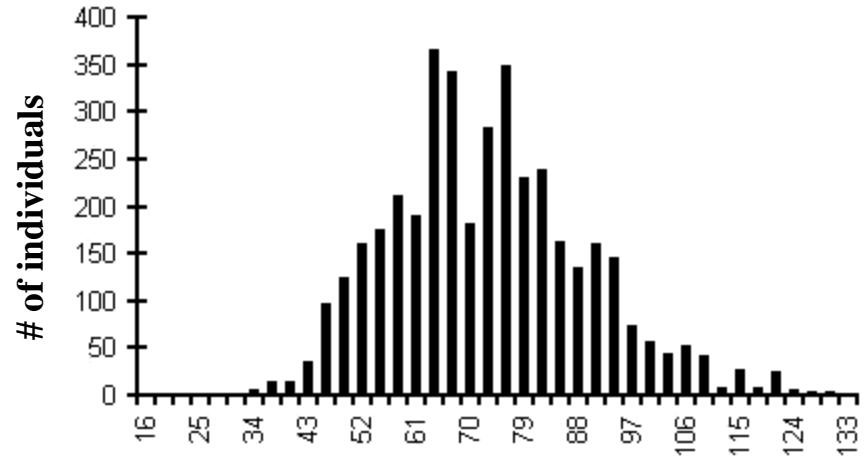


Genetic variation: the raw material of evolution



**Color pattern polymorphism
in *Cepea* snails**



Human body weight

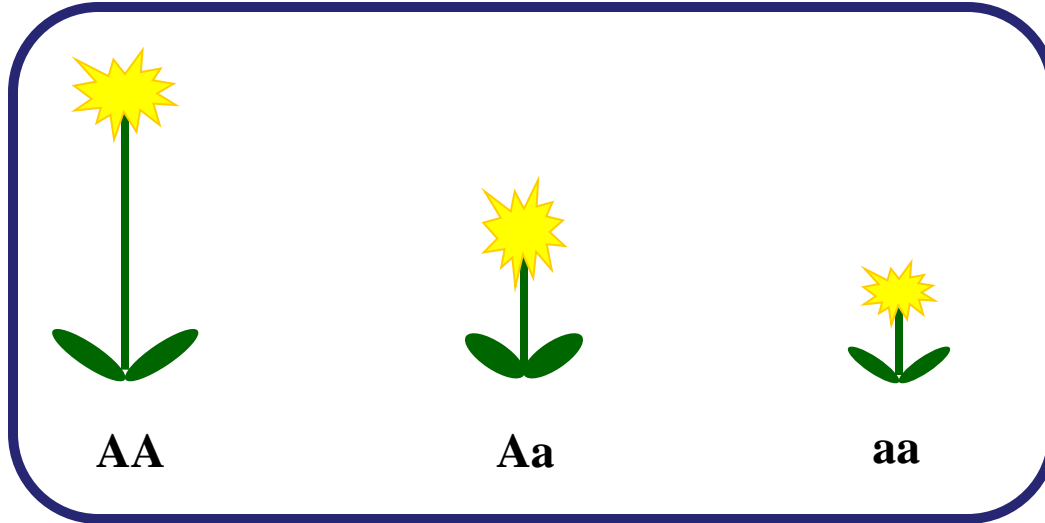
- **How much variation is there?**
- **How does novel variation arise?**

Sources of phenotypic variation

- 1. Differences in genotype – Different genotypes produce different phenotypes**
- 2. Differences in environment – Different environments produce different phenotypes**
- 3. Interactions between genotype and environment – The relative values of phenotypes produced by different genotypes depend on the environment**

