

# *Population and Quantitative Trait Genetics*

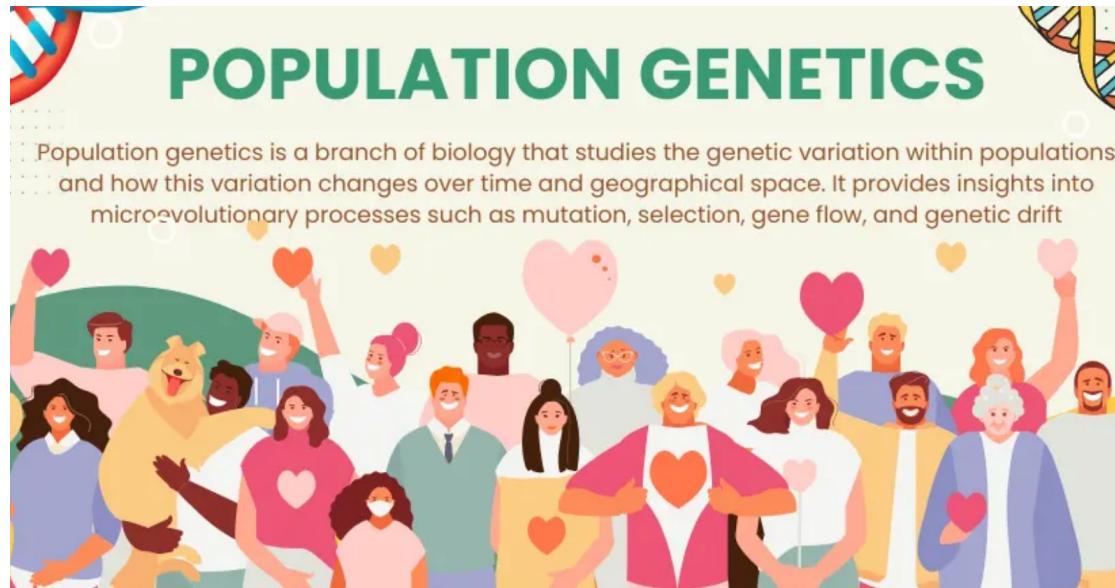
*Prof. Schoen*

## **Module: Population Genetics (first 2.5 lectures)**

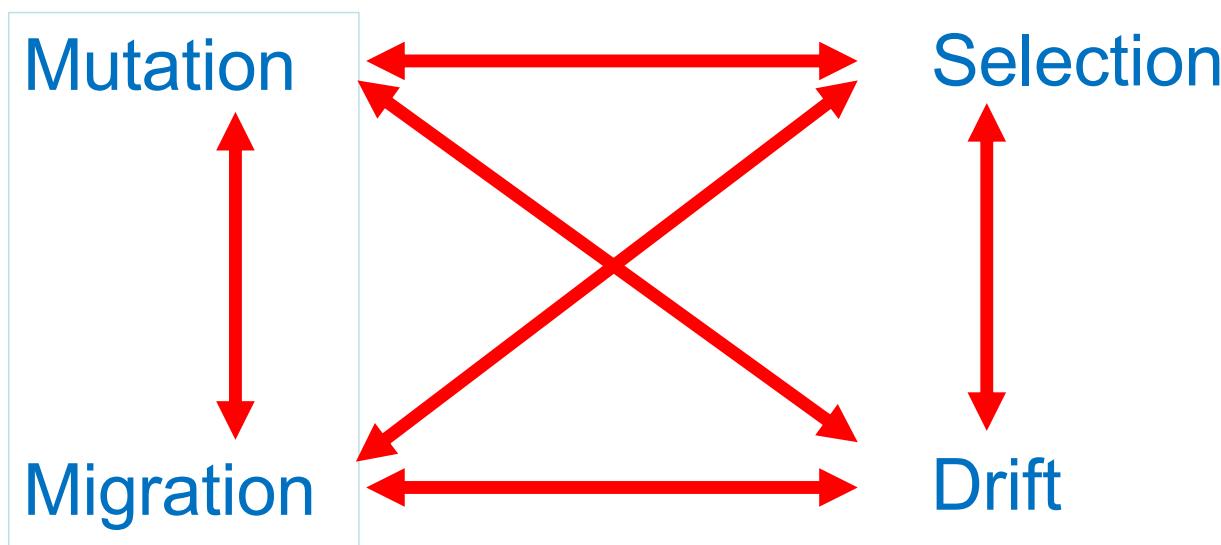
Lecture 10 — Genes in populations. Hardy-Weinberg theory.

Lecture 11 — Inbreeding. Mutation and migration. Genetic drift.

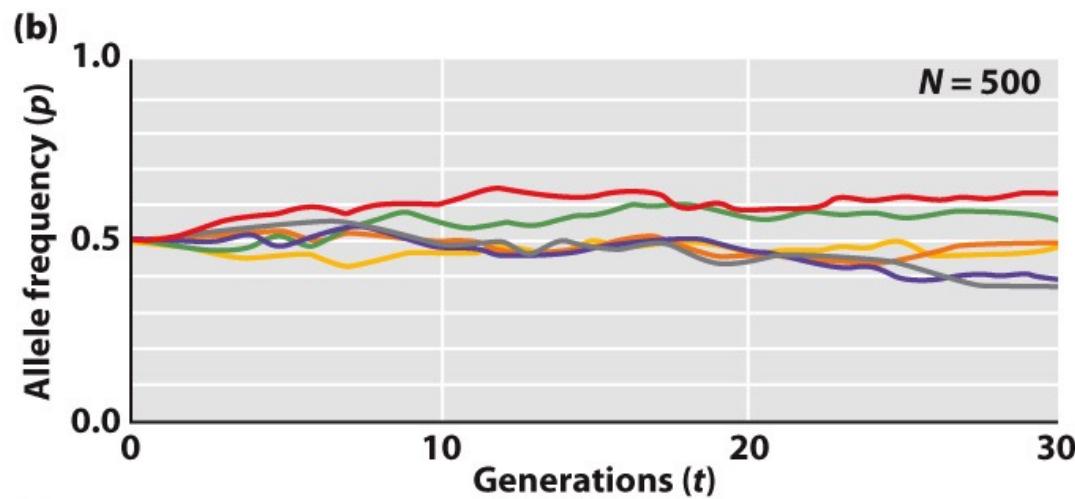
**Lecture 12 — The genetics of natural selection. Intro to quantitative genetics.**



Evolutionary processes influence genotype and allele frequencies in populations

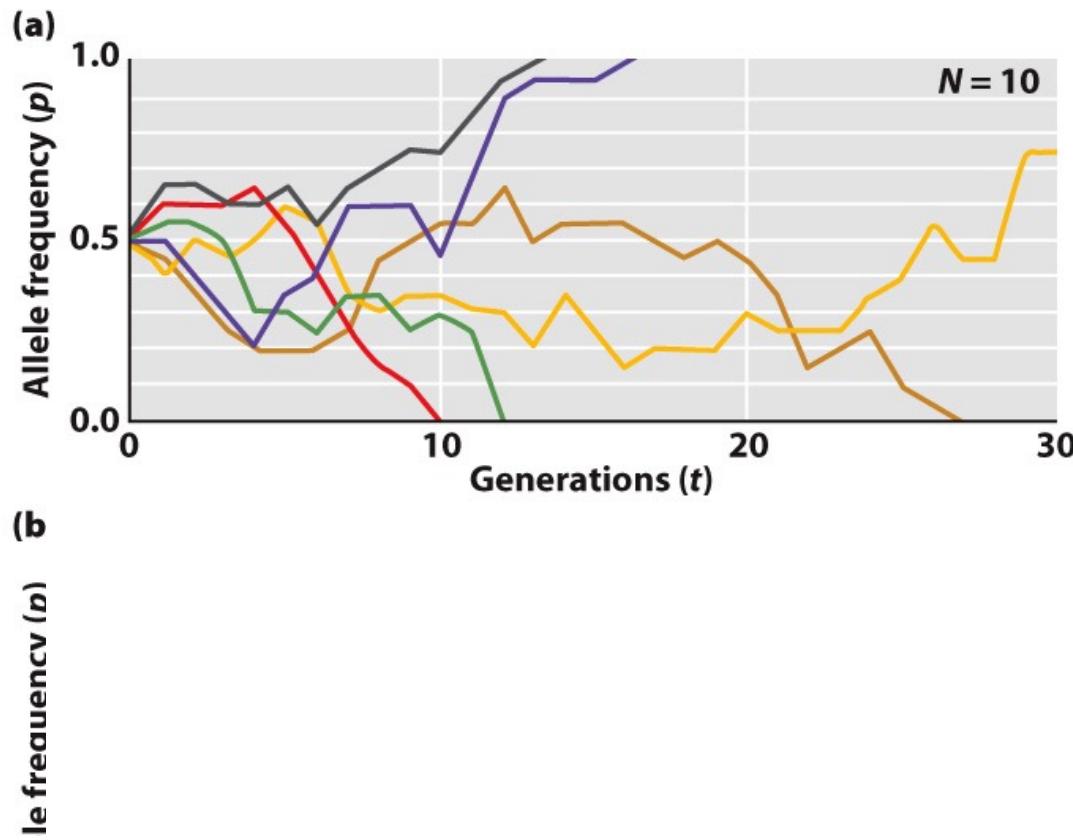


Random genetic drift is weaker in large populations



*Each colour represents the frequency of one of the alleles at a biallelic locus*

## Random genetic drift is strong in small populations



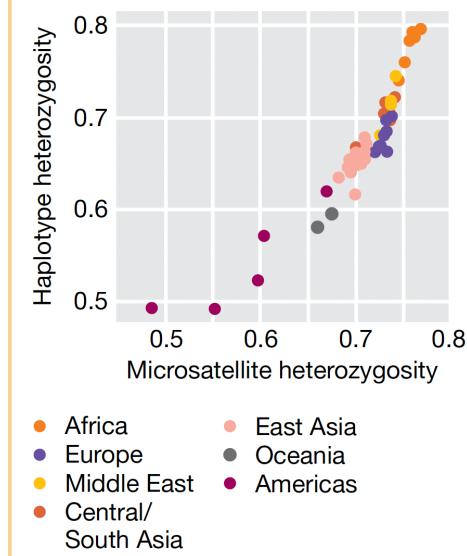
*Each colour represents the frequency of one of the alleles at a biallelic locus*

