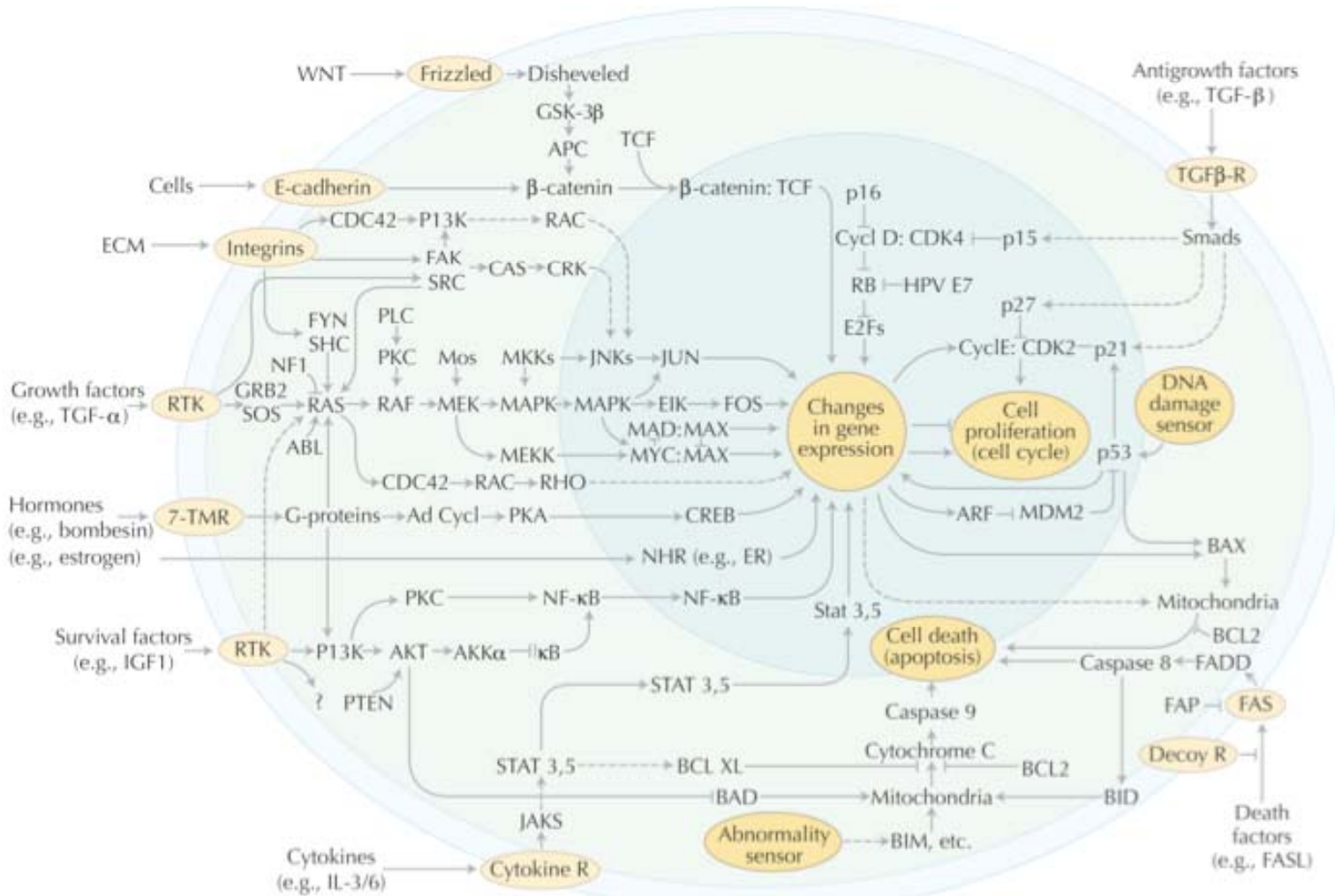
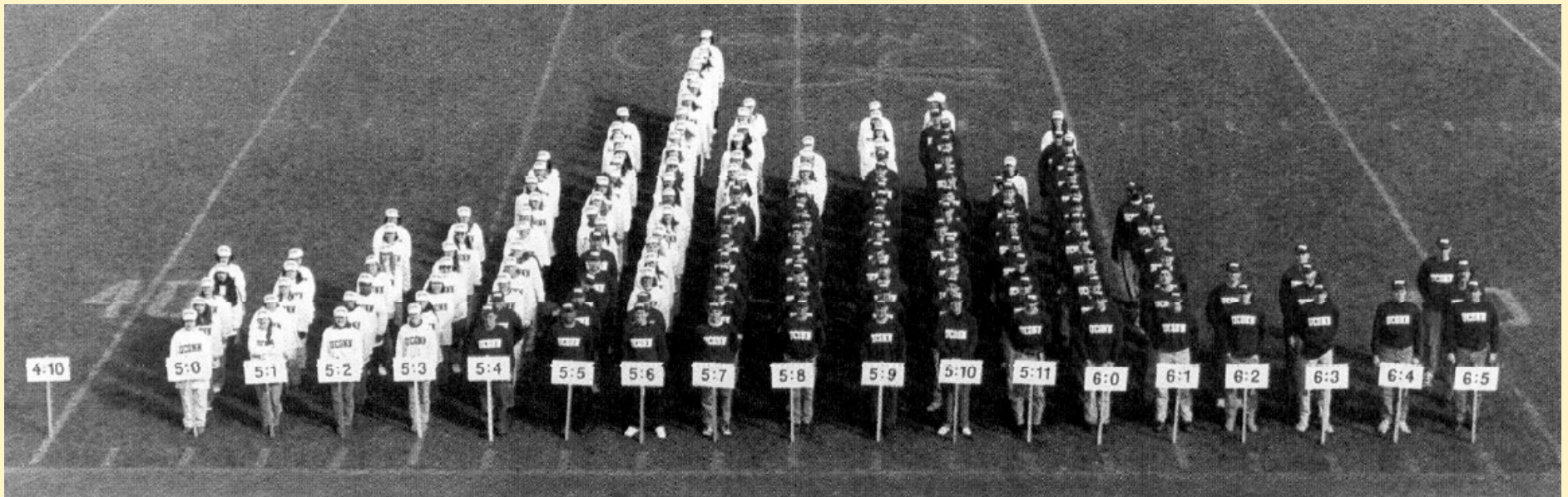


Relationship between genotype and phenotype is non-trivial



Simplified regulatory network of a eukaryotic cell

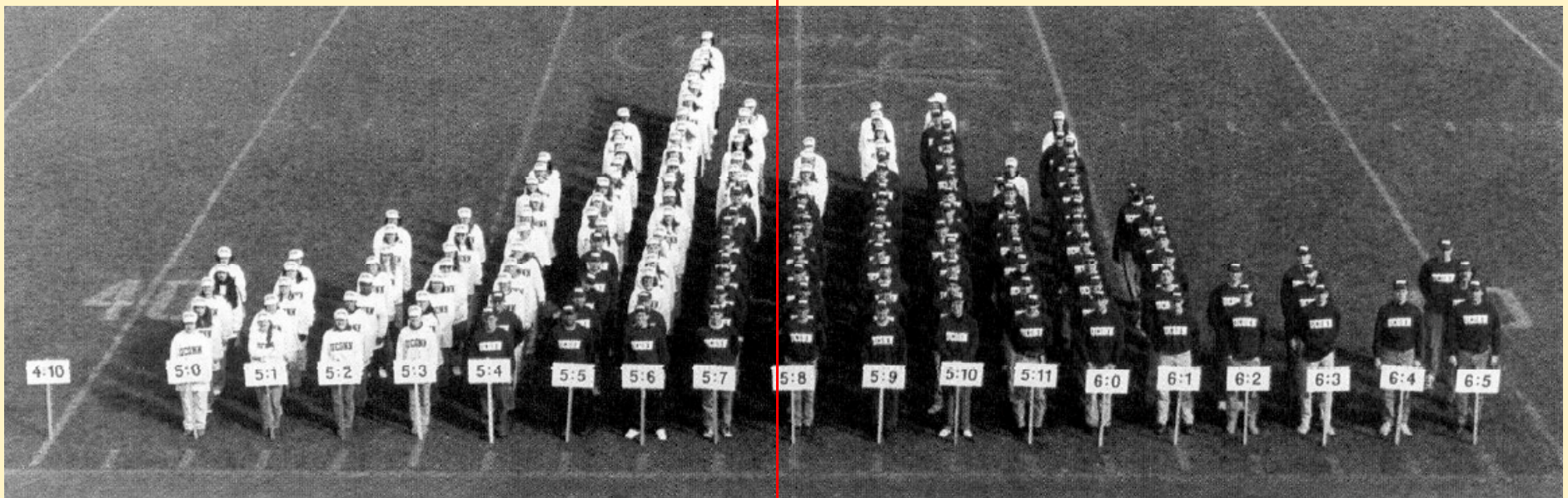
Most traits in nature show
continuous variation
= Quantitative traits



UCONN "living histogram"

The mean: a measure of central tendency

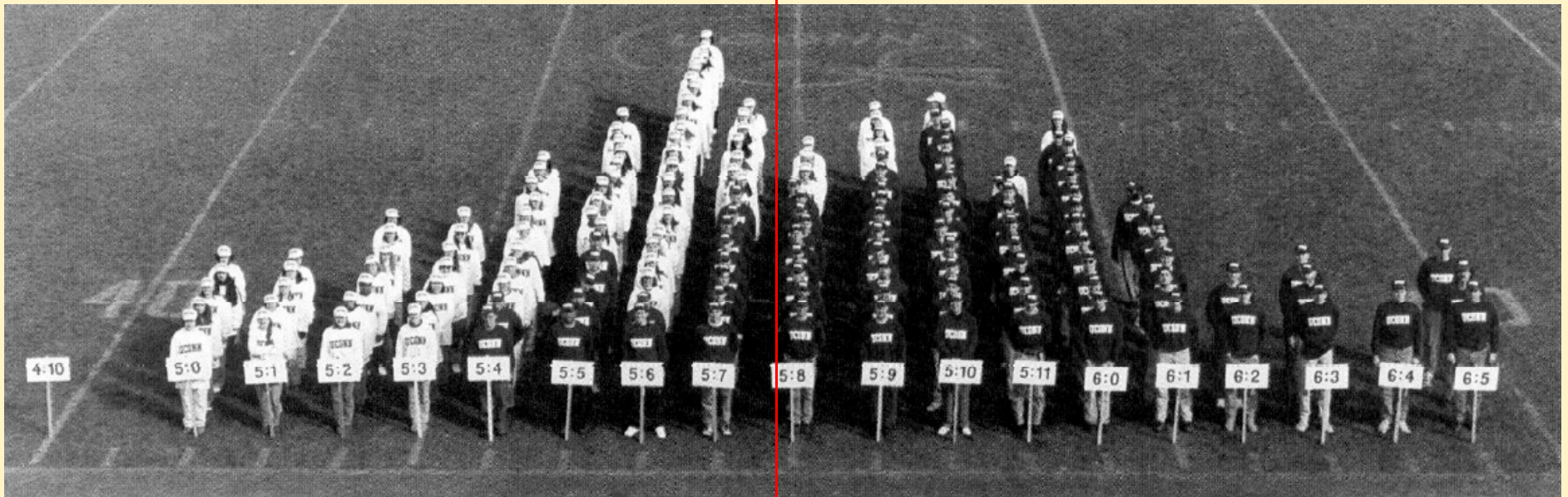
Mean



$$\text{mean} = \bar{x} = \frac{x_1 + x_2 + x_3 \cdots x_N}{N} = \frac{1}{N} \sum x_i$$

The variance measures the dispersion of the data

Mean



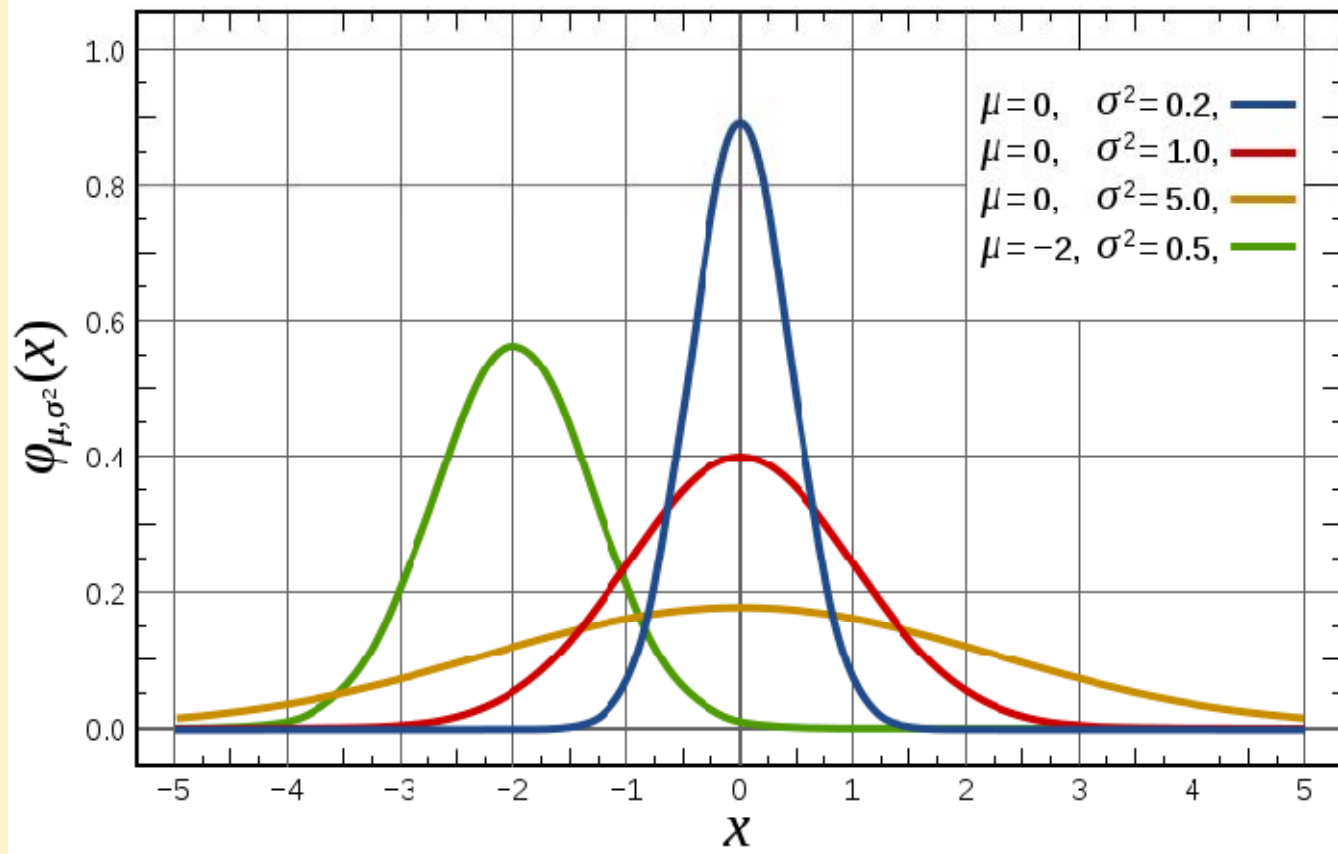
Stand. Dev.

$$\text{variance} = s^2 = \frac{(x_1 - \bar{x})^2 + (x_2 - \bar{x})^2 + (x_3 - \bar{x})^2 \cdots (x_N - \bar{x})^2}{N} = \frac{1}{N} \sum (x_i - \bar{x})^2$$

$$\text{standard deviation} = s = \sqrt{s^2}$$

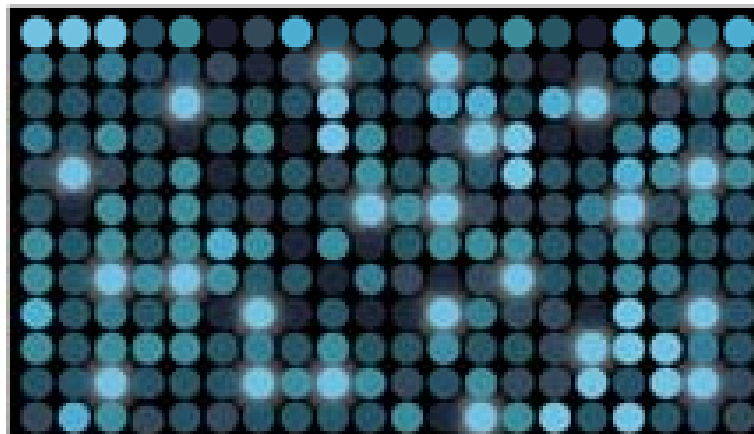
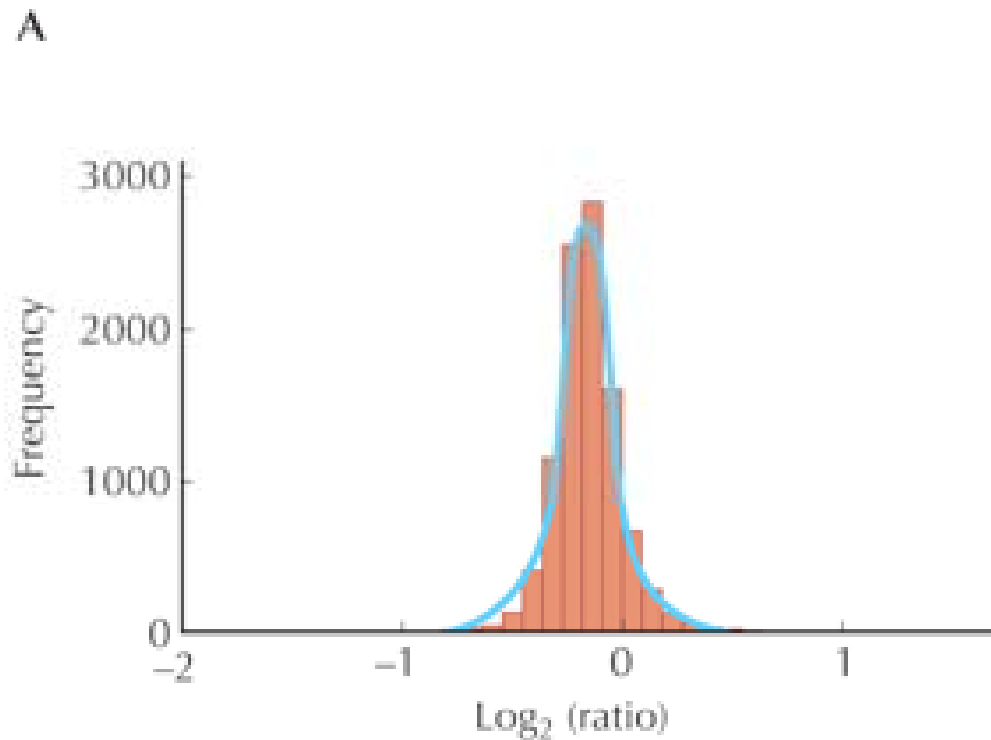
Normal distribution is a convenient way to describe natural variation

Probability mass function



$\mu = \text{mean}$

$\sigma^2 = \text{variance}$



Many observed distributions of quantitative traits approximate the normal

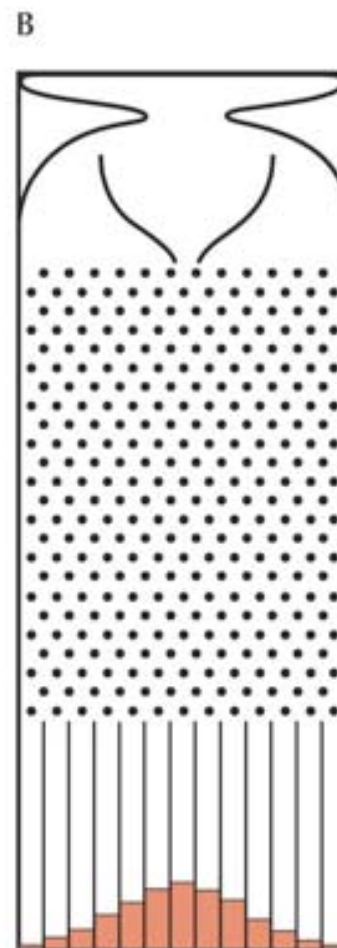
If sample size is large:
“Central limit theorem”

Conditions leading to a normal distribution:

- Underlying processes are *random*
- There are many different *independent* processes
- Outcomes of different processes are *additive* (=they simply sum up, no complex interaction)

Galton's quincunx

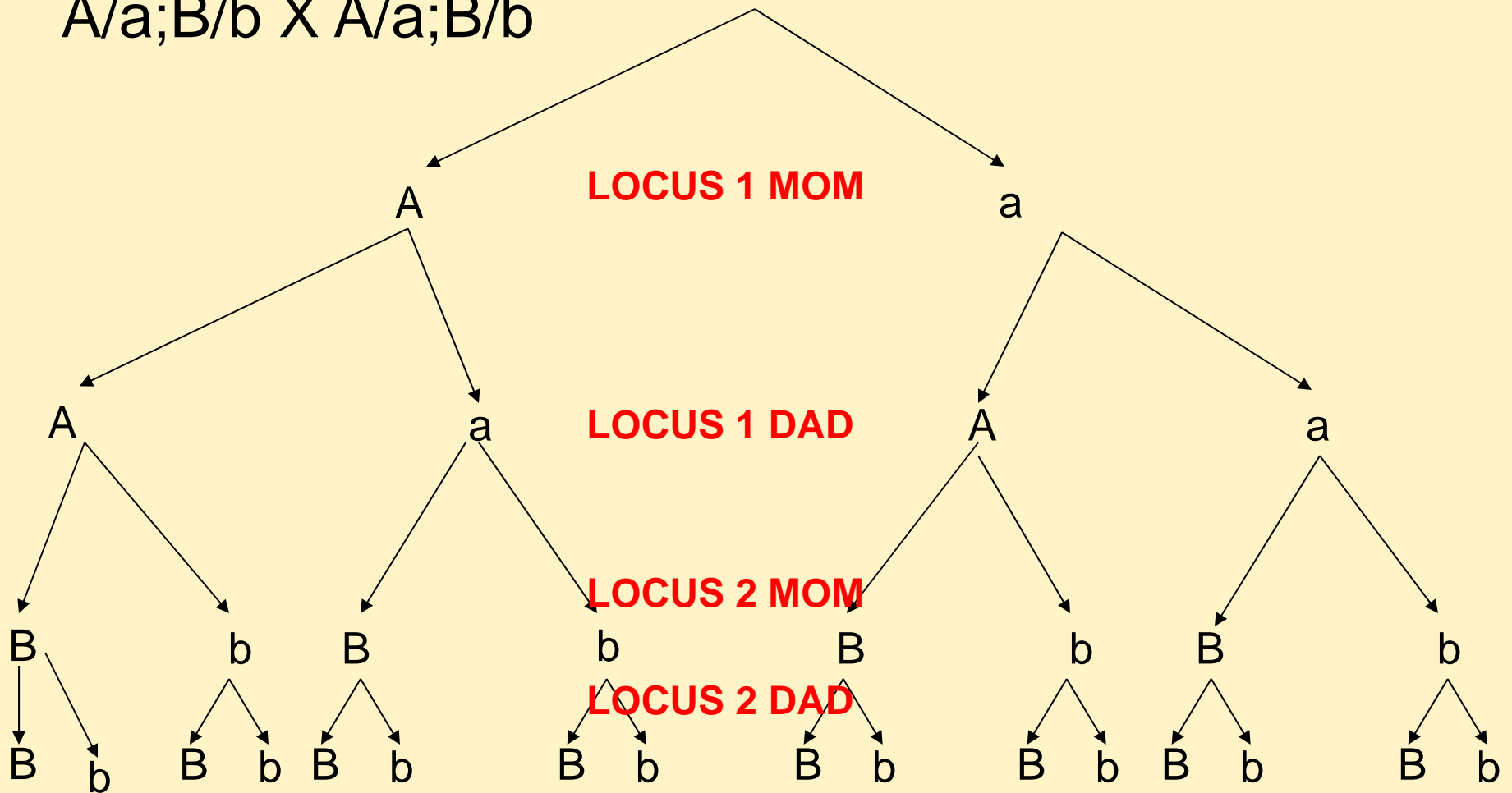
- <http://www.jcu.edu/math/iseq/quincunx/quincunx.html>



Instrument to illustrate
the principle of the
Law of Error or Dispersion,
by
Francis Galton 1868.

