
4

Genetic Drift and Effective Population Size

The views of Fisher and Wright contrast strongly on the evolutionary significance of random changes in the population. Whereas, to Fisher, random change is essentially noise in the system that renders the determining processes somewhat less efficient than they would otherwise be, Wright thinks of such random fluctuations as one aspect whereby evolutionary novelty can come about by permitting novel gene combinations.

James Crow and Motoo Kimura (1970)

Small population size can lead to loss of neutral genetic variation, fixation of mildly deleterious alleles, and thereby reduced population fitness. The rate of this process depends on the effective size of a population, N_e , rather than the actual number of living individuals, N , making the effective size of a population one of the most fundamental parameters in evolutionary and conservation biology.

Kalinowski and Waples (2002)

Since the beginning of population genetics, there has been controversy concerning the importance of chance changes in allele frequencies caused by small population size or **genetic drift** (sometimes referred to as random genetic drift or random drift to emphasize the random aspect of this effect). Part of this controversy has resulted from the large numbers of individuals observed in many natural populations, large enough to make chance effects small in comparison to the effects of other factors, such as selection and gene flow. However, if the selective effects or amount of gene flow are small relative to the population size, then long-term genetic change caused by genetic drift may be important. Consideration of this possibility, even when the population size is large, led to the development of the neutrality theory, in which selectively neutral variants are generated by mutation and changed in frequency by genetic drift (see Chapter 6 for a discussion).

Under certain conditions, a finite population may be so small that genetic drift is significant even for loci with sizable selective effects or when there is gene flow. First, some populations may be continuously small for a relatively long period of time because of limited resources in the populated area, low dispersal between suitable habitats, territoriality among individuals,

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or other factors. For example, lizard numbers can be limited by perch sites and territoriality, bird populations by nesting sites and territoriality, and the number of colonizing plants by open habitat and dispersal between habitats. Isolated populations, whether of land animals or plants on an island, vertebrates or invertebrates in a lake, or other groups living in a circumscribed area, may also have a continuously low population size.

Second, some populations may have intermittent small population sizes. Examples of such episodes are the overwintering loss of population numbers in many invertebrates, periodic crashes of populations in small rodents such as lemmings and voles, epidemics that periodically decimate populations of both plants and animals, and the seasonal desiccation of ponds that affect population numbers of many species. Such population fluctuations generate **bottlenecks**, *periods during which only a few individuals survive to continue the existence of the population*. A classic example of periodic oscillations is the relative abundance of the lynx and snowshoe hare in Canada, where both species show approximately 9- to 10-year oscillations and the population density fluctuates by an order of magnitude or more. As a result, in periods of low density, individuals of both species often become exceedingly rare.

Small population size is also important when a population grows from a few founder individuals, a phenomenon termed **founder effect**. For example, many island populations appear to have started from a very small number of founders. If a single female who was fertilized by a single male founds a population, then only four genomes, two from the female and two from the male, may start a new population. In plants, an entire population may be initiated from a single seed—only two genomes, if self-fertilization occurs. As a result, *populations descended from a small founder group may have low genetic variation or by chance have a high or low frequency of particular alleles*. Such initial restrictions in the number of founders also appear to be important in some human populations. For example, some religious isolates in North America, such as the Amish and the Hutterites, were initiated by small numbers of migrants from Europe; some remote sites, such as the island Tristan da Cunha, were settled by a few individuals (see Example 4.1, which discusses the number of founding mtDNA and Y-chromosome lineages in the Tristan da Cuhna islanders).

EXAMPLE 4.1 Tristan da Cunha is a small, remote island in the south Atlantic about 2900 km west of South Africa. The British established a garrison on the island in 1816 to prevent the French from rescuing Napoleon who was in exile on St. Helena, 2259 km to the north. From historical records, the ancestry of only seven women (indicated by their initials here) remain: M. L. who came in 1816; M. W., S. W., and M. W. in 1827; S. P. in 1863; and E. S. and A. S. in 1908. Because mtDNA is maternally inherited with no recombination, present-day mtDNA types can be used to trace the ancestry to the founding females. Table 4.1 gives the mtDNA

TABLE 4.1 The mtDNA sequence differences in Tristan da Cunha islanders showing the number of individuals with the types traced to the founding females. Adapted from H. Soodyall, *et al.*, 1997.

Founding females	mtDNA sequence	N (proportion)
S. W.	ACTTGTTTCG	46 (0.29)
M. W. and M. W.	GTTCGCTTCG	34 (0.21)
E. S. and A. S.	GCTTATCTTG	25 (0.16)
M. L.	ATCTGCCCTA	11 (0.07)
S. P.	GTCTGTCCTG	45 (0.28)
Total		161 (1.0)

types found in 161 present-day individuals for nine different mtDNA regions first found by SSO probes and then described by sequence differences (Soodyall *et al.*, 1997). S. W. and M. W. were described as sisters from the historical data, but the mtDNA show that they have distinct mtDNA types. M. W. and M. W. were mother and daughter, and E. S. and A. S. were sisters, both of which are confirmed by the mtDNA data. In other words, from the genealogical information, four founder mtDNA types were expected, but five were observed. The estimated level of mtDNA haplotype diversity using expression 2.19c is 0.768.

There are seven family names in use in Tristan, corresponding to the number of founding fathers with present-day descendants from public records (Soodyall *et al.*, 2003). Because Y chromosomes are paternally inherited with no recombination, present-day Y-chromosome haplotypes can be used to trace ancestry to the founding males. Within each family, there was a haplotype that could be traced to the known ancestors (Table 4.2). However, two other

TABLE 4.2 The seven families from Tristan da Cunha and the Y-chromosome haplotypes found in each one. The repeat numbers for the microsatellite alleles that are different from the ancestral family type are given in boldface. Adapted from H. Soodyall, *et al.*, 2003.

Family	Y-chromosome haplotype	N (proportion)
1	15-12-25-10-14-13	5 (0.066)
2	14-12-24-11-13-13	3 (0.039)
3	14-12-23-11-13-13 14-12-23- 10 -13-13 (mutant)	9 (0.118) 4 (0.053)
4	14-12-24-10-13-14 16 -12- 25 -10-11-13 (migrant)	8 (0.105) 1 (0.013)
5	14-12-23-10-14-13 14 - 14 - 22 -10-11-13 (from family 7)	16 (0.211) 3 (0.039)
6	16-13-24-10-11-13 14 - 12 - 23 -10-14-13 (from family 5)	10 (0.132) 1 (0.013)
7	14-14-22-10-11-13 14 - 12 - 23 -10-14-13 (from family 5)	14 (0.184) 2 (0.026)
Total		76 (1.0)

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haplotypes were also observed, one in family 3 that appears to be a mutation and one in family 4 that appears to be from a migrant. In addition, in families 5, 6, and 7, haplotypes from other families were also found that appear from pedigree examination to be the result of four instances of nonpaternity and the subsequent descendants. Overall, there are nine Y haplotypes, and the estimated level of Y-chromosome haplotype diversity using expression 2.19c is 0.847.

Another situation in which small population size may be of great significance is where the population (or species) in question is one of the many threatened or endangered species. For example, as few as 20 northern elephant seals are thought to have survived hunting by 1900 (Table 4.3) on Isla Guadalupe, Mexico, but their numbers have now grown exponentially to 200,000 (Hoelzel *et al.*, 2002; see also Example 4.6). Also, the Florida panther was thought extinct in the early 1970s, and today its numbers are around 100 (Culver *et al.*, 2008). Only 20 whooping cranes were alive in 1920, but their numbers have now grown to approximately 340 and new populations have been established.

Furthermore, some species, such as Przewalski's horses, California condors, black-footed ferrets, Galapagos tortoises from Espanola Island, and Mexican wolves have gone extinct, or were very near extinction, in nature (Table 4.3). All of the living individuals of these species are

TABLE 4.3 Examples of some endangered species that either went through an extreme bottleneck in the wild (top) or where some of the last individuals were captured to start a captive population (bottom). The estimated number in wild populations today are also presented.

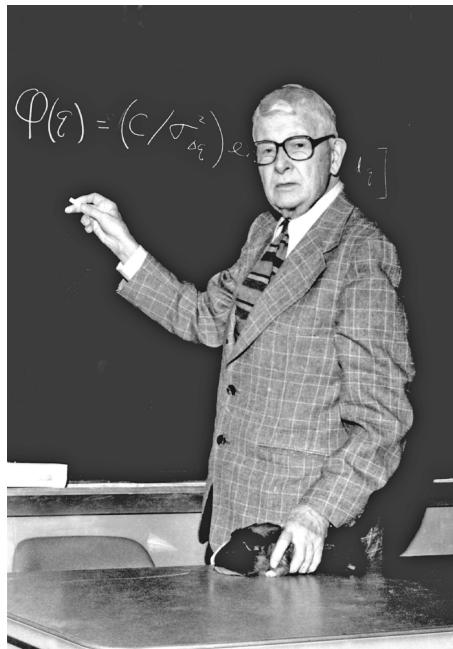
	Bottleneck or founder number (date)	Estimated number in wild today
Wild		
Elephant seal	20 (1900)	200,000
Florida panther	<10 (1960s)	100
Whooping crane	20 (1920)	340
Captive		
Black-footed ferret	6 (1986)	>600
California condor	14 (1987)	155
Galapagos tortoise (Espanola Island)	15 (1960s)	1200
Mexican wolf	7 (1970s)	50
Père David's deer	11 (1890s)	>1700
Przewalski's horse	13 (1900)	> 300

descended from a few individuals that were brought into captivity to establish a protected population. For example, black-footed ferrets, once thought extinct, are descended from six animals (Seal *et al.*, 1989), California condors, the largest bird in North America, are descended from 14 animals, Galapagos tortoises from Espanola Island are all descended from 3 males and 12 females (Milinkovitch *et al.*, 2004), Mexican wolves are descended from 7 founders (Hedrick and Fredrickson, 2008), the Chinese Père David's deer are descended from 11 founders taken to Europe in the 1890s, and Przewalski's horses, the only wild horse species, are descended from 13 founders (Boyd and Houpt, 1994). For these species, there are reintroduction programs that have used descendants of the captured individuals to establish protected populations in natural habitats: All of these programs have had both their setbacks and successes. The management of these species continues to be of great concern (Ballou *et al.*, 1995), and it remains to be seen whether these species have retained, as they passed through the bottleneck caused by their near extinction, enough genetic variation to adapt to future environmental changes.

The effect of finite population size on genetic variation was investigated in depth by Sewall Wright (see p. 192) in the 1930s and 1940s (see Wright 1969, for a summary). In the 1950s, Motoo Kimura (see p. 300) introduced the diffusion equation approach to understanding the impact of genetic drift (see Kimura and Ohta, 1971). Their elegant work has contributed greatly to our basic knowledge concerning the interplay of genetic drift and other factors such as selection, mutation, and gene flow. Here we concentrate on discrete generation models and illustrate, through some numerical examples, the dynamics of genetic variation in a finite population.

At first thought, **genetic drift** and **inbreeding** (see Chapter 8) appear to have similar overall effects on genetic variation, but when examining a given locus within a population, the predicted effect is different. Genetic drift, as we will show below, may cause a change in allele frequency but generally causes no deficiency of heterozygotes within a population. Only when averaged over replicate populations for a given locus, or averaged over independent loci within a given population, does genetic drift result in a deficiency of heterozygotes and no change in allele frequency. On the other hand, inbreeding in a large population can result in a deficiency of heterozygotes, with no change in allele frequency, for a given locus within a population.

Obviously, the fundamental importance of genetic drift in understanding molecular evolution and the very small population sizes in many threatened and endangered species make genetic drift of great significance today in applications of population genetics. Here we discuss the effective population size, an approach that allows the generalization of the effects of genetic drift. We wait to introduce the concept of coalescence—that is, how the effect of genetic drift can be traced backward in the ancestry of a contemporary population—until Chapter 6 on the neutrality theory.



Courtesy of USDA

SEWALL WRIGHT (1889–1988)

Sewall Wright, born in Massachusetts and raised in Illinois, carried out much of his early research on problems in physiological and developmental genetics and was one of the first scientists to recognize a direct relationship between genes and enzymes (Wright, 1917). Working on the guinea pig (being held in this photo), he detailed the complex inheritance patterns for a number of coat-color genes. Although he did not publish his work in book form until the late 1960s and 1970s (his four-volume work is a comprehensive treatment; Wright, 1968, 1969, 1977, 1978), his contributions to inbreeding analysis, the consideration of finite population size, and many other topics are fundamental to population genetics. In fact, genetic drift was sometimes referred to as *the Sewall Wright effect*. Wright used a number of ingenious mathematical approaches to understand the effect of finite population size, and his view of the factors (and their interactions) affecting evolutionary genetic phenomena is central to the thinking and approaches of most modern-day population geneticists. Provine (1986) wrote a biography of Wright, and Hill (1995) wrote a perspective on his early papers.

I. THE EFFECT OF GENETIC DRIFT

All the above examples of restricted population size can have the same general genetic consequence of genetic drift. **Genetic drift** is the *chance changes in allele frequency that result from the random sampling of gametes from generation to generation in a finite population*. Genetic drift has the same expected effect on all loci in the genome. In a large population, on the average, only a small chance change in the allele frequency will occur as the result of genetic drift. On the other hand, if the population size is small, then the allele frequency can undergo large fluctuations in different generations in a seemingly unpredictable pattern and can result in chance **fixation** (going to a frequency of 1.0) or the **loss** (going to a frequency of 0.0) of an allele.

Figure 4.1 illustrates the type of allele frequency change expected in a small diploid population with two alleles. This example uses Monte Carlo simulation with uniform random numbers to imitate the allele changes in four populations (see p. 19). In Figure 4.1, the solid lines are four replicates of a hypothetical diploid population of size $N = 20$ ($2N = 40$), and the broken line is the mean frequency of allele A_2 over the four replicates.

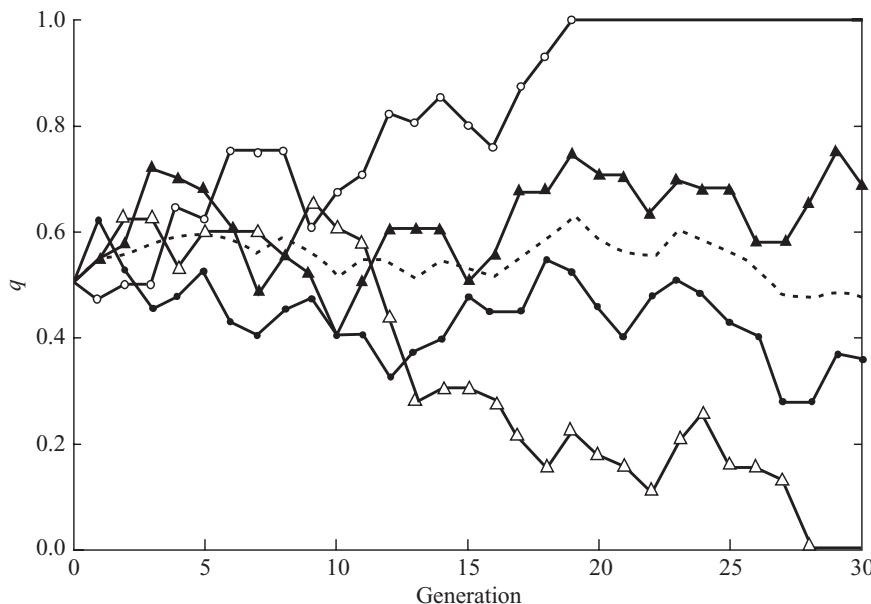


FIGURE 4.1 Frequency of allele A_2 over time for four replicates (solid lines) of a population of size 20. The mean frequency of allele A_2 for the four replicates is indicated by the broken line.

All of the replicates were initiated with the frequency of allele A_2 equal to 0.5. One of these simulated replicates went to fixation for the A_2 allele in generation 19 (open circles), and another lost the A_2 allele in generation 28 (open triangles). The other two replicates were still segregating for both alleles at the end of 30 generations. As shown here, genetic drift may cause large and erratic changes in allele frequency in a rather short time, and illustrating that small population size causes replicate populations to drift apart in allele frequency.

On the other hand, the mean of the four replicates varied much less. It ranged from 0.625 in generation 19 to 0.475 in generation 30 but was generally near to the initial frequency of 0.5. If there are enough replicate populations, then there is no expected change in the mean allele frequency, so that

$$\bar{q}_0 = \bar{q}_1 = \bar{q}_2 \dots \bar{q}_t \dots \bar{q}_\infty$$

where \bar{q}_t is the mean frequency of A_2 in generation t over all replicates. The constancy of the mean occurs because the increases in allele frequency in some replicates are cancelled by reductions in allele frequency in other replicates.

Individual replicates eventually either go to fixation for A_2 ($q = 1$) or to loss of A_2 ($q = 0$). The *proportion of populations expected to go to fixation for a given allele is equal to the initial frequency of that allele*. In other

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words, if the initial frequency of A_2 is q_0 , then the **probability of fixation** of that allele, $u(q)$ (proportion of replicate populations fixed for it), is

$$u(q) = q_0 \quad (4.1)$$

For example, if the initial frequency of A_2 is 0.1, only 10% of the time will a population become fixed for that allele. On the other hand, if A_2 has an initial frequency of 0.9, 90% of the time it will become fixed. This can be understood intuitively because the amount of change necessary to go from 0.1 to 1.0 is much greater than from 0.9 to 1.0 (there are numerical examples illustrating this below). This finding is a fundamental aspect of the neutrality theory used in molecular evolution (see Chapter 6)—that is, without differential selection, the probability of fixation of a given allele is equal to its initial frequency.

