Inbreeding

Genetic Variation - Generalization of the H-W law

Geographic variation in the three alleles of the alkaline phosphatase in humans (Roychoudhury and Nei 1988)

	S	F	I	others	n
England	0.637	0.27	0.085	0.008	597
Italy	0.661	0.256	0.075	0.007	273
West India	0.701	0.217	0.066	0.016	208
Thailand	0.746	0.081	0.165	0.008	188
Japan	0.724	0.038	0.236	0.003	294
Nigeria	0.942	0.019	0.039		130
Canadian Inuits	0.556	0.142	0.296	0.006	81
Papua New Guinea	0.880	0.05	0.068	0.002	338

The human population is not one large randomly mating population.

Inbreeding

Even though inbreeding levels have decreased in western civilizations, many studies have shown that in many other large societies **consanguineous (Lat. “of the same blood”) marriages** still predominate. In fact, in many large populations of Asia and Africa twenty to fifty percent of all unions are that of consanguineous marriages (Bittles 1991). There are several circumstances that would give a population a reason to practice inbreeding at a large scale. Some of these reasons for practicing inbreeding include **royalty**, **religion and culture**, **socioeconomic class**, and, **geographic isolation** and **small populations**.

Groups that are associated with inbreeding because of religion and culture are the small Anabaptist populations in North America. These groups include the Amish, the Mennonites, and the Hutterites. These groups settled in North America in the 18th and 19th centuries in search of religious freedom. These populations have shown increases in consanguineous marriages over time, and the hight was reached in the 1950's when some groups reached levels of consanguineous marriages as high as 85%. The reason for the high levels of inbreeding is not only due to religion; it can also be attributed to the small isolated farming communities in which these populations find themselves. These factors of religion and small communal societies lead to limited choices when searching for possible mates (Agarwala 2001).

Geographic isolation and **population size** play a large role in many populations when concerning levels of inbreeding and genetic barriers. **Migration rates** can also play a large role in inbreeding levels. Furthermore, as the number of generations since the isolated population was founded increases so should the inbreeding levels. Several of these factors were seen in studies in small communities and countries located and isolated in European mountain ranges. One such population study was performed in the country of Andora. Andora is on of the smallest countries in Europe, and it is very isolated by being surrounded by very high mountains in the Central Pyrenees. It was traditionally a small agricultural and cattle farming country that had a population between 4,000 and 6,000. The economy of Andora has grown to include areas of tourism and trade, and immigration has increased to Andora partially due to the absence of taxes and beautiful scenery. The population has grown to approximately 46,000 people, which itself can cause a decline in inbreeding levels because it increases the number of mates to choose from and brings new views and ideas to the population (Gonzalez-Martin 2002).

Inbreeding - The Hutterities

The Hutterites are a religious sect that originated in the Tyrolean Alps in the 1500's. Between the mid-1700's to mid-1800's, during their tenure in Russia, the population grew in size from approximately 120 to over 1,000 members (Hostetler 1974). In the 1870's approximately 900 of these members migrated to what is now South Dakota and roughly half settled on three communal farms. Due to a high natural fertility rate and the proscription of contraception among communal Hutterites, the population expanded dramatically since migrating to the United States. Today there are >35,000 Hutterites living on >350 communal farms (called colonies) in the northern United States and western Canada. Genealogical records, collected by Steinberg and his students in the 1950's and 1960's (Bleibtreu 1964; Mange 1964; Steinberg et al. 1967), trace all extant Hutterites to fewer than 90 ancestors who lived in the early 1700's to the early 1800's (Martin 1970). The relationships between these ancestors are unknown, but some of them may have been related.

Their isolation along with their beliefs leads to a highly inbred population. Moreover, the Hutterites are a good population to study because, like the Amish, they keep very detailed genealogical records. The Hutterites are also among the most fertile populations that commonly practice inbreeding. Furthermore, in studies concerning the Hutterites the confounding effects of socioeconomic class are not a factor, because they are relatively uniform in this population's communal lifestyle. One such study wanted to investigate some of the effects of inbreeding on the fertility of adult women. There were several measurements used to detect any adverse changes in fertility. Inbreeding coefficients, measurements of birth intervals, and family size were all measured. The offspring of the Hutterite women showed that the intervals between births decreased as levels of inbreeding increased. These intervals not only increased as inbreeding levels increased, they also increased with each generation of Hutterite women. Therefore, the deleterious effects of inbreeding can be tracked through each generation. These significantly **longer interbirth intervals** were due to lower conception rates or higher losses in embryonic stages of pregnancy. Moreover, this also caused large declines in family size. In fact, average family size shrunk from above nine from 1901 to 1920 to five from 1941 to 1960. This showed a decrease in two family members per generation in the Hutterite population. This study has shown that deleterious recessive alleles received from inbreeding can lower the fertility rates of adult woman (Ober 1999).