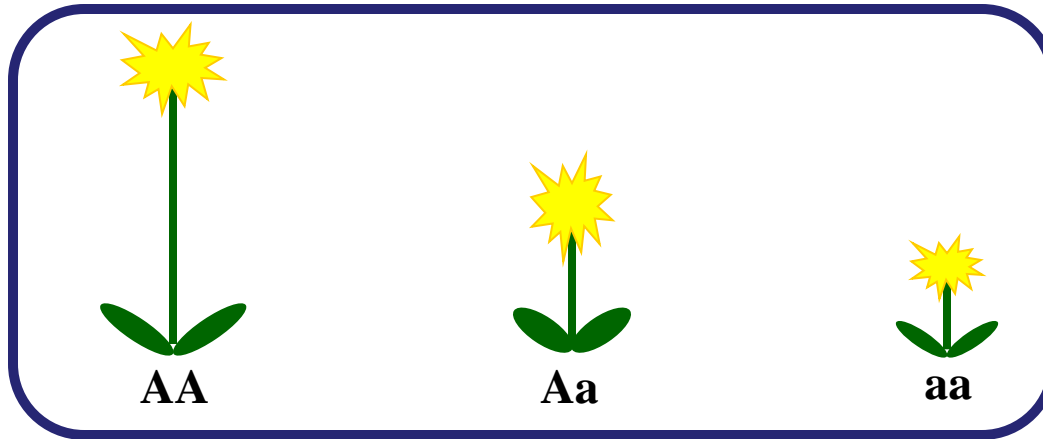
Genetic variation

Environment 1



Environmental variation

Environment 1

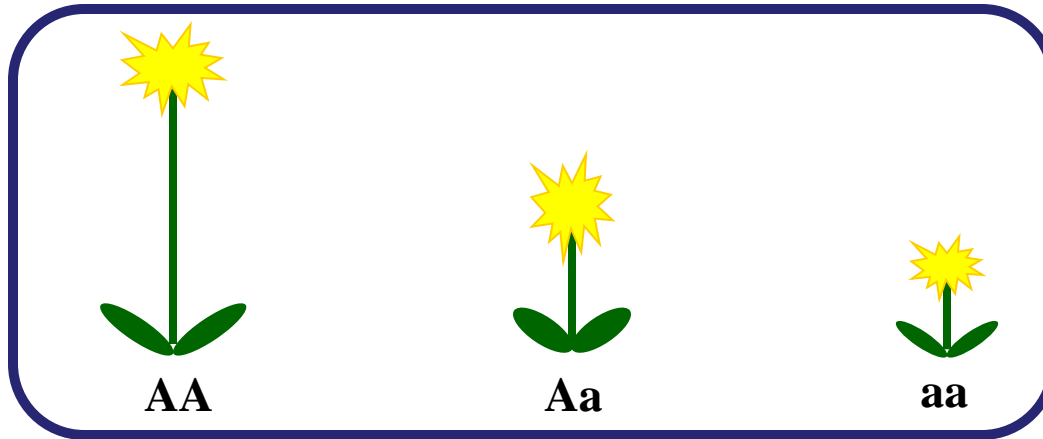


Environment 2

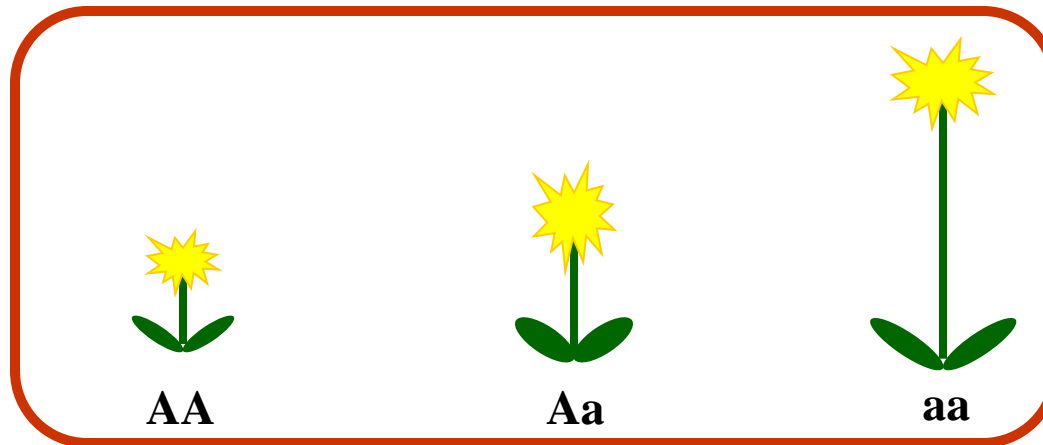


Genotype×Environment variation

Environment 1



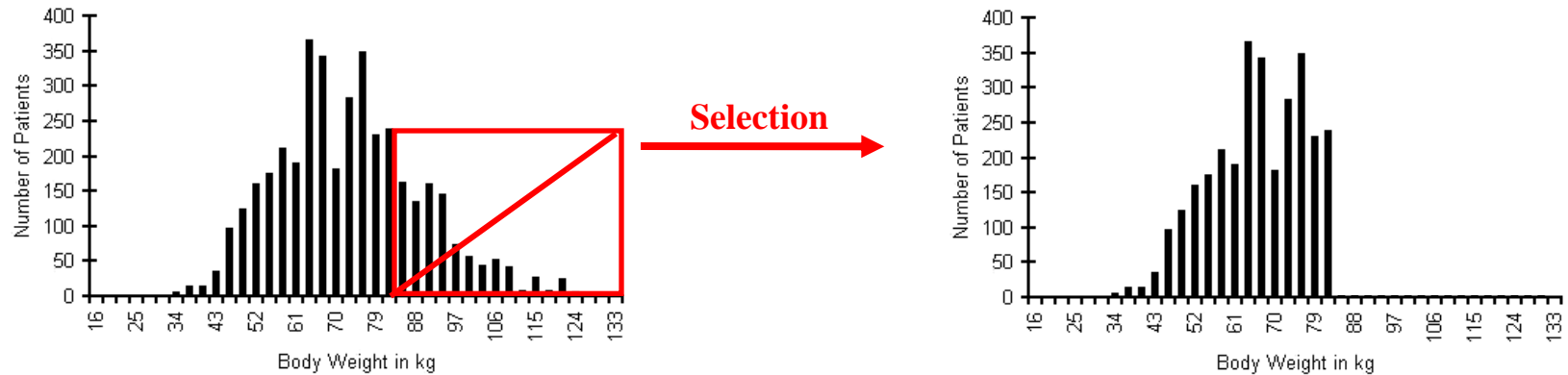
Environment 2



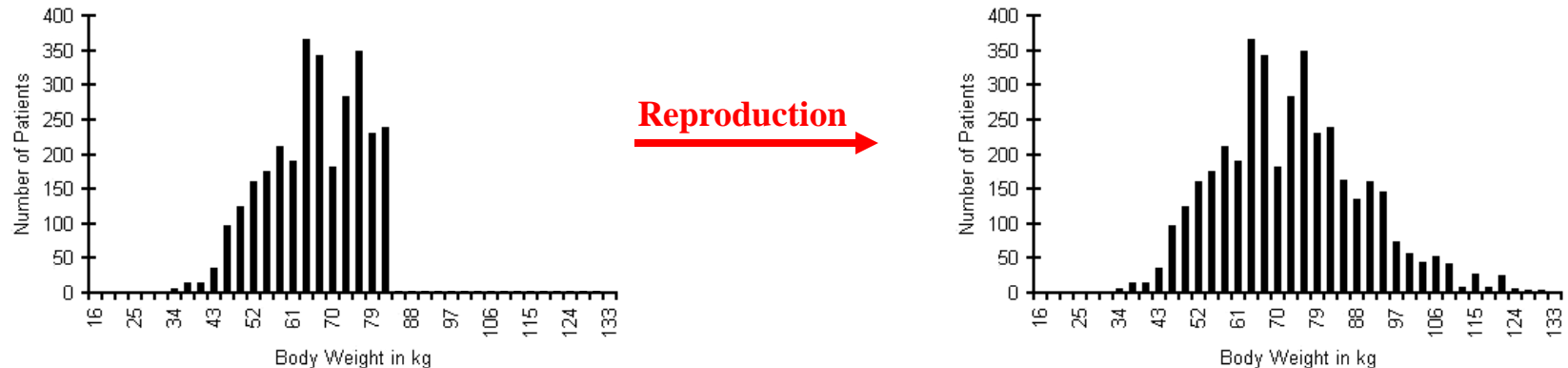
*** Although prevalent in nature, we will ignore the complication of $G \times E$ ***

It is **GENETIC** variation that is essential for evolution

- **Selection can act on purely phenotypic variation**

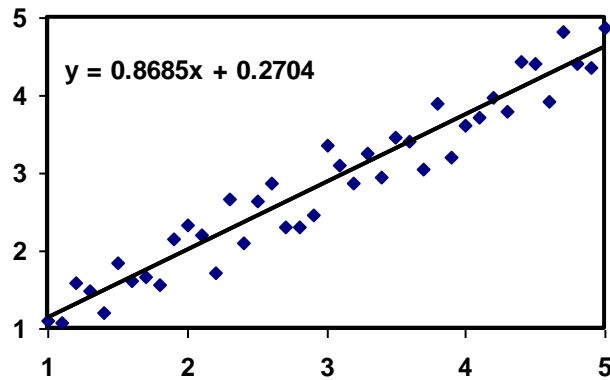


- **But without genetic variation evolution will not occur**

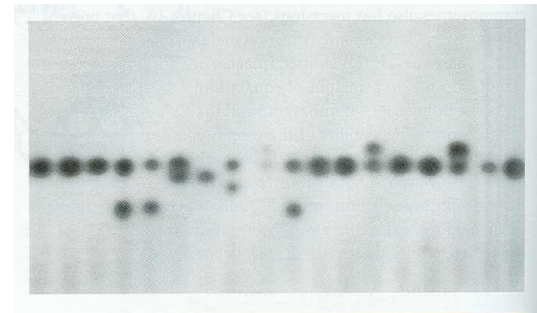


How much genetic variation is there?

1. Statistical analysis of quantitative traits

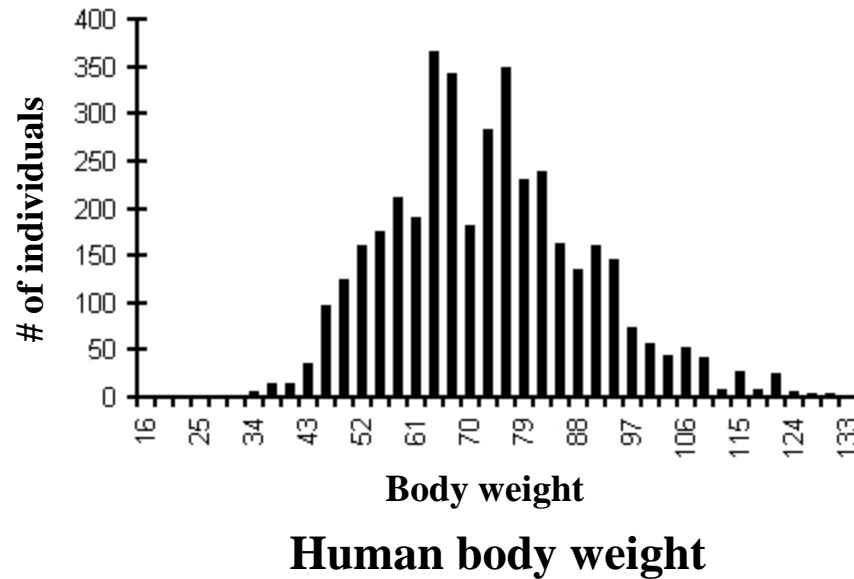


2. Studies at the molecular level



How much genetic variation is there?

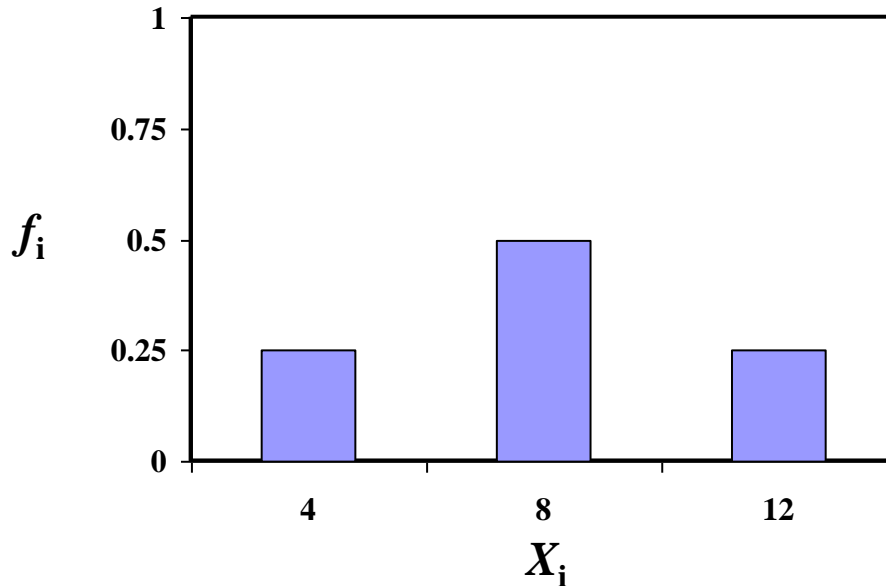
Part I. Statistical analysis of quantitative traits



How much of this phenotypic variation is genetic?