Because the mean allele frequency does not change but the distribution of the allele frequencies over replicate populations does, the overall effect of genetic drift is best understood by examining either the heterozygosity or the variance of the allele frequency over replicate populations (see Example 4.2 for a classic illustration using an eye color variant in *Drosophila*). The examples discussed so far involve the change of a given locus over replicate populations. However, we are often interested in the impact of genetic drift in all the different loci (the total genome) in a given population. If genetic drift affects different genes independently of each other, then the effect of genetic drift can also be observed by looking at multiple genes in the same organism. In reality, this is often difficult because, for example, different loci generally have different numbers of alleles, different allele frequencies, and linkage relationships with other loci that may be influenced by selection. It is still important, however, to remember in our discussion here that although we are talking about the effects of genetic drift at a given locus, genetic drift acts essentially in the same general manner over all of the loci in a given population.

EXAMPLE 4.2 A classic illustration of how finite population size affects allele frequency was provided by Buri (1956). He looked at the frequency of two alleles at the *brown* locus that affects eye color in *Drosophila melanogaster* in randomly selected populations of size 16. The alleles, bw^{75} and bw , were chosen because they appeared to be nearly neutral with respect to each other. As a result, the effect of finite population size on allele frequency could be examined almost independently of the effect of selection. Some data from his study are presented here in two ways: first in Figure 4.2 as the number of the 107 replicate populations that had from 0 to 32 bw^{75} genes in different generations, and then in Figure 4.3 as the mean and variance of the allele frequency over the populations.

The histograms in Figure 4.2 illustrate that the distribution of the allele frequencies over replicates has a greater and greater spread with time. This is a graphical way of presenting

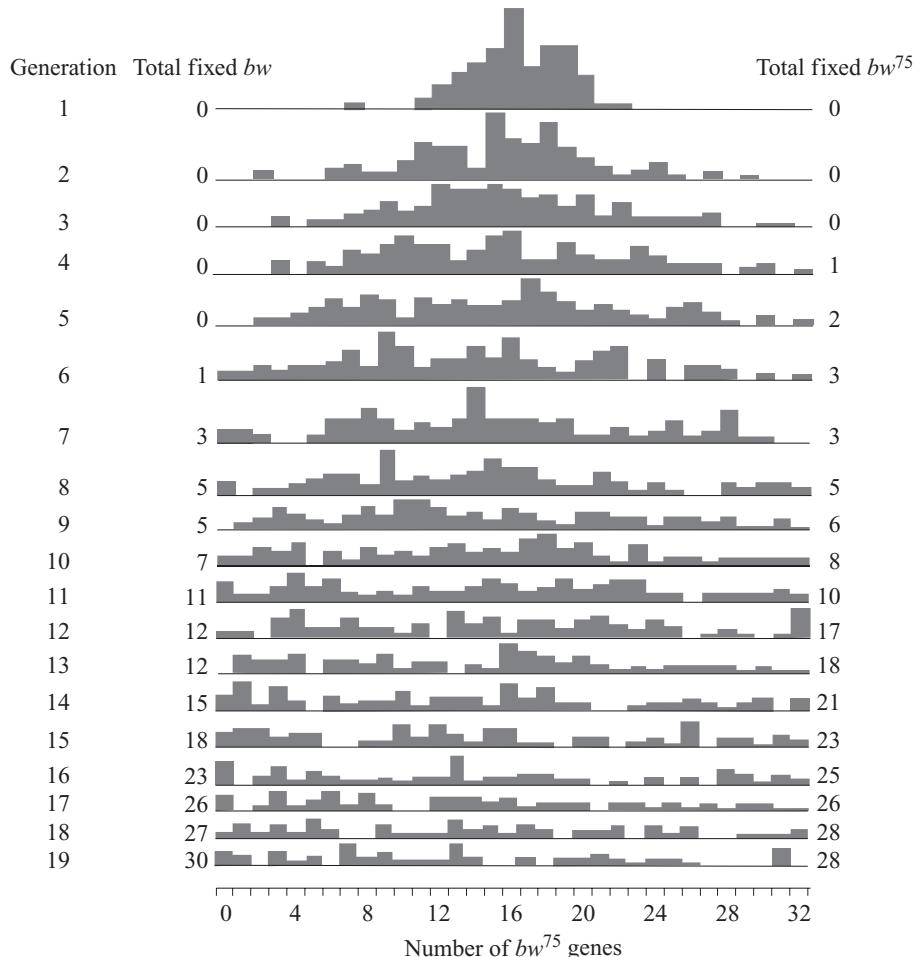
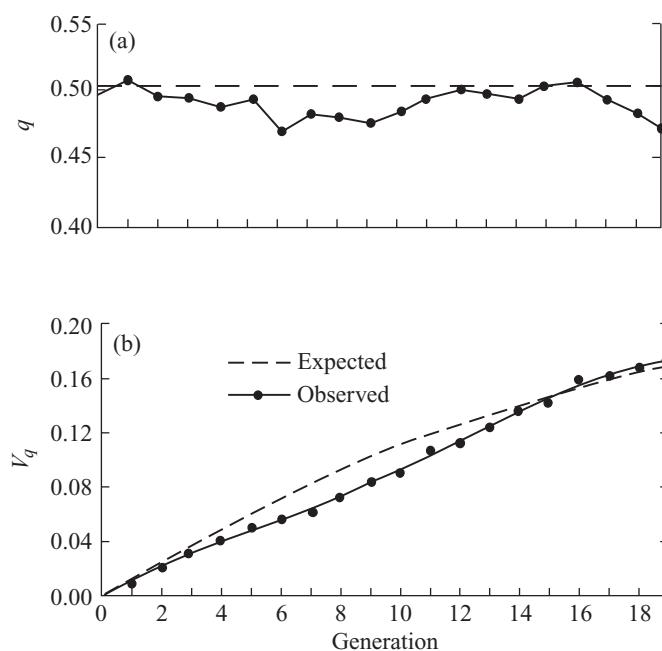


FIGURE 4.2 The distribution of bw^{75} alleles over time in 107 replicate populations of size 16 that were either polymorphic, or lost or fixed, for the bw^{75} allele in the current generation. To the left and right are the numbers of replicates that were fixed for the bw and bw^{75} alleles, respectively, in previous generations. Adapted from P. Buri, 1956.

the type of data given in Figure 4.1 (but for more replicates), with a histogram drawn for each generation. The total number of populations fixed for one of the two alleles increased at nearly a linear rate after generation 4 (see also Example 4.3), and in generation 19 it is nearly equal for the two alleles, with 30 populations fixed for bw and 28 fixed for bw^{75} .

Figure 4.3a gives the mean allele frequency over all replicates (fixed and unfixed) for Buri's experiment. As expected with little or no differential selection, the mean frequency stays very close to the initial frequency, 0.5. The observed variance of the allele frequency over all replicates in Figure 4.3b is indicated by closed circles. As expected, the variance increases

FIGURE 4.3 The observed and expected (a) mean and (b) variance in allele frequency in the experiment of Buri (1956). The expected variance was generated using expression 4.4a and a population size of nine.



with time and appears to be approaching the theoretical maximum of 0.25. A theoretical variance was calculated using expression 4.4a and is given by the broken line. The population size used in this expression as estimated by Buri was nine and gave a close fit to the observed increase in variance with time.

To derive the expected heterozygosity in a finite population, let us assume that there are N diploid individuals in the population and that each individual contributes two haploid gametes to the next generation (Crow and Kimura, 1970). To generate offspring, let us choose alleles randomly (and with replacement) from these parents. The probability that the same allele is drawn twice is $2N[1/(2N)]^2 = 1/(2N)$. Therefore, the probability that the two alleles drawn for an offspring are different is $1 - 1/(2N)$. However, even if the two alleles are different (not from the exact same allele in the parents), it is possible that these alleles are the same because they came from a common ancestor in a previous generation.

Let us assume that f_t is the **inbreeding coefficient** in generation t and that it is defined as the probability that the two alleles in a given individual are **identical by descent**, or **IBD** (see Chapter 8). Therefore,

$$f_{t+1} = \frac{1}{2N} + \left(1 - \frac{1}{2N}\right)f_t \quad (4.2a)$$

which can be rewritten (add unity to both sides of the equation in the process) as

$$1 - f_{t+1} = \left(1 - \frac{1}{2N}\right)(1 - f_t) \quad (4.2b)$$

Later, on p. 444 we will show that $1 - f = H/(2pq)$ so that

$$H_{t+1} = \left(1 - \frac{1}{2N}\right)H_t \quad (4.3a)$$

which indicates that the heterozygosity declines each generation at a rate inversely dependent on the population size.

The relationship between the heterozygosity over several generations can be generated from this expression as

$$H_t = \left(1 - \frac{1}{2N}\right)^t H_0 \quad (4.3b)$$

Thus, for a given initial heterozygosity, H_0 , the heterozygosity t generations later can be predicted. Expression 4.3b is approximately

$$H_t = H_0 e^{-t/2N}$$

From this expression, we can calculate the approximate time until a given proportion of the heterozygosity is lost. For example, the number of generations until a proportion x ($= H_t/H_0$) of the original heterozygosity is left is

$$t = -2N \ln x$$

We can also determine that the time until 50% of the heterozygosity is lost ($x = 0.5$), the half-life, is $1.39N$.

On p. 375, we show how average observed heterozygosity is affected when a population is subdivided (Wahlund effect), an effect identical to examining the average observed heterozygosity over replicate experimental populations. From that consideration, we can use expression 7.3, which relates the observed heterozygosity to the difference in the expected heterozygosity and the variance in allele frequency (V_q) as

$$H = 2pq - 2V_q$$

If we substitute this in expression 4.3b for H_t , assuming that the initial heterozygosity is $2p_0q_0$, and rearrange, the variance in allele frequency in generation t becomes

$$V_{q,t} = p_0q_0 \left[1 - \left(1 - \frac{1}{2N}\right)^t \right] \quad (4.4a)$$

As the number of generations increases—that is, as t becomes large—the variance approaches a maximum of p_0q_0 . For example, if $p_0 = 0.3$, the variance of the allele frequency will approach a maximum of 0.21 at a rate

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that is a function of the population size. After one generation ($t = 1$), the variance is

$$V_q = \frac{p_0 q_0}{2N} \quad (4.4b)$$

which is the binomial sampling variance. As a general yardstick to measure the effect of genetic drift on allele frequency and compare it with other evolutionary factors, such as selection, gene flow, or mutation, the standard deviation of q for one generation is approximately equal to the average absolute value of the allele frequency change. For example, if $p_0 = q_0 = 0.5$ and $N = 50$, then $(V_q)^{1/2} = 0.05$, which is approximately equal to the mean $|\Delta q|$.

This simple model of genetic drift that we have presented here was independently developed by Sewall Wright and Ronald Fisher and is often referred to as the **Wright–Fisher model**. In essence, this model assumes that N diploid parents produce a large number of gametes, these gametes randomly unite to produce a large number of zygotes, and from these zygotes, N progeny are randomly chosen to form the next generation. Implicit in this formulation is that individuals are hermaphrodites (produce gametes of both sexes) so that there is a small probability of $1/N$ of self-fertilization—that is, an individual will fertilize itself (see Chapter 8).

a. The Probability Matrix Approach

Although it is impossible to determine precisely how much change in allele frequency in a population is due to genetic drift, we can calculate the probability that the allele frequency will be a certain value. For example, given an allele frequency of 0.4 in a population of size 10, there is an 18% chance that the allele frequency will remain at exactly 0.4 after one generation. Such probabilities can be calculated for different population sizes and allele frequencies, and they give us a general way to examine the effect of genetic drift. These probabilities can be arranged in matrix form and can give the expected change in the distribution of alleles in a population of a given finite size over time.

Such a matrix has as its elements the probabilities of a certain number of alleles of a particular type in the next generation, given a certain number in the previous generation (see p. 29 for an introduction to using matrices). More specifically, the elements of this matrix, called a **probability transition matrix**, are the probability of $i A_2$ alleles in generation $t + 1$ given $j A_2$ alleles in generation t . These elements can be calculated from the binomial probability expression as follows:

$$x_{ij} = \frac{(2N)!}{(2N - i)!i!} \left(1 - \frac{j}{2N}\right)^{2N-i} \left(\frac{j}{2N}\right)^i$$

where the frequency of A_2 in generation t is $j/2N$ and there are $2N$ alleles in the population.

TABLE 4.4 A probability transition matrix for a population of size two ($2N = 4$), where the values indicate the probability of $i A_2$ alleles in generation $t + 1$, given $j A_2$ alleles in generation t .

Generation $t + 1$	Generation t				
	0	1	2	3	4
0	1	0.3164	0.0625	0.0039	0
1	0	0.4219	0.25	0.0469	0
2	0	0.2109	0.375	0.2109	0
3	0	0.0469	0.25	0.4219	0
4	0	0.0039	0.0625	0.3164	1

A simple example of such a matrix is given in Table 4.4 for a population of size two ($2N = 4$). The matrix has five columns corresponding to the possible states in generation t (0, 1, 2, 3, or 4 A_2 alleles) and five rows corresponding to the possible states in generation $t + 1$. The first and last columns have only one nonzero element, in the first and last rows, respectively. This occurs because once a population is homozygous either for A_1 or A_2 it will continue to be homozygous for that allele if the lost allele is not reintroduced into the population. As a result, these two states, 0 A_2 and 4 A_2 alleles, are termed **absorbing states**. On the other hand, all of the elements in the middle three columns are nonzero, which indicates that there is a probability of a population moving to all other possible states from these states. For example, the probability of 0 A_2 alleles in generation $t + 1$, given 1 A_2 allele in generation t , x_{01} , is $(0.75)^4 = 0.3164$. The probabilities in all columns sum to unity because these values specify all of the possible transitions from a given initial state.

Once we have a transition matrix that gives the probability of change from one state to another, we can evaluate how the distribution of allele frequencies for populations of a given size is expected to change with time. Such a *distribution of allele frequencies over populations of the same size* is termed the **allele-frequency distribution** (or often called the **gene-frequency distribution**). We can observe the change of this distribution by assuming some initial distribution of allele frequencies over populations and then calculating distributions in future generations using the transition matrix. More specifically, the proportion of populations that have $j A_2$ alleles in generation t is $y_{j \cdot t}$, and the sum over all possible population states is unity, or

$$\sum_{j=0}^{2N} y_{j \cdot t} = 1.0$$

If we call the matrix of probability transition values (the x_{ij} values) \mathbf{X} and the vector of population states (the $y_{j \cdot t}$ values) \mathbf{Y}_t , then we can specify the distribution of population states from one time to the next by

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multiplying the transition matrix by the vector of population states (remember, this is the allele-frequency distribution) or

$$\mathbf{Y}_{t+1} = \mathbf{X}\mathbf{Y}_t$$

In other words, the proportion of populations in state i at time $t + 1$ can be obtained by postmultiplication of the matrix \mathbf{X} by the vector \mathbf{Y}_t so that

$$y_{i,t+1} = \sum_{j=0}^{2N} x_{ij} y_{j,t}$$

Therefore, the proportion of populations in state i at time $t + 1$ is the sum for all states of the product of the transition to state i from state j and the proportion of populations in state j at time t . If the initial distribution of population states is given as \mathbf{Y}_0 , then the above recursion relationship can be generalized to

$$\mathbf{Y}_t = \mathbf{X}^t \mathbf{Y}_0$$

To illustrate how the population states change over time, let us use the transition matrix given in Table 4.4. Assume that initially all populations had equal numbers of A_1 and A_2 alleles. In other words, two of the four alleles in the zero generation are A_2 so that $y_{2,0} = 1.0$, and all other initial states are 0.0, making $q_0 = 0.5$. With this initial distribution, the distribution of allele frequencies over populations changes with time; it is given in Table 4.5. One observation is that a high proportion of the populations quickly become homozygous either for A_1 or A_2 . In fact, after only three generations, almost 50% of the populations are homozygous either for A_1 or A_2 because of the small population size. Eventually, 50% of the populations become homozygous for A_1 and 50% for A_2 .

The mean frequency of allele A_2 in generation t can be calculated as

$$q_t = \frac{1}{2N} \sum_{j=0}^{2N} j y_{j,t}$$

The frequency of A_2 in the different generations for this example is given at the bottom of Table 4.5. The frequency of A_2 remains at 0.5 even though the

TABLE 4.5 The distribution of allele frequencies and heterozygosity over generations for populations of size two ($2N = 4$) when $q_0 = 0.5$.

Number of A_2 alleles	Generation						
	0	1	2	3	4	...	∞
0	0	0.625	0.1660	0.2490	0.3117	...	0.5
1	0	0.25	0.2109	0.1604	0.1205	...	0.0
2	1	0.375	0.2461	0.1813	0.1356	...	0.0
3	0	0.25	0.2109	0.1604	0.1205	...	0.0
4	0	0.0625	0.1660	0.2490	0.3117	...	0.5
q_t	0.5	0.5	0.5	0.5	0.5	...	0.5
H_t	0.5	0.375	0.2812	0.2109	0.1582	...	0.0

distribution of the allele frequency over replicates continuously spreads until fixation of all of the replicates. Eventually, 0.5 of the replicates become fixed for A_2 ; this probability of fixation is equal to the initial frequency of A_2 .

An important observation is that there is a constant rate of decrease in heterozygosity per generation. The heterozygosity in generation t can be calculated as

$$H_t = 2 \sum_{j=0}^{2N} \left(1 - \frac{j}{2N}\right) \left(\frac{j}{2N}\right) y_{j,t}$$

The relationship of heterozygosity between generations is

$$H_{t+1} = \lambda H_t$$

where λ indicates the characteristic rate of decline of heterozygosity per generation. To illustrate, we can use the heterozygosity calculated for the early generations given in the example in Table 4.5 where H_0 , H_1 , and H_2 were 0.5, 0.375, and 0.2812, respectively. In this case, $\lambda = 0.75$ for all comparisons between adjacent generations.

This expression can be rearranged so that

$$\lambda = \frac{H_{t+1}}{H_t}$$

where λ is specific for a particular population size and is equal to

$$\lambda = 1 - \frac{1}{2N}$$

as was shown in expression 4.3a. In the example in Table 4.5, $\lambda = 1 - 1/(2N) = 0.75$, as calculated above.

