

Today:

Quantitative Genetics

Broad Heritability

Narrow Heritability

QTL Mapping

Evolutionary Genetics

Darwin's Theory

Forces Acting on Variation

Adaptive Landscapes

Molecular Evolution

Protein Evolution

Regulatory Evolution

Common Ancestry

Speciation

Last Time:

Defined Quantitative Traits

- Environmental differences & developmental noise
- Multiple genes

Norms of Reaction

- Environment -> phenotype within genotype
- “Superior” genotypes unlikely
- Breeding specific for environment

Heritability

- Must be sure not environment
- Extremes from crosses show shift from mean

Goals of a Quantitative Geneticist:

1. Is there a genetic component to the quantitative variation observed in a trait?
2. Is there genetic variation and if so what phenotypes are expected for each genotype?
3. What is the relative contribution of genetic variation verses environmental effects and developmental noise?
4. How many and which genes contribute to the trait?

Q: If there is a genetic component and an environmental component to the quantitative trait, how do we figure out what they are and how strong they are?

Ans: Let's start by defining the problem a little more specifically.

Breaking a quantitative trait into its components:

- Typically a quantitative trait is described by its *Phenotypic Variance* (s_p^2). There is potentially a genetic and environmental component to the variance.
- If different genotypes have different phenotypic distributions then the differences between genotypic means is the genetic component of the phenotypic variance (s_g^2). This is also called the *Genetic Variance*.
- The remaining phenotypic variance after accounting for the genetic variance is the *Environmental Variance* (s_e^2).

$$s_p^2 = s_g^2 + s_e^2 \quad (+ 2 \text{ cov}_{ge})$$

Broad Heritability (H^2) - Fraction of phenotypic variance contributed by genotypic variance.

$$\begin{aligned} H^2 &= s_g^2 / s_p^2 \\ &= s_g^2 / (s_g^2 + s_e^2) \end{aligned}$$

Estimation:

1. Estimate s_e^2 and infer s_g^2 . Make homozygous lines. Do paired crossings to make representative Hets. Measure phenotypic variance within offspring of each cross.

Average variance is s_e^2 .

2. Estimate directly using phenotypic and genetic similarity of relatives. Major problem with this approach is relatives often have correlated environments. This can be controlled for but it is difficult.

To emphasize:

Heritability of a trait difference is specific to each population and in each set of environments

It cannot be extrapolated from one population or set of environments to another

Also on relative contribution:

High heritability does not mean phenotypic plasticity across environments is low. It just means that average differences between genotypes are large compared with environmental variation within genotypes.

High heritability does not imply low phenotypic plasticity across environments. Example: IQ in adopted children relative to their biological and adopted parents (this is hypothetical data).

	Children	Bio. Par.	Adopt. Par.
	110	90	118
	112	92	114
	114	94	110
	116	96	120
	118	98	112
	120	100	116
Mean	<i>115</i>	<i>95</i>	<i>115</i>

- Children are perfectly correlated with biological parents and not at all with adopted parents. This is a perfectly heritable trait ($H^2 = 1.0$).
- Yet the children all have much higher IQ than their biological parents and as a group have the same mean IQ as their adopted parents.
- Therefore environment can strongly influence IQ but it played no roll in determining the variation in IQ in this group of adopted children.

Q: If genetic variance is the result of different genotypes, will traits controlled by genes with dominant and recessive alleles, vs. genes with no dominance, show different amounts of genetic variance?

Ans: Yes. Because of this, genetic variance is often broken into *Additive Genetic Variance* (s_a^2) and *Dominance Variance* (s_d^2). Additive genetic variance is due to the contribution of different alleles while dominance variance is simply due to the dominance structure of a gene.

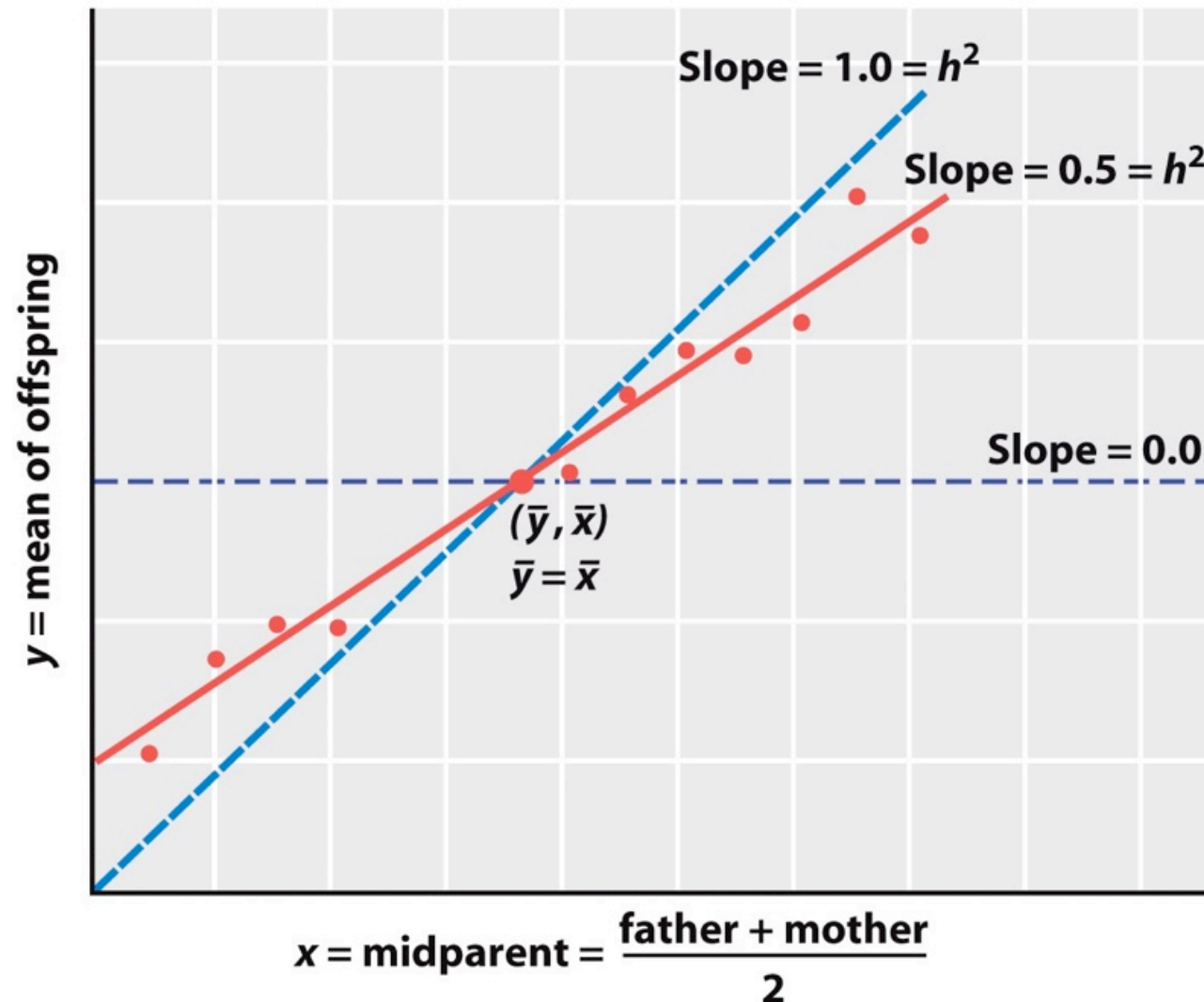
Narrow Heredity (h^2) - The heritability of a trait based just on additive genetic variance (i.e. just on variance due to different alleles).

