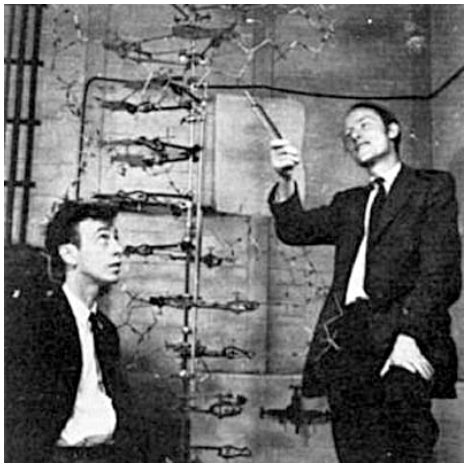
Mutations

by

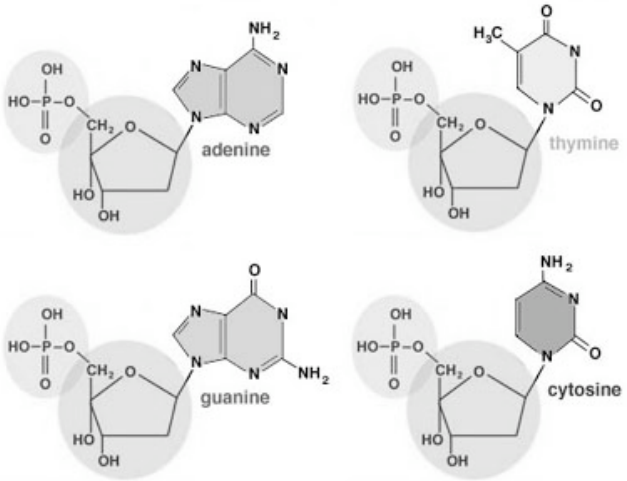
The Modern Synthesis

- The fusion of natural selection with Mendelian genetics yielded a powerful theory indeed.
- Modern synthesis evolution is still the "classic" evolutionary biology—and will form a large part of the content of this course
- To start, let's review types of mutation that are now known to occur

In case anyone forgot: in 1954, Watson and Crick described the shape of DNA as a *double helix*, two strands of nucleotides wrapped around each other.



And you should know by now that DNA is a *polymer* of subunits called *nucleotides*. (To be a little more accurate: it's two polymers wrapped around each other.)



Point Mutation

- Mis-sense mutations: one nucleotide replaced by another
  - Transition: replaces a purine with a purine (A to G or G to A) or a pyrimidine with a pyrimidine (T to C or C to T).
  - Transversion: mutation of a purine to pyrimidine (A or G to T or C), or vice versa
- Silent mutation: causes no change in the amino acid

Point Mutation

- Frameshift mutations: addition or deletion of 1 or 2 nucleotides causes triplet codon reading frame to shift
- Nonsense or termination mutations: amino acid codon converts to stop codon, creating a shortened gene product

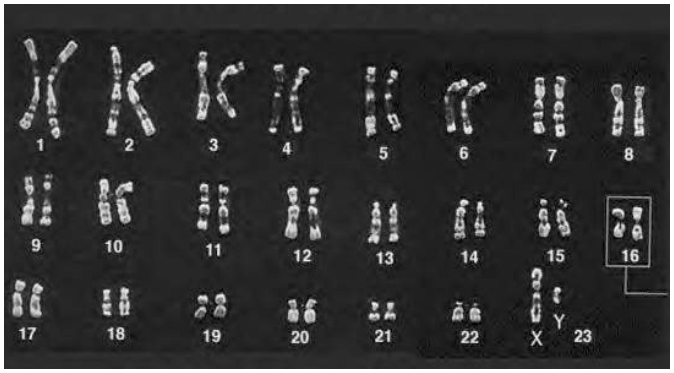
Gene Effects

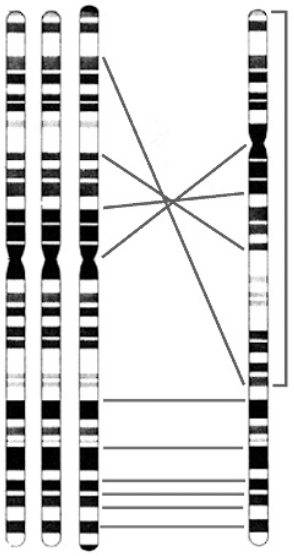
- Regulatory mutations: some genes "switch on" or "switch off" other genes—mutations in the control genes may have huge effects
- Mutations in genes for DNA repair enzymes can cause the overall mutation rate for the entire genome to increase or decrease