A second numerical example is given in Table 4.6, where initially all populations had only one A_2 allele so that $y_{1,0} = 1.0$ ($q_0 = 0.25$) and the other initial states are 0.0. As in the previous example, the distribution quickly spreads, and populations become fixed either for A_1 or A_2 . The frequency of A_2 remains at 0.25, and the rate of decline of heterozygosity, λ , is the same as in the previous example even though the initial allele frequency (as well

TABLE 4.6 The distribution of allele frequencies and heterozygosity over generations for populations of size two ($2N = 4$) when $q_0 = 0.25$.

Number of A_2 alleles	Generation						
	0	1	2	3	4	...	∞
0	0	0.3164	0.4633	0.5484	0.6038	...	0.75
1	1	0.4219	0.2329	0.1471	0.1003	...	0.0
2	0	0.2109	0.1780	0.1353	0.1017	...	0.0
3	0	0.0469	0.0923	0.0943	0.0805	...	0.0
4	0	0.0039	0.0336	0.0748	0.1137	...	0.25
q_t	0.25	0.25	0.25	0.25	0.25	...	0.25
H_t	0.375	0.2812	0.2109	0.1582	0.1187	...	0.0

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as the heterozygosity) is different. Again, the probability of fixation of A_2 is equal to the initial frequency of A_2 , 0.25 in this case.

We can use the probability matrix approach to calculate the distribution of allele frequencies over time for finite populations of different sizes. As an example, let us examine a population of size 20 ($2N = 40$) and follow its distribution over time, again initially assuming equal numbers of A_1 and A_2 alleles so that $y_{20,0} = 1.0$ and all other initial population states are 0.0. Then the distribution of allele frequencies follows the pattern given in Figure 4.4 for generations 1, 5, and 20 (this is a smoothed representation of the actual distribution). After one generation, a large proportion of the populations is still near the initial frequency of 0.5. After five generations, the spread is much greater, and after 20 generations, more than 16% of the populations are homozygous (half for A_1 and half for A_2). Obviously, the spread of the allele frequency distribution takes place very quickly, and by generation 20, there is a nearly uniform distribution among all population states in which there is still polymorphism. Eventually half the populations become fixed for A_1 and half for A_2 because the initial allele frequency was 0.5.

The **mean time until fixation** of an allele (here A_2) depends on the population size and the initial frequency of the allele. As the population size increases, the effect of genetic drift per generation becomes smaller so that it takes longer for chance changes to accumulate and result in fixation. For a given population size, the further the initial frequency is from unity (the frequency when fixed) the longer it takes for an allele to become fixed. The time can be calculated directly from the iteration of the transition matrix until all populations are fixed as

$$T(q) = \frac{1}{q} \sum_{t=1}^{\infty} t(y_{2N,t} - y_{2N,t-1}) \quad (4.5a)$$

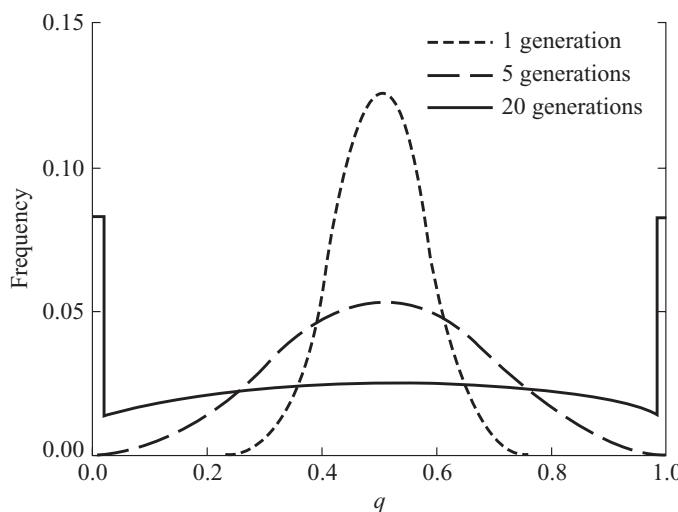


FIGURE 4.4 The smoothed distribution of allele frequency for a population of size 20 and an initial allele frequency of 0.5 after 1, 5, and 20 generations.

where the term in parentheses is the proportion of populations that become fixed in generation t . The summation is divided by the allele frequency because only q of the populations will become fixed for A_2 .

Kimura and Ohta (1971), using a diffusion approximation for a continuous time model, have given an expression for the mean time until fixation of allele A_2 with an initial frequency of q as

$$T(q) = -\frac{4N(1-q)\ln(1-q)}{q} \quad (4.5b)$$

The mean time until fixation is a linear function of population size and decreases as the initial allele frequency gets higher—that is, becomes closer to unity. For example, if the initial allele frequencies are $q = 0.2$ and 0.8 , then the mean times until fixation become $3.57N$ and $1.61N$, respectively. This approximation and the result obtained by using a transition matrix in expression 4.5a are quite close unless the population size is very small. When q is small, as for a new mutant, expression 4.5b becomes

$$T(q) = 4N \quad (4.5c)$$

because $\ln(1-q) \approx -q$. We discuss this elegant prediction from neutral theory—that is, the *expected time to fixation for a neutral mutant is four times the population size*—again in Chapters 5 and 6.

Figure 4.5 gives the proportion of populations fixed for the A_2 allele each generation for three different initial frequencies of A_2 and a population

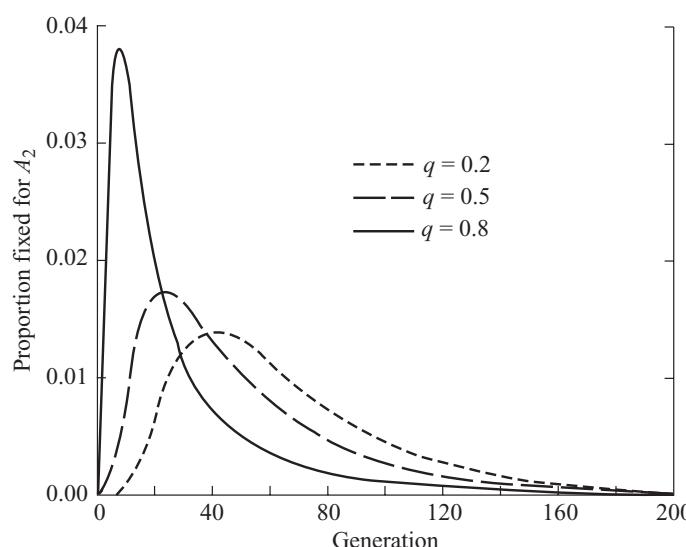


FIGURE 4.5 The smoothed distribution of populations becoming fixed for A_2 in each generation for three initial allele frequencies when $N = 20$.

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of size 20, using the transition matrix approach. When the initial frequency of A_2 is 0.8, most of the fixation takes place in the first few generations. When the initial frequency is 0.2, the peak fixation period of A_2 is delayed considerably. These differences are due to the total amount of allele frequency change necessary for fixation for these different initial frequencies. The mean times to fixation calculated from expressions 4.5a and 4.5b for $q = 0.2$ are 69.5 and 71.4 generations, respectively, in this example. These are of course somewhat less than $4N$ because the initial allele frequency is significantly greater than $1/(2N)$, the lowest it could be in a polymorphic population. Example 4.3 gives the observed and expected fixation times for the *Drosophila* experiment of Buri (1956) in Example 4.2.

EXAMPLE 4.3 We can use the data from the classic *Drosophila* experiment of Buri (1956) that we discussed in Example 4.2 to calculate the observed rate that populations become fixed and compare it with the theoretical predictions from expressions 4.5a and 4.5b. Figure 4.6 gives the observed cumulative proportion of lines fixed for the two alternative alleles, bw and bw^{75} . The expected cumulative proportion of fixation was obtained by iterating a transition matrix with $2N = 18$, the population size that Buri (1956) found that was a good fit to the observed variance in the experiment. Overall, although there is a lag in fixation for both alleles in the early generations, the observed values are generally a close fit to the expectation.

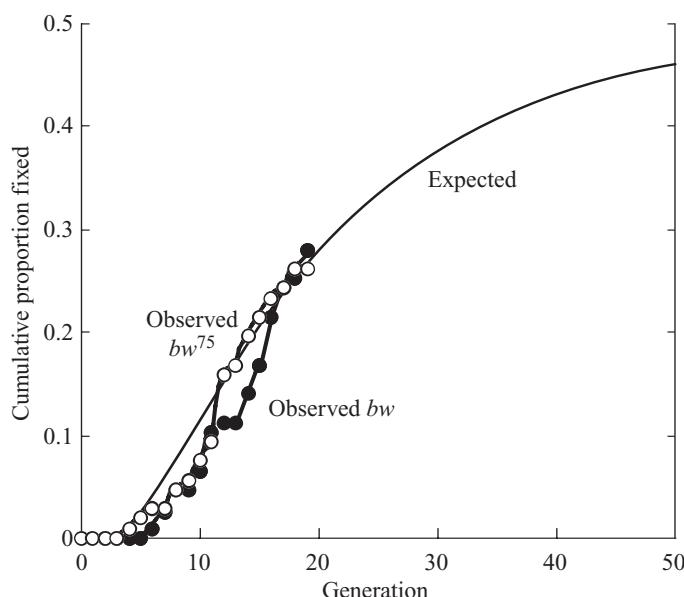


FIGURE 4.6 The observed cumulative proportion of fixed populations for alleles bw (closed circles) and bw^{75} (open circles) (Buri, 1956). Also given is the expected cumulative proportion from iteration of the transition matrix with $2N = 18$. Adapted from P. Buri, 1956.

By using expression 4.5a, we can calculate the expected time to fixation over the 19 generations of the experiment and compare it with that observed. The observed average time, 12.8 generations, is slightly longer than that expected, 11.4 generations. Although the total proportions fixed by generation 19 for that observed and expected are very close (0.542 vs. 0.531), the difference in mean times occurs because the fixations observed took place slightly later than those expected. If we use expressions 4.5a and 4.5b, the overall expected times to fixation are 23.5 and 25.0 generations. If Buri had wanted to continue his experiment until around 90% to 95% of the populations were fixed, based on transition matrix results, he would have had to continue the experiment for another 30 generations.

II. EFFECTIVE POPULATION SIZE

In examining the effects of genetic drift, we have assumed a given population size N . However, the population size that is relevant for evolutionary matters, the number of breeding individuals, may be quite different from the total number of individuals in an area, the **census population size**, that is the appropriate measure for many population ecology studies (Begon *et al.*, 2006). In some cases, the **breeding population size** may be only a small proportion of the total number of individuals; for example, in trees, mammals, or other organisms that mature only after a prolonged juvenile stage, much of the population may be prereproductive. In humans and some other vertebrates, there may be postreproductive adults as well.

The size of the breeding population may be estimated with reasonable accuracy by counting indicators of breeding activity such as nests, egg masses, and colonies in animals or by counting the number of flowering individuals in plants. However, even the breeding population number may not be indicative of the population size that is appropriate for evolutionary studies. For example, factors such as variation in the sex ratio of breeding individuals, offspring number per individual, and numbers of breeding individuals in different generations may be evolutionarily important. All of these factors can influence the genetic contribution to the next generation, and a general estimate of the breeding population size does not necessarily take them into account. As a result, the effective population size, a value that incorporates these factors and allows general predictions or statements irrespective of the particular forces responsible, is quite useful (Wright, 1931; Charlesworth, 2009). In other words, the concept of an ideal population with a given effective size enables us to draw inferences concerning the evolutionary effects of finite population size by providing a mechanism for incorporating factors that result in deviations from the ideal.

The concept of **effective population size**, N_e , makes it possible to consider an *ideal population of size N in which all parents have an equal expectation of being the parents of any progeny individual*. In this ideal, often called the Wright–Fisher model, gametes are drawn randomly from

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all breeding individuals and the probability of each adult producing a particular gamete is equal to $1/N$, where N is the number of breeding individuals. This basic model assumes that these diploid individuals can produce both male and female gametes (monoecy) and includes the possibility of self-fertilization. A straightforward approach that is often used to tell the impact of various factors on the effective population size is the **ratio of the effective population size to breeding (or sometimes census) population size**—that is, N_e/N . This ratio is important because in many natural populations only estimates of N are known, and it is often useful to have at least a relative estimate of N_e .

With this assumption, the distribution of the number of progeny (gametes) per parent (k) approaches the Poisson distribution when N is large (see p. 26 about the Poisson distribution). The general terms in the Poisson distribution are

$$P(k) = \frac{e^{-\bar{k}} \bar{k}^k}{k!}$$

where \bar{k} is the mean number of offspring per parent. Let us assume that on average each parent has two offspring ($\bar{k} = 2$), as would occur in a population that is not changing in size (remember that each offspring has two parents in a sexual, diploid organism). Then the probability that a given individual has no progeny ($k = 0$) becomes $e^{-2} = 0.135$, the probability of one offspring is $2e^{-2} = 0.27$, two offspring is 0.27, three offspring is 0.18, and so on (see Table 4.7). One of the most important characteristics of the Poisson distribution is that the mean number of progeny (\bar{k}) and the variance in the number of progeny, V_k , are equal. On p. 211, we discuss how differences from the Poisson distribution of progeny can be incorporated into an estimate of effective population size.

Three approaches have been used to calculate the effective population size: inbreeding, variance, and eigenvalue effective population sizes (Crow and Denniston, 1988). The **inbreeding effective population size** relates to increase in inbreeding in a given population to that in the ideal population, the **variance effective population size** relates to the increase in variance in allele frequency in a given population to that in the ideal population, and the **eigenvalue effective population size** relates to the loss of heterozygosity in a given population to that in the ideal population. In other words, the effective population size is the size of an idealized population that would produce the same amount of inbreeding, allele frequency variance, or heterozygosity loss as the population under consideration.

For clarity, let us show the general relationship of these definitions of effective population size to the impacts that small population size has on the different measure of genetic variation. First, expression 4.2a can be solved to give the inbreeding effective population size as

$$N_{e(inb)} = \frac{1 - f_t}{2(f_{t+1} - f_t)} \quad (4.6a)$$

Similarly, expression 4.4b can be solved to give the variance effective population size as

$$N_{e(\text{var})} = \frac{pq}{2V_q} \quad (4.6b)$$

and expression 4.3a can be solved to give the eigenvalue effective population size (indicated here as $N_{e(\text{het})}$) to show that it is related to loss of heterozygosity as

$$N_{e(\text{het})} = \frac{H_t}{2(H_t - H_{t+1})} \quad (4.6c)$$

We discuss several derivations for expressions to calculate the effective population size using the concept of the inbreeding effective number. The different types of effective population size are generally either identical or quite similar when the population is not changing in size.

When the population is increasing or decreasing in size, Kimura and Crow (1963) have shown that the inbreeding and variance effective population sizes may differ. For example, assume that the population size declines from a bottleneck (Waples, 2002). The variance effective population size reflects this change immediately because the amount of variation in allele frequency increases as the result of a small number of progeny. On the other hand, the effect of a bottleneck on the inbreeding effective population size is delayed by one generation because the small number of progeny in the first generation does not influence the level of inbreeding and only increases inbreeding in the grand-progeny generation.

The following discussion focuses on how various demographic factors, such as numbers of breeding females and males, variance in reproduction, and variance in numbers over generations, theoretically influence the effective population size.

a. Separate Sexes

Before examining how two separate sexes (dioecy) can be incorporated into the concept of effective population size, let us consider a monoecious population of size N . If the probability of an allele coming from each parent is assumed to be $1/N$, then the probability of two alleles coming from the same individual in the parental generation is $(1/N)^2$. Because there are N individuals, the probability of any of the individuals having alleles coming from the same parent is $N(1/N)^2 = 1/N$. In such an idealized population of N individuals, in which each parent has an equal probability of producing each offspring, then $N = N_e$, the effective population size (this is the inbreeding effective population size).

Now consider a dioecious organism and assume that half the gametes must come from individuals of one sex (females) and half from individuals of the other sex (males). For this case, we can use a probability argument similar to that above to derive the inbreeding effective population size.

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First, the probability that two alleles in different individuals in generation t came from a female in generation $t - 1$ is $(\frac{1}{2})(\frac{1}{2}) = \frac{1}{4}$. If we take this one step further and use the same logic as above, the probability that these two alleles came from the same female is $1/(4N_f)$, where N_f is the number of females in the population. Likewise, the probability that two alleles came from the same male in the previous generation is $1/(4N_m)$, where N_m is the number of males. The combined probability of two alleles coming from the same individual in the previous generation, whether they came from females or males, is then

$$\frac{1}{N_e} = \frac{1}{4N_f} + \frac{1}{4N_m}$$

This expression can be solved for N_e so that the effective population size becomes

$$N_e = \frac{4N_f N_m}{N_f + N_m} \quad (4.7a)$$

If there are equal numbers of females and males, $N_f = N_m = \frac{1}{2}N$, and $N_e = N$.

In some species, the number of females and the number of males are often unequal. Frequently, the number of breeding males is smaller than the number of breeding females ($N_m < N_f$) because some males mate more than once. However, the opposite is true in some species, such as honeybees, where the female may mate with and produce offspring from multiple males. Figure 4.7 shows how the effective population size may vary as the proportion of males, N_m/N , varies for different total numbers. N_e is

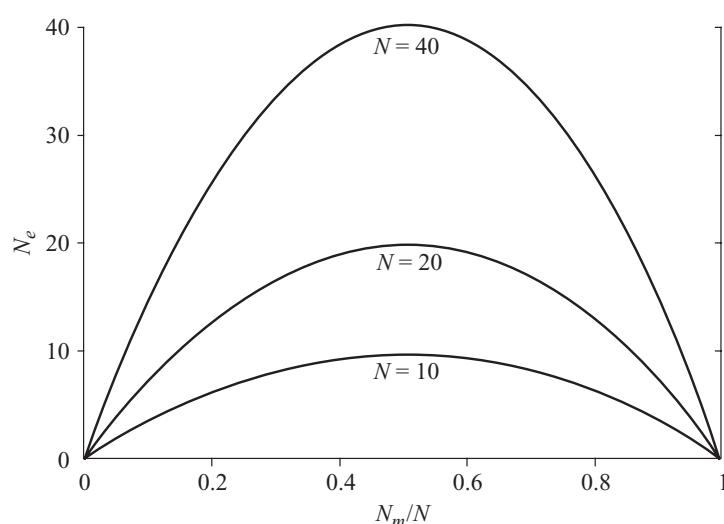


FIGURE 4.7 The effective population size as a function of the proportions of males, N_m/N , for three different total numbers of individuals.

close to N for a substantial range of the proportion of males near 0.5. However, when the proportion is near 0 or 1, then N_e is greatly reduced.

