Chapter 7

Beyond alleles: quantitative genetics and the evolution of phenotypes

What is quantitative genetics?

Kind of the study of continuous traits!

We study these from the top down!

Remember the mouse selection example from earlier chapter!?

Chapter 7

Beyond alleles: quantitative genetics and the evolution of phenotypes

- **What is quantitative genetics?**
- Two ways of estimating narrow sense heritability
  1. Parent-Offspring Regression
  2. The Breeders Equation!
- Coat color in mice-linkage and connecting genes to phenotypes.
- “Modes of selection”

Why do we study continuous traits "quantitatively"?

Because they have a complex genetic basis and are more complex than the Mendelian patterns (Punnett Squares) we considered before!

Why more complex?

- They are typically **polygenic** (what does that mean?)
- Many of the genes involved have **epistatic** interactions (what is epistasis?)
- Many are also **multifactorial** (what does that mean)?

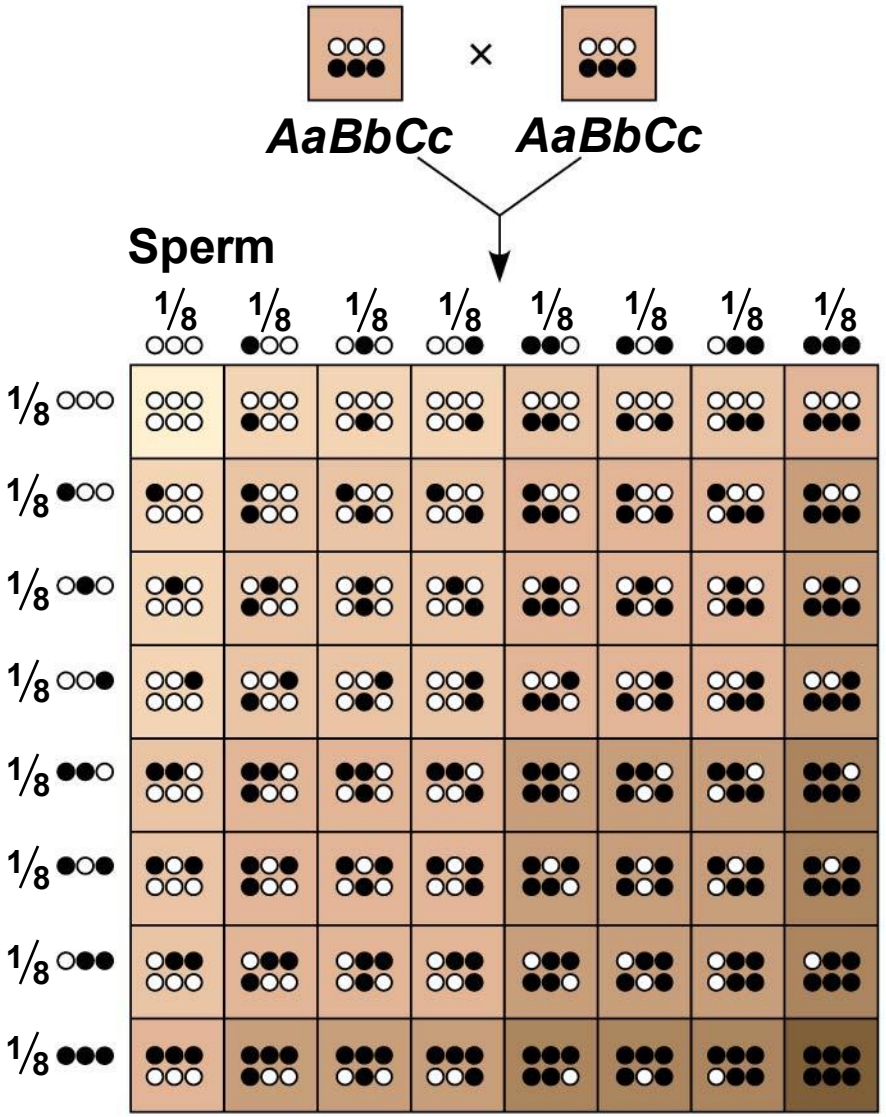
Some disorders, such as sickle cell disease and cystic fibrosis, are caused by mutations in a single gene. The causes of many other disorders, however, are much more complex. Common medical problems such as heart disease, type 2 diabetes, and obesity do not have a single genetic cause—they are likely associated with the effects of multiple genes (polygenic) in combination with lifestyle and environmental factors. Conditions caused by many contributing factors are called complex or **multifactorial** disorders.

https://ghr.nlm.nih.gov/primer/mutationsanddisorders/complexdisorders

Skin color example we saw before…

And remember three is not even remotely realistic for skin color or height!

Is skin color only a function of your genes? What about the effects of the environment during your lifetime?



So how manageable or realistic is it to study traits that are a function of many loci as well as the environment by using Punnett Squares?

What do we do?

We study these from the “top down”!

Take measurements at the population level and infer the degree to which the variation we observe in the population is a function of genetic variation.

Who cares about heritability?

If a large portion of the variance is genetic and you select for height in a population, how much would you expect the next generation to increase in height?

If genes only contribute a small amount (and the environment plays a big role) and you select for height, how much would you expect the next generation to increase in height when you selected for height?

Can you think of practical applications?

If geneticists are trying to improve a specific quantitative trait (such as crop yield or weight gain of an animal), estimates of the proportion of these variances to the total variance provide direction to their research. If a large portion of the variance is genetic, then gains can be made from selecting individuals with the metric value you wish to obtain. On the other hand if the genetic variance is low, which implies that the environmental variance is high, more success would be obtained if the environmental conditions under which the individual will be grown are optimized.

https://www.ndsu.edu/pubweb/~mcclean/plsc431/quantgen/qgen4.htm

So to Review….Questions Studied By Quantitative Geneticists

- What is the genetic and environmental contribution to the phenotype?
- How many genes influence the trait?
- Are the contributions of the genes equal?
- How do alleles at the same locus interact? Additively?
- How do loci interact? Additively? Epistatically?
- How rapidly will the trait change under selection?

Phenotype = Genetic Factors + Environmental Factors

Not required info!

$$V_P = V_G + V_E$$

Total phenotypic variance in population	Variance due to genetic differences	Variance due to environmental differences
The differences in what we look like are =	The different genes we have and the way they interact with one another	The different environments we live in

Variation due to the environment is important.

Does one genotype "win" (or have the highest yield) in every year?

https://www.ndsu.edu/pubweb/~mcclean/plsc431/quantgen/qgen2.htm

To illustrate the effect of environment on the expression of a genotype, look at the yields of winter wheat at one North Dakota location (Casselton, ND) during the last ten years. (The data was kindly provided by Dr. Jim Anderson, Dept of Plant Sciences, North Dakota State University, Fargo, ND.) Any year for year variation in yield for any one genotype is largely an effect of the environment.

	Yield (bushels/acre)		
	Genotype		
Year	Roughrider	Seward	Agassiz
1986	47.9	55.9	47.5
1987	63.8	72.5	59.5
1988	23.1	25.7	28.4
1989	61.6	66.5	60.5
1990	0.0	0.0	0.0
1991	60.3	71.0	55.4
1992	46.6	49.0	41.5
1993	58.2	62.9	48.8
1994	41.7	53.2	39.8
1995	53.1	65.1	53.5

Note: All plants in 1990 experienced winter kill.

The **broad-sense heritability** is the ratio of total genetic variance to total phenotypic variance (which is interesting but super hard to actually calculate).

$H^2 = V_G/V_P$ **Not required info!**

Therefore, we are not going to say much about this…instead we will focus on **narrow sense heritability**!

Narrow sense heritability

Not required info!

Proportion of phenotypic variance explained by *additive* genetic variation only (not variation due to things like epistasis).

We focus on this because it is the kind of genetic variation that most directly causes offspring to resemble parents.

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

Additive

Dominance

Epistasis

To review…

Broad sense heritability is the proportion of phenotypic variance due to:

- Additive effects
- Dominance effects
- Epistatic effects

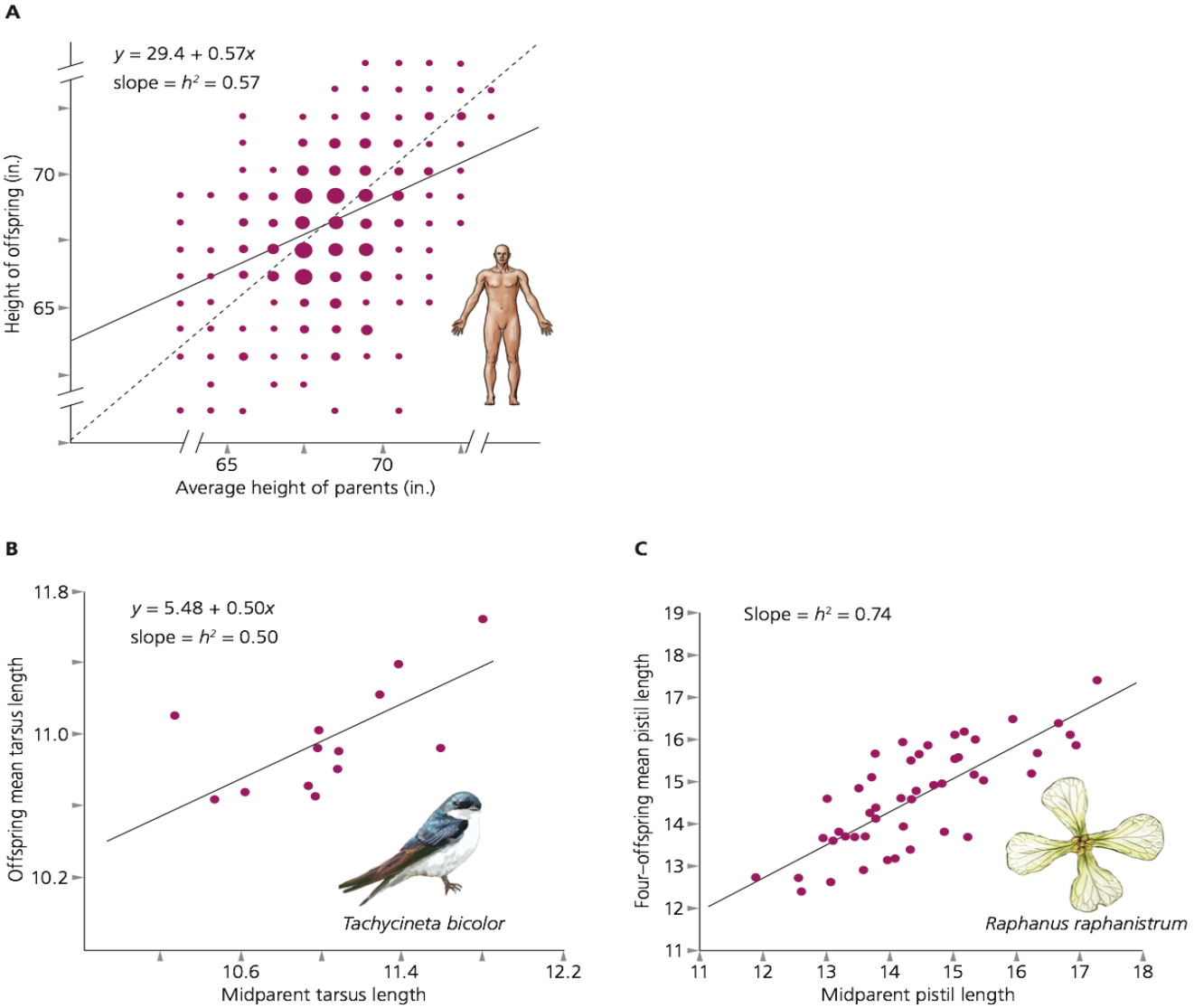
Not required info! Although you should know the difference between the terms additive, dominant and epistatic!

