Chapter 2 – Genotype Frequencies

Mendelian Genetics

Hardy-Weinberg Equilibrium

Heterozygosity & Inbreeding

Linkage and Recombination

"inbreeding" (fixation index, F)

- consanguinity or kinship between individuals
- autozygosity of alleles within an individual or sampled at random from a population
- fixation index, measured as excess homozygosity in relation to HW expectations
- description of a population's mating system
- increase in homozygosity due to:
  - finite population size (genetic drift)
  - population structure (drift within subpopulations)
- inbreeding depression (?)

fixation index and heterozygosity

- F = fixation index, measure of "excess" homozygosity (i.e., in comparison to HW expectations)
- $F = (H_e - H_0)/H_e$, where H is heterozygosity
- assortative mating
  - positive or negative (disassortative)
  - consanguineous mating (inbreeding)
  - selfing (sexual autogamy)

Penn & Potts. 1998. MHC-disassortative mating preferences reversed by cross-fostering. *Proc. Roy. Soc*. 265: 1299-1306.

- How do mice acquire their mate choice preferences?
- Where does the recognition "template" come from?
  - self (the "armpit effect"), or
  - siblings during development

Penn & Potts. 1998. MHC-disassortative mating preferences reversed by cross-fostering. *Proc. Roy. Soc.* 265: 1299-1306.

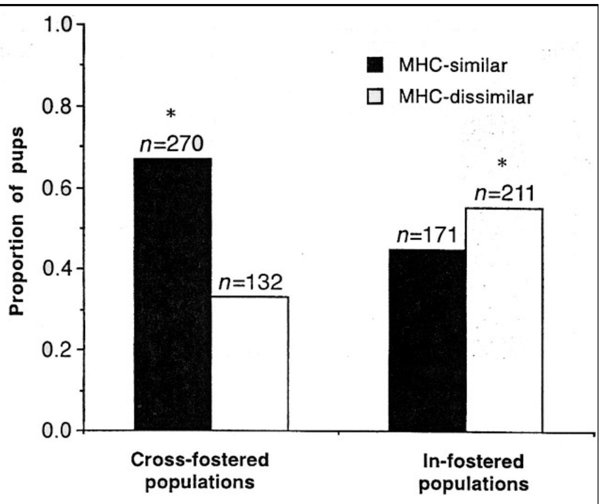


Figure 2. The proportion of pups from MHC-similar and MHC-dissimilar matings compared between cross-fostered and in-fostered female mice ($\chi^2 = 39.9$, $n = 784$, $p < 0.0001$). The type of mating was deduced from pup MHC genotypes (see § 2). The values above the bars refer to the number of pups in each category (* indicates that the standardized residuals were positive and significant at $p = 0.05$).

Multiple Alleles

$$H_e = 1 - \sum_{i=1}^{k} p_i^2 = \sum_{i=1}^{k} \sum_{j=i+1}^{k} 2 p_i p_j$$

- where k is the number of alleles

Selfing

- what's wrong here?

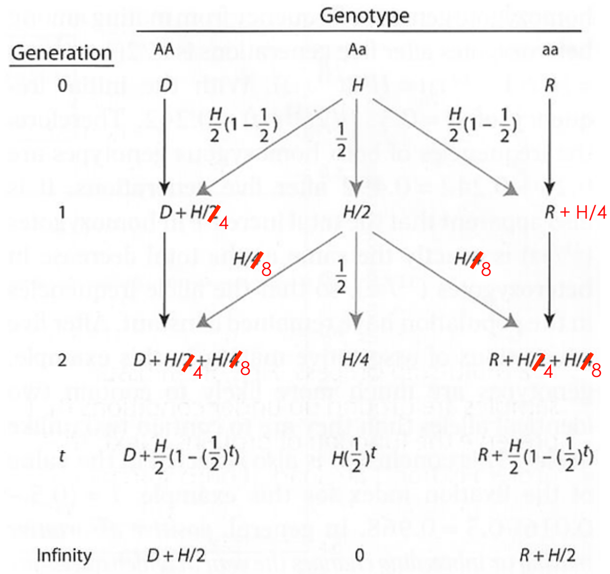


Figure 2.12 The impact of complete positive genotypic assortative mating (like genotypes mate) or self-fertilization on genotype frequencies.

Relatedness and Autozygosity

- Autozygous = "identical by descent" (IBD)
- Relatedness = the fraction of alleles that two individuals share IBD
- Inbreeding coefficient = f = probability that the two alleles at a given locus within an individual are IBD
- Relatedness between two individuals (that are not already inbred) is double the inbreeding coefficient in their potential offspring