$$\begin{aligned} h^2 &= s_a^2 / s_p^2 \\ &= s_a^2 / (s_a^2 + s_d^2 + s_e^2) \end{aligned}$$

Estimation:

- Complicated methods using covariance between relatives
- Simple method comparing mean phenotype of offspring to 'midparent' value (average phenotype of parents)

Note that this only works if there are few differences in environment across all individuals and most importantly that relatives do not have more common environments than non-relatives.

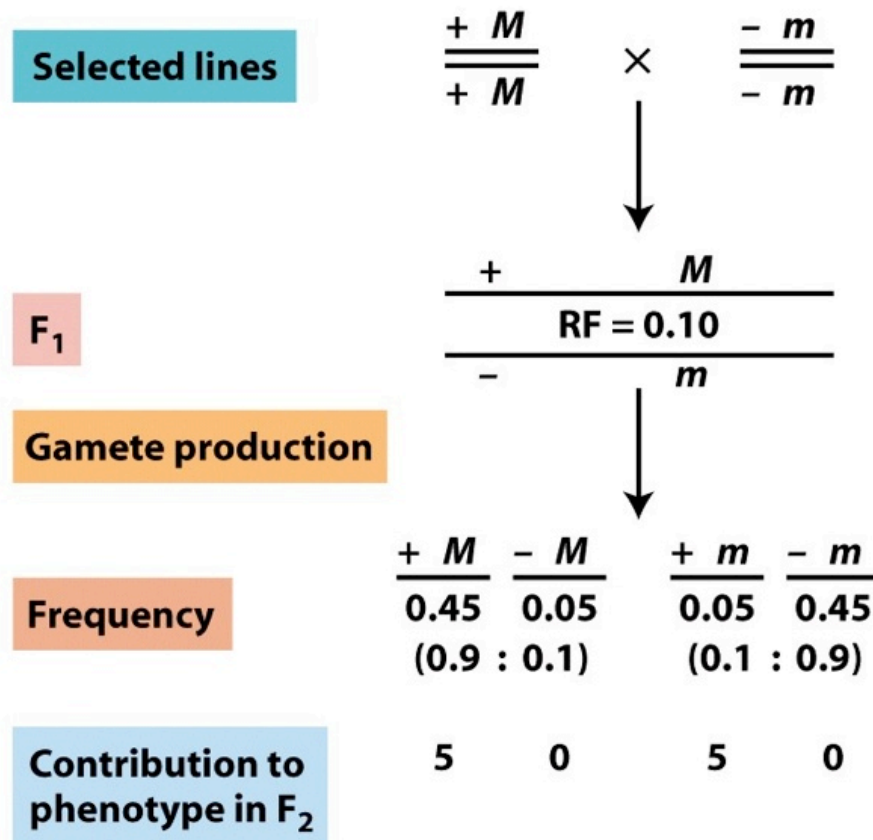


Q: OK, even though it seems like a sticky business to understand heredity in quantitative traits, we're still missing one aspect of this area of research. How do you find the genes responsible for a quantitative trait?

Ans: If you don't have good candidate genes to investigate, then similar to the linkage mapping that we discussed in classical genetics, you can do what is called Quantitative Trait Locus (QTL) Mapping in experimental organisms or Association Mapping in natural populations.

QTL and Association Mapping:

- Use either visible or other markers (RFLPs/SNPs) that have easily distinguished alleles that are distributed throughout the genome
- Look for markers that are highly correlated with your trait of interest across either:
 1. F2s from a cross between two phenotypically different individuals (QTL Mapping)
 2. Just across individuals in a natural population (Association Mapping)



Average phenotypic effect of *M* class = 5 (0.9) + 0 (0.1) = 4.5

Average phenotypic effect of *m* class = 5 (0.1) + 0 (0.9) = 0.5

**Difference between *M*-carrying gametes and *m*-carrying gametes =
4.5 – 0.5 = 4**

**Difference between average F₂ *M* / *M* homozygotes and average
F₂ *m* / *m* homozygotes = 8**

Figure 18-17
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Work on problems 3, 4 & 14 from chapter 18