Narrow sense heritability is the proportion of phenotypic variance due to

- Additive effects only… and we lump dominance and epistatic effects in with the environmental variation

Estimating **(narrow sense) heritability in two ways.**

1. Parent offspring regression.



2. The Breeders Equation!

A second way of estimating heritability involves actively selecting on a population to see how much change we can generate.

If there is **high** heritability for height and we select a population for tallness how will the next generation **RESPOND** to selection? What will happen in next generation?

How about if there is **low** heritability for height, what will the next generation look like? Or how will it **RESPOND**?

What about if we only select the really tall individuals (top 10% vs the top 50%) of the parental population? Which will result in taller offspring?

Which will have a greater **RESPONSE to selection**?

Selecting the top 10% means there is a larger **selection differential** (a larger difference between the mean of the whole original population and those you are selecting)

While selecting top 50%=smaller **selection differential**

The Breeder's Equation

In the 1977 parents graph S (**selection differential**), is equal to the difference between the mean of survivors and the mean of the original parental population. (Survivors-Original)

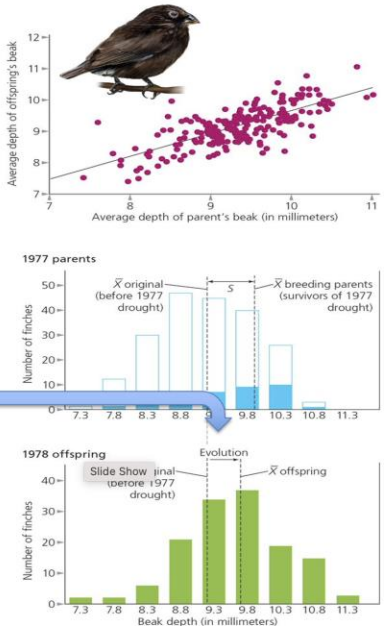
Now check out the 1978 offspring graph. Did beak depth increase in the next generation?

Did it reach the average beak depth of the surviving parents?

Selection pulled up avg but it did not reach the avg of parents.

Lets define **R (response to selection)**
So there is a cool equation that connects the response to selection with the heritability of the trait and the selection differential.

R = h^2 x S (Breeder's Equation)



So there is a cool equation that connects the response to the heritability and the selection differential

R = h^2 x S

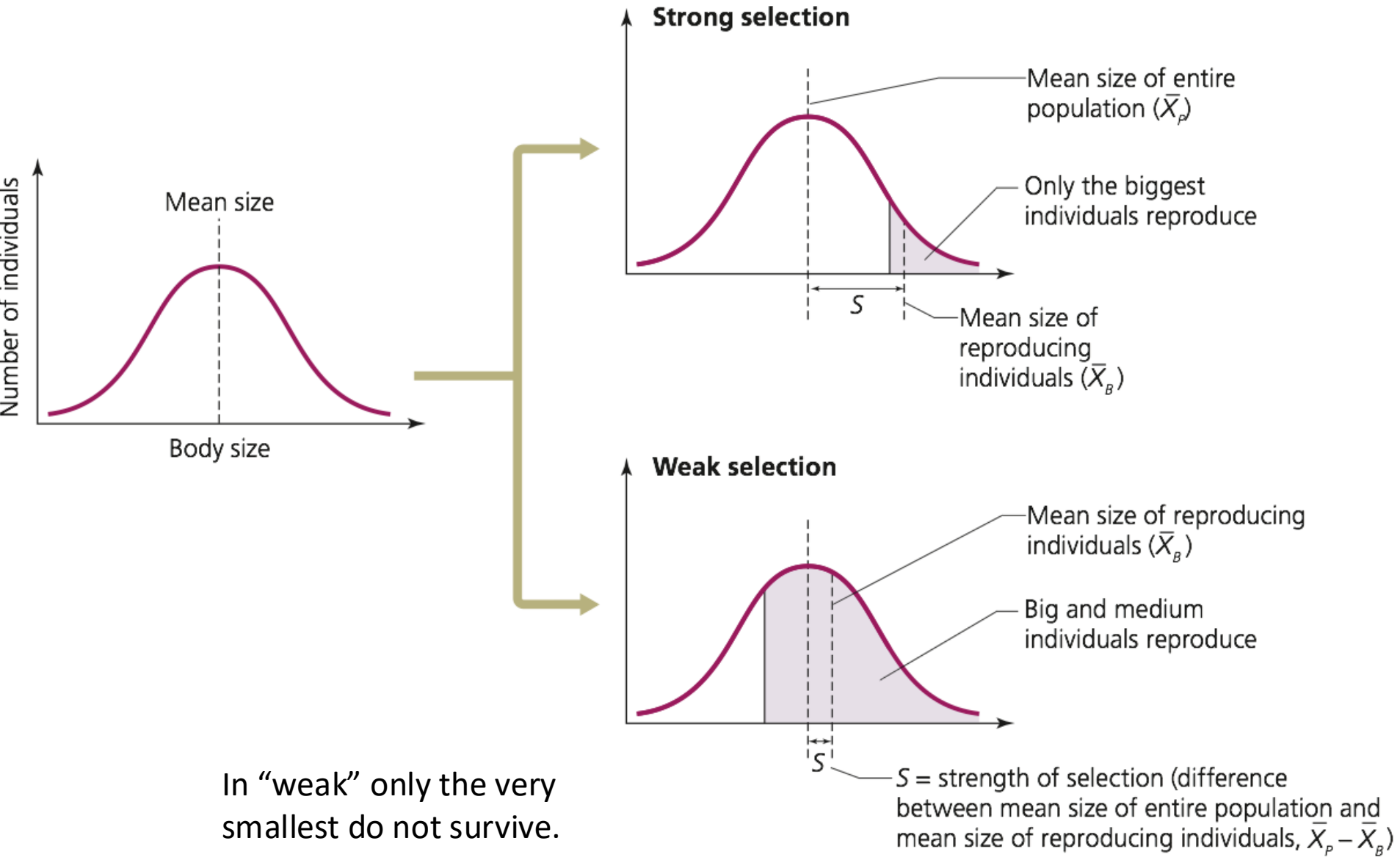
The evolutionary response to selection (R) or the degree to which a population evolves (in height for example) will be equal to the heritability (h^2) times the selection differential (S).

FYI:
I'm sharing the images just to reinforce the fact that you should review and understand on your own!

Same material as the bear handout!

