

# Lecture 10: The Interaction of Selection, Mutation, and Migration (Ch11)

*Population genetic PCB4553/6685*

# Background

- **Mutation**, is the ultimate source of all genetic variation
- Mutations constantly introducing new variation into all populations.
- Mutations are random and so mutations that affect function are often damaging.
- Mutation will, in the absence of sufficiently strong selection, degrade pre-existing adaptations and undo the work of selection that has built up functional regions of DNA over time.

# Background

- **Migration**, the movement of individuals into a population, can also increase variation to the population as the individuals bring new alleles in from surrounding populations.
- Migration can be an important source of adaptive alleles, aiding their spread amongst populations within a species.
- Adaptive alleles can even spread between species if low levels of interbreeding occur.
- Like mutation, migration can disrupt adaptations. When populations are locally adapted migration amongst populations can introduce maladaptive alleles into well adapted populations.
- If this migration pressure is sufficiently strong, it can lead to the collapse of local adaptations, or even the collapse of species.

# Mutation-selection balance

- To study mutation-selection balance, we return to the model of directional selection, where allele A1 is advantageous
- $\mu = \mu_{1 \rightarrow 2}$  : mutation rate per generation from A1 to the deleterious allele A2
- Assume no reverse mutation  $\mu_{2 \rightarrow 1} = 0$ .
- Assume selection against A2 is relatively strong compared to the mutation rate, so that that A2 is always rare, i.e.  $q_t = 1 - p_t \ll 1$

genotype	$A_1A_1$	$A_1A_2$	$A_2A_2$
absolute fitness	$W_{11}$	$\geq W_{12} \geq$	$W_{22}$
relative fitness	$w_{11} = 1$	$w_{12} = 1 - sh$	$w_{22} = 1 - s.$

# Mutation-selection balance

- Change in frequency due to selection
  - assuming  $q^2 \approx 0$ ,  $p \approx 1$ ,  $\bar{w} \approx w_1$
  - The change in frequency of A2 due to selection

- $$\Delta_S q_t = \frac{\bar{w}_2 - \bar{w}_1}{\bar{w}} p_t q_t \approx -hsq_t.$$

- If initial frequency of A2 is  $q_0$ , then its frequency at time t is approximately

- $$q_t = q_0(1 - hs)^t.$$

# Mutation-selection balance

- $\mu = \mu_{1 \rightarrow 2}$  : mutation rate per generation from A1 to the deleterious allele A2
- $q' = \mu p_t + q_t = \mu(1 - q_t) + q_t$
- Assuming  $\mu \ll 1$ ,  $q \ll 1$ 
  - change in the frequency of allele A2 due to mutation can be approximated by
- $\Delta_M q_t = q' - q_t = \mu.$
- \*When A2 is rare and the mutation rate is low, mutation acts to linearly increase the frequency of the deleterious allele A2.

# Mutation-selection balance

- To find the frequency for A2 at the mutation–selection equilibrium, we set

- $\Delta_M q_t + \Delta_S q_t = 0$

- $\Delta_M q_t = q' - q_t = \mu.$

- $\Delta_S q_t = \frac{\bar{w}_2 - \bar{w}_1}{\bar{w}} p_t q_t \approx -hsq_t.$

- $q_e = q_t = \frac{\mu}{hs}$

# Mutation-selection balance

- $q_e = q_t = \frac{\mu}{hs}$
- A2A2 homozygote has not entered this calculation, as A2 is so rare that it is hardly ever found in the homozygous state.
- The deleterious effect of A2 in a heterozygous state (i.e. if  $h > 0$ ), determines the frequency at which A2 is maintained in the population.
- If an allele is truly recessive, we can make a similar argument

- $q_e = \sqrt{\frac{\mu}{s}}.$



### Question 1.

Oblong-winged katydids (*Amblycorypha oblongifolia*) are usually green. However, some are bright pink, thanks to an erythrism mutation. This pink condition is thought to be due to a dominant mutation (Crew, 2013). Assume that roughly one in ten thousand katydids is bright pink and that the mutation rate at the gene underlying this condition is  $10^{-5}$ . What is the relative fitness of heterozygotes for the pink mutation?

