Population Genetics

- Population Genetics
- Hardy-Weinberg equilibrium
- Microevolution
- Mutation
- Genetic Drift
- Migration
- Non-random mating
- Natural selection
- Heterozygote advantage

Population Genetics

- Population
- gene pool
- allele frequency
- polymorphism

Determining allele frequency

- starch gel electrophoresis

TABLE 16.2 Determining Allele Frequencies for Codominant Genes

		BY COUNTING ALLELES		
GENOTYPE	MM	MN	NN	TOTAL
Number of individuals:	54	26	20	100
Number of M alleles:	108	26	0	134
Number of N alleles:	0	26	40	66
Total	108	52	40	200

Frequency of M in population: 134/200 = 0.67 = 67%
Frequency of N in population: 66/200 = 0.33 = 33%

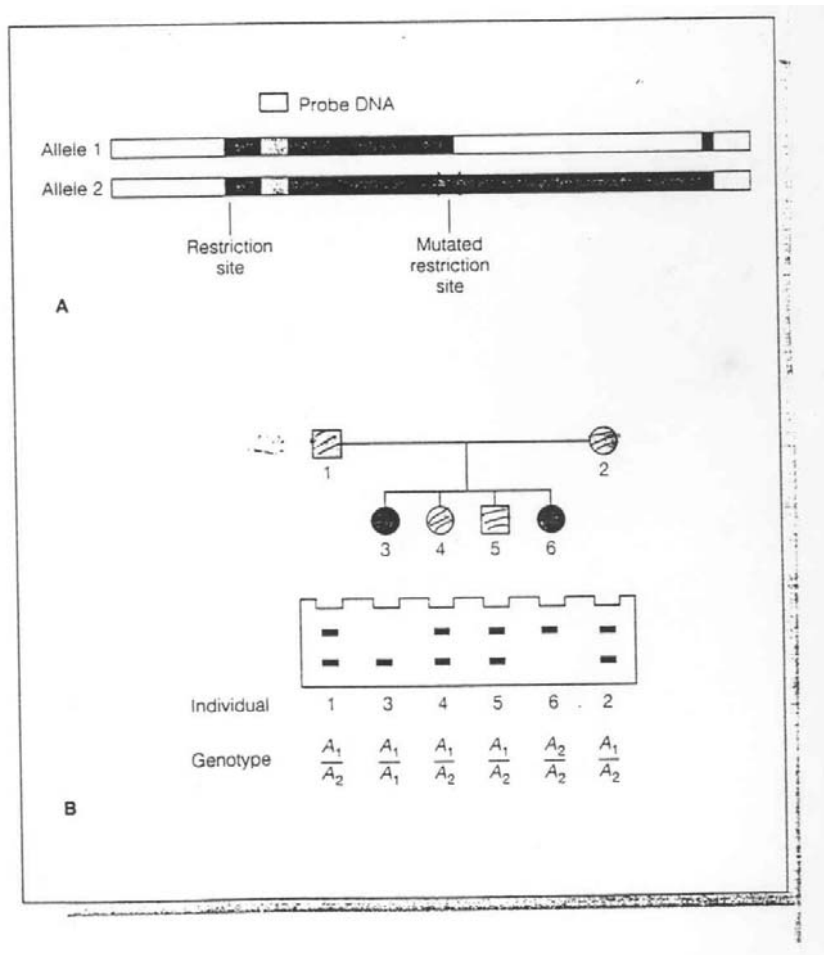
TABLE 16.3 Frequencies of M and N Alleles in Various Populations

	GENOTYPE FREQUENCY (%)			ALLELE FREQUENCY	
POPULATION	MM	MN	NN	M	N
US Indians	60.00	35.12	4.88	0.776	0.224
US Blacks	28.42	49.64	21.94	0.532	0.468
US Whites	29.16	49.38	21.26	0.540	0.460
Eskimos (Greenland)	83.48	15.64	0.88	0.913	0.087

DNA Markers

Figure 8–2

Restriction fragment size variation in DNA. A. Nucleotide substitution (marked with ×) in a DNA molecule eliminates a restriction site. The result is that, in the region detected by the probe DNA, alleles 1 and 2 differ in the size of a restriction fragment. B. Segregation of a restriction fragment length polymorphism like that in part A. In the pedigree, both parents (individuals 1 and 2) are heterozygous A_1 / A_2. Expected progeny resulting from segregation are A_1 / A_1, A_1 / A_2, and A_2 / A_2 in the proportions 1 : 2 : 1. The diagram of the electrophoresis gel shows the expected patterns of bands in a Southern blot. Homozygous individuals numbered 3 (A_1 / A_1) and 6 (A_2 / A_2) yield a single restriction fragment that hybridizes with the probe DNA. The heterozygous individuals show both bands.



