


Figure 18. Selection when there is overdominance. (a) The allele frequencies converge to an equilibrium value irrespective of the initial frequency. In this example, $w_{11} = 0.9$, $w_{12} = 1$, $w_{22} = 0.8$, and the equilibrium frequency of the A allele is 0.667. (b) Average fitness \bar{w} against p for the same example as in (a). Note that \bar{w} is a maximum at equilibrium.

cell anemia. Homozygous $Hb\beta^S/Hb\beta^S$ individuals are severely anemic owing to sickling of red blood cells; $Hb\beta^+/Hb\beta^+$ individuals have normal hemoglobin but are sensitive to the type of malaria caused by the mosquito-borne protozoan parasite *Plasmodium falciparum*; and $Hb\beta^+/Hb\beta^S$ heterozygotes are mildly anemic but tend to be resistant to falciparum malaria, perhaps because red blood cells infested with the parasite undergo sickling and are removed from circulation. The viabilities of $Hb\beta^S/Hb\beta^S$, $Hb\beta^+/Hb\beta^S$, and $Hb\beta^+/Hb\beta^+$ individuals in high-malaria regions in Africa have been estimated as $w_{11} = 0$, $w_{12} = 1$, and $w_{22} = 0.85$, respectively (Allison 1964). Substitution into Equation 2.32 leads to a predicted equilibrium allele frequency for $Hb\beta^S$ of $(1 - 0.85)/(2 - 0 - 0.85) = 0.13$. This value is reasonably close to the average allele frequency of 0.09 observed in West Africa, but there is considerable variation in allele frequency among local populations.

PROBLEM 23

Anderson et al. (1968) established experimental populations of *Drosophila pseudoobscura* and periodically treated the flies with weak doses of the insecticide DDT. One population was initially polymorphic for five different inversions of the third chromosome, in approximately equal frequencies. After 13 generations, three of the inversions had essentially disappeared from the population. The two that remained were Standard (ST) and Arrowhead (AR). Changes in frequency of each inversion were monitored, and from the values for the first nine generations, DuMouchel and Anderson (1968) estimated the relative fitnesses of ST/ST, ST/AR, and AR/AR genotypes as 0.47, 1.0, and 0.62, respectively. Because the inversions undergo almost no recombination with one another, each type can be considered as an "allele." What equilibrium frequency of ST is predicted? What equilibrium value of \bar{w} is predicted?

ANSWER Let \hat{p} represent the equilibrium frequency of ST. Then, using Equation 2.32, $\hat{p} = (1.0 - 0.62)/(2.0 - 0.47 - 0.62) = 0.42$. (The value of $\langle p \rangle$ after 13 generations was actually 0.43.) Predicted \bar{w} from Equation 2.24 equals $(0.42)^2(0.47) + 2(0.42)(0.58)(1.0) + (0.58)^2(0.62) = 0.78$.

PROBLEM 24

Warfarin is a blood anticoagulant used for rat control during and after World War II. Initially highly successful, the effectiveness of the rodenticide has gradually diminished owing to the evolution of resistance among some target populations. Among Norway rats in Great Britain, resistance results from an otherwise harmful mutation *R* in a gene in which the normal nonresistant allele may be denoted *S*. In the absence of warfarin, the relative fitnesses of *SS*, *SR*, and *RR* genotypes have been estimated as 1.00, 0.77, and 0.46, respectively. In the presence of warfarin, the relative fitnesses have been estimated as 0.68, 1.00, and 0.37, respectively (Greaves, quoted in May 1985). Calculate the equilibrium frequency \hat{q} of *R* in the presence of warfarin. Noting that, in the absence of warfarin, *R* and *S* are nearly additive in their effects on fitness, estimate the approximate number of generations required for the allele frequency of *R* to decrease from \hat{q} to 0.01 in the absence of the poison.

ANSWER From Equation 2.32, the equilibrium frequency \hat{p} of *S* equals $(1.00 - 0.37)/[2(1.00) - 0.68 - 0.37] = 0.66$, so $\hat{q} = 0.34$. Setting $q_0 = 0.01$ and $q_t = 0.34$ in Equation 2.30, with $s = 1.00 - 0.46 = 0.54$, yields $t = 14.6$ generations. The overdominance that occurs in the presence of warfarin appears to result from the homozygous *RR* genotypes having an excessive requirement for vitamin K.