To evaluate the impact of different numbers of the two sexes on the ratio N_e/N , assume that $x_f = N_f/N$ and $x_m = N_m/N$ are the proportions of females and males, respectively, and $x_m = 1 - x_f$, then

$$\frac{N_e}{N} = \frac{4x_f N x_m N}{N^2} = 4x_f(1 - x_f) \quad (4.7b)$$

Taking the derivative of this expression, setting it to 0, and solving for x_f , the maximum N_e/N ratio of unity occurs when $x_f = 0.5$. As examples of values, if 10% or 90% of the breeding animals are females ($x_f = 0.1$ or 0.9), then $N_e/N = 0.36$ from these unequal sex ratios.

Let us assume the most extreme situation possible: one male mates with all of the females in a colony or harem, as is thought to occur in some vertebrate populations in which males control female harems, such as bighorn sheep (see Example 4.9). In this case, expression 4.7a becomes

$$N_e = \frac{4N_f}{N_f + 1} \quad (4.7c)$$

The maximum value of this expression, when N_f becomes large, is 4.0. In other words, because each sex must contribute half the genes to the progeny, restricting the number of breeding individuals of one sex can greatly reduce the effective population size. Figure 4.8 gives the effective population size for different numbers of females when $N_m = 1$, $N_f/2$, or N_f to illustrate the impact of unequal number of the two sexes on N_e .

In the past, the numbers of breeding females and males generally have been estimated from behavioral observations. However, genetic examinations

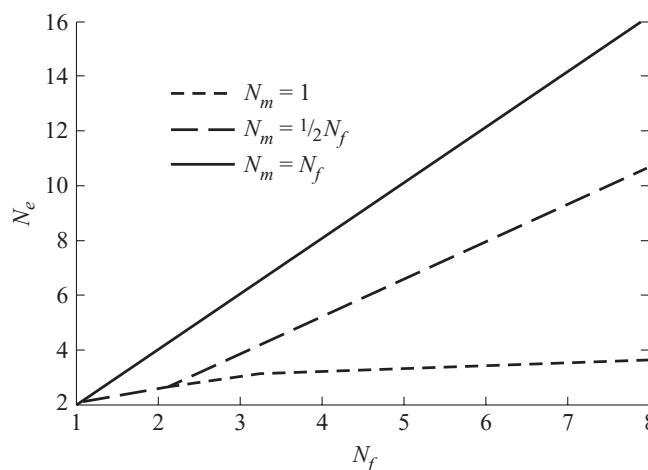


FIGURE 4.8 The effective population size when $N_m = N_f$, $\frac{1}{2}N_f$, and 1.

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in a number of cases have found that behavioral data are not consistent with actual paternity or other genetic data. For example, an examination of the mtDNA and nuclear DNA variation in the southern elephant seal suggests that the estimated sex ratio based on behavioral observations of approximately 40 females per male may greatly overestimate the sex ratio (Slade *et al.*, 1998). The effective sex ratio estimated indirectly from the genetic data is only approximately four or five females per male. The difference in these estimates may be partly due to an overestimate of copulatory success in the behavioral estimate and the short time that a dominant male is a “beachmaster” (1 or 2 years), but other factors may also influence the indirect genetic estimates.

For alleles at an **X-linked gene** or alleles in a **haplo-diploid organism**, the effective population size is somewhat different than that for autosomal genes because females contain two-thirds and males one-third of the alleles. In this case, the effective population size is (Wright, 1931)

$$N_e = \frac{9N_f N_m}{2N_f + 4N_m} \quad (4.8a)$$

If there are equal numbers of females and males ($N_f = N_m = \frac{1}{2}N$) then $N_e = \frac{3}{4}N$ as expected because the males are haploid. In some social Hymenoptera, there may be only one breeding female or queen. When this is so ($N_f = 1$), this expression becomes

$$N_e = \frac{9N_m}{2 + 4N_m} \quad (4.8b)$$

The maximum of this expression when N_m becomes large is 2.25. This equation is plotted in Figure 4.9 along with the effective population size when

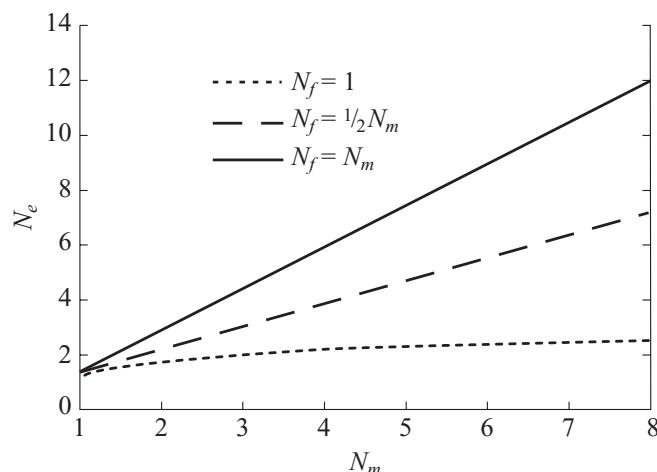


FIGURE 4.9 The effective population size for an X-linked or haplo-diploid gene when $N_f = N_m$, $\frac{1}{2}N_m$, and 1.

$N_f = N_m$ and when $N_f = \frac{1}{2}N_m$. Effective population size is important when we are considering a honeybee colony with 20,000 or more bees (most of which are nonreproductive, worker females), of which only one is a breeding female who mates with perhaps a dozen males to produce all of the progeny.

b. Variation in Number of Gametes

There may be a nonrandom (non-Poisson) distribution of progeny (gametes) per parent because of genetic, environmental, or accidental factors. For example, some birds have strongly determined numbers of eggs in a clutch so the variance of egg number in a clutch may be near zero. In some human populations, a relative uniform number of offspring per parent may lower variation because of efforts to control population growth. On the other hand, if whole clutches or broods survive or perish as a group, then the variance of progeny number may be larger than Poisson. Even more extreme, in some organisms with very high reproductive potential, a substantial proportion of the progeny may come from only a few highly successful parents.

In general, to include variance in the number of progeny and the population is changing in size so that $\bar{k} \neq 2$, the effective population size is approximately

$$N_e = \frac{N\bar{k} - 1}{\bar{k} - 1 + \frac{V_k}{\bar{k}}} \quad (4.9a)$$

where V_k is the variance in the number of progeny (Kimura and Crow, 1963; Crow and Denniston, 1988). The ratio of the effective size to the census size in this case is approximately (Crow, 1954)

$$\frac{N_e}{N} = \frac{2}{1 + \frac{V_k}{\bar{k}}} \quad (4.9b)$$

If $V_k = \bar{k}$, then this ratio is equal to unity, as expected.

When the population is constant in size, $\bar{k} = 2$, the effective population size is

$$N_e = \frac{4N - 2}{V_k + 2} \quad (4.9c)$$

using expression 4.9a. If $V_k = \bar{k}$, a Poisson distribution of progeny, then for both expressions 4.9a and 4.9c, $N_e \approx N$ (see Table 4.7).

If $V_k = 0$, as it may in an artificial population where exactly two progeny from each individual are allowed to survive and reproduce, then $N_e \approx 2N$ or $N_e/N = 2$ (Table 4.7). Therefore, if V_k is kept low, the effects of finite population size can be avoided to some extent, and the effective population size may actually be larger than the breeding or census number.

TABLE 4.7 The expected number of progeny when the mean number of progeny (\bar{k}) is two and there is (a) a Poisson distribution of progeny, (b) all parents have two progeny, and (c) all progeny have the same parent. In the three right-hand columns are the variance of the number of progeny (V_k), the effective population size, and the ratio of the effective population size to the adult number for the three situations.

	Number of progeny (k)							V_k	N_e	N_e/N	
	0	1	2	3	4	...	$2N$	$(e^{-2}2^{2N})/(2N)!$			
(a) Poisson	0.135	0.270	0.270	0.180	0.090	...	$(e^{-2}2^{2N})/(2N)!$	2	N	1	
(b) Two progeny/parent	0	0	1	0	0	...	0	0	$2N$	2	
(c) One parent	$(N - 1)/N$	0	0	0	0	...	$1/N$	$4(N - 1)$	2	$1/N$	

In some human populations, such as in Japan and Sweden, the family size has become fairly uniform through birth control, and this trend may actually make N_e greater than the breeding population size (Example 4.4 discusses a change in the N_e/N ratio over time in the Japanese).

EXAMPLE 4.4 Birth records in human populations are often useful sources of demographic information. Imaizumi *et al.* (1970) examined in detail the records for approximately 1000 families over several generations in a rural community in Japan. One measure of fertility that they used was the total number of children surviving beyond the age of 18. The families were divided in five cohorts according to birthdate of the female parent so that any temporal trends in fertility could be recognized. A summary of these data is given in Table 4.8, where \bar{k} and V_k are the mean and variance of family size. The ratio of the effective population size to the actual size can be calculated from expression 4.9b.

It is obvious from Table 4.8 that both the mean and the variance of family size decreased substantially over time. The mean and variance were nearly equal in the early cohorts, but in the last cohort (1921–1930) the variance was much smaller. As a result, the N_e/N ratio is 1.43; that is, the effective size is substantially larger than the actual size. Imaizumi *et al.* attributed this to the widespread use of birth control and the desire in most families to have only a few—generally two—children.

TABLE 4.8 The mean and variance of total births for five cohorts in a rural Japanese population and the ratio of effective to actual population size using expression 4.8b. Adapted from Y. Imaizumi, M. Nei, and T. Furusho, 1970.

Birthdate of mother					
	1881–1890	1891–1900	1901–1910	1911–1920	1921–1930
\bar{k}	4.60	4.80	4.28	3.28	2.74
V_k	4.58	5.12	4.79	2.75	1.09
N_e/N	1.00	0.97	0.94	1.09	1.43

Often, however, the variance in progeny number may also be larger than the mean, and as a result, N_e/N is lower than unity. Evaluating data

from *D. melanogaster* and taking into account the variance in the number of gametes, Crow and Morton (1955) found that the ratio N_e/N was between 0.74 and 0.90 in several populations and that the ratio of N_e/N in human populations was between 0.69 and 0.95. Nunney (1993, 1996) has shown that, theoretically, the N_e/N ratio within a generation for many organisms should usually be within the range of 0.25 to 0.75.

However, in some organisms, such as shellfish or fishes (Hedgecock *et al.*, 1992; Li and Hedgecock, 1998; Turner *et al.*, 2006), there may be both very high fecundities and very high mortalities of the early life stages (type III survivorship curves; Begon *et al.*, 2006). In addition, in a given year, most of the small number of recruited young, relative to the very large number of offspring produced, may be from a few parents. This combination of high fecundity and chance success of the progeny of broods of a few parents may result in a quite high variance in progeny number, and consequently, the N_e/N ratio may be quite small (Hedrick, 2005a).

To illustrate this effect, assume as an extreme that one individual produces all of the progeny. The value of the variance is

$$V_k = \sum_i x_i(k_i - \bar{k})^2$$

where x_i is the proportion of progeny produced by parents with k_i progeny. Using the x_i values in the bottom row of Table 4.7,

$$V_k = \frac{N-1}{N}(0-2)^2 + \frac{1}{N}(2N-2)^2 = 4(N-1) \quad (4.10a)$$

In other words, the variance in progeny number is equal to nearly four times the number of progeny produced by the successful parent. Using expression 4.8b and with $V_k = 4(N-1)$, then

$$\frac{N_e}{N} = \frac{2}{1+2(N-1)} \approx \frac{1}{N} \quad (4.10b)$$

As the number of progeny produced by the successful individual increases, this ratio approaches 0.

Sometimes it is useful to calculate the effective population size for the two sexes separately because the variance in progeny number may be significantly different between the two sexes. The **female effective population size** and **male effective population size** are

$$N_{ef} = \frac{N_f \bar{k}_f - 1}{\bar{k}_f - 1 + \frac{V_{kf}}{\bar{k}}} \quad (4.11a)$$

$$N_{em} = \frac{N_m \bar{k}_m - 1}{\bar{k}_m - 1 + \frac{V_{km}}{\bar{k}}} \quad (4.11b)$$

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respectively (Lande and Barrowclough, 1987; see Example 4.7 later). These values can then be combined to calculate the overall effective population size as

$$N_e = \frac{4N_{ef}N_{em}}{N_{ef} + N_{em}} \quad (4.11c)$$

This approach has been used to estimate the effective population size in a population of pumas from Yellowstone Park (Culver *et al.*, 2008; see Example 4.5). Nomura (2002) has given expressions for the joint effects of variance in progeny number due to different mating systems and unequal sex ratios.

EXAMPLE 4.5 Only limited published data exist on the number of lifetime offspring produced by individual females and males in a population. One such data set is that of the northern Yellowstone pumas collected from 1987 to 1995 (Murphy, 1998; Culver *et al.*, 2008) to estimate effective population size using a demographic approach. In this case, using microsatellite markers, parentage of 70% of the litters was determined over a 9-year period, a nearly complete reproductive history of a single generational cohort (Table 4.9). Two males fathered 23 and 15 offspring, 72% of all of the genotyped kittens. Also, 15 males that were present on the study area did not have any offspring during this period.

From these data, the mean number and variance in number of offspring for females and males can be calculated. The variance in offspring in males is 11.8 times its mean, reflecting the very unequal reproduction noted above. Using these values in expressions 4.11a and 4.11b, $N_{ef} = 9.14$ and $N_{em} = 4.45$. The ratio of the effective population size to the census number of

TABLE 4.9 The number of kittens for different females and males in northern Yellowstone Park for cougar litters born from 1987 to 1995. Adapted from K. Murphy, 1998, and from M. Culver, *et al.*, 2008.

<i>Females</i>		<i>Males</i>	
<i>Number of kittens</i>	<i>Number of females</i>	<i>Number of kittens</i>	<i>Number of males</i>
0	2	0	15
2	1	2	1
3	3	3	4
4	1	4	2
5	2	15	1
7	2	23	1
8	1		
9	1		
17	1		
$\bar{k}_f = 5.21 \quad V_{kf} = 19.10 \quad N_{ef} = 9.14$		$\bar{k}_m = 2.50 \quad V_{km} = 29.39 \quad N_{em} = 4.45$	

potentially breeding adults for females is $N_{ef}/N_f = 9.14/14 = 0.653$ and for males is $N_{em}/N_m = 4.45/24 = 0.185$ (the census number used here is a low estimate because a number of other animals were present on the study area at some time between 1987 and 1995). If there were random reproduction, these values should approach unity, but here, particularly for males, it is much below unity. The effective population sizes for each sex can then be used in expression 4.11c to obtain an estimate of the overall effective population size $N_e = 11.97$. The ratio of this to the overall census number of potentially breeding adults is $N_e/N = 11.97/38 = 0.315$.

For genes that are inherited only through one sex such as mtDNA, cpDNA, and the Y chromosome, the effective population size for the appropriate sex determines the effect of genetic drift on those genes. In all three of these cases, if there is an equal sex ratio, the expected effective population size is $N_e/4$ because these genes are transmitted in only one sex, and in this sex, they are of only one type—that is, they are haploid. Because mtDNA is generally maternally inherited and cpDNA appears always maternally inherited, the **mtDNA effective population size** and the **cpDNA effective population size** are

$$N_e = \frac{N_{ef}}{2} \quad (4.12a)$$

or half the female effective population size. However, for hermaphroditic species (all individuals are both female and male), as are many plants and some mollusks, $N_e = N_{ef}$ (Latta, 2006).

If the number of males breeding or the male effective population size is small, then the effective size for such a gene may actually be greater than for a nuclear gene in the same organism. For example, if N_m is 1, as discussed above, then the maximum value of N_e for a nuclear gene is 4. Because N_{ef} can be much larger than 8, obviously N_e for an organellar gene can be larger than for a nuclear gene. As an example, consider elephant seals (see Example 4.6 later) in which one male may have a harem of many females so that in a population $N_{em} = 4$ and $N_{ef} = 200$. In this case, N_e for mtDNA is 100, and N_e for nuclear genes is 15.7, approximately 16% of that for mtDNA genes.

The **Y chromosome effective population size**, and for mtDNA when it is inherited paternally as in conifers, is

$$N_e = \frac{N_{em}}{2} \quad (4.12b)$$

or half the male effective population size. In organisms with a low male effective size, the effective size for such a gene could be much smaller than that of a nuclear gene in the same organism. Again, for the elephant seal example used above ($N_{em} = 4$ and $N_{ef} = 200$), for Y chromosome genes, $N_e = 2$, approximately one-eighth of the 15.7 estimated N_e for a nuclear gene.

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TABLE 4.10 The estimated effective population sizes for autosomal, X chromosomal, mitochondrial DNA, and Y chromosomal genes in an Eskimo population, the N_e/N ratios, and the observed and expected N_e/N , relative to that for autosomal genes. Data from S. Matsumura and P. Forster, 2008.

