

Inbreeding and Inbreeding Depression

Inbreeding is

- mating among relatives
- which increases homozygosity

Why is Inbreeding a Conservation Concern:

Inbreeding may or may not lead to ***inbreeding depression***, which is a reduction in the fitness in the offspring produced by inbred matings.

As populations size ↓, probability of mating among relatives ↑

If this reduces fitness, then a feedback loop can be established:

small N → ↓ fitness → further ↓ N → further ↓ fitness →→→

Dropping below the pop size threshold into this feedback loop was dubbed an '***extinction vortex***' by Gilpin & Soule (1986, *Conservation Biology* - this is just one of four extinction vortices they described).

Does inbreeding reduce fitness?

1. Population genetic ***theory*** predicts that inbreeding ***should*** reduce fitness in most cases.

Harmful alleles are normally rare.

Harmful alleles are normally recessive (why is this so)?

Recessive alleles must be homozygous to affect phenotype, and thus affect fitness.

So harmful alleles are unlikely to be expressed, as long as mating is random.

Suppose a harmful recessive has $q = 0.01$. Odds of getting a homozygote, with random mating, are $q^2 = 0.0001$. One in ten thousand.

But within families, if one individual has a single copy of the harmful allele (a "carrier" that doesn't express the phenotype), 50% of its siblings will also be carriers. Odds that full-sib mating will express the phenotype = $0.5^2 = 0.25$. One in 4.

2500X more likely to express harmful recessive than with random mating (for this example).

So inbreeding should affect fitness.

The magnitude of the effect depends on how many harmful recessive alleles are found in the population, and how harmful they are. This is called the **genetic load**.

Genetic load will tend to be lower in species (populations) in which inbreeding has been common in the past (e.g. species with small population sizes) — simply because *past inbreeding will have exposed harmful recessives to selection, and thus reduced their frequency, or eliminated them "purging inbreeding depression"*.

Conversely, genetic load will be highest in species that have large population sizes and little inbreeding due to factors such as social organization (which can subdivide the population and cause non-random mating).

2. **Empirical data** show that inbreeding depression is **common and often produces strong effects on fitness**, but is not universal.

Measuring inbreeding depression:

If each locus has independent (multiplicative) effects on fitness, then log of fitness will be a function of the degree of inbreeding.

(Ohead: Keller & Waller Fig 1 p 233)

(Ohead: Keller & Waller Box 5)

(Ohead: Ralls & Ballou Table 1a, p. 166 ff, Tables 2, 3, 4)

(Ohead: Keller & Waller Table 1, p.236)

Defining and Measuring Inbreeding

Measures of the level of inbreeding are **relative**, not absolute. Suppose, a set of matings is observed in a population - if some of these include matings among relatives, is the pattern strong enough to be considered non-random? The answer depends on what is chosen as the **reference population**, which defines the set of matings that would be expected by chance.

Differences in the reference population used produce three different (but related) measures of inbreeding:

- (1) **Pedigree Inbreeding**: inbreeding due to parents sharing recent direct ancestors.
 - F = prob. that two homologous alleles in an individual are identical by descent (IBD)

For a pedigree that goes back to an ancestor A, the inbreeding coefficient (F) of individual I is:

$$F_I = \sum (0.5)^i (1 + F_A)$$

where i = the number of individuals (except I) in a closed pedigree path through a common ancestor leading to both of I's parents. A closed path is one that involves inbreeding.

The summation (Σ) is across all possible closed paths in the pedigree that lead to individual I.

(Ohead: Lande & Barrowclough page 117)

- Note that an individual can be homozygous for the same allele without the two alleles being IBD.