Heterozygote inferiority refers to the opposite situation from overdominance, and it occurs when the fitness of the heterozygous genotype is smaller than that of both homozygotes (w_{12} less than w_{11} and w_{22}). A third equilibrium also exists in this case, and its value is given by Equation 2.32. However, in the case of heterozygote inferiority, the equilibrium is *unstable*, whereas the equilibria at $p = 0$ and $p = 1$ are both locally (but not globally) stable. An example of heterozygote inferiority is depicted in Figure 19(a), where the arrows again denote the direction of change in allele frequency. If the initial allele frequency is exactly equal to the equilibrium value (in this example, $\hat{p} = 1/3$), then the allele frequency remains at that value. In all other cases,

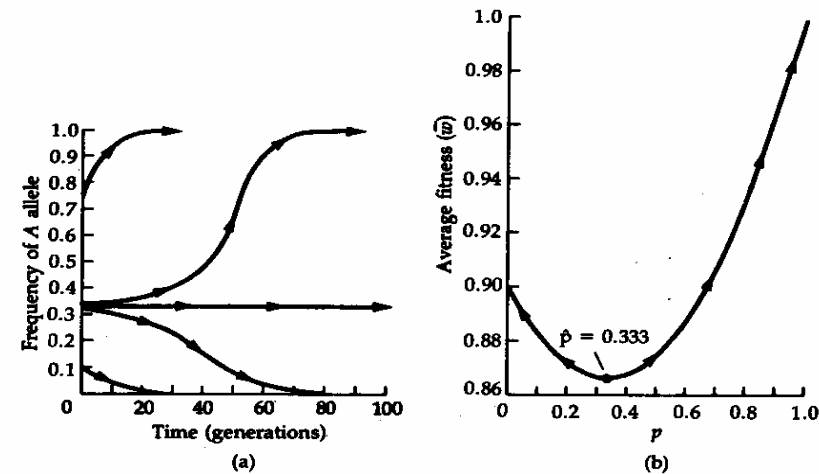


Figure 19. Selection when there is heterozygote inferiority. (a) The allele frequency goes to 0 or 1, depending on the initial frequency. In this example, $w_{11} = 1$, $w_{12} = 0.8$, $w_{22} = 0.9$, and there is an unstable equilibrium when the frequency of the *A* allele is $p = 0.333$. An infinite population with $p = 1/3$ maintains this frequency, but any slight upward change in the frequency of *A* results in eventual fixation of *A*, and any slight downward change in the frequency of *A* results in ultimate loss of *A*. (b) Average fitness \bar{w} against p for same example as in (a). The unstable equilibrium represents the minimum of \bar{w} .

p goes to 1 or 0, depending on whether the initial allele frequency was above or below the equilibrium value.

Figure 19(b) shows the situation regarding average fitness when there is heterozygote inferiority. Note that the unstable equilibrium at $\hat{p} = 1/3$ represents a minimum of average fitness. The shape of the \bar{w} curve has an important implication, especially in more complex examples. Imagine a population with an allele frequency near 0, where $\bar{w} = 0.9$. In terms of average fitness, the population would be better off if the allele frequency were near 1, because \bar{w} would then be close to 1.0. However, as shown by the direction of the arrows, the population cannot evolve toward $p = 1$ because it cannot get through the "valley." To say the same thing in a somewhat different way, $p = 0$ represents a locally stable equilibrium. The population has no way to escape from the equilibrium even though, in doing so, it would eventually end up with a greater average fitness. This consideration would seem to limit the ability of natural selection to increase average fitness in such cases, but one way out of the impasse is suggested in the next section.

Adaptive Topographies and the Role of Random Genetic Drift

Any graph of \bar{w} against allele frequency, even the simple example in Figure 19(b), is called an **adaptive topography**. In order to generalize the discussion a bit, try to imagine an adaptive topography in many dimensions, which would occur in more realistic situations in which \bar{w} depended on the allele frequencies of many genes instead of only one. In many dimensions, the adaptive topography is a complex surface and, on this surface, there may be "peaks" and "pits" and even "saddle-shaped" regions. In this context, the peaks represent locally stable equilibria, and natural selection ordinarily changes the allele frequencies so as to move \bar{w} to the top of some peak. However, the peak that a population perches upon may not be the highest peak that exists on the whole surface. However, as illustrated in Figure 19(b), the population may become stuck there because the peak is a locally stable equilibrium.