Hardy-Weinberg equilibrium

- gene and genotype frequency do not change due to sexual reproduction alone

- **<u>Five assumptions</u>**
- large population
- no selection
- no mutation
- no migration
- random mating

Hardy-Weinberg

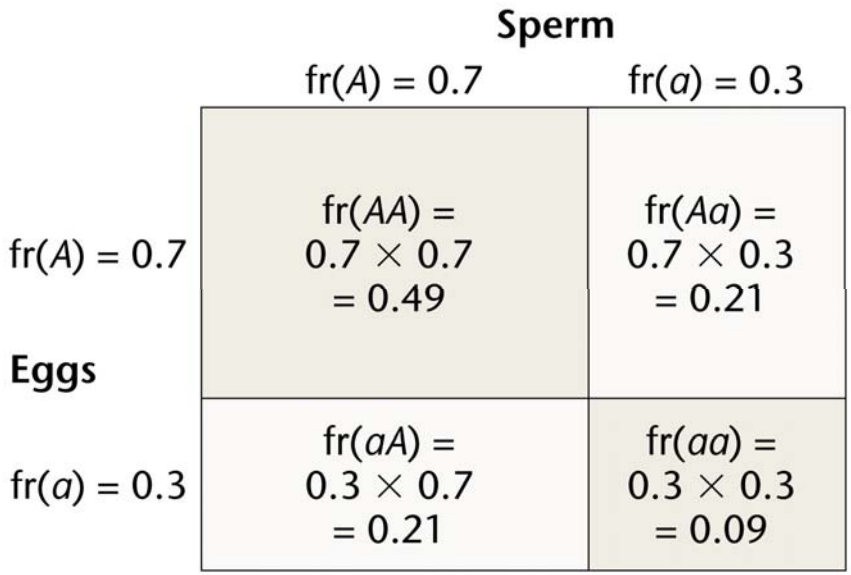
- allele frequency:

$p + q = 1.0$

- genotype frequency:

$p^2 + 2pq + q^2 = 1.0$

determine if population is in HW equilibrium



Multiple alleles

TABLE 16.5 Genotype and Phenotype Frequencies in Multiple-Allele Systems

GENOTYPE	GENOTYPIC FREQUENCY	PHENOTYPE	PHENOTYPIC FREQUENCY
AA	$p^2 = (0.38)^2 = 0.14$	A	0.53
AO	$2pr = 2(0.38 \times 0.51) = 0.39$		
BB	$q^2 = (0.11)^2 = 0.01$	B	0.12
BO	$2qr = 2(0.11 \times 0.51) = 0.11$		
AB	$2pq = 2(0.38 \times 0.11) = 0.082$	AB	0.08
OO	$r^2 = (0.51)^2 = 0.26$	O	0.26

The Frequency of Multiple Alleles Can Be Calculated

Until now we have discussed allele frequencies in genes that have only two alleles. For other genes more than two alleles can be present in the population. In ABO blood types, three alleles of the isoagglutinin locus (I) are present in the population. The alleles A and B are codominant, and both are dominant to O. This system has six possible genotypic combinations:

$$AA, AO, BB, BO, AB, OO$$

Homozygous AA and heterozygous AO individuals have the same phenotype (type A blood), as do BB and BO individuals (type B blood). This dominance relationship among the alleles results in four phenotypic combinations, known as blood types A, B, AB, and O.

The Hardy-Weinberg Law can be used to calculate both the allele and genotype frequencies for this three-allele system by adding another term to the equation. For the three blood group alleles

$$p(A) + q(B) + r(O) = 1$$

In other words, when you add together the frequencies of the A, B, and O alleles, you have accounted for 100% of the alleles for this gene in the population. The genotypic frequencies are given by the equation

$$(p + q + r)^2 = 1$$

Allele frequencies for A, B, and O can be calculated from the phenotypic frequencies in a population if random mating is assumed.

Once we know the frequency of the A, B, and O alleles for a given population, we can then calculate the genotypic and phenotypic frequencies for all combinations of these alleles. The genotypic combinations can be calculated by an expansion of the Hardy-Weinberg equation:

$$p^2\,(AA) + 2pq\,(AB) + 2pr\,(AO) + q^2\,(BB) + 2qr\,(BO) + r^2\,(OO) = 1$$

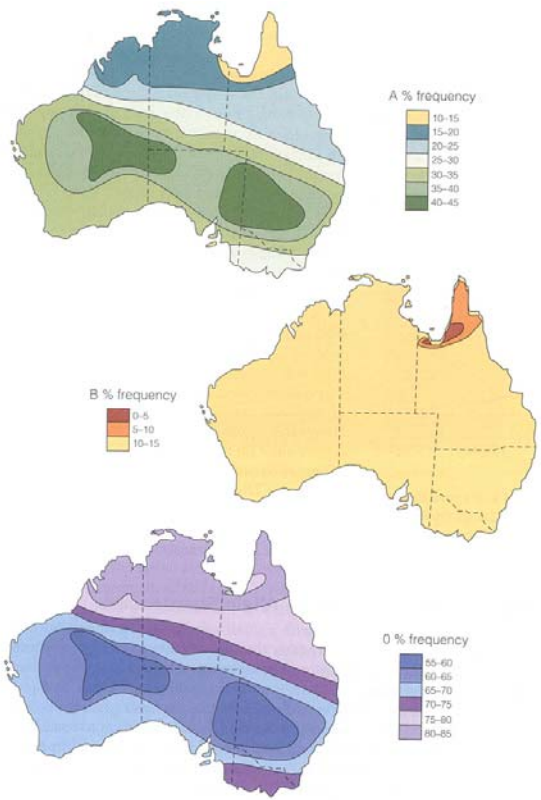


FIGURE 18.1 A reconstruction of the geographic distribution of the ABO alleles in the prehistoric population of Australia.

Calculations

- recessive allele frequency
- heterozygote frequency
- sex-linked genes

and allele frequency

fied by their distinctive phenotype. Suppose that 1 in 2,500 individuals in a population is affected with cystic fibrosis. These individuals have the genotype *aa*. According to the Hardy-Weinberg equation, the frequency of this genotype in the population is equal to q^2. The frequency of the *a* allele in this population is therefore equal to the square root of q^2:

$$q^2 = 1/2500 = 0.0004$$

$$q = \sqrt{0.0004}$$

$$q = 0.02 = 1/50$$

Once we know that the frequency of the *a* allele is 0.02 (2%), we can calculate the frequency of the dominant allele *A* by subtraction:

$$p + q = 1$$

$$p = 1 - q$$

$$p = 1 - 0.02$$

$$p = 0.98 = 98\%$$

In this population, 98% of the alleles for gene *A* are dominant (*A*), and 2% are recessive (*a*). This method can be used to calculate the allele and genotype frequencies for any dominant or recessive trait.

Heterozygotes

TABLE 16.6 Heterozygote Frequencies for Recessive Traits

FREQUENCY OF HOMOZYGOUS RECESSIVES (q^2)	FREQUENCY OF HETEROZYGOTES INDIVIDUALS ($2pq$)
1/100	1/5.5
1/500	1/12
1/1000	1/16
1/2500	1/25
1/5000	1/36
1/10,000	1/50
1/20,000	1/71
1/100,000	1/158
1/1,000,000	1/500
1/10,000,000	1/1582

TABLE 16.7 Heterozygote Frequency for Some Recessive Traits in the United States

TRAIT	HETEROZYGOTE FREQUENCY
Cystic fibrosis	1/22 whites, much lower in blacks, Asians
Sickle cell anemia	1/12 blacks, much lower in most whites and in Asians
Tay-Sachs disease	1/30 among descendants of Eastern European Jews, 1/350 among others of European descent
Phenylketonuria	1/55 among whites, much lower in blacks, those of Asian descent

Sex-Linked Genes

TABLE 16.4 Frequency of X-Linked Traits in Males and Females

MALES WITH TRAIT	FEMALES WITH TRAIT
1/10	1/100
1/100	1/10,000
1/1000	1/1,000,000
1/10,000	1/100,000,000

Microevolution

- Change in allele frequencies
- 5 mechanisms
- Which assumption not valid?

Mechanism	Action on Gene Pool	Usually Adaptive?*
Genetic drift	Random change in small gene pool due to sampling errors in propagation of alleles	No
Gene flow	Change in gene pools due to immigration or emigration of individuals between populations	No
Mutation	Change in allele frequencies due to net mutation	No
Nonrandom mating	Inbreeding or selection of mates for specific phenotypes (assortative mating) reduces frequency of heterozygous individuals	Unknown
Natural selection	Differential reproductive success increases frequencies of some alleles and diminishes others	Yes

