

Lecture Handout 12

Outbreeding: mating individuals are less closely related than those drawn by chance from a population.

Inbreeding: mating individuals are more closely related than those drawn by chance from a population.

Effects of inbreeding:

- Genotype changes affect all loci in the genome
- Effects on genotype frequencies might be easily reversible
- Inbreeding and genetic drift have similar effects on heterozygosity, but through different mechanisms (heterozygote deficiency and loss of alleles, respectively)

Coefficient of inbreeding, f , is the probability that 2 homologous alleles are identical by descent (IBD)

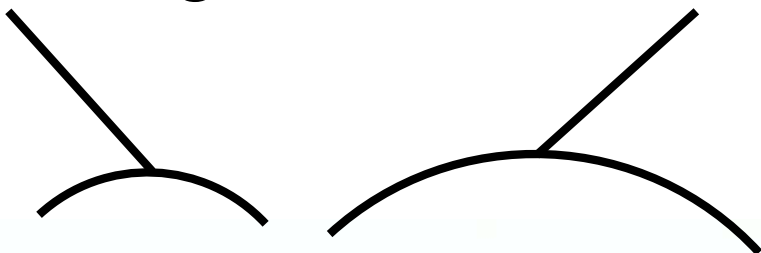
Identical by descent (IBD): derived from one particular allele possessed by a very recent common ancestor

As opposed to **identity in state**: two identical alleles that are not derived from a very recent common ancestor

In a population with some inbreeding,
the frequency of genotype A_1A_1 is:

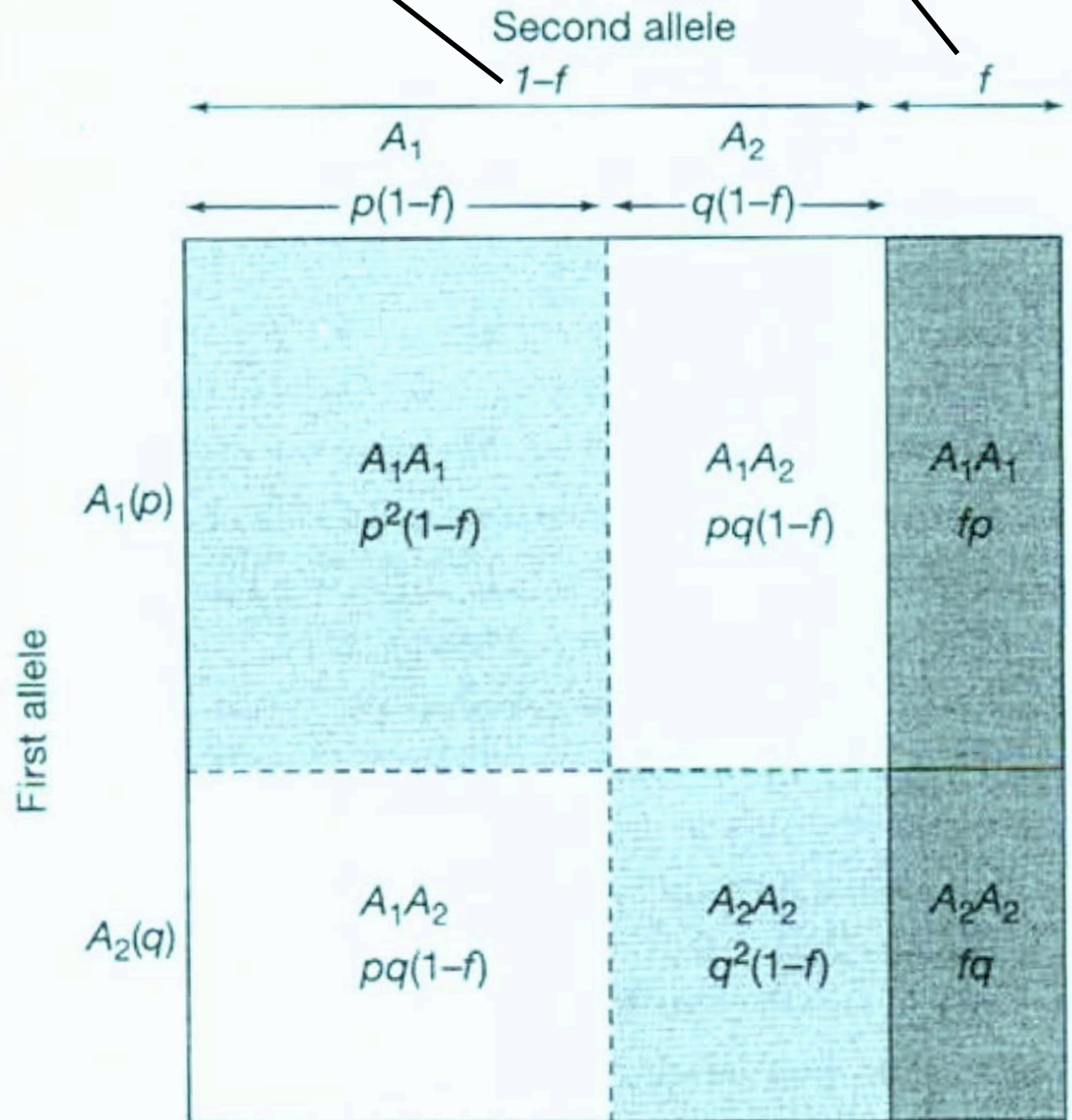
Due to inbreeding

Due to random mating


$$P = pf + p^2(1 - f)$$
$$= p^2 + fpq$$

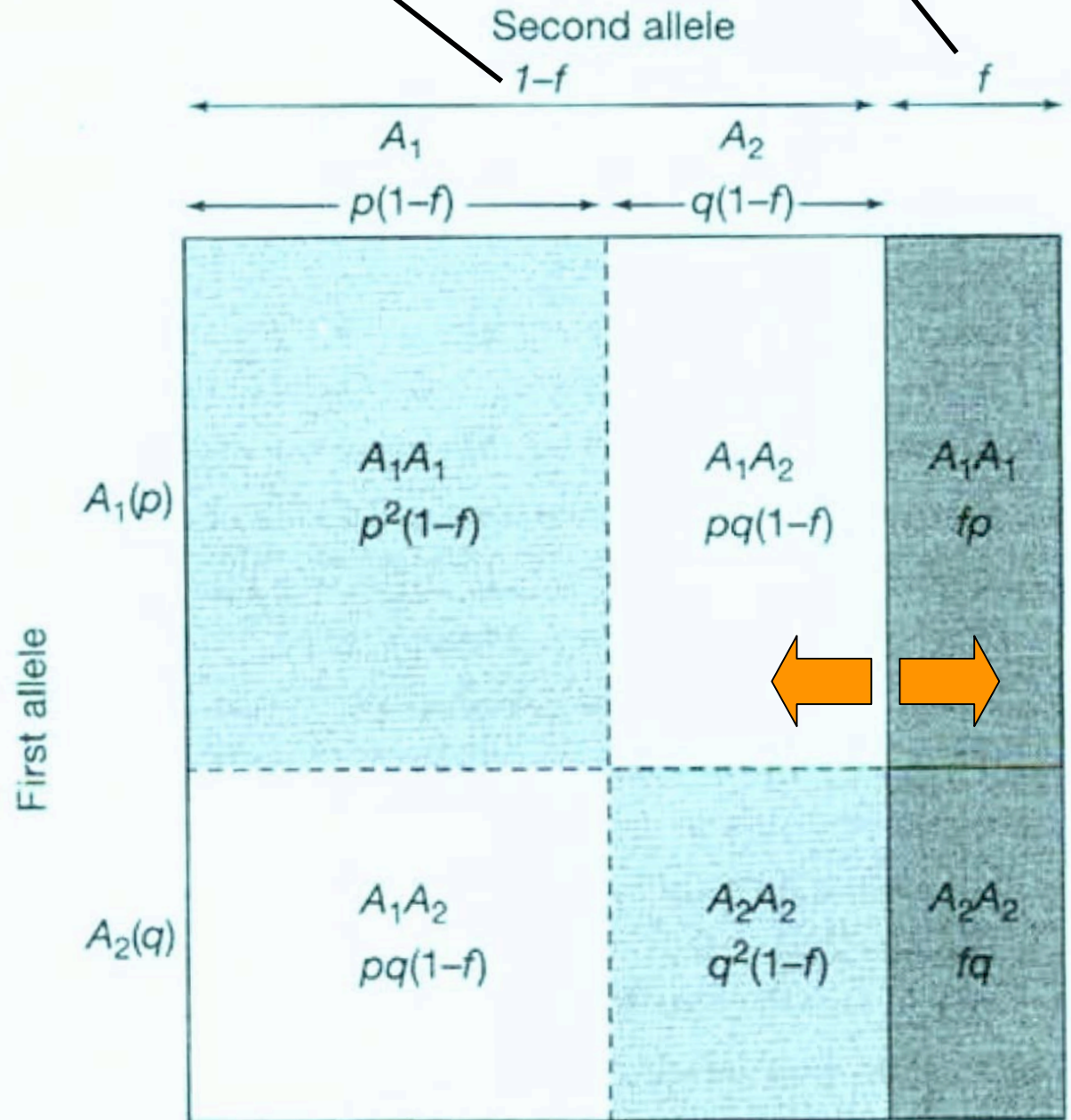
non-inbred component, Inbred component

Figure 5.1. The proportions of homozygous genotypes that are the result of inbreeding or IBD (darkly shaded area) and homozygotes that are the result of identity in state (lightly shaded area) using a unit square.



Note that
inbreeding
affects only
genotype and
not allele
frequencies
*(if distinguished
from genetic
drift in small
populations)*

non-inbred component, Inbred component



Proportion of three genotypes with
inbreeding level of f

$$P = p^2 + f p q$$

$$H = 2 p q - 2 f p q$$

$$Q = q^2 + f p q$$

Frequency of heterozygotes:

$$H = 2pq(1 - f)$$

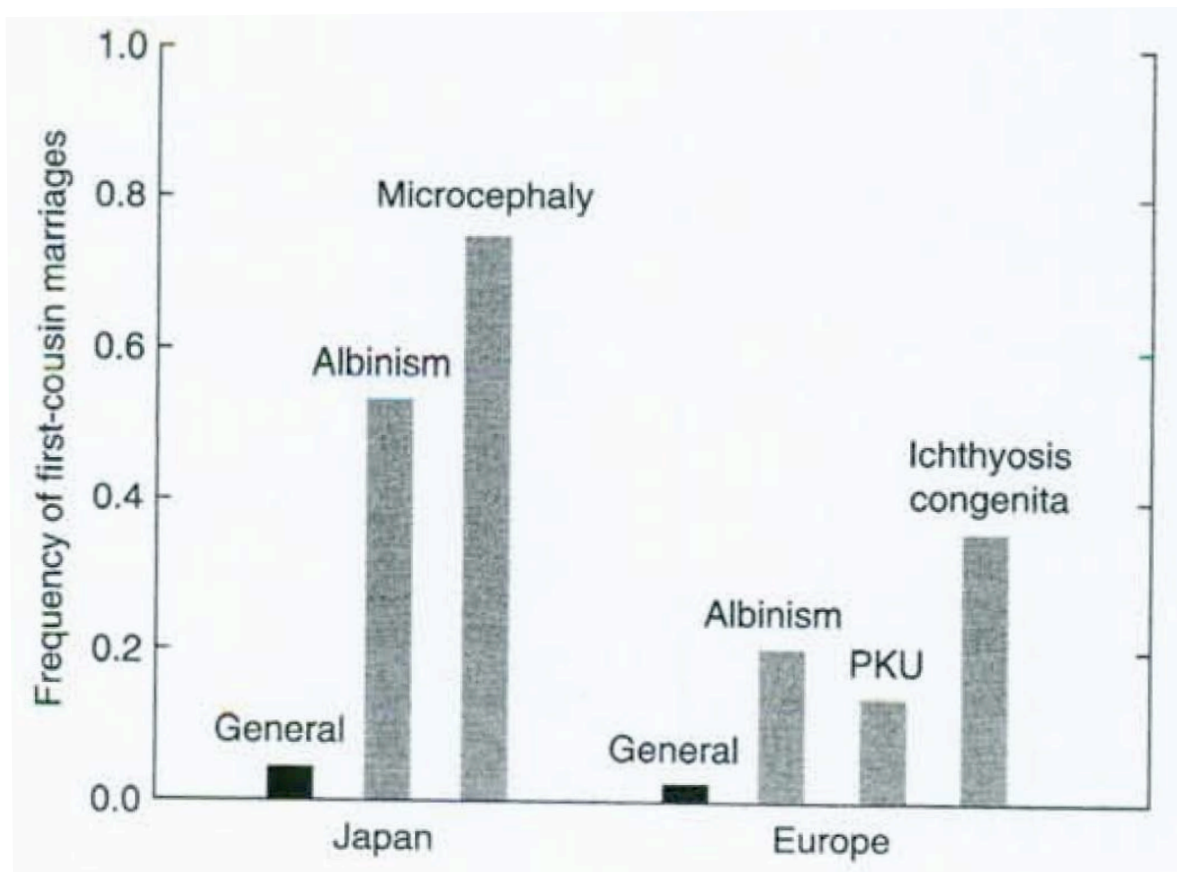
Therefore:

$$f = 1 - \frac{H}{2pq}$$

Observed
heterozygosity

Hardy-Weinberg
heterozygosity

Inbreeding can have dramatic effects on relative genotype frequencies for genes with alleles in a dominant-recessive relationships: recessive genotypes become much more common.



Pedigree showing **consanguineous** (between-relatives) matings (double lines) and incidence of a rare recessive disease (shaded)