# The genetic load of deleterious alleles

- What effect do such deleterious mutations at mutation–selection balance have on the population?
- Common to quantify the effect of deleterious alleles in terms of a reduction of the mean relative fitness of the population.
- Given

- $q_e = q_t = \frac{\mu}{hs}$

- We find

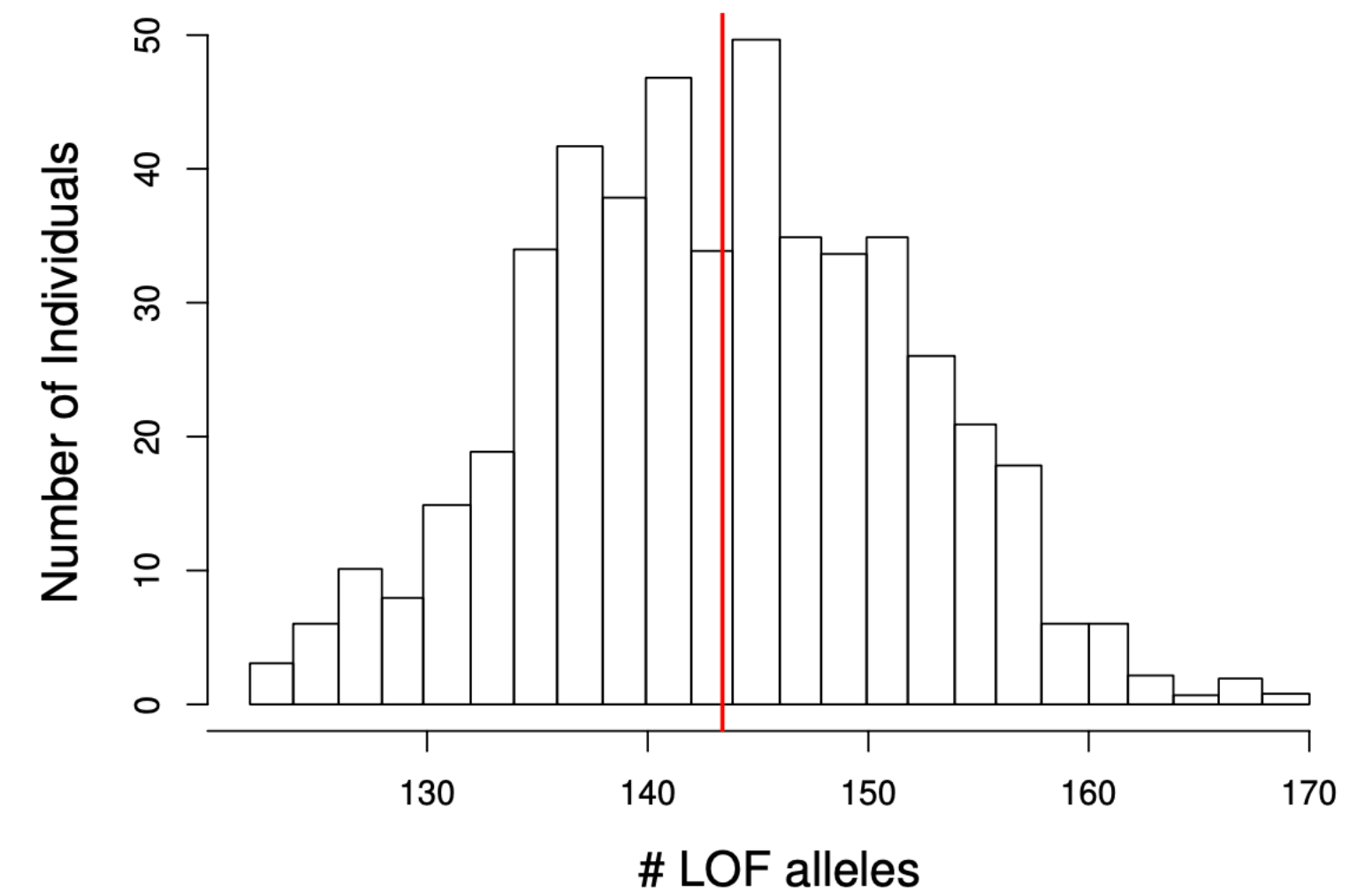
- $\bar{w} = 1 - 2p_e q_e h s - q_e^2 s \approx 1 - 2\mu.$