Mutation

- Mutation rate (μ): 10^{-5} to 10^{-6} per generation

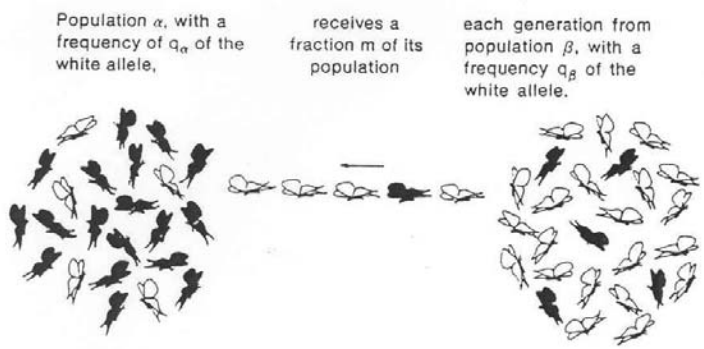
- $P_t = P_o e^{-\mu t}$ t= # of generations

- To reduce P by ½, if μ= 10^{-5} & P_o =0.96
- Requires 69,000 generations
- Mutation source of genetic variation does not really cause rapid evolutionary change

Gene Flow

- homogenizing force
- calculate changes in allele frequency due to migration

- **$\Delta p = m(p_m - p_o)$**
- **M= fraction of migrants to original population**
- **P_m= allele freq of migrating population**
- **P_o= allele freq of original population**



6 EVOLUTION BY GENE FLOW. Population α (*left*), with a frequency of q_α of white alleles, receives a fraction (m) of its individuals from population β (*right*), which has a frequency q_β of white alleles.

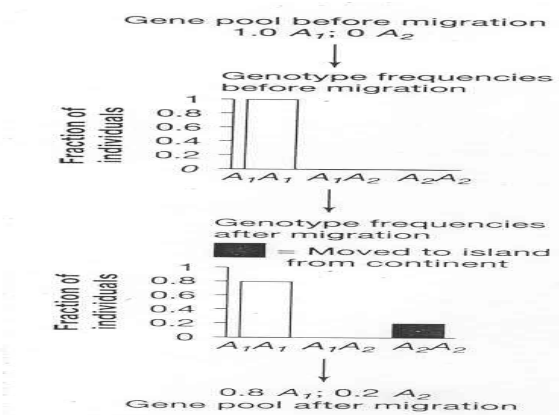
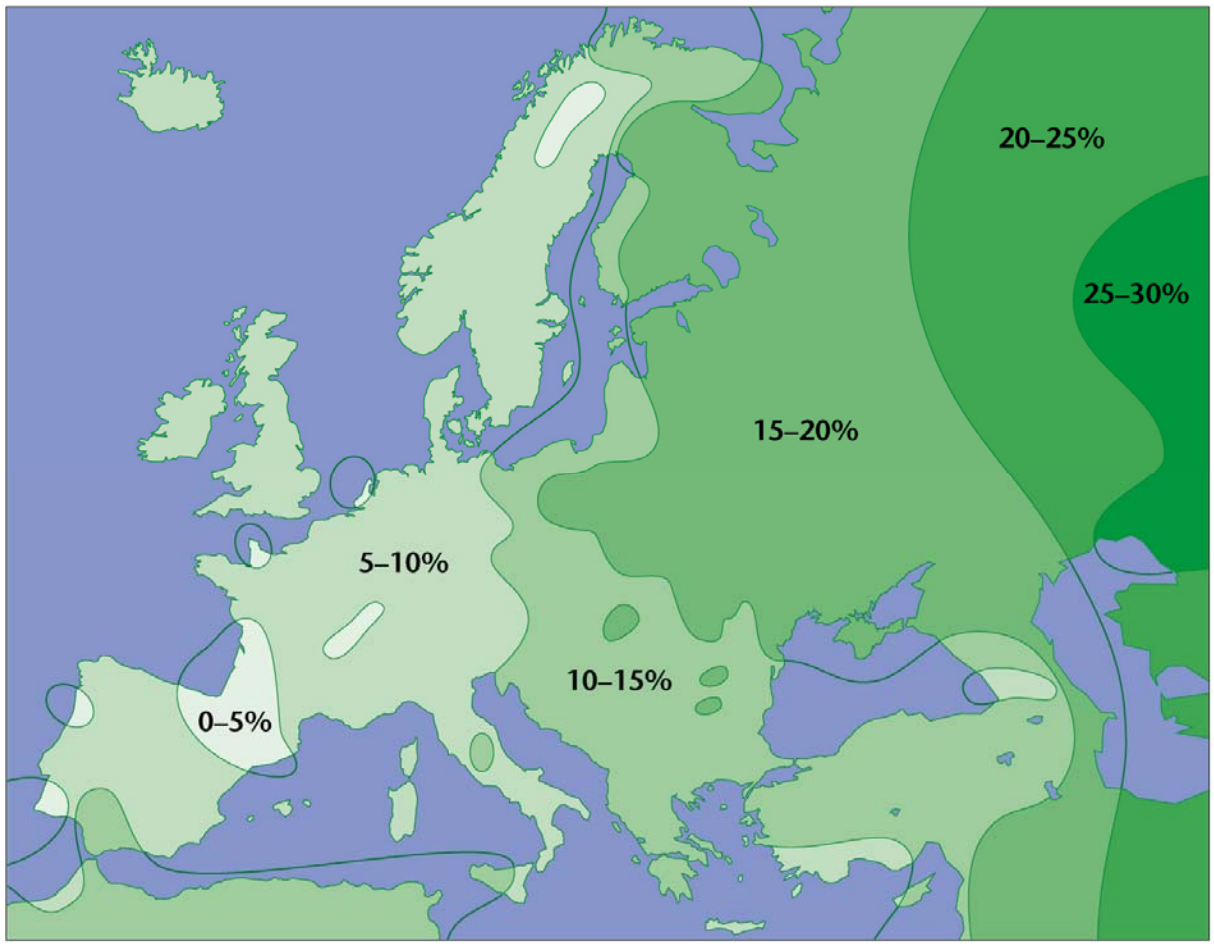