Some basic statistics I: The mean

$$\bar{x} = \sum_{i=1}^n f_i X_i$$

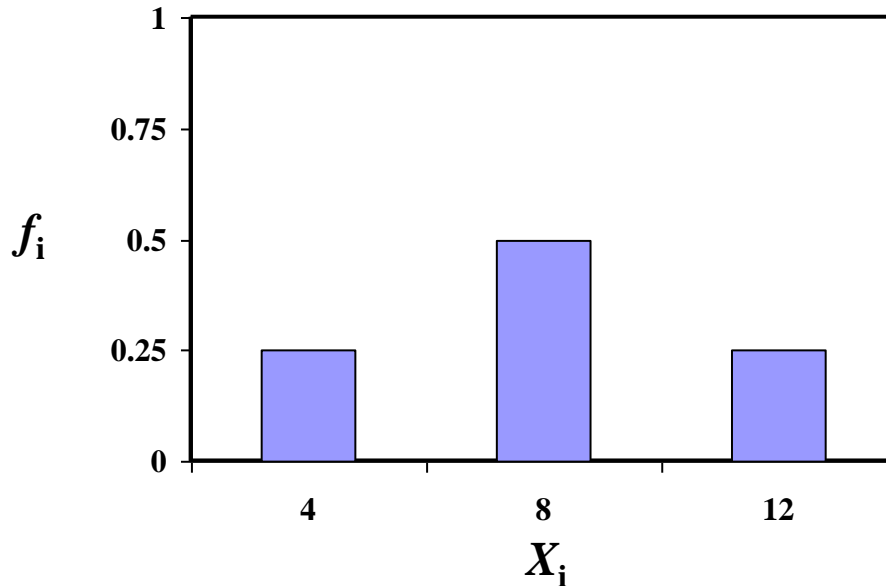


$$\bar{x} = .25(4) + .5(8) + .25(12) = 8$$

Where n is the number of different phenotype classes

Basic statistics II: The variance

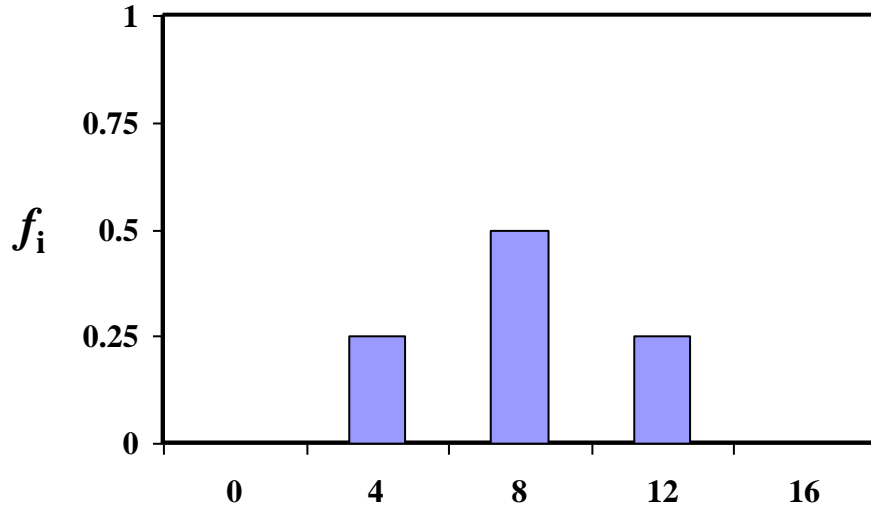
$$V = \sum_{i=1}^n f_i (X_i - \bar{x})^2$$



$$V = .25(4-8)^2 + .5(8-8)^2 + .25(12-8)^2 = 8$$

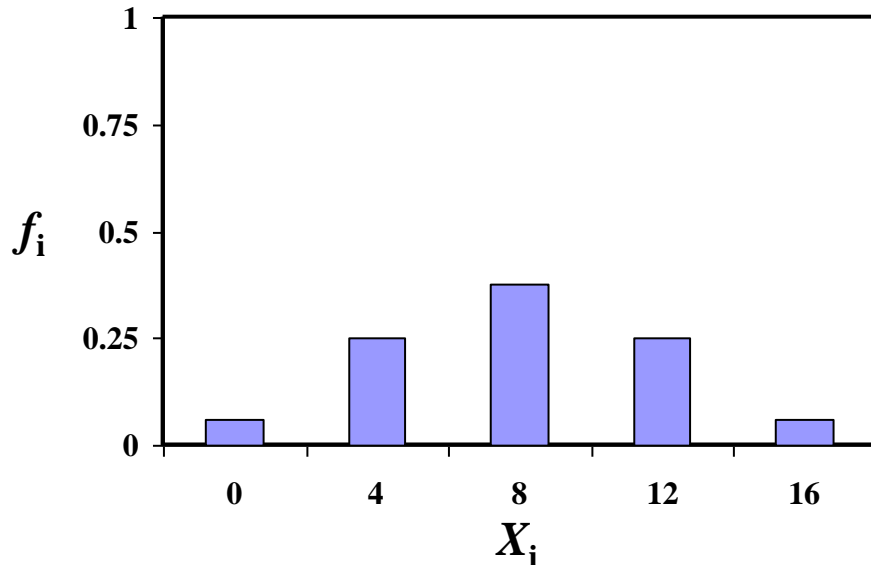
Where n is the number of different phenotype classes

Basic statistics II: The variance



Population with variance = 8

$$V = 0(0-8)^2 + .25(4-8)^2 + .5(8-8)^2 + .25(12-8)^2 + 0(16-8)^2 = 8$$



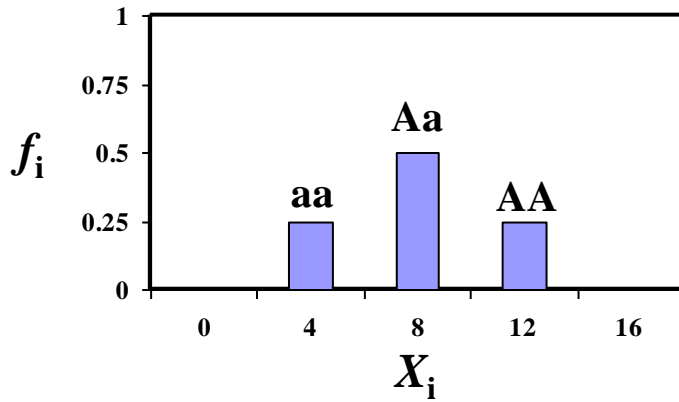
Population with variance = 16

$$V = .0625(0-8)^2 + .25(4-8)^2 + .375(8-8)^2 + .25(12-8)^2 + .0625(16-8)^2 = 16$$

Using basic statistics to decompose phenotypic variation

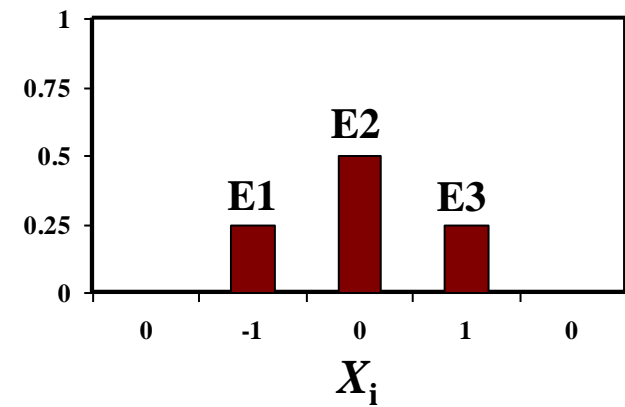
$$V_P = V_G + V_E$$

Genetic Variance

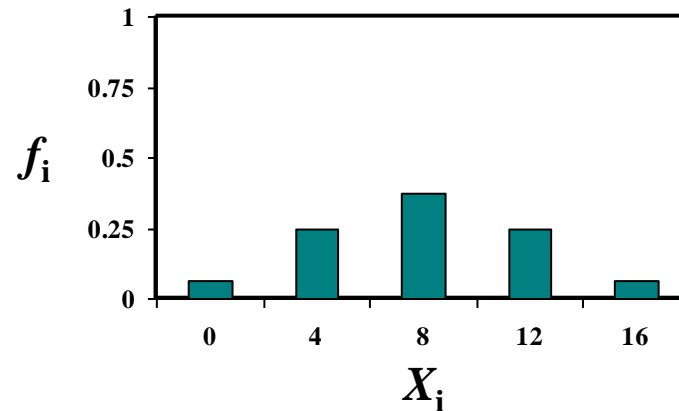


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Environmental Variance



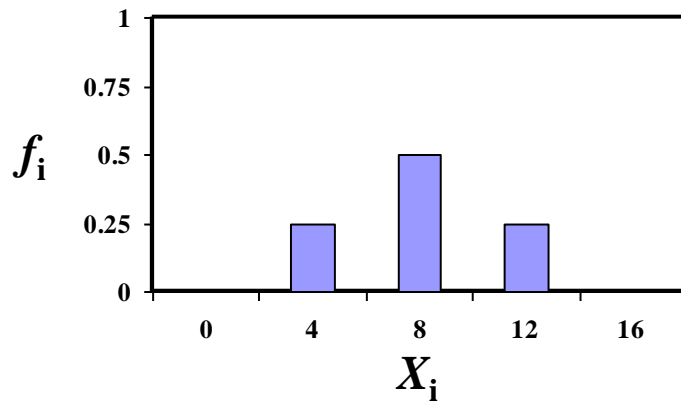
Phenotypic Variance



Genetic variation can be further decomposed

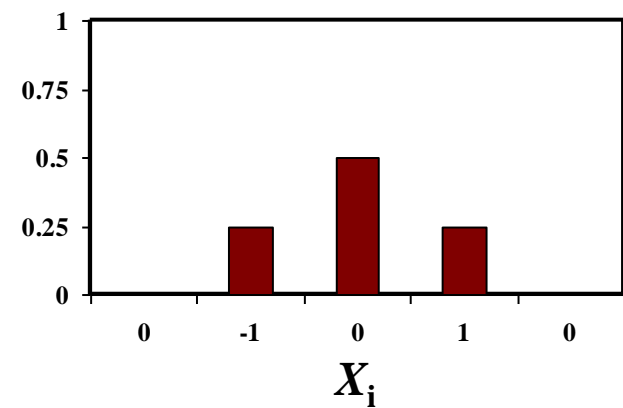
$$V_G = V_A + V_I + V_D$$

Additive Genetic Variance

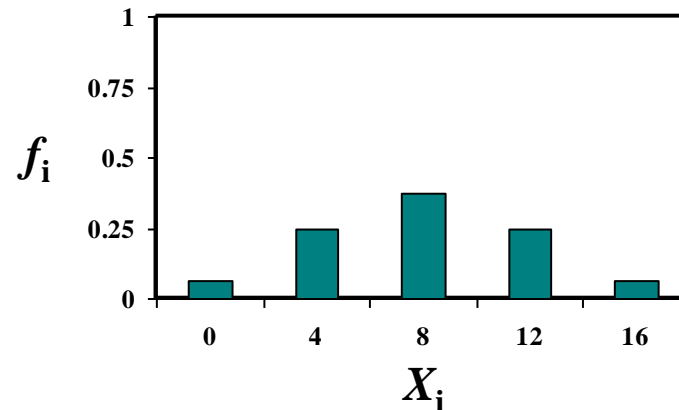


+

Epistasis and Dominance Variance



Genotypic Variance



What mechanisms contribute to each component?