# The genetic load of deleterious alleles

- $\bar{w} = 1 - 2p_e q_e h s - q_e^2 s \approx 1 - 2\mu.$
- Drop in mean fitness is independent of the selection coefficient against the heterozygote; it depends only on the mutation rate
- $\mu$  on the order of  $10^{-5}$ , so reduction in mean fitness is very small
- Genetic load: if there are many loci segregating at mutation–selection balance, small fitness reductions can add up to have substantial effects
- A major cause of variation in fitness-related traits among individuals.

# Loss of function mutations in humans

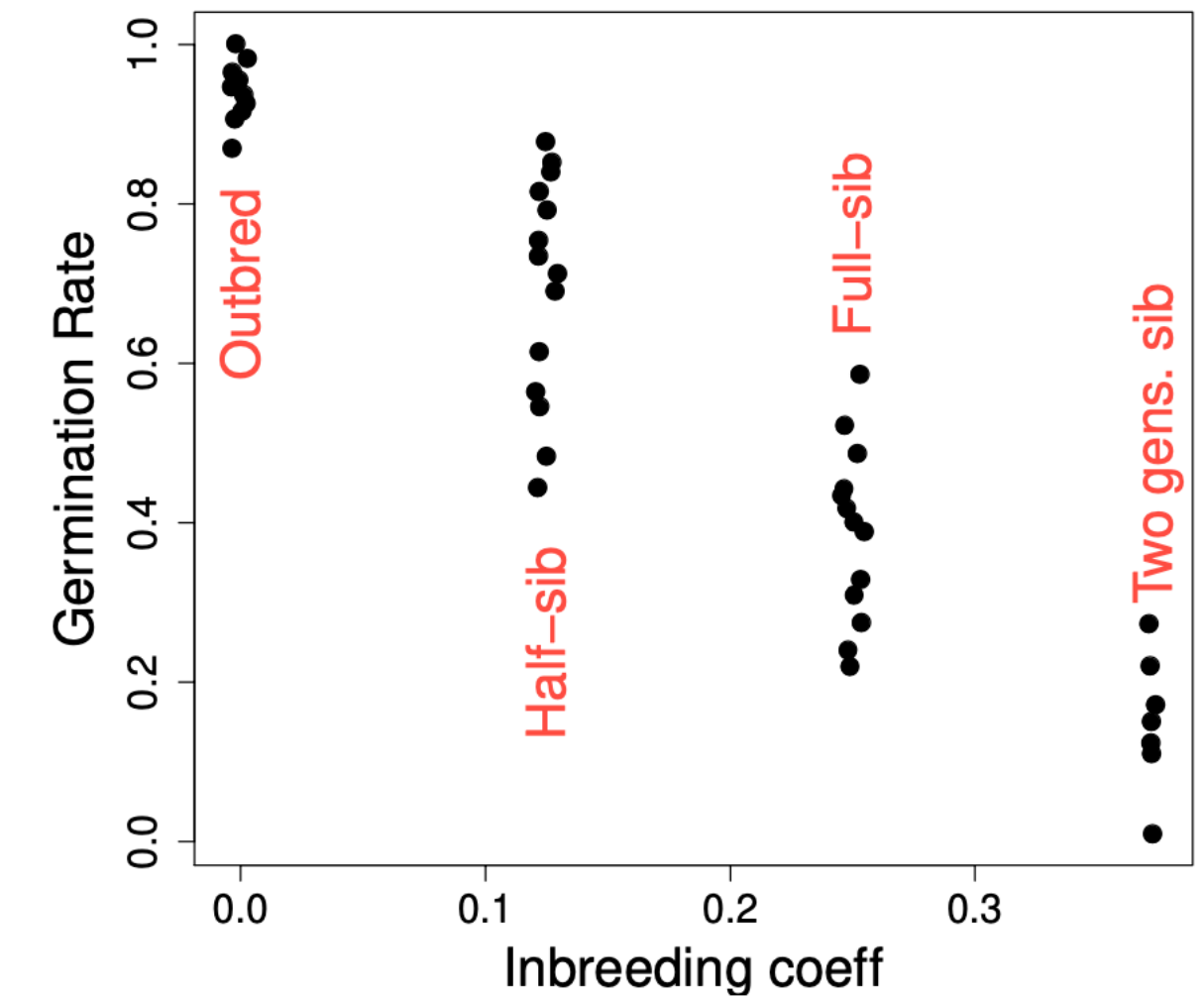
- Loss of function (LOF) variants: mostly severely disrupt a protein-coding gene, typically found at low frequencies but each human genome typically carries over a hundred LOF variants
- Combined load of these LOF alleles must on average lower our fitness, otherwise selection wouldn't be removing them from the population.
- Each human genome typically carries over a hundred LOF variants
- The individuals who carry fewer of these LOF alleles will on average likely have higher fitness than those individuals with more.
- Variation in LOF alleles may be a major source of variation in fitness.