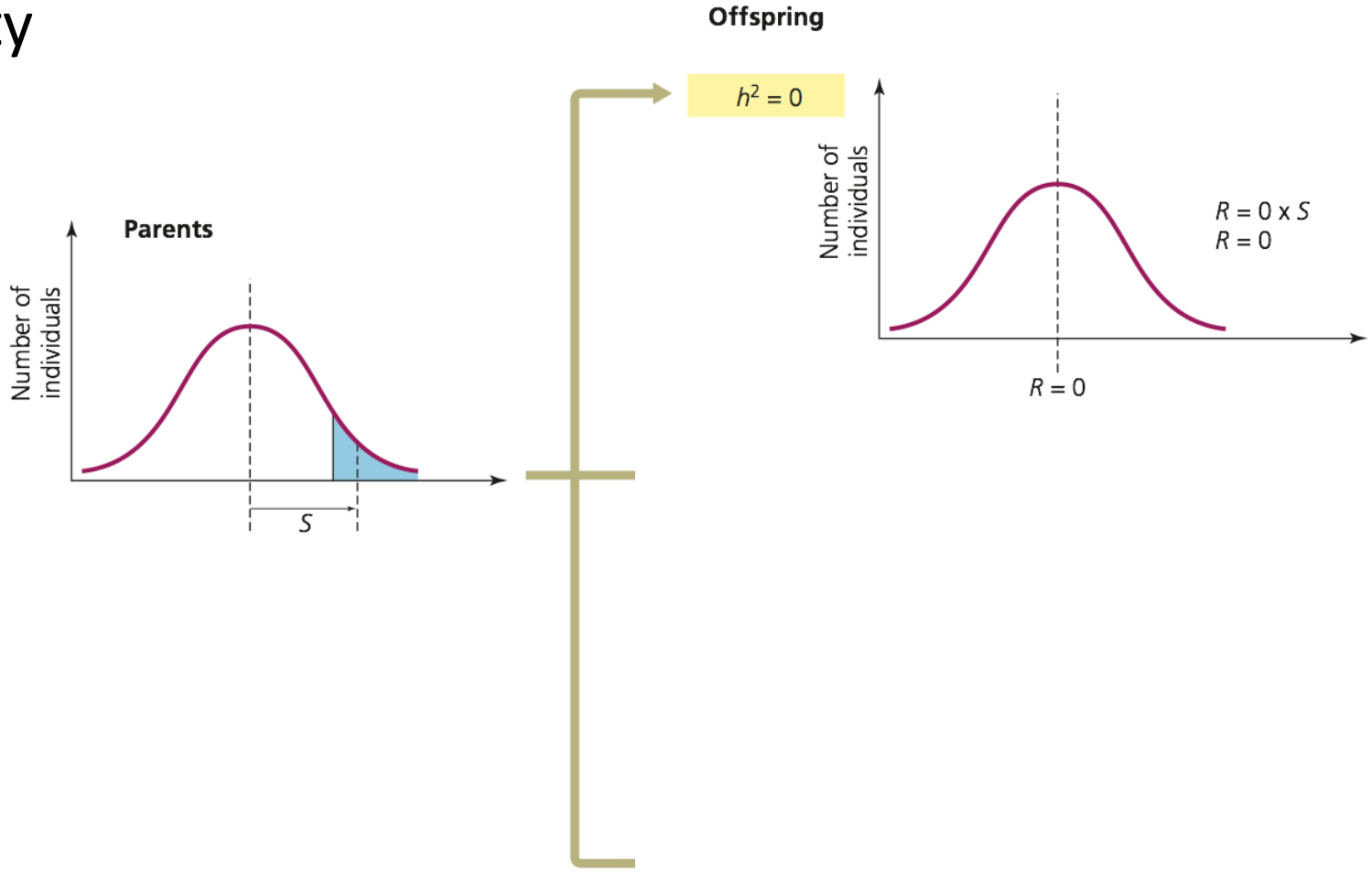
What are they showing??

How do we measure the selection differential (S)?



In "weak" only the very smallest do not survive.

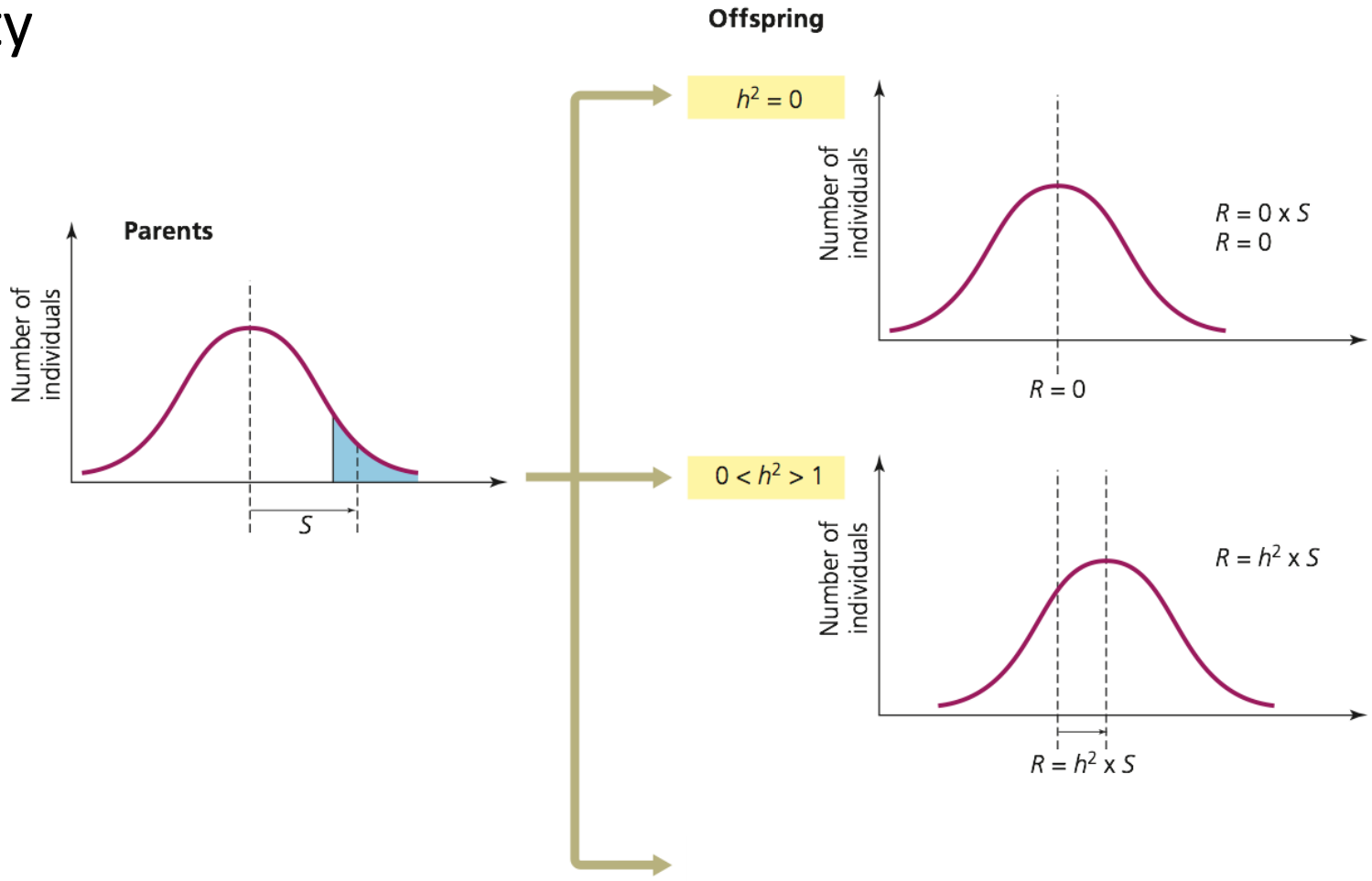
Response to selection (R) will differ depending on heritability



R = h^2 x S

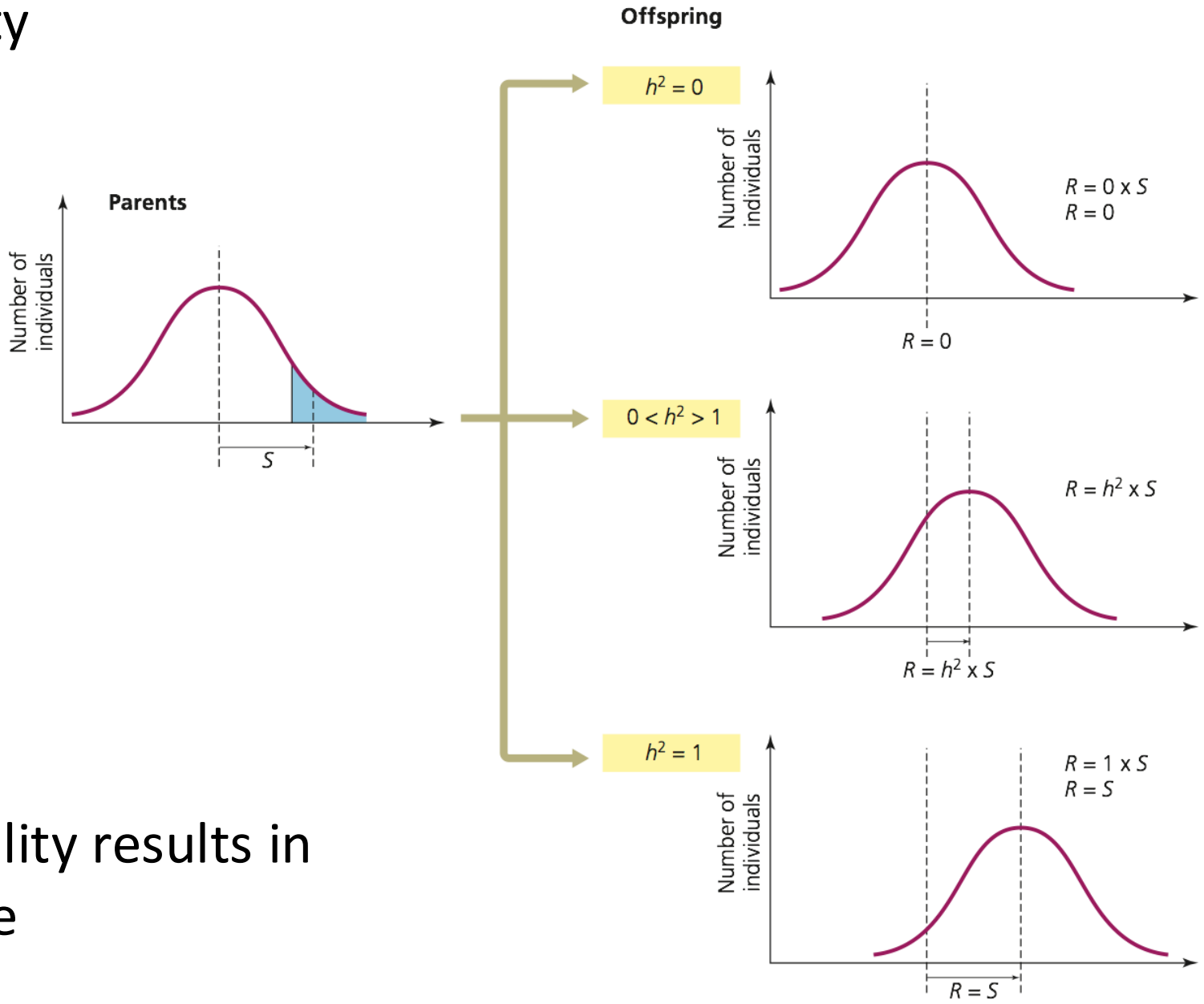
High heritability results in larger change