Additive genetic variance (V_A) – Due to the additive effects of alleles

Genotype	Phenotype
AA	2
Aa	1
aa	0

Dominance variance (V_D) – Due to dominance

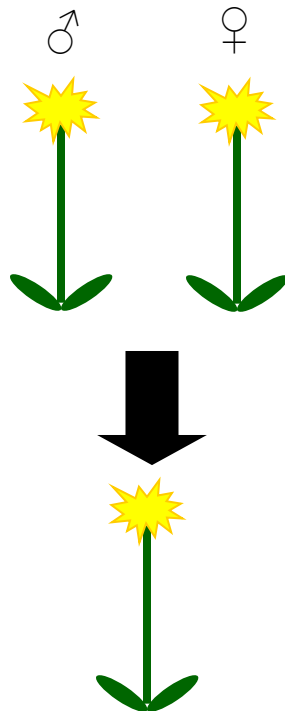
Genotype	Phenotype
AA	2
Aa	1
aa	2

Interaction variance (V_I) – Due to epistasis

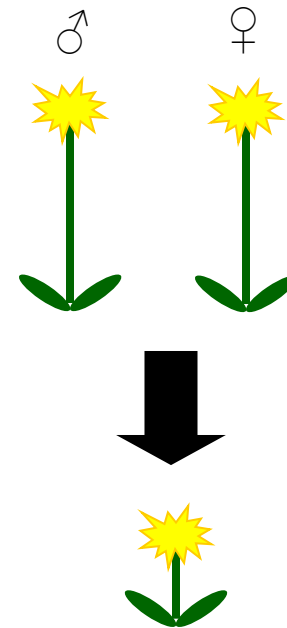
Genotype	Phenotype
AA (BB)	2
AA (Bb)	1
AA (bb)	2

It is **additive genetic variance** that determines the resemblance of parents and offspring

Additivity



Epistasis or Dominance



Offspring need not look like parents!

How do we know how much additive genetic variation exists within a population?

The proportion of phenotypic variation that is genetic can be estimated by calculating “heritability”

- **Broad sense heritability** – Measures the proportion of phenotypic variation that is genetic

$$H_B^2 = V_G / (V_G + V_E) = V_G / V_P$$

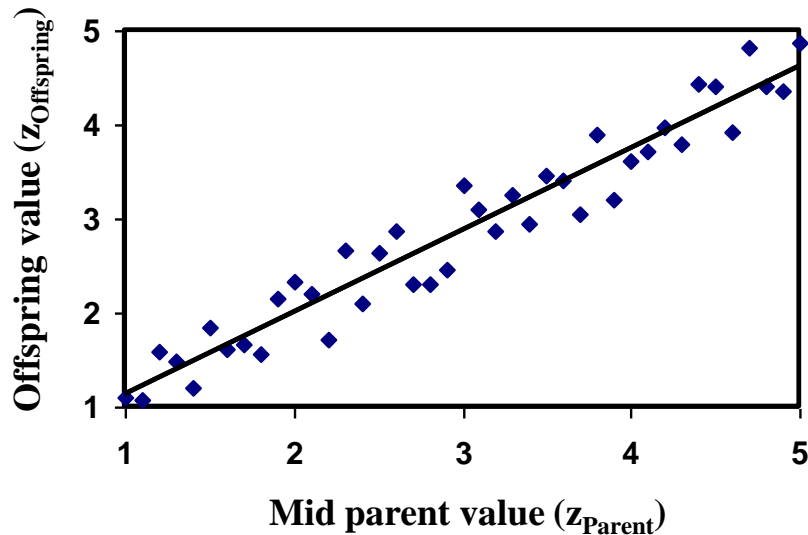
- **Narrow sense heritability** – Measures the proportion of phenotypic variation attributable to the additive action of genes. This is the measure relevant to N.S.

$$h_N^2 = V_A / (V_A + V_I + V_D + V_E)$$

How can we measure narrow sense heritability?

One possibility is a parent-offspring regression

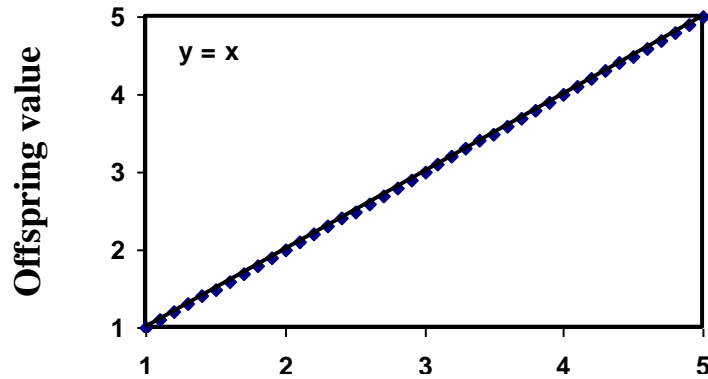
- The slope of the linear regression is an estimate of heritability



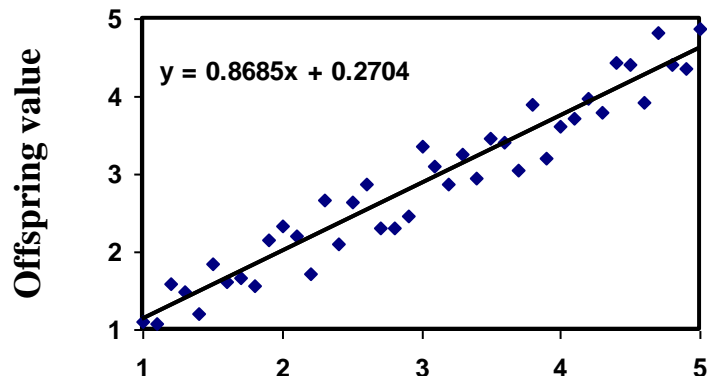
$$h^2 = \frac{Cov[z_{Parent}, z_{Offspring}]}{V[z_{Parent}]}$$

$$Cov[z_{Parent}, z_{Offspring}] = \frac{\sum_{i=1}^n (z_{Parent,i} - \bar{z}_{Parent})(z_{Offspring,i} - \bar{z}_{Offspring})}{n}$$

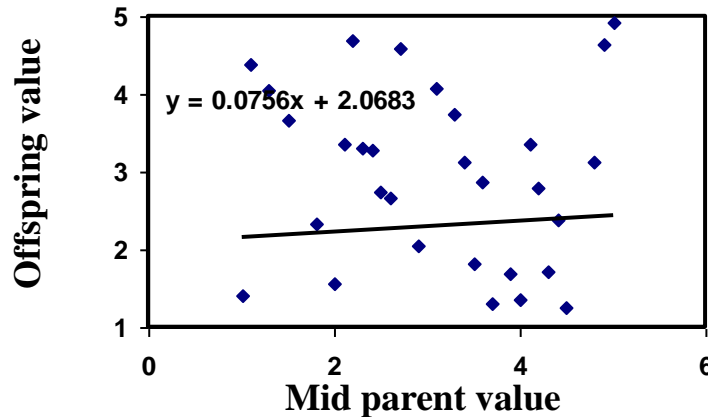
One possibility is a parent-offspring regression



Perfectly heritable – Slope is 1.0



High heritability – Slope is 0.8685



Low heritability – Slope is 0.0756

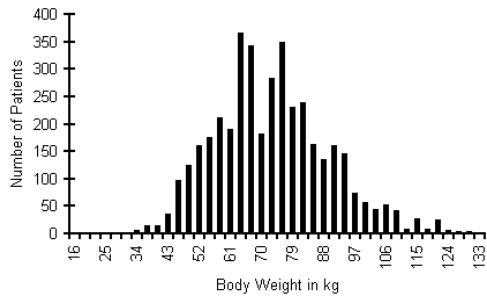
How heritable are most traits?

<i>Trait</i>	<i>Heritability</i>
Milk Yield in Cattle	.3
Body length in pigs	.5
Litter size in pigs	.15
Wool length in sheep	.55
Egg weight in chickens	.6
Age at first laying In chickens	.5
Tail length in mice	.6
Litter size in mice	.15

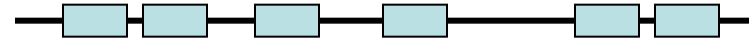
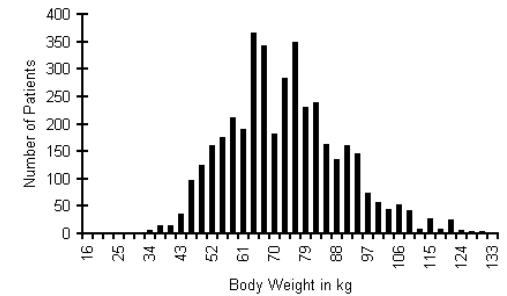
After Falconer (1981)

For almost any trait ever measured, there is abundant additive genetic variation!

