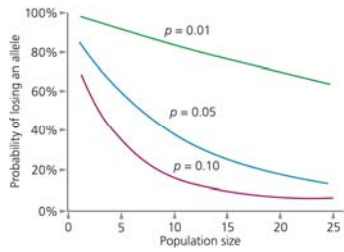


Bottlenecks reduce genetic variation – Genetic Drift



Northern Elephant Seals were reduced to ~30 individuals in the 1800s.

Rare alleles are likely to be lost during a bottleneck



Two important determinants of the severity of a bottleneck are the duration and population size (N_e)

NON-RANDOM MATING

▪ **Inbreeding:** mating between close relatives leads to deviations from H-W equilibrium by causing a deficit of heterozygotes.

▪ In the extreme case of self-fertilization:

Generation	AA	Aa	aa
0	p^2	$2pq$	q^2
1	$p^2 + (pq/2)$	pq	$q^2 + (pq/2)$
2	$p^2 + (3pq/4)$	$pq/2$	$q^2 + (3pq/4)$

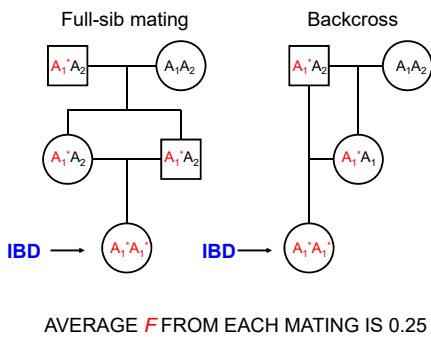
HOW CAN WE QUANTIFY THE AMOUNT OF INBREEDING IN A POPULATION?

- The inbreeding coefficient,

F

- The probability that a randomly chosen individual carries two copies of an allele that are *identical* by descent from a recent ancestor.
- The probability that an individual is *autozygous*

- Consider two pedigrees:



LOSS OF HETEROZYGOSITY IN LINE OF SELFERS

- Population Size (N) = 1

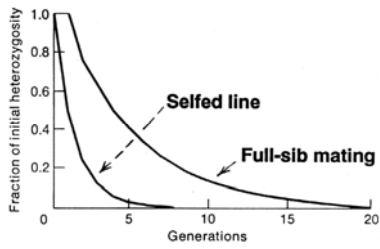
Heterozygosity after one generation, $H_1 = (1/2) \times H_0$

Heterozygosity after two generations, $H_2 = (1/2)^2 \times H_0$

After t generations of selfing, $H_t = (1/2)^t \times H_0$

- Example: After $t = 10$ generations of selfing, only 0.098% of the loci that were heterozygous in the original individual will still be so. The inbred line is then essentially completely homozygous.

DECLINE IN HETEROZYGOSITY DUE TO INBREEDING



HETEROZYGOSITY IN A POPULATION THAT IS PARTIALLY INBRED

- In an inbred population the frequencies of homozygous individuals are higher than expected under HWE. Thus, the observed heterozygosity will be lower than expected under HWE.

$$H_{obs} = 2pq(1-F) = H_{exp}(1-F).$$

- F ranges from 0 (no inbreeding) to 1 (completely inbred population)

F CALCULATED FROM HETEROZYGOTE DEFICIT

$$F = (H_{exp} - H_{obs}) / H_{exp}$$

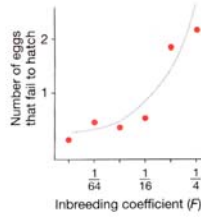
Where,

H_{exp} = frequency of heterozygotes if all matings were *random*

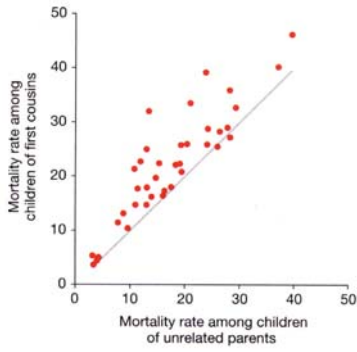
INBREEDING COEFFICIENT, F



- As the inbreeding coefficient (F) increases, fitness often decreases.
- **INBREEDING DEPRESSION**



INBREEDING DEPRESSION IN HUMAN POPULATIONS



Science 8 February 2008:
Vol. 319, no. 5864, pp. 813 - 816

An Association Between the Kinship and Fertility of Human Couples

Helgason et al.