Response to selection (R) will differ depending on heritability



High heritability results in larger change

Response to selection (R) will differ depending on heritability



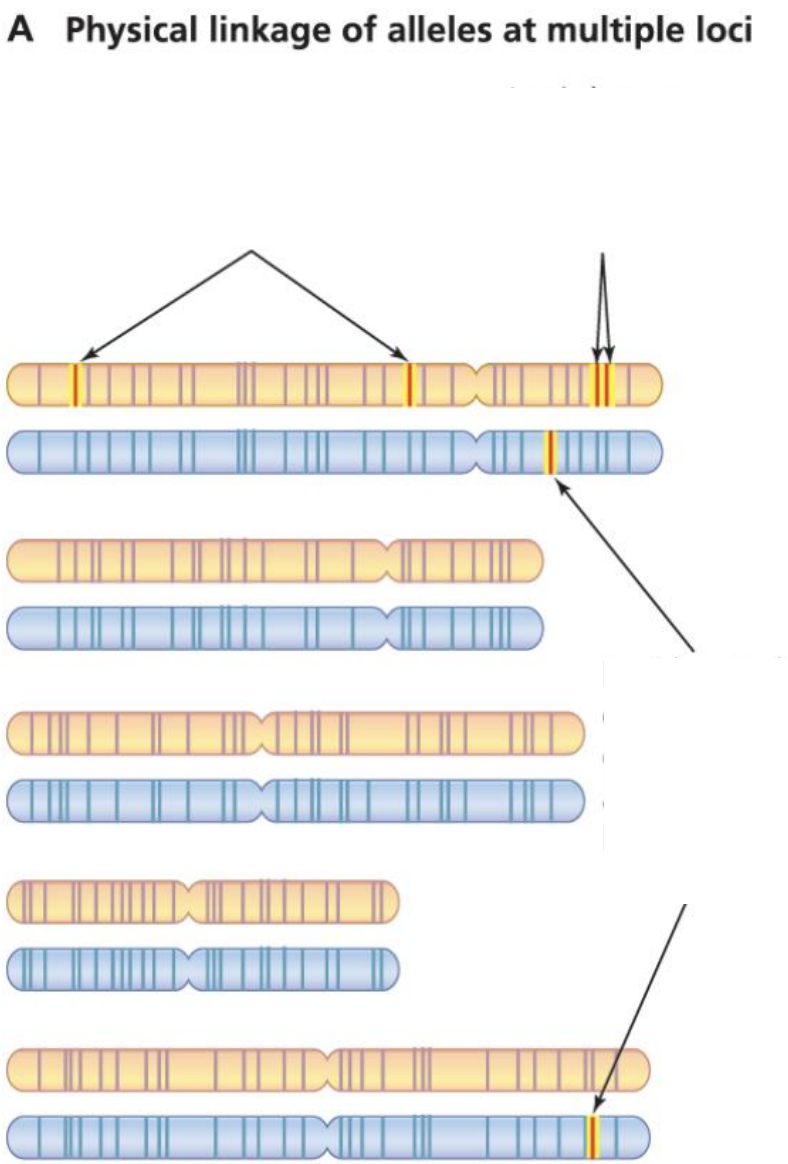
High heritability results in larger change

Chapter 7

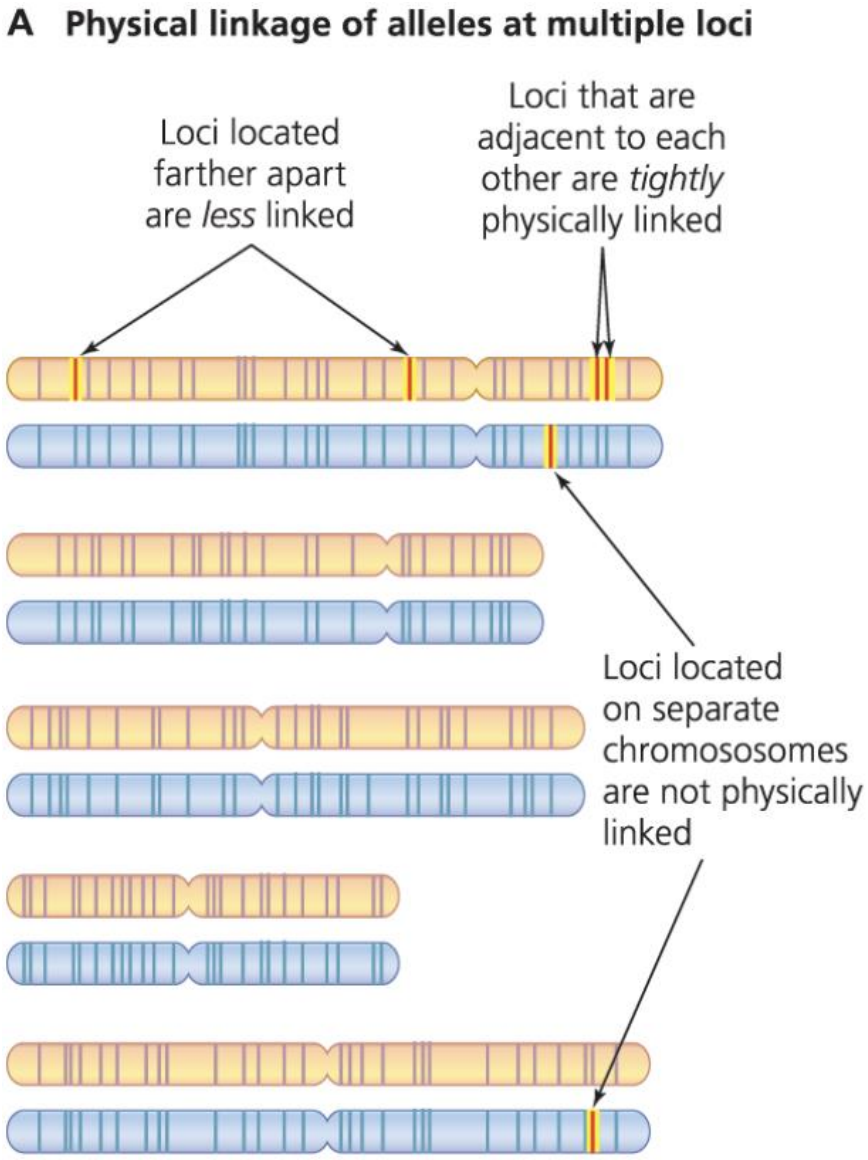
Beyond alleles: quantitative genetics and the evolution of phenotypes

- What is quantitative genetics?
- Extending Hardy-Weinberg to polygenic traits
- Two ways of estimating narrow sense heritability
  1. Parent-Offspring Regression
  2. The Breeders Equation!
- **Coat color in mice-linkage and connecting genes to phenotypes.**
- "Modes of selection"

- **Coat color in mice-linkage and connecting genes to phenotypes.**



Which loci or genes will be more or less likely to show linkage?



Remember that this connects with concept of **hitchhiking** in lactase persistence example.

QTL analysis of coat color in mice (quantitative trait loci)

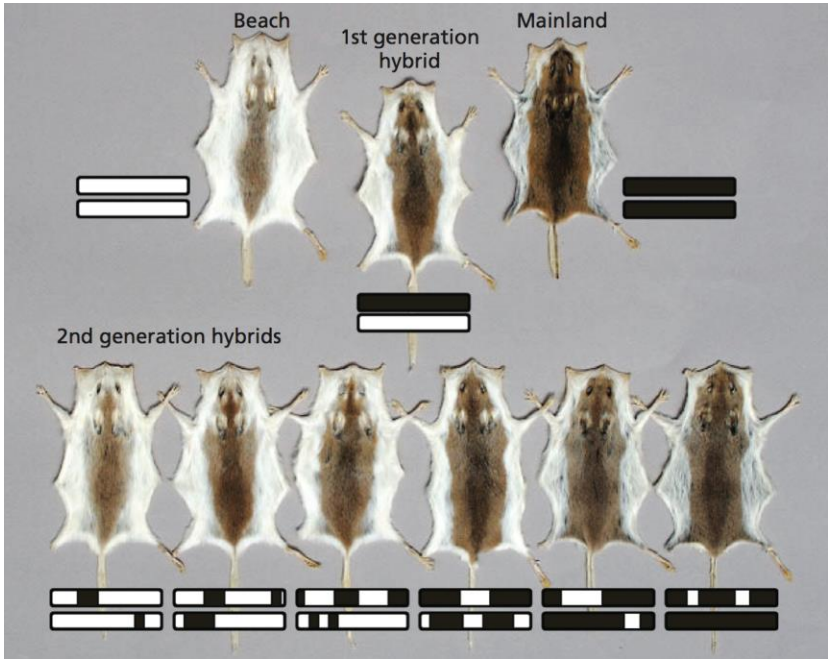
Basically searching for **genetic markers** correlated with light or dark coloration.

No need to know exactly what QTL analysis is!

What are **genetic markers**?

Regions that are correlated or associated with a certain trait or phenotype.

When we find markers we ask-are they actually important genes directly affecting the trait of interest OR are they just hitchhiking because they are near the gene that is actually affecting coat color?



They found two genes in two regions that were associated with coat color!