	Autosomal	X chromosome	mtDNA	Y chromosome
N_e	179.2	139.3	53.8	39.7
N_e/N	0.60	0.47	0.18	0.13
Observed (relative to autosomal N_e/N)	1.0	0.78	0.30	0.22
Expected (relative to autosomal N_e/N)	1.0	0.75	0.25	0.25

Matsumura and Forster (2008) estimated the effective population size for Polar Eskimos in North Greenland using genealogical records collected from 1805 to 1974. Table 4.10 gives the estimated autosomal, X chromosomal, mitochondrial DNA, and Y chromosomal N_e , N_e/N ratios, and the observed and expected N_e/N , relative to that for autosomal genes, in this population. Although the observed ratios are similar to that expected, the observed effective population size (and ratios) is slightly larger for females (mtDNA) and slightly smaller for males (Y chromosome) than that expected.

The effect of different ratios of female and male effective population sizes on the relative effective population size for genes on different chromosomes is given in Figure 4.10 (Hedrick, 2007a). As we mentioned above

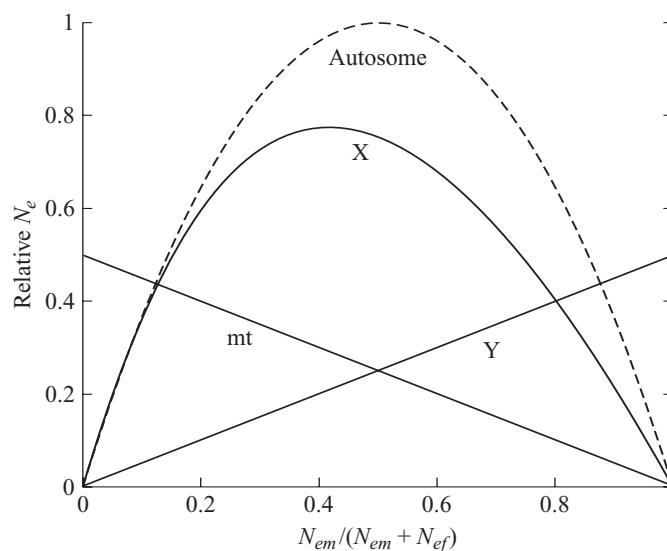


FIGURE 4.10 The effective population size for genes on autosomes, the X chromosome, mitochondrial DNA, and the Y chromosome, relative to that for genes on autosomes with equal sex ratios, when the ratio of male to female effective population size varies. Adapted from P. W. Hedrick, 2007a.

for both autosomal and X-linked genes, when the ratio of the input of either sex is low, the overall reduction in relative effective N_e is largest. For genes that are inherited only through one sex, the effective population size for the appropriate sex determines the relative N_e on those genes. In these cases, if there is an equal sex ratio and random progeny production for both sexes, the expected effective population size is $N_e/4$. Or, when the effective size of appropriate sex is large, the relative N_e may be larger for mtDNA or Y chromosome genes than for autosomal or X-linked genes.

As discussed earlier, the ratio of the effective size for X-linked to autosomal loci is 0.75 when the number of males and females are the same. In general, using expressions 4.7a and 4.8a, and incorporating the effective number of the two sexes, this ratio is

$$\frac{N_{eX}}{N_{eA}} = \frac{9(N_{em} + N_{ef})}{8(2N_{em} + N_{ef})} \quad (4.12c)$$

When the male effective population size becomes small, relative to the female effective size, this ratio becomes larger than 1 and approaches 1.125 at the limit (Cabarello, 1995). Based on the higher than expected observed variation in humans for X-linked genes, relative to autosomal genes, Hammer *et al.*, (2008) estimated that the N_{eX}/N_{eA} ratio was substantially higher than 0.75 and averaged nearly 1 over six populations (however, see Keinan *et al.*, 2009). They concluded that this finding was the result of a very low N_{em} , relative to N_{ef} , because of a very high variance in male reproductive success.

c. Variation in Time

When the population size varies greatly in size in different generations, it can have a large impact on the overall effective population size. The variation in population size could result from regular cyclic variation in population numbers, periodic decimation of the population because of disease or other factors, or seasonal variation in population numbers. When this occurs, the lowest population numbers determine, to a large extent, the overall effective population size because after these bottlenecks, all remaining individuals are descendants of the bottleneck survivors.

The effect of variation in population size can be shown by examining the heterozygosity over time (Crow and Kimura, 1970). Previously, we saw that

$$H_t = \left(1 - \frac{1}{2N}\right)^t H_0$$

If N varies from generation to generation, then

$$\begin{aligned} \frac{H_t}{H_0} &= \left(1 - \frac{1}{2N_0}\right)\left(1 - \frac{1}{2N_1}\right)\left(1 - \frac{1}{2N_2}\right) \dots \left(1 - \frac{1}{2N_{t-1}}\right) \\ &= \prod_{i=0}^{t-1} \left(1 - \frac{1}{2N_{e,i}}\right) \end{aligned}$$

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where $N_{e,i}$ is the effective population size in generation i . Example 4.6 gives an application of variation of N_e over time to explain the low genetic variation in the northern elephant seal.

EXAMPLE 4.6 The northern elephant seal was thought to have been hunted to extinction at the end of the 19th century when the “last” 153 animals were killed by collectors in 1884. Fortunately, some animals apparently survived on a remote beach on Isla Guadalupe, Mexico, and their descendants were rediscovered in 1892. However, the ancestors of the present-day population of approximately 200,000 stretching up to central California may have numbered as few as 20.

Hoelzel *et al.* (2002) found two mtDNA haplotypes with estimated frequencies of 0.27 and 0.73 in the contemporary northern elephant seal population, giving a haplotype diversity estimate of 0.40. Hoelzel *et al.* (2002) also determined mtDNA haplotypes in prebottleneck museum and midden samples and estimated the mtDNA diversity in these samples as 0.80.

To determine what bottleneck size could result in this loss of variation, assume that the loss of mtDNA diversity can be described by the expression

$$H_t = H_0 \prod_{i=1}^t \left(1 - \frac{1}{N_{ef,i}}\right)$$

where the original mtDNA diversity is $H_0 = 0.80$, the observed contemporary diversity is $H_t = 0.40$, and $N_{ef,i}$ is the effective female population size in generation i . Using the approach of Hedrick (1995b) and examining various sizes and duration of the bottleneck, but allowing the population to grow to known census levels in 1922 and 1960, a one-generation bottleneck of census size 15 ($N_{ef} = 3.8$) is consistent with this observed loss of mtDNA variation. If the effective population size of females grew from the bottleneck as $N_{ef,0} = 3.8$, $N_{ef,1} = 6.4$, $N_{ef,2} = 11.0$, $N_{ef,3} = 18.7\dots$, then the mtDNA diversity initially declined rather quickly as $H_0 = 0.804$, $H_1 = 0.592$, $H_2 = 0.501$, $H_3 = 0.455$, $H_4 = 0.431\dots$ and then asymptoted at 0.40 because of the very large population size after a few generations. These results are similar to the conclusions Hoelzel *et al.* (2002) reached using a detailed demographic model and following the loss in the number of mtDNA haplotypes.

The overall effective population size is the one that causes the same reduction in heterozygosity as the varying $N_{e,i}$ values, and thus,

$$\prod_{i=0}^{t-1} \left(1 - \frac{1}{2N_{e,i}}\right) = \left(1 - \frac{1}{2N_e}\right)^t$$

Solving this, the overall effective population size is

$$N_e = \frac{1}{2 \left\{ 1 - \left[\prod_{i=0}^{t-1} \left(1 - \frac{1}{2N_{e,i}}\right) \right]^{1/t} \right\}} \quad (4.13a)$$

If the $N_{e,i}$ values are not too small, then the effective population size becomes approximately

$$N_e = \frac{t}{\sum \frac{1}{N_{e,i}}} \quad (4.13b)$$

Therefore, the effective population size is approximately the harmonic mean of the effective population sizes in individual generations.

For example, assume that the population in subsequent generations has effective population sizes of 10, 100, and 1000. Given that $H_0 = 0.5$, we expect that $H_1 = 0.475$, $H_2 = 0.473$, and $H_3 = 0.472$ because of these finite population sizes. Applying expression 4.13b gives the effective population size as 27.0. Therefore, the heterozygosity declines so that $H_1 = 0.491$, $H_2 = 0.482$, and $H_3 = 0.473$, reaching essentially, in generation 3, the same heterozygosity as when the population size was variable.

To illustrate the importance of a bottleneck in determining effective population size, assume that a population of insects increases 10-fold each of two generations in the summer and then returns to its original low level because of winter mortality; for example, the population sizes are N , $10N$, and $100N$. The mean census number (arithmetic mean) over the three different generations is $36.7N$. However, the effective population size as calculated from expression 4.13b is only $2.7N$, more than an order of magnitude less. In this case, the N_e/N ratio is only 0.074—that is, the effective population size is only 7.4% of the average census number. Example 4.7 shows how variation in progeny number in the two sexes and variation over generations can be included in an overall estimate of effective population size.

EXAMPLE 4.7 As we have seen, the effective population size may be influenced by several factors, including unequal sex ratio, nonrandom variance in progeny number in the two sexes, and variation in effective size over generations. Lande and Barrowclough (1987) gave a useful example to illustrate how all these factors may be incorporated into one estimate of effective population size. Table 4.11 gives the number of progeny produced by individual females and males over three generations in the growing population in their example. Note that there are more females than males contributing each generation, so the mean number of progeny produced per female is less than that per male (Table 4.12). In addition, the variance in progeny reproduction per female is lower than that per male. Using expression 4.11a and these data, we find that the effective population size for females in the first generation is

$$N_{ef} = \frac{(4)(3) - 1}{3 - 1 + \frac{2}{3}} = 4.12$$

Likewise, $N_{em} = 1.38$.

TABLE 4.11 The number of progeny for females and males in an example of a growing population over three generations. Data from R. Lande and G.F. Barrowclough, 1987.

<i>Generation</i>	<i>Females</i>	<i>Number of progeny</i>	<i>Males</i>	<i>Number of progeny</i>
1	A,B	4	M	9
	C	3	N	3
	D	1		
2	A	5	M	9
	B,C	4	N	5
	D	3	O,P	3
	E,F	2		
	G,H	0		
3	A,B	5	M	12
	C,D	4	N	9
	E,F,G	3	O	7
	H,I,J,K	2	P	5
	L	1	Q	3
			R,S,T	0

TABLE 4.12 The mean and variance in the number of progeny for females and males in the three generations of data given in Table 4.11.

<i>Generation</i>	<i>Number of females</i>	<i>Number of males</i>	\bar{k}_f	\bar{k}_m	v_{kf}	v_{km}
1	4	2	3.0	6.0	2.00	18.00
2	8	4	2.5	5.0	3.43	8.00
3	12	8	3.0	4.5	1.64	2.086

Note that the effective population size for females is slightly greater than the census number, because the female variance in progeny number is lower than the mean progeny number, and that the effective number of females is over three times larger than the effective number of males. The overall effective size for this generation is then

$$N_e = \frac{4(4.12)(1.38)}{4.12 + 1.38} = 4.13$$

For generations 2 and 3, the effective sizes for males are again lower than those for females because of the higher variance in progeny number and number of individuals. Using these values, the overall effective sizes for generations 2 and 3 are 8.97 and 13.10, respectively. Substituting these effective population sizes for each generation in expression 4.13a yields the overall effective population size:

$$N_e = \frac{1}{2\left\{1 - \left[\left(1 - \frac{1}{(2)(4.13)}\right)\left(1 - \frac{1}{(2)(8.97)}\right)\left(1 - \frac{1}{(2)(13.10)}\right)\right]^{1/3}\right\}} \\ = 6.91$$

In other words, the loss of genetic diversity in the population is the same as though there were a constant effective population size of 6.91. In this example, the arithmetic mean of the effective sizes over generations is 8.73, somewhat greater than the estimated effective size of 6.91. This indicates that the low effective size in the first generation served to lower the overall effective size. The effective sizes for the generations can also be substituted in expression 4.13b to give

$$N_e = \frac{3}{(1/4.13) + (1/8.97) + (1/13.10)} = 6.98$$

In this case, with only a few generations and not much variation in effective size over generations, the harmonic mean approximation is very close to the exact formula.

Frankham (1995) examined 102 published estimates of effective population size in vertebrate, invertebrate, and plant species. The overall low observed ratio for N_e/N of 0.11 that he calculated for these species appeared to be primarily the result of variable effective population size over time. Subsequently, Vucetich *et al.* (1997) demonstrated analytically that variable population size over generations can greater lower the N_e/N ratio. However, these conclusions are potentially confounded by a statistical artifact in the computation of the N_e/N ratio (Waples, 2002; Kalinowski and Waples, 2002). Specifically, in these studies, N_e/N was calculated as the ratio of the harmonic mean of N_e divided by the arithmetic mean of N . Recently, Palstra and Ruzzante (2008) have compiled data published since the Frankham (1995) study and found that the median N_e/N ratio was 0.14 for a selected data set.

d. Other Factors That May Influence Effective Population Size

First, the amount of **inbreeding** in a population can reduce the effective population size. In a general way, the effective population size, as a function of the amount of inbreeding, is

$$N_e = \frac{N}{1 + f} \quad (4.14)$$

where f is the inbreeding coefficient (see Chapter 8). In other words, inbreeding decreases N_e only slightly when it is on the order found in human populations (mean f ranges from 0.0 to approximately 0.05). However, in highly selfed plants or animals, f may approach 1 and result in N_e approaching $\frac{1}{2}N$. This can be understood intuitively because with nearly complete inbreeding the loss of variation is similar to that in a haploid population of size N . However, in a haploid population of size N , there are only N gametes, which makes it equivalent to a diploid population of size $\frac{1}{2}N$ (Cabarelo, 1994).

Charlesworth (2003) summarized the studies comparing the sequence diversity in taxa with either populations of congeneric species or different populations within the same species that have different levels of inbreeding. Overall, the level of variation in the highly inbreeding populations was much lower than the outcrossing populations, generally even more than predicted by the maximum 50% reduction predicted when the inbreeding coefficient approaches unity (see also Siol *et al.*, 2007). She suggested that the reduced effective recombination in inbreeders (see p. 547) and different life history characteristics in inbreeders and outbreeders may also contribute to differences in variation between the types. Example 4.8 gives the nucleotide diversity of a mustard plant for low, intermediate, and high selfing populations where there is an inverse relationship between the levels of self-fertilization and genetic variation.

EXAMPLE 4.8 Comparisons of the effect of the mating system on genetic variation are most appropriate when different populations of the same species vary in level of inbreeding. Charlesworth (2003) documented the amount of nucleotide diversity at six genes in the mustard plant, *Leavenworthia crassa*. She examined three different types of populations, those that were self-incompatible (low selfing or inbreeding), those with some self-compatibility (intermediate selfing values), and those with self-compatibility (high selfing). Table 4.13 gives the mean nucleotide diversity within the three types of populations. Although there is significant variation over loci, the observed amount of variation for each population is consistent with its level of selfing: highest variation for low selfing and lowest variation for high selfing.

TABLE 4.13 DNA sequence diversity for six loci in *L. crassa* populations with different levels of selfing. Data from D. Charlesworth, 2003.

<i>Locus</i>	<i>Level of selfing</i>		
	<i>Low</i>	<i>Intermediate</i>	<i>High</i>
<i>Adh1</i>	0.036	0.000	0.000
<i>Adh2</i>	0.008	0.006	0.014
<i>Adh3</i>	0.017	0.007	0.000
<i>Gapc</i>	0.028	0.017	0.014
<i>Nir1</i>	0.023	0.022	0.007
<i>PgiC</i>	<u>0.000</u>	<u>0.013</u>	<u>0.011</u>
Mean	0.019	0.013	0.008

Second, many organisms have populations that contain prereproductive (and some postreproductive) individuals as well as reproductive individuals. In addition, individuals of different ages may vary in both their birth and death rates because of environmental and genetic factors. As a

result, individuals of different ages can potentially make very different contributions to the genetic continuity of a population. For example, a postreproductive individual will make no additional contribution to the population even if it remains alive for a long period. On the other hand, an individual that is just reaching reproduction can potentially make a large genetic contribution to the population.

Incorporating detailed **age structure** into an estimation of the effective population size is complicated, particularly when generations overlap and there are age differences in survival and fecundity, and several different approaches have been developed (see Cabarello, 1994; Engen *et al.*, 2007). For example, Nei and Imaizumi (1966) suggested that the effective population size is approximately

$$N_e = TN_a \quad (4.15)$$

where T is the mean age of reproduction in years, **generation length**, and N_a is the number of individuals born per year who survive to reproductive age. For example, if we assume that $T = 5$, similar to that in many larger mammals, and $N_a = 50$, then the approximate effective population size is 250.

The generation length (or generation time) is generally assumed to be 20 or 25 years for prehistoric humans. However, some studies have estimated that the mean age of reproduction is somewhat larger. For example, Matsumura and Forster (2008) examined data from Polar Eskimos born from 1805 to 1974, and Figure 4.11 gives the distribution of the parental ages for these births. The mean mother–daughter interval was 27.0 years

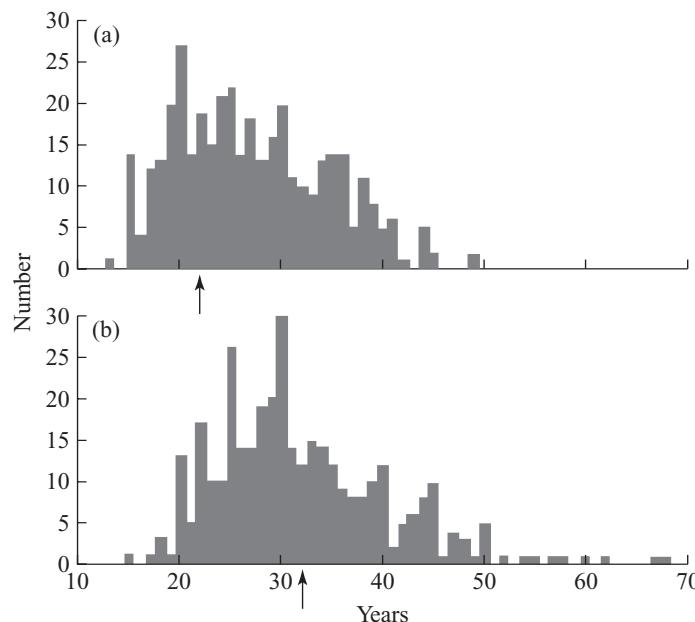


FIGURE 4.11 From a population of Polar Eskimos, the distribution of (a) mother–daughter and (b) father–son intervals where the means are given by arrows. Adapted from S. Matsumura and P. Forster, 2008.