Figure 5.16 **Migration can change both genotype and allele frequencies** This figure follows the imaginary island population described in the text as migrants arrive from the continent.

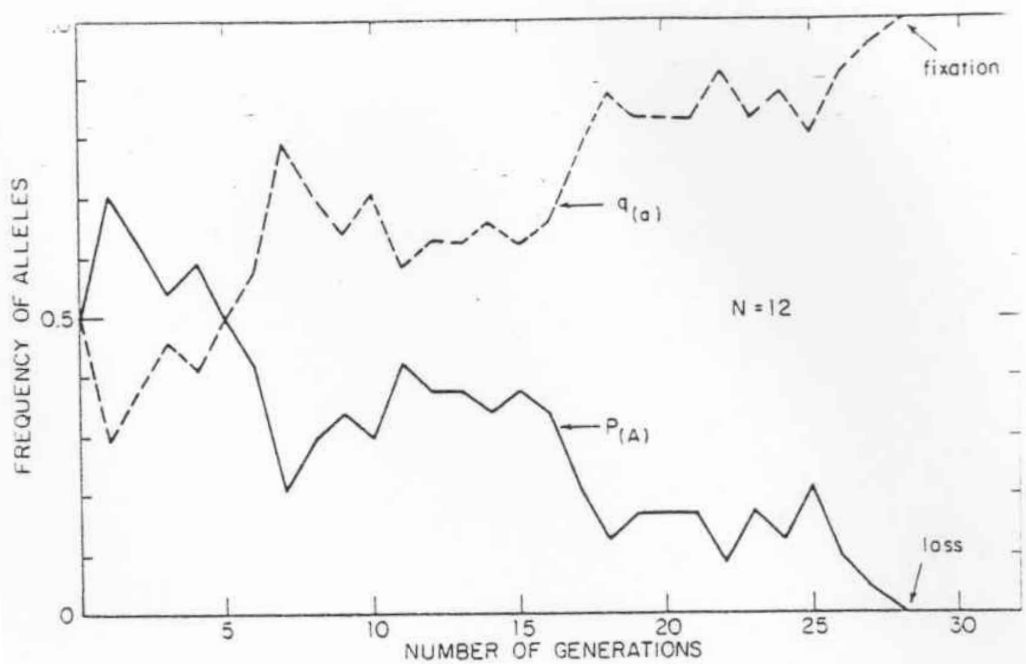
Migration

B allele of Blood types



Genetic Drift

- small population
- fixed alleles and extinction



12 GENETIC DRIFT, simulated by the aid of a computer, led to fixation of *a* and loss of *A* in a population consisting of only 12 individuals. In general, the smaller the population, the more rapid will be the drift to these end points.