Because mice are a model organism we had some previous info on what these genes do

Mc1r gene

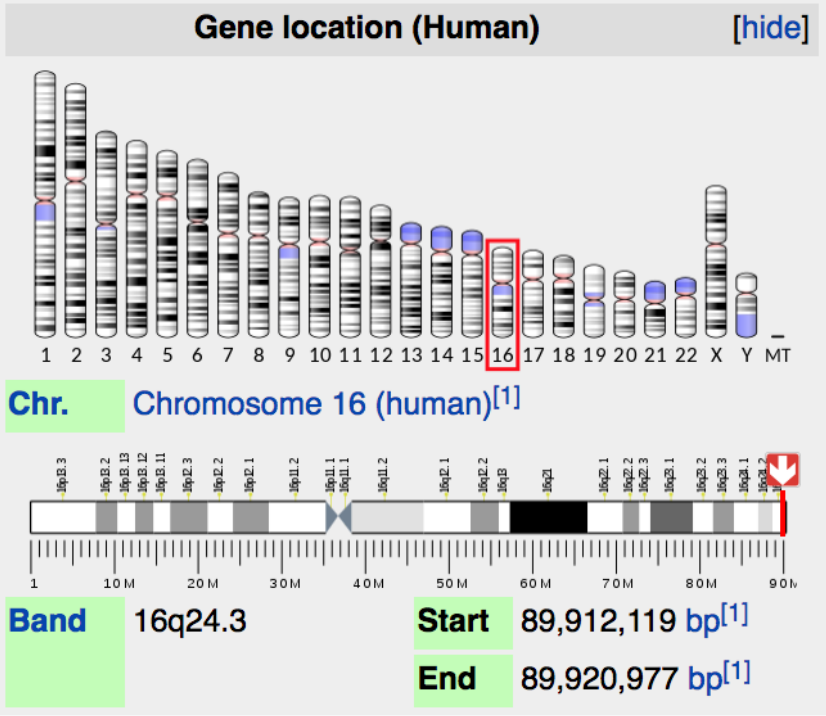
Agouti gene

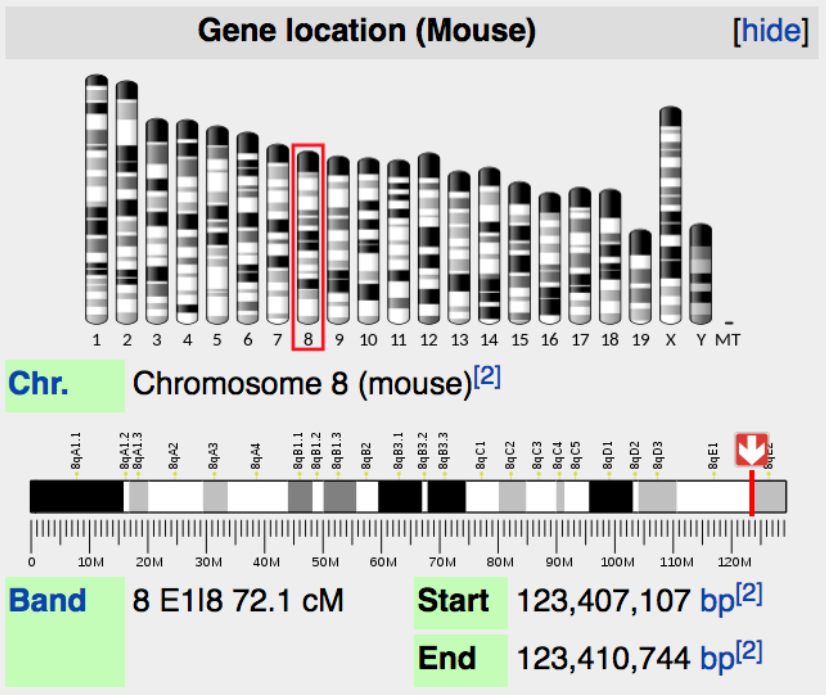
(actually called Agouti Signaling Protein that in humans is encoded by the ASP gene.)

Mc1r

If you look up a gene in Wikipedia you can learn lots of things!

What do you notice?





How do these genes affect coat color?

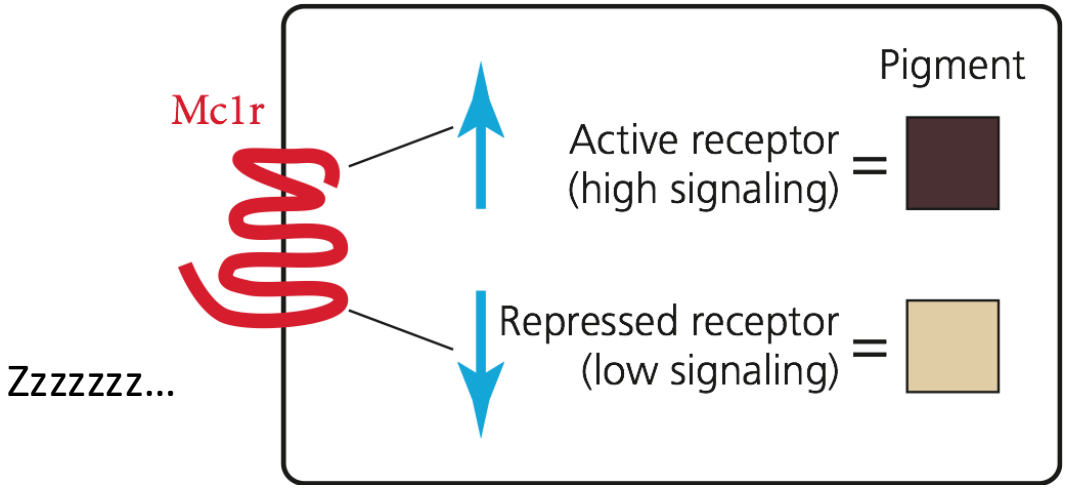
There is a dark pigment called melanin.

Both genes affect the biochemical pathway that makes this pigment.

Mc1R

This gene makes a protein that is a receptor on cell surface. One mutation decreased activity or **sensitivity of the receptor (made it kind of lazy)** so message to make more melanin did not go through =lighter coat.

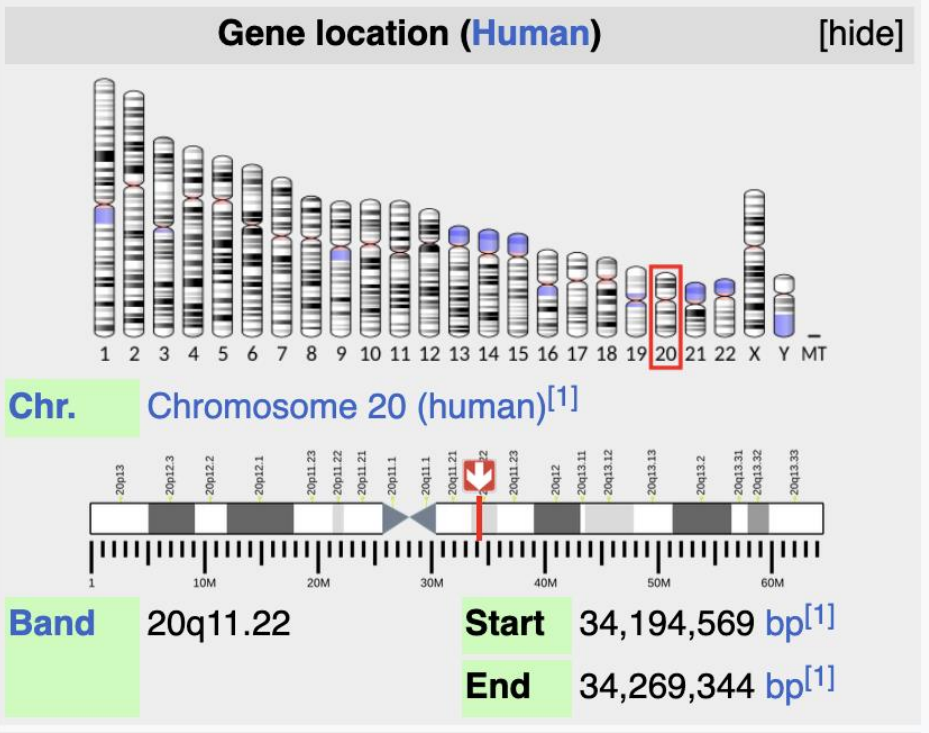
Kind of makes the receptor dysfunctional!

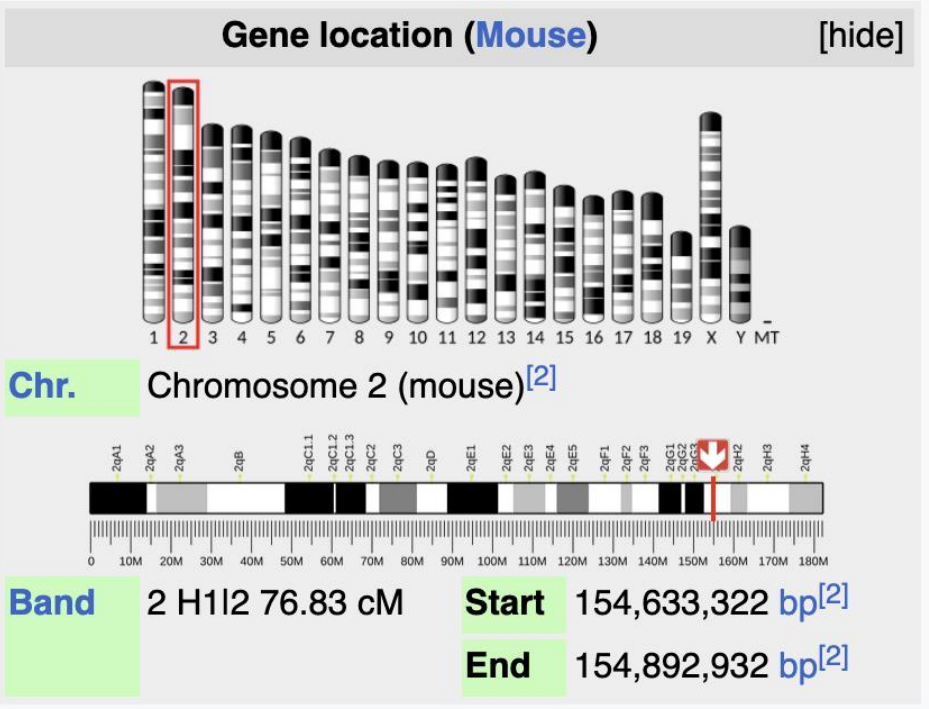


Agouti gene

If you look up a gene in Wikipedia you can learn lots of things!

What do you notice?