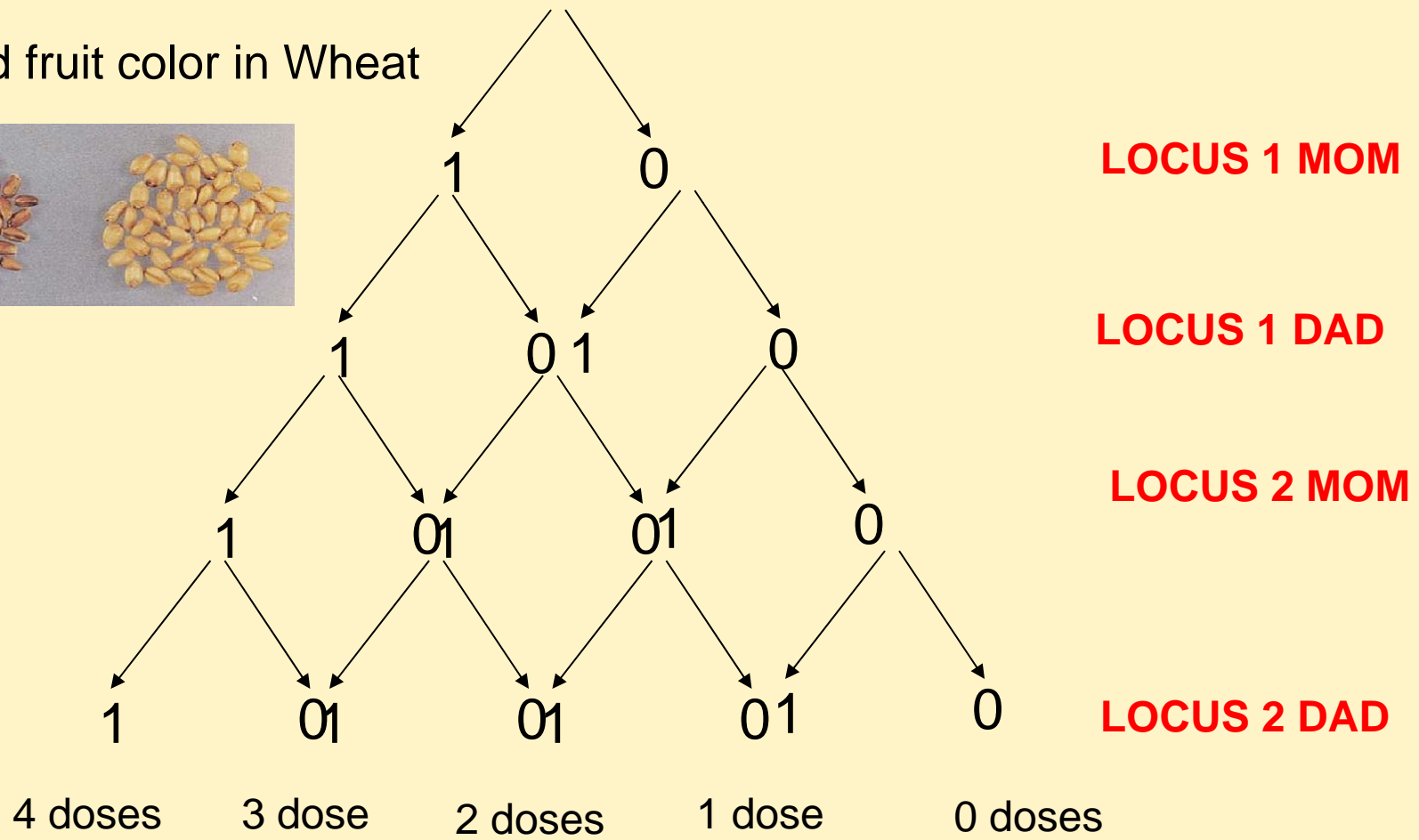
Resemblance to a multi-hybrid cross?

$A/a;B/b \times A/a;B/b$



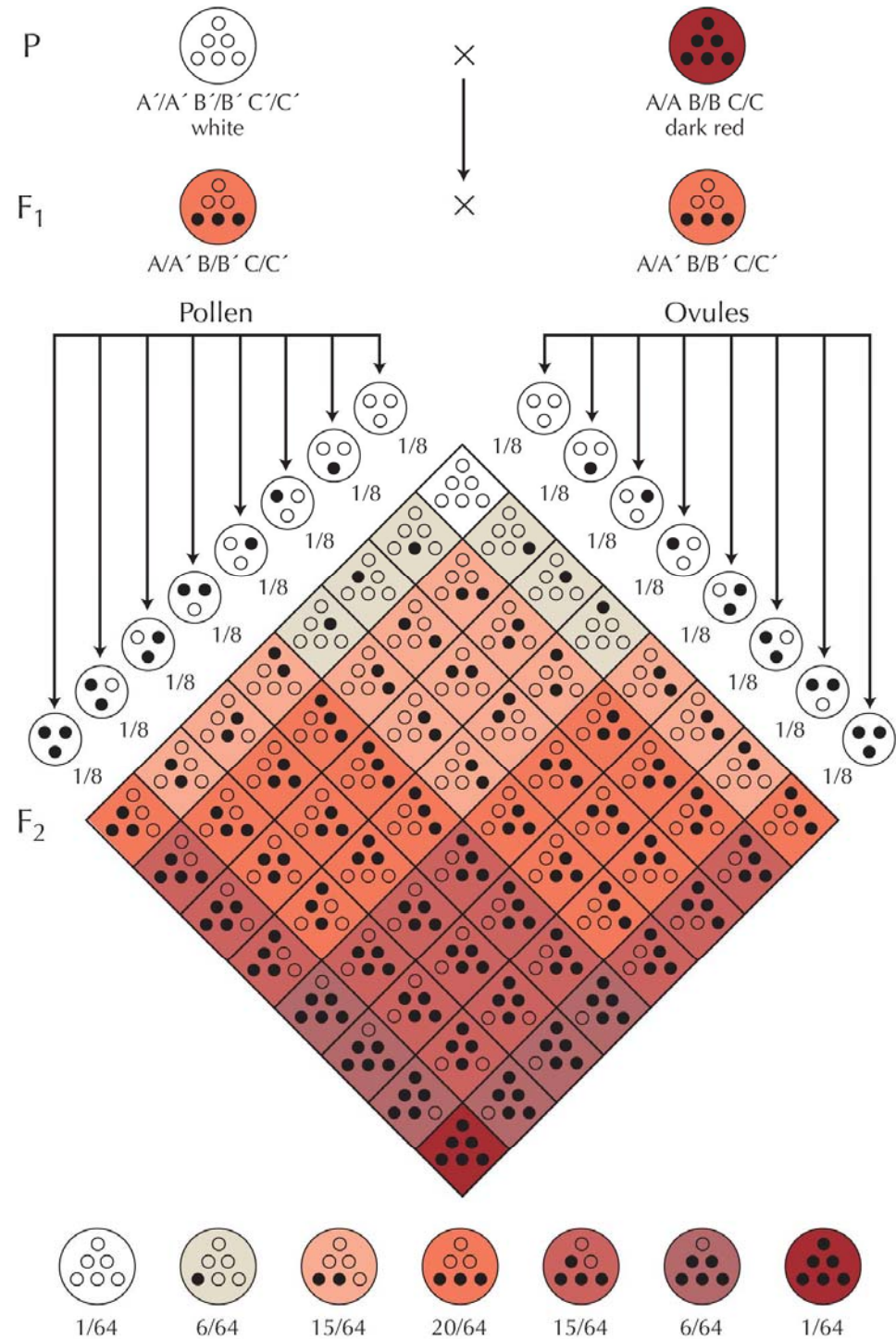
Direct correspondence to a multi-hybrid cross with additive alleles

E.g. Red fruit color in Wheat



Tri-hybrid cross

Fruit color in wheat



Randomly segregating polygenes will produce normal distributions

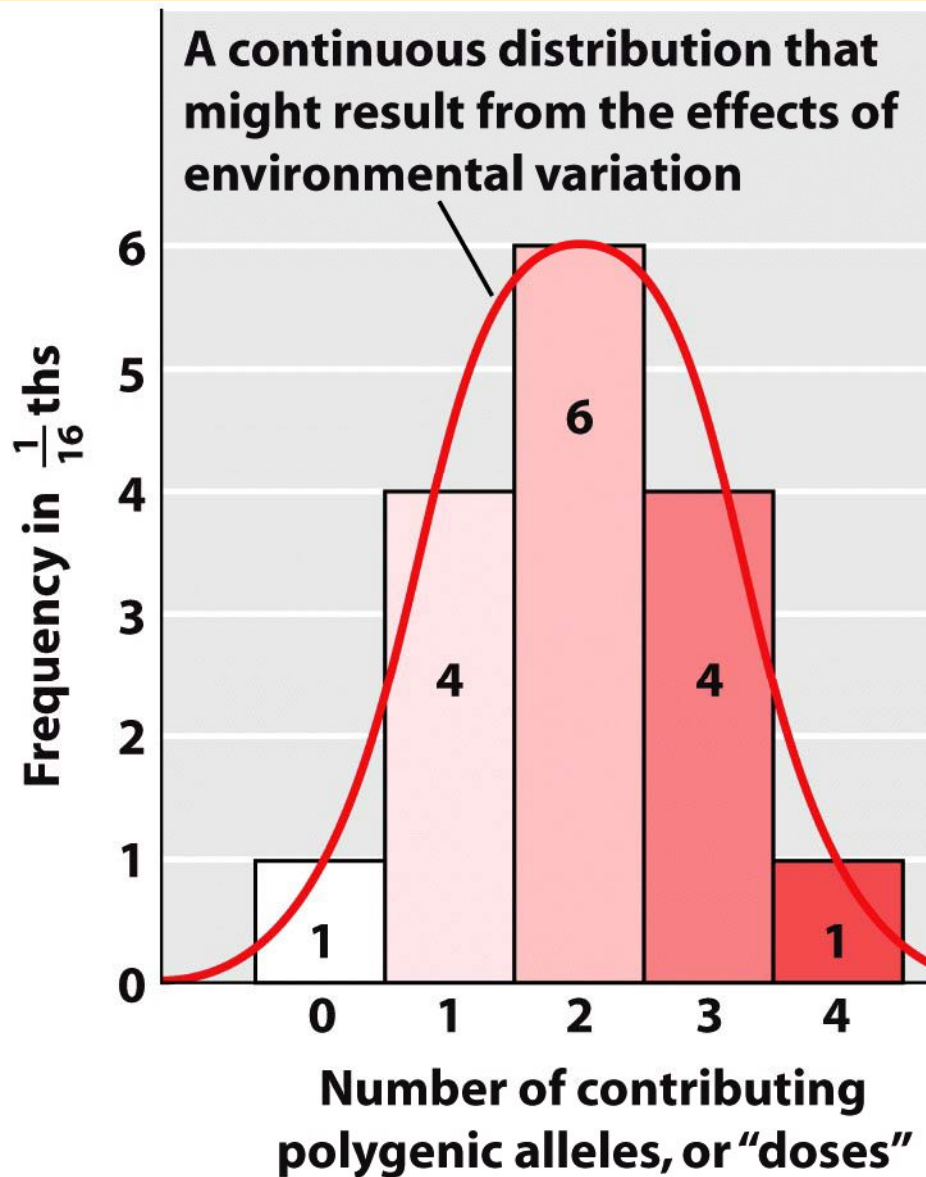


Figure 3-16
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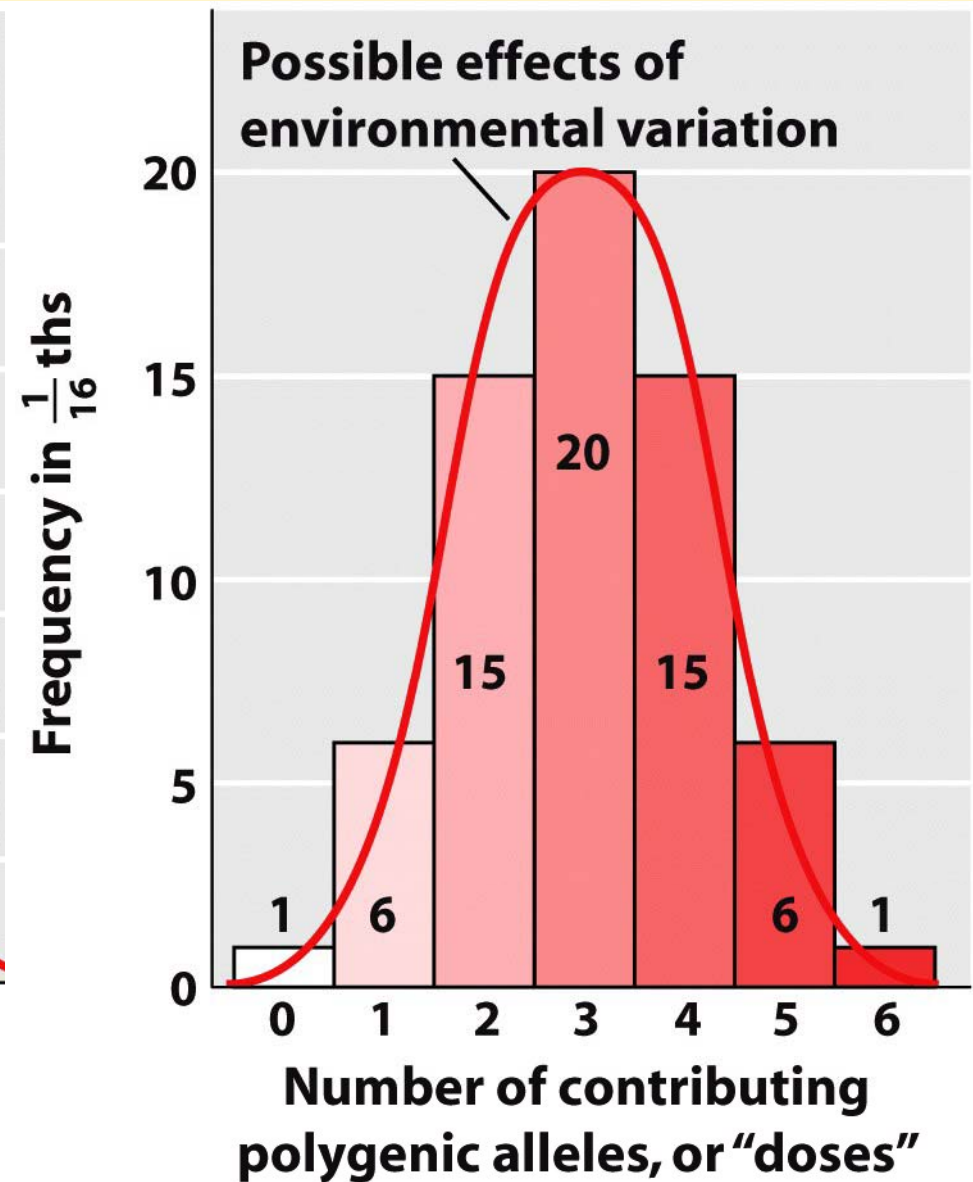
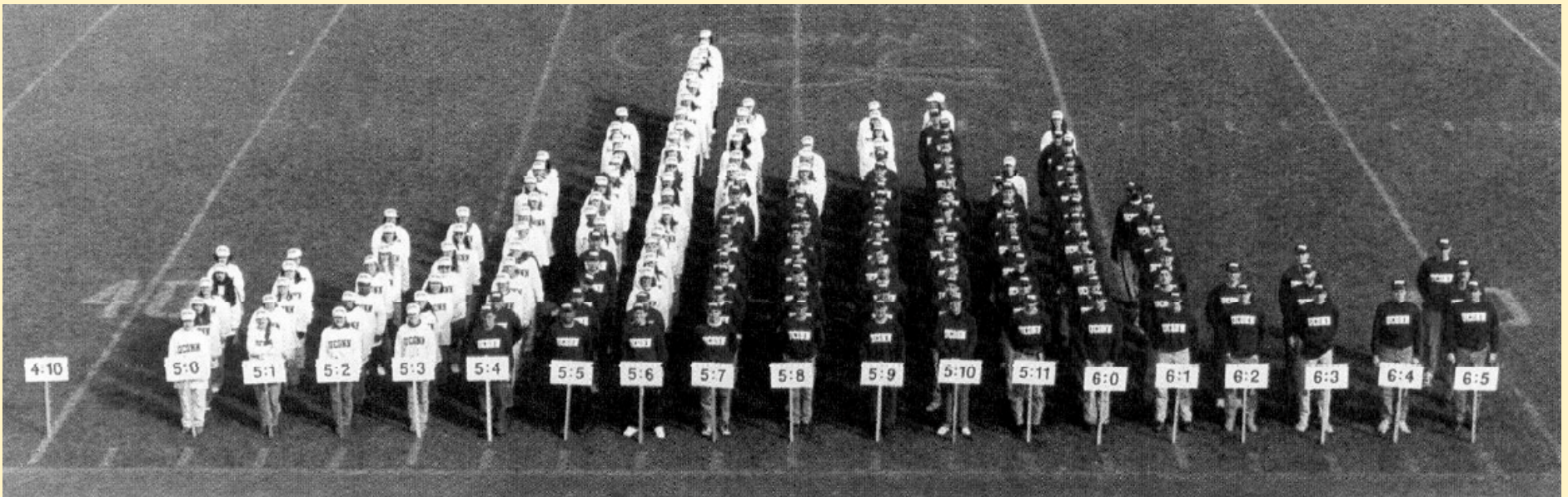


Figure 3-17
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Does this explain all observed normal distributions?



- What factors determine body height in humans?

Quantitative genetics

- Describes variation
- Partitions variation into genetic and non-genetic contributions
- Asks how many and what genes underlie a quantitative trait

A model of additive variation

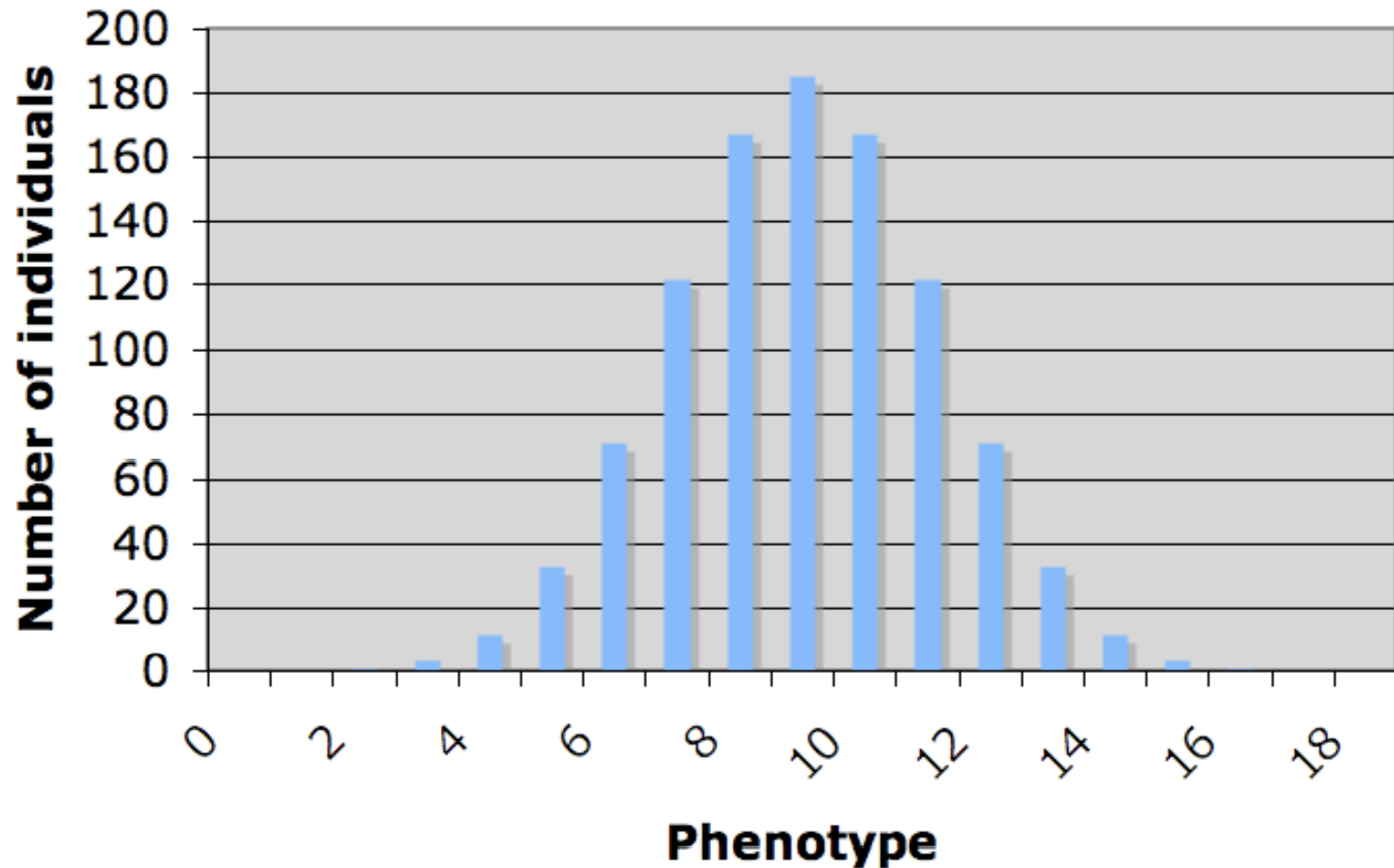
Homologous chromosome

Locus

	1	2	3	4	5	6	7	8	9
Mom's	+	+	-	+	+	-	+	-	+
Dad's	-	-	-	+	-	+	+	-	-

- The phenotype is simply the sum of all +
- In this case 9
- How many potential phenotypes are there?

Each phenotype can have multiple underlying genotypes with the same number of additive doses



- But if mating is random we expect this distribution of phenotypes

E.g. phenotype 12

	1	2	3	4	5	6	7	8	9
Mom's	+	+	+	+	+	-	+	+	+
Dad's	-	-	+	+	-	+	+	-	-

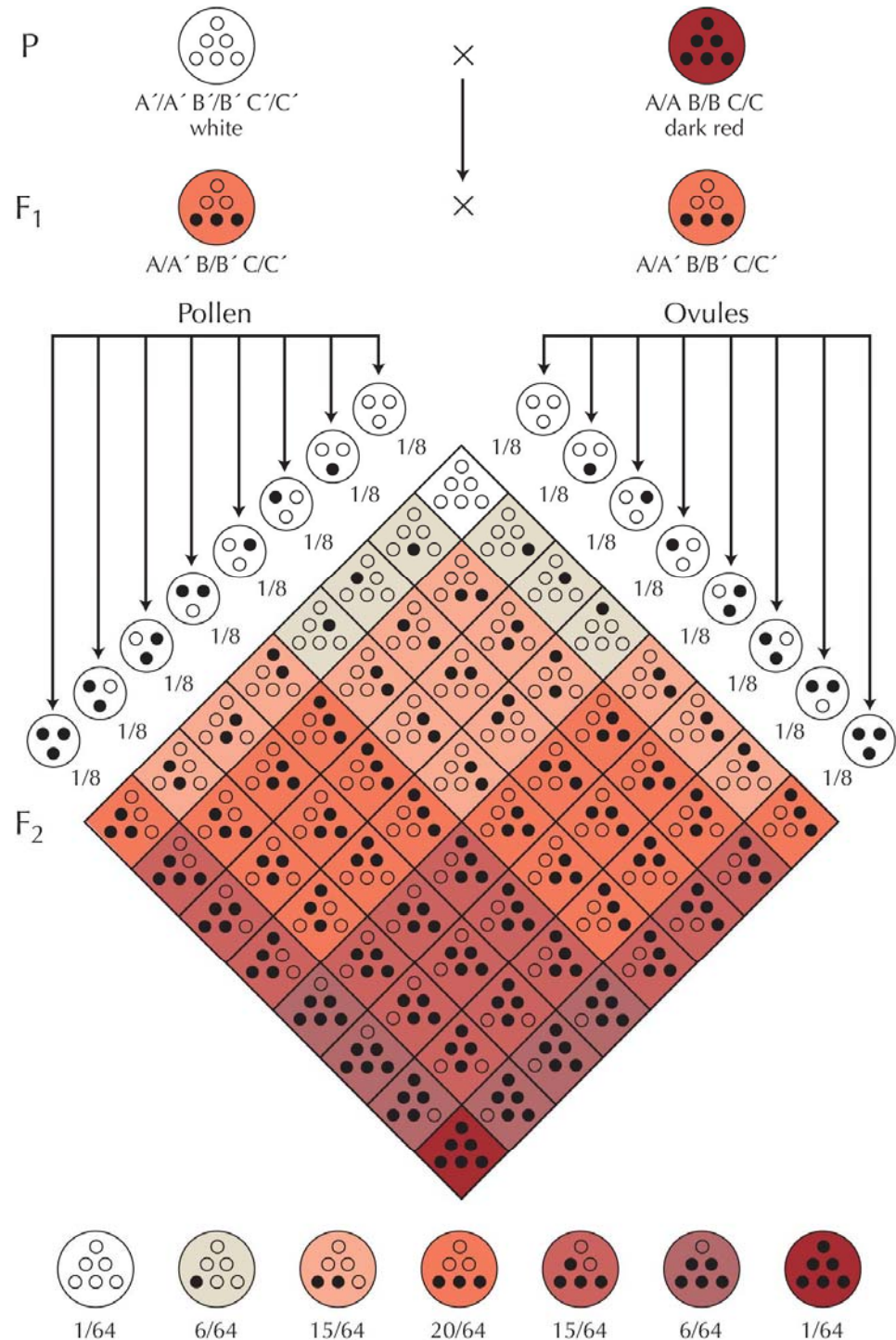
	1	2	3	4	5	6	7	8	9
Mom's	+	+	-	+	+	-	+	+	+
Dad's	-	+	+	+	-	-	+	+	-

	1	2	3	4	5	6	7	8	9
Mom's	-	-	+	+	+	+	+	+	-
Dad's	-	-	+	+	+	+	+	+	-

Etc., etc...