Inbreeding - Inbreeding coefficent

Inbreeding is the mating of individuals related by ancestry. The consequence of mating with a relative is that offspring have an increased probability of inheriting alleles that are recent copies of the same allele (i.e. identical by descent, or autozygous). **This leads to increased frequencies of homozygotes.**

We can use the predictable increase in homozygosity and decrease in heterozygosity resulting from inbreeding to measure the effect of inbreeding.

The inbreeding coefficient of an individual (F) is the probability that an individual has two alleles at a locus that are identical by descent. It measures the amount of inbreeding by comparing the frequency of heterozygotes (H) in the population to the frequency expected under random mating (H_e).

$$F = 1 - \frac{H}{H_e} = \frac{H_e - H}{H_e} \rightarrow \frac{H}{H_e} = \frac{2pq(1-F)}{2pq} = 1 - F$$

when population in HWE H_e=H and F=0 (random mating) - F:[-1,1]

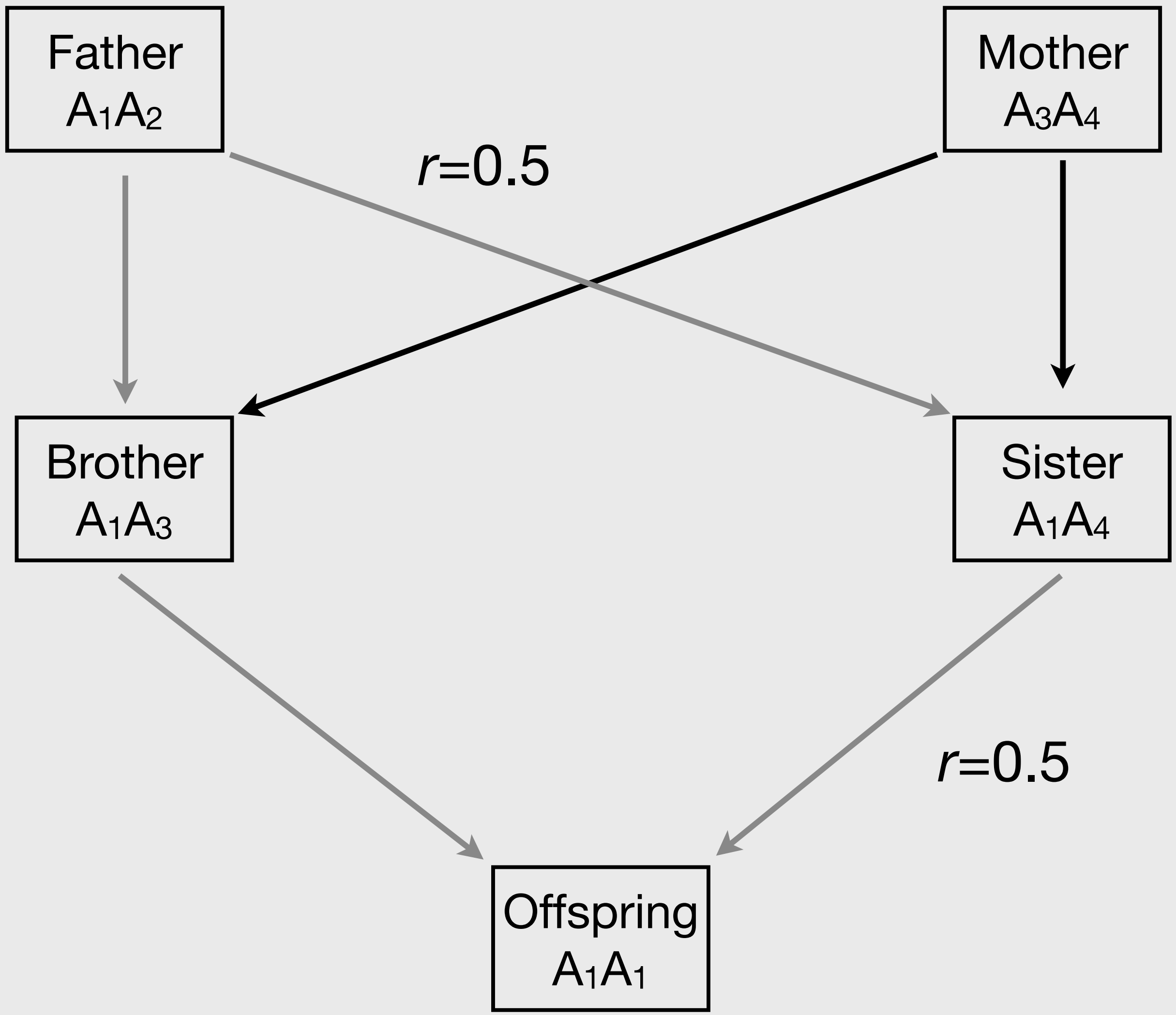
The following genotype frequencies in a plant species that engages in mixed selfing and outcrossing:

Genotype	A_1A_1	A_1A_2	A_2A_2
Frequency	0.828	0.144	0.028

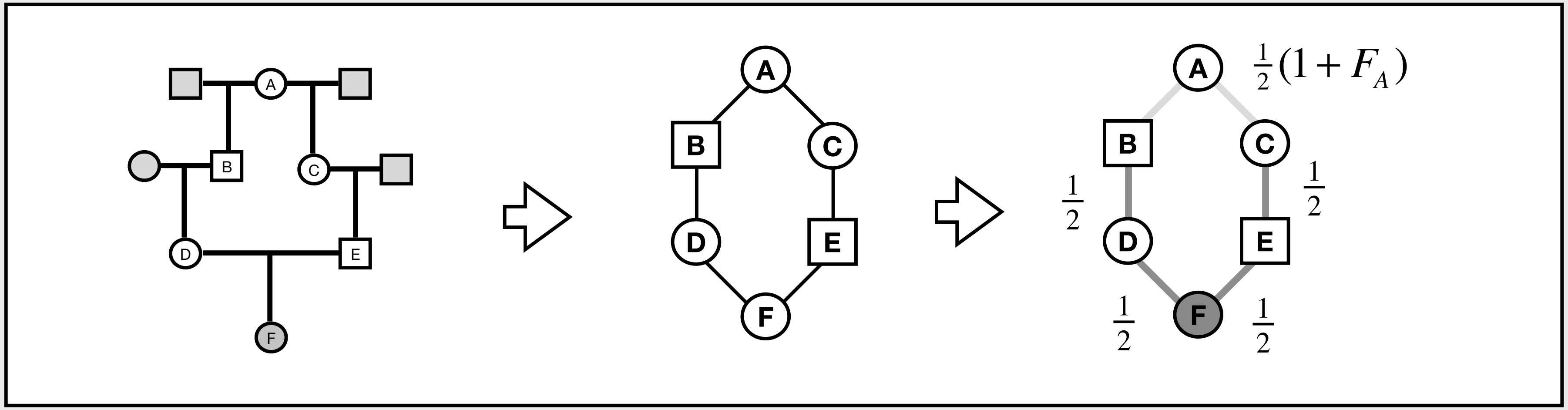
$$p = 0.828 + \tfrac{1}{2}0.144 = 0.9$$
$$q = 1 - 0.9 = 0.1$$
$$H_e = 2pq = .018$$
$$F_I = \frac{0.18 - 0.144}{0.18} = 0.2$$

What is the frequency of selfing if the population is at equilibrium?

Inbreeding - Coefficient for relatedness (*r*)



Inbreeding : Calculation of inbreeding coefficient



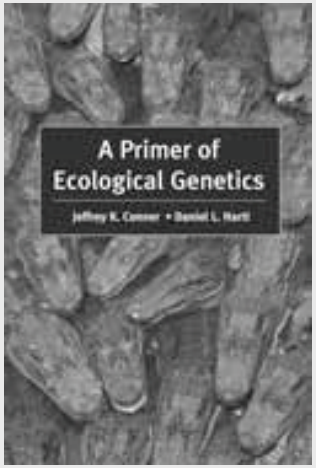
a. identify all common ancestors in the pedigree => A

b. trace all the paths of gametes (DBACE)

c. calculate inbreeding coefficient F_I

$$F_I = \left(\tfrac{1}{2}\right)^i \left(1 + F_A\right) \overset{F_A = 0}{\Longrightarrow} \left(\tfrac{1}{2}\right)^5 = \frac{1}{32}$$

Inbreeding - Consequences of inbreeding



"...genetic drift increases homozygosity and decreases heterozygosity without changing allele frequencies..."

"...exactly the same pattern produced by inbreeding..."

"...Sewall Wright used this similarity between genetic drift and inbreeding to create **F-statistics**, which provide an integrated view of genetic variation at three hierarchical levels of population structure..."

> the "inbreeding" due to small population size is actually a consequence of genetic drift, not mating with relatives more often than expected by chance

> inbreeding increases the frequencies of both homozygotes (AA and aa) and therefore the sub-population deviates from HWE

> genetic drift increases the frequencies of only one - the homozygote as one allele randomly heads to fixation, and the sub-population stays in HWE.

> Departure from HW expected genotype frequencies, the autozygosity or inbreeding coefficient and the fixation index are all interrelated.