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Adaptive Landscapes

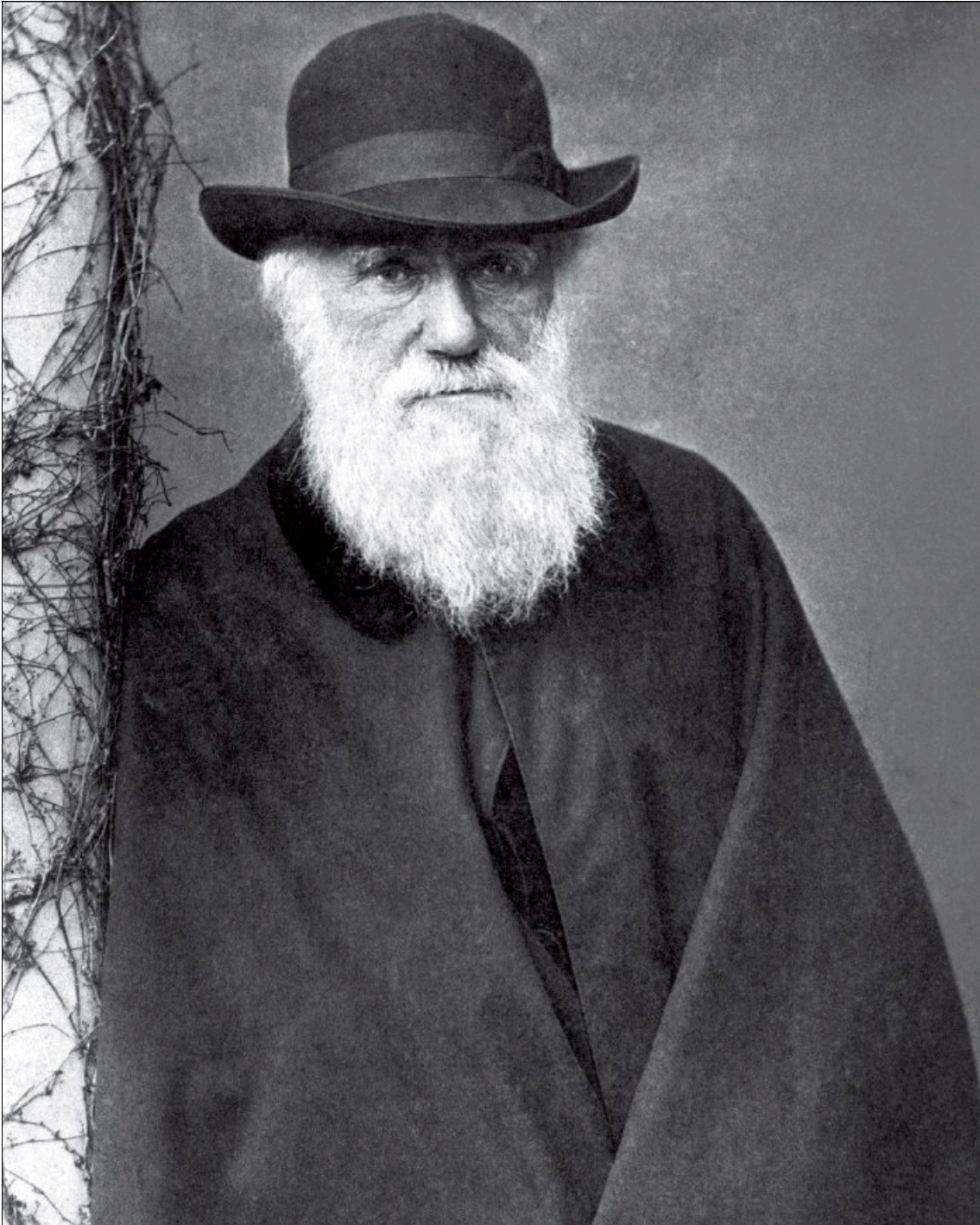
Molecular Evolution

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Common Ancestry

Speciation



Charles Darwin proposed a new explanation for evolution in 1859 (*Origin of Species*) that has been the basis for evolution analysis ever since.

“The preservation of favorable variations and the rejection of injurious variations I call Natural Selection.”

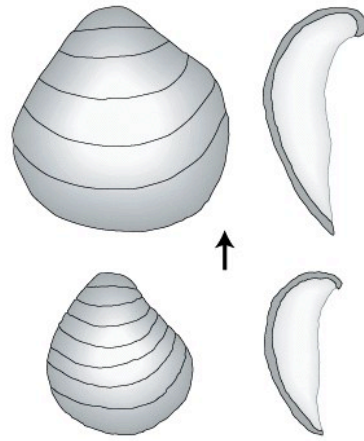
On the Origin of Species, Chapter 4

Major principles of Darwin's theory of evolution:

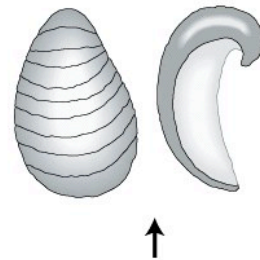
1. *Principle of variation* - Among individuals within any population, there is variation in morphology, physiology & behavior
2. *Principle of heredity* - Offspring resemble their parents more than they resemble unrelated individuals
3. *Principle of selection* - Some forms are more successful at surviving and reproducing than other forms in a given environment

A.

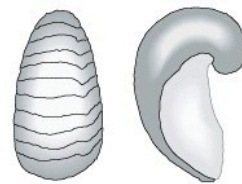
G. gigantea



G. mccullochii



G. arcuata incurva



G. arcuata obliquata



Figure 19-1
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Darwin's theory provided a mechanistic explanation for both (A) phyletic evolution and (B) diversification.

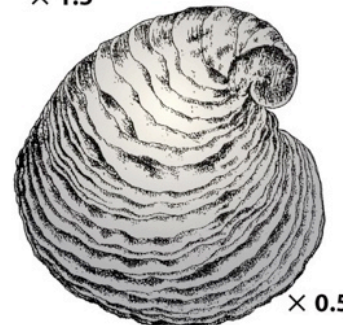
B.



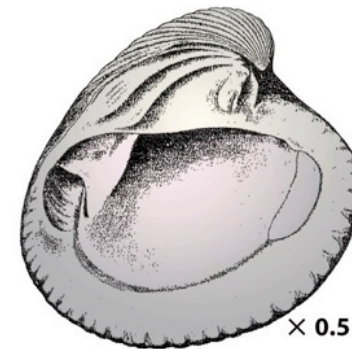
Exogyra arietina Roemer.
Late Cretaceous