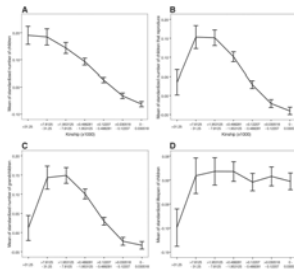


Fig. 1. The relationship between kinship and reproduction among Icelandic couples. The four panels show means and 95% confidence intervals of standardized variables relating to the reproductive outcome of Icelandic couples as a function of seven intervals of kinship. (A) shows the total number of children, (B) the number of children who reproduced, (C) the number of grandchildren, and (D) the mean life expectancy of children. *The first interval of kinship represents all couples related at the level of second cousins or closer, the second interval represents couples related at the level of third cousins and up to the level of second cousins, and so on, with each subsequent category representing steps to fourth, fifth, sixth, and seventh cousins and the final category representing couples with no known relationship and those with relationships up to the level of eighth cousins.*

INBREEDING VERSUS RANDOM GENETIC DRIFT

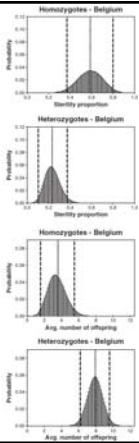
- **Inbreeding** is caused by non-random mating and leads to changes in genotype frequencies but **not** allele frequencies.
- **Random genetic drift** occurs in finite populations, even with completely random mating, and leads to changes in **both** genotype and allele frequencies.
- Both processes cause a decline in heterozygosity.

Homozygosity at a class II MHC locus depresses female reproductive ability in European brown hares

- Why does inbreeding cause a decrease in fitness?
- What genetic mechanisms, or type of **gene action** are responsible?



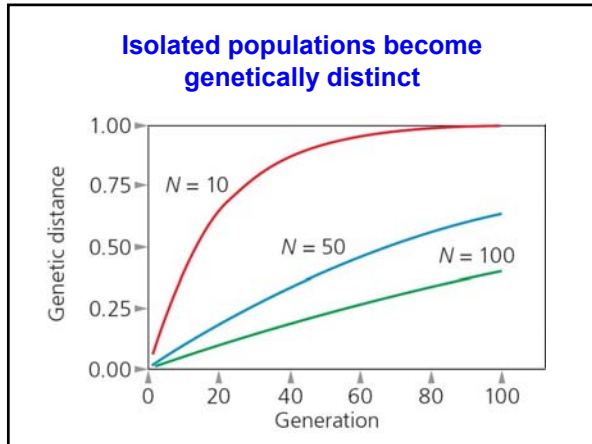
Smith et al. Molecular Ecology (2010) 19, 4131–4143

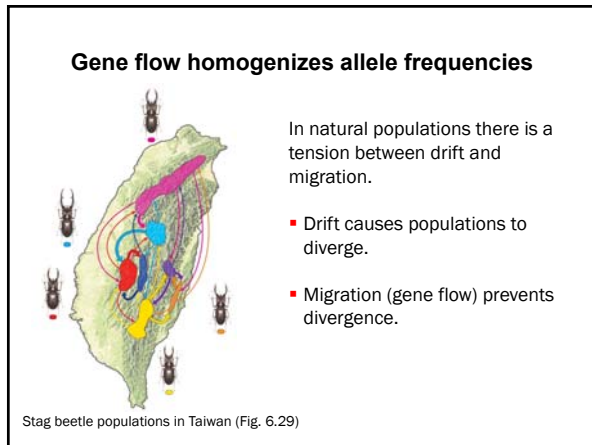


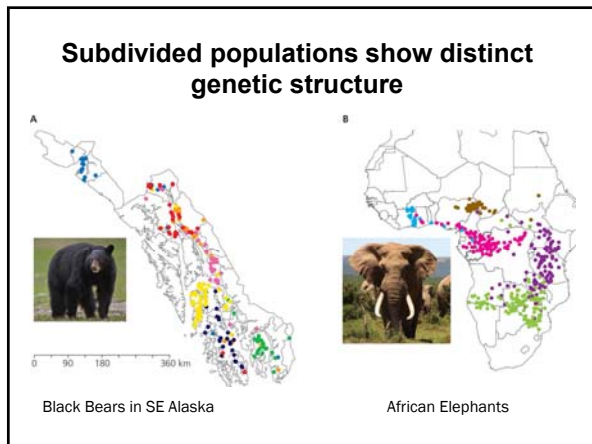
Many organisms occupy ranges that are discontinuous