# Genetic Drift ( “founding events”)

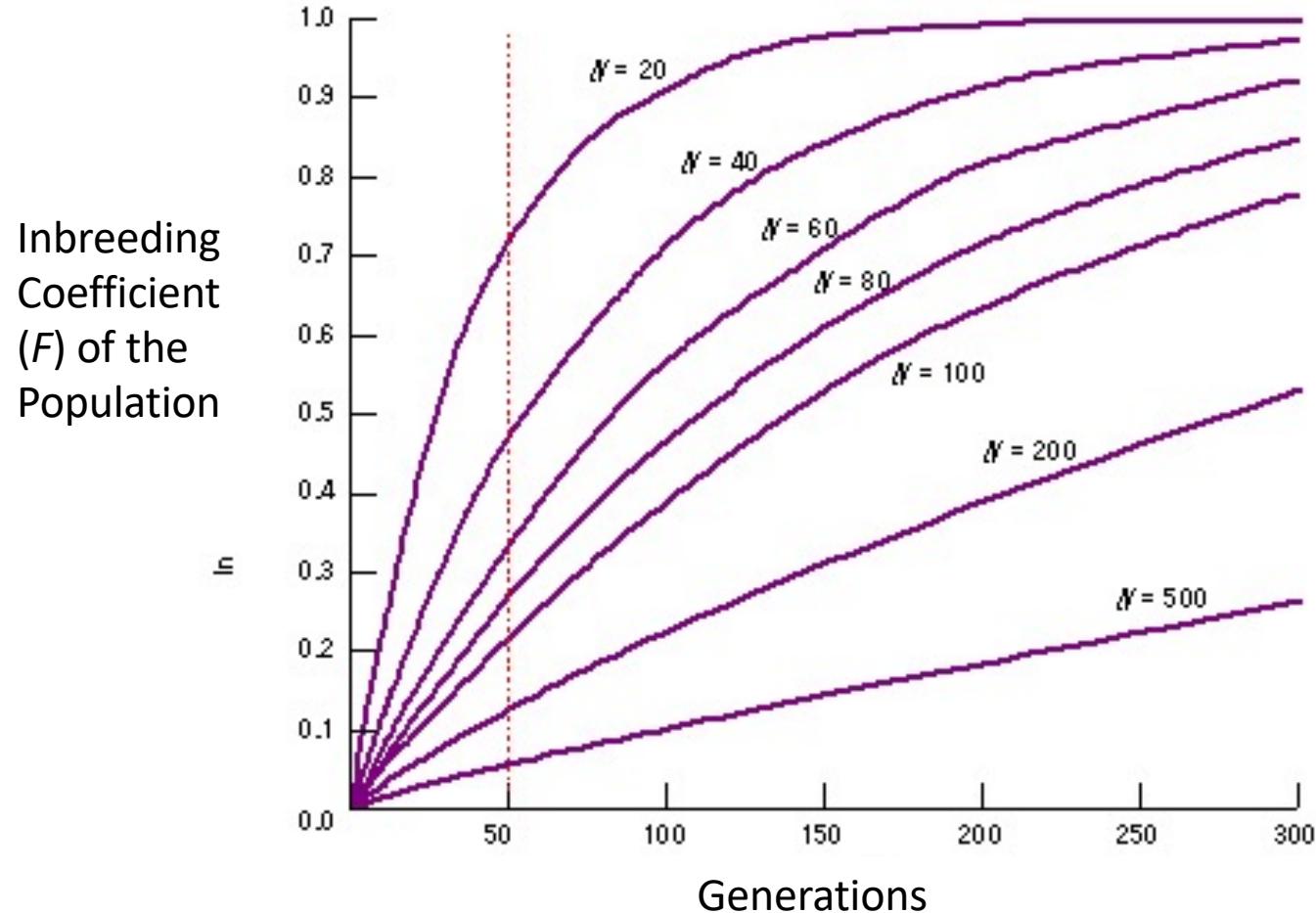
Figure 1: Human migration out of Africa.



Human populations have different levels of genetic diversity



Successive generations of small population size → Inbreeding levels build up



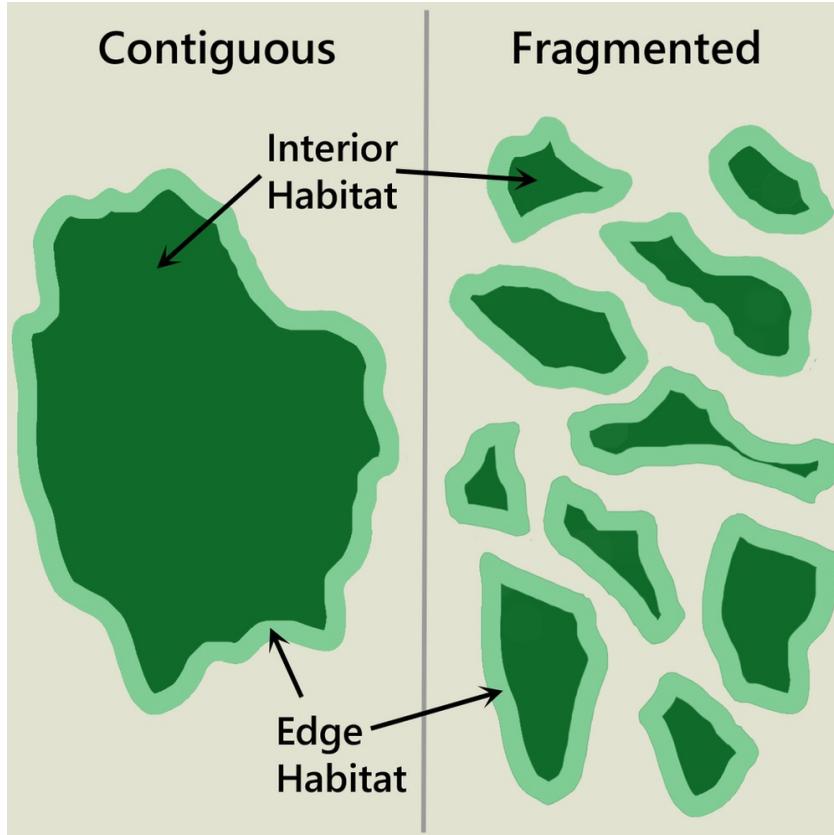
# Habitat fragmentation can reduce population sizes



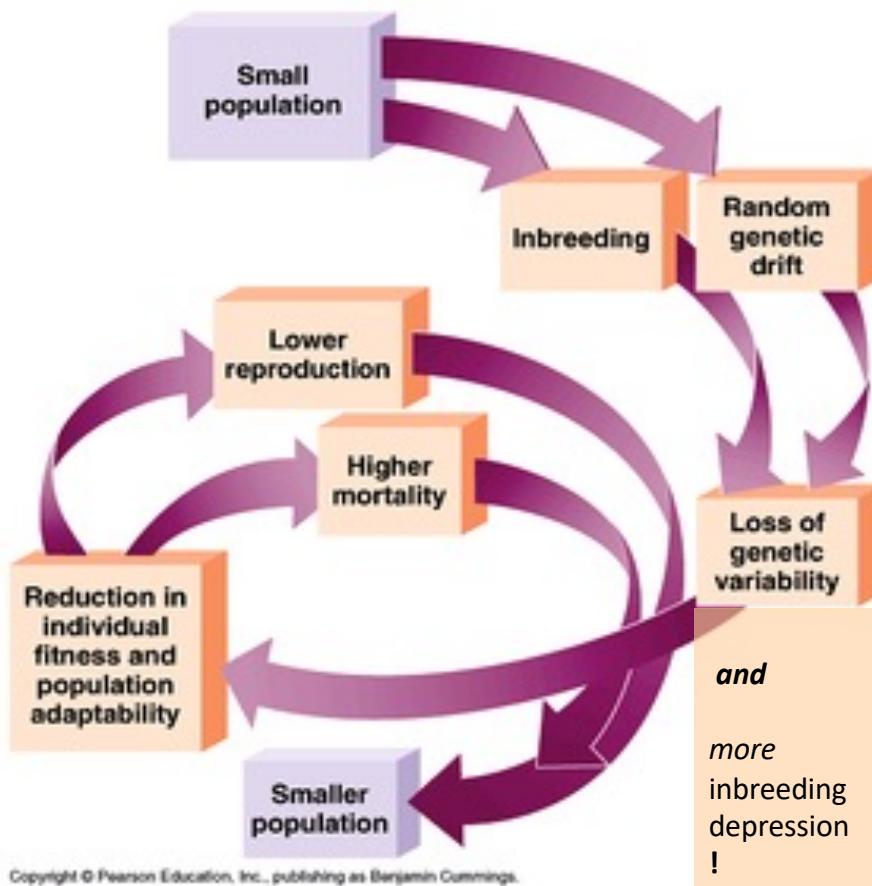
**Article**  
**Global meta-analysis shows action is needed to halt genetic diversity loss**

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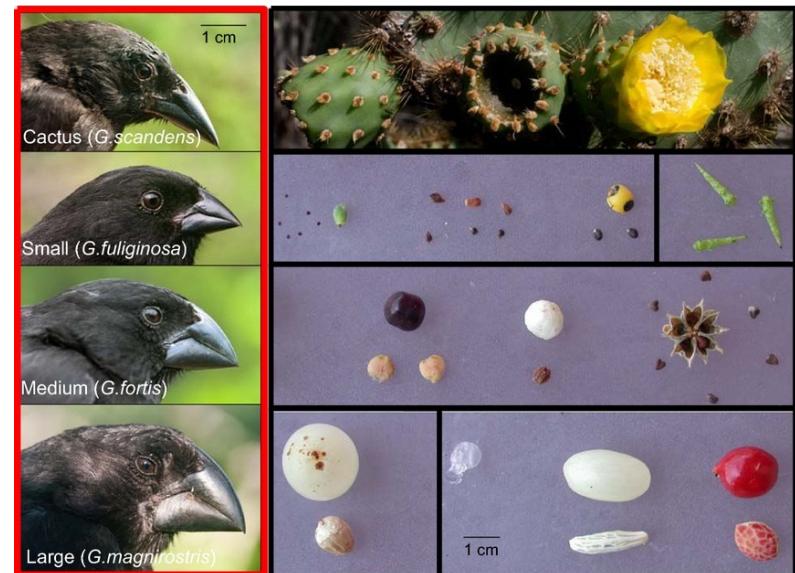


## Small populations and the “Extinction Vortex”



# Processes influencing allele frequencies

- *Mutation*
- *Migration*
- *Genetic Drift*
- *Natural Selection*



# Module: Population Genetics



## *Lecture 12—The population genetics of natural selection*

- Genetics of Natural Selection (Ch18 – section 5) skip subsection on "Recombination" and "Linkage Disequilibrium" and Box 18.5)
- Quantitative (or complex) trait genetics: genes and environment (Ch19 section 1)

# Population genetic models of selection allow us to:

- Predict the outcome of selection (i.e., the equilibrium allele frequency at a locus)
- Predict rate of evolutionary change (i.e., the rate of change in allele frequency at a locus)
- Examine the interaction of selection with other population processes.