Each mating
between
individuals is a
multi-hybrid
cross

Example of tri-hybrid
cross



Individuals of phenotype 12 can have offspring with different phenotypic values

	1	2	3	4	5	6	7	8	9
Mom's	+	+	+	+	+	-	+	+	+
Dad's	-	-	+	+	-	+	+	-	-

X

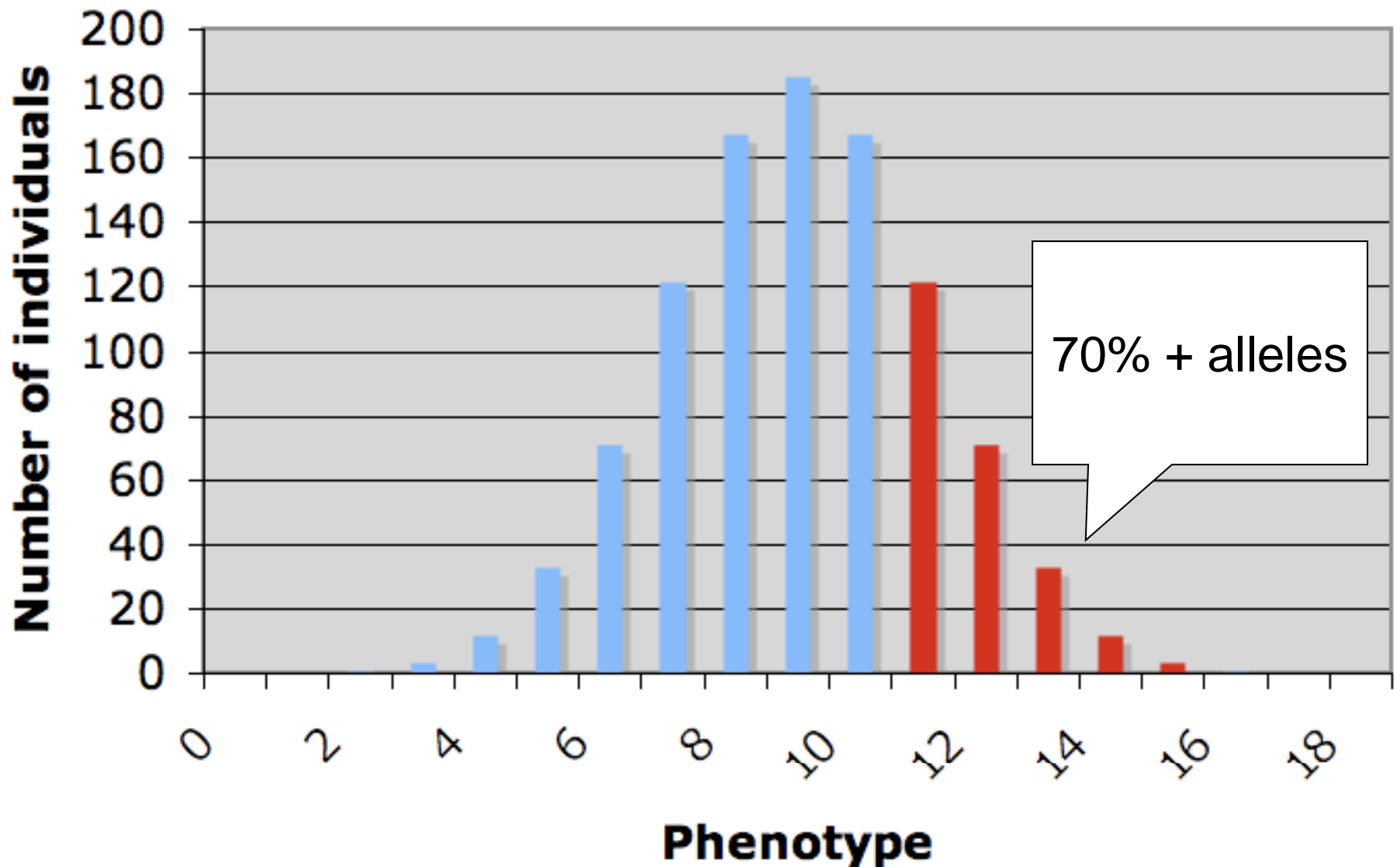
	1	2	3	4	5	6	7	8	9
Mom's	+	+	-	+	+	-	+	+	+
Dad's	-	+	+	+	-	-	+	+	-



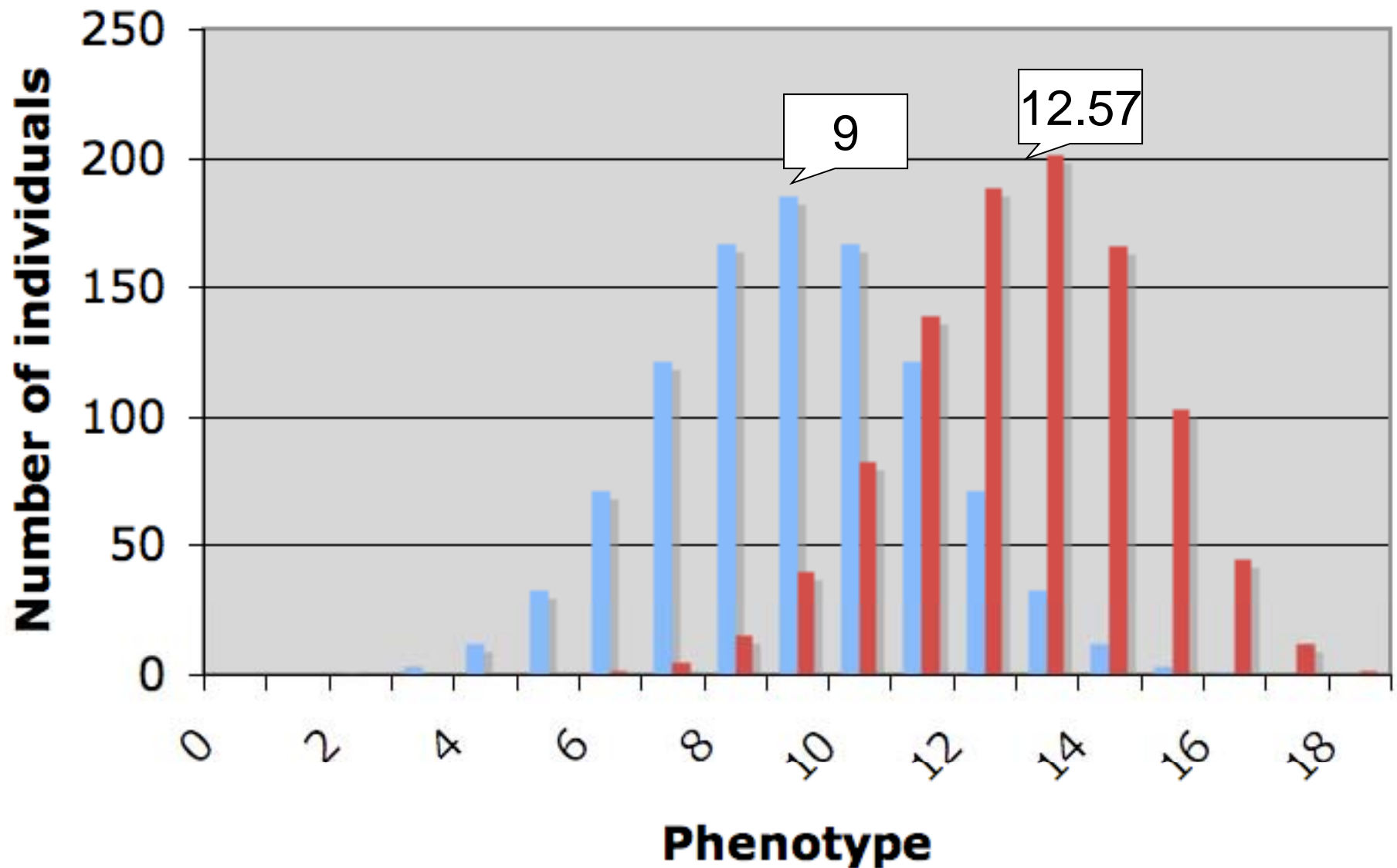
	1	2	3	4	5	6	7	8	9
Mom's	-	+	-	+	-	-	+	+	+
Dad's	-	-	+	+	-	-	+	+	-

Phenotype 9

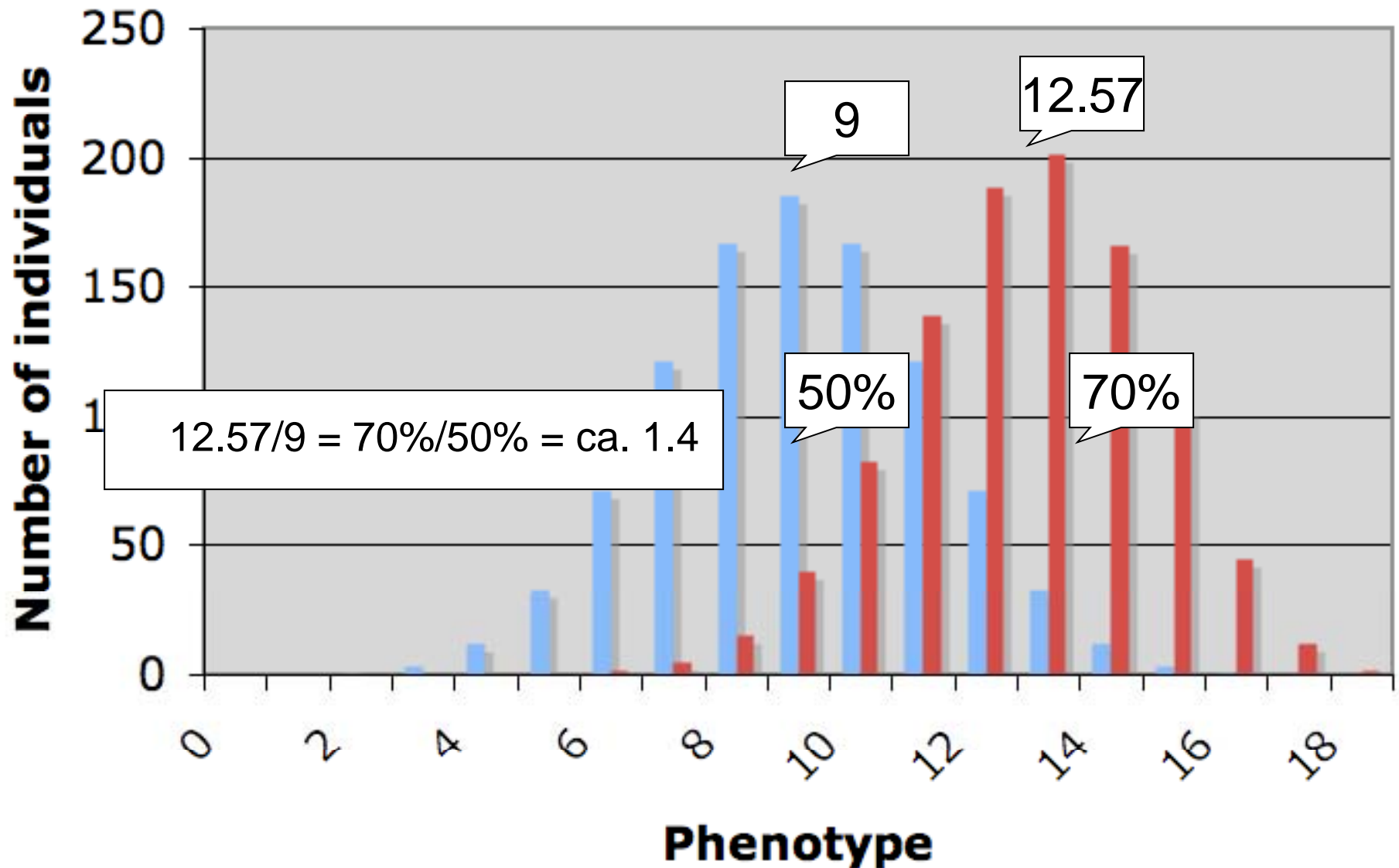
Select phenotype ≥ 12 (i.e. only individuals that breed)



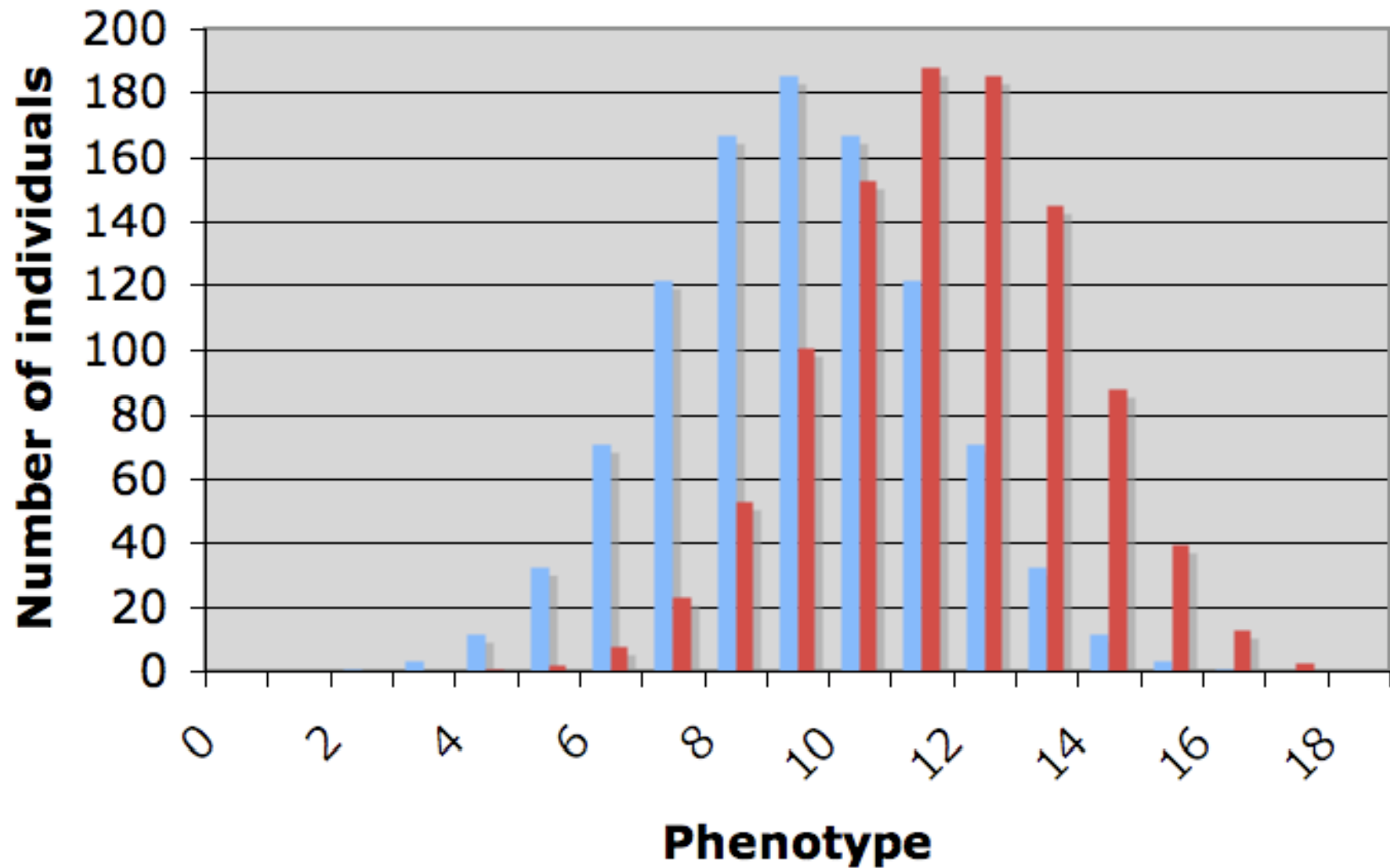
The mean of the population has shifted in the next generation



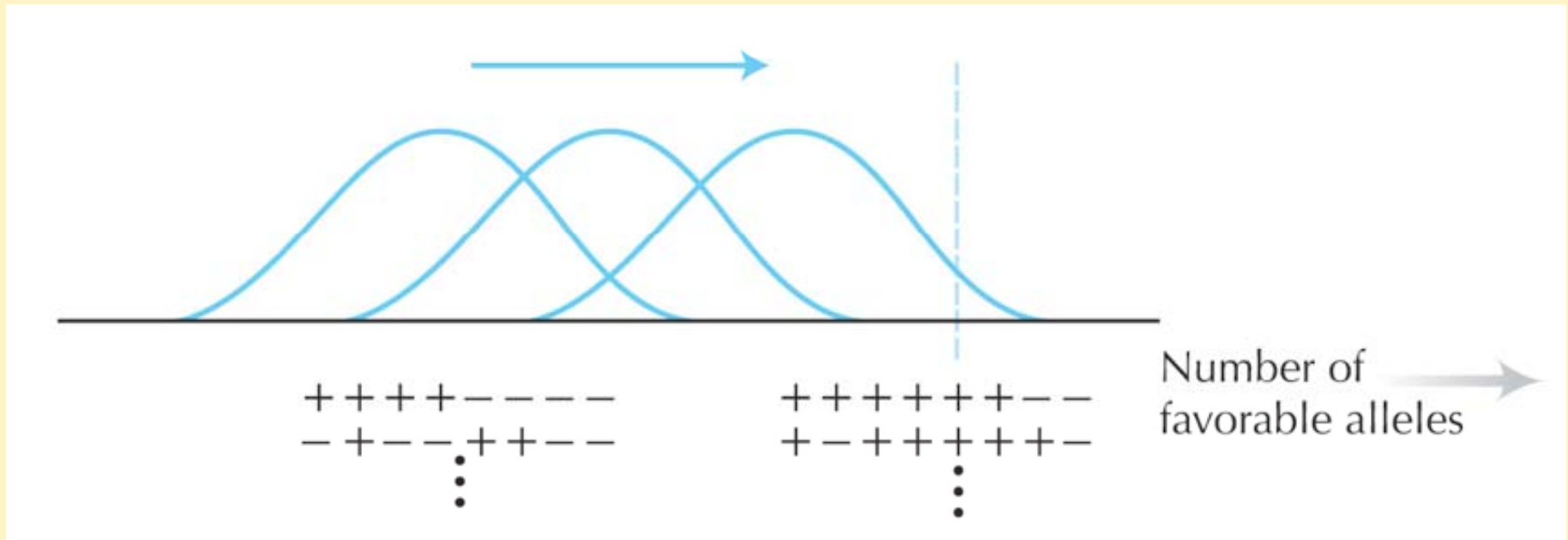
The shift in the population proportion of + has been completely converted into an equivalent change of the mean



What may be the reason for incomplete conversion?



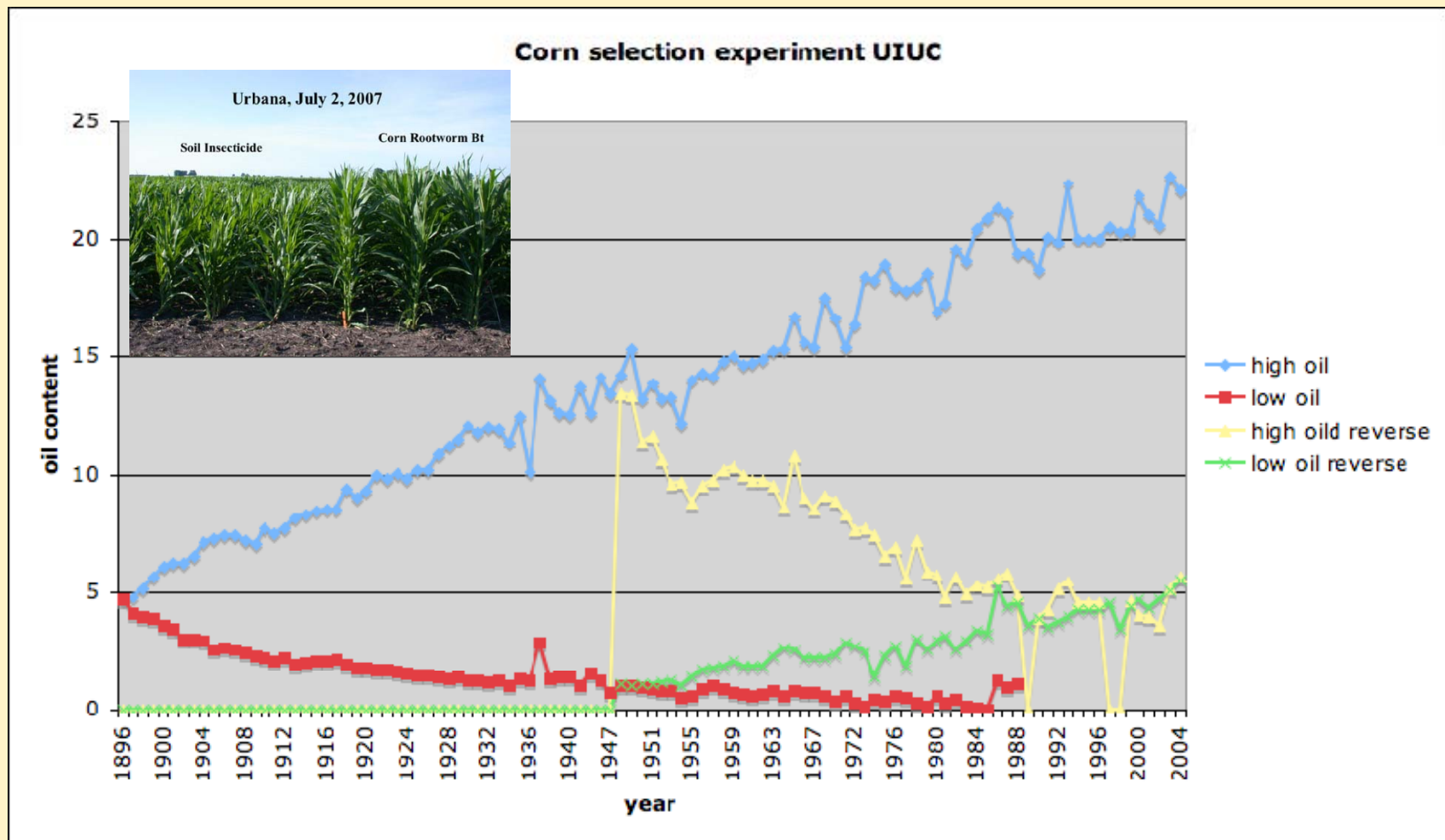
Directional Selection is shifting the mean of a trait distribution



- + = favorable alleles

Quantitative genetics can describe to what degree a trait responds to selection

Selecting for oil content in corn

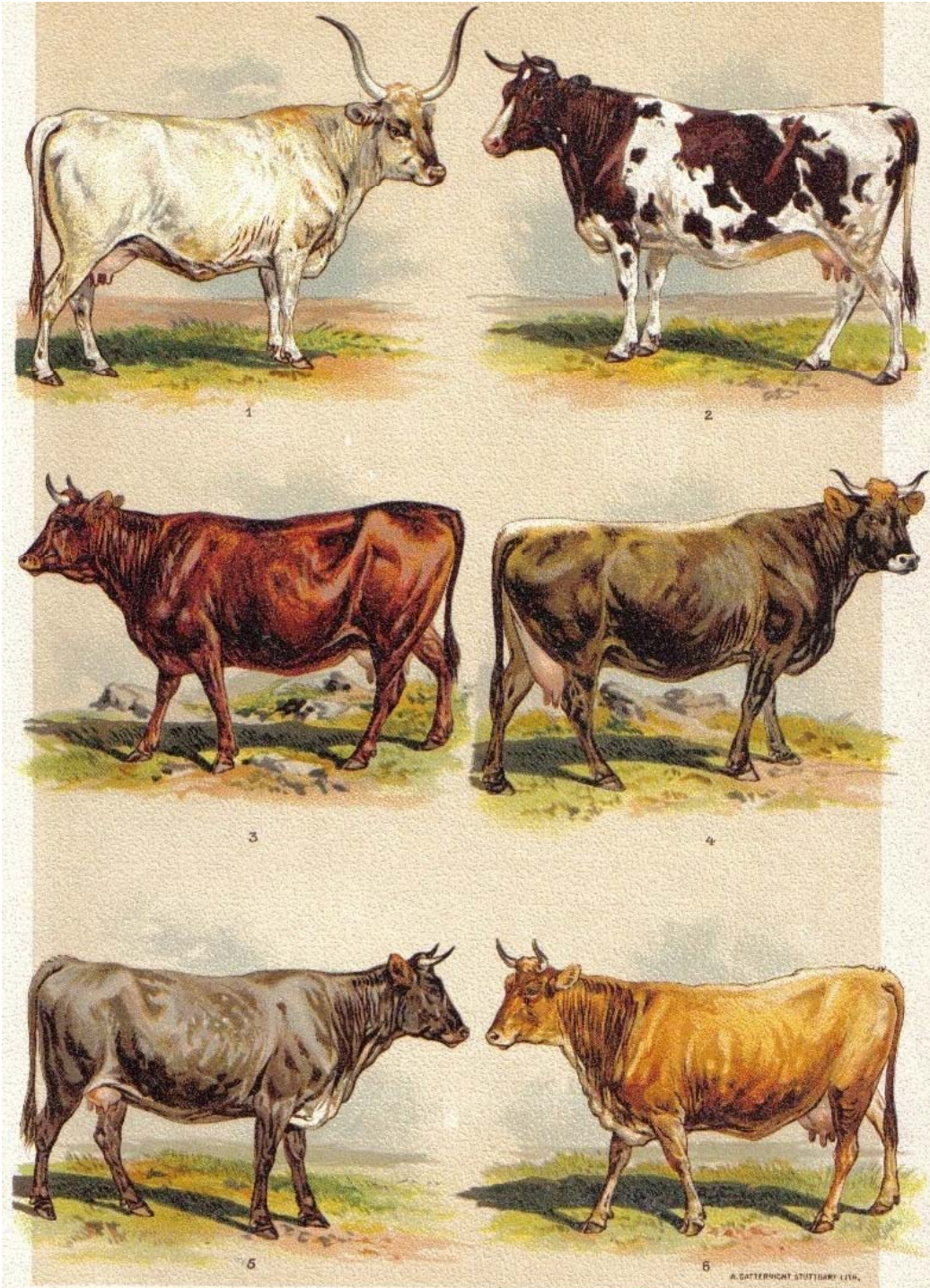


“Recreating” extinct species



Aurochs (*Bos primigenius*)

Last one killed in 1627



Is the
Aurochs still
around?