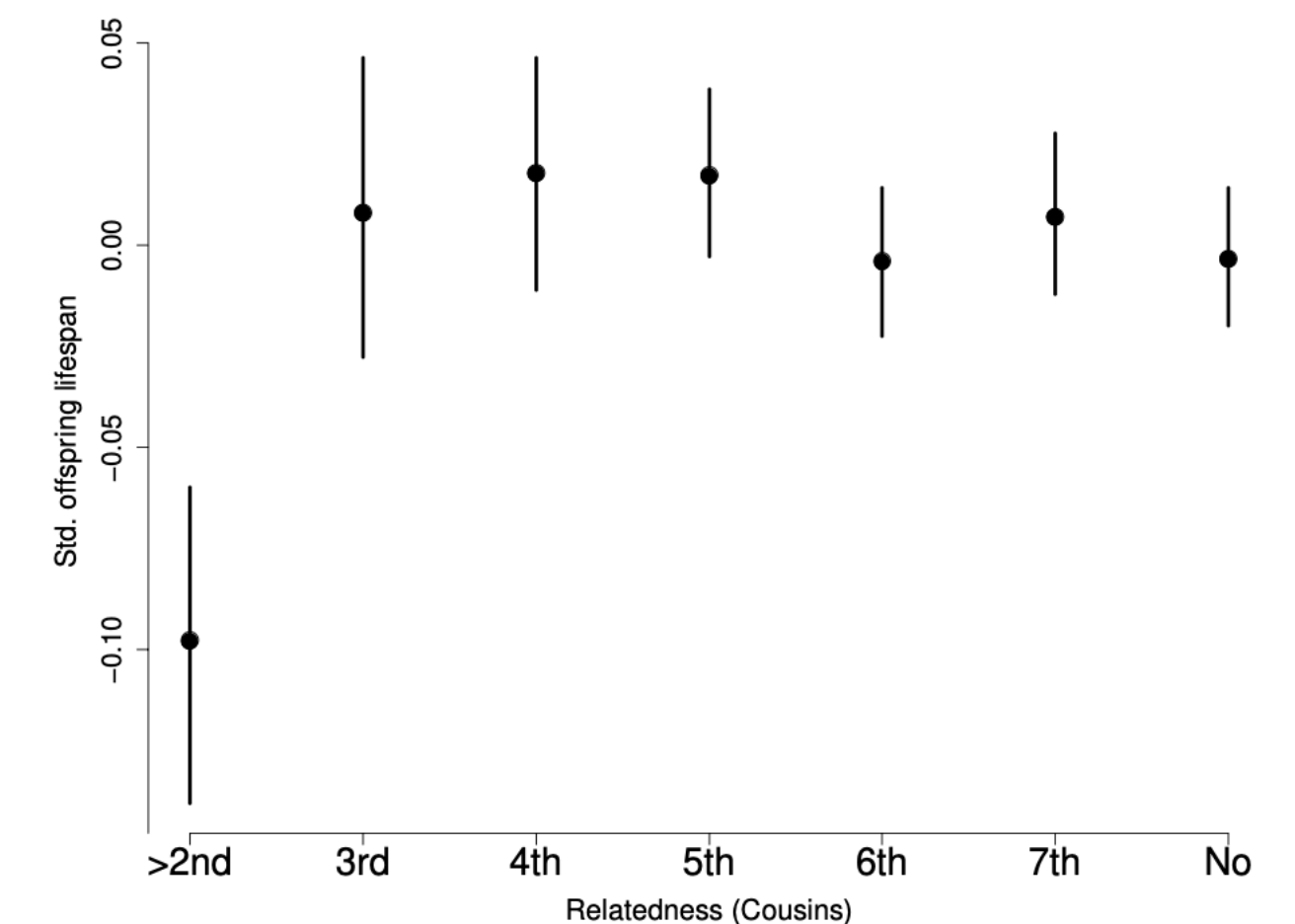
# Inbreeding depression

- Alleles that have strongly deleterious effects in the homozygous state can still segregate at low frequencies in the population, as long as they do not have too strong a deleterious effect in heterozygotes.
- Outbred populations may have many alleles with recessive deleterious effects segregating within them.

- One consequence of segregating for low-frequency recessive deleterious alleles is that inbreeding can reduce fitness.
- primarily a consequence of being homozygous at many loci for alleles with recessive deleterious effects.



Inbreeding depression over different degrees of inbreeding in *S. latifolia*. Each point is the mean seed germination rates for different family crosses.



Inbreeding depression for offspring lifespan in humans in Iceland.

# Purging the inbreeding load

- Inbreeding help expose many recessive deleterious alleles in a homozygous state, and so selection can more readily remove these alleles from the population.
- Populations that regularly inbreed over sustained periods of time are expected to partially purge the load of deleterious alleles.
- Assuming the mutation-selection model, now with inbreeding, the equilibrium frequency is

$$q_e = \frac{\mu}{(h(1 - F) + F)s}$$

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### Question 2.

Assume that a deleterious allele has a relative fitness 0.99 in heterozygotes and a relative fitness 0.2 when present in the homozygote state. Assume that the deleterious allele is at a frequency  $10^{-3}$  at birth and the genotype frequencies follow from HWE. Only considering the fitness effects of this locus, and measuring fitness relative to the most fit genotype, answer the following questions:

- A) What is the average fitness of an individual in the population?
- B) What is the average fitness of the child of a full-sib mating?



# Migration–selection balance

- Local adaptation
- Interaction strength between migration and selection depends on the spatial scale of local adaptation and migration
- Migration cause influx of maladaptive alleles