By what process can a population stranded on a submaximal fitness peak get off the peak, through a nearby valley, and onto a place where natural selection can carry it to the top of an even higher fitness peak? This is something that natural selection acting alone cannot accomplish because it entails a temporary reduction in fitness. There is, however, a process that can accomplish the task—random genetic drift. In a sufficiently small population, the allele frequencies can change by chance, even producing a reduction in average fitness. Theoretically, random genetic drift can shift a population from a locally stable equilibrium, through a nearby valley, and into a region where it is attracted by another locally stable equilibrium as-

sociated with a higher fitness peak. Random genetic drift can therefore play a crucial role in evolution by allowing a population to explore the full range of its adaptive topography. This role of random genetic drift has been particularly emphasized by Wright (1977 and earlier) in his proposed **shifting balance theory** of evolution. Additional discussion of the theory is found in the section below on interdemic selection, and also in Hartl (1979) and Provine (1986).

Mutation–Selection Balance

Recall from Chapter 1 that outcrossing species typically contain a large amount of hidden genetic variability in the form of recessive or nearly recessive harmful alleles at low frequencies. This situation is to be expected. Selection cannot completely eliminate harmful alleles because of their continual creation through recurrent mutation. To be specific, suppose a is a harmful allele, and consider the simple model of directional selection for A . Suppose mutation of A to a occurs at the rate μ per generation. (Because q , the allele frequency of a , remains small, reverse mutation of a to A can safely be ignored.) The calculation of p' carried out for Equation 2.25 is still valid, except that a proportion μ of A alleles mutate to a in the course of one generation. Thus,

$$p' = \frac{p(pw_{11} + qw_{12})(1 - \mu)}{\bar{w}} \quad (2.33)$$

In the following, it is again convenient to use the fitness symbols defined in Equation 2.27, namely $w_{11} = 1$, $w_{12} = 1 - hs$, and $w_{22} = 1 - s$.

When selection is balanced by recurrent mutation, there is a globally stable equilibrium at an allele frequency of \hat{p} , where \hat{p} can be found by solving Equation 2.33 with $p' = p = \hat{p}$. The equilibrium frequency of the harmful a allele is therefore $\hat{q} = 1 - \hat{p}$, and two important cases arise:

1. When the harmful allele is *completely recessive* ($h = 0$), then

$$\hat{q} = \sqrt{\mu/s} \quad (2.34)$$

2. When the harmful allele is *partially dominant* ($h > 0$), then, approximately,

$$\hat{q} = \mu/hs \quad (2.35)$$

(Equation 2.35 is an excellent approximation for realistic values of μ , h , and s .)

The Huntington disease (formerly called Huntington's chorea) serves as an example of the use of Equation 2.35. The disease is a severe degenerative disorder of the neuromuscular system that typically appears after age 35. Although the disease itself results from a "dominant" gene, Reed and Neel

(1959) estimated the fitnesses as $\langle w_{11} \rangle = 1$, $\langle w_{12} \rangle = 0.81$, and $\langle w_{22} \rangle = 0$, where w_{12} and w_{22} refer, respectively, to genotypes which are heterozygous or homozygous for the Huntington allele. Therefore, we may estimate $\langle s \rangle = 1 - \langle w_{22} \rangle = 1$ and $\langle hs \rangle = 1 - \langle w_{12} \rangle = 0.19$, so $\langle h \rangle = 0.19$. In terms of neuromuscular degeneration, the Huntington allele is dominant. In terms of fitness, however, the allele is only partially dominant owing to the late age of onset of the disease.

Because we are dealing with a partial dominant in the case of Huntington disease, Equation 2.35 is appropriate. Using Equation 2.35, we could estimate q if the value of μ were known, or we could estimate μ if q were known. In the Michigan population studied by Reed and Neel (1959), $\langle q \rangle = 5 \times 10^{-5}$, so (assuming that the population is in equilibrium) we have $\langle \mu \rangle = (5 \times 10^{-5})(0.19) = 9.5 \times 10^{-6}$. This example illustrates one of the common indirect methods for the estimation of mutation rates in humans.