## Natural selection in mid-19<sup>th</sup> Britain favoured the dark form of the Peppered Moth

*Light  
Form*



*Dark  
Form*



*Hungry  
sparrow*



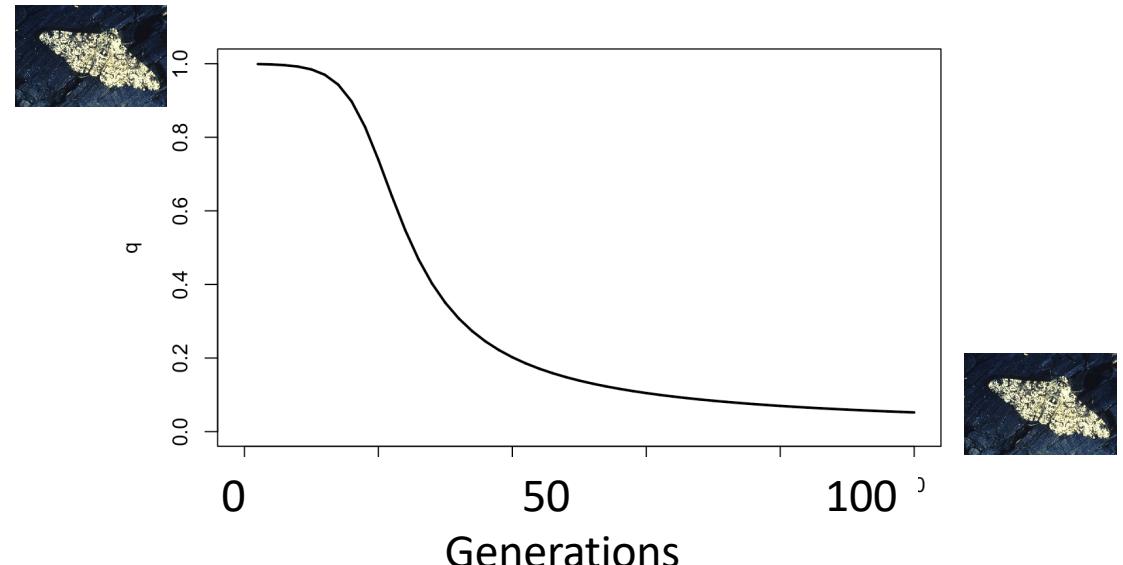
*When coal was “king”  
(mid-19<sup>th</sup> century Britain)*

During the era of heavy coal burning in Britain, it took about a hundred years for the white form of the Peppered Moth to be nearly replaced by the dark form

*Light Form*



*Dark Form*



*“light form”*

*Genotype aa*



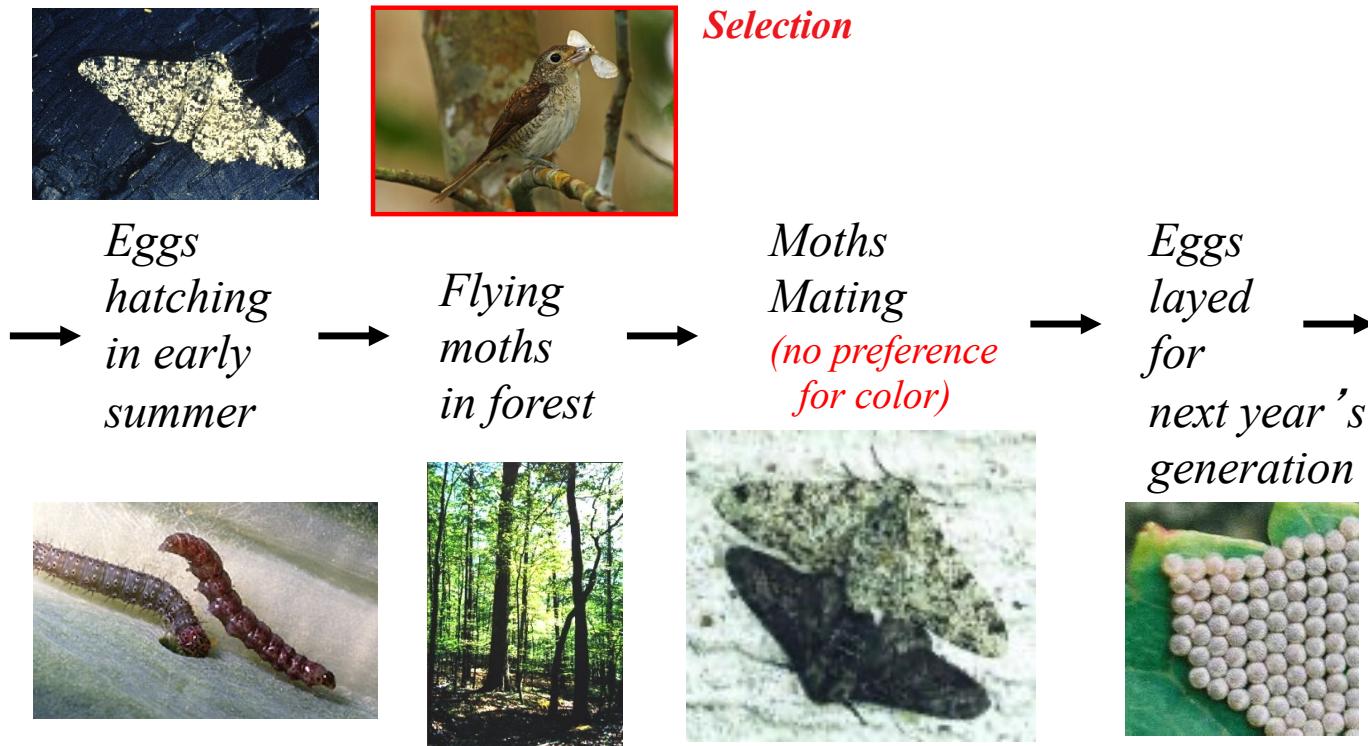
*“dark form”*

*Genotype AA or Aa*



*Peppered Moth*

## How will natural selection act to alter frequency of allele **a** ("light") in a coal-polluted forest environment?



Natural selection typically works by favouring the form with the highest **relative fitness**

<b>Genotype</b>	<b>Absolute Fitness</b> <i>(Percent survival to reproductive age)</i>	<b>Relative Fitness</b> <i>(in coal-polluted forest)</i>
AA (dark)	30%	$w_{AA} = 1.0$
Aa (dark)	30%	$w_{Aa} = 1.0$
aa (light)	21%	$w_{aa} = 21\% / 30\% = 0.7$
<i>(i.e., <math>s = 0.3</math>)</i>		

## Using a model of selection to calculate genotype frequencies after selection

<u>Genotype</u>	<u>Phenotype</u>	<u>Relative fitness</u>	<u>Starting frequencies the genotypes</u>	<u>Genotype frequencies weighted by fitness</u>
AA	dark	$w_{AA} = 1$	$f_{AA} = 0.01$	$w_{AA} f_{AA} = 0.01$
Aa	dark	$w_{Aa} = 1$	$f_{Aa} = 0.18$	$w_{Aa} f_{Aa} = 0.18$
aa	light	$w_{aa} = 1-s$ = 0.7	$f_{aa} = 0.81$	$w_{aa} f_{aa} = 0.567$

$$\begin{aligned}W_{avg} &= f_{AA} w_{AA} + f_{Aa} w_{Aa} + f_{aa} w_{aa} \\&= 0.01 (1) + 0.18 (1) + 0.81 (0.7) \\&= 0.757\end{aligned}$$

*NOTE: A population average value is equal to the sum of individual values times their respective frequencies*

## Using a model of selection to calculate genotype frequencies after selection

<u>Genotype</u>	<u>Phenotype</u>	<u>Relative fitness</u>	<u>Starting frequencies the genotypes</u>	<u>Genotype frequencies weighted by fitness</u>	<u>Genotype frequencies after selection</u>
AA	dark	$w_{AA} = 1$	$f_{AA} = 0.01$	$w_{AA} f_{AA} = 0.01$	$w_{AA} f_{AA} / W_{avg} = 0.0132$
Aa	dark	$w_{Aa} = 1$	$f_{Aa} = 0.18$	$w_{Aa} f_{Aa} = 0.18$	$w_{Aa} f_{Aa} / W_{avg} = 0.2378$
aa	light	$w_{aa} = 1-s = 0.7$	$f_{aa} = 0.81$	$w_{aa} f_{aa} = 0.567$	$w_{aa} f_{aa} / W_{avg} = 0.7490$

The frequency of the "a" allele after selection =  $0.2378/2 + 0.7490 = 0.8679$

\*where  $W_{avg} = 0.757$  as we calculated in the previous slide

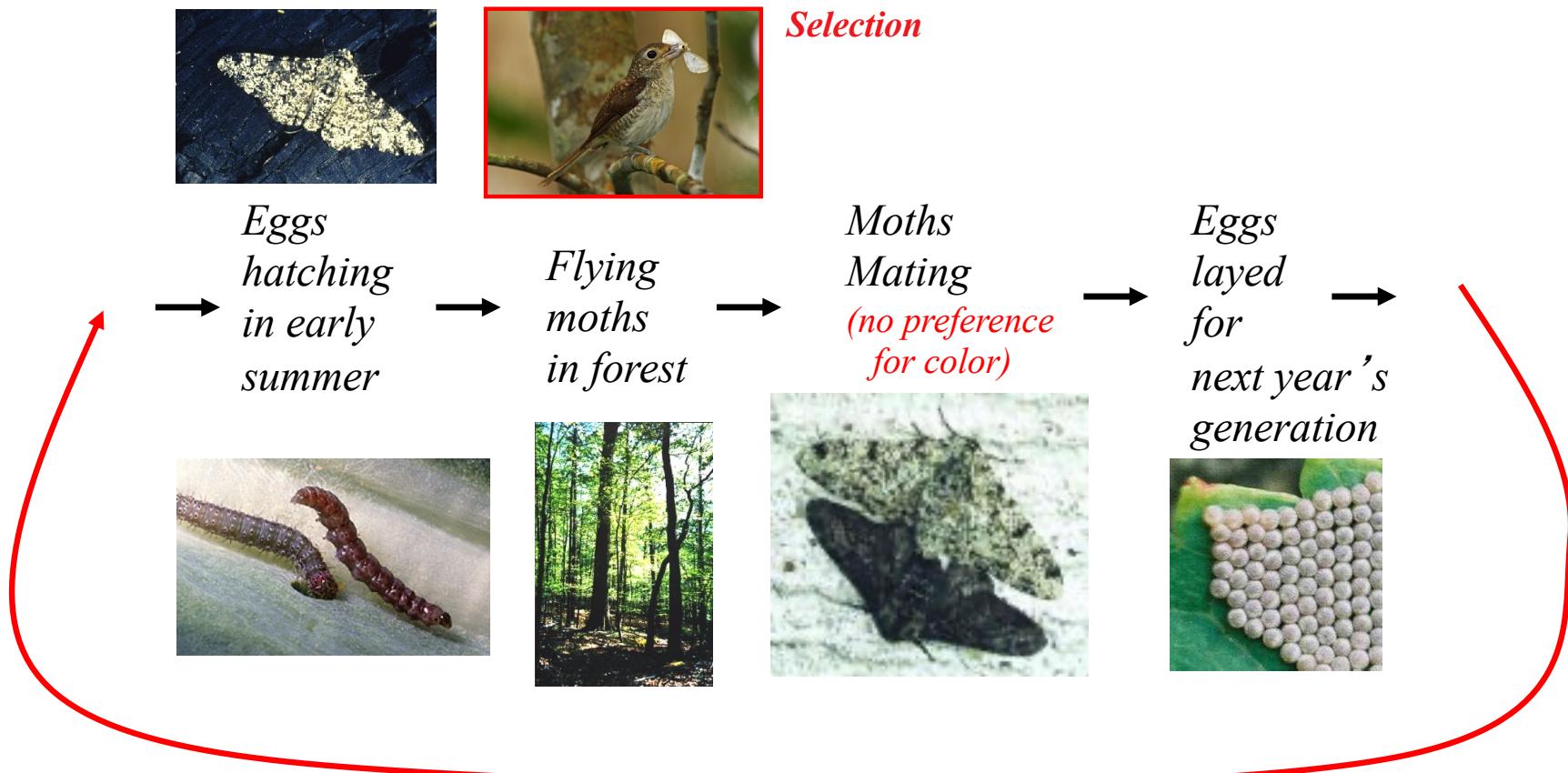
## Using a model of selection to calculate genotype frequencies after selection