Agouti

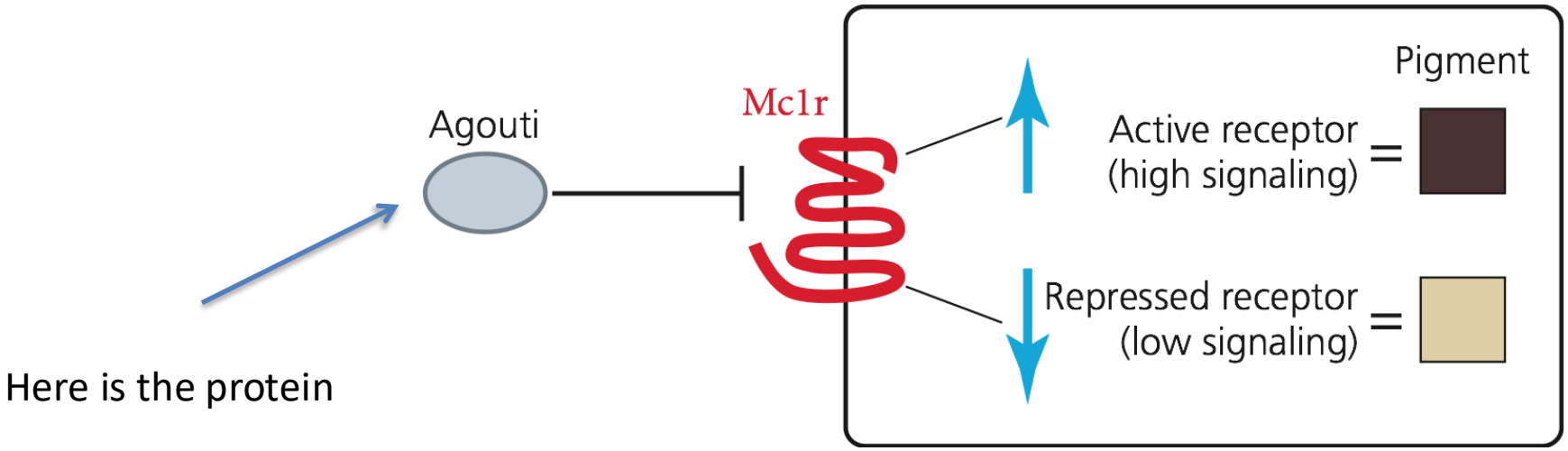
Another gene makes a **protein (called agouti)** that can partially **shut down** the Mc1r receptor so again message to make pigment does not go through.

They call Agouti an "antagonist."

Mutation → more agouti production →more shutting down and less melanin production=lighter coat

Does this sound familiar??? Labs? Epistasis?

Interaction between the two genes!



How much of this do you understand?

Comparative Study > Anim Genet. 2000 Jun;31(3):194-9.
doi: 10.1046/j.1365-2052.2000.00639.x.

Identification of a premature stop codon in the melanocyte-stimulating hormone receptor gene (MC1R) in Labrador and Golden retrievers with yellow coat colour

R E Everts [1], J Rothuizen, B A van Oost

Affiliations + expand

PMID: 10895310 DOI: 10.1046/j.1365-2052.2000.00639.x

Abstract

We have examined whether black/yellow coat colour in Labrador retrievers is controlled by allelic variants at the extension locus. As the gene encoding the melanocyte-stimulating hormone receptor (MC1R) has been shown to correspond to the extension locus in several species, we have determined **the genomic MC1R sequence in Labrador retrievers with black and with yellow coat colour. Using primers based on the fox (*Vulpes vulpes*) MC1R sequence we initially isolated and sequenced the innerpart of the canine MC1R. By means of inverse PCR we succeeded in the characterization of both flanking regions of the MC1R gene (Genbank: AF064455). Comparison of the complete MC1R sequences of a yellow and a black Labrador retriever revealed a single C-->T mutation at nucleotide position 916 in the yellow dog. This transition changed the codon for arginine at position 305 into a stop codon,** resulting in the elimination of the evolutionary strongly conserved 10 carboxyterminal amino acid residues. With an allele-specific-oligonucleotide (ASO) test it was shown that the mutation cosegregated with the recessively inherited yellow coat colour in the Labrador retriever. **Golden retrievers also appeared to be homozygous for the mutation. Seventeen other breeds were all negative for the mutation. Since the Labrador and Golden retriever are closely related, we suggest a common founder for the yellow coat colour in Labrador and Golden retrievers.**

A bit more about the Agouti gene in humans.
Since it relates to coat or fur color in many animals, and we humans are animals - does it relate to skin color in humans?

Wikipedia!
Human homologue *(what does homologue mean?)*
Agouti signaling protein (ASP) is the human homologue of murine *agouti*. It is encoded by the human agouti gene on chromosome 20 and is a protein consisting of 132 amino acids.

It is expressed much more broadly than murine *agouti* and is found in adipose tissue, pancreas, testes, and ovaries, whereas murine *agouti* is solely expressed in melanocytes.[6] ASP has 85% similarity to the murine form of *agouti*.[31]

What is it called when one gene/locus has effects on many different traits (or in this case tissues)?
In humans the agouti gene is pleiotropic!

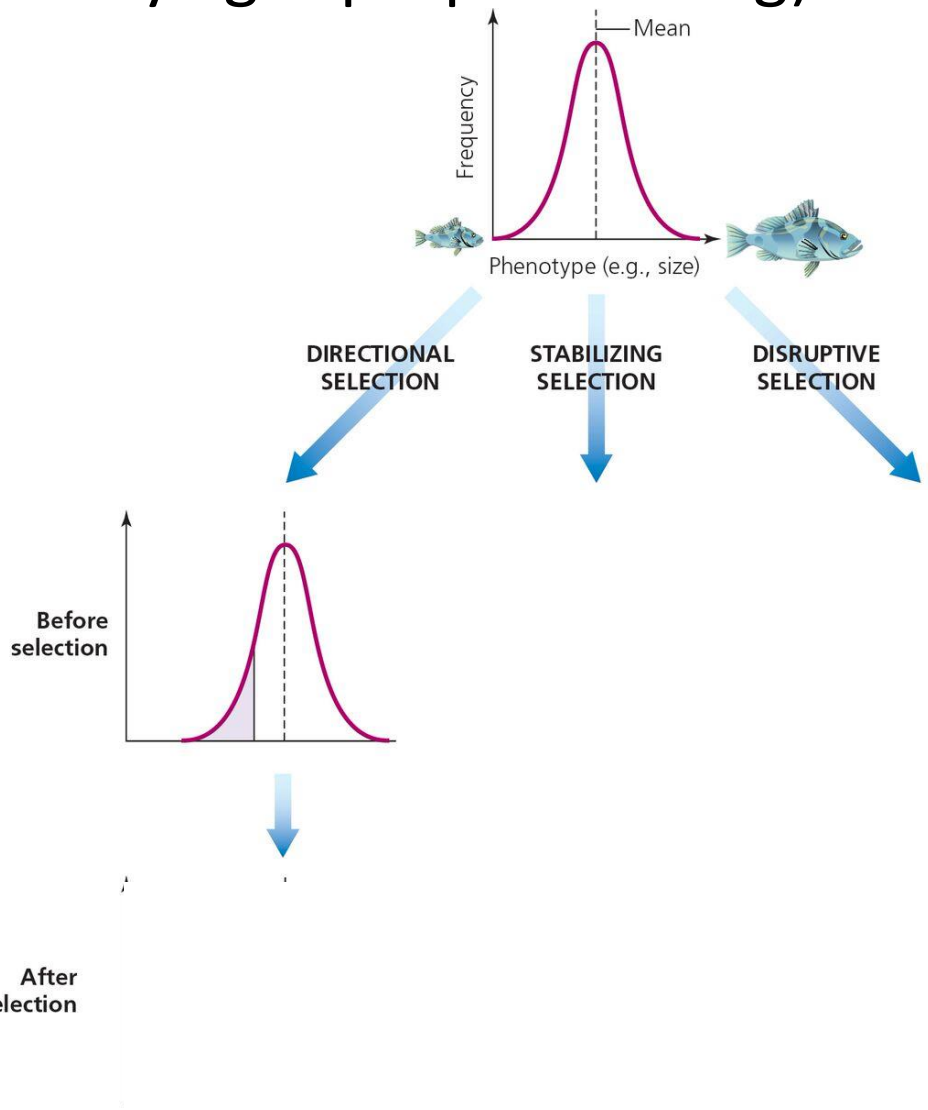
Chapter 7

Beyond alleles: quantitative genetics and the evolution of phenotypes

- What is quantitative genetics?
- Extending Hardy-Weinberg to polygenic traits
- Two ways of estimating narrow sense heritability
  1. Parent-Offspring Regression
  2. The Breeders Equation!
- **Coat color in mice-linkage and connecting genes to phenotypes.**
- "Modes of selection" - Make sure to review on your own!