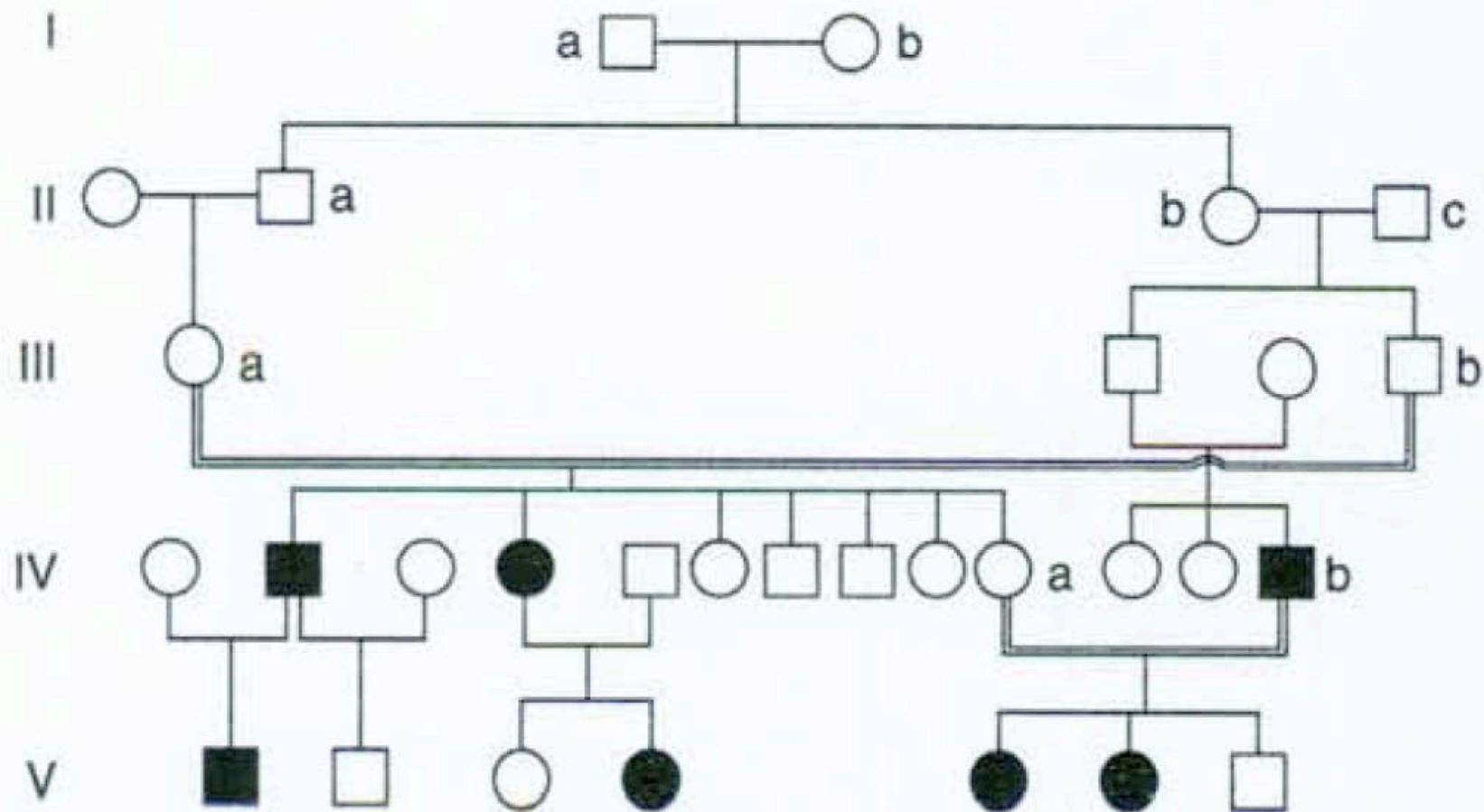


TABLE 5.1 The ratio of the proportion of recessives with a given inbreeding coefficient (f) to the Hardy–Weinberg proportion of recessives for several allele frequencies.

q	f		
	$\frac{1}{32}$	$\frac{1}{16}$	$\frac{1}{8}$
0.001	32.2	63.4	125.9
0.025	13.5	25.9	50.9
0.01	4.1	7.2	13.4
0.1	1.3	1.6	2.1
0.5	1.0	1.0	1.1

By “unveiling” recessive deleterious genotypes (ie increasing homozygotes), inbreeding can lower the overall fitness of the population... yet paradoxically it may help purge the deleterious alleles.

Self-fertilization in plants is the most extreme form of inbreeding--can quickly divide the population into highly homozygous lines.

TABLE 5.2 The mating types and frequency of progeny when there is complete self-fertilization.

<i>Mating type</i>	<i>Frequency</i>	<i>Progeny</i>		
		A_1A_1	A_1A_2	A_2A_2
$A_1A_1 \times A_1A_1$	P_0	P_0	—	—
$A_1A_2 \times A_1A_2$	H_0	$\frac{1}{4}H_0$	$\frac{1}{2}H_0$	$\frac{1}{4}H_0$
$A_2A_2 \times A_2A_2$	Q_0	—	—	Q_0
Total	1	$P_0 + \frac{1}{4}H_0$	$\frac{1}{2}H_0$	$Q_0 + \frac{1}{4}H_0$