<u>Genotype</u>	<u>Phenotype</u>	<u>Relative fitness</u>	<u>Starting frequencies the genotypes</u>	<u>Genotype frequencies weighted by fitness</u>	<u>Genotype frequencies after selection</u>
AA	dark	$w_{AA} = 1$	$f_{AA} = 0.01$	$w_{AA} f_{AA} = 0.01$	$w_{AA} f_{AA} / W_{avg} = 0.0132$
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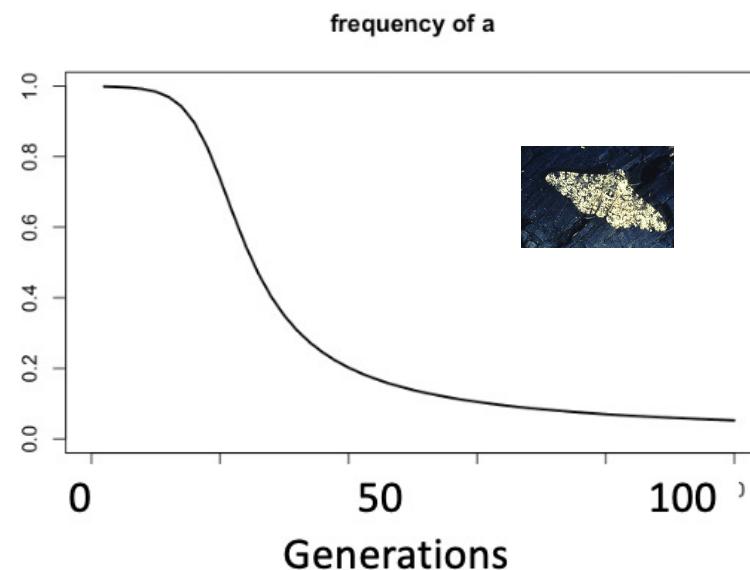
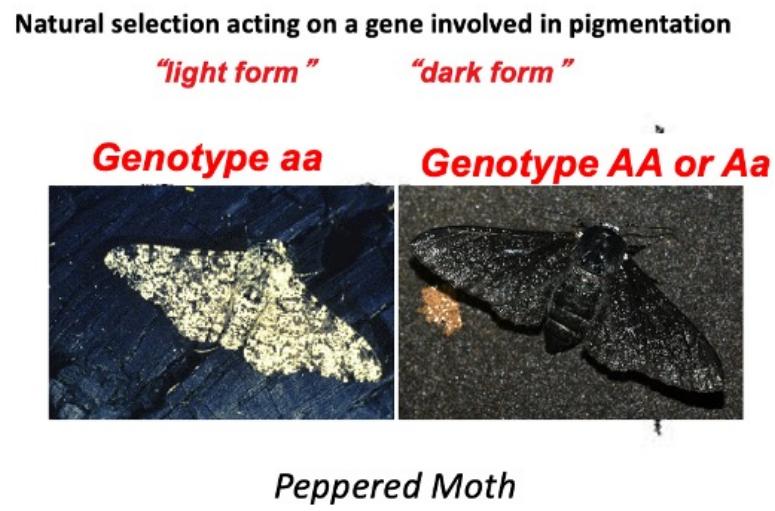
The frequency of the “a” allele **after selection** =  $0.2378/2 + 0.7490 = 0.8679$

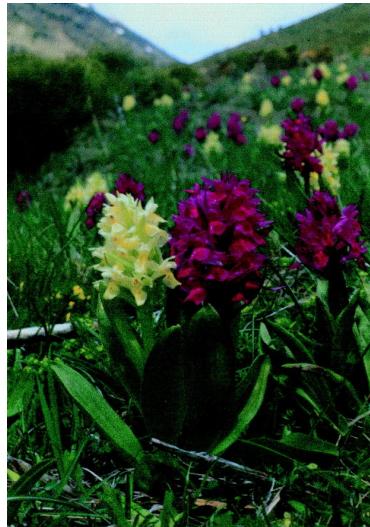
After one generation of selection, the frequency of the “a” allele went from **0.9 → 0.8679**

## How will natural selection act to alter frequency of allele **a** ("light") in a coal-polluted forest environment?

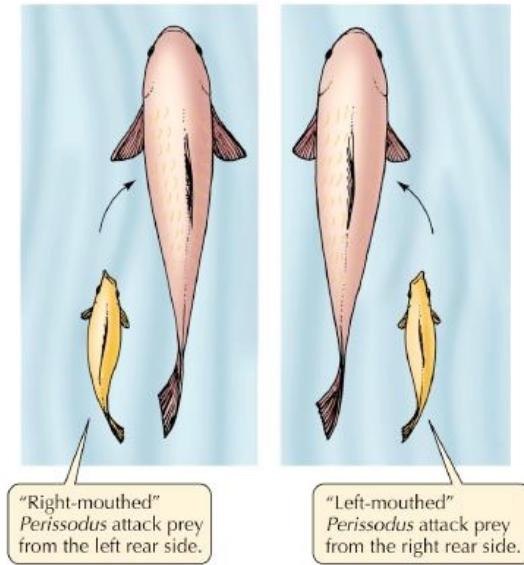


**Directional selection will eventually drive the less fit form from the population**





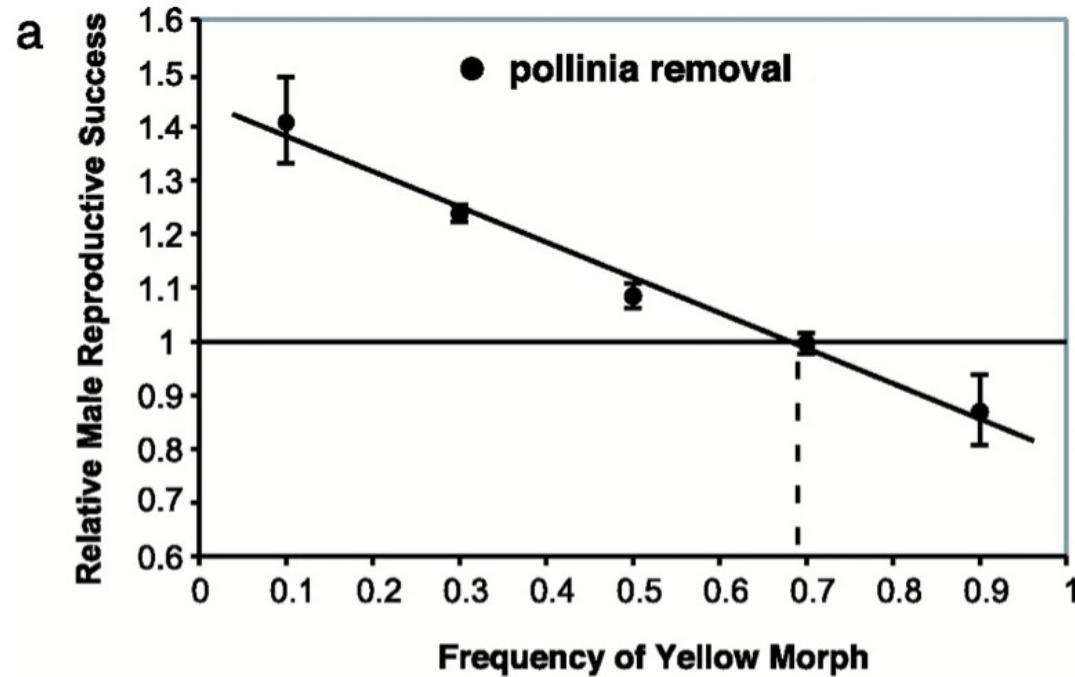
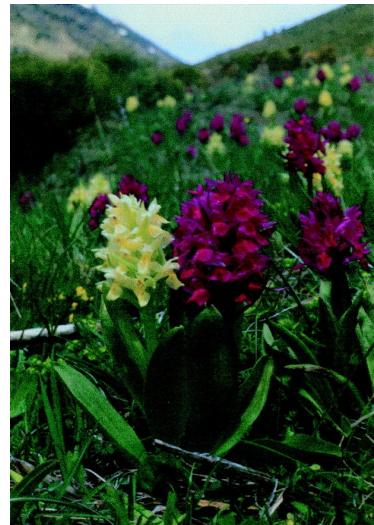
*Not all selection  
is directional*



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We've just considered an example of **DIRECTIONAL selection**,  
but **BALANCING selection** can also occur in nature

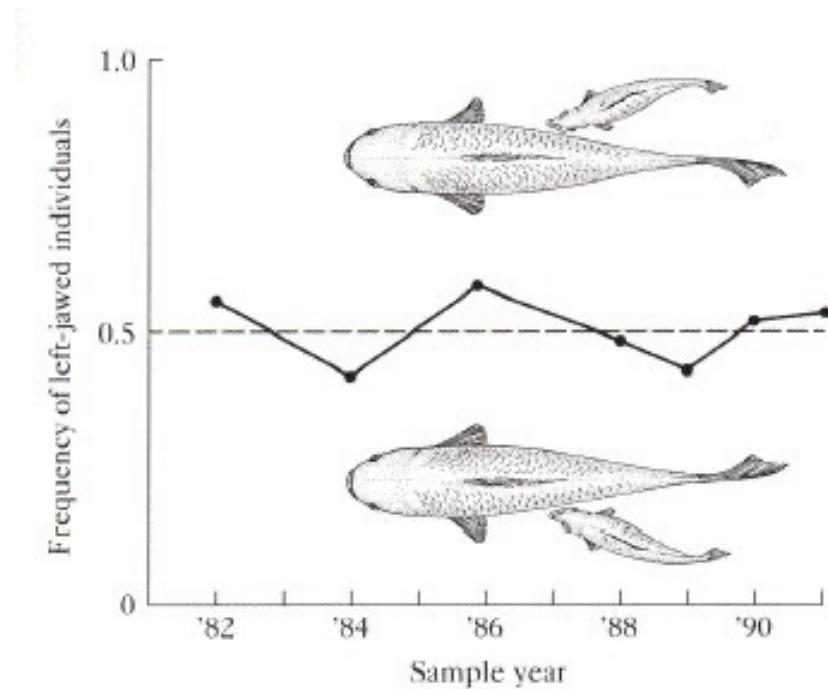
*(frequency-dependent selection is a type of balancing selection)*



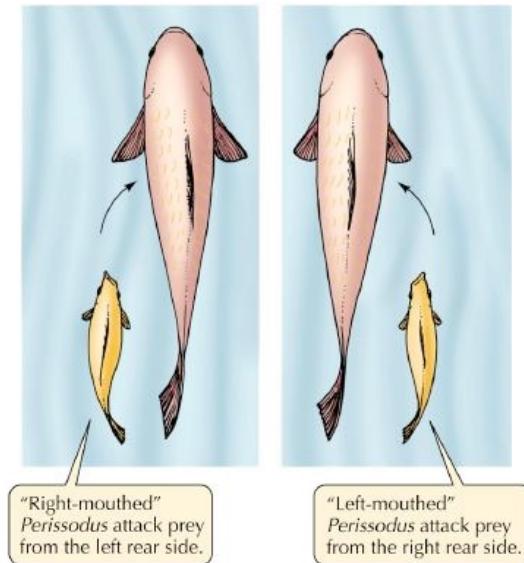
*Frequency-  
dependent  
selection of  
flower color*

We've just considered an example of **DIRECTIONAL selection**,  
but **BALANCING selection** can also occur in nature

*(frequency-dependent selection is a type of balancing selection)*



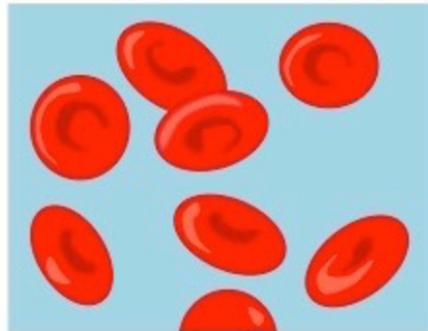
Predator-prey relations in Lake Tanganyika cichlid fish that eat other fishes' scales.