Relatedness and Autozygosity

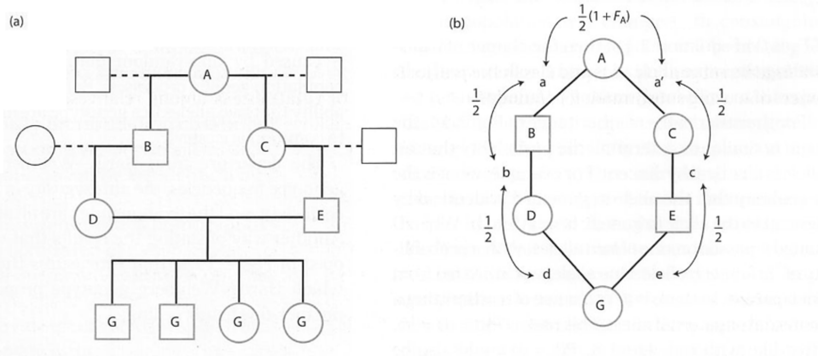
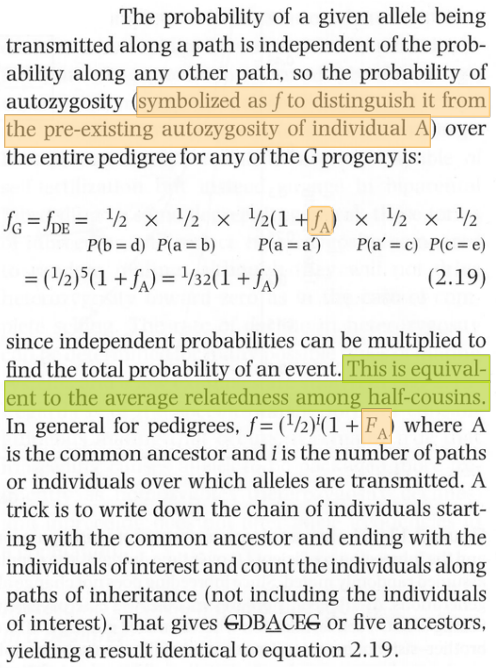


Figure 2.14 Average relatedness and autozygosity as the probability that two alleles at one locus are identical by descent. (a) A pedigree where individual A has progeny that are half-siblings (B and C). B and C then produce progeny D and E, which in turn produce offspring G. (b) Only the paths of relatedness where alleles could be inherited from A, with curved arrows to indicate the probability that gametes carry alleles identical by descent. Upper-case letters for individuals represent diploid genotypes and lower-case letters indicate allele copies within the gametes produced by the genotypes. The probability that A transmits a copy of the same allele to B and C depends on the degree of inbreeding for individual A, or F_A.

Calulating *f*

- what's wrong here?
- pg. 37: relatedness = 2 x autozygosity



The probability of a given allele being transmitted along a path is independent of the probability along any other path, so the probability of autozygosity (symbolized as *f* to distinguish it from the pre-existing autozygosity of individual A) over the entire pedigree for any of the G progeny is:

$$f_G = f_{DE} = \underset{P(b=d)}{{}^1/_2} \times \underset{P(a=b)}{{}^1/_2} \times \underset{P(a=a')}{{}^1/_2(1+f_A)} \times \underset{P(a'=c)}{{}^1/_2} \times \underset{P(c=e)}{{}^1/_2}$$

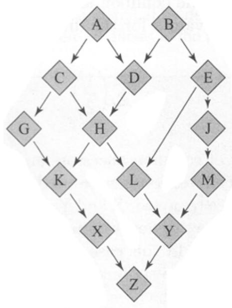
$$= ({}^1/_2)^5(1+f_A) = {}^1/_{32}(1+f_A) \qquad (2.19)$$

since independent probabilities can be multiplied to find the total probability of an event. This is equivalent to the average relatedness among half-cousins. In general for pedigrees, $f = ({}^1/_2)^i(1+F_A)$ where A is the common ancestor and *i* is the number of paths or individuals over which alleles are transmitted. A trick is to write down the chain of individuals starting with the common ancestor and ending with the individuals of interest and count the individuals along paths of inheritance (not including the individuals of interest). That gives ~~G~~DB$\underline{\text{A}}$CE~~G~~ or five ancestors, yielding a result identical to equation 2.19.

Calulating *f*

- example with multiple common ancestors

FIGURE 8.7 A hypothetical pedigree with a complicated history of inbreeding.



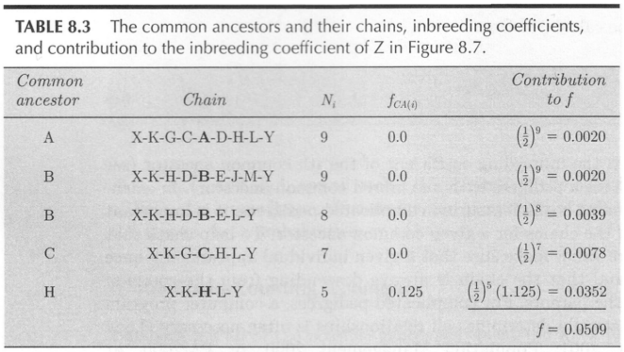


TABLE 8.3 The common ancestors and their chains, inbreeding coefficients, and contribution to the inbreeding coefficient of Z in Figure 8.7.

Common ancestor	*Chain*	N_i	$f_{CA(i)}$	*Contribution to f*
A	X-K-G-C-**A**-D-H-L-Y	9	0.0	$\left(\frac{1}{2}\right)^9 = 0.0020$
B	X-K-H-D-**B**-E-J-M-Y	9	0.0	$\left(\frac{1}{2}\right)^9 = 0.0020$
B	X-K-H-D-**B**-E-L-Y	8	0.0	$\left(\frac{1}{2}\right)^8 = 0.0039$
C	X-K-G-**C**-H-L-Y	7	0.0	$\left(\frac{1}{2}\right)^7 = 0.0078$
H	X-K-**H**-L-Y	5	0.125	$\left(\frac{1}{2}\right)^5 (1.125) = 0.0352$
				$f = 0.0509$

Inbreeding Depression

- Dominance hypothesis
  - deleterious recessives
  - fitness of *aa* lower than *AA* or *Aa*
  - predicts gradual elimination of a from population
- Overdominance hypothesis
  - heterosis or heterozygote advantage
  - fitness of *Aa* higher than *AA* or *aa*
  - predicts ongoing maintenance of both *A* and *a*