**PROBLEM
25**

A small amount of dominance can have a major effect in reducing the equilibrium frequency of a harmful allele. To confirm this for yourself, imagine an allele that is lethal when homozygous ($s = 1$) in a population of *Drosophila*. Suppose that the allele is maintained by selection-mutation balance with $\mu = 5 \times 10^{-6}$. Calculate the equilibrium frequency of the allele in the cases (1) complete recessive and (2) partial dominant with $h = 0.025$.

ANSWER Case 1: $q = \sqrt{\mu/s} = \sqrt{[(5 \times 10^{-6})/1]} = 2.24 \times 10^{-3}$. Case 2: $q = (\mu/hs) = [(5 \times 10^{-6})/(0.025)(1)] = 2.00 \times 10^{-4}$. The equilibrium allele frequency is reduced more than tenfold, and the frequency of homozygous recessive genotypes at equilibrium is reduced more than a hundredfold. It is of interest that $h = 0.025$ is near the average degree of dominance estimated for "recessive" lethals in *Drosophila* (Simmons and Crow 1977).

MORE COMPLEX TYPES OF SELECTION

We have considered only the simplest type of selection involving two alleles of a single gene with constant fitnesses determined by differences in viability. Actual mechanisms of selection in natural populations are usually more complex. As mentioned earlier, when fertilities differ among genotypes, then the simple model of selection on viability is inadequate except in special cases. Additional complications arise in actual situations because fitness is determined by many genes that may interact with each other. Simple models of selection have validity only when the genes interact in an extremely simple manner (for example, when fitness effects are additive or multiplicative across genes), or when one gene has such major effects on fitness that it overwhelms

the effects of other genes. Still more complications arise because the fitnesses of the genotypes may not actually be constants, but may vary from generation to generation depending on, for example, the weather, or from place to place depending on local conditions, such as availability of food, water, or nesting sites. Hedrick (1986) has reviewed the subject of environmental heterogeneity in relation to its possible role in the maintenance of genetic polymorphisms. Realistic models of natural selection with varying fitnesses or other complications are often complex. (See Hartl 1980 for specific references.)

Allele frequencies in natural populations may vary systematically according to geographical location. The frequency of an allele may increase or decrease in a regular trend which accompanies a change in an environmental variable such as temperature, salinity (for marine organisms), population density, or some combination of environmental variables. Geographical trends in allele frequency are called clines.

A particularly dramatic example of a cline is found in the hemoglobin- I^1 allele in the eelpout fish *Zoarces viviparus*, the allele frequency of which drops from a value of nearly 1 in the North Sea to a value of nearly 0 in the Baltic Sea (Christiansen and Frydenberg 1974). In human aboriginal populations, there is a cline of increasing frequency of the I^B allele in the ABO blood groups from Southwest to Northeast Europe. Although clines can result from selection—for example, when one genotype is favored at one extreme of the environmental gradient but disfavored at the other extreme—clines can also result from other processes. For example, differences in allele frequency in local populations at the extremes of the range may result from founder effects, and migration of organisms from the extremes into the intermediate zone produces the cline.

Interdeme Selection and the Shifting Balance Theory

Two types of selection should be singled out for brief discussion here because they involve extended concepts of "fitness." One type is called **interdeme selection**, and it occurs between semi-isolated populations (demes) of the same species. If populations containing certain genotypes are more likely to become extinct and have their vacated habitats recolonized by migrants from other populations that are more persistent due to the particular genotypes that they contain, then the more successful populations can in some sense be considered as having a greater "fitness" than the less successful ones. Since this concept of **population fitness** is a characteristic of the entire population and not merely the average fitness of the genotypes within it (\bar{w}), interdeme selection is outside the realm of most conventional models of selection. Interdeme selection is one type of *group selection* (Wilson 1983).