Crosses and breeding of domestic cattle produced the Heck cattle



Why could the phenotype of the Aurochs be recreated?

Was the Aurochs resurrected?

How can this example inform our understanding of natural evolution?

Impact of the environment

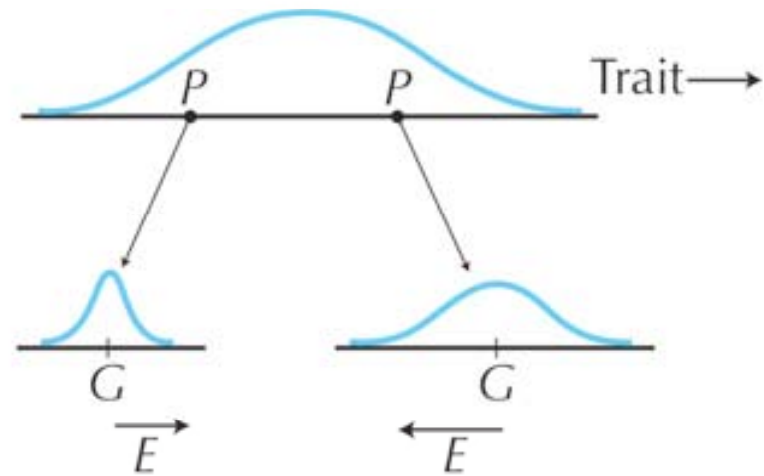
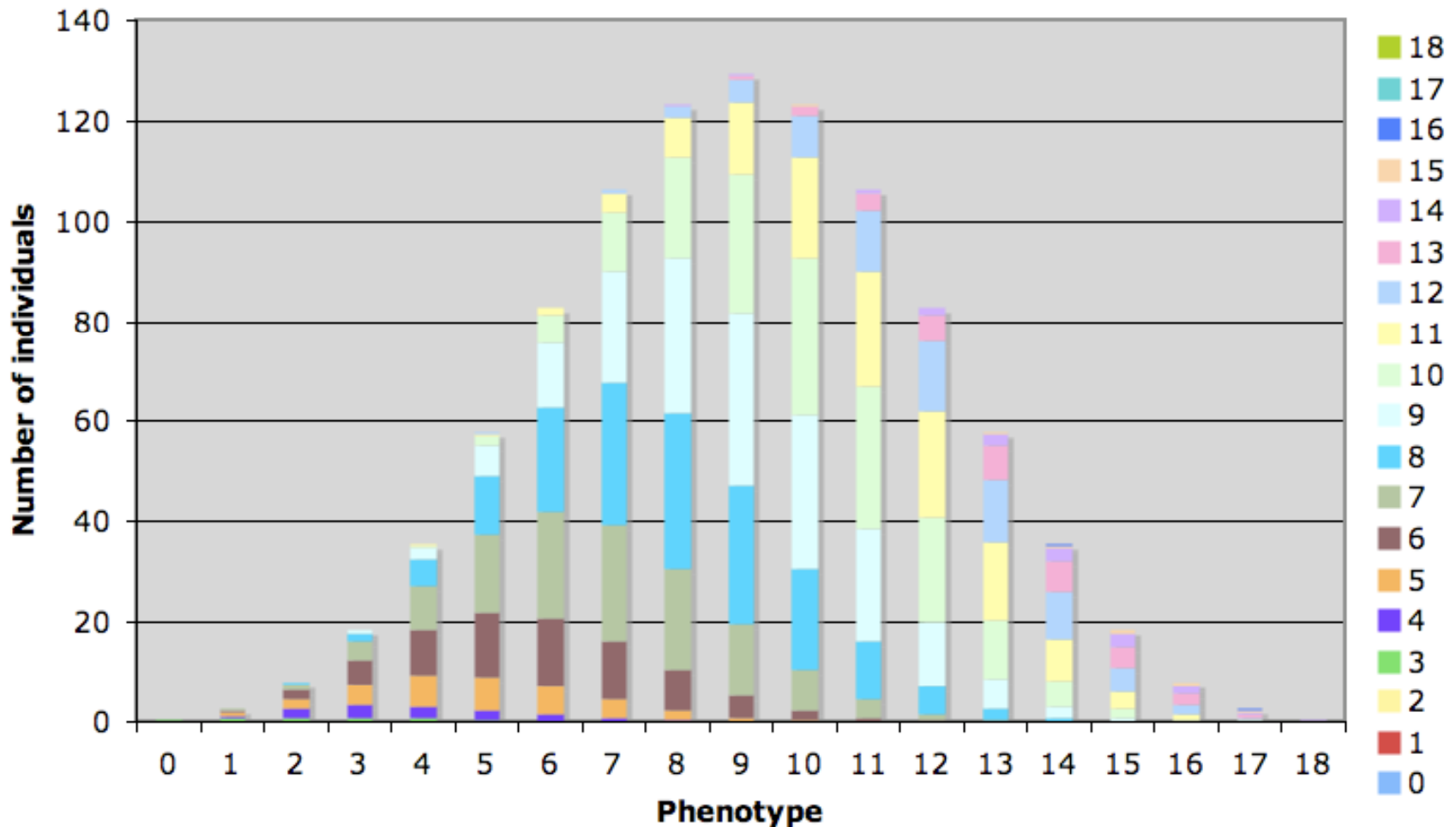


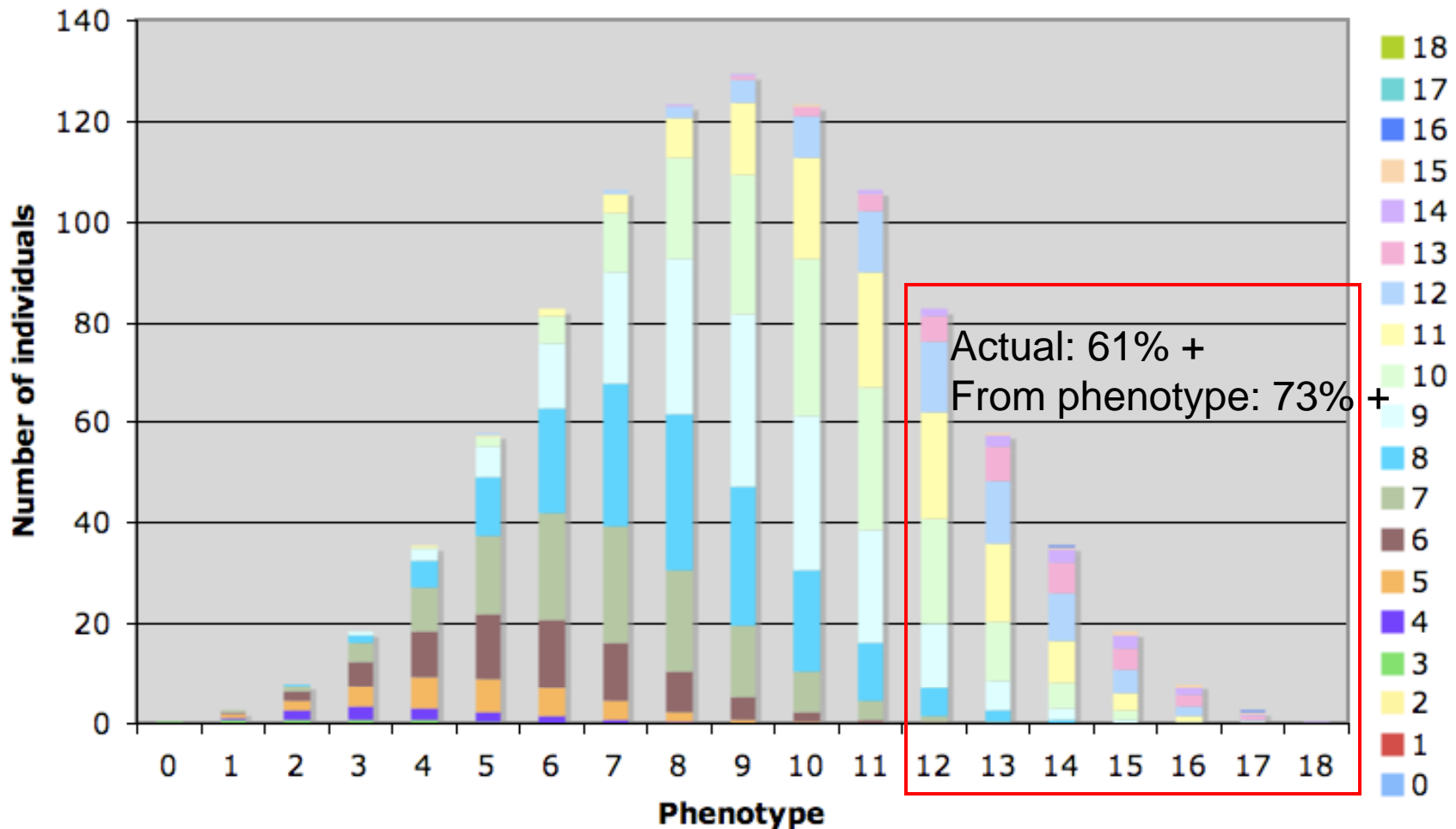
FIGURE 14.6. An individual's phenotype can be separated into a genotypic and an environmental component: $P = G + E$. The *curve at the top* shows the distribution of phenotype in the whole population. If we take any one individual and rear very many genetically identical copies, these will have a distribution (*lower curves*). The mean is the genotypic value G and the difference between this and the actual phenotypic value P is the environmental deviation E .

Including the environment in our model



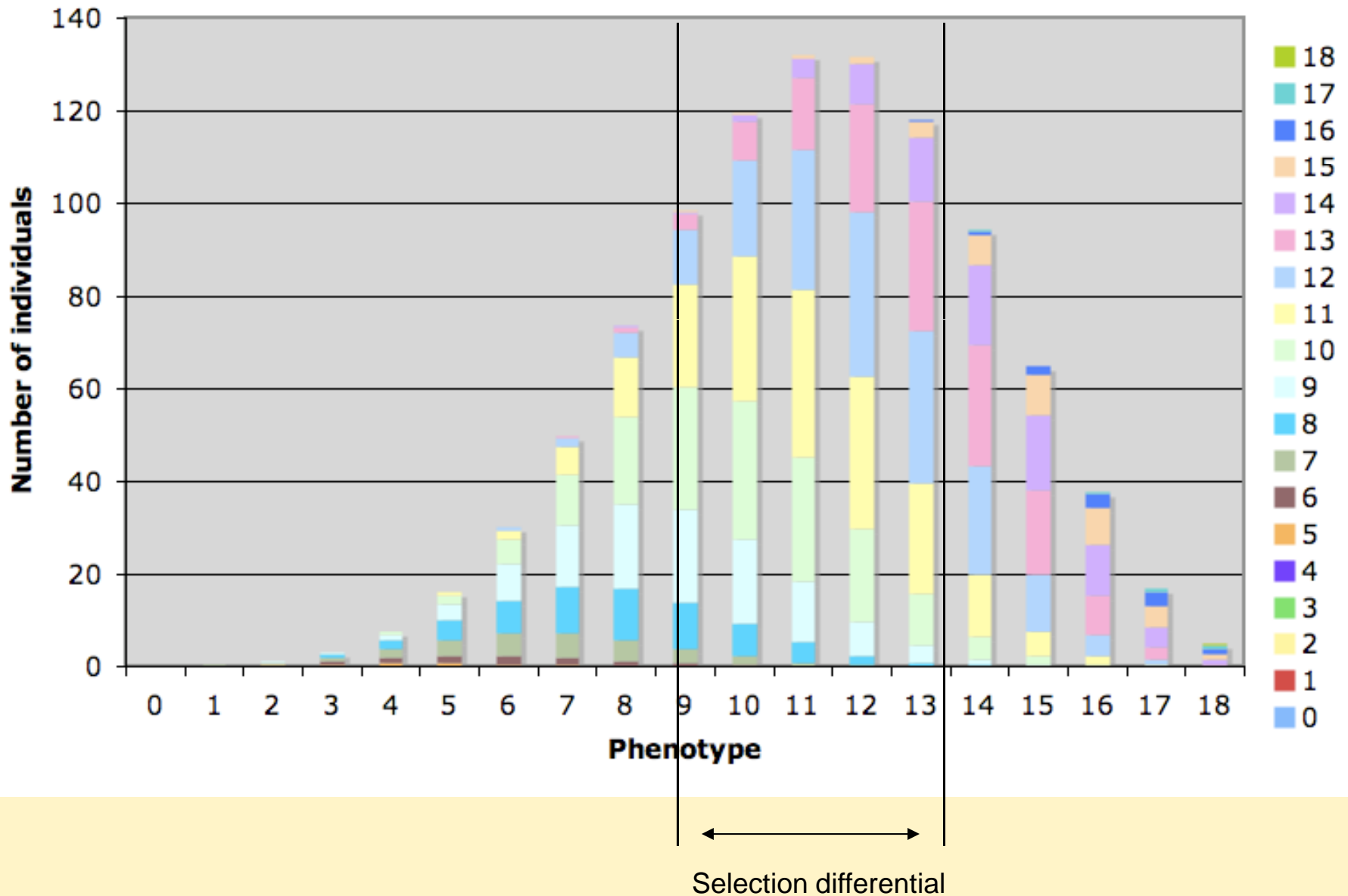
- There is an environmental error when converting doses into phenotype

Genotypes with different doses underlie each phenotype

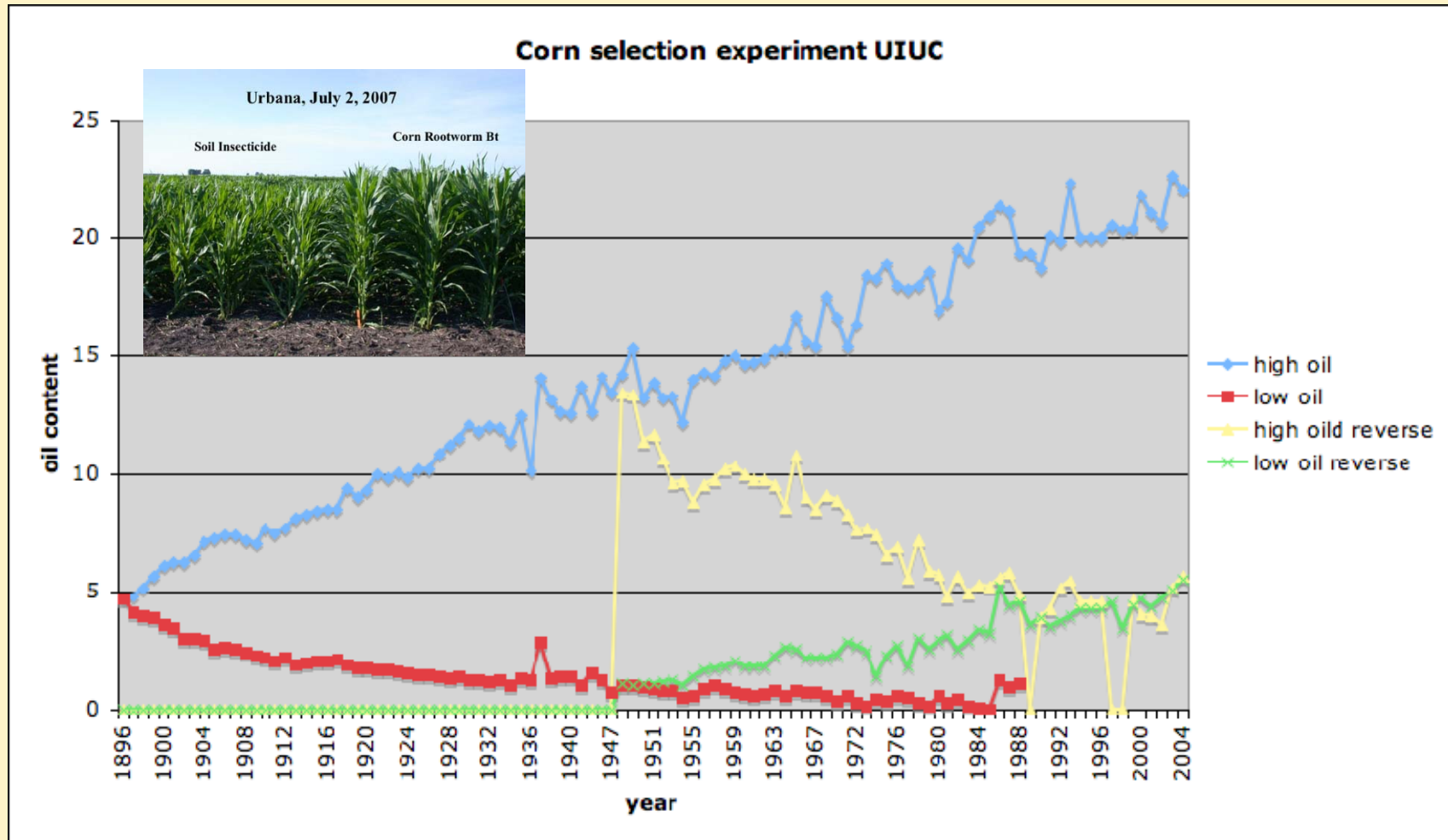


- When selecting individuals the allele frequency will be different from what could be expected from the phenotypes

The selective shift is not fully realized



Heritability provides information on the potential for artificial selection



Using variances

$$V_X = V_g + V_e$$

Total phenotypic variance = Genetic variance + Environmental variance

What fundamental assumption do we make about the relationship of genetics and environment?

What consequences does this have for experimental design?

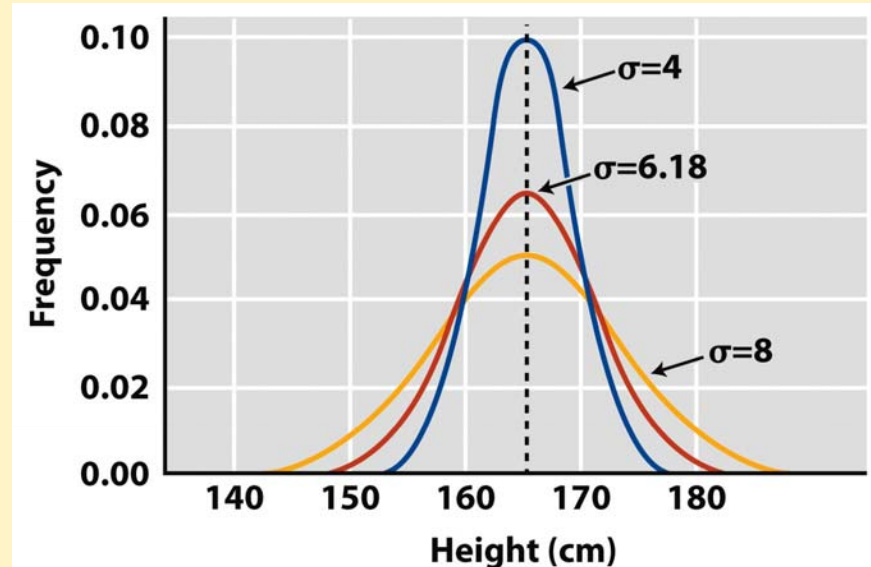


Figure 19-2c
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Heritability (broad-sense)

$$H^2 = \frac{V_g}{V_X} = \frac{V_g}{V_g + V_e}$$

Heritability is the proportion of the total phenotypic variance that is explained by genetic factors.

Table 19-4 Broad-Sense Heritability for Some Traits in Humans as Determined by Twin Studies

Trait	H^2
Physical attributes	
Height	0.88
Chest circumference	0.61
Waist circumference	0.25
Fingerprint ridge count	0.97
Systolic blood pressure	0.64
Heart rate	0.49
Mental attributes	
IQ	0.69
Speed of spatial processing	0.36
Speed of information acquisition	0.20
Speed of information processing	0.56
Personality attributes	
Extraversion	0.54
Conscientiousness	0.49
Neuroticism	0.48
Positive emotionality	0.50
Antisocial behavior in adults	0.41
Psychiatric disorders	
Autism	0.90
Schizophrenia	0.80
Major depression	0.37
Anxiety disorder	0.30
Alcoholism	0.50–0.60
Beliefs and political attitudes	
Religiosity among adults	0.30–0.45
Conservatism among adults	0.45–0.65
Views of school prayer	0.41
Views on pacifism	0.38

Sources: J. R. Alford et al., *American Political Science Review* 99, 2005, 1–15; T. Bouchard et al., *Science* 250, 1990, 223–228; T. Bouchard, *Curr. Dir. Psych. Sci.* 13, 2004, 148–151; P. J. Clark, *Am. J. Hum. Genet.* 7, 1956, 49–54; C. M. Freitag, *Mol. Psychiatry* 12, 2007, 2–22.