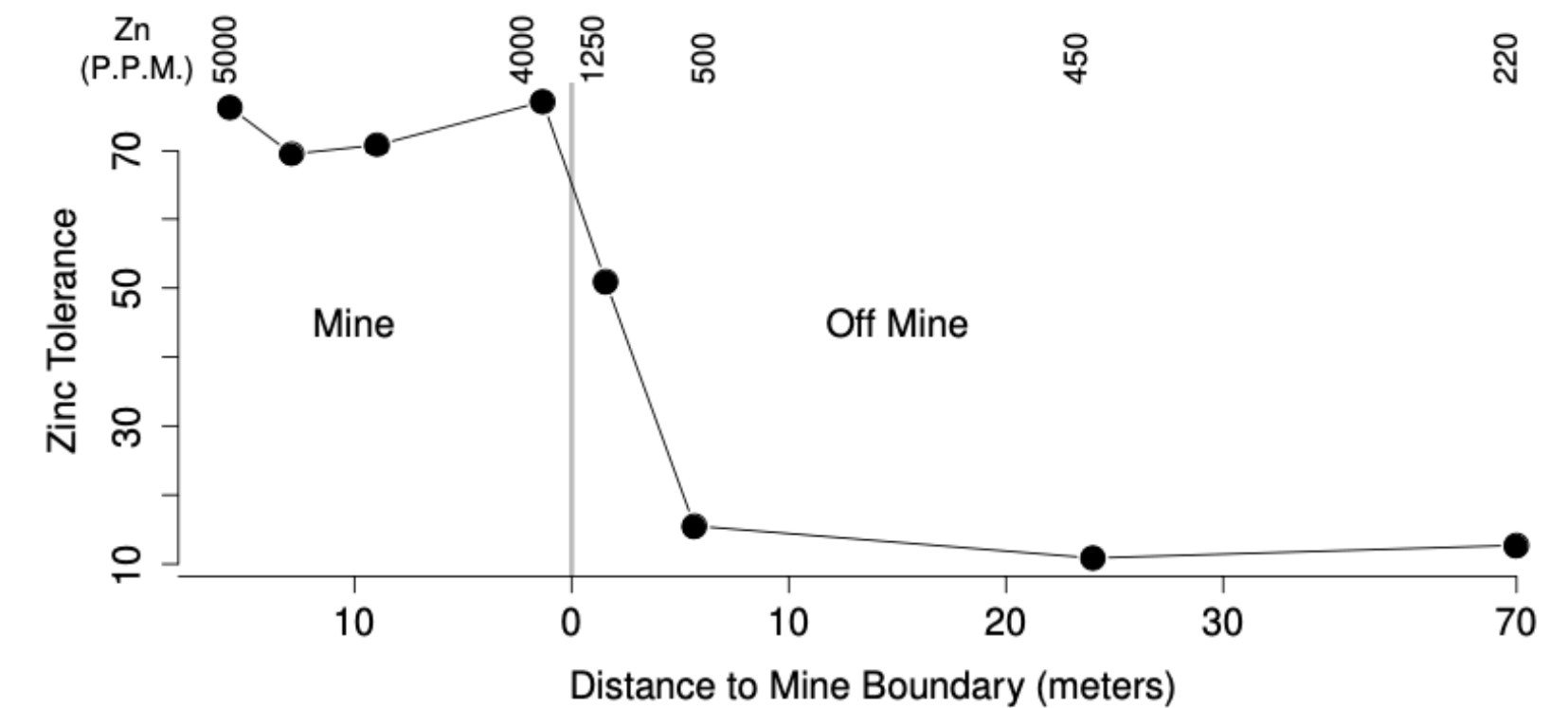


Figure 11.7: Data showing the zinc tolerance of *Anthoxanthum odoratum* on and off of the Trelogan Mine, Flintshire, North Wales. The numbers along the top give the soil contamination of zinc in parts per million. Data from [JAIN and BRADSHAW \(1966\)](#). Code [here](#).

# Haploid two-allele mode

- assume that selection is strong compared to migration ( $s \gg m$ )
- such that allele 1 will be almost fixed in population 1 and allele 2 will be almost fixed in population 2.
- migration changes the frequency of allele 2 in population 1 ( $q_1$ ) by