($N = 379$), and the mean father–son interval was 32.1 years ($N = 352$). In other words, the estimated generation length for autosomal genes is about 30 years, for mtDNA is about 25 to 30 years, and for Y chromosome genes is about 30 to 35 years.

In applying such an approach to demographic information on white females in the United States, Felsenstein (1971) found that the ratio of effective population size to census number was approximately 0.34. Nunney and Elam (1994) have suggested an approach in which summary demographic data can be incorporated in an estimate of the ratio of the effective population size to the number of adults. They evaluated estimates in a number of species, including spotted owls, grizzly bears, and the snail *Cepea nemoralis*, and found that their approach was generally robust.

Finally, in many natural situations, no sharp boundaries separate populations, and thus, it is impossible to estimate the effective size of a distinct population. To evaluate the effect of finite population size in species where there is a continuous distribution over space, Wright (1943b) introduced the concept of **neighborhood size**. The size of a neighborhood is the number of individuals in a circle with a radius twice the standard deviation of the per generation gene flow ($2V^{1/2}$) in one direction. Therefore, if we know the density of individuals (d) and area of the neighborhood circle ($4\pi V$), we can estimate the effective population size in the neighborhood as

$$N_e = 4\pi Vd \quad (4.16)$$

Rousset (2000) developed an indirect estimator for Vd , which has been evaluated under different mutation rates and models (Leblois *et al.*, 2003) and variation in different demographic parameters (Leblois *et al.*, 2004).

As an example, Beattie and Culver (1979) estimated directly that in a violet (*Viola pedata*) population, $V = 4.54 \text{ m}^2$ and $d = 9.6/\text{m}^2$ so that the estimate of effective size is 547. In animals, such estimates are complicated because gene flow is a function of a number of factors, including density, food sources, and genetic variation. In plants, estimates of neighborhood size may need to account for gene flow in different life stages. For instance, in the violet example, dispersal was in gametes mediated by pollinators and in seeds, both by ants and ballistic ejection from the capsule.

e. The Founder Effect and Bottlenecks

A population may descend from only a small number of individuals either because the population is initiated from a small number of individuals, causing a founder effect, or because a small number of individuals survived in a particular generation or consecutive generations, resulting in a population bottleneck. These situations can lead to chance changes in genetic variation so that allele frequencies are different from those in the ancestral population, resulting in lower heterozygosity and fewer alleles.

First let us examine the potential importance of the founder effect or a bottleneck on the amount of genetic variation. One simple way to understand this effect is to compare the heterozygosity in the population in which the founder group came from, or that before the bottleneck, and that in the population after the event. For example, expression 4.3a can be solved for the effective population size as

$$N_e = \frac{H_t}{2(H_t - H_{t+1})} \quad (4.17a)$$

where H_t and H_{t+1} are the heterozygosities in the original population and the founding group. Assuming that there are t generations of small numbers as in a bottleneck with size N_e , then expression 4.3b can be solved as

$$N_e = \frac{1}{2(1 - e^{[\ln(H_t/H_0)]/t})} \quad (4.17b)$$

where H_0 is the heterozygosity before the bottleneck. For example, if $H_0 = 0.7$, $H_t = 0.6$, and $t = 5$, then $N_e = 16.4$. Obviously the greater the **reduction in heterozygosity** from the founding event or the bottleneck, the lower the estimate of effective population size in the founder group or the bottleneck generations.

In an effect related to the reduction in heterozygosity, a founder event (or a bottleneck) can also quickly **generate genetic distance** between the ancestral population and the newly founded or bottlenecked population. Genetic distance varies from 0 when two groups have exactly the same allele frequencies to either 1 or ∞ (depending upon the genetic distance measure) when two groups do not share any alleles (see the discussion on p. 378). The effect of a founder event can be understood intuitively if we assume that there are 10 alleles in the ancestral population, and the founder (or bottleneck) generation consists of one fertilized female ($2N = 4$). As a result, at least six alleles must be lost in the bottleneck, resulting in significant changes in allele frequencies in the descendant population and generating genetic distance from the ancestral population in one generation. The expected standard genetic distance (Nei, 1987) after a founder event or a bottleneck is (Chakraborty and Nei, 1977; Hedrick, 1999b)

$$D_t = -\frac{1}{2} \ln \left(\frac{1 - H_0}{1 - H_t} \right) \quad (4.18a)$$

Assuming that there is a founding event or bottleneck of t generations,

$$D_t = -\frac{1}{2} \ln \left[\frac{1 - H_0}{1 - H_0 \left(1 - \frac{1}{2N_e}\right)^t} \right] \quad (4.18b)$$

where N_e is the effective population size in the generations during the founder event or bottleneck.

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FIGURE 4.12 The expected genetic distance for different initial heterozygosities generated by a bottleneck that results in a reduction of heterozygosity.

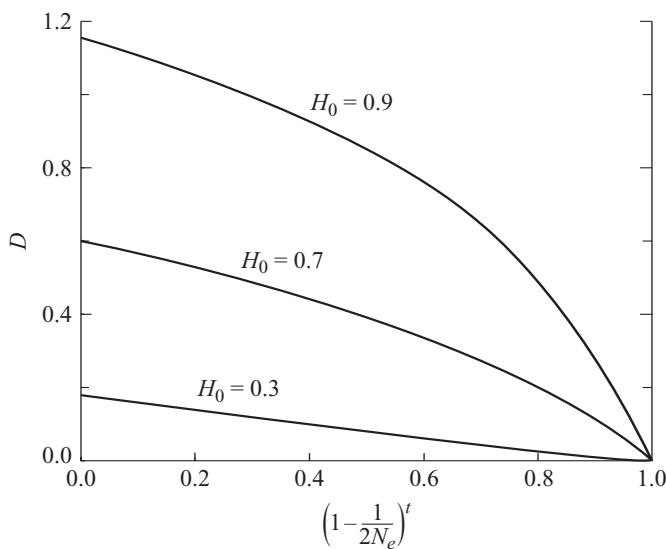


Figure 4.12 gives the expected genetic distance generated by a bottleneck that results in heterozygosity that is $[1 - 1/(2N_e)]^t$ of that before the bottleneck for different initial heterozygosities. When there is high initial heterozygosity, such as found for microsatellite loci, the effect can be quite large. For example, say there is a one-generation bottleneck of two individuals (0.75 on the horizontal axis). Then for H_0 of 0.7 and 0.9, the genetic distances generated are 0.230 and 0.589, respectively (see Example 4.9 for an application of these approaches to bighorn sheep from Tiburon Island in Mexico).

EXAMPLE 4.9 Bighorn sheep (*Ovis canadensis*) have greatly declined in numbers and distribution in the past century because of disease, hunting, and other factors. As a result, there have been a number of introductions throughout western North America in an effort to establish more viable populations. For example, in early 1975, 20 desert bighorn sheep (4 males and 16 females) were captured in mainland Sonora, Mexico, and translocated to nearby Tiburon Island in the Sea of Cortez (Montoya and Gates, 1975). The translocated population grew quickly, and by 1999, an estimated 650 sheep were on the island, all descended from this small founder group.

In 1998, 14 wild sheep were captured and analyzed for genetic variation at 10 microsatellite loci (Hedrick *et al.*, 2001a). As shown in Table 4.14, these data were compared with the variation from three populations of the same subspecies from neighboring Arizona. The heterozygosity was much lower in the Tiburon Island population than in the Arizona populations.

TABLE 4.14 The number of alleles n and heterozygosity H (95% confidence intervals in parentheses) in the introduced Tiburon Island population of desert bighorn sheep and that for three populations of the same subspecies for 10 microsatellite loci. Adapted from P. W. Hedrick, *et al.*, 2001a.

Population	n	H
Tiburon Island, Mexico	2.5	0.42 (0.38, 0.46)
Arizona		
Kofa Mountains	3.7	0.60 (0.55, 0.64)
Stewart Mountains	3.1	0.54 (0.50, 0.58)
Castle Dome Mountains	3.9	0.58 (0.55, 0.62)
Mean (Arizona)	3.6	0.57

If we use the mean heterozygosity for the microsatellite loci for Arizona and Tiburon populations as H_t and H_{t+1} , respectively, then from expression 4.17a, $N_e = 1.92$, a very low value.

The four founder males were ages 1, 1, 2, and 7 years, so that it is likely that the oldest ram made a greater initial contribution than the other males. If it is assumed that the oldest ram was initially the only breeding male, then the effective size of the founder generation could have been, using expression 4.6a, $N_e = 4(16)(1)/(16 + 1) = 3.8$. Although this does not explain all of the loss of heterozygosity, it may explain much of it. In addition, in the subsequent early generations, there may have been more loss of variation due to small numbers, particularly because of few effective breeding rams.

In addition, the average observed genetic distance between the Tiburon Island population and the Arizona populations was 0.312. Using the observed heterozygosities in these populations in expression 4.18a, the genetic distance expected from genetic drift was 0.154, 49.5% of the total observed. In other words, approximately half of the genetic distance between these populations appears to be the result of the recent loss of genetic variation and approximately half because of prior genetic differentiation.

Nei (1987) suggested that genetic distance can be corrected for this effect by assuming that the genetic identity (see p. 379) is

$$I = \frac{J_{xy}}{J_x} \quad (4.18c)$$

where J_{xy} is the product of the allele frequencies in the two populations and J_x is the homozygosity in the population that has not gone through a founder event or a bottleneck. For example, Paetkau *et al.* (1997) found that brown bears on Kodiak Island and black bears on Newfoundland Island had much lower heterozygosities for microsatellite loci than found in other

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samples and also a higher genetic distance between these island populations and mainland populations (1.50) than predicted by geographic distance. The corrected value using expression 4.18c was 1.06, illustrating that loss of genetic variation and genetic differentiation had both contributed to this high genetic distance value.

Another way to illustrate the impact of a founder effect on genetic variation is to calculate the **probability of polymorphism** in the founders. When there are Hardy–Weinberg proportions in the parental population, the probability of polymorphism in a founder group of size N is

$$R = 1 - \left[(p_1^2)^N + (p_2^2)^N + \dots + (p_i^2)^N \right] = 1 - \sum p_i^{2N} \quad (4.19)$$

which is one minus the probability of monomorphism. Figure 4.13 gives the value of R as a function of founder size for several allele frequencies when there are only two alleles. If the alleles are equal in frequency, then the founder size does not need to be very large for a high probability of inclusion of both alleles. For example, the founder population need be only three individuals or larger for there to be a greater than 95% chance of including both alleles when they are equal in frequency. If the frequencies in the parental population of the two alleles are far from equal (e.g., 0.95 and 0.05), then the founder number needs to be 30 or larger for there to be a 95% chance of including both alleles (in reality, of including the rarer allele). For application of this approach and related ideas for genetic conservation of wild plant species in seed banks, see Schoen and Brown (2001) and references therein.

For highly variable loci in particular, the **loss of alleles** occurs more rapidly than the loss of heterozygosity. For example, a microsatellite locus with 20 alleles in a bottleneck of five ($2N = 10$) would lose at least half of

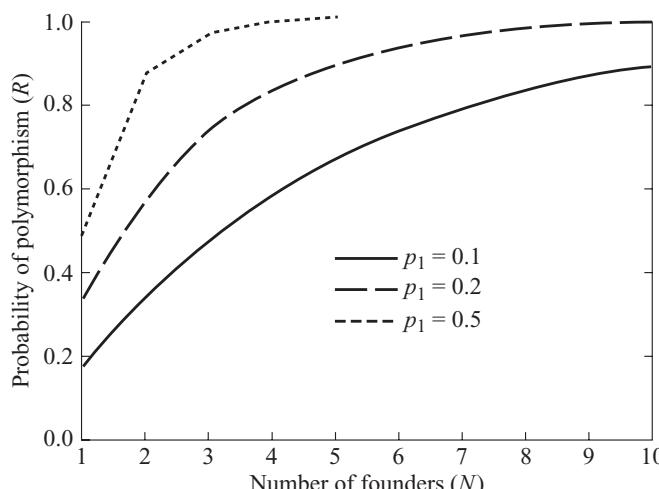


FIGURE 4.13 The probability of polymorphism, given different numbers of founders in a sample for three different allele frequencies.

its alleles, but only 10% of its heterozygosity would be expected to be lost. One way to quantify this effect is to calculate the expected number of alleles remaining after a bottleneck or a founder event

$$\begin{aligned} n_{t+1} &= n_t - [(1 - p_1)^{2N} + (1 - p_2)^{2N} + \cdots (1 - p_i)^{2N}] \\ &= n_t - \sum (1 - p_i)^{2N} \end{aligned} \quad (4.20a)$$

where $(1 - p_i)^{2N}$ is the probability that allele A_i is lost from the population (Denniston, 1978).

To illustrate this effect, assume the “triangular” distribution of allele frequencies used by Pudovkin *et al.* (1996). In this case, the frequency of allele i when there are n alleles is

$$p_i = \frac{i}{n(n + 1)/2} \quad (4.20b)$$

For example, when there are two alleles, $p_1 = 0.333$ and $p_2 = 0.667$, and when there are three alleles, $p_1 = 0.167$, $p_2 = 0.333$, and $p_3 = 0.5$. This distribution is intermediate between assuming that all allele frequencies are equal to $1/n$ and the neutrality distribution (see Chapter 6), in which there are generally one or a few common alleles and a number of rare alleles. The standardized allele number measure suggested by Allendorf (1986)

$$A' = \frac{n_{t+1} - 1}{n_t - 1} \quad (4.20c)$$

is useful here because it scales the loss of alleles between 0 and 1 so that it can be compared to the loss of heterozygosity.

Figure 4.14 shows the loss of alleles for three different founder sizes when there are different numbers of alleles with a triangular distribution. For example, when $N = 5$ and $n_t = 5$, then $n_{t+1} = 4.09$ and $A' = 0.77$.

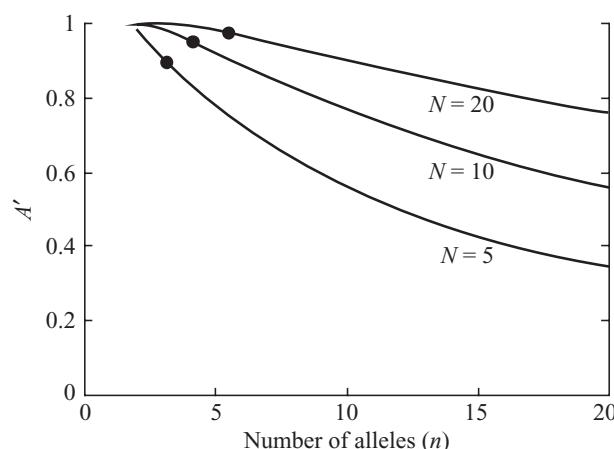


FIGURE 4.14 The standardized number of alleles A' after a one-generation founder event of size N given the number of alleles (n) in the ancestral population before the founder event in a triangular distribution. The solid circles indicate the expected proportion of heterozygosity retained for the three founder sizes.

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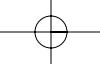
This 23% reduction in the number of alleles is much greater than the 10% reduction in heterozygosity for $N = 5$. In fact, when $N = 5$ and there are four alleles or more, the reduction in the standardized allele number is greater than the loss of heterozygosity. Of course, when there are many alleles, even when the founder size is larger, the loss of allele number is much greater than the loss of heterozygosity. When the founder or bottleneck size is small, rare alleles will be lost quite easily. On the basis of this differential rate of loss and using the neutrality distribution, Cornuet and Luikart (1996) have devised tests to detect bottlenecks, and Luikart and Cornuet (1998) gave a number of examples of populations that have gone through a genetic bottleneck (see p. 271). Under given conditions, Anderson and Slatkin (2007) and Leblois and Slatkin (2007) have provided methods for estimating the number of founders, and Ross and Shoemaker (2008) estimated the number of founders in the invasive fire ant in the United States.

III. TECHNIQUES FOR ESTIMATING EFFECTIVE POPULATION SIZE

There are several different approaches, mainly using genetic techniques, that can be used to estimate the current or recent (sometimes called short-term) effective population size based on the effect of small population size on genetic variation (Leberg, 2005; Wang, 2005; see also Nomura, 2008). For estimation when there is a large effective population size, the effect of sampling may be more important than the small effect of genetic drift. However, small N_e estimates appear to be a good indicator that the effective population size is in fact small. Later (see p. 358), we will discuss the use of DNA sequence variation to estimate the long-term effective population size further back in evolutionary time.

a. Demographic Approach

Estimating the effective population size in many situations from demographic data is dependent on information that is unavailable or difficult to obtain from natural populations, such as the variance in the number of progeny. As a result, approaches to estimate effective population size using genetic data have a great appeal. One approach that uses genetic information is to determine the paternity and maternity of a progeny cohort and then use the demographic approaches given above to estimate the consequent effective population size. For example, the puma data given in Example 4.5 determined maternity and paternity from a known number of parents using microsatellite loci, and the winter run Chinook data set given in Example 4.10 uses microsatellite loci to determine maternity and paternity from known spawners (and matings) used to produce progeny.



EXAMPLE 4.10 Winter run Chinook salmon (*Oncorhynchus tshawytscha*) from the Sacramento River (California) are federally listed as an endangered species. A program to mitigate the factors causing endangerment has included the annual supplementation of young raised at a fish hatchery. In the 1994 brood year, 43,346 progeny from 16 female and 10 male wild-caught spawners were released. After spending more than 2 years in the Pacific Ocean, 93 returning spawners from this cohort were identified and their maternity and paternity were determined by microsatellite loci (Table 4.15).