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We've just considered an example of **DIRECTIONAL selection**,  
but **BALANCING selection** can also occur in nature

*(Heterozygote advantage is another type of balancing selection)*



**AA**

Susceptible to malaria  
but no sickle cell disease



**Aa**

Resistant to malaria  
and only mild sickle cell disease



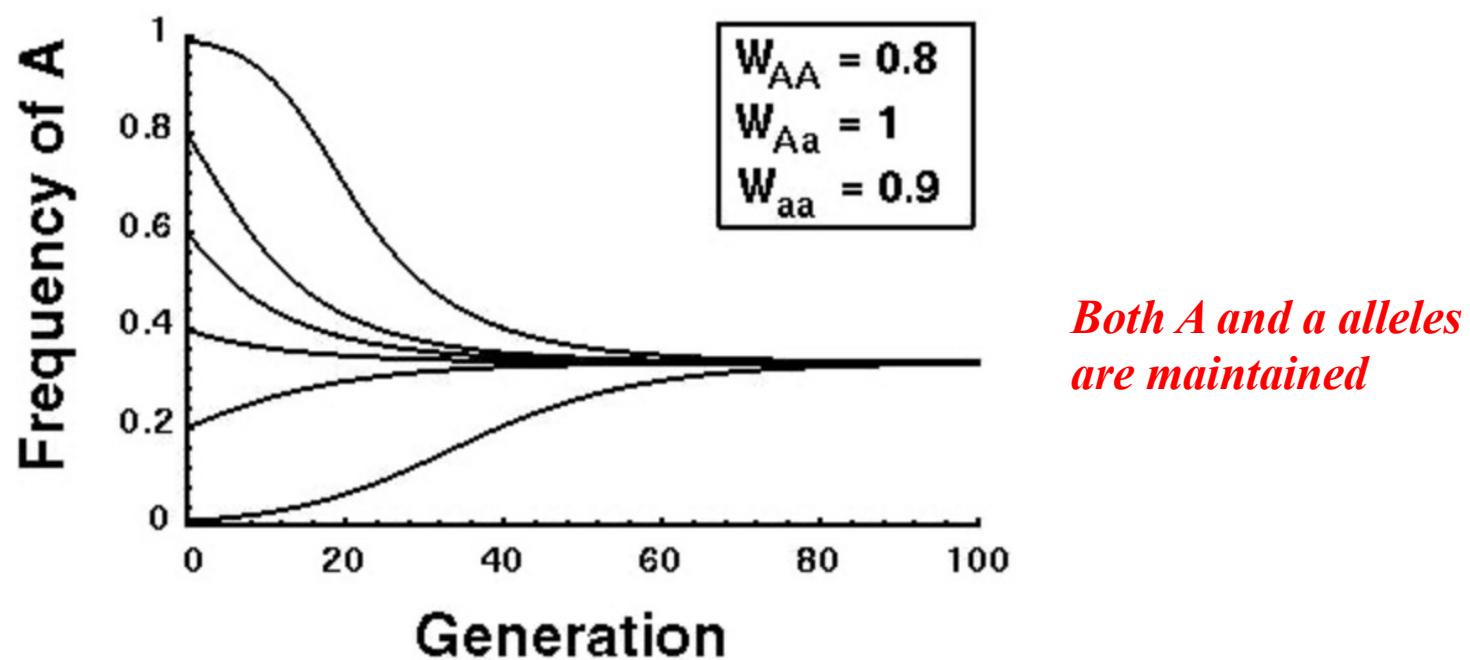
**aa**

Resistant to malaria  
but has fatal sickle cell disease

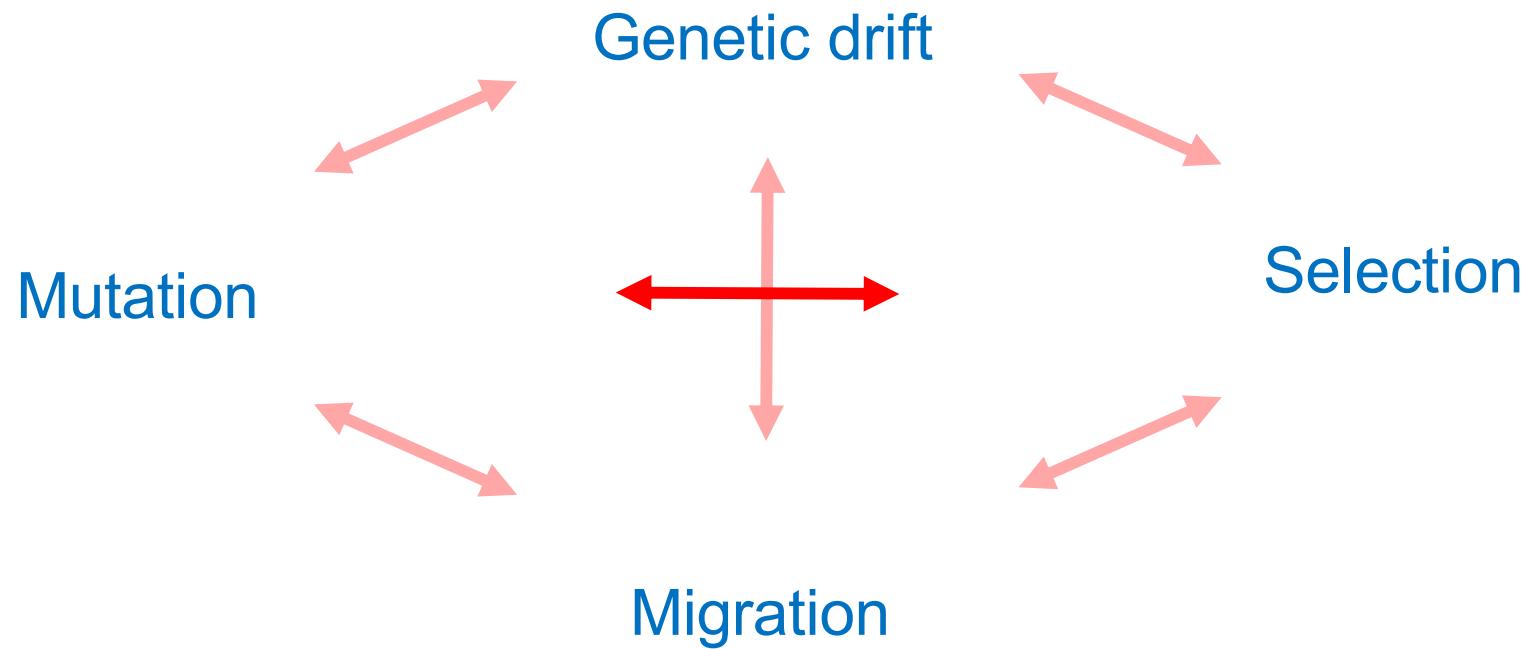
## Model for heterozygote advantage

<u>Genotype</u>	<u>Form</u>	<u>Relative fitness</u>
$AA$	<i>phenotype 1</i>	$w_{AA} = 1-t$
$Aa$	<i>phenotype 2</i>	$w_{Aa} = 1$
$aa$	<i>phenotype 3</i>	$w_{aa} = 1-s$

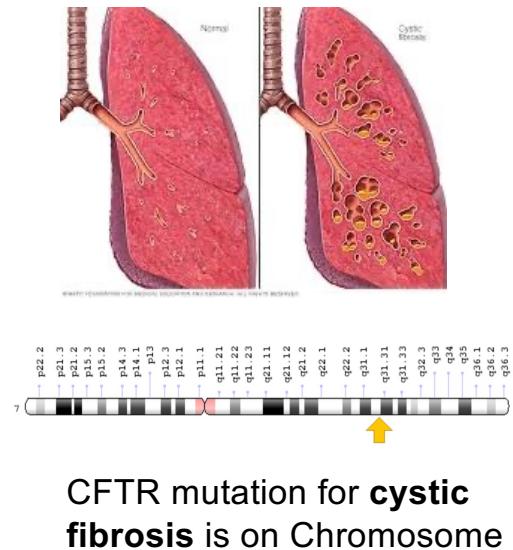
## Allele frequency change under heterozygote advantage



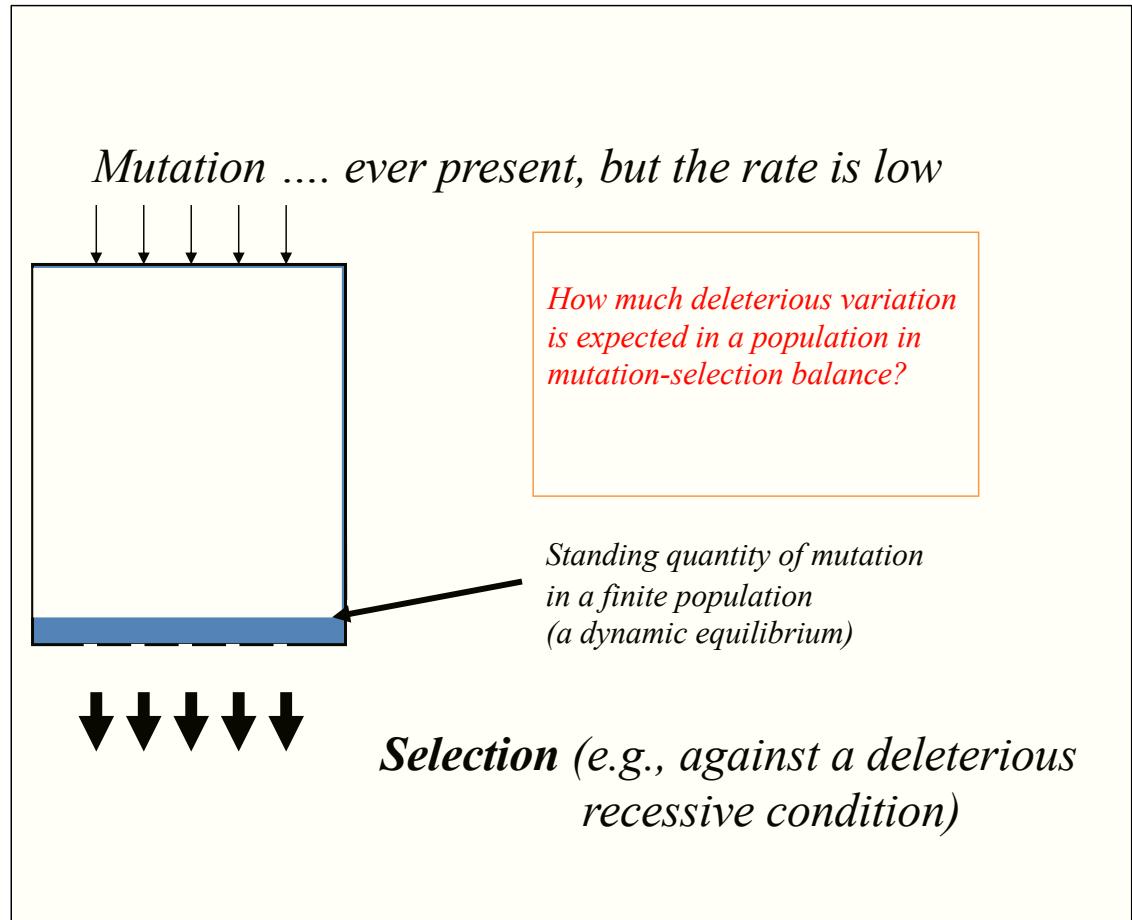
Processes influencing allele frequencies interact !