Table 19-4

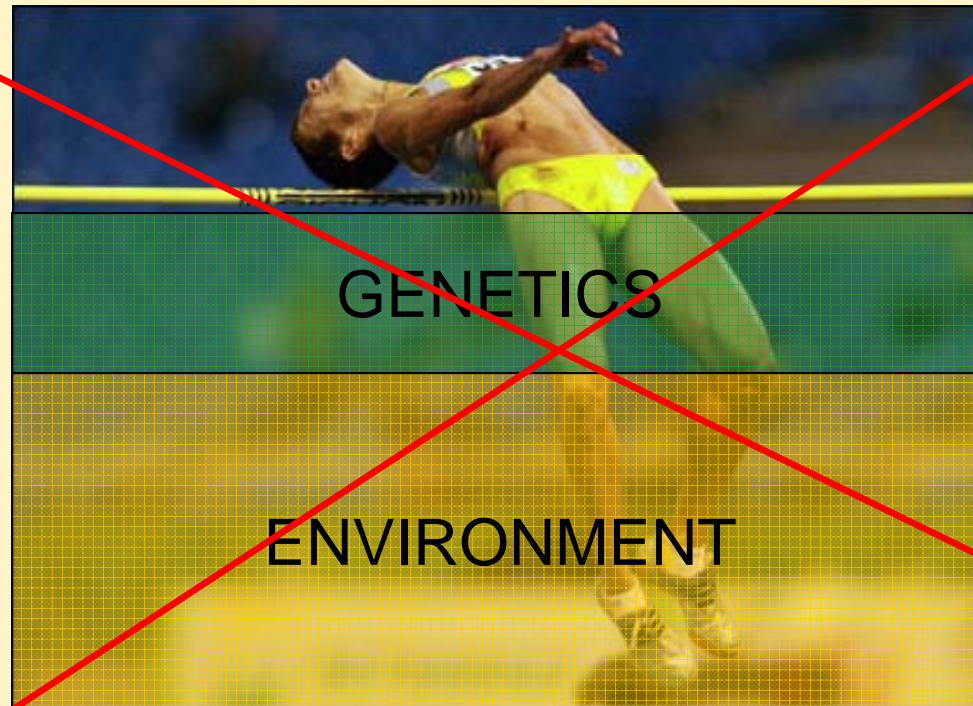
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Nature vs.
Nurture:
Heritability
estimates derived
from twin studies

Common misconceptions about heritability

- Heritability describes the contribution of genetics to the phenotypic **VARIANCE** in the **POPULATION**, not to the actual trait value of an individual

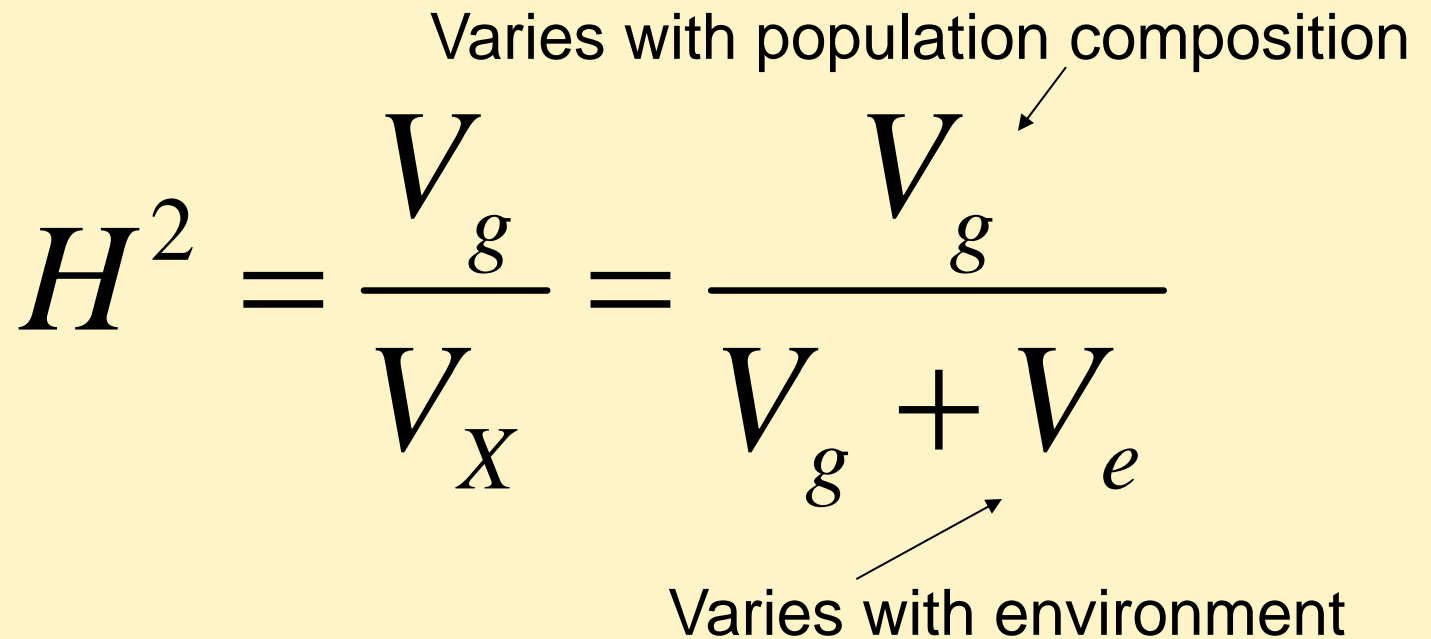


Common misconceptions about heritability

Varies with population composition

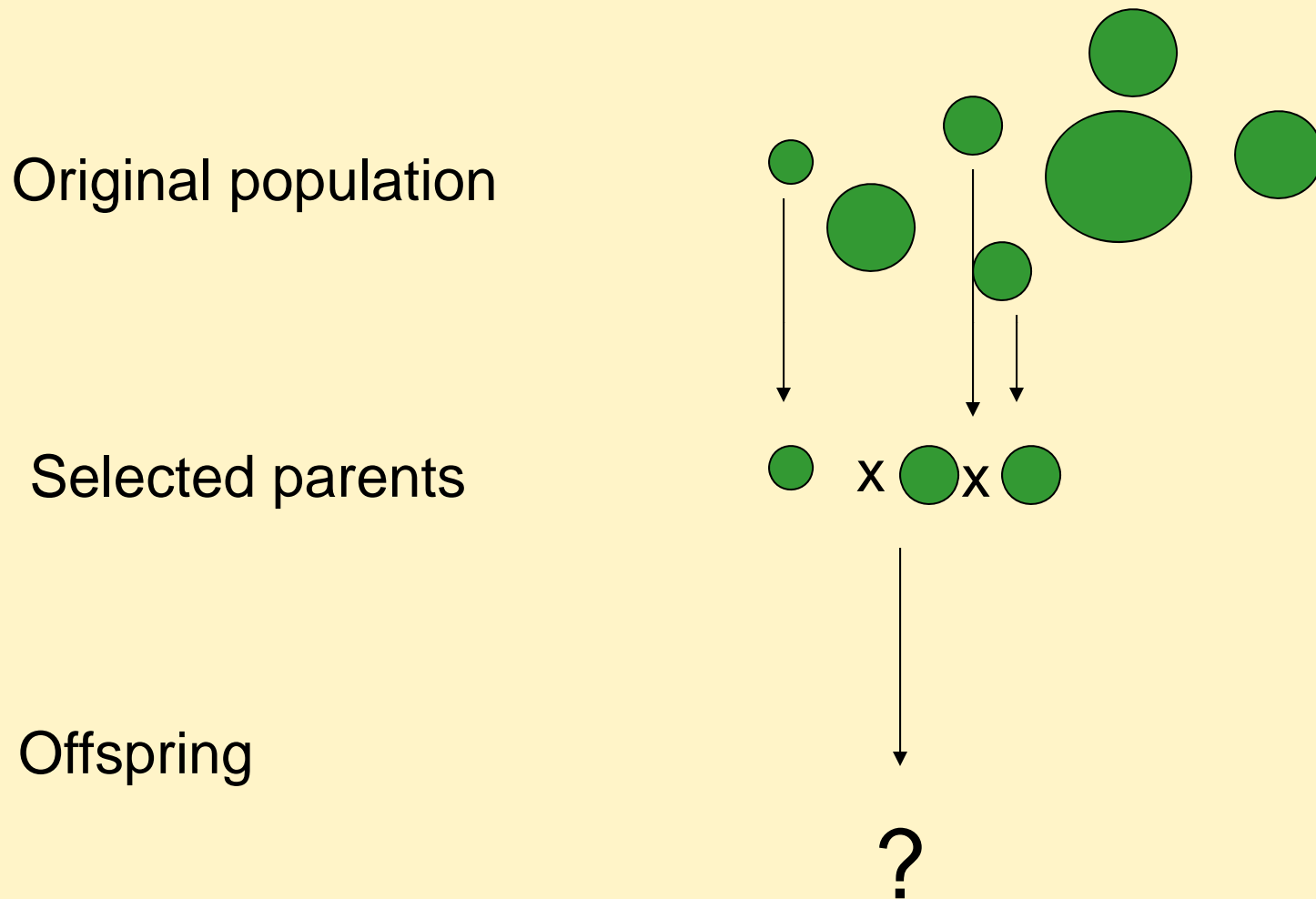
$$H^2 = \frac{V_g}{V_X} = \frac{V_g}{V_g + V_e}$$

Varies with environment



- Heritability is not a constant property of a certain trait but its estimate varies with population composition and the environment

Selection experiments in controlled environments



Selection experiments in controlled environments

- Alternative: environment alone causes variation

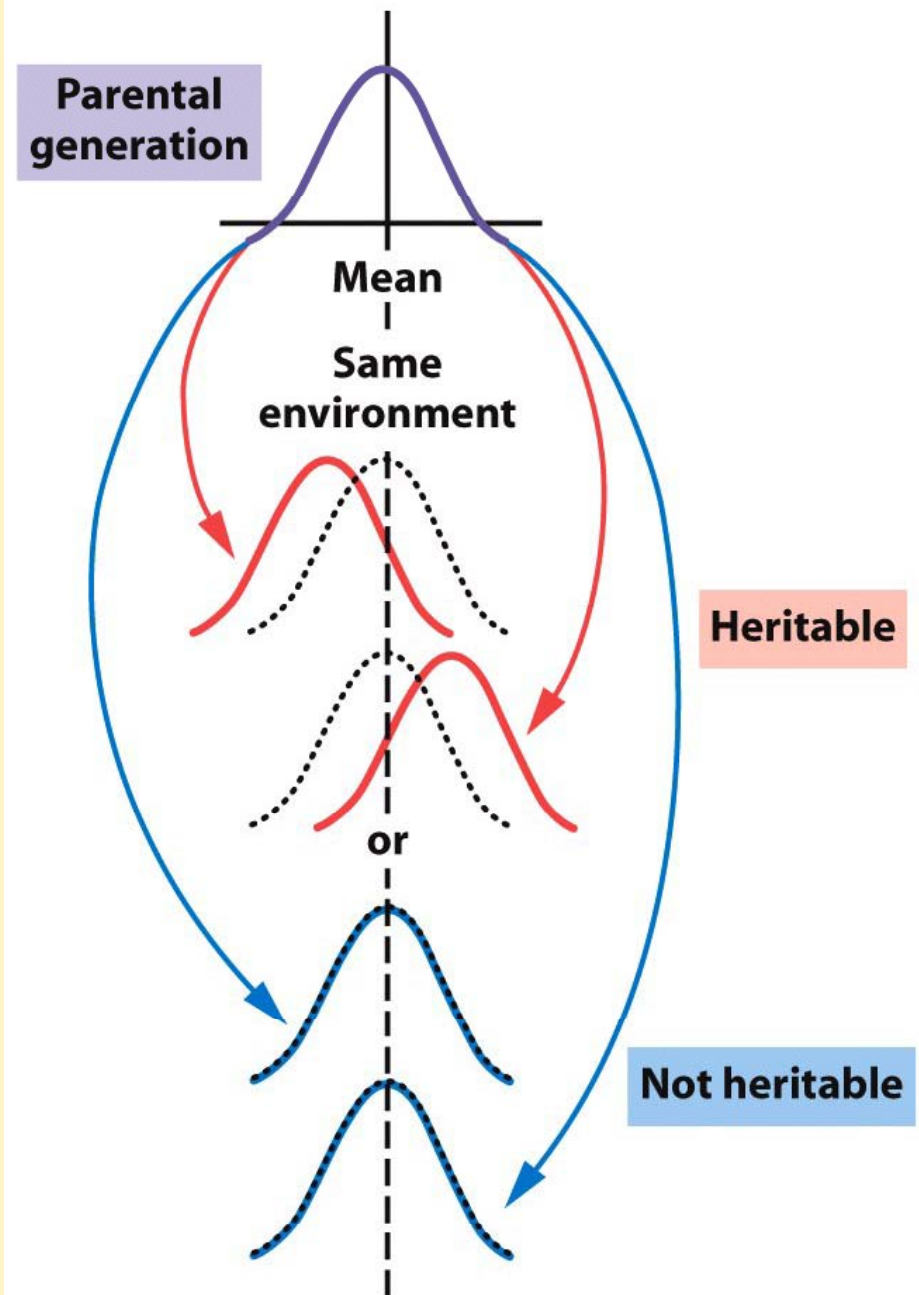
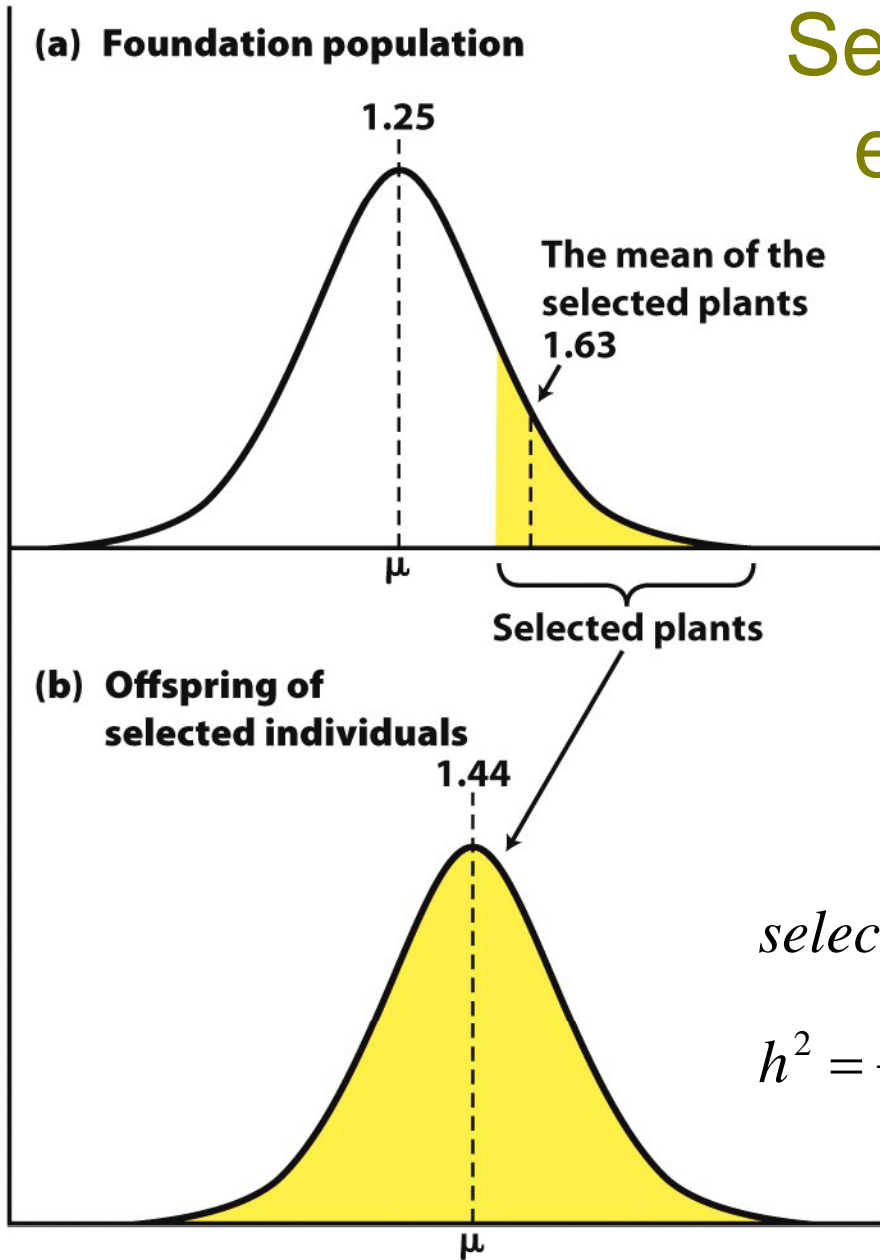


Figure 18-11
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Selection experiments can estimate narrow-sense heritability (h^2)

- **Selection differential** = difference between population mean and the mean of the selected parents in a selection experiment
- **Selection response** = difference between the mean of the original population and the mean of the offspring of the selected parents



$$\text{selection response} = h^2 \times \text{selection differential}$$

$$h^2 = \frac{\text{selection response}}{\text{selection differential}}$$

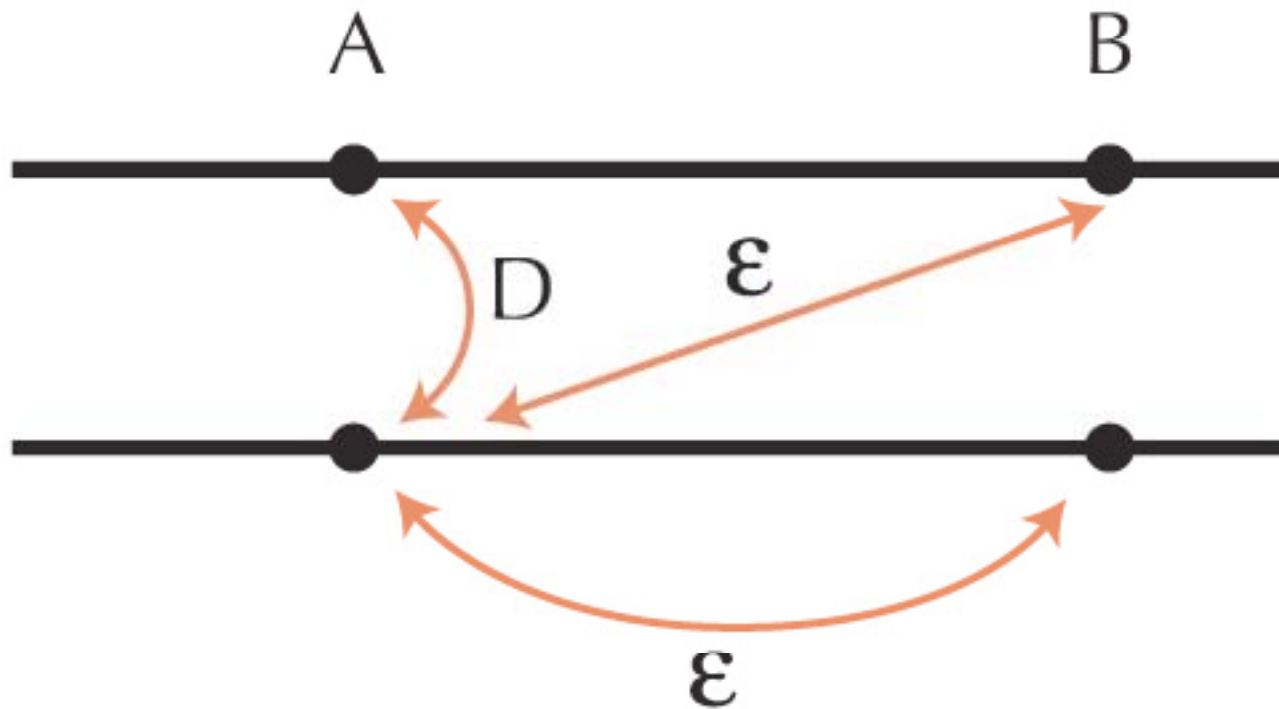
What does h^2 describe?

How can we interpret narrow-sense heritability?

$$\begin{aligned} h^2 &= \frac{\textit{additive_genetic_variance}}{\textit{total_phenotypic_variance}} \\ &= \frac{\textit{additive_genetic_var}}{\textit{additive_gen_var} + \textit{dominance_var} + \textit{environmental_variance}} \\ &= \frac{V_a}{V_a + V_d + V_e} \end{aligned}$$

- h^2 = proportion of of the complete phenotypic variance that is due to **additive** genetic variance (**selectable** variance)
- V_g has been split up

Genetic Interactions: Dominance and Epistasis



- D = Dominance, alleles at same locus
- Epsilon=Epistasis, between alleles at different loci

Dominance variance

Additive gene action

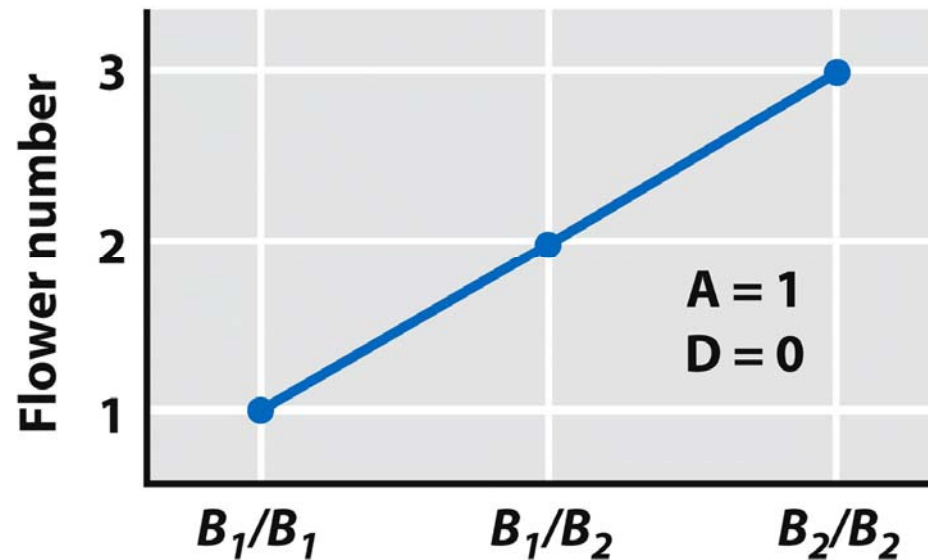


Figure 19-6a
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Dominant gene action

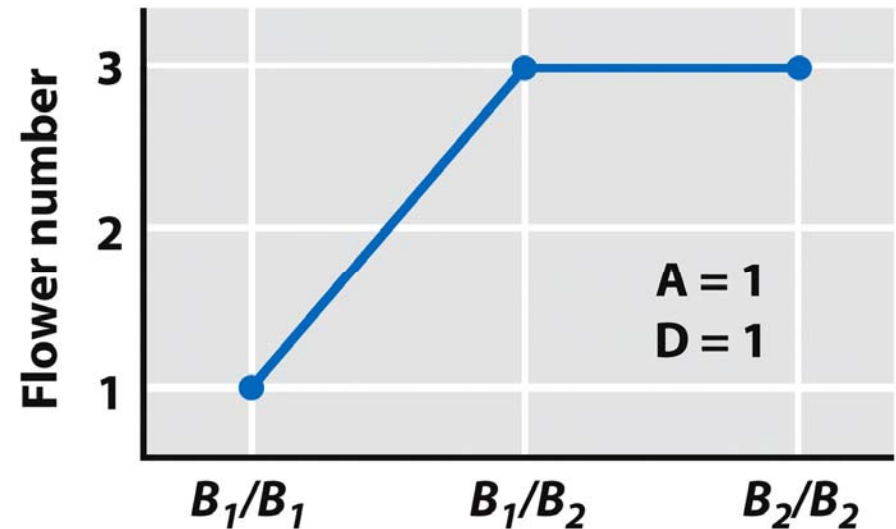


Figure 19-6b
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B_1/B_2 has the same phenotype as B_2/B_2 .

But crossing $B_1/B_2 \times B_1/B_2$ will also produce B_1/B_1 offspring. The offspring population will have fewer flowers than the parental population.

Epistatic interactions

- Beware: Epistasis in evolutionary biology implies any kind of non-additive interaction...not only genes in pathways

Additive interaction

Pairs of mutations in *Drosophila* have epistatic effects

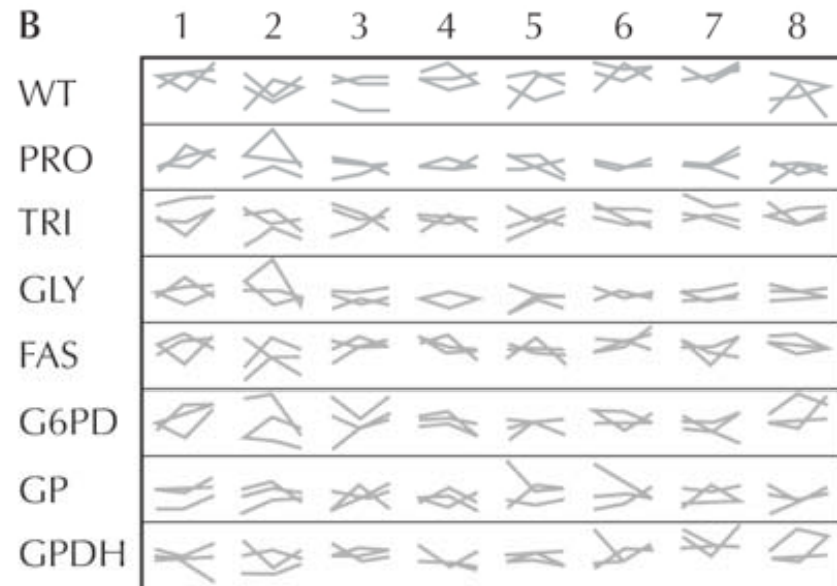
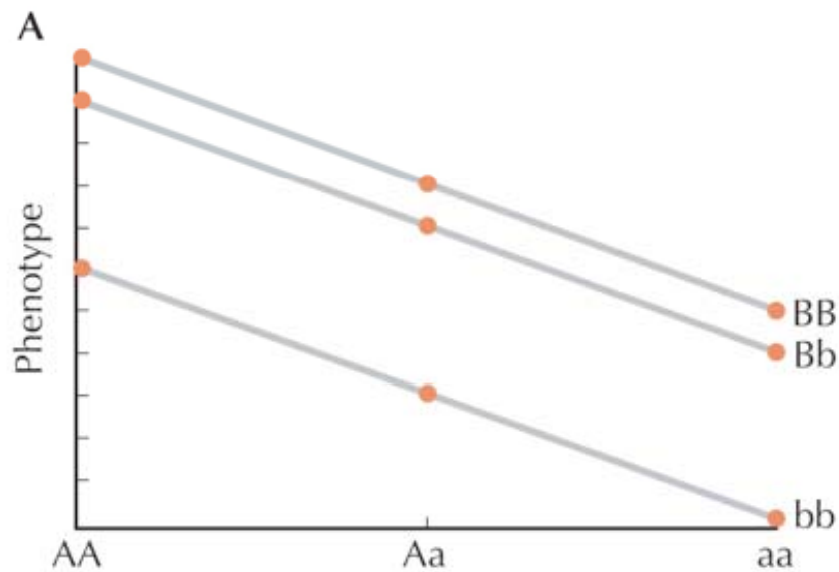


Table 19-5 Narrow-Sense Heritability for Some Traits in Several Different Species

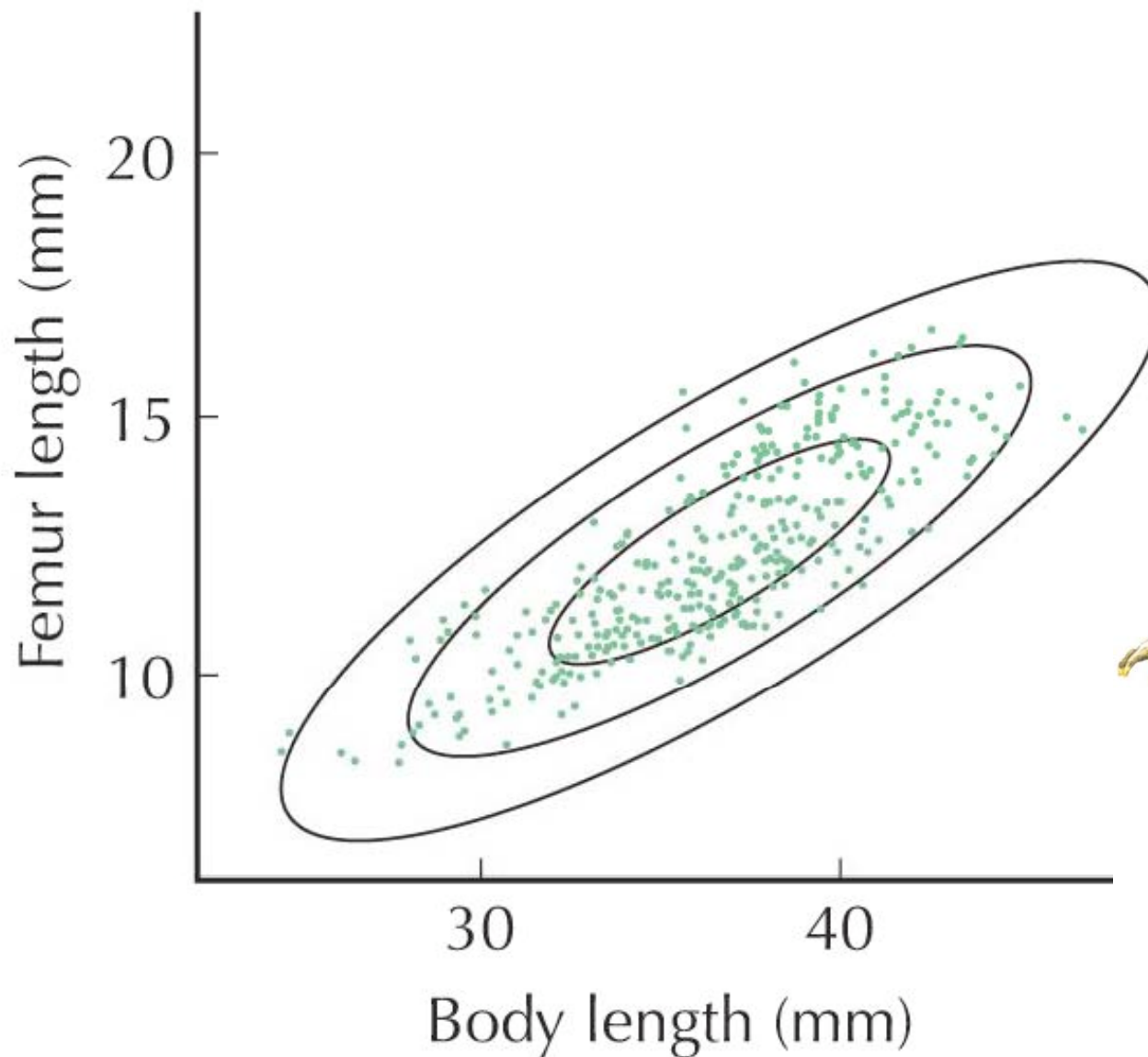
Trait	h^2 (%)
Agronomic species	
Body weight in cattle	65
Milk yield in cattle	35
Back-fat thickness in pig	70
Litter size in pig	5
Body weight in chicken	55
Egg weight in chicken	50
Natural species	
Bill length in Darwin's finch	65
Flight duration in milkweed bug	20
Plant height in jewelweed	8
Fecundity in red deer	46
Life span in collared flycatchers	15

Source: D. F. Falconer and T. F. C. Mackay, *Introduction to Quantitative Genetics*, Longman, 1996; J. C. Conner and D. L. Hartl, *A Primer in Ecological Genetics*, Sinauer, 2004.

