

# Population Subdivision

## Homework 3 due next Tuesday

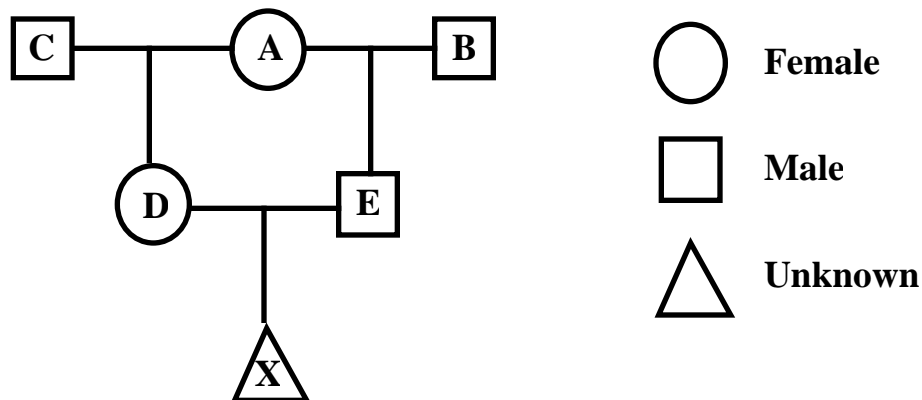
- First Violation of HWE was population substructure.
  - $F_{is}$  is a measure of inbreeding on the individual level.
- I) Inbreeding – the production of offspring by individuals that share a common ancestor.

### A) Terms

- 1) Consanguineous – individuals that have one or more ancestors in common.
- 2) Inbreeding – individuals are consanguineous
- 3) Identical by descent (IBD) – copies of the same (i.e., 1 allele) gene (copied in the previous generation)
- 4) Identical by state (IBS) – genes indistinguishable in effect or form but not IBD
- 5) Allozygous – homozygotes that carry genes IBS
- 6) Autozygous – homozygotes that carry genes IBD

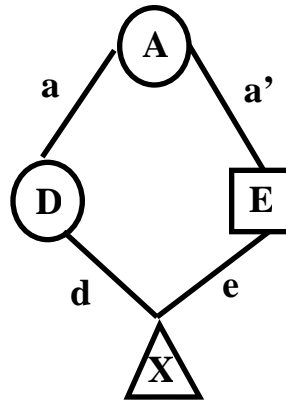
### OH A

- B) Pedigree Analysis – when the family history of an individual is known an accurate estimate of the degree of inbreeding can be determined



Is individual X inbred and if so, by how much?

1) Remove all unnecessarily individuals



a, a', d, and e are all alleles that are being transmitted

2) Calculate individual transmission probabilities

$F_x$  = the probability that individual X is autozygous

= Inbreeding coefficient

$F_x = P(d, e: IBD)$

=  $P(a, a': IBD \ \& \ d, a: IBD \ \& \ e, a': IBD)$

$$P(d, a: IBD) = \frac{1}{2}$$

$$P(e, a': IBD) = \frac{1}{2}$$

$P(a, a': IBD)$  = is a little more complicated (but not much)

Consider: The genotype of individual A is  $\alpha_1\alpha_2$

a, a' could be  $\alpha_1$

a, a' could be  $\alpha_2$

a, a' could be  $\alpha_1$  &  $\alpha_2$  and  $\alpha_1 = \alpha_2$  with probability  $F_A$

a, a' could be  $\alpha_2$  &  $\alpha_1$  and  $\alpha_1 = \alpha_2$  with probability  $F_A$

These are all the possible ways that a & a' can be autozygous and are equal in frequency.

$$\begin{aligned}
 P(a, a': \text{IBD}) &= \frac{1}{4}\alpha_1\alpha_1 + \frac{1}{4}\alpha_2\alpha_2 + \frac{1}{4}\alpha_1\alpha_2F_A + \frac{1}{4}\alpha_2\alpha_1F_A \\
 &= \frac{1}{2} + \frac{1}{2}F_A \\
 &= \frac{1}{2}(1 + F_A)
 \end{aligned}$$

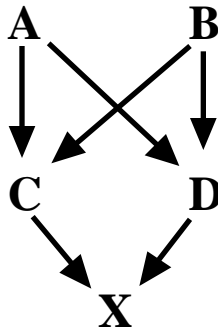
So combining all probabilities:

$$\begin{aligned}
 F_X &= \frac{1}{2} \times \frac{1}{2} \times \frac{1}{2}(1 + F_A) \\
 &= \frac{1}{2}^3 (1 + F_A) \\
 &= \frac{1}{8} \text{ assuming individual A is not inbred}
 \end{aligned}$$

3) In General:

$$F_X = \frac{1}{2}^{n-1} (1 + F_A) \text{ where } n = \text{number of individuals in the path}$$

4) More complicated example



**Note:** parents of X have two common ancestors, A and B.

- a) include all paths from one parent of X to the common ancestor and back to the other parent of X.
- b) use only one parent of X.
- c) individuals are included only once per path.
- d) paths switch directions relative to arrows ONLY at the common ancestor (and only once).
- e) inbreeding coefficient of individuals in the paths are only included for the common ancestors.