Genetic Drift

- founder effect
- bottleneck effect

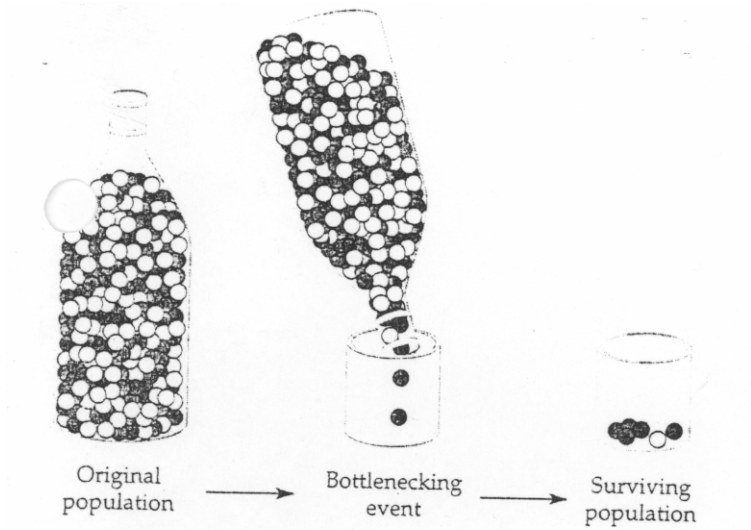


Figure 21.4
The bottleneck effect. A gene pool can drift by chance when the population is drastically reduced by a disaster that kills victims unselectively. In this analogy, a population of magenta and white marbles in a bottle is reduced in the bottleneck. Notice that the composition of the surviving population in the bottleneck is not representative of the makeup of the larger, original population. By chance, the magenta marbles are overrepresented.

Non-Random Mating

- assortative mating
- loss of heterozygotes
- disassortative mating
- Inbreeding depression
- Higher levels of genetic diseases

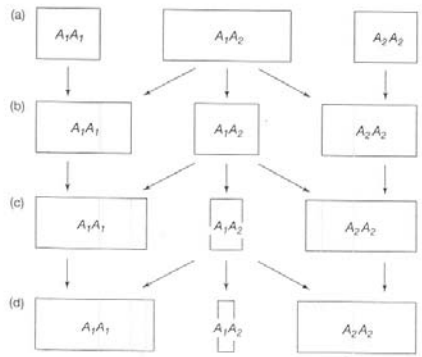


Figure 5.25 **Selfing increases the frequency of homozygotes** Row (a) represents, with the area of each box, the genotype frequencies in a population with two alleles, each at frequency 0.5, in Hardy-Weinberg equilibrium. Row (b) represents the genotype frequencies in the next generation that will result if every individual in the population mates only with itself. If selfing continues, homozygotes consititute an ever-larger fraction of the population every generation; see rows (c) and (d).

TABLE 5.3 Changes in genotype frequencies with successive generations of selfing

The frequency of allele A_1 is p and the frequency of allele A_2 is q. Note that allele frequencies do not change from generation to generation—only the genotype frequencies. After Crow (1983).

Generation	Frequency of A_1A_1	Frequency of A_1A_2	Frequency of A_1A_2
0	p^2	2pq	q^2
1	$p^2 + (pq/2)$	pq	$q^2 + (pq/2)$
2	$p^2 + (3\,pq/4)$	pq/2	$q^2 + (3\,pq/4)$
3	$p^2 + (7\,pq/8)$	pq/4	$q^2 + (7\,pq/8)$
4	$p^2 + (15\,pq/16)$	pq/8	$q^2 + (15\,pq/16)$

Natural selection

- Differential reproductive success
- Selection coefficient
- Relative fitness of genotypes

