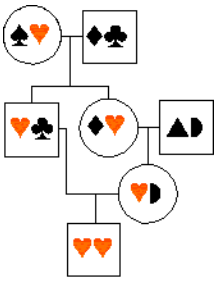
BIOL2007
INBREEDING AND NEUTRAL EVOLUTION

Tutorials: exercise now online; tutor details soon...



Regular systems of inbreeding, (vs. small population sizes, that also lead to **genetic drift** and inbreeding)

MEASURING INBREEDING: If an individual mates with a relative, offspring may be homozygous for an allele which is **identical by descent** from one of the ancestors. In the diagram, a male is homozygous for two copies of an allele - ♥ - inherited from a single copy in an ancestor. His mum is his dad's niece.

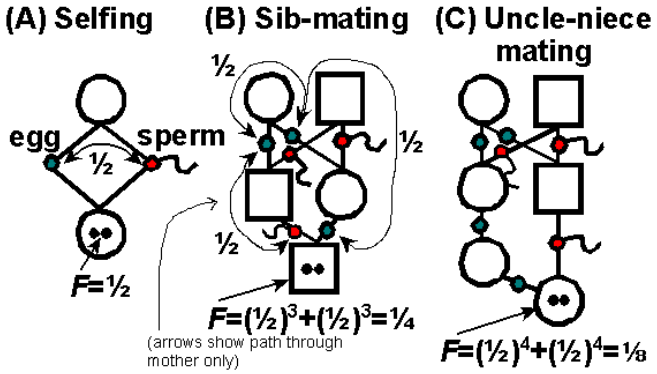
The **INBREEDING COEFFICIENT, *F*,** is used to gauge the strength of inbreeding.

F = probability that two alleles in an individual are **identical by descent** (**IBD**). ***F*** stands for **fix**ation index, because of the increase in homozygosity, or "fixation", that results from inbreeding.

Note: two alleles that are **identical by descent** must be **identical in state**. However, a homozygote for an identifiable allele can often be produced *without* inbreeding in its recent ancestry. Therefore **identity in state** does not necessarily imply **identity by descent**.

REGULAR SYSTEMS OF INBREEDING

We can measure ***F*** easily in regular systems of inbreeding, using Sewall Wright's method of "path analysis":



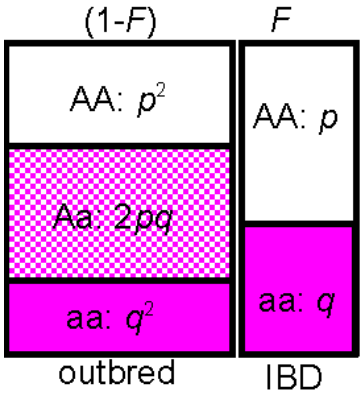
1) Find each path that alleles may take to become **IBD**.
2) Find the no. of path segments (***x***) between gametes (eggs or sperm) through a single ancestor in common in each path.
3) Calculate the probability of **IBD** for each path. The probability that an allele is **IBD** between two gametes connected through an individual is **1/2**. Thus, the probability of **IBD** for each path is $(1/2)^x$.
4) Add up the probabilities of each path to get the total probability of **IBD**.

EFFECT OF INBREEDING ON POPULATIONS

Consider two alleles, **A**, and **a** with frequencies *p,q* with inbreeding (**IBD**) at rate ***F***:

Frequency of homozygotes:
AA = $(1\text{-}F)p^2$ [outbred]
+ Fp [inbred]
(see figure at right)
= $p^2 + F(p\text{-}p^2)$
= $p^2 + Fp(1\text{-}p)$
= $p^2 + Fpq$

Similarly frequency of other homozygotes, **aa** = $q^2 + Fpq$



All genotype frequencies must add to 1, so the extra $2Fpq$ AA and aa homozygotes must have come from the heterozygotes (which cannot be IBD, since they aren't even identical in state), and so overall, the frequencies are:

genotype	**AA**	**Aa**	**aa**	
frequency	p^2+Fpq	$2pq(1\text{-}F)$	q^2+Fpq	Sum = 1

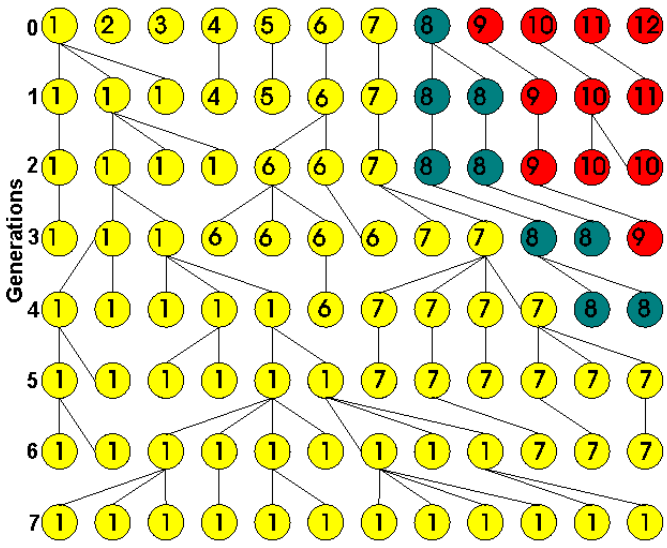
So, **inbreeding** leads to a **reduction in heterozygosity**. **Heterozygosity** (***Het***, i.e. the proportion that are heterozygotes under inbreeding) is reduced by a fraction ***F*** compared with the outbred (Hardy-Weinberg) expectation $Het_{HW} = 2pq$:

$$Het = Het_{HW}(1 - F)$$

Therefore, ***F*** measures reduction of heterozygosity, ***heterozygote deficit*** compared to Hardy-Weinberg, as well as ***probability of identity by descent***!