Complete self-fertilization in plants

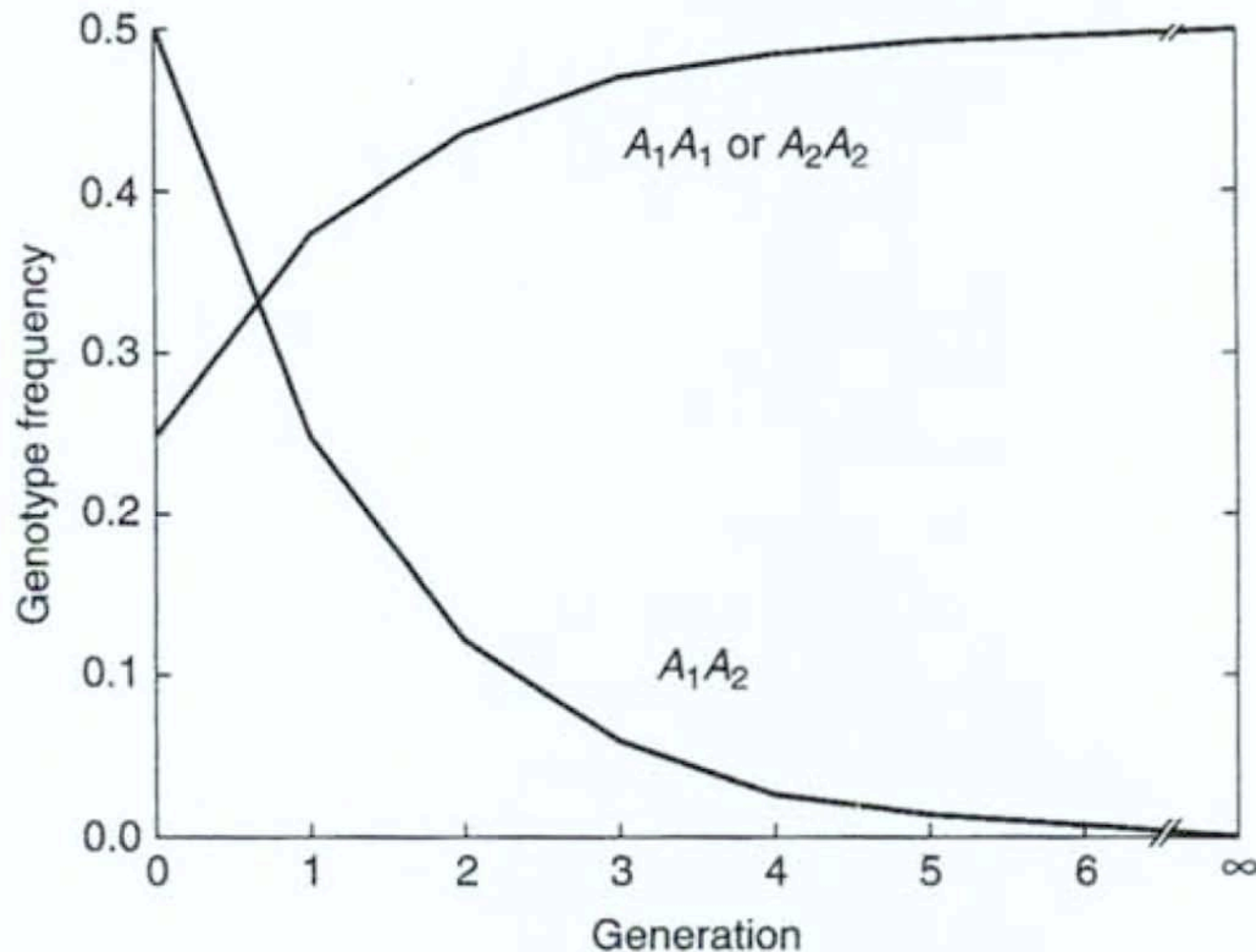


Figure 5.6. The genotype frequencies over time when there is complete self-fertilization and Hardy–Weinberg proportions existed initially with $p_0 = q_0 = 0.5$.

Partial self-fertilization in plants: a proportion **S** of the progeny are due to **self-fertilization**, while the remaining proportion **T** are **outcrossed** ($S+T = 1$)

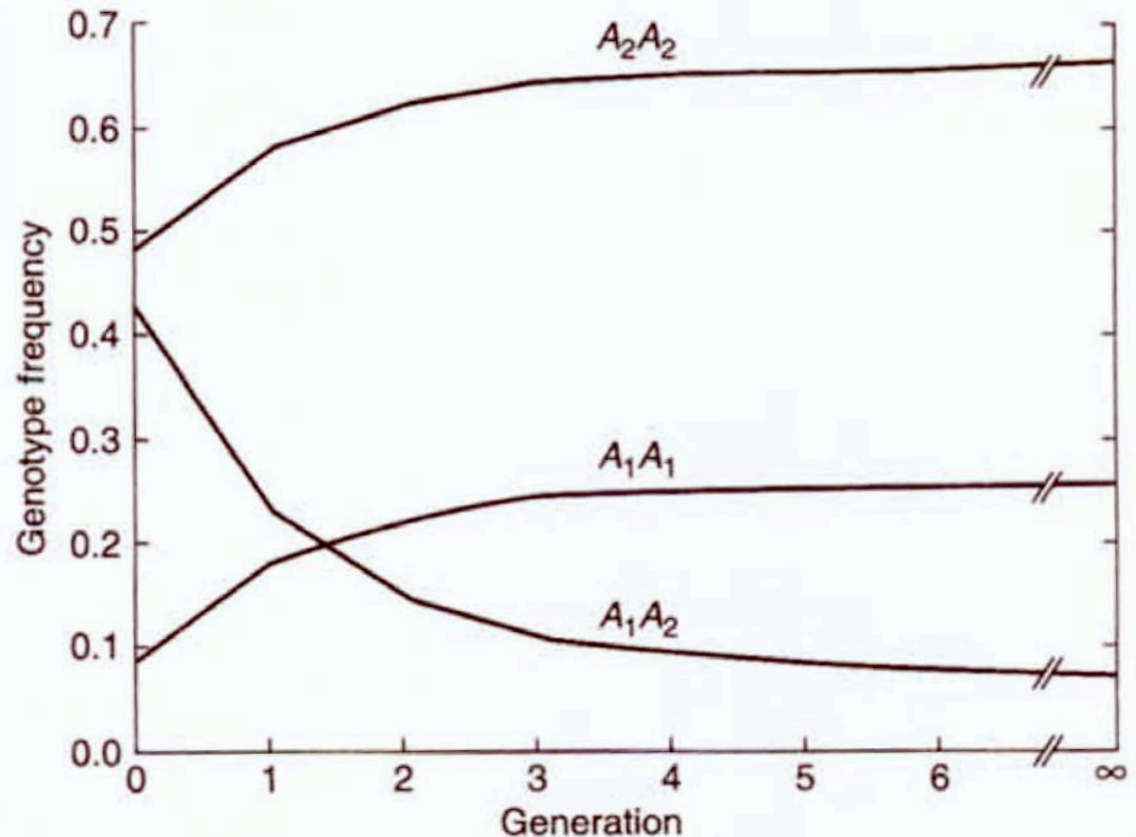
TABLE 5.3 The mating types and frequencies of progeny when there is a proportion S of the progeny produced by self-fertilization and a proportion T produced by outcrossing.