Gene Effects

- Epistasis: one trait may be influenced by several genes, and a mutation in one might have unpredictable effects
- Pleiotropy: one gene might affect multiple traits, and again a mutation in one might have unpredictable effects

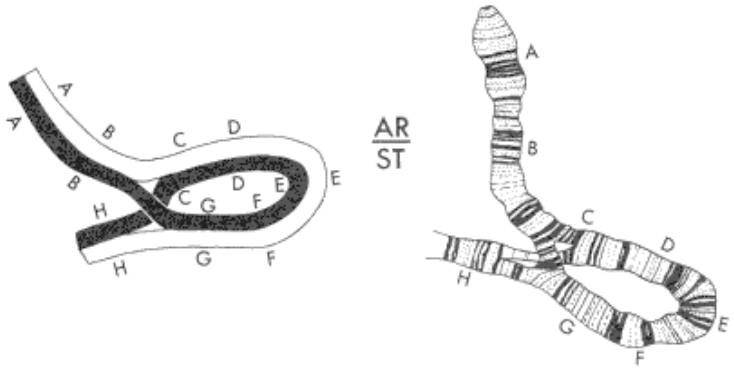
Bear in mind for what follows that chromosomes show distinctive *banding pattterns* when stained with suitable dyes. These allow us to trace certain things that can happen to chromosomes. . .



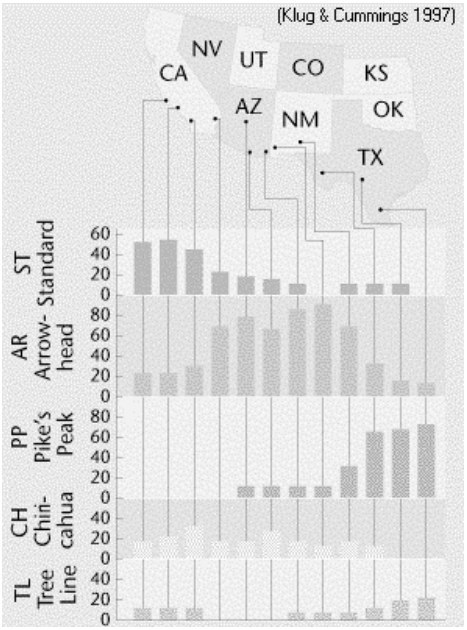


Inversion is another possible genetic change. The diagram shows chromosomes from four closely related animal species. The one on the right shows an inversion relative to the other three, as you can see if you try to match up the banding patterns.

(Left to right: human, chimp, gorilla, and orangutan chromosome 3)

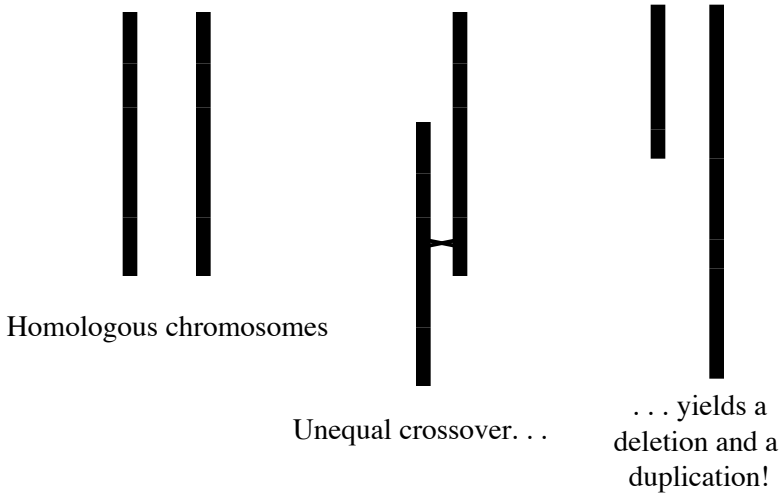


In the species of fruit fly *Drosophila pseudoobscura*, inversions are easily seen, because in an individual with both a "normal" and "inverted" chromosome, the chromosomes must form loops in order to pair up.