Interdeme selection plays an essential role in the shifting balance theory

of evolution (Wright 1977 and earlier). In Wright's view, subdivision of a population into small semi-isolated demes gives the best chance for the populations to explore the full range of their adaptive topography. Temporary reductions in fitness which would be prevented by selection in large populations become possible in small ones because of the random drift in allele frequencies that occurs in small populations. The lucky subpopulations which reach higher adaptive peaks on the fitness surface increase in size and send out more migrants than other subpopulations, and the favorable gene combinations are gradually spread throughout the entire set of subpopulations by means of interdeme selection. The shifting balance process includes three distinct phases:

1. An exploratory phase, in which random genetic drift plays an important role in allowing small populations to explore their adaptive topography;
2. A phase of mass selection, in which favorable gene combinations created by chance in phase (1) become rapidly incorporated into the genome of local populations by the action of natural selection; and
3. A phase of interdeme selection, in which the more successful demes increase in size and rate of migration, and the excess migration shifts the allele frequencies of nearby populations until they also come under the control of the higher fitness peak. The favorable genotypes thereby become spread throughout the entire population in ever-widening concentric circles. Where the region of spread from two such centers overlaps, a new and still more favorable genotype may occur and itself become a center for interdeme selection. In this manner, the whole of the adaptive topography can be explored, and there is a continual shifting of control from one adaptive peak to control by a superior one.

The shifting balance theory has played an important role in evolutionary thinking, in part because of the prominent role assigned to random genetic drift in the initial phase of the process. However, as a comprehensive theory of evolution, many aspects of the theory remain to be tested. For the theory to work as envisaged, the interactions between alleles must often result in complex adaptive topographies with many peaks and valleys. The population must be split up into smaller demes, which must be small enough for random genetic drift to be important, but large enough for mass selection to fix favorable combinations of alleles. While migration between demes is necessary, neighboring demes must be sufficiently isolated for genetic differentiation to occur, but sufficiently connected for favorable gene combinations to spread. Because of uncertainty about the applicability of these assumptions, the shifting balance process remains a picturesque metaphor which is still largely untested.

One implication of interdeme selection is that selection for genes that are

beneficial to the group may, in some cases, override effects that are harmful to the individuals. This principle is illustrated in the model in Table 4, where the allele A' is harmful to individuals within demes but favorable to the deme as a whole. Equation 2.26 implies that, within the i th deme, $\Delta q_i = -cq_i(1 - q_i)$ (assuming that $\bar{w} = 1$). Averaging across all of n subpopulations, the change in allele frequency resulting from selection within subpopulations Δq_w equals $-c\bar{q}(1 - \bar{q})(1 - F)$. At the same time within-population selection occurs, interdeme selection favors demes containing A' , and the change in allele frequency in the i th population resulting from between-population selection equals $2(b - c)q_i(1 - q_i)$ (assuming $\bar{v} = 1$). Averaging this across all n subpopulations gives the total change in allele frequency resulting from between-population selection as $\Delta q_b = 2(b - c)\bar{q}(1 - \bar{q})(1 - F)$. Putting both processes together, the total change in the frequency of A' is

$$\Delta q = \Delta q_w + \Delta q_b = \bar{q}(1 - \bar{q})[2F(b - c) - c(1 - F)] \quad (2.36)$$

Equation 2.36 implies that $\Delta q > 0$ if

$$\frac{b - c}{c} > \frac{1 - F}{2F} \quad (2.37)$$

This is the condition necessary for selection between demes to override selection within demes, and the formulation is quite general (Crow and Aoki 1982). (A biological interpretation of Equation 2.37 is given in the following section on kin selection.)

If there are n demes, each of size N , which exchange migrants in such a way that m is the proportion of genes in each deme that are exchanged each generation for genes chosen at random from the other demes, then the approximate value of F at equilibrium is

$$F = \frac{1}{4Nm\alpha + 1} \quad (2.38)$$

where $\alpha = [n/(n - 1)]^2$ (Crow and Aoki 1984). Note that Equation 2.38 does not depend on the mutation rate to new alleles or on the number of alleles,

Table 4. Model of interdeme selection.

Genotype	AA	AA'	$A'A'$
Frequency in deme i	p_i^2	$2p_iq_i$	q_i^2
Within-population fitness (w)	1	$1 - c$	$1 - 2c$
Between-population fitness of deme i (v)		$1 + 2(b - c)q_i$	

and when n is reasonably large, $\alpha = 1$, and the equation reduces to the familiar form in Equation 2.21.

Equation 2.38 implies that, for large n , $(1 - F)/2F = 2Nm$, which equals the number of migrant diploid individuals per generation (two times the number of migrant alleles). We therefore conclude from Equation 2.37 that selection between demes overrides selection within demes only when the benefit to the group ($b - c$), relative to the cost to the individual (c), is greater than the average number of migrant individuals per generation. This principle defines a rather stringent limit above which migration among demes cancels any possible effects of interdeme selection.