A limitation of the statistical approach



vs.



Can never accurately reveal how many genetic loci are responsible for observed levels of variation

How much genetic variation is there?

Part II: Molecular variability

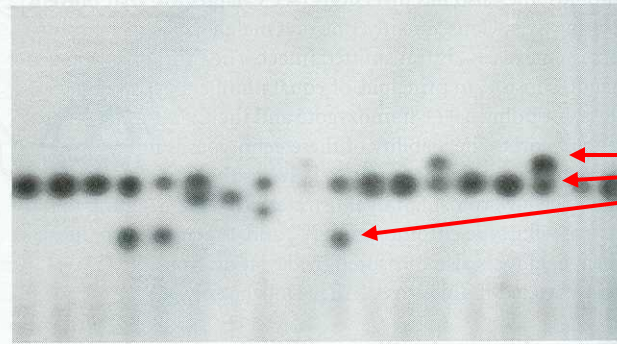
- **Prior to 1966, it was generally assumed that populations were, in large part, genetically uniform**

- **In 1966, two landmark papers (Lewinton and Hubby, 1966; Harris, 1966) turned this conventional wisdom on its head, demonstrating an abundance of *GENETIC POLYMORPHISM***

So what did these landmark studies really show?

Genetic polymorphism – The presence of two or more alleles in a population, with the rarer allele having a frequency greater than .01.

FIGURE 9.8 An electrophoretic gel, showing genetic variation in the enzyme phosphoglucosmutase among 18 individual killifishes (*Fundulus zebrinus*). Five electromorphs (alleles) can be distinguished by differences in mobility. The fastest, at top, is allele 1; the slowest, at bottom, is allele 5. The enzyme is a monomer, so homozygotes (such as “2/2”) display a single band and heterozygotes (such as “2/5”) display two bands. From left to right, the genotypes are 2/2, 2/2, 2/2, 2/5, 2/5, 2/3, 3/3, 2/4, 1/2, 2/5, 2/2, 2/2, 1/2, 2/2, 2/2, 1/2, 2/2, 2/2. (Courtesy of J. B. Mitton.)



In this example, there are 5 alleles

Separates protein variants (alleles) by size and charge

Using protein gel electrophoresis, these studies showed that roughly 1/3 of all loci are polymorphic in both humans and *Drosophila*.

Subsequent studies found the same thing!

	NUMBER OF SPECIES EXAMINED	AVERAGE NUMBER OF LOCI PER SPECIES	AVERAGE PROPORTION OF LOCI	
			POLYMORPHIC PER POPULATION	HETEROZYGOUS PER INDIVIDUAL
Insects				
<i>Drosophila</i>	28	24	0.529	0.150
Others	4	18	0.531	0.151
Haplodiploid wasps ^a	6	15	0.243	0.062
Marine invertebrates	9	26	0.587	0.147
Marine snails	5	17	0.175	0.083
Land snails	5	18	0.437	0.150
Fishes	14	21	0.306	0.078
Amphibians	11	22	0.336	0.082
Reptiles	9	21	0.231	0.047
Birds	4	19	0.145	0.042
Rodents	26	26	0.202	0.054
Large mammals ^b	4	40	0.233	0.037
Plants ^c	8	8	0.464	0.170

Source: Futuyma, *Evolutionary Biology*, 3rd Edition

Suggests that almost every individual in a sexually reproducing species is genetically unique!

- **Even with only two alleles per locus, the estimated 3000 polymorphic loci in humans could generate $3^{3000} = 10^{1431}$ different genotypes!**

The bottom line:

**No matter how you cut it,
there is abundant genetic variation **WITHIN** populations,
and thus ample opportunity for selection to act**

Assessing genetic variation and Hardy-Weinberg I: a practice problem

The scenario: A group of biologists was studying a population of elk in an effort to quantify genetic variation at disease resistance locus. Through DNA sequencing, the biologists have determined that there are two alleles at this locus, **A** and **a**. Sequencing analysis of many individuals has also allowed the frequency of the alleles and the corresponding diploid genotypes to be estimated

The data:

Frequency of the **A** allele is $p = 0.4$

Frequency of the **a** allele is $q = ?$

Frequency of the **AA** genotype is: 0.06

Frequency of the **Aa** genotype is: 0.80

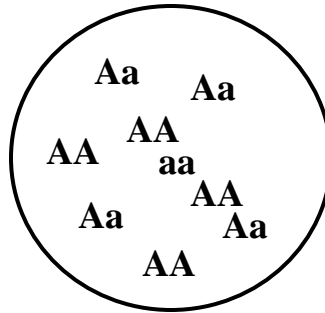
Frequency of the **aa** genotype is: 0.14

The question:

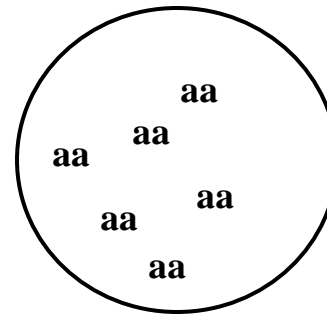
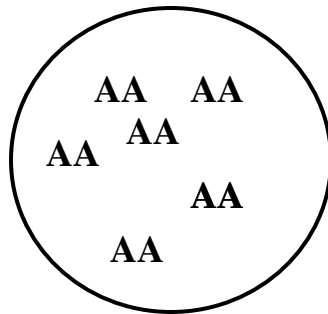
Is this population in Hardy-Weinberg Equilibrium? Justify your response.

Increasing the scale: Genetic variation among populations

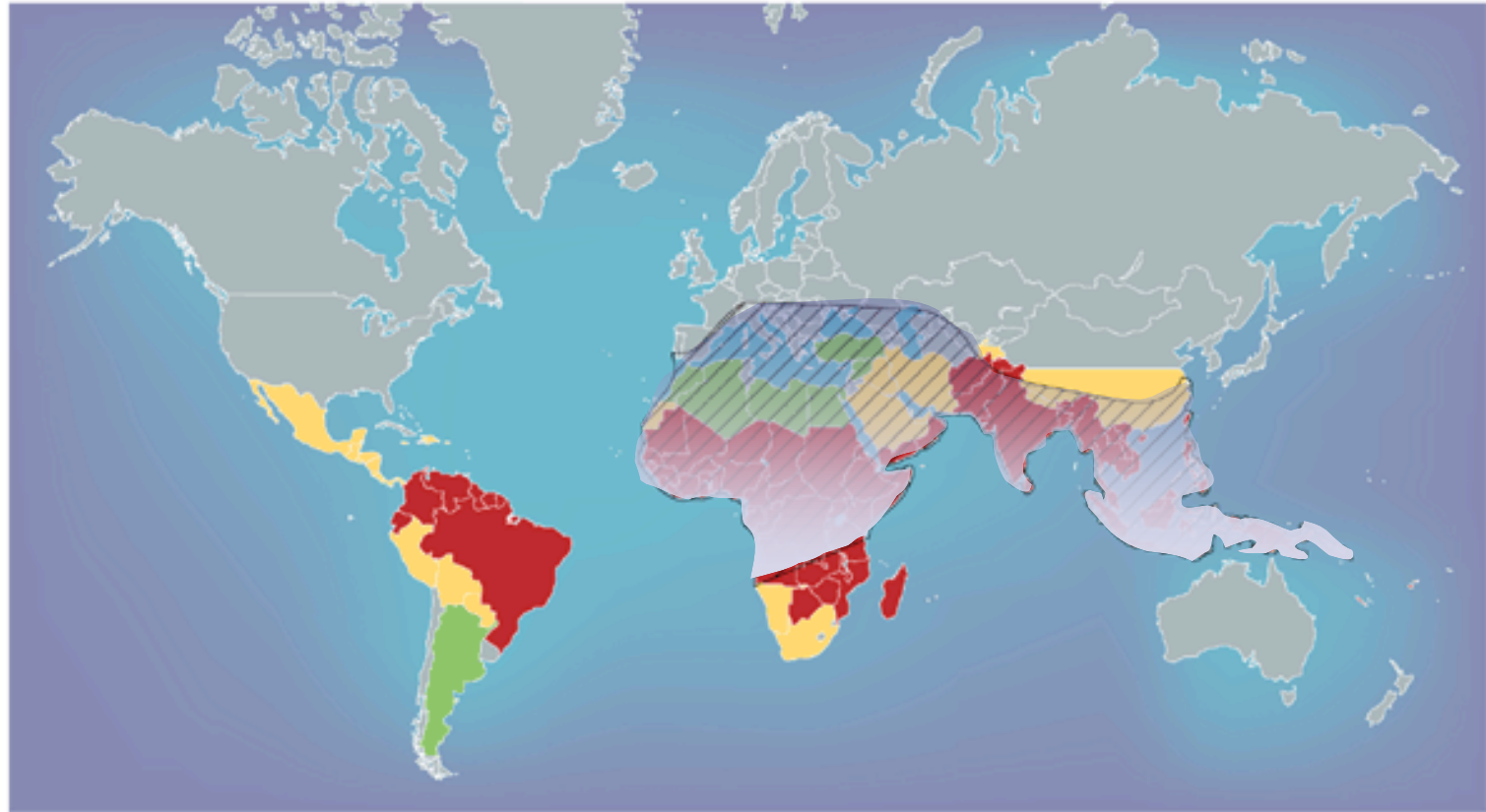
Genetic variation within a single population