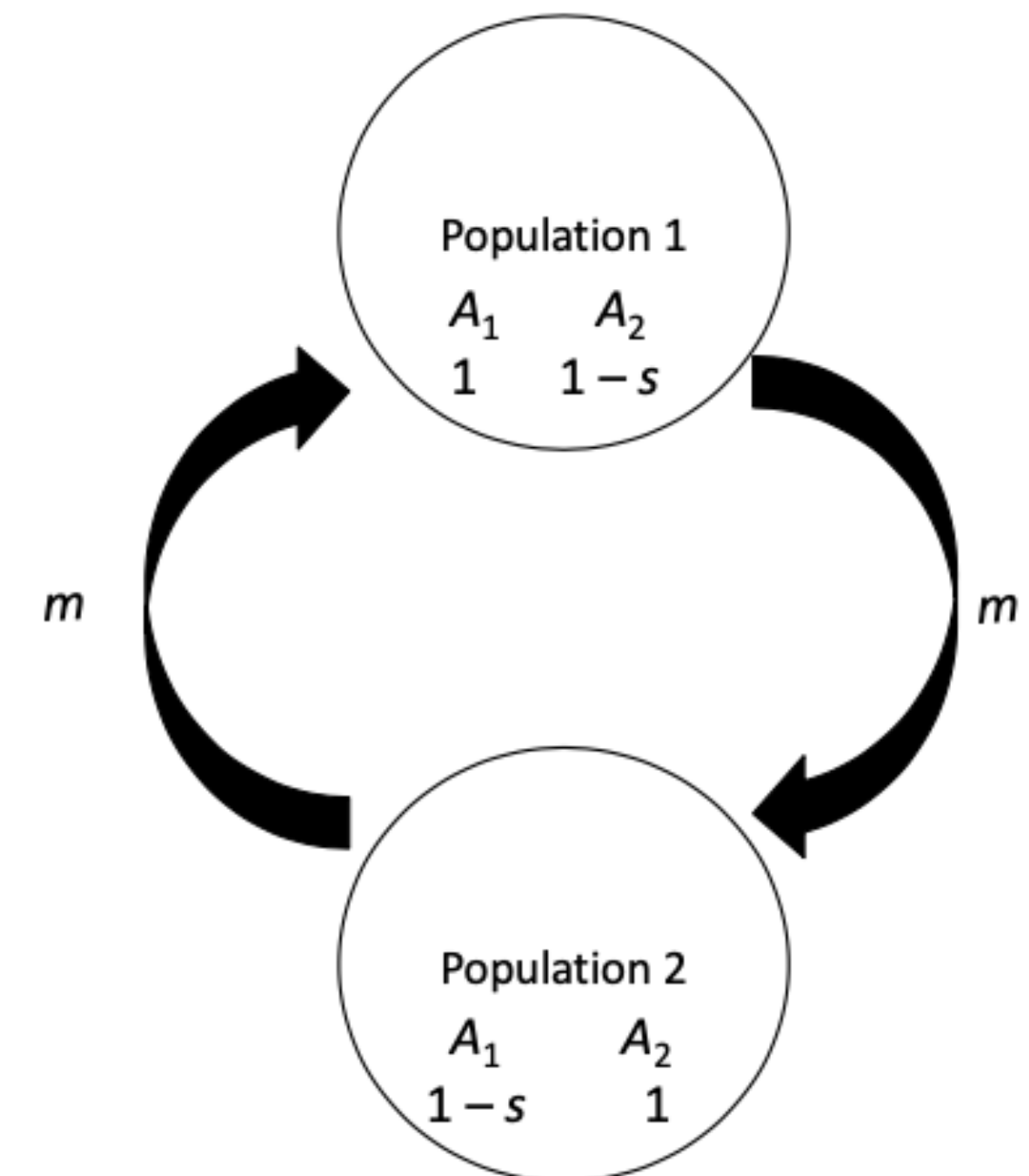
- $\Delta_{Mig} q_1 \approx m$

- $\Delta_s q_1 = -s q_1$

- equilibrium frequency of allele 2 in population 1

- $q_{e,1} = \frac{m}{s}$

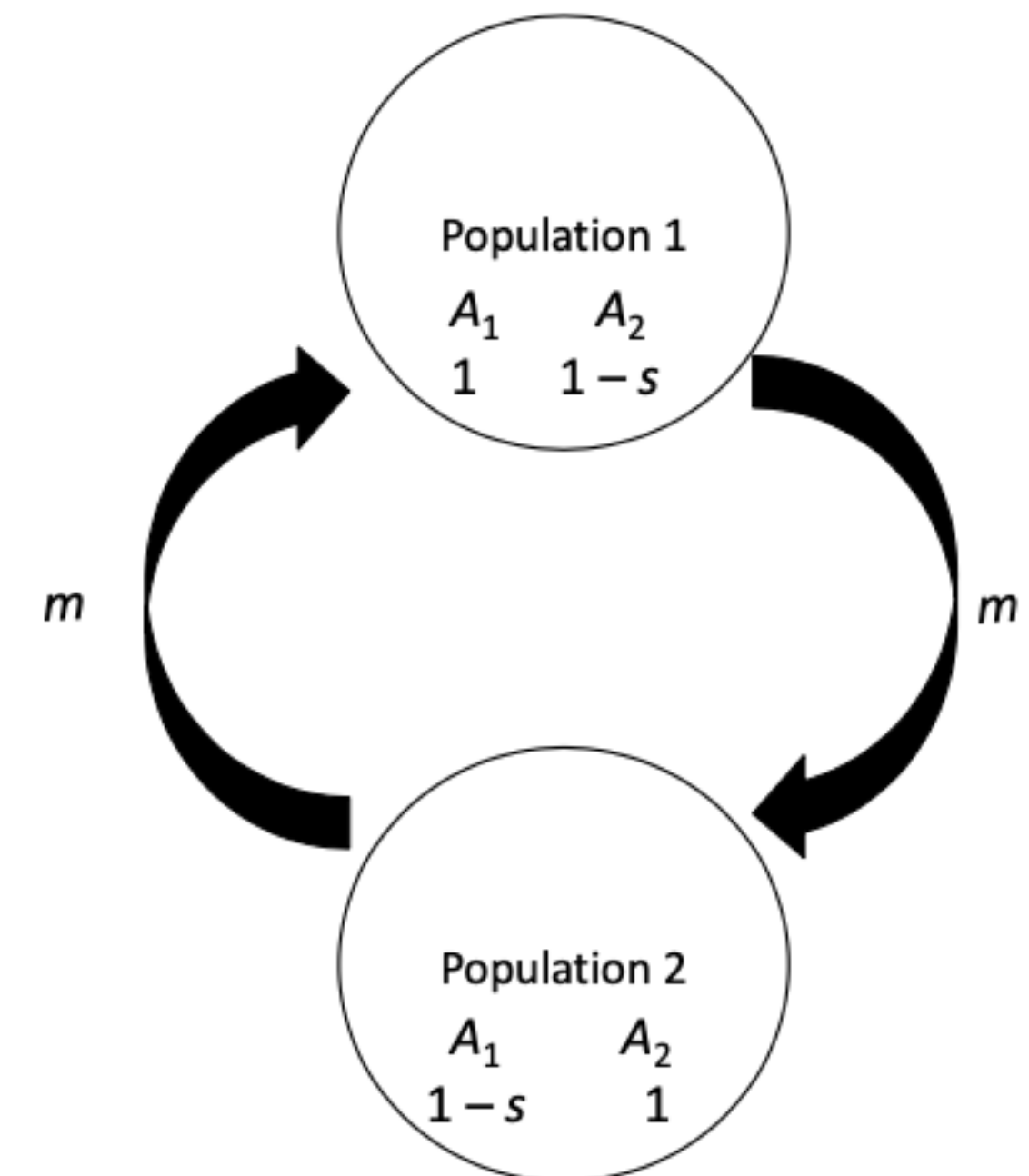
allele	1	2
population 1	1	1-s
population 2	1-s	1



# Diploid two-allele mode

- $\Delta_{Mig}q_1 \approx m$
- $\Delta_Sq_1 \approx -hsq_1$
- equilibrium frequency of allele 2 in population 1
  - $q_{e,1} = \frac{m}{hs}$

allele	1	2
population 1	1	1-s
population 2	1-s	1



### Question 3.

HOEKSTRA *et al.* (2004) found that the dark  $D$  allele was at 3% frequency at the Tule Mountains study site. Using  $F_{ST}$ -based approaches, for unlinked markers, they estimated that the per individual migration rate was  $m = 7.0 \times 10^{-4}$  per generation between this site and the Pinacate lava flow. What is the selection coefficient acting against the dark  $D$  allele at the Tule Mountains site?

- If selection is weaker and only of the order of migration  $s \approx m$  our migration-selection polymorphism collapses,
- Because selection can not maintain the difference in the face of gene flow.
- Under this situation, both populations are expected to have roughly the same frequency of the alleles. Migration has swamped out local adaptation.