## Deleterious mutation-selection interaction (why bad things happen to good populations)



CFTR mutation for **cystic fibrosis** is on Chromosome 7



The B locus has two alleles  $B$  and  $b$  with frequencies of  $p = 0.95$  and  $q = 0.05$ , respectively. The genotypic relative fitnesses at this locus are  $w_{B/B} = 0.8$ ,  $w_{B/b} = 1.0$ , and  $w_{b/b} = 0.7$ . What will the frequency of the  $b$  allele be in the next generation?

- A. 0.0602
- B. 0.1182
- C. 0.0501
- D. 0.1002

The B locus has two alleles  $B$  and  $b$  with frequencies of  $p = 0.95$  and  $q = 0.05$ , respectively. The genotypic relative fitnesses at this locus are  $w_{B/B} = 0.8$ ,  $w_{B/b} = 1.0$ , and  $w_{b/b} = 0.7$ . What will the frequency of the  $b$  allele be in the next generation?

- A. 0.0601
- B. 0.1182
- C. 0.0501
- D. 0.1002

	Genotype	HW fqs	Rel. Fitness	Product	Fq after selection
A. 0.0601	B/B	0.9025	0.8	0.722	0.881832061
B. 0.1182	B/b	0.095	1	0.095	0.116030534
C. 0.0501	b/b	0.0025	0.7	0.00175	0.002137405
Pop fitness=					0.81875

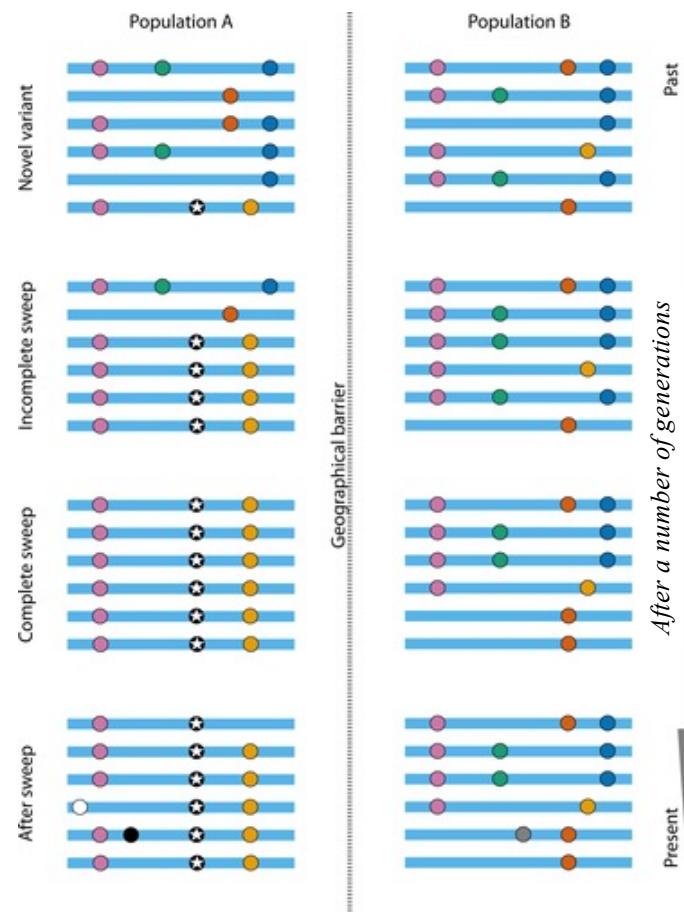
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- A. 0.0601
- B. 0.1182
- C. 0.0501
- D. 0.1002

	Genotype	HW fqs	Rel. Fitness	Product	Fq after selection
B. 0.1182	B/B	0.9025	0.8	0.722	0.881832061
C. 0.0501	B/b	0.095	1	0.095	0.116030534
D. 0.1002	b/b	0.0025	0.7	0.00175	0.002137405

$q \text{ (next gen)} = 0.1160/2 + 0.0021 = 0.0602$

**Selective sweeps** can reduce diversity in genomic regions, especially those with low rates of recombination

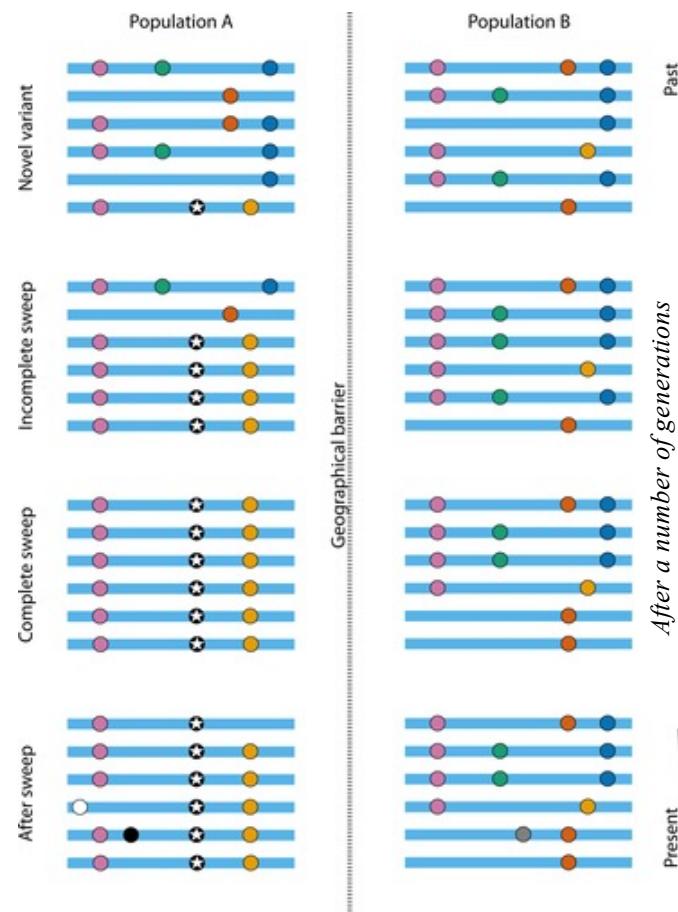


Note that this one chromosome becomes common as a result of the sweep in the Population (Population A) where the nucleotide mutation is strongly selected

(In Population B the nucleotide mutation did not occur)

**Selective sweeps** can reduce diversity in genomic regions, especially those with

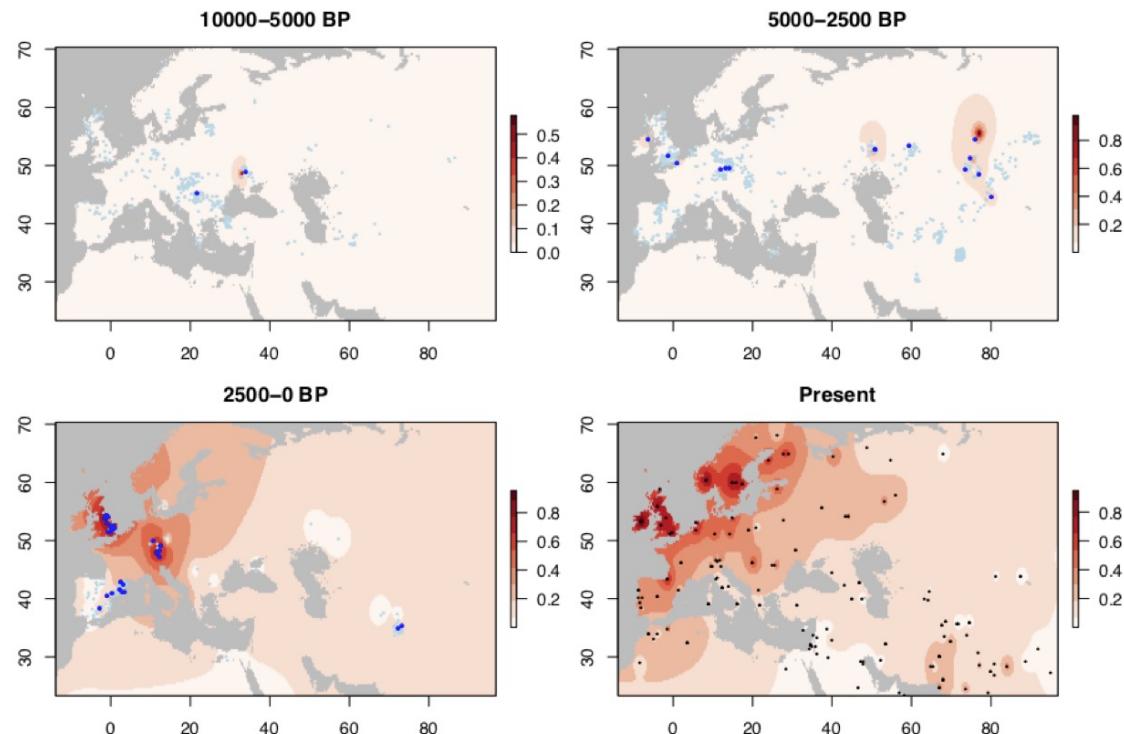
low rates of recombination—they leave behind a trace of past events that have influenced the genome.



*We have detected “GHOST OF SELECTION PAST” in Population A.*

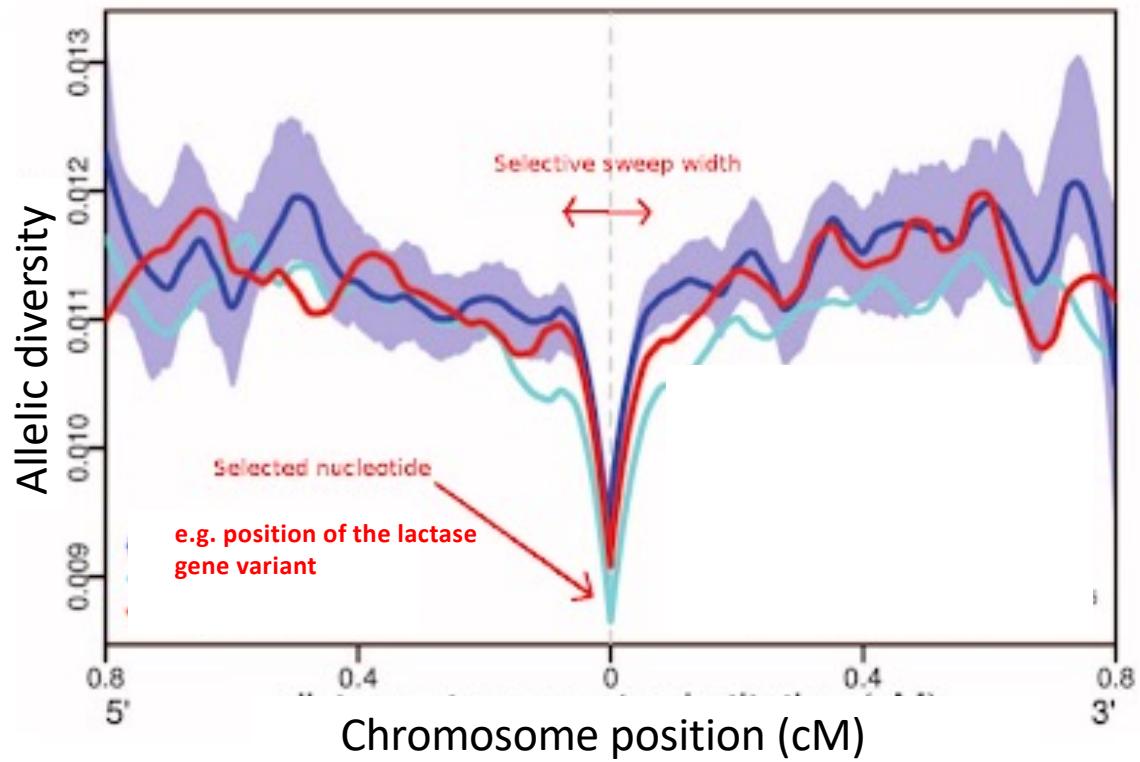


## *Lactase allele variant that causes lactase to persist through life*



**Figure 2.99: Increase in allele frequency of the lactase variant in Europe (from ancient DNA).** The maps indicate locations of samples with ancestral alleles (light blue) and derived alleles (dark blue) in each time period (BP = years Before Present); as well as spatially smoothed maps of the derived allele frequency in each period (red color scale beside each panel). Credit: Iain Mathieson blog post (2019) [[Link](#)]. Used with permission of the author.