TABLE 4.15 The number of winter run Chinook salmon progeny released and the number of returning spawners from the different females and males indicated by their identifier (ID) in the 1994 brood year and the ratio of the returns to release for each parent. Adapted from P. W. Hedrick, *et al.*, 2000.

Female parents				Male parents			
ID	Releases	Returns	Ratio	ID	Releases	Returns	Ratio
3	3444	10	1.35	B	4433	9	0.95
4	3055	5	0.77	C	3152	9	0.95
5	2499	7	1.29	D	4360	16	1.61
6	2361	6	1.12	E	6013	8	0.62
7	2421	3	0.57	F	5223	15	1.34
8	2292	2	0.42	G	5098	6	0.51
9	2338	5	1.00	H	4432	10	1.06
11	2230	7	1.39	I	6353	16	1.17
12	2701	3	0.52	J	3012	3	0.46
13	3946	8	0.93	K	1270	1	0.38
14	1364	2	0.69				
15	3426	10	1.37				
16	2855	10	1.64				
17	2766	7	1.17				
18	3088	4	0.61				
19	2270	4	0.75				
Total	43,346	93			43,346	93	

The numbers released were fairly even across both females and males, with percentage parentage ranging from 3.2% (ID 14) to 9.2% (ID 13) for females and from 2.9% (ID K) to 14.7% (ID I) for males. The ratio of the variance to mean reproduction was 0.43 and 0.45 for females and males, respectively, much less than unity. This low variance resulted primarily from a breeding protocol at the hatchery instituted to equalize the production over different females and males (Hedrick *et al.*, 1995).

Every female and male parent was represented in the 93 returning spawners, and the numbers were spread fairly evenly over the 16 females and 10 males (Table 4.15). The ratio of the proportion released to the proportion returning for a given individual gives a perspective on the relative return rate; these ratios ranged from 0.38 (ID K) to 1.64 (ID 16). The ratio of

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the variance to mean reproduction for the returning spawners was 0.51 and 0.55 for the females and males, only slightly higher than that in the released individuals. If we use expression 4.11c, the observed effective population size calculated for the returning spawners was 30.2, not significantly different from that predicted if the salmon returning were a random sample of those released. Overall, the breeding protocol resulted in a rather even distribution of releases, and there was only a small increase in the variance of reproduction across parents in the returning spawners.

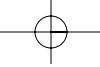
In most situations, such detailed information on parents and offspring is not available. As a result, several different techniques have been developed to estimate the relatively short-term effective population by determining the effect of genetic drift on various population genetic measures. In all approaches, a very small effective population size has the largest effect, and in larger populations, there may be very little signal from genetic drift. One of the general problems with these measures is that they have poor precision, although this can be overcome with larger numbers of marker loci and improved statistical techniques.

b. Temporal Method

The most widely used genetic technique to estimate recent effective population size depends on the fact that, given that no other evolutionary factors are important, genetic drift results in an expected change in allele frequency over generations. As the population size becomes smaller and the number of generations is longer, a greater change in allele frequency from genetic drift is expected. The estimation method using **temporal change of allele frequencies** is based on the expected variance in allele frequency that we discussed in expression 4.4a. However, the variance is a function of the initial allele frequencies so that estimates need to contain a standardization to account for different initial allele frequency values (Waples, 1989). In recent years, there have been a number of developments in the application of this approach (Anderson, 2005; Wang, 2005; Jorde and Ryman, 2007; Waples and Yokota, 2007).

Let us assume that the initial frequency of allele A_i is $p_{i,0}$ and that after t generations of genetic drift it is $p_{i,t}$. The theoretical value of the standardized variance (F) (Wright, 1931) is

$$F = \frac{(p_{i,0} - p_{i,t})^2}{p_{i,0}(1 - p_{i,0})} \quad (4.21a)$$



The expectation E of the numerator in this expression is

$$E[(p_{i.0} - p_{i.t})^2] = p_{i.0}(1 - p_{i.0}) \left[1 - \left(1 - \frac{1}{2N}\right)^t \right]$$

so that the expectation of F becomes

$$E(F) = \left[1 - \left(1 - \frac{1}{2N}\right)^t \right]$$

If t is not too large, then an estimate of the variance effective population size becomes

$$\hat{N}_e = \frac{t}{2F} \quad (4.21b)$$

To estimate the effective population size, we need an estimate of the standardized variance. Nei and Tajima (1981) suggested the expression

$$\hat{F} = \frac{1}{n} \sum_{i=1} \frac{(\hat{p}_{i.0} - \hat{p}_{i.t})^2}{(\hat{p}_{i.0} + \hat{p}_{i.t})/2 + \hat{p}_{i.0}\hat{p}_{i.t}} \quad (4.22a)$$

where n is the number of alleles at a locus. In addition, F is influenced by the size of the two samples such that it is increased by the sampling effects at both sampling times. To adjust for this effect, the estimate of F can be reduced by the reciprocals of the two sample sizes, $2N_0$ and $2N_t$, as

$$\hat{F}' = \hat{F} - \frac{1}{2N_0} - \frac{1}{2N_t} \quad (4.22b)$$

Therefore, an estimate of the effective population size is

$$\hat{N}_e = \frac{t}{2\hat{F}'} \quad (4.22c)$$

For an application of this approach to a Swedish population of brown trout monitored for many years, see Example 4.11.

EXAMPLE 4.11 A natural population of brown trout (*Salmo trutta*) in central Sweden has been studied since the 1970s and changes in both allozyme frequencies and mtDNA haplotypes have been monitored. Table 4.16 gives the frequency of the most common mtDNA haplotype (the frequency of the other haplotype is the complement of this) for 14 annual cohorts (Laikre *et al.*, 1998). Using expression 4.22a, the estimate of the standardized variance between adjacent cohorts was then estimated, and it ranged from a high of 0.286 for the comparison between 1975 and 1976, because of the large increase in the common haplotype frequency between these two cohorts, to near zero in several comparisons.

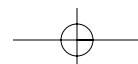


TABLE 4.16 The estimated frequency of the most common mtDNA haplotype p_i , the sample size N , and the estimated \hat{F} and sample size–corrected \hat{F}'_{mt} between adjacent years in 14 annual cohorts from a population of brown trout in central Sweden. Data from L. Laikre, P. E. Jorde, and N. Ryman, 1998.

Cohort	p_i	N	Cohorts for estimate	\hat{F}	\hat{F}'_{mt}
1975	0.640	50			
1976	0.880	50	1975 and 1976	0.286	0.246
1977	0.694	49	1976 and 1977	0.199	0.159
1978	0.800	50	1977 and 1978	0.057	0.017
1979	0.596	52	1978 and 1979	0.190	0.151
1980	0.621	66	1979 and 1980	0.002	-0.032
1981	0.700	50	1980 and 1981	0.028	-0.007
1982	0.675	40	1981 and 1982	0.003	-0.042
1983	0.620	50	1982 and 1983	0.013	-0.032
1984	0.760	50	1983 and 1984	0.091	0.051
1985	0.735	49	1984 and 1985	0.003	-0.037
1986	0.680	50	1985 and 1986	0.014	-0.026
1987	0.660	50	1986 and 1987	0.002	-0.038
1988	0.521	48	1987 and 1988	0.077	0.036
Mean/total	0.680	704		0.074	0.032

Because the sample size for mtDNA haplotypes is half that of a nuclear gene, expression 4.22b needs to be modified to

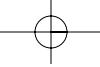
$$\hat{F}'_{mt} = \hat{F} - \frac{1}{N_t} - \frac{1}{N_{t+1}}$$

where N_t is the sample size in year t (Laikre *et al.*, 1998). The sample size–corrected F estimates are somewhat lower than the uncorrected F estimates (Table 4.16), and some of them become negative because the expected effect of sampling is larger than the uncorrected F estimate.

Because brown trout have a generation length much longer than 1 year, they have overlapping generations, and mtDNA gives only an estimate of the female effective population size, expression 4.22c needs to be modified to

$$\hat{N}_{ef} = \frac{C}{G\hat{F}'_{mt}}$$

where C is a correction because of the overlapping generations and G is the estimated female generation length. From demographic data, Laikre *et al.*, (1998) estimated that $C = 18.1$ and $G = 8.3$. Using the mean sample size–corrected \hat{F} of 0.032 over all adjacent cohort pairs at the bottom of Table 4.16, the estimated female effective size is 68.5. Although a good estimate of the actual census numbers in the lake is not available, the numbers appear to be much larger than this estimate of effective population size, suggesting that N_e/N is much less than unity.



c. Heterozygote Excess

The effective population size (actually the effective number of parents or breeders) can be estimated from the **heterozygote excess** found in their progeny. When there are small numbers of parents, the allele frequencies in the female and male parents will differ because of binomial sampling error (Pudovkin *et al.*, 1996; see also Balloux, 2004; Wang, 2005). On p. 76, we discussed how differences in parental female (p_f) and male (p_m) frequencies for allele A_1 resulted in an excess of heterozygotes in their progeny but did not specify the cause of differences. The observed heterozygosity from expression 2.6b is

$$H = 2\bar{p}\bar{q} + \frac{1}{2}(p_f - p_m)^2 \quad (4.23a)$$

where $\bar{p} = \frac{1}{2}(p_f + p_m)$ and $\bar{q} = \frac{1}{2}(q_f + q_m)$. When N parents of each sex are randomly drawn from an infinite population with allele frequencies p and q , the right-hand term in the above expression is half of the variance of the difference in allele frequencies between the sexes and can be given as the variance in the difference between two binomial samples, or $2pq/N$ (Pudovkin *et al.*, 1996), so that

$$H = 2\bar{p}\bar{q} + \frac{pq}{N_e} \quad (4.23b)$$

Assuming that $\bar{p} = p$ and $\bar{q} = q$, solving for the effective number of parents gives the estimate

$$\hat{N}_e = \frac{pq}{H - 2pq} \quad (4.23c)$$

Pudovkin *et al.* (1996) also gave a slightly different, more exact derivation (see also Balloux, 2004).

Although this estimation approach has some advantages (e.g., only one cohort needs to be sampled), theoretical evaluation by Luikart and Cornuet (1999) showed that the confidence intervals were quite large except when the effective number of parents was less than 10 and there were large numbers of both offspring and loci. Furthermore, when they used this approach on 10 data sets where there were known to be only a few parents, half of the estimates were very large or negative, and in most of the rest, the upper confidence interval was infinity.

d. Linkage Disequilibrium

Genetic drift also generates **linkage disequilibrium**, the *statistical association between alleles at different loci* (see Chapter 9). As we will see later, theory predicts that there is an expected amount of linkage disequilibrium

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between neutral loci in a finite population. If we measure linkage disequilibrium by the correlation coefficient r between the allele frequencies at two loci, and assume that the loci are unlinked, then the expected value of r^2 is

$$r^2 = \frac{1}{3N_e} + \frac{1}{N}$$

where N is the sample size. This expression can be solved for N_e as

$$N_e = \frac{1}{3(r^2 - 1/N)} \quad (4.24a)$$

If the rate of recombination (c) between the two loci is known, then the expected value is

$$r^2 = \frac{(1 - c)^2 + c^2}{2N_e c(2 - c)} + \frac{1}{N}$$

(Weir and Hill, 1980) and

$$N_e = \frac{(1 - c)^2 + c^2}{2c(2 - c)(r^2 - 1/N)} \quad (4.24b)$$

For both estimates, N_e varies inversely with r^2 . For example, if $r^2 = 0.5$ and $c = 0.1$ (and large N), then from expression 4.24b, $N_e = 43$.

The linkage disequilibrium approach to estimating N_e is appealing because it is based on only one sample, unlike the temporal method that requires at least two samples. In addition, the linkage disequilibrium approach estimates the effective population size in the very recent past if unlinked loci are used or in the more distant past if tightly linked loci are used. As a general rule for tightly linked loci, the amount of linkage disequilibrium reflects the ancestral effective population size about $1/(2c)$ generations ago (Hayes *et al.*, 2003). Therefore, if $c = 0.0005$, then the estimated N_e reflects that about 1000 generations ago. England *et al.* (2006) and Waples (2006) have suggested that this N_e estimate is biased when the sample size is small, a concern when the approach is applied to conservation genetics. Example 4.12 provides an application of the linkage disequilibrium approach using about 20 million tightly linked SNP pairs in human populations.

EXAMPLE 4.12 Most of the past estimates of N_e using linkage disequilibrium have used a relatively small number of locus pairs. In contrast, Tenesa *et al.* (2007) used data from about 1 million SNPs in four human samples from Nigeria (Yoruba), Europe (CEPH), China (Han), and Japan that provided about 20 million SNP pairs between 5 kb and 100 kb apart. The number of closely linked SNP pairs per chromosome in each sample ranged from about 240,000 on chromosome 19 to well over 2 million on chromosome 8.

Figure 4.15 gives the estimates of N_e from these data for the 22 autosomes and the X chromosome. The average N_e estimates over all chromosomes for the Nigerian, European, Chinese, and Japanese samples are 6286, 2772, 2620, and 2517, respectively. The European, Chinese, and Japanese populations have very similar N_e estimates for nearly all the chromosomes, and the overall N_e estimate for the Nigerian sample is about 2.4 times as large. This pattern is consistent with the hypothesis that the non-African populations descended from a migrant African population that represented a subset of the variation present in Africa at that time. However, these estimates are smaller than estimates using molecular variation (see p. 358). As an explanation, Tenesa *et al.* suggest that the linkage disequilibrium N_e estimate reflects a more recent point in time during which populations have experienced population bottlenecks.

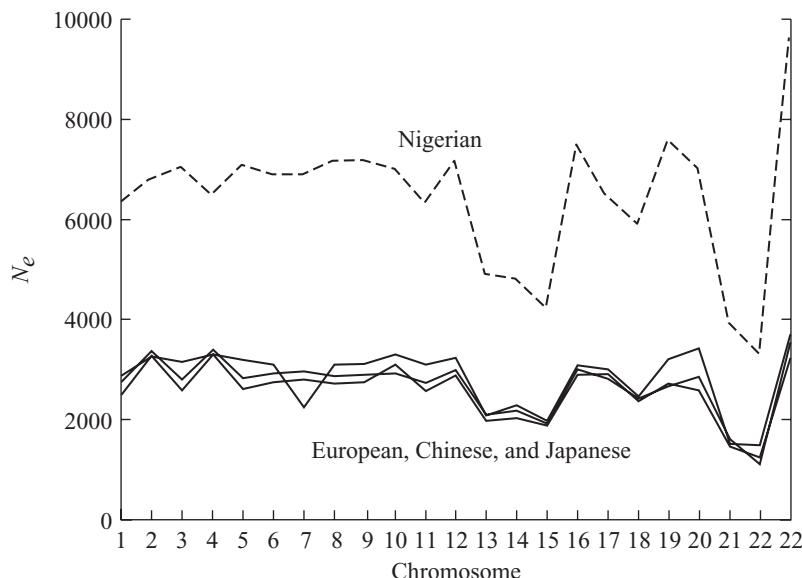


FIGURE 4.15 The effective population size for each chromosome estimated from linkage disequilibrium between about 20 million closely linked SNPs in four human populations. Adapted from A. Tenesa, *et al.*, 2007.

IV. SELECTION IN FINITE POPULATIONS

Remember that when there is no differential selection at a locus, an allele may become fixed or lost as a result of genetic drift. The probability of fixation is equal to the initial frequency of the allele so that when the allele is rare, the probability of fixation is quite low. In contrast, in an infinite population, which by definition has no genetic drift, a selectively favorable allele always increases and asymptotically approaches fixation. In a finite

population, however, a favorable allele may not always be fixed because it may be lost because of the chance effects of genetic drift.

The **probability of fixation** of a favorable allele in a finite population, $u(p)$, is a function of the initial frequency of the allele, the amount of selection favoring the allele, and the finite population size. For a model in which it is assumed that time is continuous, Kimura (1962) developed a general diffusion equation to incorporate these factors and to calculate the probability of fixation of allele A_1 . For a relatively easy-to-follow exposition of the derivation of this general equation, see Kimura and Ohta (1971).

a. Directional Selection

If it is assumed that the relative fitnesses of the three genotypes A_1A_1 , A_1A_2 , and A_2A_2 are $1 + s$, $1 + hs$, and 1, respectively, the values given for directional or positive selection in row c2 of Table 3.5, then the general diffusion equation becomes

$$u(p) = \frac{\int_0^p e^{-2Ns[(2h-1)x(1-x)+x]} dx}{\int_0^1 e^{-2Ns[(2h-1)x(1-x)+x]} dx} \quad (4.25a)$$

where in this section it is assumed $N = N_e$. This general expression for the probability of fixation depends on the initial frequency of allele $A_1(p)$, the level of dominance (h), the effective population size (N), and the selective advantage (s). There are four parameters involved, but the system reduces to three parameters because N and s always appear as a product. Even though the deviation of this expression contains several basic assumptions, the expression appears to be generally accurate even for discontinuous-time models unless the population size is fairly small. When there is additivity ($h = 0.5$), this expression reduces to the much simpler form

$$u(p) = \frac{1 - e^{-2Ns p}}{1 - e^{-2Ns}} \quad (4.25b)$$

The relationship between the different parameters and their effect on the probability of fixation is illustrated in Figures 4.16 and 4.17. In Figure 4.16, the probability of fixation is calculated for three levels of dominance and different initial allele frequencies for $Ns = 2.0$. An Ns value of 2.0 can result, for example, from a combination of $N = 1000$ and $s = 0.002$ or $N = 100$ and $s = 0.02$. The initial allele frequency has a large effect on the probability of fixation, with $u(p)$ increasing quickly as p increases from a low value. The difference in $u(p)$ for different levels of dominance is also substantial at low allele frequencies. For example, if $p = 0.1$, the probabilities of fixation for $h = 0.0$, 0.5 , and 1.0 are 0.223 , 0.335 , and 0.461 , respectively

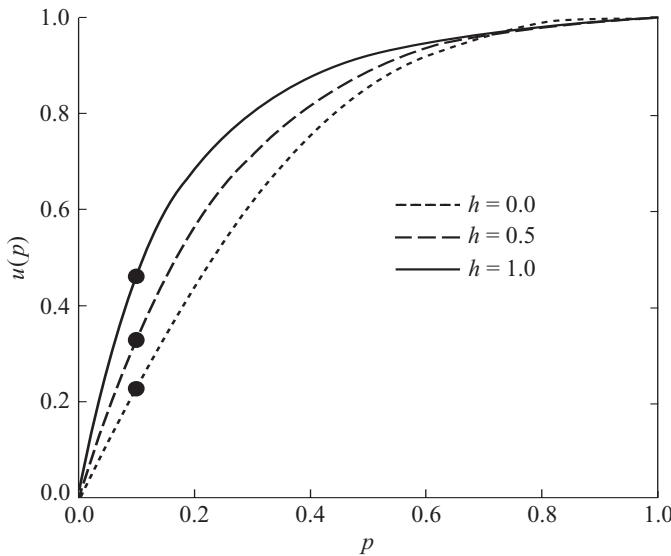


FIGURE 4.16 The probability of fixation for different initial allele frequencies and three levels of dominance when $N_s = 2.0$. The closed circles indicate $u(p)$ for $p = 0.1$.