Kin Selection

A second extended concept of fitness arises in the context of **kin selection**, which refers to indirect selection for alleles that occurs through the relatives of carriers of those alleles rather than by direct selection through an increased fitness of the carriers themselves. Kin selection has been postulated in attempts to account for the evolution of altruism. **Altruism** consists of behavioral traits or other attributes that increase the fitness of other individuals at the expense of one's own fitness. Altruistic behavior is exhibited most dramatically by social insects such as termites, ants, and bees, in which certain worker castes exert their labors for the care, protection, and reproduction of the queen and her offspring but do not reproduce themselves. Other, less dramatic, examples of altruistic behavior include phenomena such as the care of offspring by their parents.

A central consideration in kin selection is that relatives have genes in common. Therefore, a gene that causes altruistic behavior can increase in frequency if the increase in the recipient's fitness as a result of altruism is sufficiently large to offset the decrease in the altruist's own fitness. The essentials of the situation can be made clear by considering the case of identical twins. Because identical twins are genetically identical, the reproduction of one's twin is genetically equivalent to reproduction by oneself. Thus, it makes no difference if an altruistic individual decreases its own fitness for the sake of an equal increase in fitness of an identical twin; from an evolutionary point of view, it is an even trade because the combined number of offspring from both twins remains unchanged. By the same token, if an altruistic act decreases the fitness of an individual by an amount less than the increase gained by an identical twin, then the altruism results in a net increase in the combined number of offspring. One would, therefore, expect altruism between identical twins to be favored by natural selection as long as the risk to the altruist is no greater than the benefit to the recipient.

These considerations of identical twins can be extended to other degrees

of relationship as well, but the risk to the altruist must be correspondingly smaller than the benefit to the recipient because other types of relatives share fewer genes than identical twins. The break-even points for altruism toward various degrees of relationship have been trenchantly summarized by J. B. S. Haldane, who is said to have quipped that he would lay down his life for two brothers, four nephews, or eight cousins. In any case, fitness considerations that take into account not only an individual's own fitness but also the fitness of relatives (other than direct descendants) constitute what is called the **inclusive fitness** of the individual.

To be concrete, suppose that altruism results in a decrease in fitness c of the altruist which is offset by an increase in fitness b in the recipient. The gene for altruism increases in frequency if the ratio of cost to benefit is great enough, relative to the genetic relationship between the individuals. That is, the gene for altruism increases in frequency if

$$c/b < r \quad (2.39)$$

as shown by Hamilton (1964) and discussed in detail by Cavalli-Sforza and Feldman (1978) and Uyenoyama and Feldman (1980). The appropriate measure of genetic relationship r in this context is defined as

$$r = \frac{2F_{XY}}{(1 + F_X)} \quad (2.40)$$

where F_X is the inbreeding coefficient of X , and F_{XY} is the inbreeding coefficient of a hypothetical offspring of X and Y . As illustrated in Figure 20, r equals the probability that two gametes from X and Y contain alleles that are identical by descent (F), relative to the probability that two gametes from X contain alleles that are identical by descent $[(1 + F)/2]$. The cost-benefit

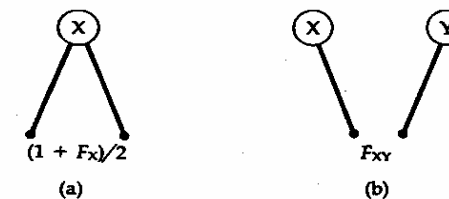
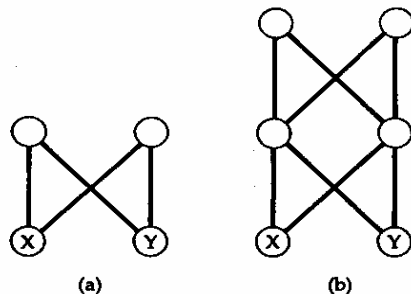


Figure 20. (a) Two genes chosen at random from an individual X are identical by descent with probability $(1 + F_X)/2$ (see Figure 23 in Chapter 1). (b) Two genes chosen at random, one from individual X and the other from individual Y , are identical by descent with probability F_{XY} , which is the inbreeding coefficient of a hypothetical offspring of X and Y . The ratio of F_{XY} to $(1 + F_X)/2$ is the appropriate measure of genetic relationship in consideration of kin selection.

tradeoff in Equation 2.39 is generally valid for weak selection when $F_X = 0$, and valid for additive alleles when $F_X \neq 0$ (Aoki 1981).