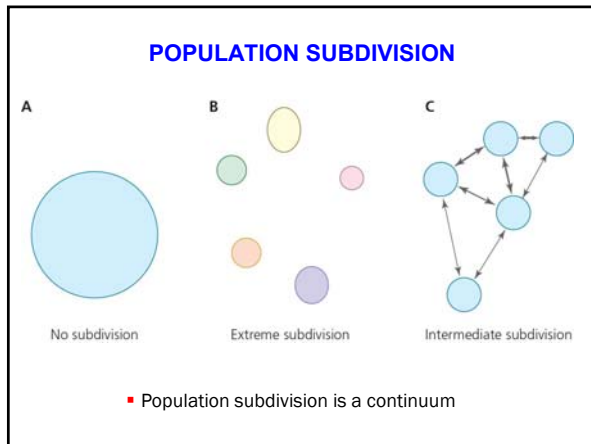


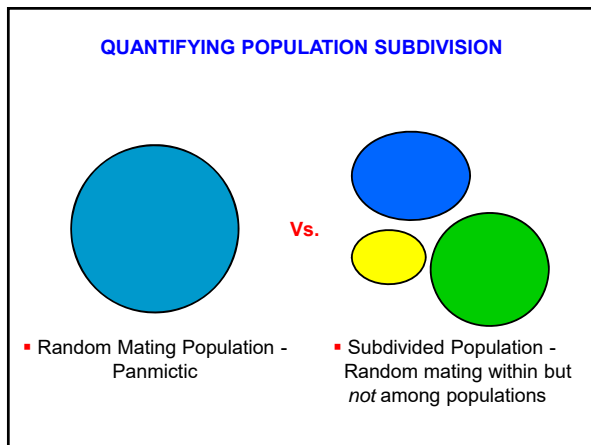
Rocky Mountain Big Horn Sheep

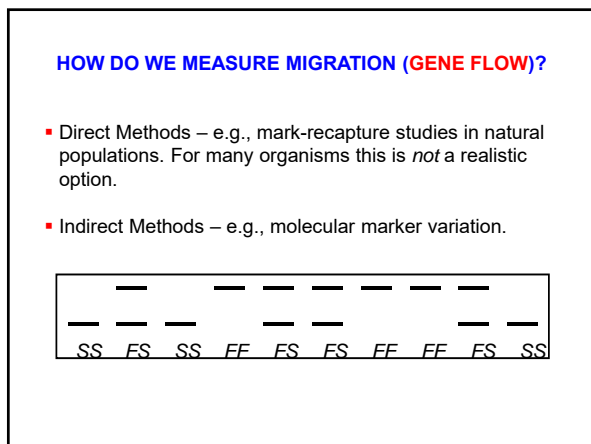












CONSIDER TWO COMPLETELY ISOLATED POPULATIONS

- Due to random genetic drift, the allele frequencies in the populations diverge.
- In an extreme case, they can be fixed for alternate alleles:

	A ₁ A ₁	A ₁ A ₂	A ₂ A ₂
Population 1	1.0	0	0
Population 2	0	0	1.0
Overall HWE	0.25	0.50	0.25

- Individuals in population 1 are clearly more closely related to one another than they are to individuals in population 2.
- In this context, the inbreeding coefficient (*F*) represents the probability that two gene copies within a population are the same, relative to gene copies taken at random from all populations lumped together.

QUANTIFYING POPULATION SUBDIVISION WITH F_{ST}

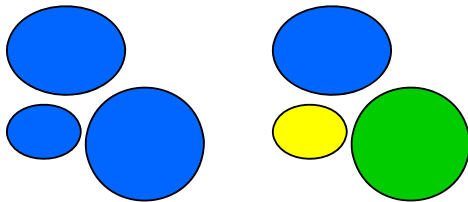
- F_{st} measures variation in allele frequencies among populations.

Ranges from 0 to 1

- F_{st} compares the *average expected heterozygosity* of individual subpopulations (*S*) to the *total expected heterozygosity* if the subpopulations are combined (*T*).

$$F_{ST} = \frac{(H_T - H_S)}{H_T} = 1 - \left(\frac{H_S}{H_T} \right)$$

F_{ST} AND POPULATION SUBDIVISION



- At Panmixis, F_{ST} = 0
- All subpopulations have the same allele frequencies.
- Complete Isolation, F_{ST} = 1
- All subpopulations are fixed for different alleles.