(Ohead: Hartl Fig 13, p 43)

- This estimate of F depends on the "depth" of the pedigree, so it is always relative to a particular ancestral generation (F_A in the equation).
- $=F_{IT}$ when averaged across all individuals in a population

$$F_{IT} = \frac{H_T - H_I}{H_T}$$

Data sets that accumulate data on mating patterns over several generations are not common. But where data exist to build "deep" pedigrees, substantial inbreeding can often be found:

(Ohead: Keller & Waller Fig. 1 p 231, Creel 1991 appendix figs)

(2) **Inbreeding due to Nonrandom Mating:** Offspring are 'inbred' if parents are more closely related than a random pair of individuals from that population

$=F_{IS}$, the deficiency of heterozygotes relative the level expected with random mating

$$F_{IS} = \frac{\bar{H}_s - H_I}{\bar{H}_s} = \frac{H_{EXP} - H_{OBS}}{H_{EXP}}$$

(EXP = expected with random mating, OBS = observed)

$F_{IS} = 0 \rightarrow$ random mating

$F_{IS} > 0 \rightarrow$ positive assortative mating (similar genotypes mate)

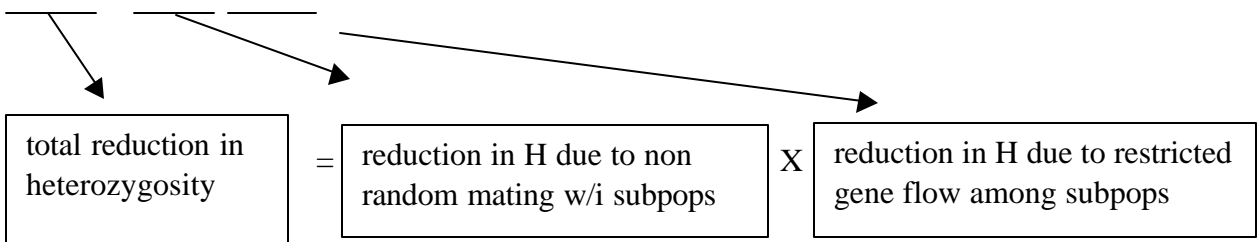
In small populations, *even random mating will sometimes produce matings among close relatives.* ($F_{IS} = 0$, but $F_{IT} > 0$, perhaps high if population is very small).

Just one generation of random mating returns F_{IS} to zero (because only one generation of random mating is needed to bring genotype frequencies back to Hardy-Weinberg equilibrium). F_{IT} does *not* return to zero, because it explicitly looks back into the pedigree: current mating patterns do not remove past matings among close relatives.

3) *Inbreeding due to Population Subdivision:*

Even if pedigree inbreeding is rare, and mating is random within subpopulations, population subdivision will increase the likelihood that an individual inherits alleles that are identical by descent (IBD). From this perspective F_{ST} is also a measure of inbreeding due to population subdivision. So to estimate total inbreeding:

$$(1-F_{IT}) = (1-F_{IS})(1-F_{ST})$$



$F_{IT} > 0$: individuals are less variable than expected for level of allelic variation seen in total population

- less than full mixture of individuals across entire population (all subpops)
- due to combination of all processes *within* subpop and *among* subpops

How much is heterozygosity reduced by a given level of inbreeding?

Begin with the definition of F_{IS} , inbreeding due to nonrandom mating:

$$F_{IS} = \frac{\bar{H}_s - H_I}{\bar{H}_s} = \frac{H_{EXP} - H_{OBS}}{H_{EXP}}$$

or

$$F_{IS} = 1 - \frac{H_{OBS}}{H_{EXP}}$$

If mating IS random, then the frequency of heterozygotes will be $2pq$ (HW equilibrium)

$$F_{IS} = 1 - \frac{H_{OBS}}{2pq}$$

$$2pq(F_{IS}) = 2pq - H_{OBS}$$

$$H_{OBS} = 2pq - 2pq(F_{IS})$$

$$H_{OBS} = 2pq(1 - F_{IS})$$

F_{IS} = the reduction in heterozygosity (H), relative to H for a random mating population.

Same logic applies to other measures of F.

So the answer to the question heading this section is "by (1-F)".

CHEETAH CASE STUDY