What if we cannot make
controlled crosses?

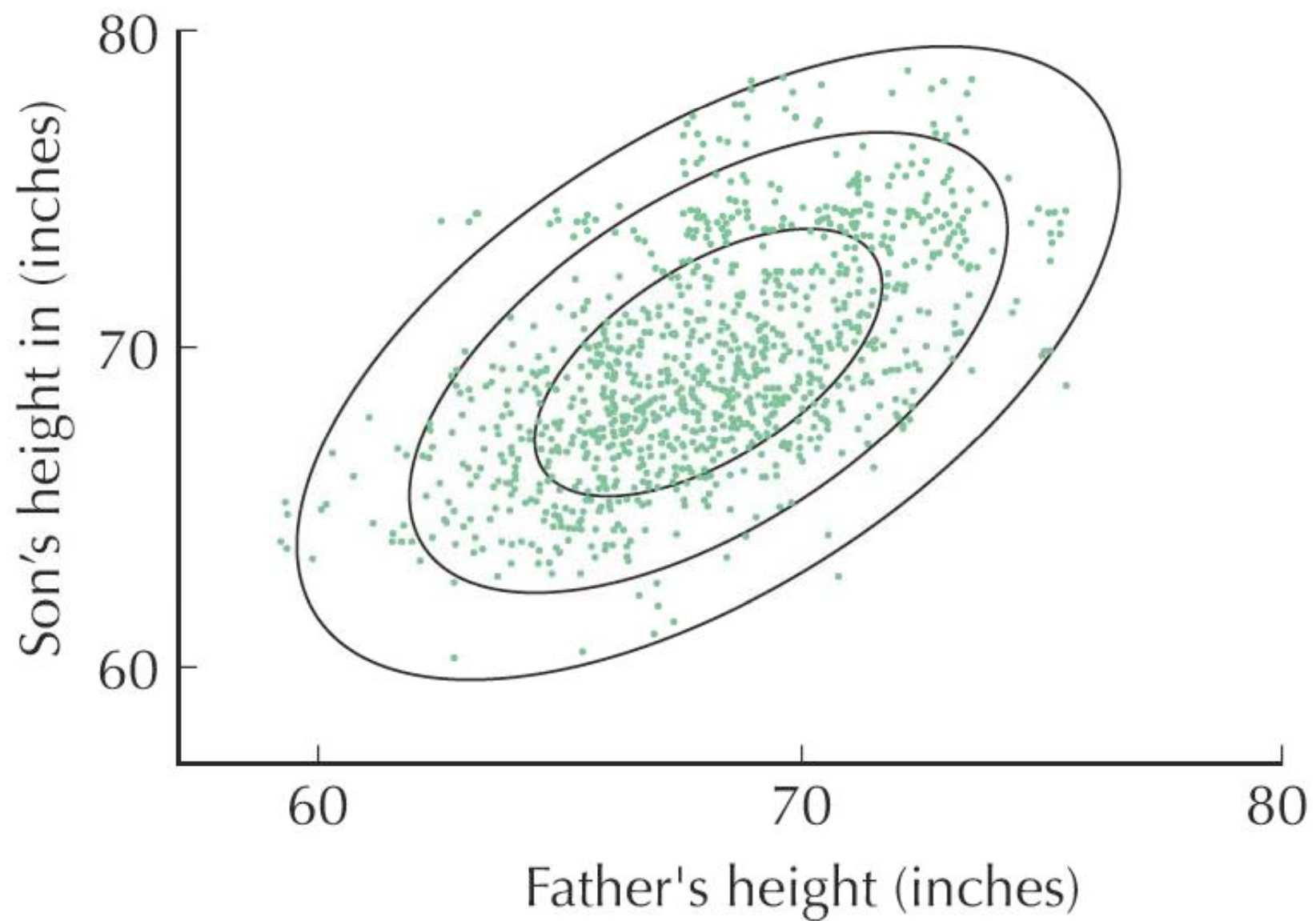


We can also describe co-variation between different traits

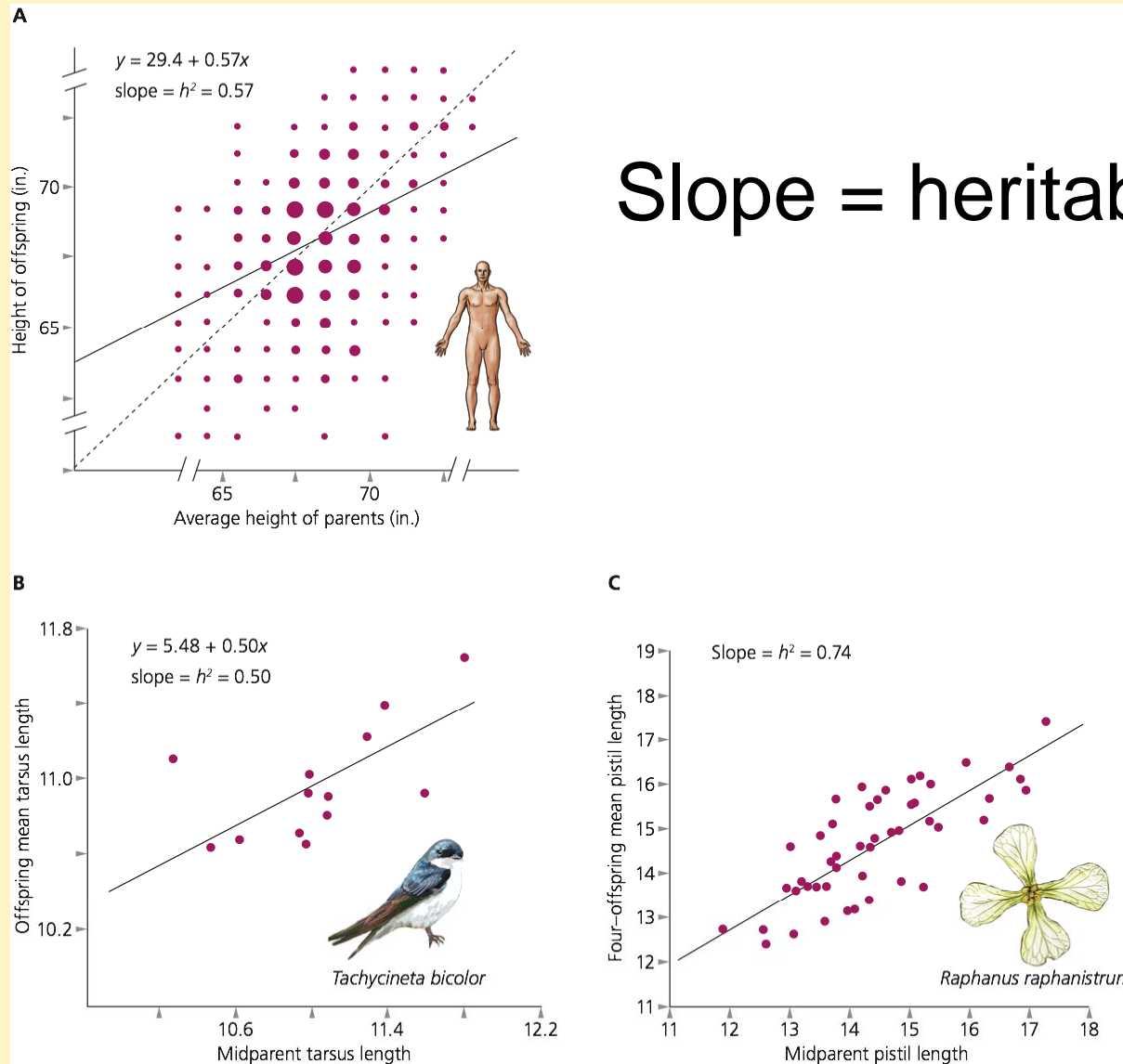


Yellow-bellied toad

... and co-variation in the same trait in different generations

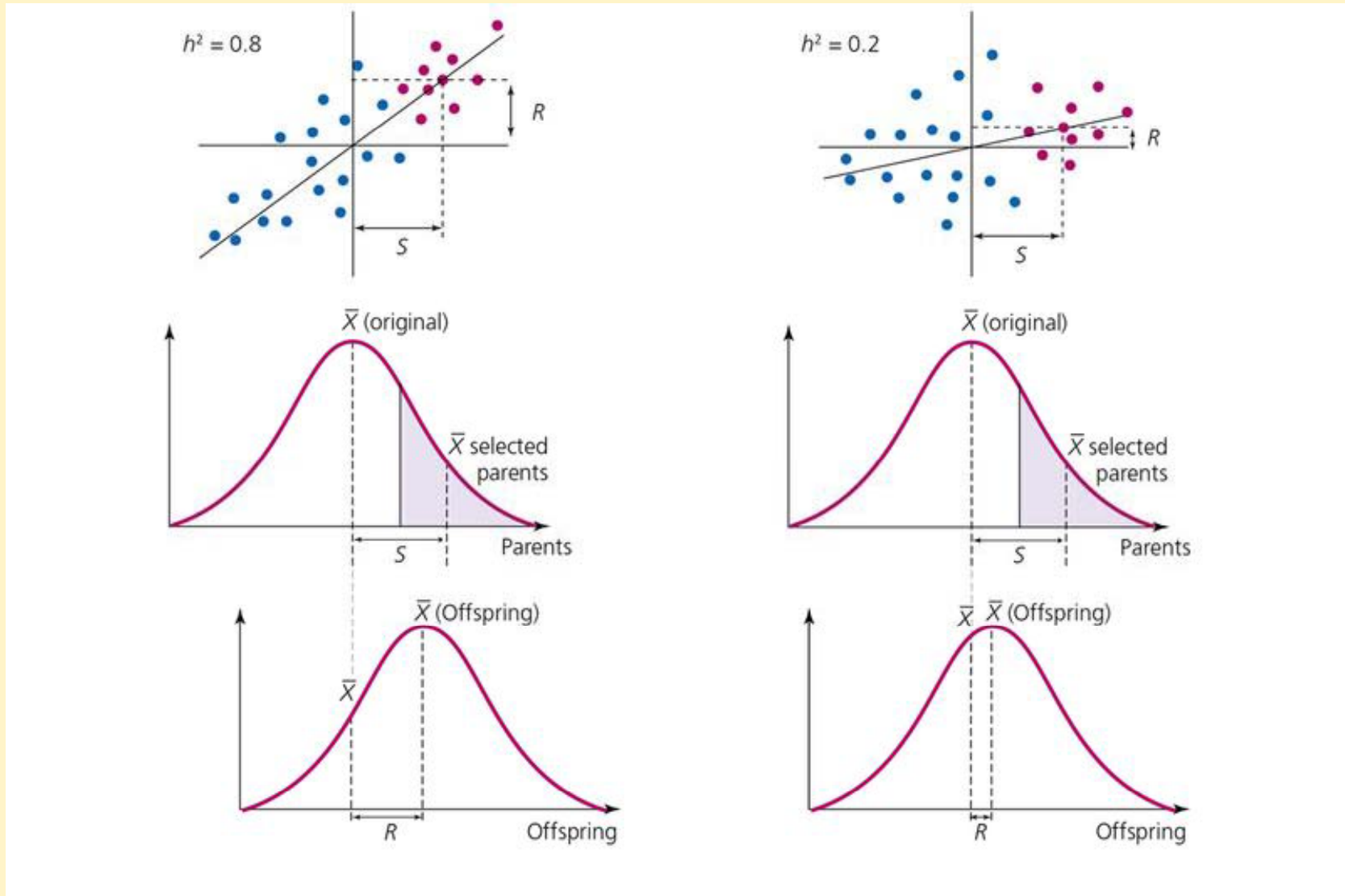


Estimating heritability



Slope = heritability

How are parent offspring-regression and selection experiments related?
Why does h^2 equal the slope of a parent-offspring regression?



Narrow sense heritability

- Proportion of phenotypic variance explained by *additive* genetic variation
 - Causes offspring to resemble parents

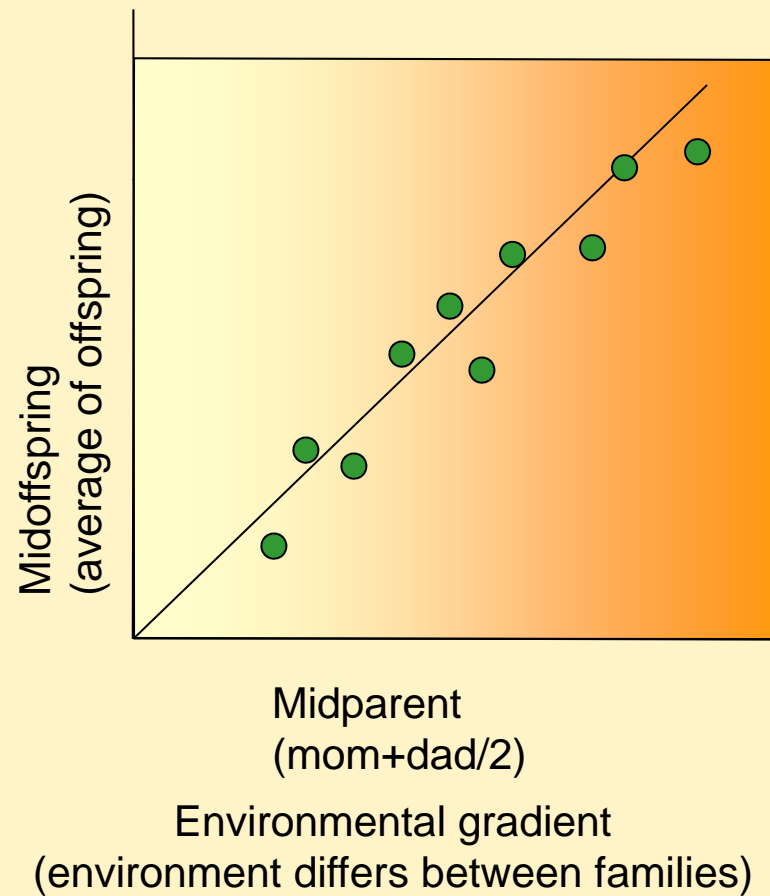
$$h^2 = V_A / V_P = V_A / V_A + V_D + V_I + V_E$$

Additive

Dominance

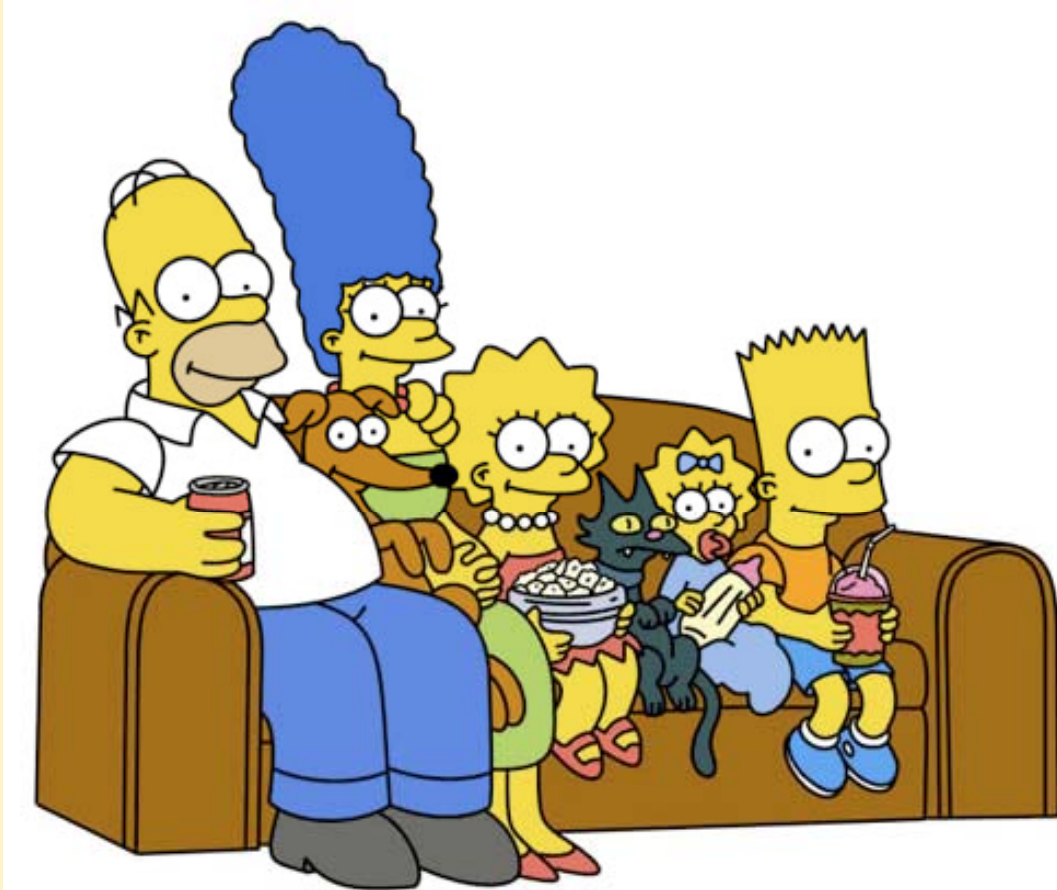
Epistasis

Violating the assumptions: environment covaries with family



Familiarity: Related individuals have similar phenotypes

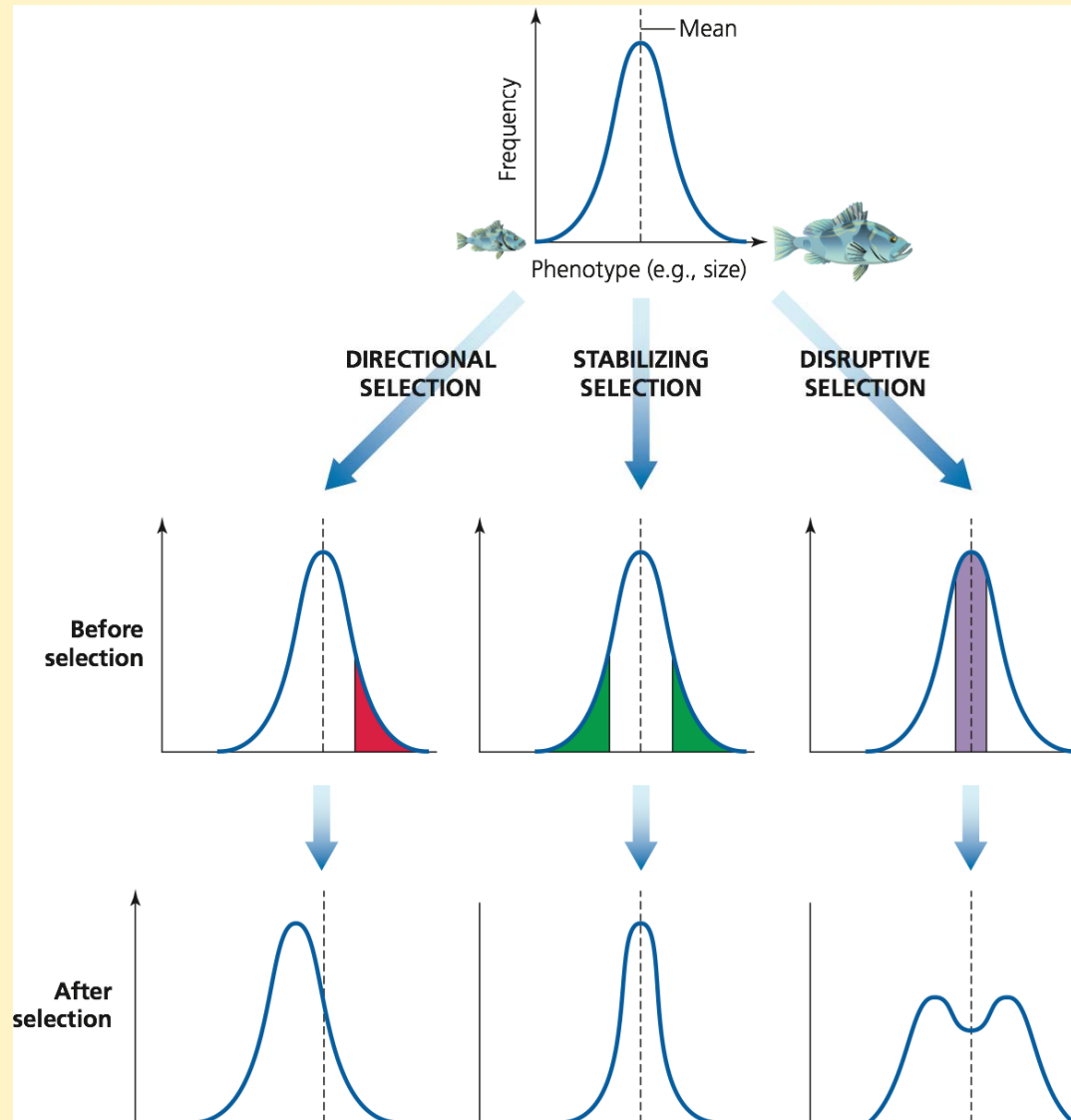
Does *familiarity* equal *heritability*?