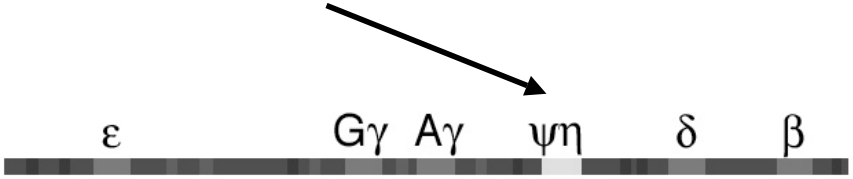


In *Drosophila pseudoobscura* there are several different inversions on chromosome 2 (which have various names, shown on the left). These have different frequencies in different parts of the fly's range.

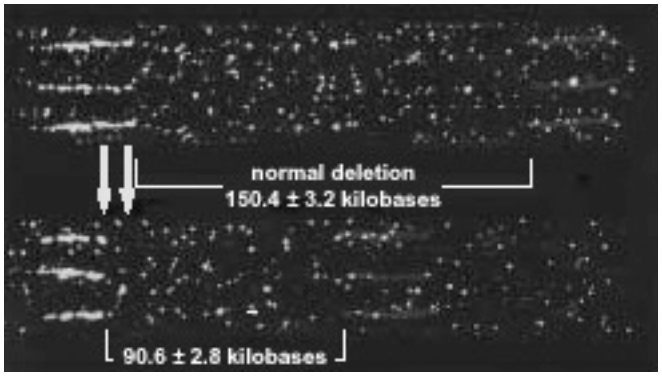
Gene duplication and deletion usually results from unequal crossover in meiosis.



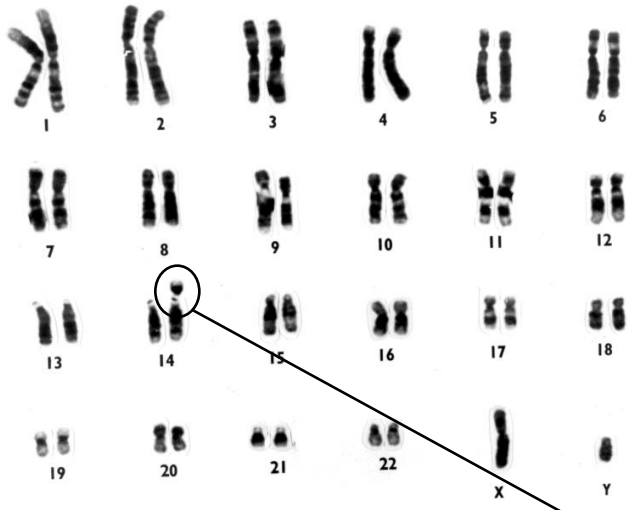
Duplication explains the existence of several closely related beta-globin genes (including a nonfunctional sequence, or *pseudogene*) on human chromosome 16



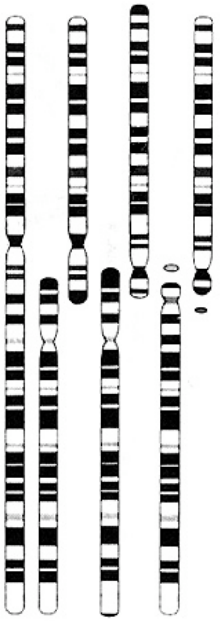
Deletion can be visualized clearly by the DNA combing technique.