(closed circles in Figure 4.16). In general, an increasing level of dominance significantly increases $u(p)$ unless $u(p)$ is already near 1.0.

When $N_s \ll 1$, that is, $s \ll 1/N$, the change in allele frequency is primarily determined by genetic drift, and $u(p) \approx p$. On the other hand, if $N_s \gg 1$, then the change in allele frequency is primarily determined by selection, and $u(p) \gg p$. To illustrate the effect of the size of N_s on $u(p)$, Figure 4.17 gives the probability of fixation for several initial allele frequencies for various levels of N_s when there is additivity ($h = 0.5$). As N_s

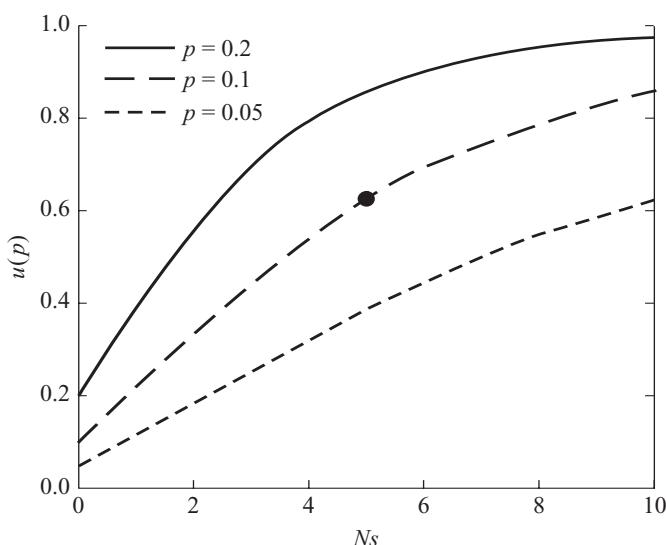


FIGURE 4.17 The probability of fixation for different N_s values and three initial allele frequencies when there is additive gene action ($h = 0.5$). The closed circle indicates $u(p)$ for $p = 0.1$ and $N_s = 5$.

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increases, the probability of fixation also increases quite dramatically so that even if p is only 0.1, the probability of fixation when $N_s = 5$ is already 0.631 (closed circle in Figure 4.17).

The effect of the initial frequency of the favorable allele on the probability of fixation is greatest when comparing adaptation from **standing variation** where the initial allele frequency may be substantial and that from new beneficial mutants (Hermisson and Pennings, 2005; Barrett and Schulter, 2008). In addition, when adaptation is the result of new beneficial mutants, not only is the initial frequency low, there may also be a substantial waiting time until a mutant is generated, making the average time for adaptive change much longer.

When time is discontinuous, the transition matrix approach can be used to calculate the probability of fixation of a favorable allele and to follow the change in allele frequency distribution over time. In such a situation, the elements in the matrix must be modified to reflect selection as well as genetic drift. This can be done by assuming that selection changes allele frequency before sampling so that

$$x_{ij} = \frac{(2N)!}{(2N-1)! i!} (p')^{2N-i} (q')^i \quad (4.26a)$$

where

$$q' = \frac{(1+hs)pq + q^2}{1 + 2hspq + sp^2} \quad (4.26b)$$

and where $q = j/2N$ and $p = 1 - j/2N$. An example is given in Figure 4.18, where $N = 20$, $s = 0.1$, $h = 0.5$, and the initial frequency of A_1 in all the

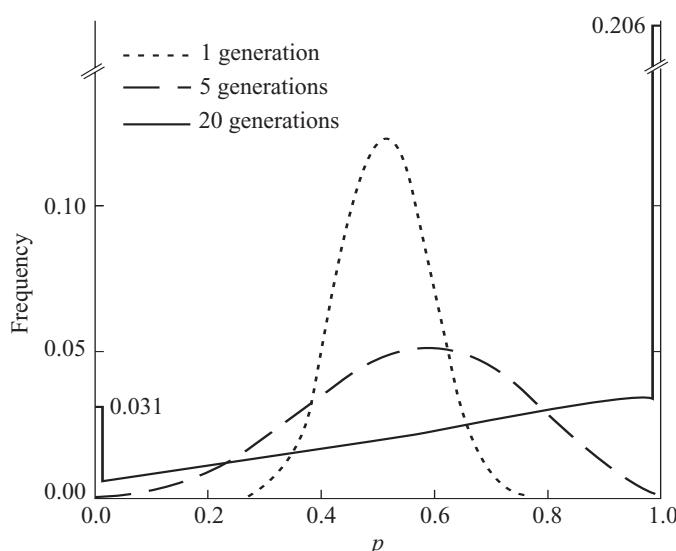


FIGURE 4.18 The smoothed distribution of allele frequency for a population of size 20 and an initial allele frequency of 0.5 with selection such that the fitnesses of A_1A_1 , A_1A_2 , and A_2A_2 are 1.1, 1.05, and 1.0, respectively, after 1, 5, and 20 generations.

populations was 0.5. The probability of fixation for these parameter values, from expression 4.25b, is 0.78. The distribution of the frequency of the favorable allele reflects the effect of directional selection even after five generations. After 20 generations, 20.6% of the populations are fixed for the favorable allele and only 3.1% for the unfavorable allele. To appreciate the effect of selection, compare Figure 4.4 and Figure 4.18, which have identical parameters except for the presence of selection in the latter figure.

In an infinite population, a selectively **detrimental allele** always decreases in frequency and asymptotically approaches loss. In contrast, in a finite population, an unfavorable allele, particularly if its detrimental effects are not large, may increase in frequency by chance and may potentially become fixed. This effect, in which a detrimental allele behaves much like a neutral allele in a small population was pointed out by Wright (1931). Ohta (1973) discussed this phenomenon in terms of molecular evolution and described it as the **nearly neutral model** (see p. 305). She suggested that the relative impact of genetic drift and selection varies with the population size so that detrimental variants may be effectively neutral in a small population, whereas in large populations, they become selected against.

Important concerns for many endangered species are that the existing population generally is small, the species has gone through a bottleneck in recent generations, or the captive or extant population descends from only a few founder individuals. All of these factors may cause extensive genetic drift with a potential loss of genetic variation for future adaptive selective change. In addition, small effective population sizes may result in chance increases in the frequency of detrimental alleles because the absolute value of N_s is so low. For example, the captive population of Scandinavian wolves, initiated from four founders, had a high frequency of hereditary blindness (Laikre *et al.*, 1993), and the captive California condor population, initiated from 14 founders, had a high frequency of a lethal form of dwarfism (Ralls *et al.*, 2000). Although a management strategy of selecting against carriers may reduce the frequency of these detrimental alleles, it may also result in a reduction in variation at other genes. In addition, human populations started from a small founder group may have a chance high frequency of some detrimental alleles (Slatkin, 2004) (see Example 4.13, which discusses a rare type of dwarfism in the Amish).

EXAMPLE 4.13 The Amish population of Lancaster County, Pennsylvania, has a high incidence of a recessive disorder known as six-fingered dwarfism (Figure 4.19) or Ellis–van Creveld (EvC) syndrome (McKusick, 1978). From a population of about 13,000, 82 affected individuals in 40 affected sibships were diagnosed as having this disease. If inbreeding is taken into account, the frequency of the recessive allele is estimated to be about 0.066 and the incidence



FIGURE 4.19 An X-ray of the hands of an Amish person with Ellis–van Creveld syndrome, a form of dwarfism in which affected individuals have six fingers on each hand. Courtesy of Dr. Charles I. Scott, Jr., MD

of the disease is about 0.005. Indicative of the restricted number of founders in this population, the 80 parents in these 40 sibships all trace their ancestry to Samuel King and his wife, early members of the community. From this pedigree information, it appears quite certain that the high incidence can be primarily attributed to founder effect. Either Samuel King or his wife carried the recessive allele; and because many individuals in the population are their descendants, the incidence of the disease is now high.

b. Balancing Selection

A good approach to understand the impact of balancing selection in a finite population is to compare the effect to the situation when there is no selection, or neutrality. For neutrality, we know that the expected rate of loss of heterozygosity per generation is $1 - 1/(2N)$. For any given balancing selection regime, we can define the asymptotic decline (decay) in heterozygosity per generation as d so that the heterozygosity decays as

$$H_{t+1} = (1 - d)H_t$$

where d indicates the asymptotic—that is, independent of the starting allele frequency distribution—amount of loss from unfixed allele frequency states and the amount of gain for the absorbing states. When there is no selection, $d = 1/(2N)$, and this expression reduces to the neutrality expression 4.3a.

The ratio of the rate of decay for a neutral locus over that for a locus undergoing selection is called the **retardation factor** (Robertson, 1962) and is

$$rf = \frac{1}{2Nd} \quad (4.27)$$

The retardation factor is unity when there is no selection—that is, when $d = 1/(2N)$. Selection can slow the rate of fixation compared with neutrality, $d < 1/(2N)$, and can make rf greater than one. Selection can also increase the rate of fixation, $d > 1/(2N)$, making the retardation factor smaller than one. The effect of virtually any selection model can be examined by calculating the effect of selection on allele frequency and then using these values to calculate the elements in the transition matrix as shown in expression 4.26a.

The retardation factor is particularly useful in assessing the impact of various balancing selection models on retaining genetic variation in finite populations. For example, Robertson (1962) investigated in detail the effect of finite population size when selection favored the heterozygote. He assumed that the relative fitnesses of genotypes A_1A_1 , A_1A_2 , and A_2A_2 were $1 - s_1$, 1, and $1 - s_2$, respectively, and then calculated the retardation factor for different values of $N(s_1 + s_2)$. These are plotted in Figure 4.20 for different equilibrium values in an infinite population.

First, notice that the vertical axis is plotted on a logarithmic scale. This is done because when $N(s_1 + s_2)$ is 16 and the equilibrium frequency is near 0.5, the rate of loss of heterozygosity is quite low and the retardation factor becomes large (see Example 4.14, which calculates the retardation factor for an MHC locus in bighorn sheep). One of the most revealing findings of this analysis is that even though selection may result in a balanced polymorphism in an infinite population, in a finite population, less genetic variation may be retained than in a population with no selection. When q_e is below 0.2 or above 0.8, the retardation factor is generally smaller than unity. In other words, in populations with heterozygote advantage and relatively unequal homozygote fitness values, genetic variation is actually eliminated faster than in populations with neutrality.

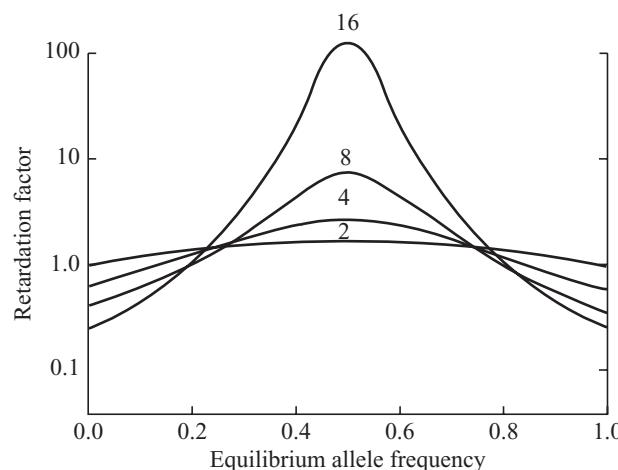


FIGURE 4.20 The retardation factor for the heterozygote advantage model of different values of $N(s_1 + s_2)$. Adapted from A. Robertson, 1962.

EXAMPLE 4.14 There are few comparisons for the loss of genetic variation from genetic drift for loci undergoing balancing selection relative to that of neutral loci (see Glémén *et al.*, 2005, for data on the self-incompatibility locus in a rare *Brassica* species and Zayed *et al.*, 2007, for data on the sex-determination locus *csd* in a solitary bee). In the bighorn sheep populations discussed in Example 4.9, genetic variation at an MHC locus, thought to be important in pathogen resistance, was examined as well as neutral microsatellite loci. Table 4.17 gives the number of alleles and heterozygosity observed for these loci in both the large Arizona populations and the bottlenecked Tiburon population. Notice that there was a greater loss of genetic variation for the microsatellite loci than for the MHC locus.

TABLE 4.17 For the introduced Tiburon Island population and the Arizona populations of desert bighorn sheep, the average number of alleles n , the heterozygosity H , and the ratio of heterozygosities (H_{t+1}/H_t) in the two groups, for 10 microsatellite loci and an MHC locus. Adapted from P. W. Hedrick, *et al.*, 2001a.

Population	Microsatellite		MHC	
	n	H	n	H
Tiburon Island	2.5	0.42	5	0.74
Arizona	3.6	0.57	7.3	0.89
Tiburon/Arizona (H_{t+1}/H_t)		0.74		0.83

We can obtain a rough estimate of the retardation factor for the MHC locus by assuming the following: The cumulative loss over time from only genetic drift for the microsatellite loci is $H_{t+1}/H_t = 0.74$, $d = 1/2N$ for these loci, and $N = 1.92$. For the MHC locus, $1 - d = H_{t+1}/H_t = 0.83$ so that $d = 0.17$. Therefore, the MHC retardation factor, which is the result of both genetic drift and balancing selection, is $rf = 1/[(3.84)(0.17)] = 1.53$. This value is somewhat larger than 1, but is not very large. The relatively small size occurs presumably because the effective population size is so small and genetic drift is so important, and this makes $N(s_1 + s_2)$ relatively small.

PROBLEMS

1. In how many generations will the expected heterozygosity be 5% of the initial value in populations of size 10 and in populations of size 100?
2. Calculate the probability matrix for $N = 2$ with no selection. Assuming that the initial gene-frequency distribution is $(0.2, 0.2, 0.2, 0.2, 0.2)$, what are the gene-frequency distribution and heterozygosity after one and two generations?

3. What is the expected time to fixation for an allele with an initial frequency of 0.1 when the population sizes are 10, 100, and 1000? Why does the time to fixation depend on population size?
4. What is the probability of polymorphism in a founder group of size 4 when there are 2 alleles of equal frequency? What is the probability of polymorphism in a founder group of size 4 when there are 10 alleles of equal frequency?
5. What is the expected increase in genetic distance between two populations when there is a 1-generation bottleneck of $N = 3$ in one of the populations when the initial heterozygosity is 0.6? What is the expected increase in genetic distance between two populations when there is a 10-generation bottleneck of $N_e = 10$ in one of the populations when the initial heterozygosity is 0.8?
6. What is N_e when $N_f = 5$ and $N_m = 1$ for a diploid organism? What is N_e when $N_f = 1$ and $N_m = 10$ for a haplo-diploid organism?
7. We can calculate the effective numbers of founders for the Tristan da Cuhna population discussed in Example 4.1. If the proportions of contribution are standardized so that the mean number of progeny per female or male is 2 ($\bar{k}_f = \bar{k}_m = 2$), then $V_{kf} = 0.66$ and $V_{km} = 2.01$. Using expressions 4.11a and 4.11b, what are the effective number of female and male founders? What is the overall effective number of founders?
8. What is N_e if in four consecutive generations the population sizes are 5, 50, 10, and 100? How different are your answers using expressions 4.13a and 4.13b?
9. From demographic data in a bighorn sheep population, the estimated effective population size for females is $N_{ef} = 100$ and for males is $N_{em} = 10$. What are the expected effective population sizes for an mtDNA gene, a Y-chromosome gene, and an autosomal gene?
10. What is the probability of fixation for an additive favorable allele when its initial frequency is 0.1, $N = 10$, and its selective advantage is 0.01, 0.1, and 0.25?
11. Calculate the probability matrix for $N = 2$ when $\Delta q = \frac{1}{2}sq(1 - q)$ and $s = 0.1$. Given the same initial gene-frequency distribution as in question 2 (0.2, 0.2, 0.2, 0.2, 0.2), find the gene-frequency distribution after one and two generations. Compare these distributions with those for no selection.
12. How would you determine empirically and experimentally the importance of genetic drift affecting variation at a given locus?
13. In the northern elephant seals discussed in Example 4.6, there was no allozyme variation. However, estimates of pre-bottleneck and modern microsatellite variation showed more modern variation than predicted from mtDNA data. Discuss other factors besides the bottleneck that may account for these differences.
14. Calculate the top three estimates of F and the sample size-corrected F in Table 4.16.
15. If you were going to design a laboratory experiment, and assuming that resources and labor are not limiting, to follow the effect of genetic drift, how would you improve upon the experiment of Buri discussed in Examples 4.2 and 4.3?