GENETIC DRIFT: Deterministic vs. stochastic evol.

Hardy-Weinberg assumes ***no*** gene frequency change. In large populations; evolution is ***deterministic***. Only approximately true in populations of finite size. Below: picture of drift. Suppose rare species kept in a zoo with ***N*** = 6 diploid individuals. Total of ***2N*** = 12 alleles (numbered 1-12 in generation 0). Evolution assumed neutral. May be genetically distinguishable, "different in state" (colours).



If wild population large, all the alleles in generation 0 come from different ancestors; none would be ***identical by descent*** (***IBD***). But by chance some alleles are lost in each generation. After a number of generations, every allele becomes ***IBD***. In the diagram, ***IBD*** by the 7th generation.

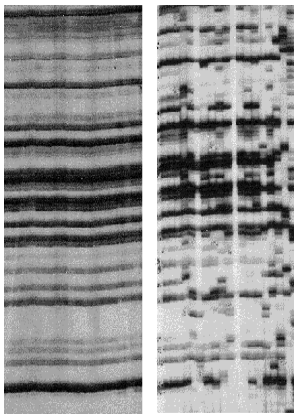
Alleles that are ***IBD*** must also be ***identical in state*** (barring mutation). Because the population has become fixed for allele 1, it has also become fixed for the allelic state to which allele 1 belongs ("yellow"). Usually, there are fewer allelic states than alleles, so that fixation of state (gen. 5, above) can happen earlier than identity by descent (gen. 7).

Predictable unpredictability (remember, science = accurate prediction!) We can't predict *exactly* what is going to happen in genetic drift, but the *distribution* of results is known, and useful. We can quantify the following:

1) The **mean gene frequency**. The mean, or **expected frequency** in the future = binomial probability ***p.*** (similarly, the av. fraction of heads is 0.5; pro. of a head).
2) The **variance of gene frequency** after one generation. The variance given by the binomial is:

$$\mathrm{var}(p) = \frac{pq}{2N}$$

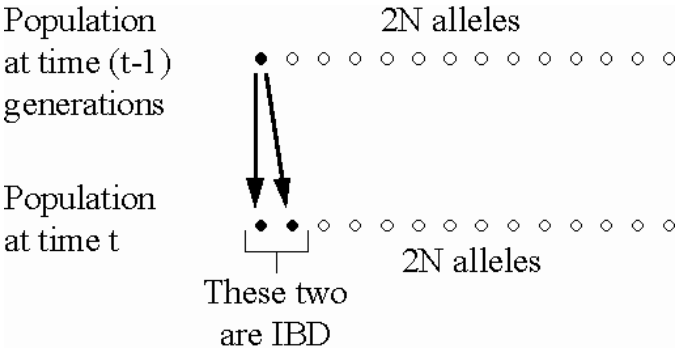
EXAMPLE OF GENETIC DRIFT



Asian bramble (*Rubus alceifolius*), introduced on Pacific islands. Genetic variation studied by means of DNA fingerprint technique: "Amplified Fragment Length Polymorphisms" - AFLP for short. Native range (Vietnam, right), versus an introduced population (the island of Réunion, left) (from Amsellem L et al. 2000.Mol. Ecol. 9: 443-455, reproduced by permission).

GENETIC DRIFT AS A CAUSE OF INBREEDING

As we have seen, **inbreeding results from drift** because alleles become ***identical by descent*** (IBD). We can therefore measure drift in terms of our inbreeding coefficient, ***F***:



In a population of size ***N***, the probability that two alleles picked during random mating in generation ***t*** are **IBD** due to copying from generation ***t*-1** is

$$F_t = \frac{1}{2N}$$

(on average). This is the ***rate of inbreeding*** due to drift per generation.

BUT the ***2N*** alleles in the previous generation may be IBD themselves from inbreeding in previous generations. The fraction of alleles in generation ***t*** that are IBD because of inbreeding before generation ***t*-1** is:

$$F_t = \left(1 - \frac{1}{2N}\right) F_{t-1}$$

Summing the inbreeding in the current generation with inbreeding from previous generations, we have at time ***t***:

$$F_t = \frac{1}{2N} + \left(1 - \frac{1}{2N}\right) F_{t-1} = \frac{1}{2N}\left(1 - F_{t-1}\right) + F_{t-1}$$

By definition, the heterozygosity after a single generation of inbreeding, $Het = Het_{HW}\,(1 - F)$. See above. From the above equation relating F_t to F_{t-1} and cancelling Het_{HW}'s:

$$Het_t = Het_{t-1}\left(1 - \frac{1}{2N}\right)$$

After t generations:

$$Het_t = Het_0\left(1 - \frac{1}{2N}\right)^t$$

Thus, **heterozygosity declines** approximately by a factor $\frac{1}{2N}$ per generation (essentially, this is the rate of drift). However, ...

(a) This is true only **on average** because a single allele may have zero, one, two or more copies in the next generation. The factor $\frac{1}{2N}$ is an average only.

(b) ***F*** can also measure inbreeding as a result of subdivision into two or more finite populations. When we sample from a number of sub-populations with different gene frequencies, the heterozygote deficit gives us identity by descent produced by subdivision. Usually written F_{ST}, inbreeding (***F***) due to subdivision into **S**ubpopulations relative to the **T**otal population.

EFFECTIVE POPULATION SIZE

Alleles usually do not have identical probability of being passed on, as required in simple models. Population geneticists get around this by calculating ***effective population size*** that produces the same rate of genetic drift in their simple models as he actual population with all its complexity.

Effective population size may differ from actual population size.

READINGS

Freeman & Herron Chapter 6.
Futuyma Chapter 11 (pp. 297-314).