**Paths:**

$$F_{X.1} = CAD = \frac{1^3}{2} (1 + F_A)$$

$$F_{X.2} = CBD = \frac{1^3}{2} (1 + F_B)$$

$$F_X = F_{X.1} + F_{X.2}$$

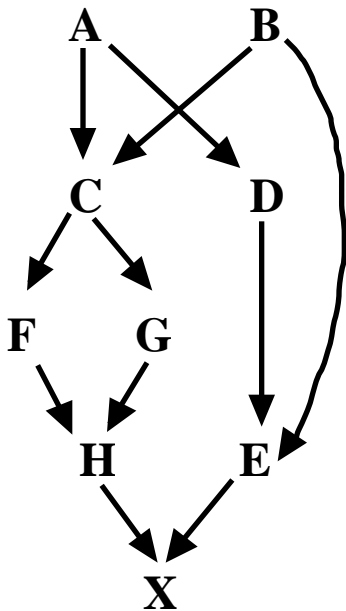
$$= \frac{1}{8} + \frac{1}{8} = \frac{1}{4}$$

5) General, general formula:

$$F_X = \prod_{i=1}^A \frac{1}{2} (1 + F_A)_i$$

Where A is the number of ancestors and n is the number of individuals (excluding the focal one) in the path.

6) Even more complicated:



Common Ancestors = A & B

Path	n	F
HFC <u>A</u> DE	6	$\frac{1}{2}^6 (1 + F_A) = \frac{1}{64}$
HGC <u>A</u> DE	6	$\frac{1}{2}^6 (1 + F_A) = \frac{1}{64}$
HFC <u>B</u> E	5	$\frac{1}{2}^5 (1 + F_B) = \frac{1}{32}$
HGC <u>B</u> E	5	$\frac{1}{2}^5 (1 + F_B) = \frac{1}{32}$

C) Sex-linked genes (i.e., X linked)

- 1) Omit all male => male paths
- 2) n = number of females in the path only (i.e., the probability of getting an X from a male and NOT then being a male to male path = 1.0)

$$F_X = \prod_{i=1}^A \frac{1}{2} (1 + F_A)_i$$

Note:  $F_X$  is also the coefficient of consanguinity ( $F_{ij}$ ) for the parents of X.

In other words:  $F_{HE}$  = the probability that a gene from H is IBD to one from E


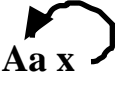
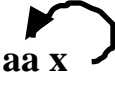
$r_{ij}$  = the coefficient of relationship (useful for male – male calculations, etc)

$$r_{ij} = \frac{2F_{ij}}{(1 + F_i)(1 + F_j)} = 2 F_{ij} \text{ if I and J are not inbred and } \frac{1}{2} F_{ij} \text{ if I and J are maximally inbred}$$

**OH 6.2** – fairly quickly after inbreeding it is unlikely to have alleles IBD (i.e.,  $F_X$  approaches 0.0 quickly without inbreeding)

#### D) Inbreeding on The Population Level

Pure Selfing:

Genotype	AA	Aa	aa
Frequency	U	V	W
Selfing			
Offspring	AA	$\frac{1}{4}AA, \frac{1}{2}Aa, \frac{1}{4}aa$	aa
Frequency	$U + \frac{1}{4}V$	$\frac{1}{2}V$	$W + \frac{1}{4}V$

In each generation of pure selfing the frequency of the heterozygotes decreases by  $\frac{1}{2}$  every generation and the frequency of each homozygotes increases by  $\frac{1}{4}V$

Written differently:

$$F = \frac{H_o - H_I}{H_o} \text{ where } H_o = 2pq \text{ (i.e., expected heterozygote frequency) and } H_I = \text{observed heterozygote frequency.}$$

$$= \frac{H_o}{H_o} - \frac{H_I}{H_o}$$

$$= 1 - \frac{H_I}{H_o}$$

$$H_I = H_o (1 - F) = 2pq(1 - F)$$

In other words:

$$\Delta F(Aa) = 2pq (1 - F)$$

$$\Delta F(AA) = p^2 + pqF$$

$$\Delta F(aa) = q^2 + pqF$$

Consider:

$$P(AA) = P(AA | \text{allozygous}) + P(AA | \text{autozygous})$$

$$= p^2(1 - F) + pF$$

$$= p^2 - p^2F + pF$$

$$= p^2 + pF(1 - p)$$

$$= p^2 + pqF$$

**Thus: Genotype ratios change from one generation to the next as a function of the magnitude of inbreeding**

**Notes:**

- 1)  $0.0 \leq F \leq 1.0$**
- 2)  $F = 0.0$  is HWE**
- 3)  $F = 1.0$  is all homozygotes (quickly)**
- 4)  $\Delta p = 0.0$**