Modes of selection

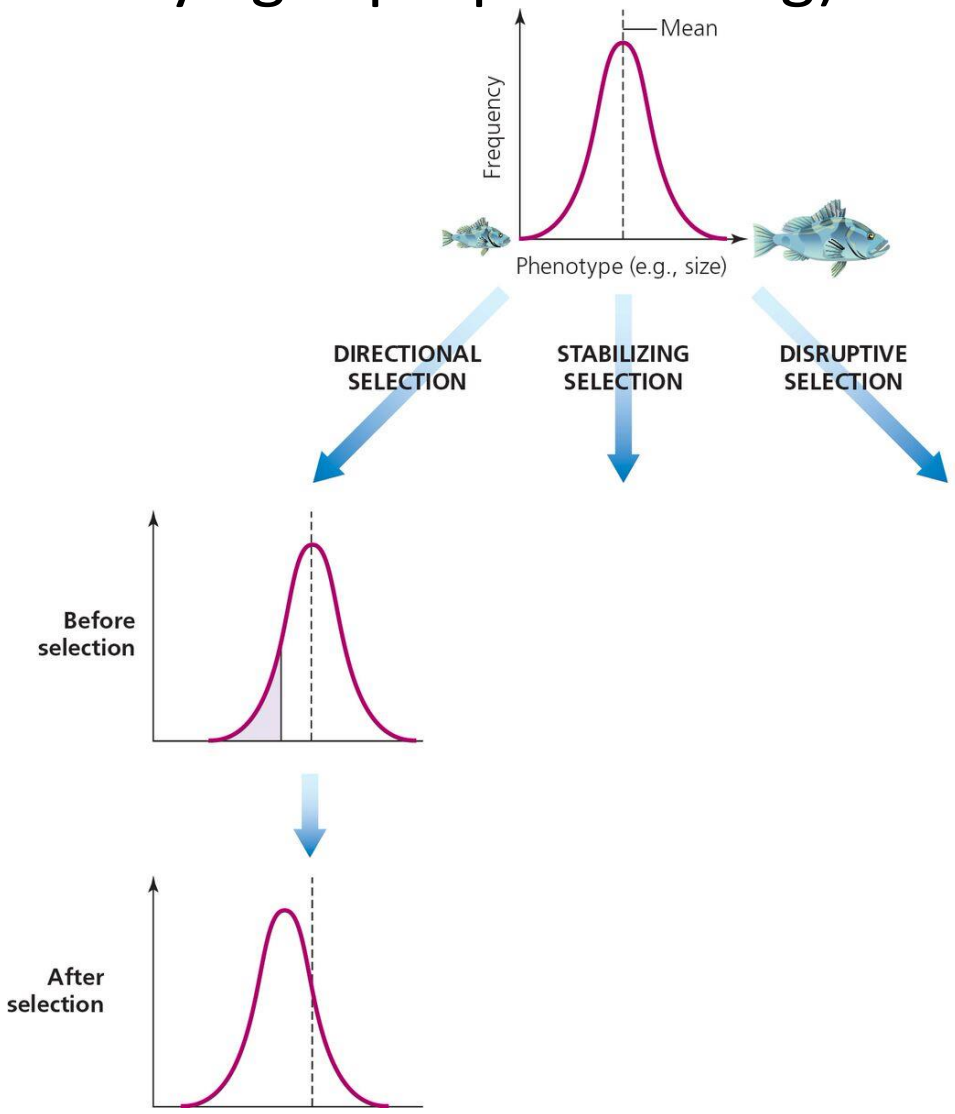
Who is surviving and reproducing in the left hand graph? (represented by light purple shading)



If only small fish survive what will curve look like in next generation?

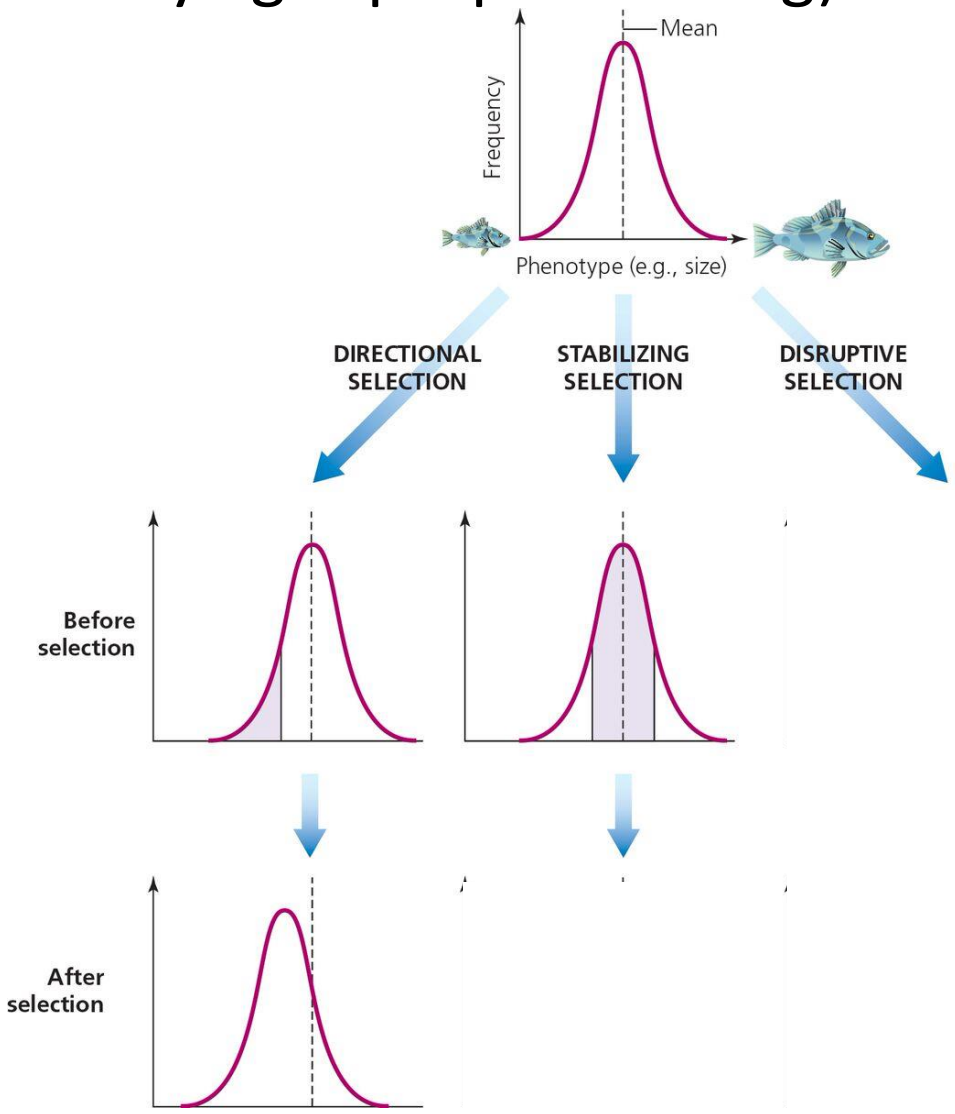
Modes of selection

Who is surviving and reproducing in the left hand graph? (represented by light purple shading)



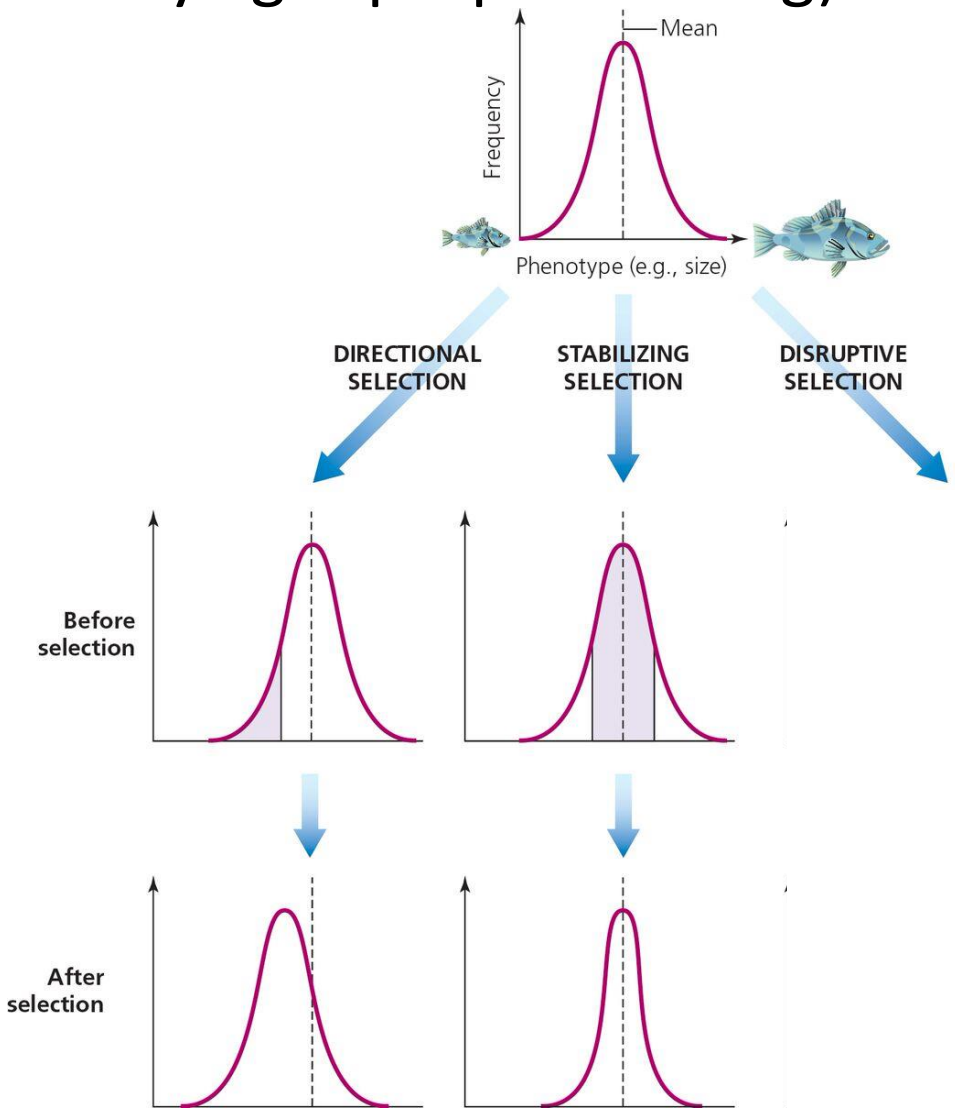
Modes of selection

Who is surviving and reproducing in the left hand graph? (represented by light purple shading)