## Selective sweep

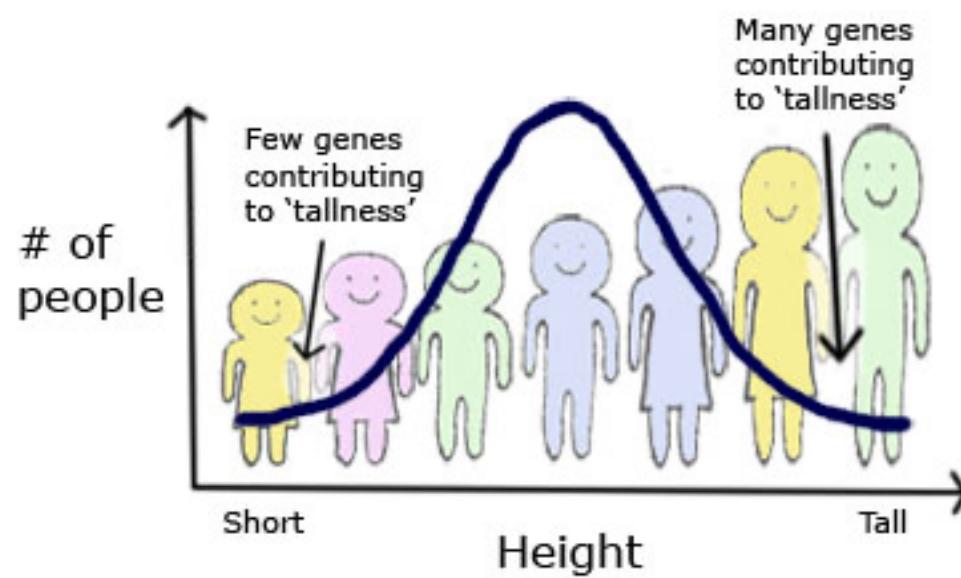


## Main points—natural selection

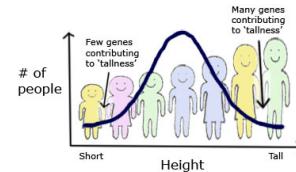
- Simple genetic models of selection predict allele frequency change over time
- Selection may be directional or balancing
- Genome level analyses can be used to detect past selection
- Selection and deleterious mutation when they interact can maintain genetic diseases in populations

Questions about population genetics?

## Module: Complex trait genetics



## Module – Complex Trait (Quantitative) Genetics



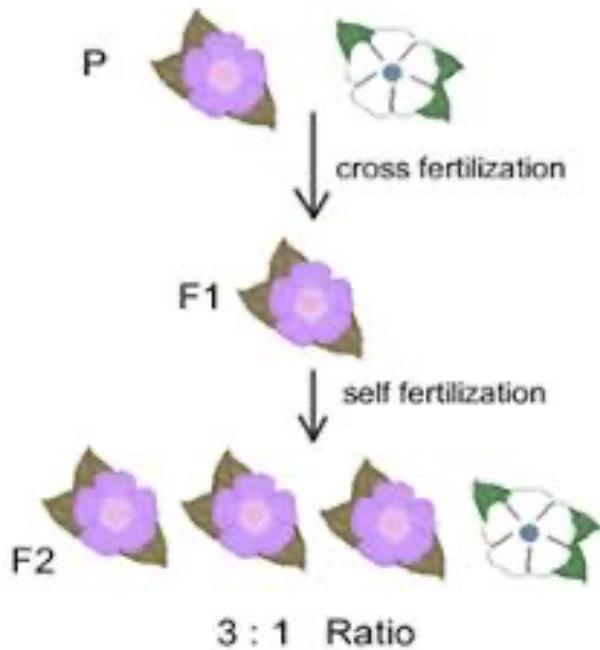
*Lecture 12/13— When many genes and many environmental effects influence trait expression and variation*

- |   |
|---|
| 1. Complex trait variation (Ch19 Section 1)   |
| 2. Measuring components of phenotypic trait variation (Ch19 Sections 2,3)                             |
| 3. Using molecular markers to infer the presence of genes affecting genetic variance (Ch19 Section 6) |

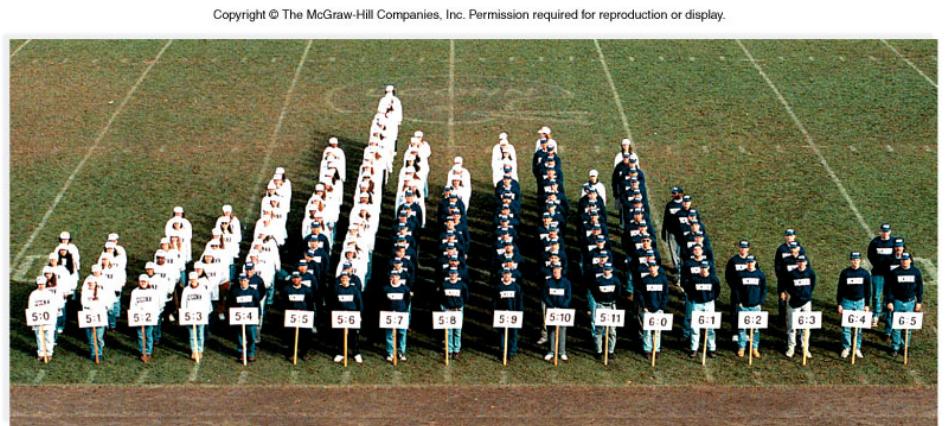
PRIMER—Quantitative Genetics (see myCourses page for Biology 202)

## Simple traits versus complex traits

Simple trait



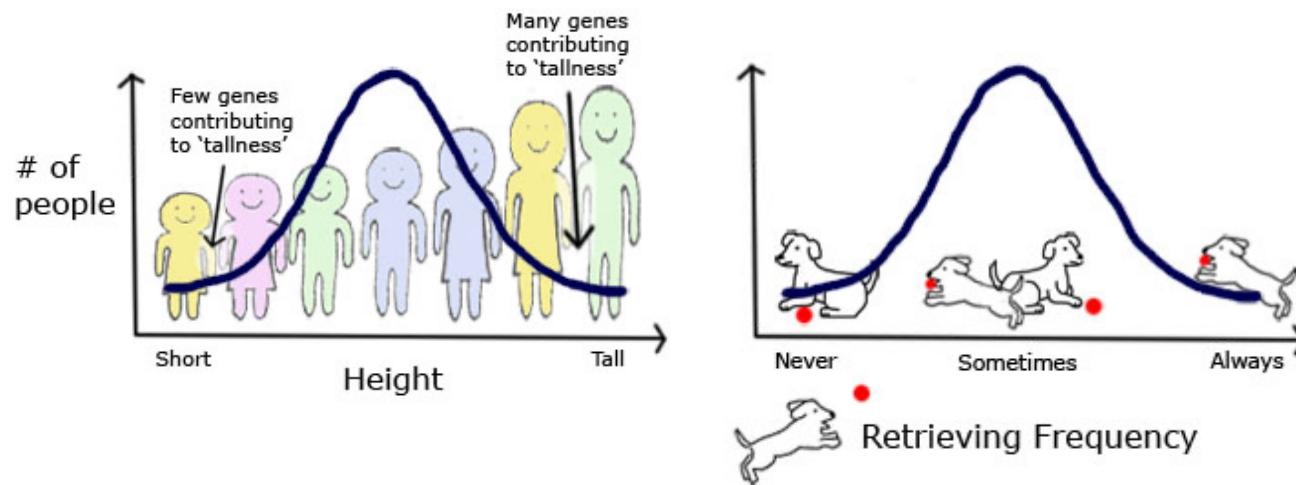
Complex (also called “quantitative” trait)



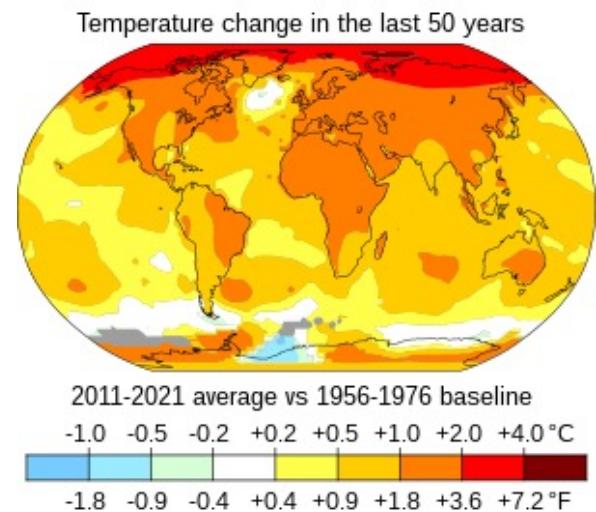
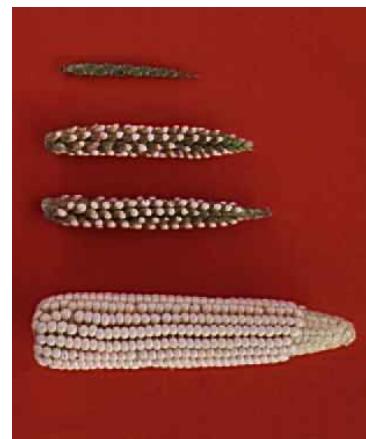
Population variation controlled by one /two genes ..... by many (e.g., 100 genes)

# Complex (quantitative) trait genetics

The nature of quantitative variation:  
Distribution of phenotypic states is often “bell-shaped”

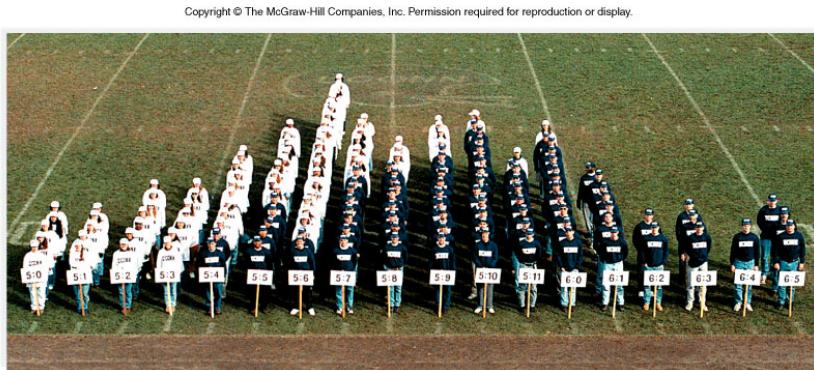


Quantitative genetic variation: Important for understanding the evolution of common diseases, crop improvement, and the rate of evolutionary change