Genetic variation among populations



Genetic variation among populations



Nature Reviews | **Genetics**

Genetic variation in human resistance to Malaria

Increasing the scale: Genetic variation among species



Chum < 32 lbs



Chinook < 100 lbs



Coho < 26 lbs



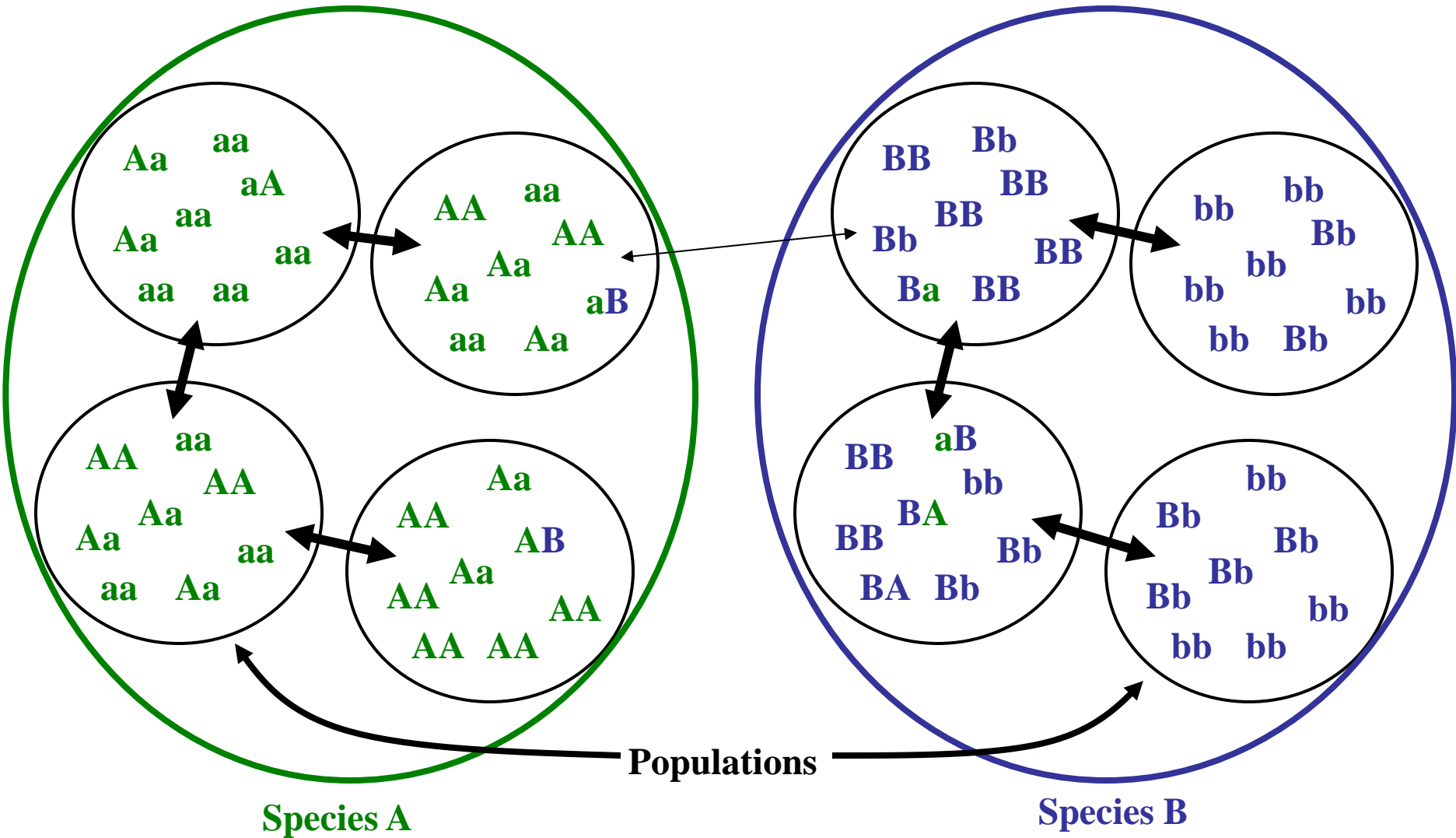
Pink < 12 lbs



Sockeye < 16 lbs

These different species are genetically differentiated with respect to adult size

We now know that genetic variation is hierarchical



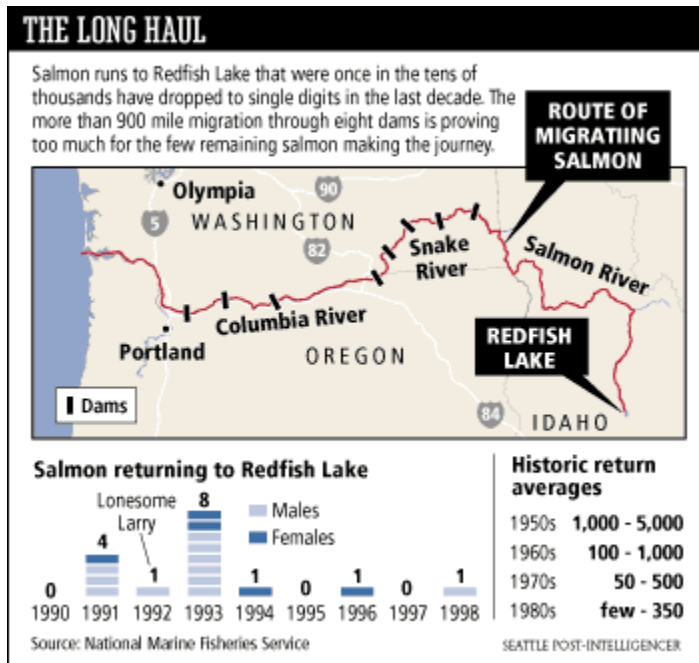
An applied problem: genetic variation and conservation



Sockeye Salmon



Redfish Lake, Idaho



**Populations vs. Species:
Which is more relevant?**

Assessing genetic variation and Hardy-Weinberg II: a practice problem

The scenario: A group of biologists is studying a population of flowers where flower color is controlled by a single diploid locus with two alleles. Individuals with genotype **AA** make white flowers, individuals with genotype **Aa** make red flowers, and individuals with genotype **aa** make red flowers.

The data:

Frequency of the white flowers is $f(\text{white}) = 0.4$

Frequency of red flowers is $f(\text{red}) = ?$

The questions:

1. Which allele, **A** or **a** is dominant?
2. Assuming that this population is in Hardy-Weinberg Equilibrium, what is the frequency of the **A** allele?
3. Assuming that this population is in Hardy-Weinberg Equilibrium, what is the frequency of the **a** allele?

Where does genetic variation come from?

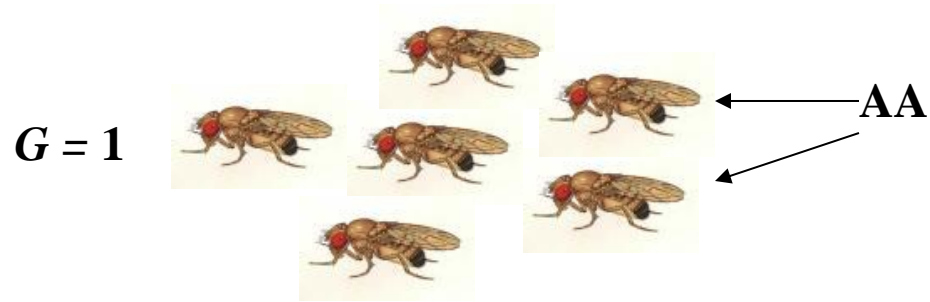
- 1. Mutation – An alteration of a DNA sequence that is inherited**
- 2. Recombination – The formation of gametes with combinations of alleles different from those that united to form the individual that produced them.**
- 3. Gene flow – The incorporation of genes into the gene pool of one population from one or more other populations.**
- 4. Hybridization – The incorporation of genes into the gene pool of one species from another species.**

Estimating the mutation rate

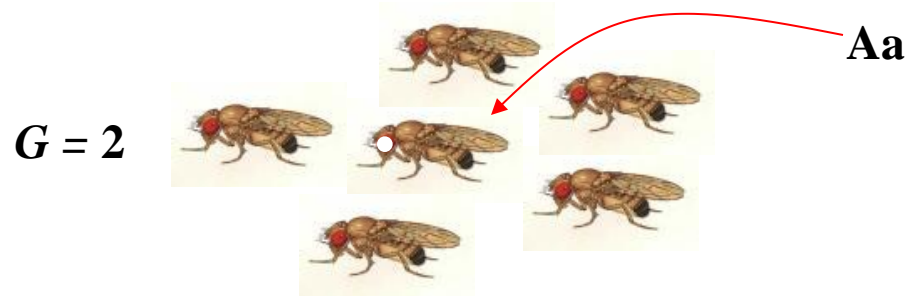
- **Direct methods – Simply counting new mutations**

- **Statistical methods – Based on increases in phenotypic variance**

Direct estimation of the mutation rate



50,000 flies all homozygous for the (hypothetical) recessive red eye allele (A)



50,000 flies but now 1 has white eyes indicating genotype (Aa)

We could then estimate that the per locus mutation rate as $1/100,000 = .00001$

Implications of these estimates for mutation rates

- As a gross average, the per locus mutation rate is 10^{-6} - 10^{-5} mutations per gamete per generation.
- As a gross average, humans have 150,000 functional genes
- $10^{-5} (150,000) = 1.5$

This suggests that EVERY gamete carries a new, phenotypically detectable mutation somewhere in its genome!!!