Gryphaea arcuata
Lamarck. Early Jurassic



Exogyra ponderosa
Roemer. Late Cretaceous



Venericardia planicosta Lamarck.
Eocene



Myalina subquadrata
Shumard

Figure 19-2
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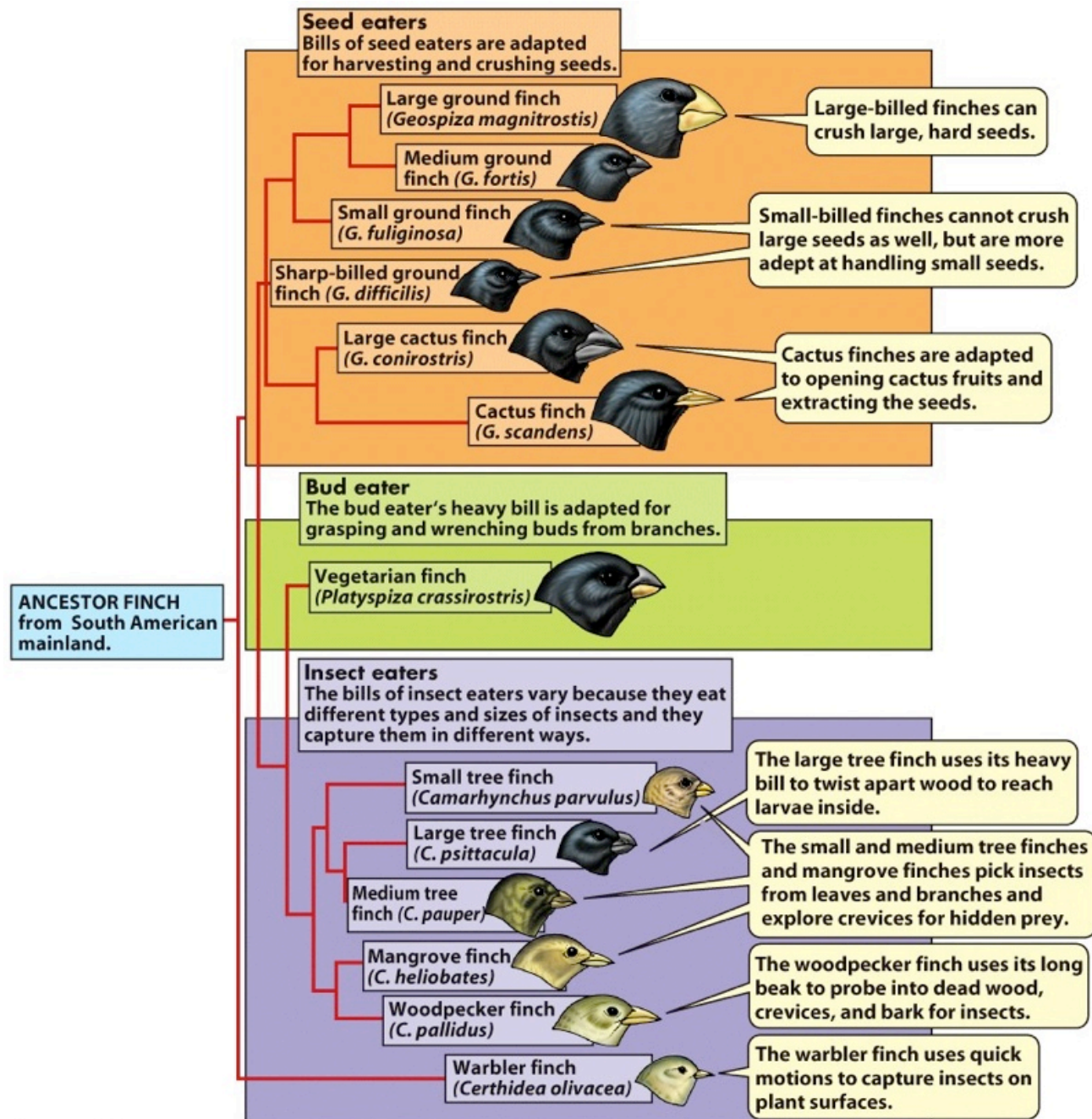


Figure 19-3
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Q: What forces act to increase or decrease variation within and between species? This seems key to understanding how new species evolve.

Ans: There are many and we've learned about the major ones already.

Table 19-1 **How the Forces of Evolution Increase (+) or Decrease (–) Variation Within and Between Populations**

Force	Variation within populations	Variation between populations
Inbreeding or genetic drift	–	+
Mutation	+	–
Migration	+	–
Directional selection	–	+/–
Balancing	+	–
Incompatible	–	+

Q: We talked about the size of the population affecting how big a role drift plays. How does that influence these counter-acting forces?

Ans: Well, in small populations drift can quickly remove variation while its very slow in large populations. So depending on the rate of mutation and migration, which counter-act drift by adding variation, you may have a population that is losing variation or gaining it. As we discussed, when different sub-populations lose variation then variation between these populations increases, leading to new species.

The rule of thumb for migration and mutation is if:

$$Nm \geq 1 \text{ or } N\mu \geq 1$$

where N is the population size, m is the migration rate of new alleles per generation and μ is the mutation rate to new alleles per generation, then the population will not be losing variation due to drift.

So if $N = 100,000$ then to prevent loss of variation the mutation rate must be greater than 10^{-5} .

The interpretation for migration is even simpler. Having one or more migrants per generation is sufficient to maintain variation.

Work on problems 2 & 5 from chapter 19

Q: OK, so I see how sub-populations can drift apart and then lead to new species. But what about selection? How does it contribute to differences between populations?

Ans: Certainly if two populations are in different environments then the fitness advantage of one allele over another might be quite different, leading to differences between the populations. That said, even in identical environments where populations are subject to the same selection pressures, populations often adapt to the same environment in different ways. Let's discuss how this might happen.

Suppose you have two loci that influence a trait and that intermediate phenotypes are most fit. Let's say the heterozygotes produce the intermediate phenotypes and the homozygotes produce the extreme phenotypes. How will selection act on these genotypes to increase fitness?

W represents the mean fitness of the population (mean over genotypes). If we calculate **W** for all possible combinations of allele frequencies then you can get a global picture of how selection might act. This is called a *Fitness Landscape* (or *Adaptive Surface/Landscape*).