Key Concepts

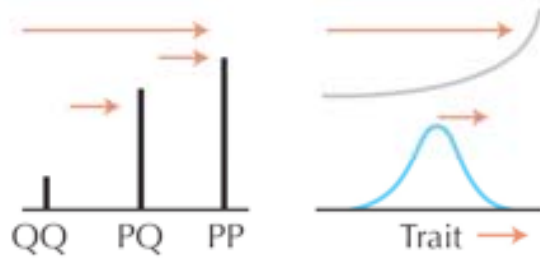
- When components of variation are additive, genetic and environmental variance sum to total phenotypic variance
- Heritability is the proportion of phenotypic variance due to genetic differences
- Broad sense heritability includes:
 - Additive effects
 - Dominance effects
 - Epistatic effects
 - Maternal/Paternal environmental effects

Modes of selection

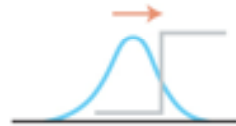


Modes of selection

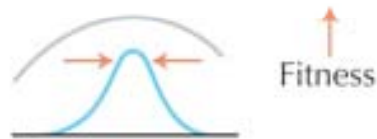
Directional selection



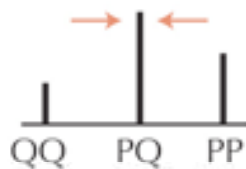
Truncation selection



Stabilizing selection



Balancing selection



Disruptive selection

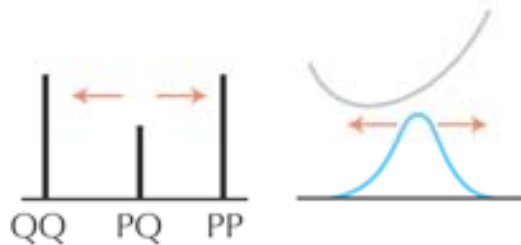
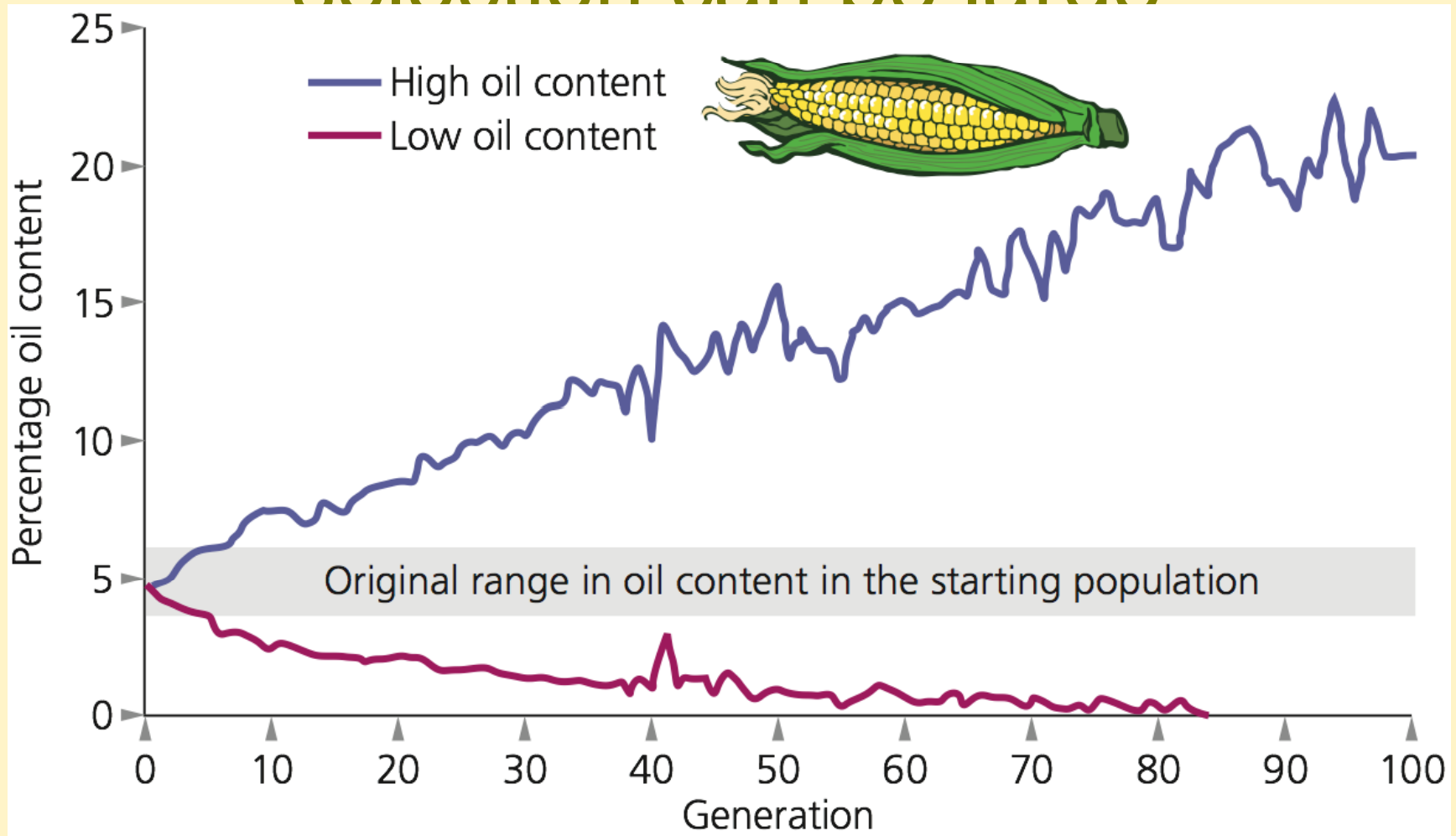
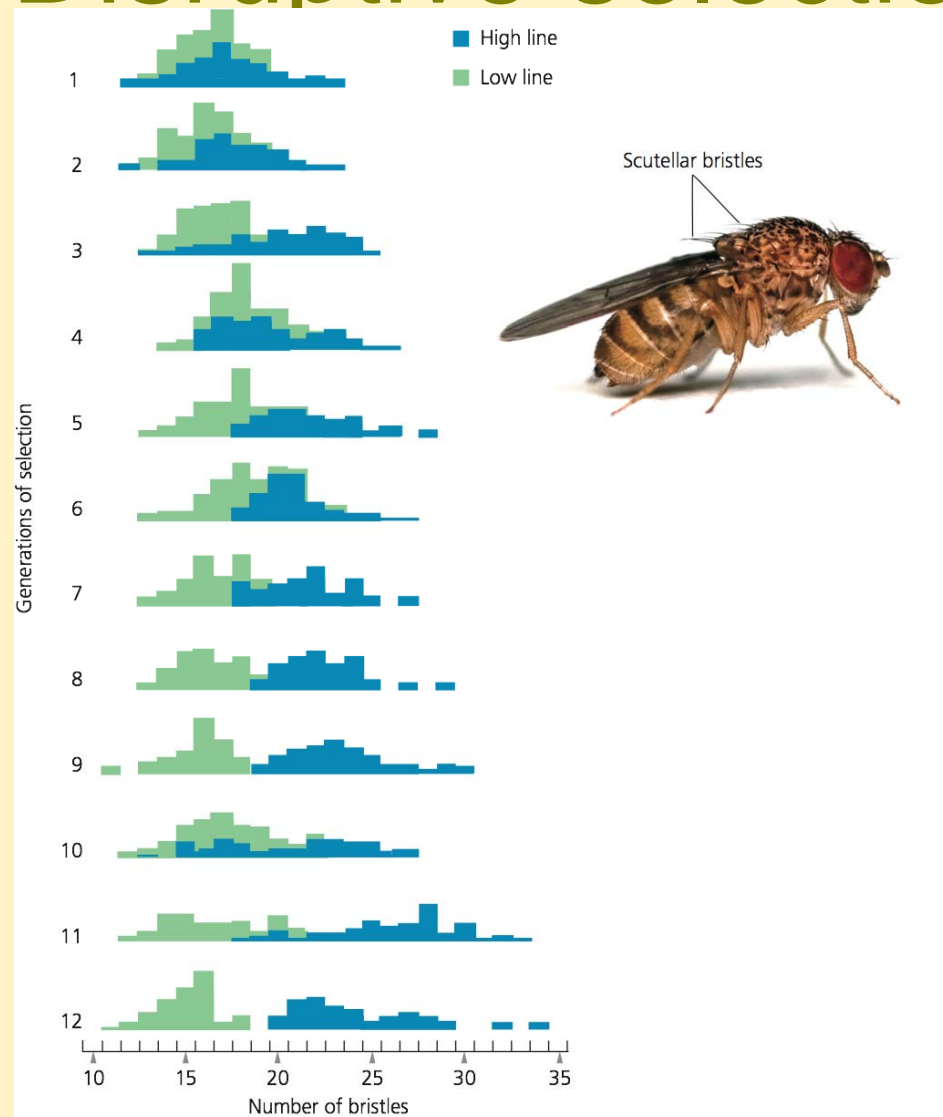


FIGURE BOX 17.2. Modes of Selection

Cumulative effects of directional selection can be large



Disruptive selection



Evolutionary response to selection

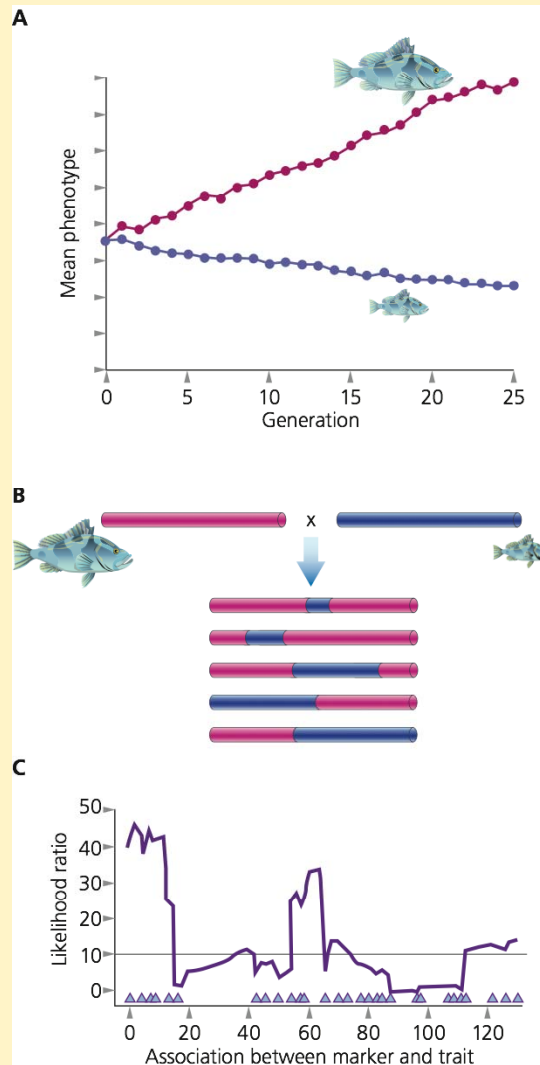
- How much the population changes depends on:
 - Selection differential (S)
 - Heritability

Fisher's fundamental theorem

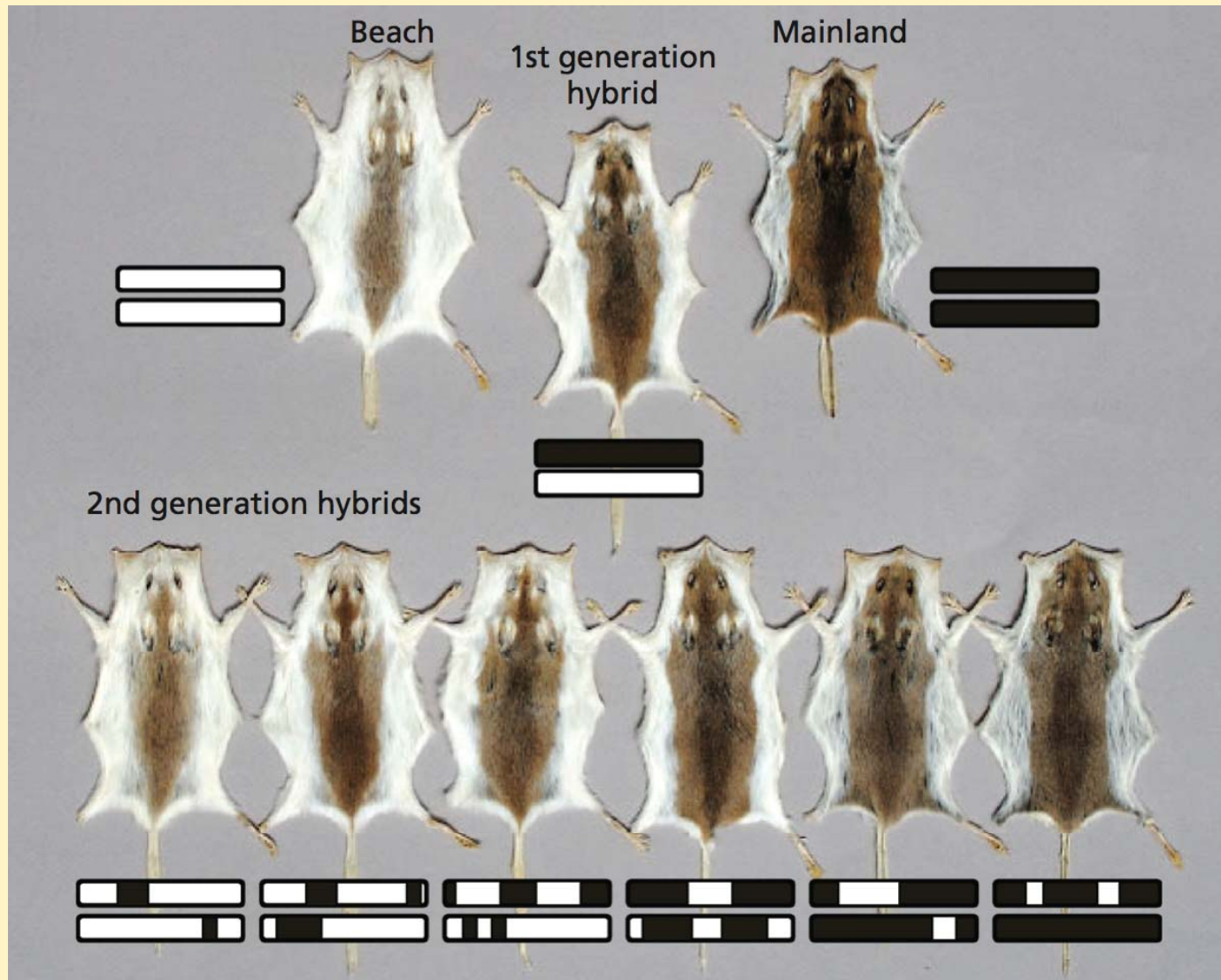
$$\Delta \overline{W} = \text{var}_A(W) / \overline{W}$$

- The change in mean fitness of a population is due to the additive genetic variance in fitness divided by the current average fitness
- The higher the variance in fitness due to heritable additive factors the greater the effect of natural selection

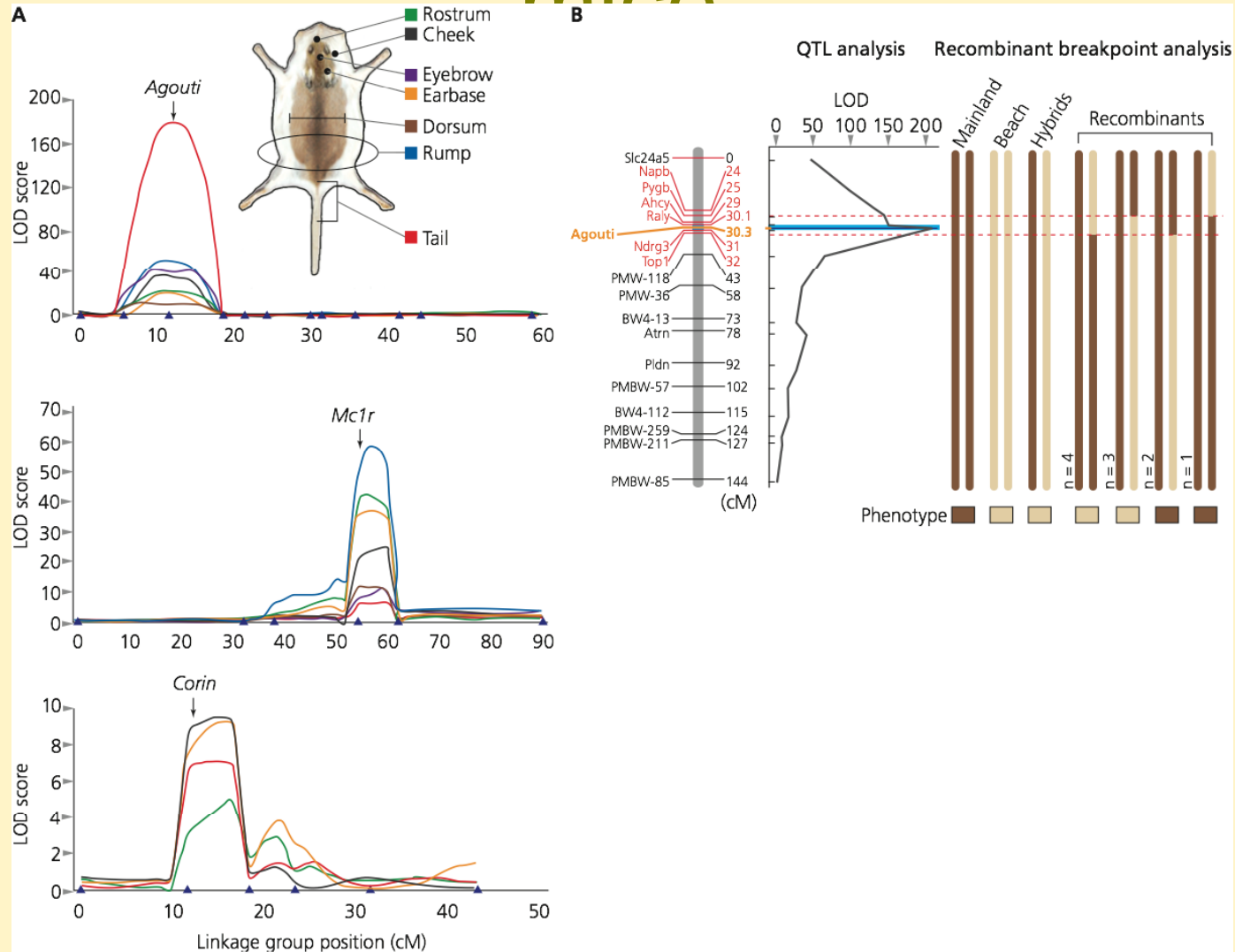
Quantitative trait locus (QTL) analysis links traits with



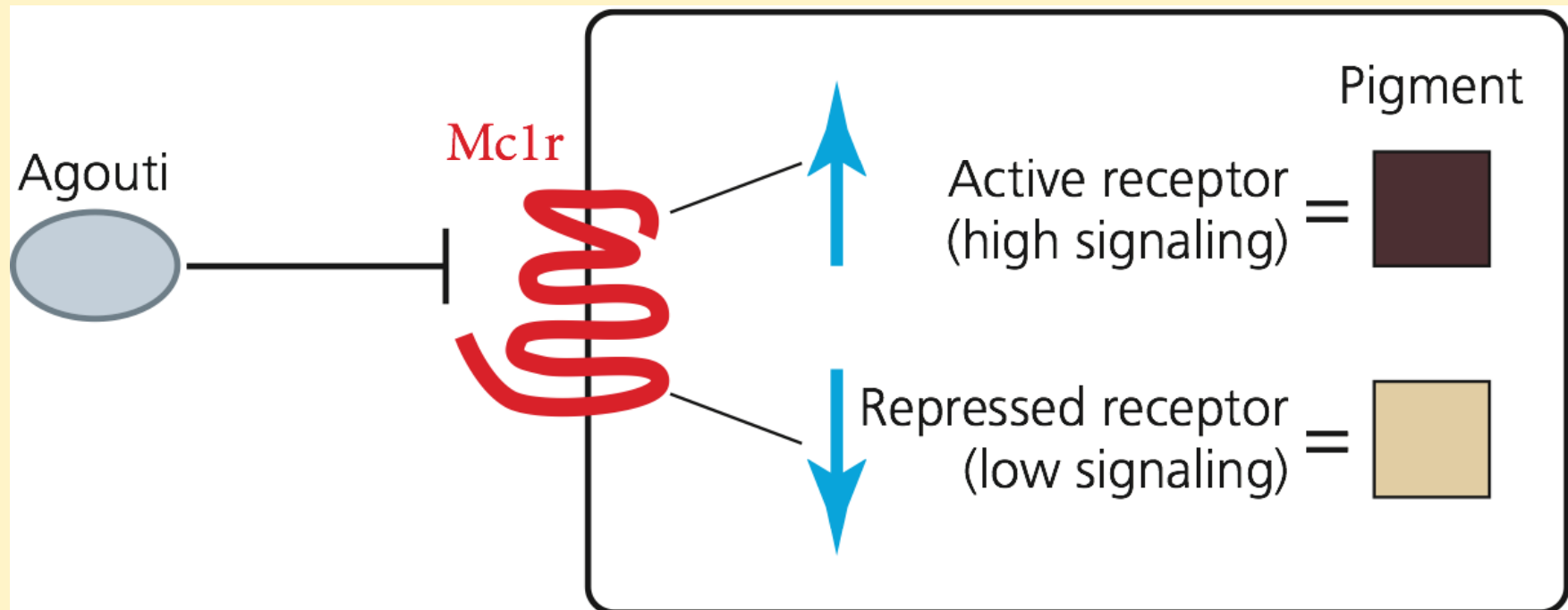
QTL analysis of coat color in mice



QTL analysis of coat color in mice

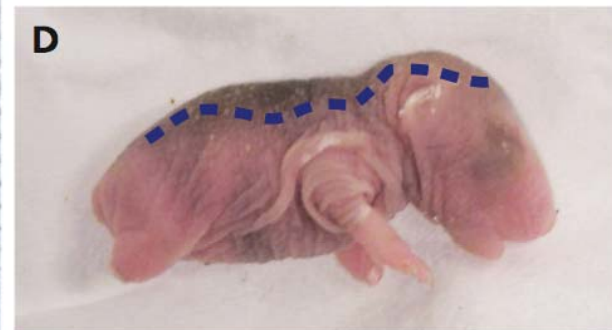
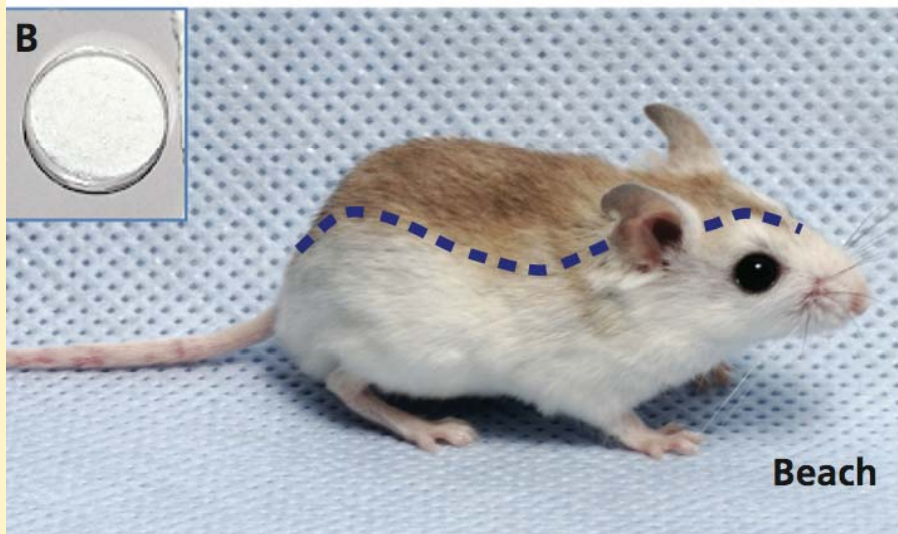
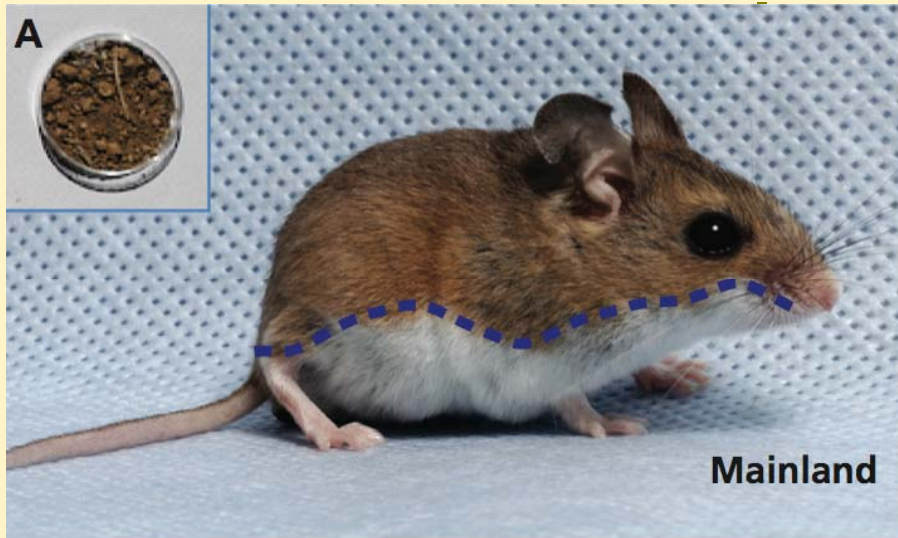