PROBLEM 26 For the illustrated pedigrees (a) and (b) of full siblings, calculate the break-even value of the benefit b to the recipient of altruism Y, relative to a cost value $c = 1$ to the donor X, in order to ensure an increase in frequency of an additive gene for altruism. Why are the answers different in the two cases?



ANSWER In case (a), a hypothetical offspring of X and Y has an inbreeding coefficient of $F_{XY} = (1/2)^3 + (1/2)^3 = 1/4$, and $F_X = 0$. Therefore, $r = 2(1/4) = 1/2$, and the break-even value of $c/b = 1/2$. Hence, for $c = 1$, $b = 2$. This is the theoretical basis of Haldane's quip about laying down his life for two brothers. In pedigree (b), $F_{XY} = 4(1/2)^5 + 2(1/2)^3 = 3/8$ and $F_X = 2(1/2)^3 = 1/4$. Therefore $r = 2(3/8)/(1 + (1/4)) = 3/5$. For a cost of $c = 1$, the break-even value of b equals $5/3$. The values differ in the two cases because of the differing inbreeding. In case (b), even though X is inbred, the break-even value of b is smaller because of the closer genetic relationship between X and Y.

Comparison of Equations 2.37 and 2.39 reveals a connection between kin selection and group selection of other types, which occurs because individuals within subpopulations are related. With random mating within subpopulations, the average value of r within subpopulations equals $2F/(1 + F)$, where F is given by Equation 2.38. Expressing the inequality in 2.37 in terms of r yields $c/b < r$, which is identical to Equation 2.39.

This chapter has focused on the evolutionary processes which determine the type and extent of genetic variation maintained in natural populations. It is still obscure whether the majority of genetic polymorphisms observed at the protein level are maintained by selection or a balance between the mutation and random genetic drift of selectively neutral or nearly neutral alleles. The issue is complex because the selective mechanisms by which polymorphisms are maintained may differ from gene to gene, and some

polymorphic genes may experience so little selection as to be effectively neutral. Indeed, some alleles may be subject to selection, whereas other alleles of the same genes may be neutral. However, important findings regarding the neutrality hypothesis and other principles of population genetics have emerged from studies at the molecular level. The next chapter serves as an introduction to these aspects of population genetics.

SUMMARY

Random genetic drift refers to the progressive dispersion of allele frequencies among small populations and the accompanying accumulation of fixed populations. The effects of random genetic drift are conveniently measured in terms of individual heterozygosity (H_i), subpopulation heterozygosity (H_s), and total heterozygosity (H_T), and in terms of the associated F -statistics $F_{IS} = (H_s - H_i)/H_s$, which measures the effects of nonrandom mating within subpopulations, $F_{ST} = (H_T - H_s)/H_T$, which measures the effects of random genetic drift among subpopulations, and $F_{IT} = (H_T - H_i)/H_T$, which measures the combined effects of nonrandom mating and random genetic drift. When there is random mating within subpopulations, then $F_{IS} = 0$, and the genotype frequencies in any one population are given by the Hardy-Weinberg principle in terms of the allele frequencies appropriate to that subpopulation; the overall genotype frequencies, averaged across subpopulations, are given by the usual formula for inbreeding (Chapter 1) with $F = F_{ST}$. For a large group of subpopulations, each of size N , the increase in F_{ST} resulting from random genetic drift is given by $F_{ST} = 1 - (1 - 1/2N)^t$, where t represents time in generations.

The effective number of a population N_e is the size of an ideal population which has the same rate of increase in F_{ST} as the actual population. When population size varies from generation to generation, the average effective size equals the harmonic mean of the various numbers. If N_m is the number of males and N_f is the number of females, then the effective size is given by $4N_mN_f/(N_m + N_f)$. If the population is spread out uniformly in two dimensions, then the effective size is given by $4\pi\delta\sigma^2$, where δ is the density of breeding individuals per unit area and σ^2 is the one-way variance in distance between birthplace and breeding site.