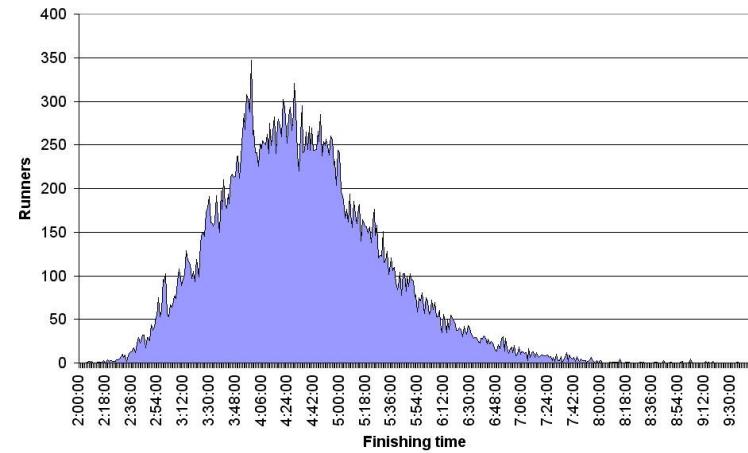


## Types of complex traits

### Continuous



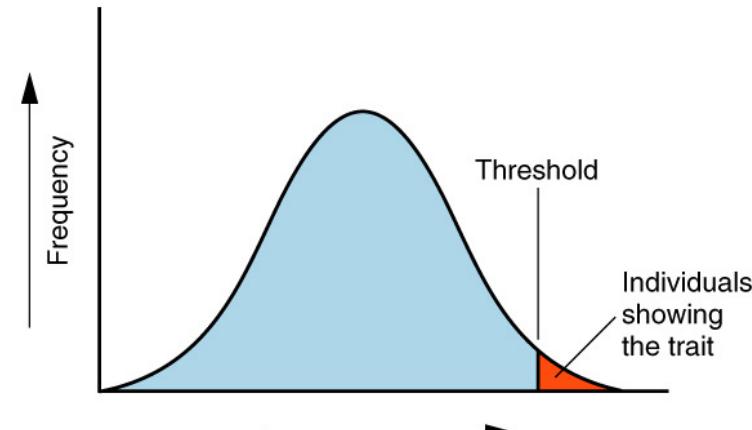
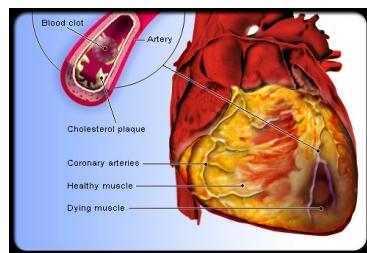
*Body size (height)*



*Running speed  
(e.g., finishing time in a marathon)*

## Types of complex traits

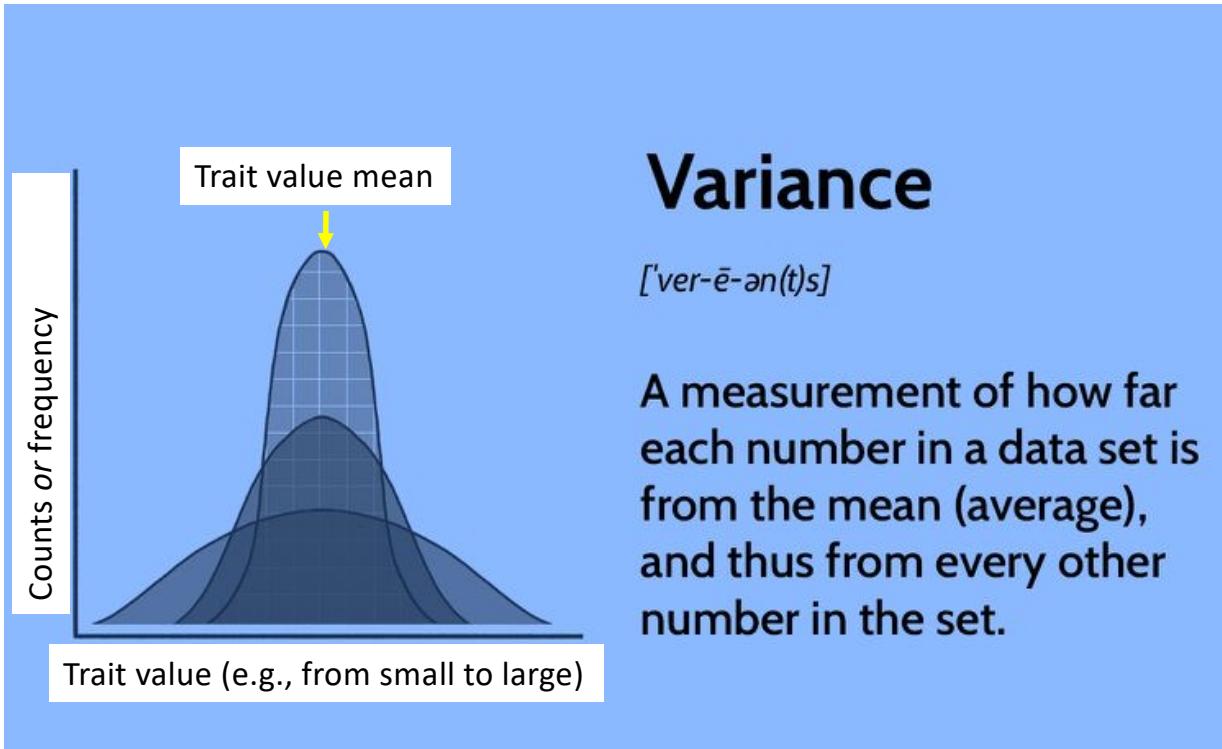
Threshold (“either / or”)



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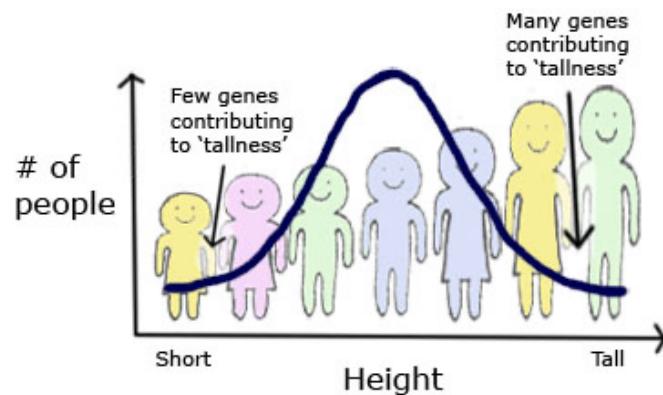
*Environmental liability  
Genetic liability*

Threshold traits  
(e.g., cancers, heart diseases)

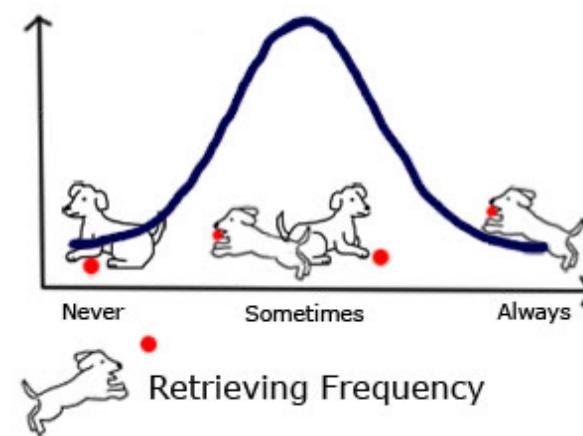


**Phenotypic variance of a trait:** How much is due to differences in the environment that individuals experience *and* how much is due to genetic differences among individuals

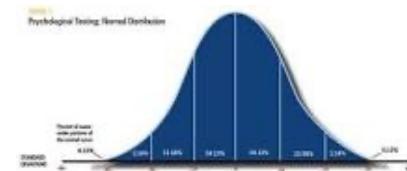
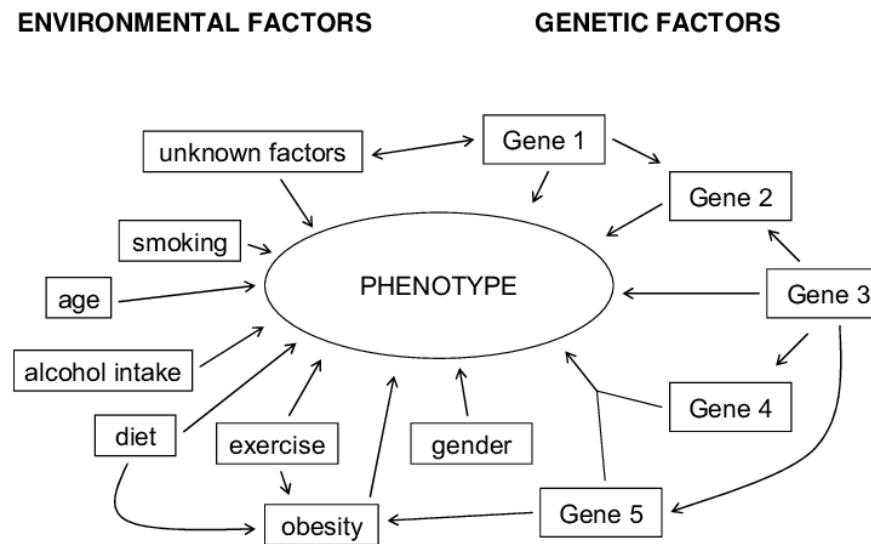
Phenotypic variance of height



Phenotypic variance of retrieving frequency

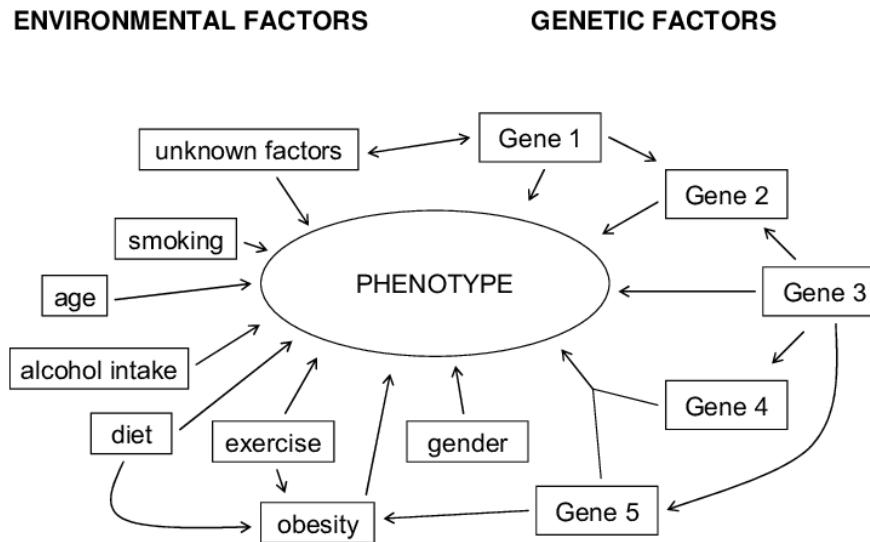


# The “Multifactorial Model” for complex trait variation



e.g. *blood pressure*

The phenotypic variance can be decomposed in variance that is attributable to environmental factors and genetic factors



*blood pressure*

## Main points—Complex (quantitative) traits

- Complex traits can be continuous or show threshold characteristics.
- We are often interested in how much variance there is in the population for the complex trait (the “phenotypic variance”).
- Complex trait variance is typically influenced by genetic variation and environmental variation.  
(we will also be interested in “genetic variance” and “environmental variance”)