▪ Example:

▪ Consider three subpopulations with 2 alleles at frequencies p and q ,

	p	q	$H_s=2pq$
▪ Subpop 1:	0.7	0.3	0.42
▪ Subpop 2:	0.5	0.5	0.50
▪ Subpop 3:	0.3	0.7	0.42

Average $H_s = 0.446$

▪ The *total expected heterozygosity* across all subpopulations is calculated from the average allele frequency,

	p	q
Subpop 1:	0.7	0.3
Subpop 2:	0.5	0.5
Subpop 3:	0.3	0.7
	$\bar{p} = 0.5$	$\bar{q} = 0.5$

$H_T = 2\bar{p}\bar{q} = 0.5$

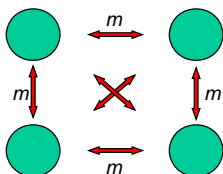
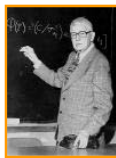
Remember that,

$$F_{ST} = \frac{(H_T - H_s)}{H_T} = 1 - \left(\frac{H_s}{H_T} \right)$$

$F_{ST} = (0.50 - 0.466) / (0.50) = 0.11$

WRIGHT'S ISLAND MODEL:

▪ Consider n subpopulations that are diverging by drift alone, not by natural selection, and with an equal exchange of migrants between populations each generation at rate m



▪ What is the equilibrium level of population subdivision (F_{ST})?

RELATIONSHIP BETWEEN F_{ST} AND Nm IN THE ISLAND MODEL

- Nm is the absolute number of migrant organisms that enter each subpopulation per generation.

- At equilibrium: $\hat{F} = F_t = F_{t-1}$

- And:
$$F_{ST} = \frac{1}{1 + 4Nm}$$

- When $Nm = 0$, $F_{ST} = 1$

$Nm = 0.25$ (1 migrant every 4th generation), $F_{ST} = 0.50$
 $Nm = 0.50$ (1 migrant every 2nd generation), $F_{ST} = 0.33$
 $Nm = 1.00$ (1 migrant every generation), $F_{ST} = 0.20$
 $Nm = 2.00$ (2 migrants every generation), $F_{ST} = 0.11$

RELATIONSHIP BETWEEN F_{ST} AND Nm IN THE ISLAND MODEL

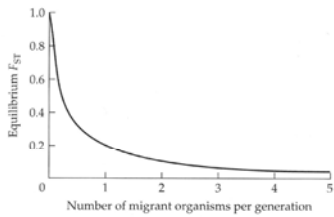
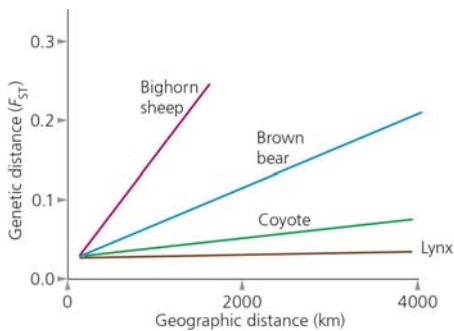


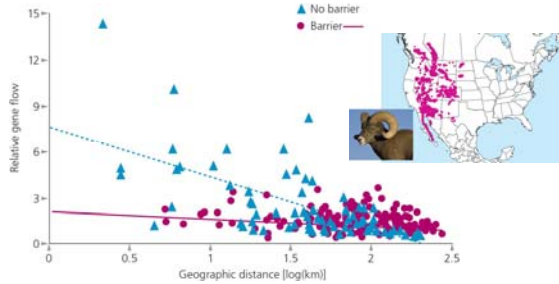
Figure 5.17 Decrease in the fixation index F_{ST} among subpopulations at equilibrium in the island model of migration. The curve is that in Equation 5.17 giving \hat{F} as a function of Nm . In the island model, Nm is the number of migrant organisms that come into each subpopulation in each generation.

In: Hartl and Clark. 1997. *Principles of Population Genetics*. Sinauer Assoc.

Amount of gene flow varies with the biology of the organism



Anthropogenic activities can alter population structure



ROLE OF DRIFT IN POPULATION DIVERGENCE

$$F_{ST} = \frac{1}{1 + 4Nm}$$

- If $Nm \gg 1$, little divergence by drift;
- If $Nm \ll 1$, drift is very important