F_{ST} can also be used as an index of genetic differentiation among populations. The amount of genetic differentiation associated with F_{ST} values of 0 to 0.05 is considered little, 0.05 to 0.15 is considered moderate, 0.15 to 0.25 is considered great, and above 0.25 is considered very great.

Mutation provides the raw material for evolutionary change, but, by itself, mutation pressure is a very weak force for changing allele frequency. If allele

A mutates to allele *a* at a rate μ per generation, and *a* undergoes reverse mutation at a rate ν per generation, then the equilibrium frequency of *A* is $\nu/(\mu + \nu)$, but the population may require tens of thousands or hundreds of thousands of generations to reach equilibrium. In finite populations, the equilibrium value of F_{ST} for genes with neutral alleles is given by $1/(4N\mu + 1)$, where μ is the mutation rate to selectively neutral alleles and $4N\mu + 1$ is called the effective number of alleles of the gene.

Wahlund's principle refers to the reduction in the frequency of rare homozygous recessive genotypes when populations become fused by extensive migration. The frequency of homozygous genotypes is reduced by the quantity $F_{ST}\bar{p}\bar{q}$, where \bar{p} and \bar{q} are the average allele frequencies in the pre-fusion populations. The reduction in frequency of homozygotes can also be expressed as σ^2 , where σ^2 is the variance in allele frequency among pre-fusion populations. Thus $F_{ST} = \sigma^2/\bar{p}\bar{q}$.

On the whole, migration hinders genetic divergence among subpopulations. In finite populations, the equilibrium value of F_{ST} with migration is given by $1/(4Nm + 1)$, and only a few migrants per generation are sufficient to keep F_{ST} below 10 percent.

Natural selection can have many different mechanisms. The simplest case involves two alleles of one gene with constant fitnesses resulting from viability differences among genotypes. In this simple case, four outcomes are possible: (1) *A* becomes fixed; (2) *a* becomes fixed; (3) there is a globally stable equilibrium at $\hat{p} = (w_{12} - w_{22})/(2w_{12} - w_{11} - w_{22})$, where \hat{p} represents the allele frequency of *A* and the fitnesses of *AA*, *Aa*, and *aa* are given by w_{11} , w_{12} , and w_{22} , respectively; or (4) there is an unstable equilibrium at the same value of \hat{p} . Case 3 refers to overdominance (w_{12} greater than both w_{11} and w_{22}); case 4 refers to heterozygote inferiority (w_{12} less than both w_{11} and w_{22}).

When a harmful allele is maintained in a population by a balance between selection and mutation the equilibrium frequency of the harmful allele is given by $\hat{q} = (\mu/s)^{1/2}$ when the allele is recessive and by $\hat{q} = (\mu/hs)$ when the allele is partially dominant. In these formulas, s is the selection coefficient against genotypes which are homozygous for the recessive allele, h is the degree of dominance of the harmful allele, and μ is the rate of mutation from the normal to the harmful allele.

Extended concepts of fitness can include the effects of selection acting on subpopulations or groups of relatives. Interdeme selection occurs when the differential growth or success of subpopulations results in changes in gene frequency. When interdeme selection occurs, some alleles that are harmful to their carriers within populations can nevertheless increase in frequency in the population as a whole because they have beneficial effects for selection between populations. Likewise, genes for altruism can increase in frequency if the loss in fitness of the altruist is offset by the increase in inclusive fitness

to the beneficiaries. For additive alleles, the condition for the increase in frequency of an allele predisposing to altruism is $c/b < r$ where c and b are the fitness cost to altruist *X* and benefit to relative *Y*, respectively, and $r = 2F_{XY}/(1 + F_X)$.

Interdeme selection plays an important role in the shifting balance theory of evolution. According to this theory, adaptive topographies are highly complex surfaces with many peaks and valleys. In small, partially isolated subpopulations, random genetic drift promotes the random exploration of the topography. When, by chance, a subpopulation comes under the control of a higher fitness peak, mass selection occurs and rapidly multiplies the favored gene combinations. Excess migration from the successful subpopulation shifts gene frequencies in surrounding subpopulations, and through repetition of the selection process, the favored gene combinations progressively spread in waves throughout the entire population. Influential as a metaphor, the shifting balance theory has not yet been adequately evaluated as an accurate description of the principal mechanism of evolutionary change.

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