Mating type	Frequency	Progeny		
		A_1A_1	A_1A_2	A_2A_2
Selfing (S)				
$A_1A_1 \times A_1A_1$	SP	SP	—	—
$A_1A_2 \times A_1A_2$	SH	$\frac{1}{4}SH$	$\frac{1}{2}SH$	$\frac{1}{4}SH$
$A_2A_2 \times A_2A_2$	SQ	—	—	SQ
Outcrossing (T)				
$A_1A_1 \times A_1A_1$	TP^2	TP^2	—	—
$A_1A_1 \times A_1A_2$	$T2PH$	TPH	TPH	—
$A_1A_1 \times A_2A_2$	$T2PQ$	—	$T2PQ$	—
$A_1A_2 \times A_1A_2$	TH^2	$\frac{1}{4}TH^2$	$\frac{1}{2}TH^2$	$\frac{1}{4}TH^2$
$A_1A_2 \times A_2A_2$	$T2HQ$	—	THQ	THQ
$A_2A_2 \times A_2A_2$	TQ^2	—	—	TQ^2
Total	1	$Tp^2 + S(P + \frac{1}{4}H)$	$2Tpq + \frac{1}{2}SH$	$Tq^2 + S(Q + \frac{1}{4}H)$

(Stable) **inbreeding equilibrium**: for a given amount of self fertilization and a given allele frequency:

$$H_e = 2Tpq + \frac{1}{2}SH_e$$
$$= \frac{4pq(1 - S)}{2 - S}$$

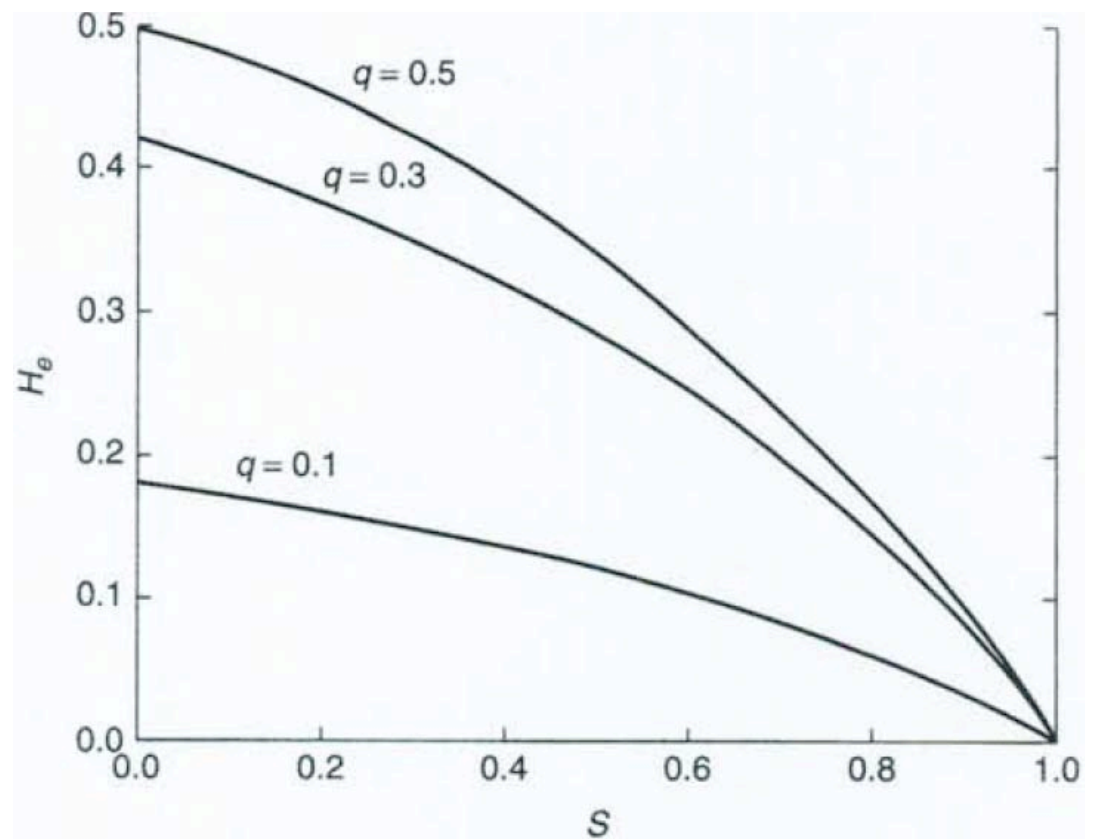
Figure 5.7. The genotype frequencies over time for an example with partial selfing ($S = 0.9$) where Hardy-Weinberg proportions existed initially with $q_0 = 0.7$.



Equilibrium heterozygote frequency for different levels of partial selfing (S), for 3 different allele frequencies for q .