Spontaneous mutation rates of specific genes detected by phenotypic effects

Estimates of mutation rates (per genome, per generation)

Single celled organisms

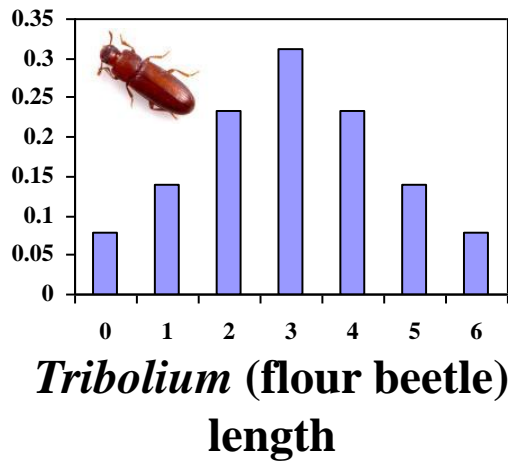
Species	Taxonomic group	Number of mutations
<i>E. Coli</i>	Bacteria	0.0025
<i>S. acidocaldarius</i>	Archaea	0.0018
<i>N. crassa</i>	Fungi	0.0030
<i>S. cerevisiae</i>	Fungi	0.0027

Multicellular organisms

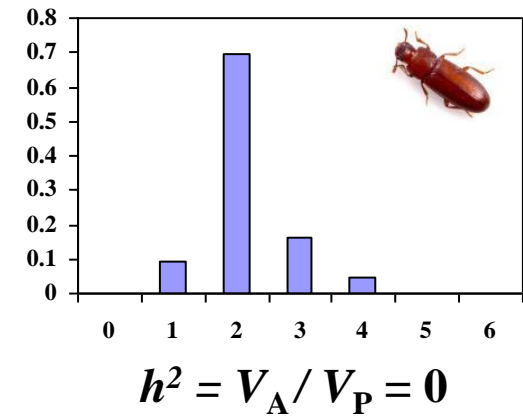
Species	Taxonomic group	Number of mutations
<i>C. elegans</i>	Roundworms	0.0360
<i>D. Melanogaster</i>	Insects	0.1400
<i>M. Musculus</i>	Mammals	0.9000
<i>H. sapiens</i>	Mammals	1.6000

Source: Evolutionary analysis: third edition. Freeman and Herron.

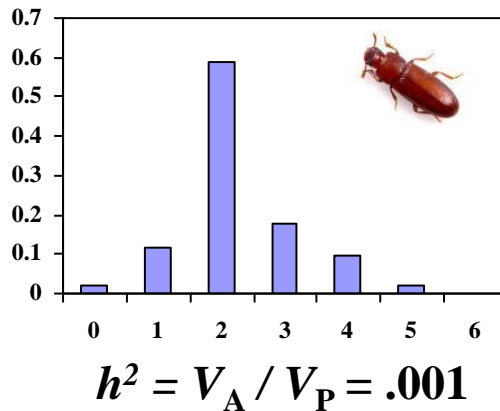
Statistical estimation of new mutational genetic variance