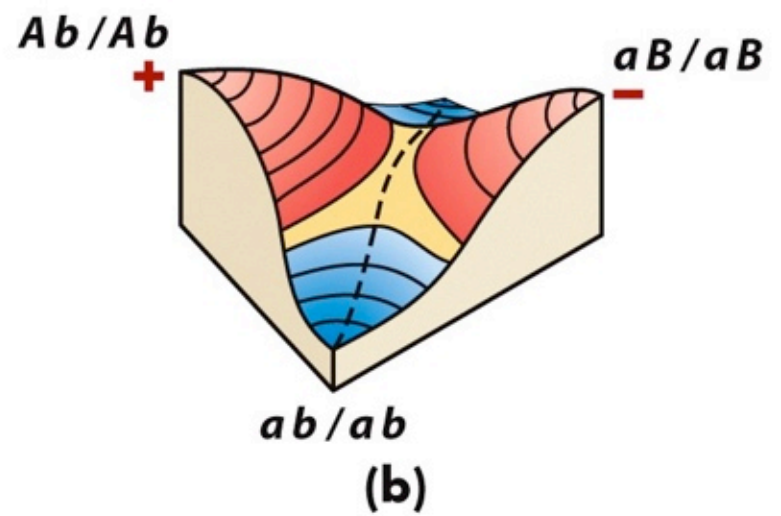
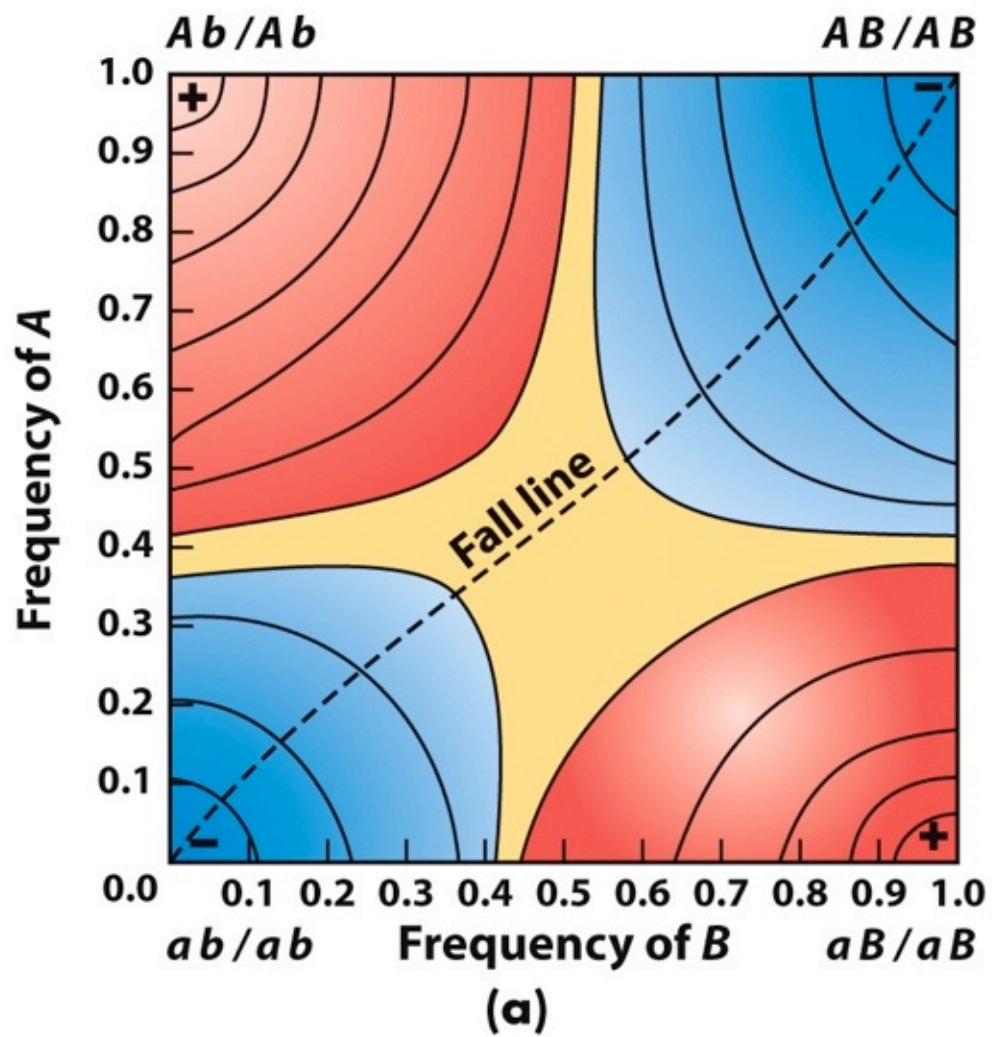


Figure 19-5
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Q: Do populations always march up the steepest gradient in a fitness landscape?

Ans: No. Genetic drift usually causes populations to wander about before, in successful cases, reaching a peak. Note that because of drift populations do not always ascend the closest fitness peak nor do they always make it to a peak at all.