Complete selection against recessive

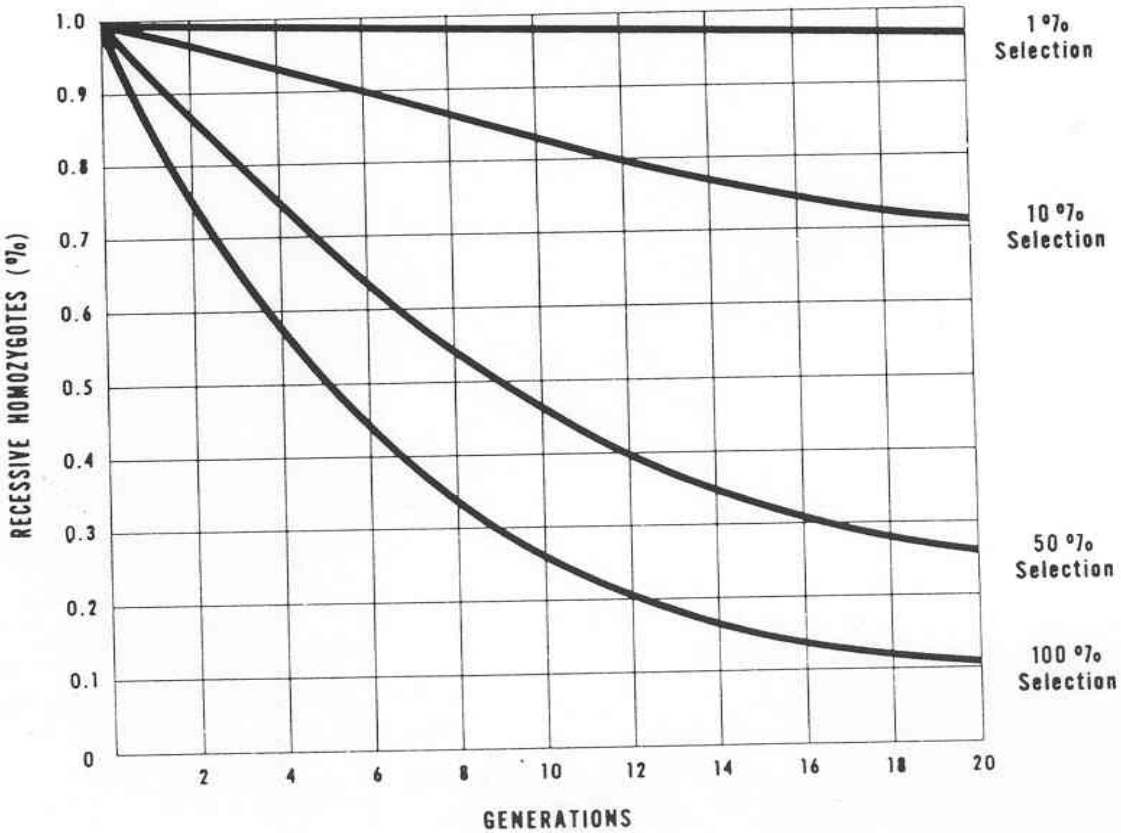
$q_n = q_o / (1 + nq_o)$

Table 5.3
Effects of Complete Selection against a Recessive Trait

Generations	Gene Frequency	Recessive Homozygotes %	Heterozygotes %	Dominant Homozygotes %
0	0.500	25.00	50.00	25.00
1	0.333	11.11	44.44	44.44
2	0.250	6.25	37.50	56.25
3	0.200	4.00	32.00	64.00
4	0.167	2.78	27.78	69.44
8	0.100	1.00	18.00	81.00
10	0.083	0.69	15.28	84.03
20	0.045	0.20	8.68	91.12
30	0.031	0.10	6.05	93.85
40	0.024	0.06	4.64	95.30
50	0.020	0.04	3.77	96.19
100	0.010	0.01	1.94	98.05

Selection

Figure 5.3 Different intensities of selection against recessive homozygotes occurring initially ("0" generation) at a frequency of 1.0 percent. The elimination of recessive individuals per generation proceeds at a slower pace as the strength of selection decreases.



Calculating relative fitness

II. ESTIMATING FITNESS FROM DATA TAKEN BEFORE AND AFTER SELECTION WITHIN THE SAME GENERATION

NUMBER OF INDIVIDUALS IN EACH GENOTYPE
(Obtained by counting)

	AA	*Aa*	*aa*
Before selection	4,000	5,100	2,300
After selection in the same generation	3,800	4,200	1,200

SURVIVAL RATE

λ_{AA} survival rate of $AA = 3{,}800/4{,}000 = 0.95$

λ_{Aa} survival rate of $Aa = 4{,}200/5{,}100 = 0.82$

λ_{aa} survival rate of $aa = 1{,}200/2{,}300 = 0.52$

RELATIVE FITNESS
(Compared with *AA*, the most fit)

W_{AA} fitness of $AA = \lambda_{AA}/\lambda_{AA} = 0.95/0.95 = 1.00$

W_{Aa} fitness of $Aa = \lambda_{Aa}/\lambda_{AA} = 0.82/0.95 = 0.86$

W_{aa} fitness of $aa = \lambda_{aa}/\lambda_{AA} = 0.52/0.95 = 0.55$

SELECTION COEFFICIENT

s_{AA} selection coefficient of $AA = 1 - W_{AA} = 0$

s_{Aa} selection coefficient of $Aa = 1 - W_{Aa} = 0.14$

s_{aa} selection coefficient of $aa = 1 - W_{aa} = 0.45$

III. ESTIMATING FITNESS FROM DATA TAKEN IN THE FIRST GENERATION BEFORE SELECTION, AND IN THE SECOND GENERATION AFTER SELECTION HAS OCCURRED

NUMBER OF INDIVIDUALS IN EACH GENOTYPE
(Obtained by counting)

	AA	*Aa*	*aa*	*Total*
Mating population of first generation (before selection)	3,000	3,900	2,000	8,900
Mating population of second generation (after selection)	3,800	4,400	1,800	10,000

GENE FREQUENCY IN FIRST GENERATION
(For calculating expected frequency in second generation in the absence of selection)

p frequency of $A = \dfrac{6{,}000 + 3{,}900}{17{,}800} = 0.56$

q frequency of $a = 1 - p = 0.44$

CORRECTED RATE OF INCREASE
(Ratio of actual number in the second generation to the number expected in the absence of selection)

R_{AA} rate of increase of $AA = \dfrac{3{,}800}{p^2 \times 10{,}000} = \dfrac{3{,}800}{0.31 \times 10{,}000} = 1.23$