Much of variation in coat color explained by differences in two genes

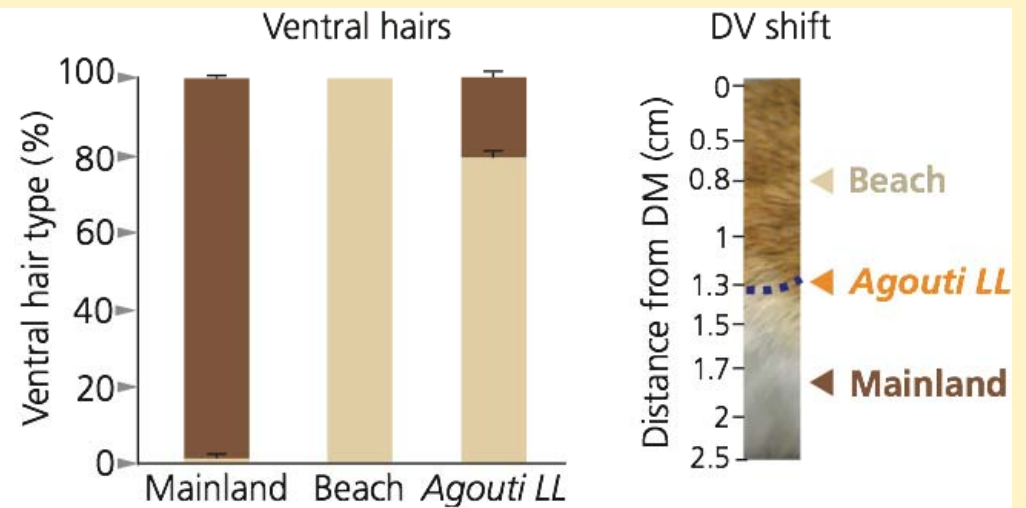
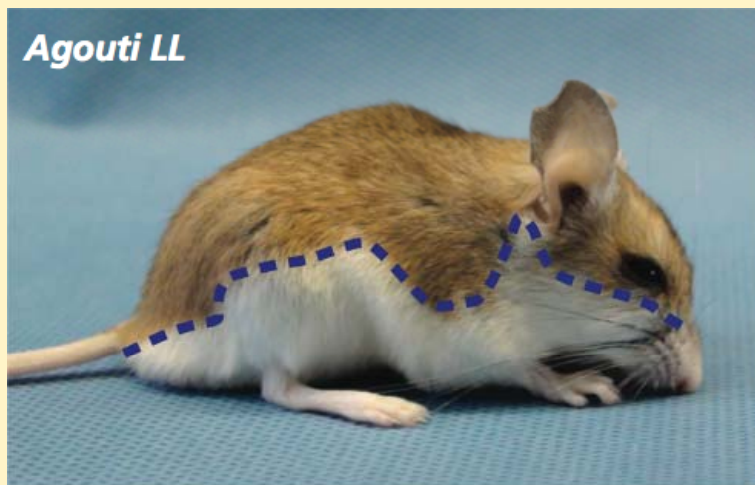


Corin also explains a small amount of variation

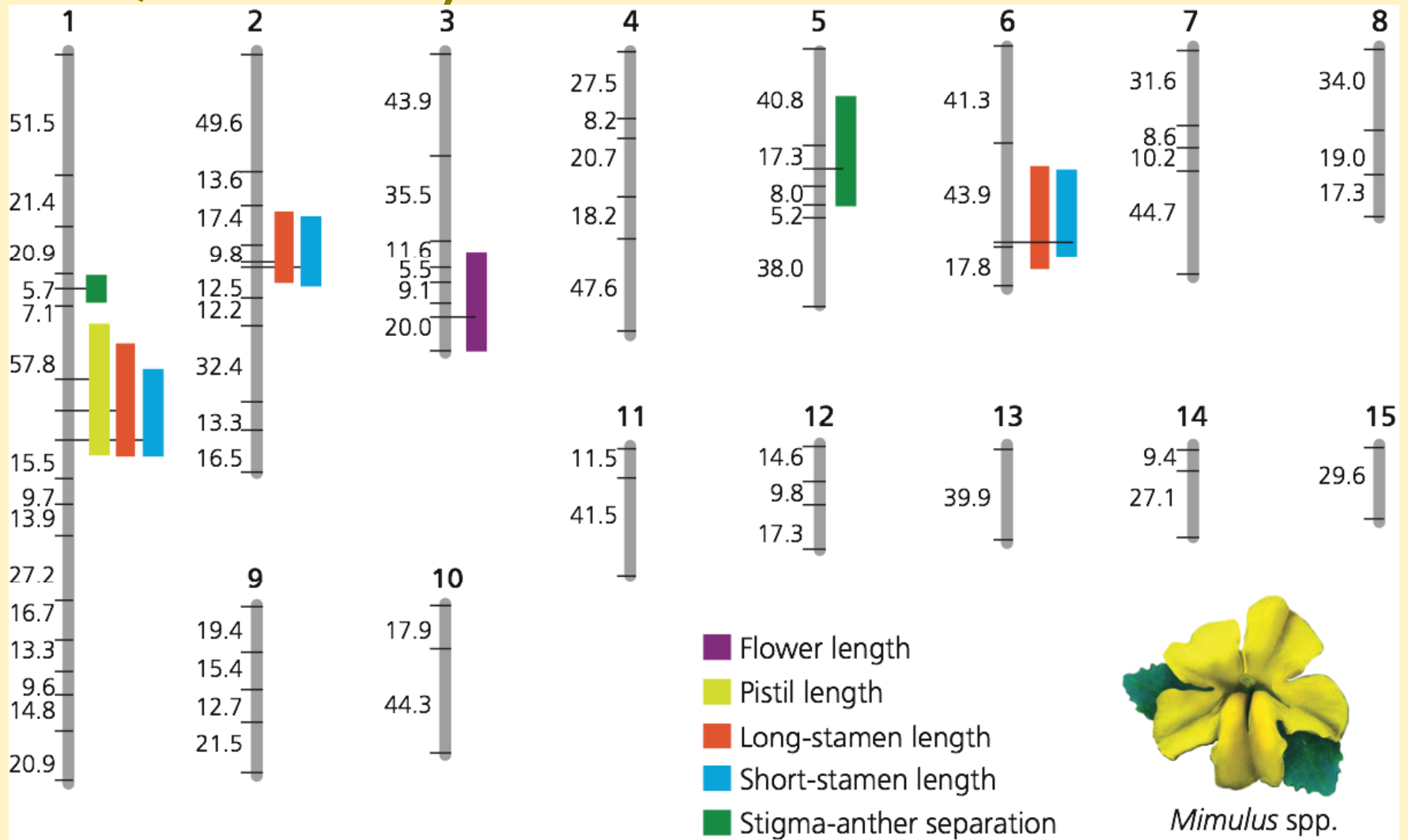
Expression of *Agouti* during development influences coat



Genetic manipulation of dark mice makes them lighter



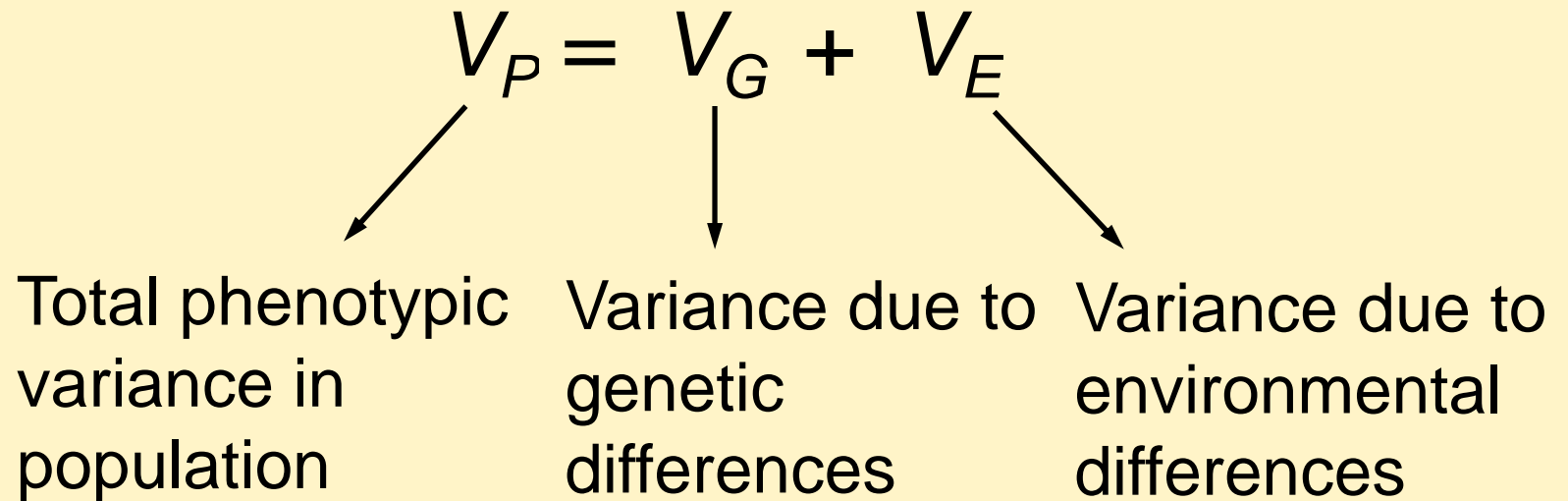
QTL analysis of traits in *Mimulus*



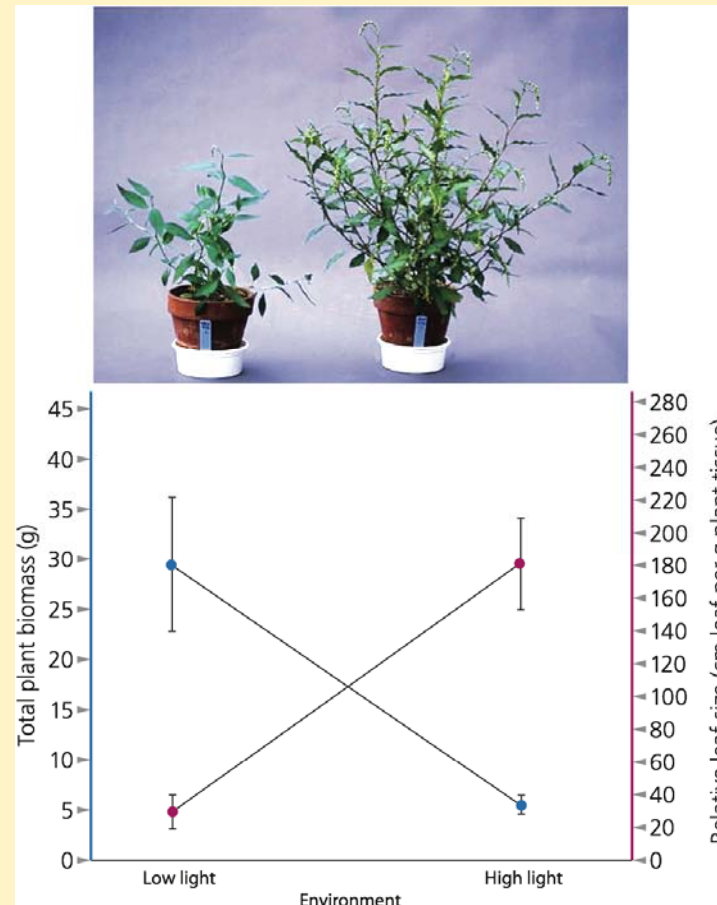
Key Concepts

- QTL analysis identifies regions of the genome associated with phenotypic variation

Environmental influences on quantitative traits

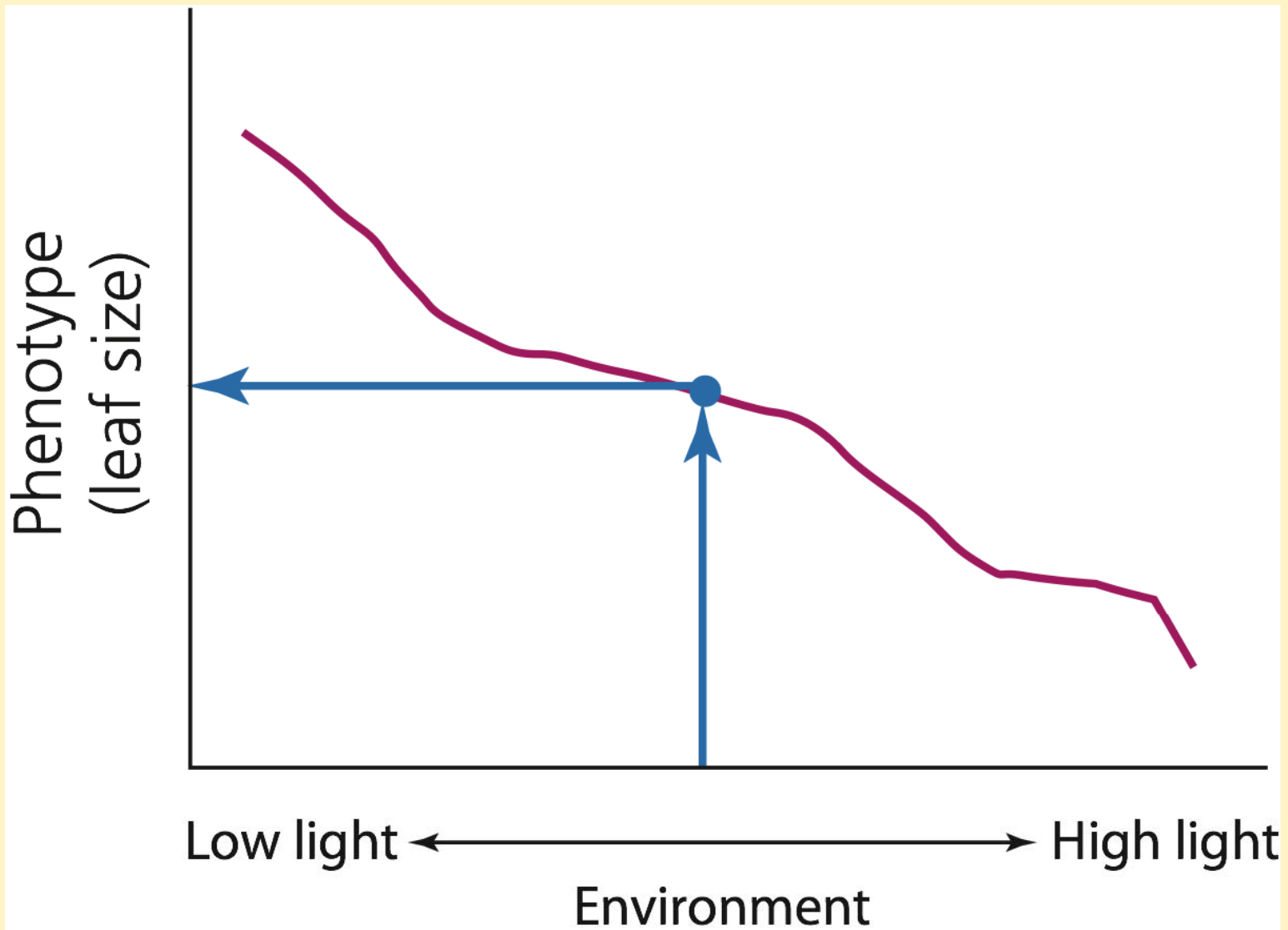


Phenotypic plasticity

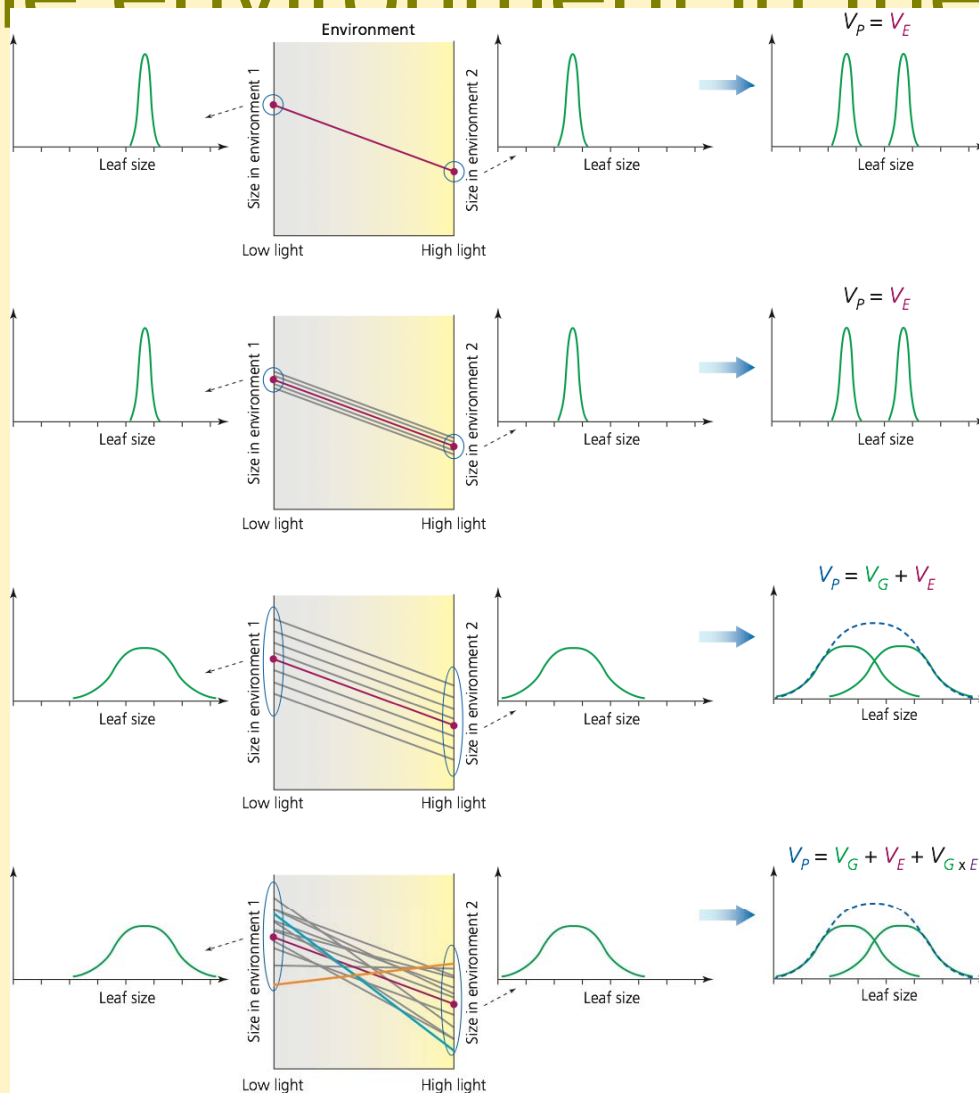


- A single genotype produces different phenotypes depending on the environment

Reaction norm

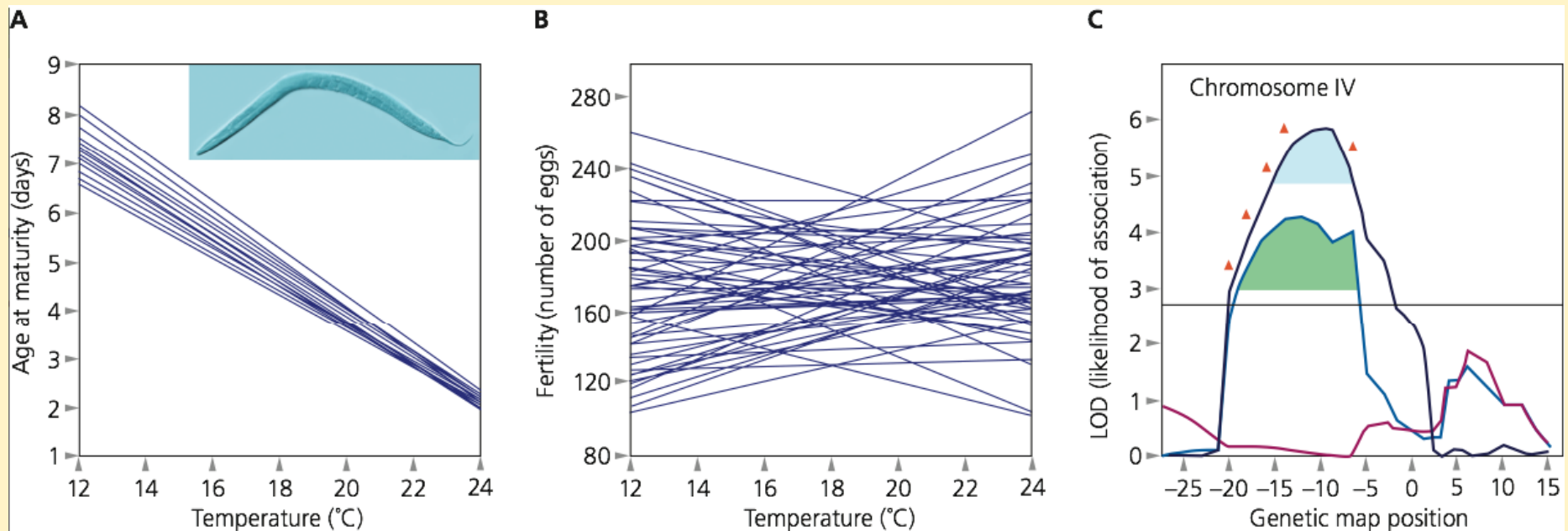


All genotypes may not respond to the environment in the same way

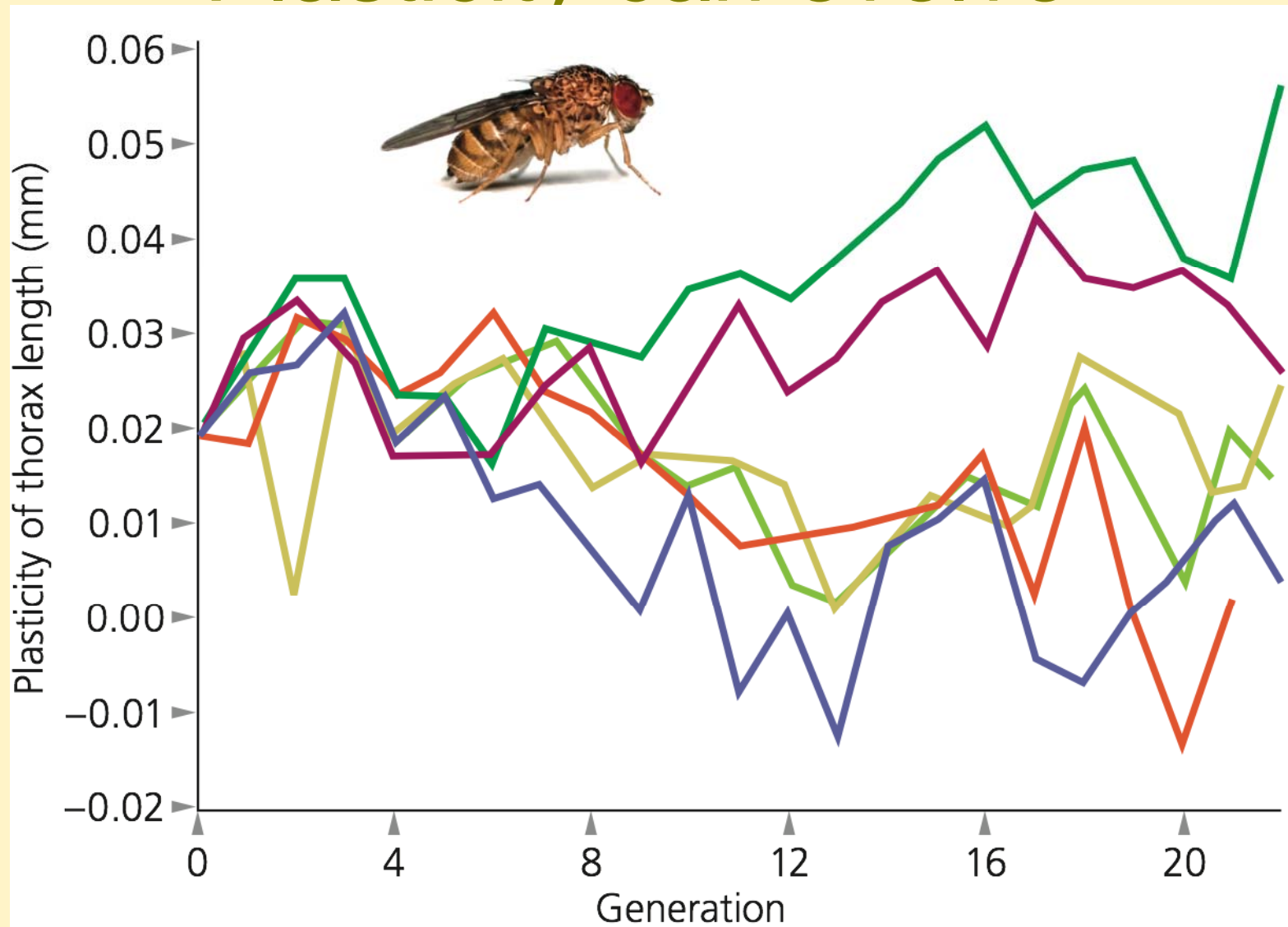


Genotype x
environment
interaction

Phenotypic plasticity in *Caenorhabditis elegans*



Plasticity can evolve



Rapid change can lead to mismatch between plastic traits and environment