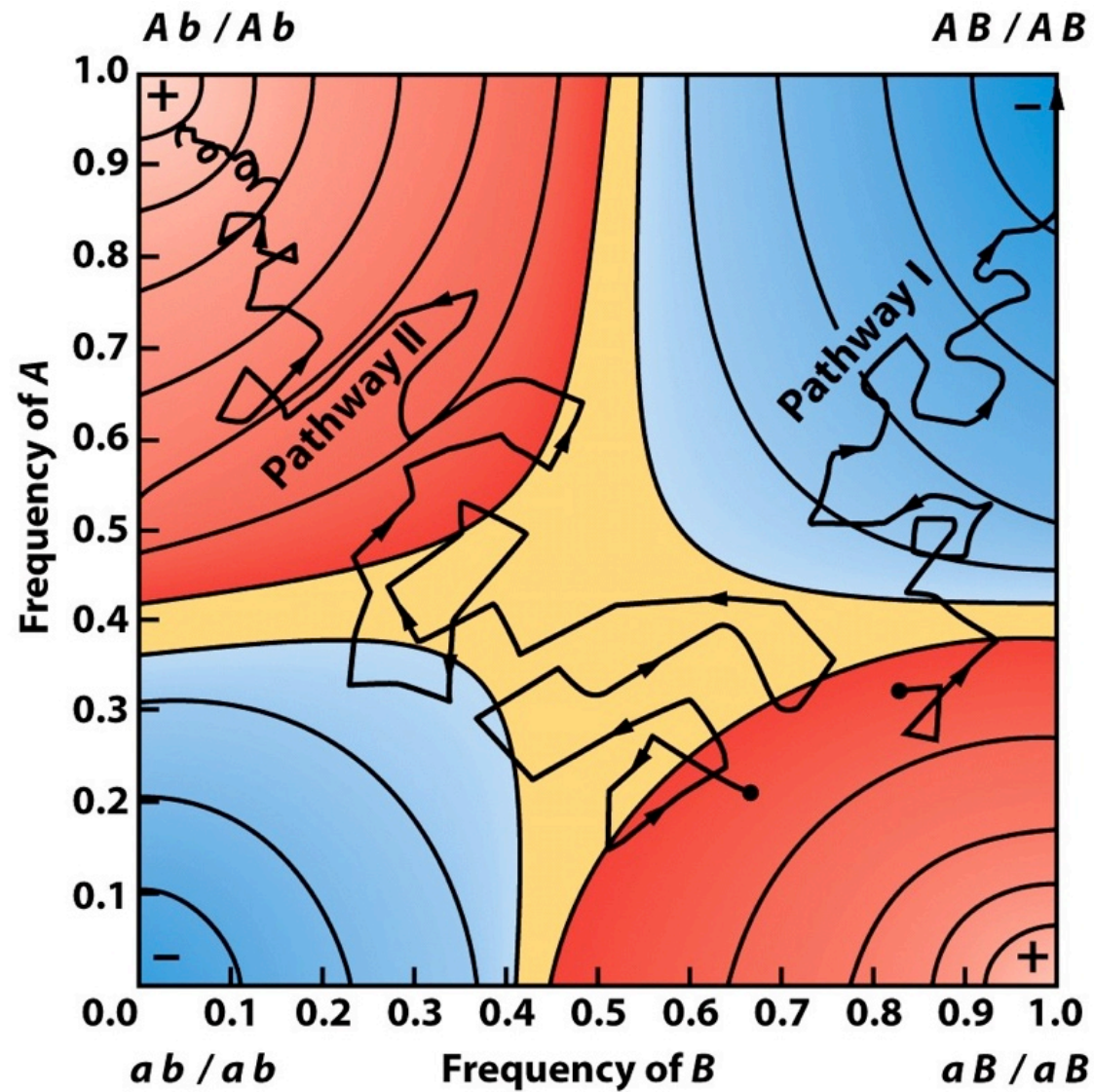


Figure 19-6
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Work on problem 8 from chapter 19

Q: If all these forces are acting in the context of genetic drift to cause populations to accumulate genetic differences, why are some DNA sequences more similar than others as we discussed when talking about comparative genomics?

Ans: Mutations can and will occur at every position in the genome. There are three possible effects on fitness for each new mutation: decrease, increase or no effect.

Mutations at many bases in the genome, because of the function and the fitness of the wildtype allele, tend to be deleterious and therefor these bases accumulate few changes. Mutations in relatively fewer positions in the genome are advantageous but these positions accumulate many changes. Most mutations fall in bases that have no appreciable fitness effect and therefor most of the genome accumulates changes at the mutation rate (neutral rate).