$$f_e = \frac{S}{2 - S}$$

$$f_e = \frac{1 - T}{1 + T}$$



Regular systems of inbreeding

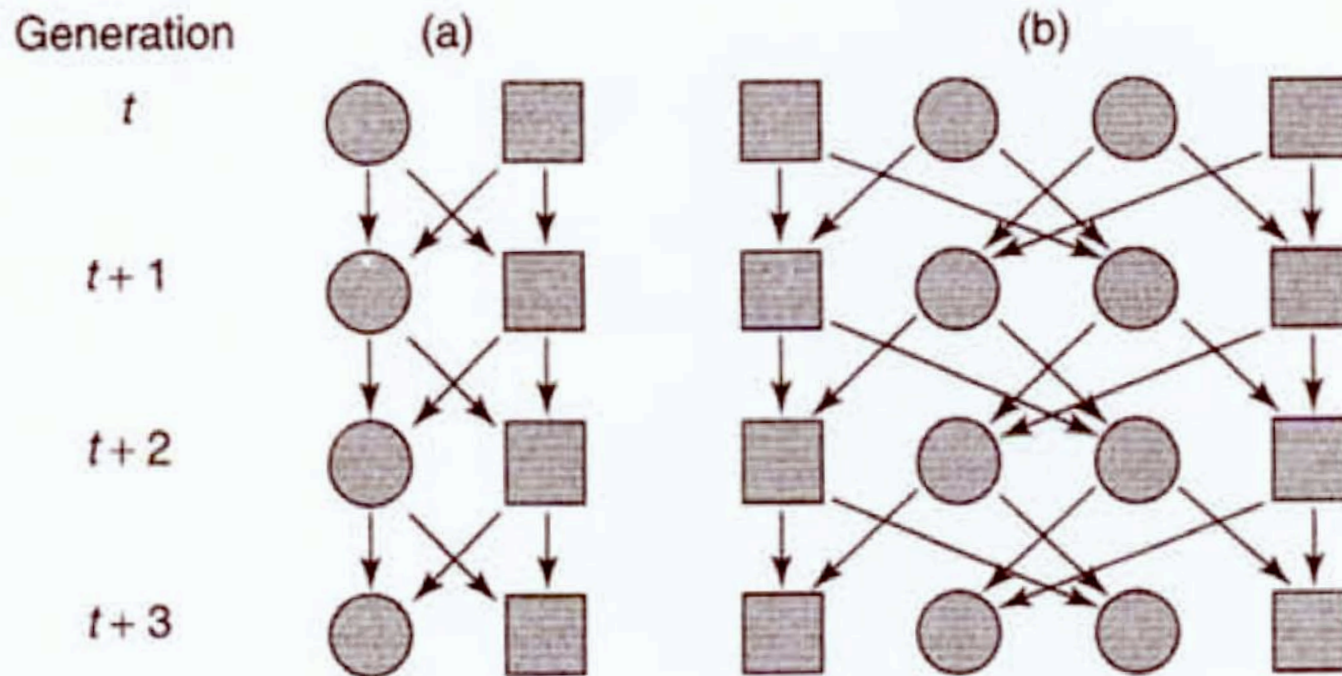
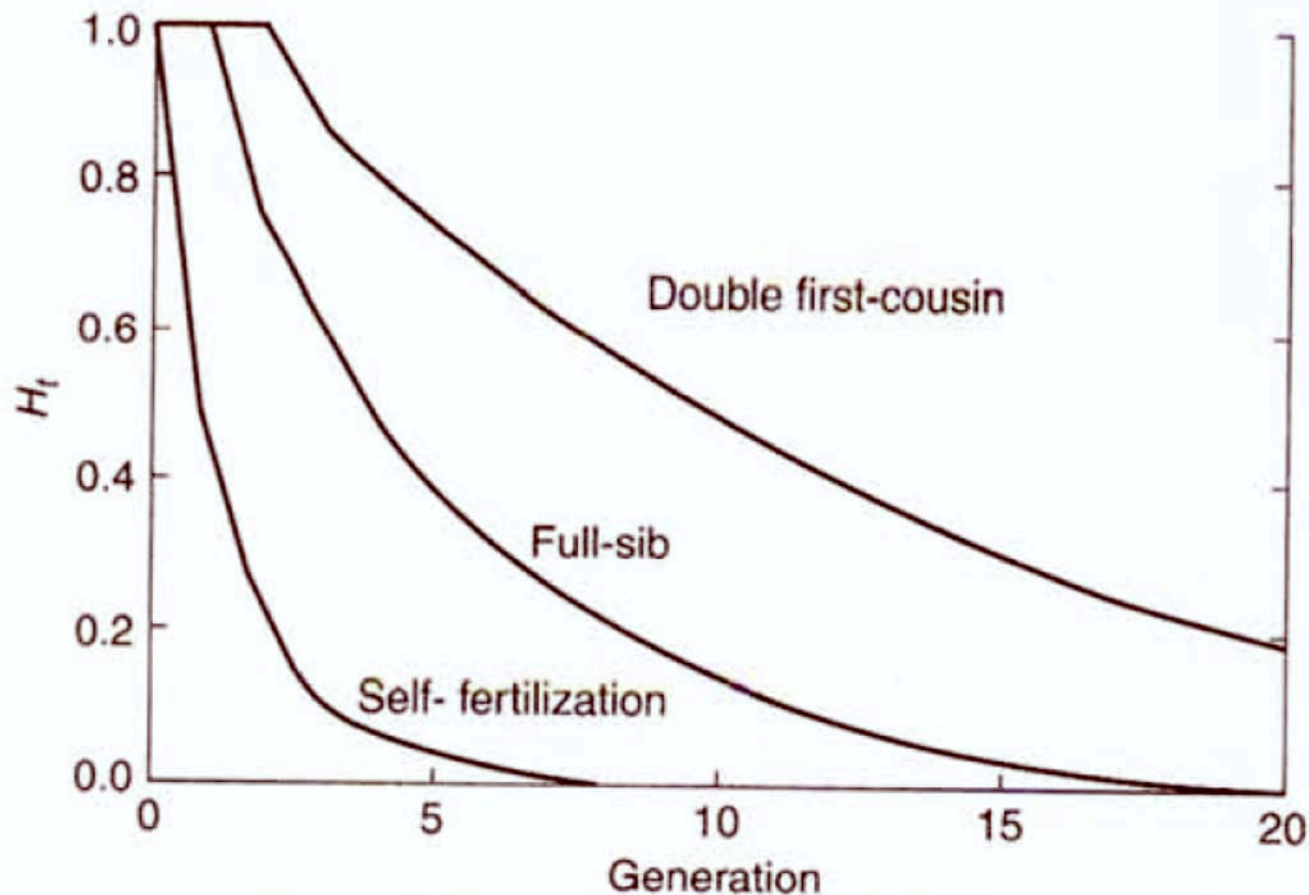


Figure 5.10. Pedigrees showing the regular mating systems of (a) full-sib mating and (b) double first-cousin mating. Circles and squares indicate females and males, respectively, and arrows indicate a parent-to-offspring relationship. The individuals in generation t are assumed to be unrelated.