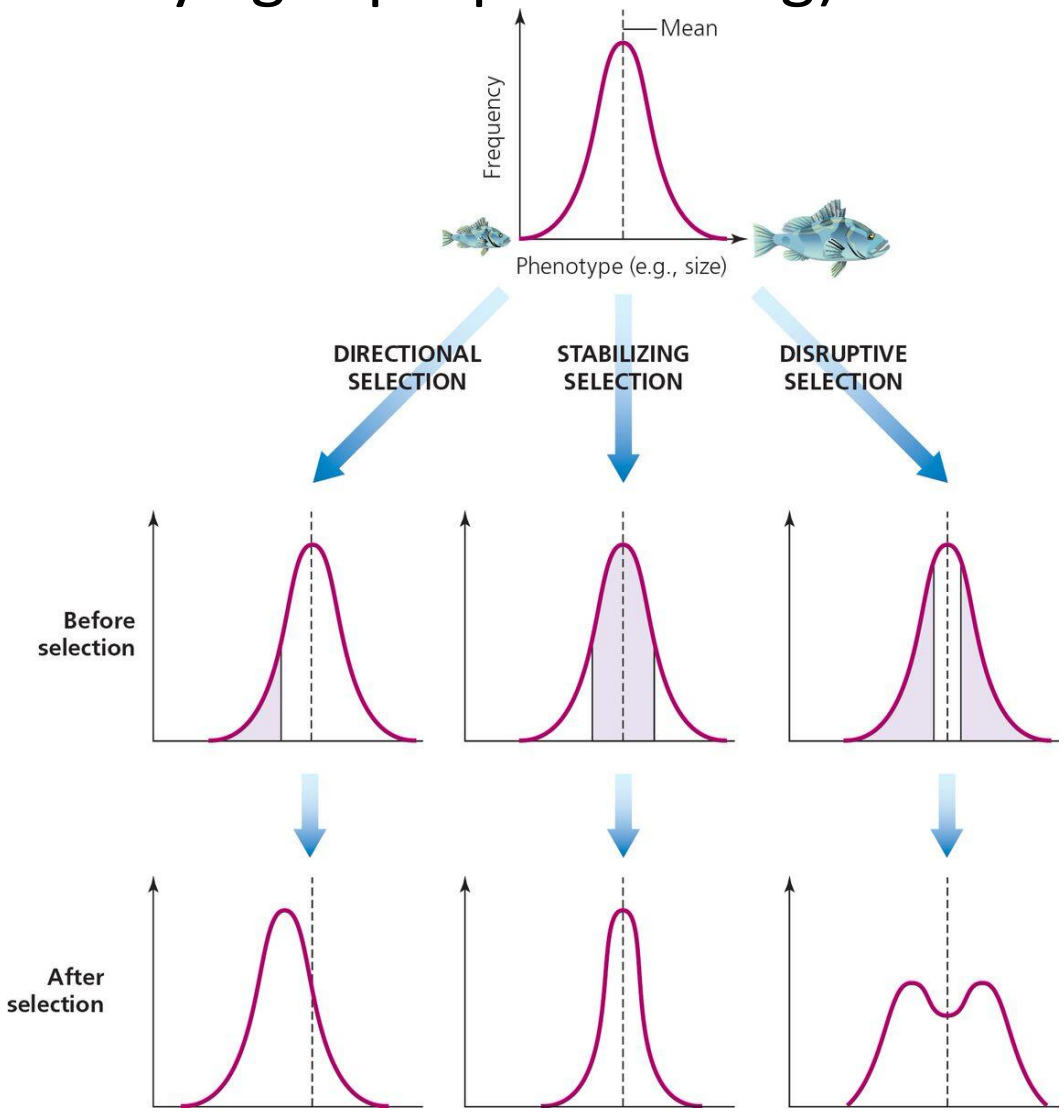
Modes of selection

Who is surviving and reproducing in the left hand graph? (represented by light purple shading)



Modes of selection

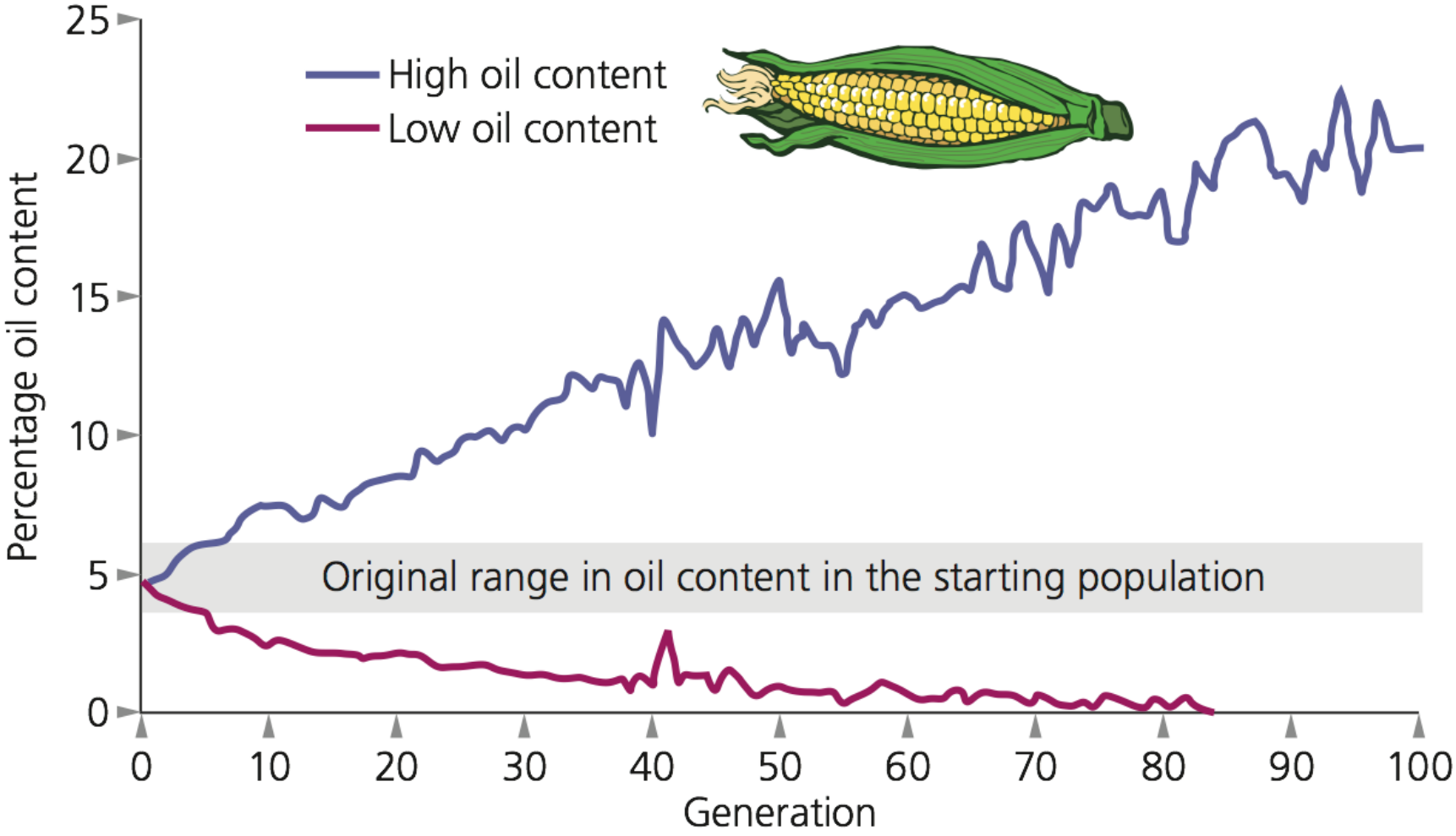
Who is surviving and reproducing in the left hand graph? (represented by light purple shading)



Directional artificial selection (in both directions!)

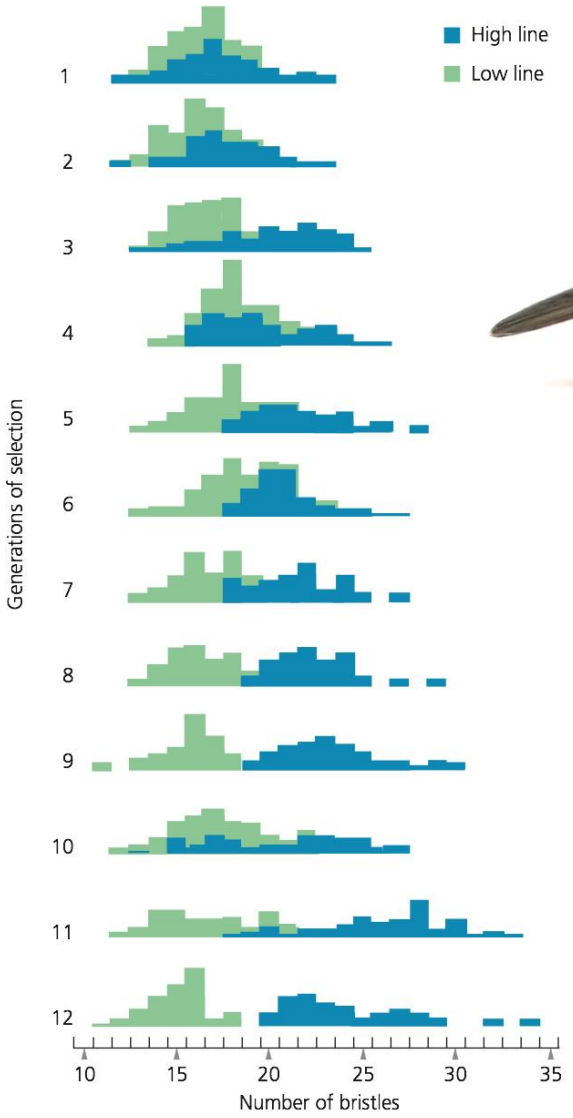
What is with all the zigs and zags???

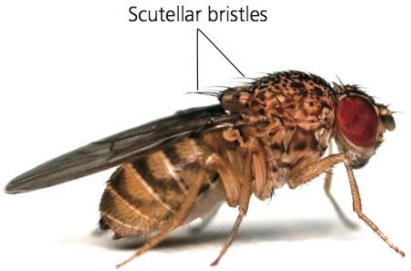
Recombination?



Selected 24 plants in each generation with hi and low

Disruptive selection in a lab population of fruit flies!





Why is the response to selection so erratic (at least in high line). What could be going on?

Recombination?