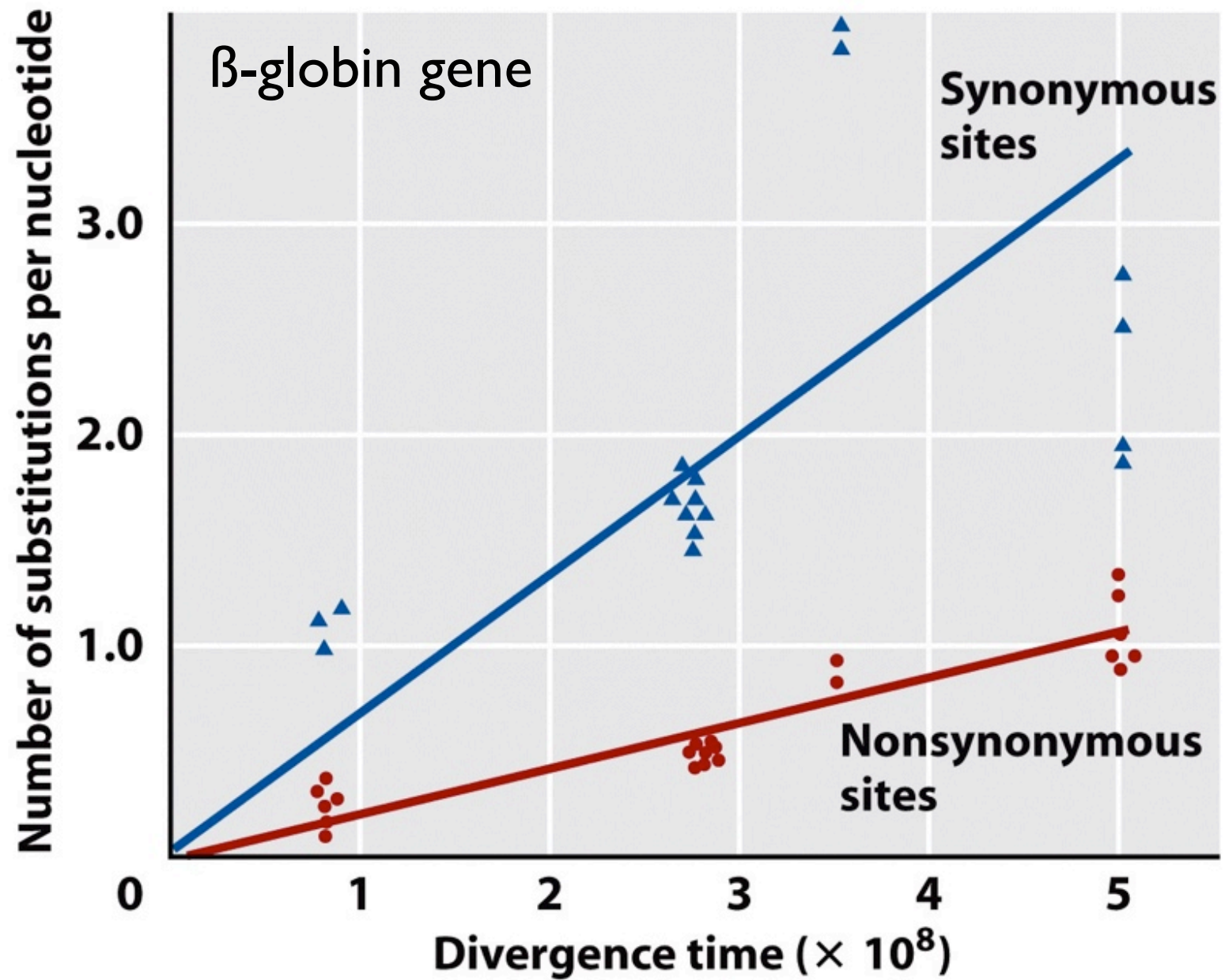


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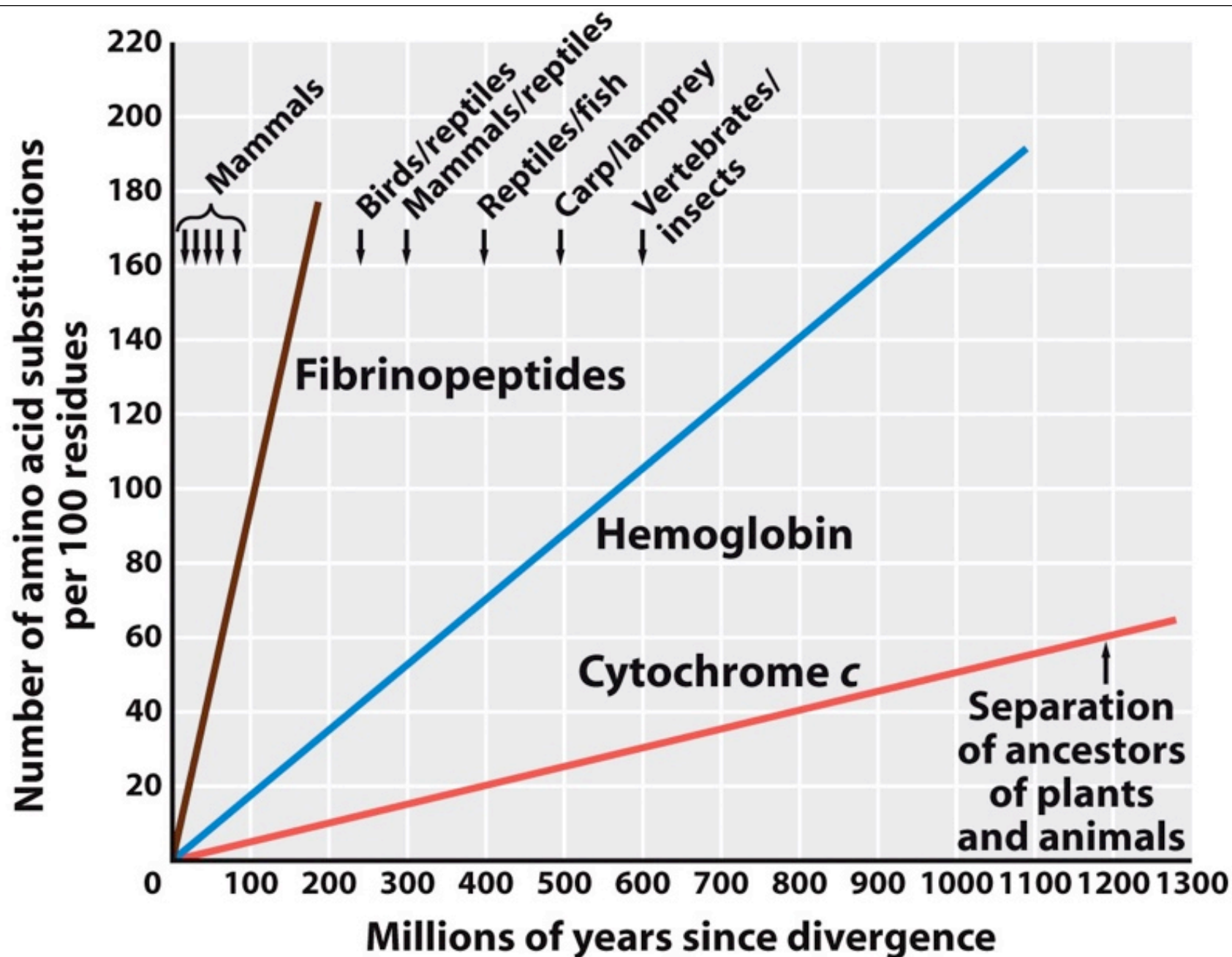


Figure 19-9

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Note: Just because a gene's sequence has changed a lot does not mean that its function or a phenotype it controls has. Genes can accumulate many changes that have little effect on their function. This is due to either the function of the gene being concentrated in a small part of the coding sequence or because many sequences are capable of producing a structurally or functionally equivalent protein.

That said, there are ways of using the rate of change in gene sequences to explore how selection might be acting on genes.

Adaptive changes for higher fitness alleles during the speciation process can result in an increase in the number of amino acid replacement changes observed between species than expected from looking within a population.

Table 19-3 Synonymous and Nonsynonymous Polymorphisms and Species Differences for Alcohol Dehydrogenase in Three Species of *Drosophila*

	Species differences	Polymorphisms
Nonsynonymous	7	2
Synonymous	17	42
Ratio	0.29:0.71	0.05:0.95

Source: J. McDonald and M. Kreitman, "Adaptive Protein Evolution at the *Adh* locus in *Drosophila*," *Nature* 351, 1991, 652–654.

Table 19-3
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Morphological evolution can happen quickly through adaptive selection on advantageous alleles in genes. Genes involved in development, particularly in regulatory pathways, are obvious targets for such selection.



Figure 19-11
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Example: MC1R controls melanin (pigment) production.