R_{Aa} rate of increase of $Aa = \dfrac{4{,}400}{2pq \times 10{,}000} = \dfrac{4{,}400}{0.50 \times 10{,}000} = 0.88$

R_{aa} rate of increase of $aa = \dfrac{1{,}800}{q^2 \times 10{,}000} = \dfrac{1{,}800}{0.19 \times 10{,}000} = 0.95$

RELATIVE FITNESS
(Compared with *AA*, the most fit)

W_{AA} fitness of $AA = R_{AA}/R_{AA} = 1.23/1.23 = 1.00$

W_{Aa} fitness of $Aa = R_{Aa}/R_{AA} = 0.88/1.23 = 0.72$

W_{aa} fitness of $aa = R_{aa}/R_{AA} = 0.95/1.23 = 0.77$

SELECTION COEFFICIENT

s_{AA} selection coefficient of $AA = 1 - W_{AA} = 0$

s_{Aa} selection coefficient of $Aa = 1 - W_{Aa} = 0.28$

s_{aa} selection coefficient of $aa = 1 - W_{aa} = 0.23$

Heterozygote advantage

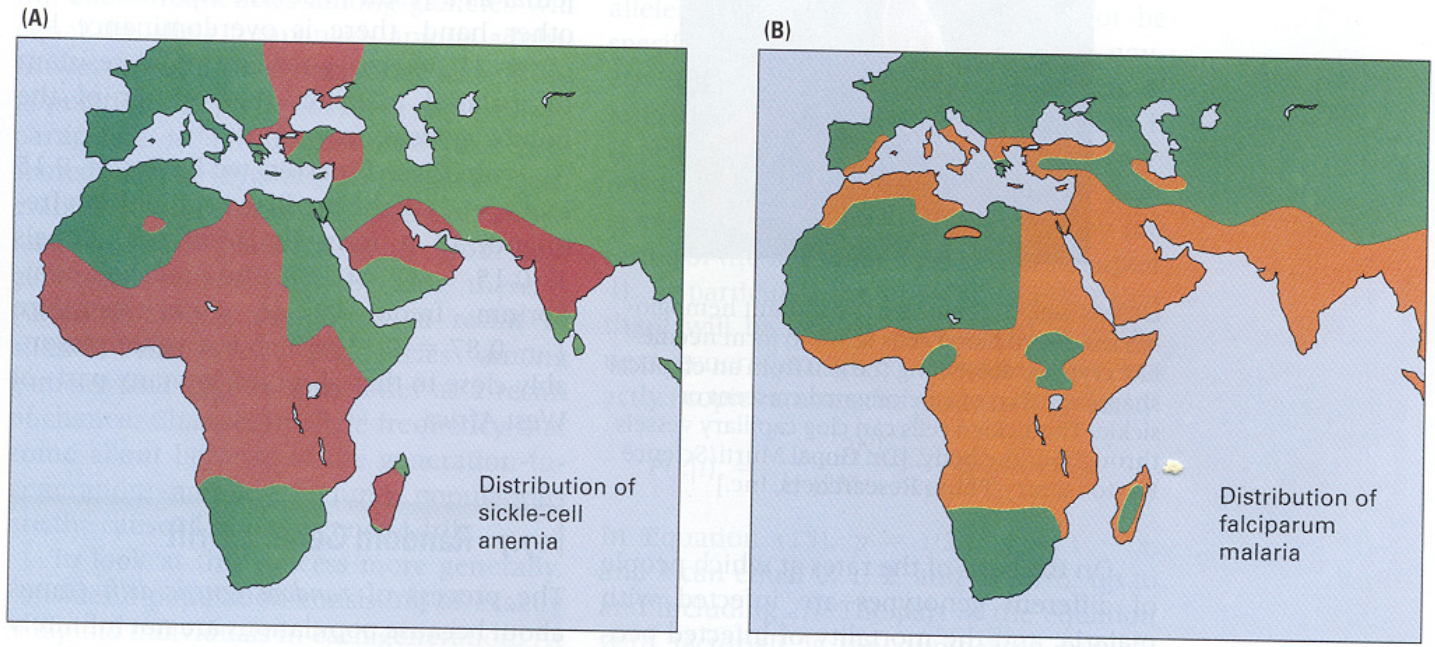


Figure 17.28 Geographic distribution of (A) sickle-cell anemia and (B) falciparum malaria in the 1920s, before extensive malaria-control programs were launched. Shades of brown indicate the areas in question.

Heterozygote advantage

- Sickle cell anemia
- balanced polymorphism
- Why is Hbs maintained in the population?
- What happens in US to allele frequency?

- $Q_{eq} = S_1 / (S_1 + S_2)$