→
Inbreed until all additive
genetic variance for some trait of
interest is lost

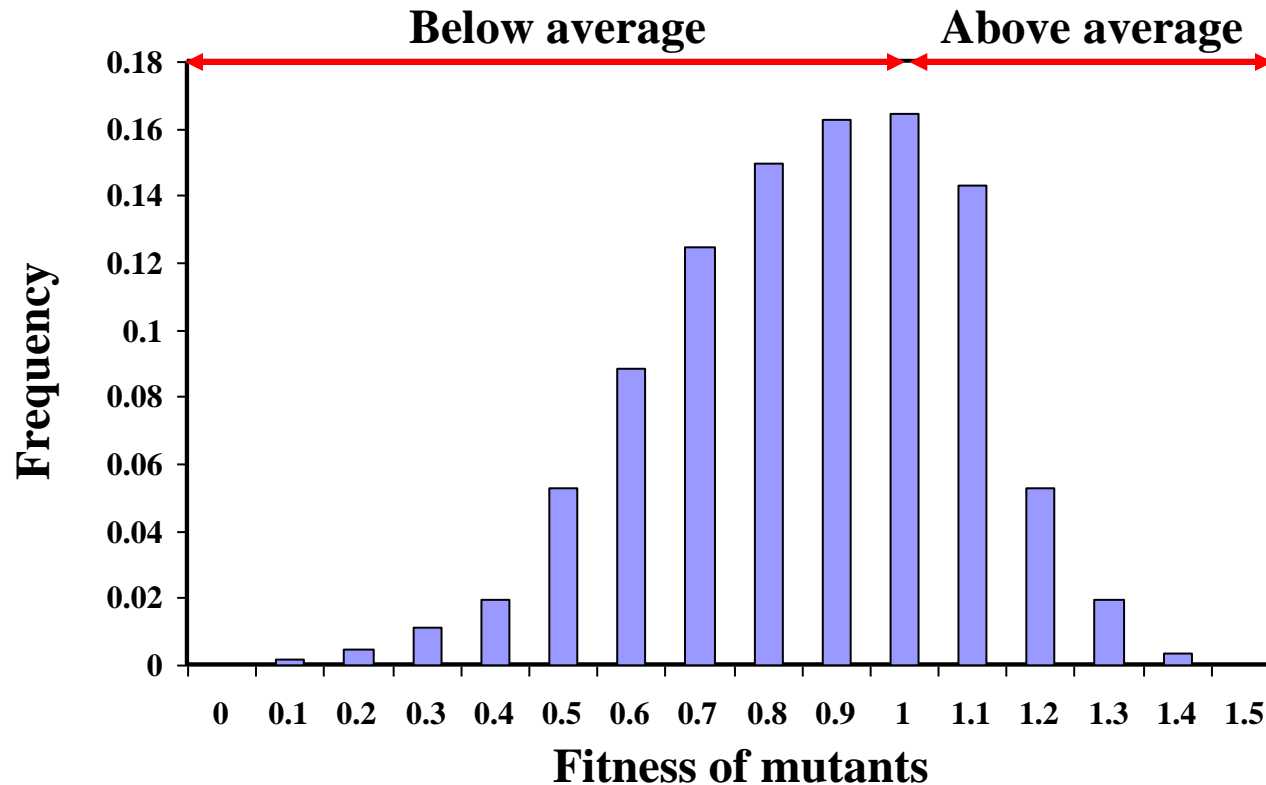


↙
Mate at random and
measure heritability



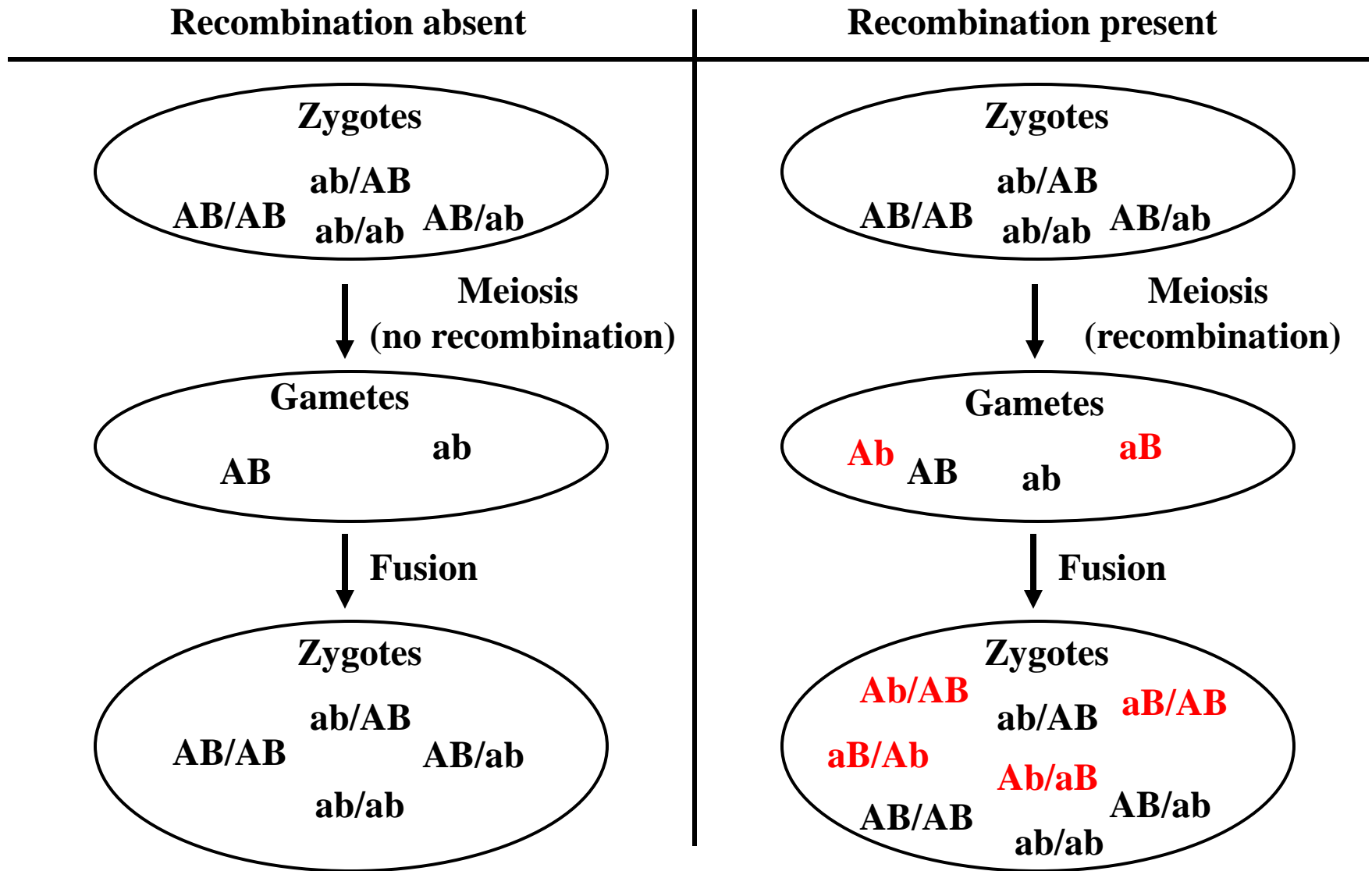
It would then take only 100 generations for h^2 to equal .1!

What effect do mutations have on fitness?



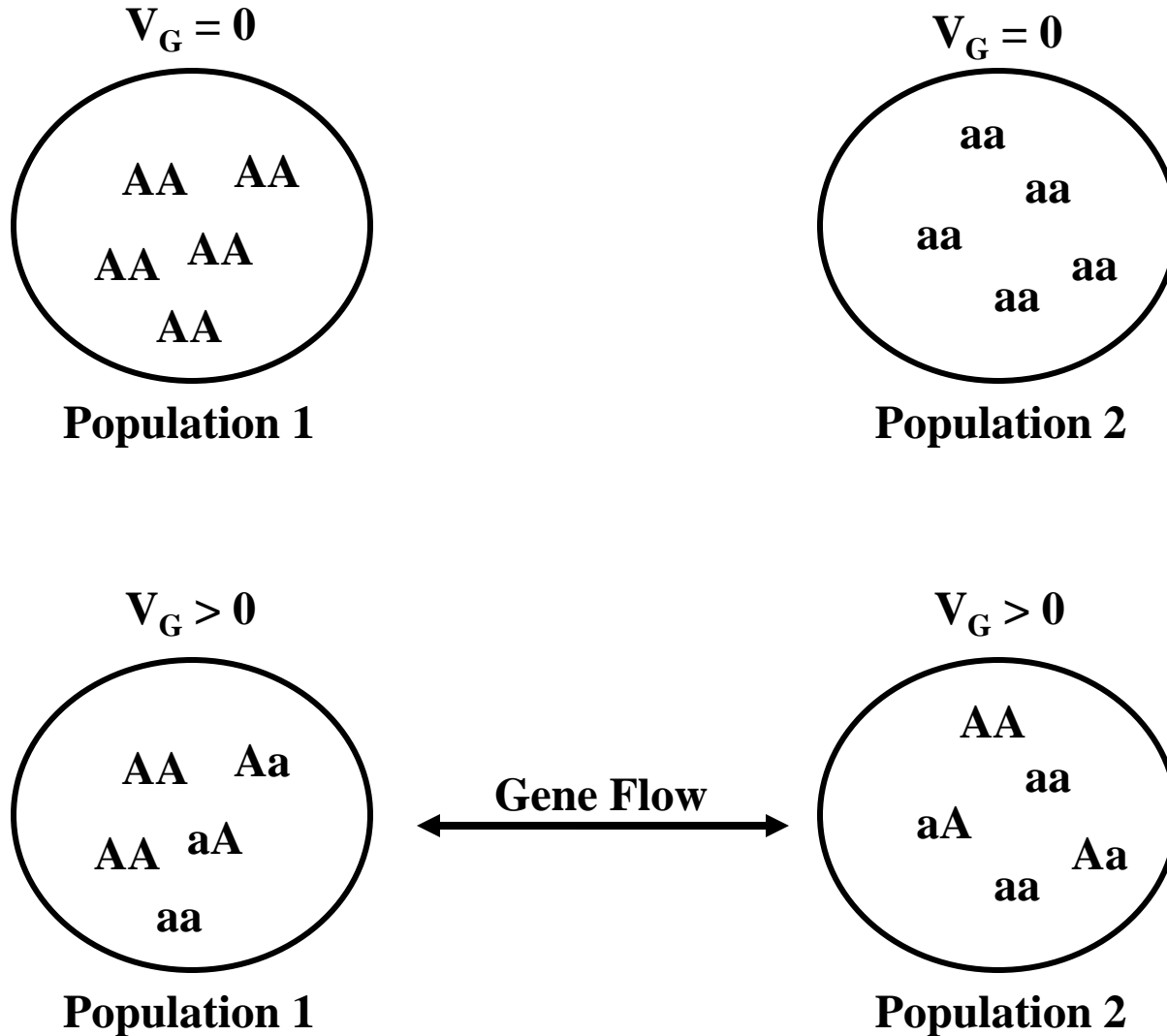
Although we know very little, we know that new mutations are generally **deleterious**

Recombination as a source of variation

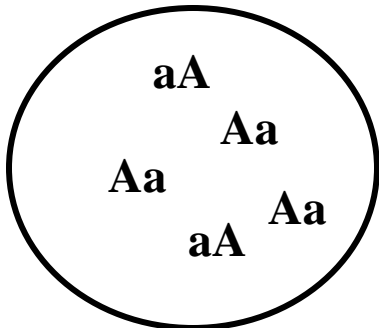
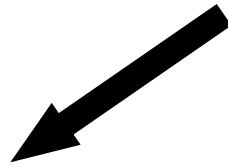
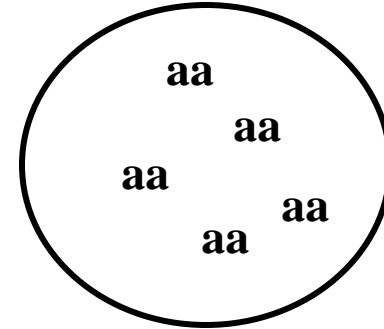
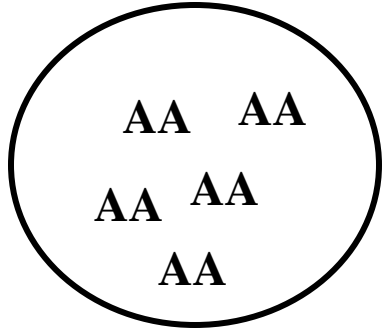


Recombination generates new COMBINATIONS of genes

Gene flow as a source of variation



Hybridization as a source of genetic variation



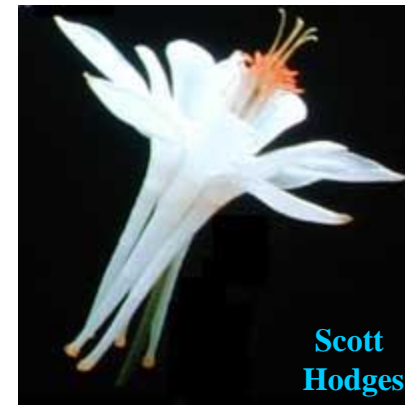
- Hybridization reshuffles genes between species
- Often has dramatic phenotypic effects
- *IF* offspring are viable and fertile, hybridization can be an important source of new genetic variation

Hybridization as a source of genetic variation



Aquilegia formosa

Lower elevations (6000-10,000 ft)



Aquilegia pubescens

High elevations (10,000-13,000 ft).

Both species grow in the Sierra Nevada mountains of California

Hybridization as a source of genetic variation



Formosa - Pubescens hybrid zone

Summary

- **There is abundant genetic variation in natural populations**
- **Mutation is the ultimate source of genetic variation**
- **Recombination, gene flow, and hybridization redistribute genetic variation**

Practice Problem

You are studying a population of Steelhead Trout and would like to know to what extent body mass is heritable. To this end, you measured the body mass of male and female Steelhead as well as the body mass of their offspring. Use the data from this experiment (below) to estimate the heritability of body mass in this population of Steelhead.

Maternal Body Mass (Kg)	Paternal Body Mass (Kg)	Average Offspring Body Mass (Kg)
2.1	2.6	2.3
2.5	2.9	2.5
1.9	3.1	2.7
2.2	2.8	2.4
1.8	2.7	2.3
2.4	2.4	2.2
2.3	2.9	2.7