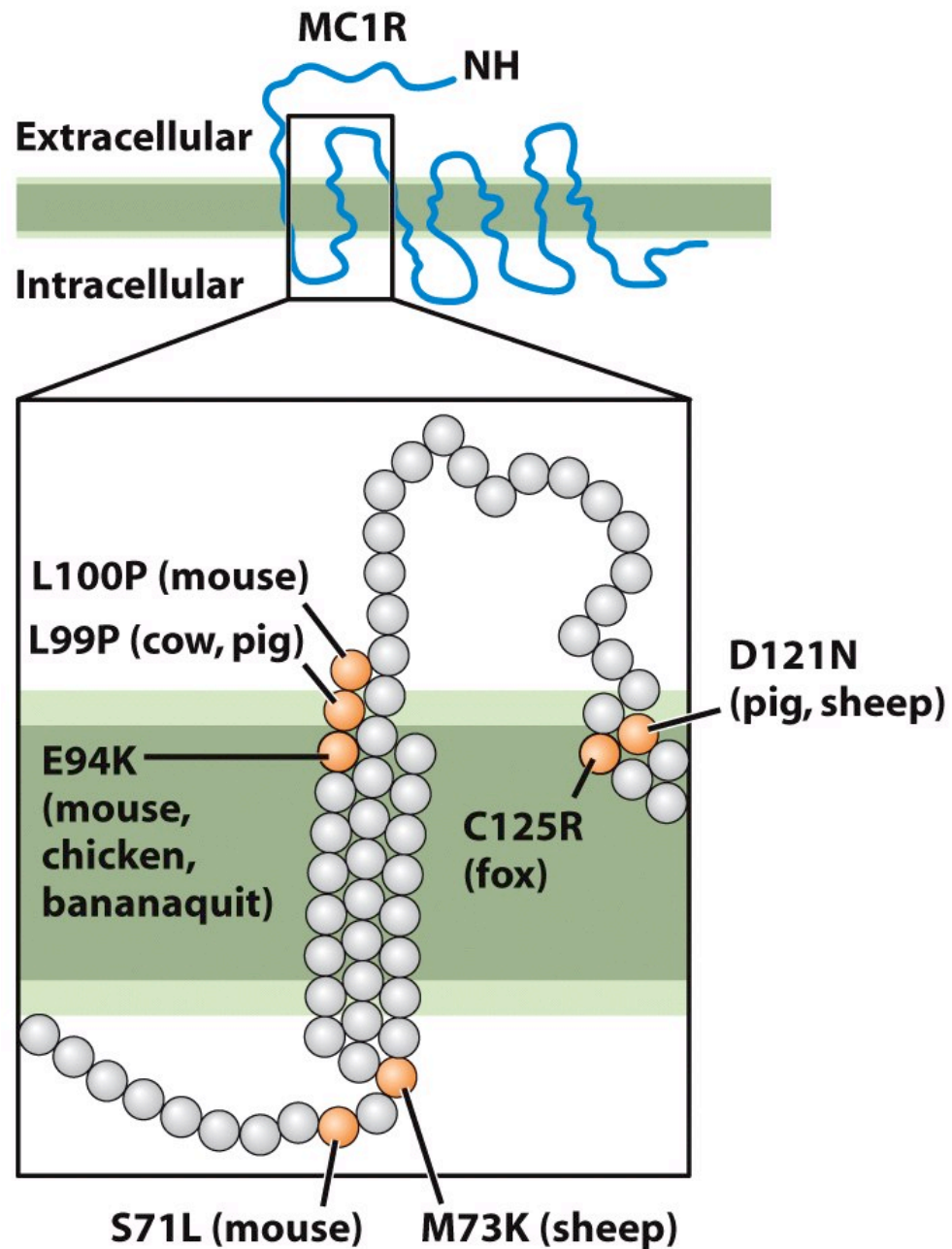


Figure 19-12

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Q: If evolution in proteins can affect differences in phenotypes between species, can evolution in cis-regulatory sequences do the same thing?

Ans: Yes. And for reasons which we will go into now, its likely that many evolutionary changes and adaptations have been the result of mutations in cis-regulatory sequences.



Figure 19-14
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Yellow gene controls production of black pigment throughout the body of *Drosophila*. How does one species turn up the amount of pigment just on the tips of the wings without affecting the amount of pigment in the rest of the body? This must be different than the MC1R example from mice.

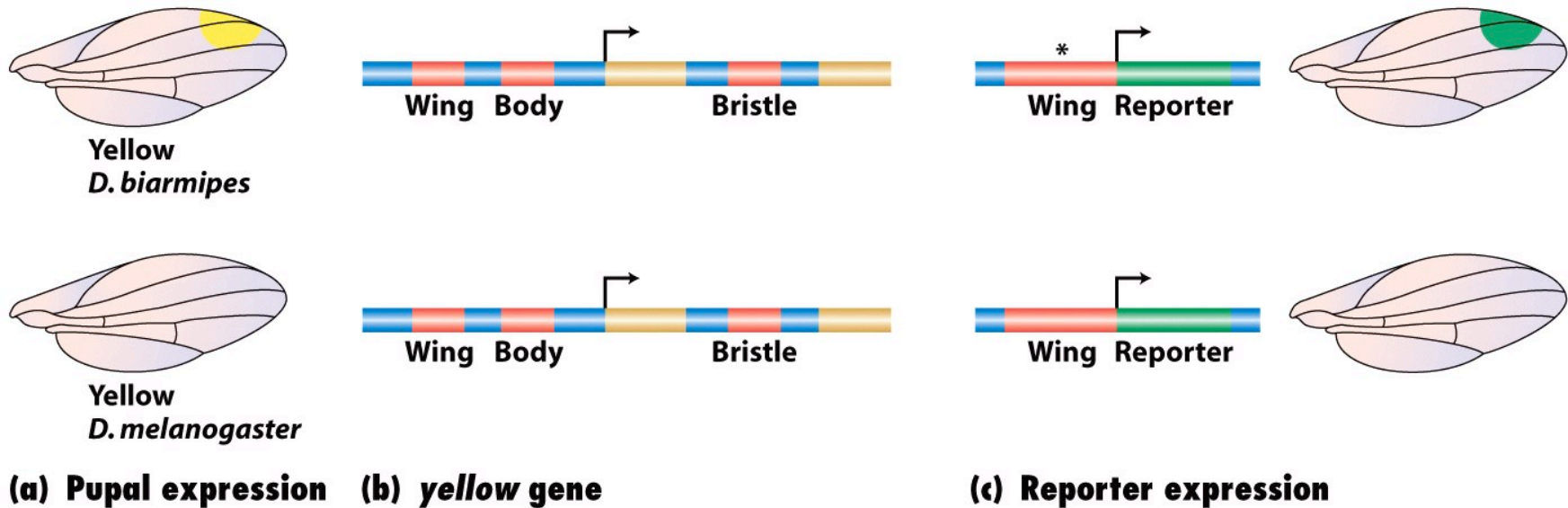


Figure 19-15
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Cis-regulatory sequences are modular with little pleiotropy (each sequences controls a distinct part of the total expression pattern). Therefore evolutionary changes occur without affecting other functions.

Work on problems 10 & 13 in chapter 19

Q: Darwin's theory of evolution describes how all living organisms could have diversified from a single common ancestor but is there further evidence to support this idea?

Ans: Yes. Lots. The major evidence is that all organisms share many genes in common and that these genes act together in similar ways. The odds of this happening independently across organisms are infinitesimally small.

Q: OK, so I accept that everything has a common ancestor and I understand how various forces act to increase genetic differences between populations. I'm still unclear on what exactly a species is verses a sub-population and how a sub-population comes to be a species.

Ans: There are a few working definitions of what a species is but the most common one is a population of individuals that can and do mate with each other and do not mate with other populations. Notice I didn't say that they cannot but just that they don't. Here's where other definitions come in. Sometimes species means the population cannot mate with other populations.

Q: So how does a population get to the point where it does not or cannot mate with other populations?

Ans: This is a very hard problem to study because you can't cross things once they can't mate anymore and events leading up to speciation may not tell us much about the actual event. That said there are different ways that speciation seems to occur that are somewhat understood.

Allopatric Speciation - Geographically isolated habitats (Darwin's finches)

Sympatric Speciation - Speciation with overlapping habitats (Bee vs bird Monkeyflower pollination)

Prezygotic Isolation - Failure to form zygotes (Flower blooming in different seasons)

Postzygotic Isolation - Failure of zygotes to contribute gametes to future generations (Horse x Ass = Mule not fertile)

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Congratulations!

You are done with lectures!