Regular systems of inbreeding, decline in heterozygosity: λ (*asymptotic*) = 0.809 for continuous full-sib mating, and 0.920 for continuous double first cousin mating



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

For full-sib, use $H_{t+2} = (0.5 \times H_{t+1}) + (0.25 \times H_t)$

Estimation of inbreeding from pedigrees:

Inbreeding coefficient, f , is the probability of identity by descent (IBD), in which the two alleles in an individual are descended from a very recent common ancestor.

“Unrelated” parents: no possibility of IBD

Same individual $\Pr(\text{IBD}) = 0.5$

How can a pedigree be used to obtain f , the inbreeding coefficient?

Estimation of inbreeding from pedigrees:

All unrelated individuals are omitted, since they can't contribute to IBD; $\Pr(\text{IBD}) = 0$

Inbred ancestors of both sexes are shown as diamonds (not circles or squares)

Common ancestor(s) are indicated and assumed heterozygous

Probabilities are calculated across the generations

Estimation of inbreeding from pedigrees:

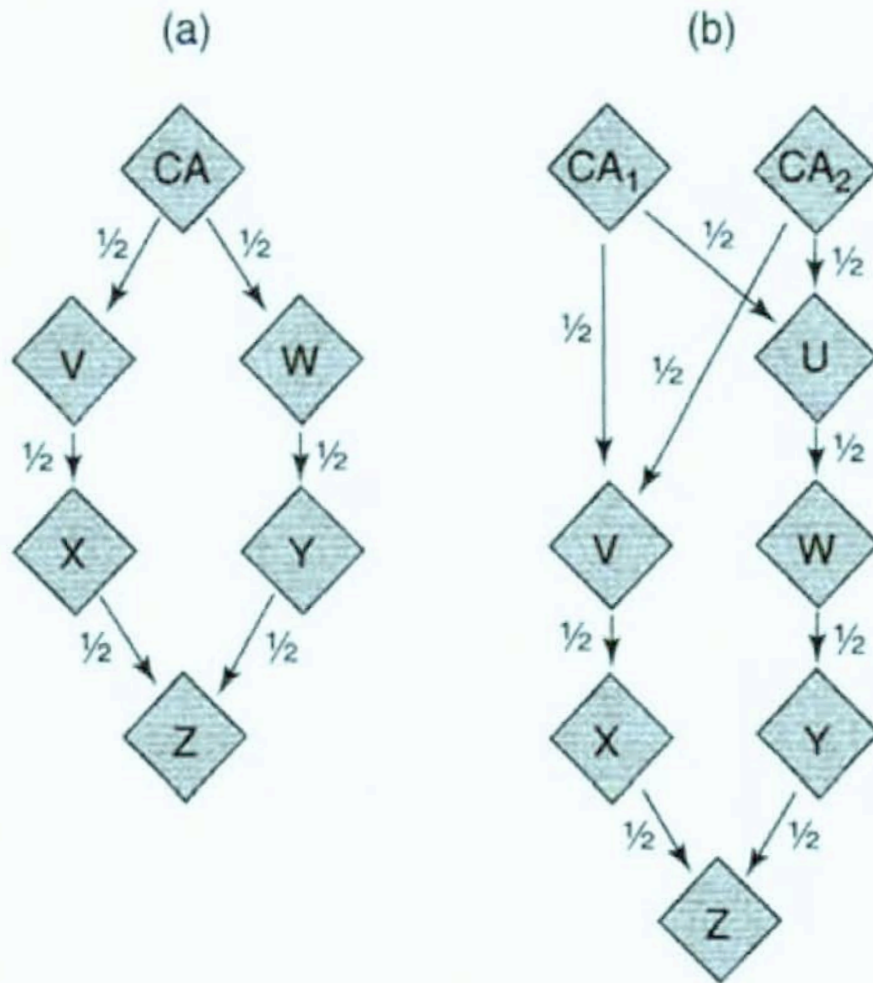


Figure 5.13. Pedigrees for (a) a half-first-cousin mating and (b) a mating between first cousins once removed. Diamonds indicate individuals of either sex, CA the common ancestors, and $1/2$ the probability of segregation between generations.

Chain-counting technique: starts with parent of inbred individual, goes up to the common ancestor, and back down to the other parent (ignores actual inbred individual). The number of individuals in this chain (excluding the inbred individual of interest) is designated ***N***, and the inbreeding coefficient...

$$f = (1/2)^N$$

If more than one common ancestor:

$$f = \sum_{i=1}^m (1/2)^{N_i}$$

Kinship coefficient (between 2 individuals): the probability that alleles drawn at random between two individuals are identical by descent (IBD). Will be equal to the inbreeding coefficient (f) of an offspring from them.

Coefficient of relationship, or relatedness (r) between 2 individuals: the fraction of alleles that the two individuals share that are identical by descent (IBD). For non-inbred diploid individuals, is twice the inbreeding coefficient in possible offspring.

$$r = 2f$$