Top: DNA strands from three normal people.
Bottom: DNA strands from three people with a 60,000-bp deletion.
(Image taken from Herrick and Bensimon 2001)



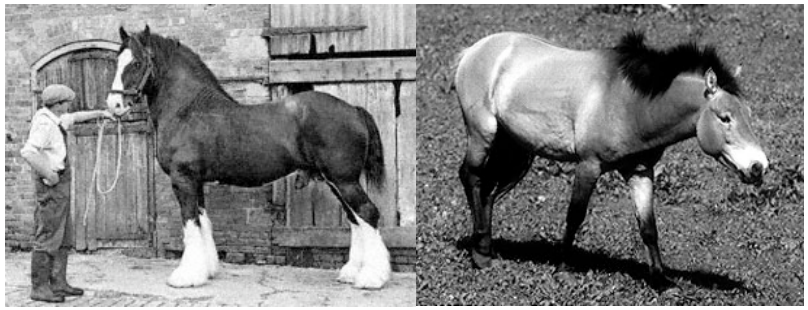
Translocation in a human—note that an extra copy of chromosome 21 has attached to chromosome 14.



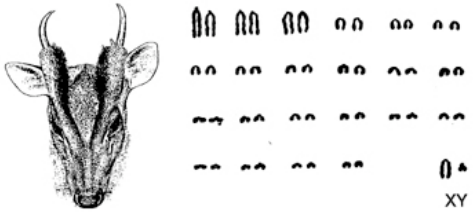
Chromosome fusion or fission shown in four closely related animal species. The first one has a single chromosome that matches with the banding pattern of two separate chromosomes of each of the other three species. (In this case, fusion is the most likely reason why—we'll get to that later. . . .)

(Left to right: human, chimp, gorilla, and orangutan chromosome 2 homologues)

Chromosome fusion probably explains why domestic horses have 64 chromosomes. . .



. . . and the closest living wild species and probable ancestor of domestic horses, Przewalski's horse, has 66 chromosomes.



Chinese muntjac deer
Muntiacus reevesi

Indian muntjac deer
Muntiacus muntjak

Translocation, chromosome fusion, and/or fission explain why these two very similar species of hoofed mammal, the Chinese and Indian muntjac deer, have such different karyotypes.

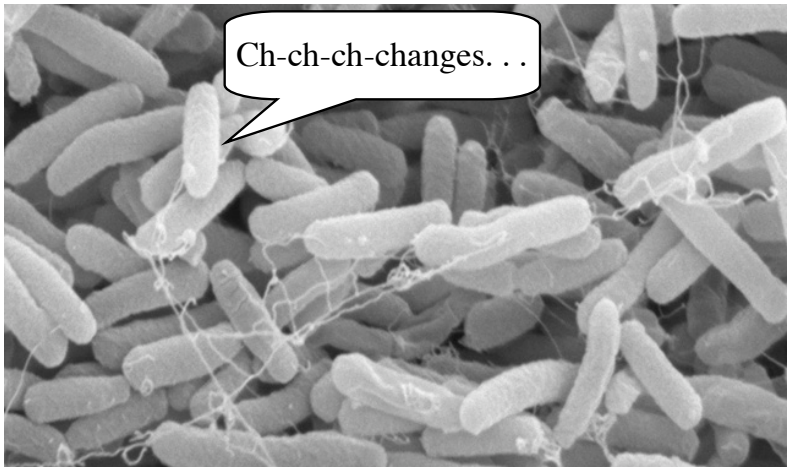
Duplication of a chromosome (polysomy) or a genome (polyploidy) can also occur as a result of a meiotic error.

Compare these two windflowers (genus *Anemone*) and their karyotypes—the one on the right is double the one on the left

So are mutations good or bad?

- We commonly think of mutations as a "bad" thing
  - Many human diseases are caused by mutant genes
- The majority of mutations are thought to be neutral, with no effect on phenotype
  - Japanese biologist Motoo Kimura developed this idea as the *neutral theory of molecular evolution*
  - Neutral mutations, said Kimura and colleagues, create an unseen "reservoir" of genetic diversity within a population

Can mutations ever be "good"?



Can mutations ever be "good"?

- In the 1980s, Barry Hall developed a strain of the bacterium *Escherichia coli* with its gene for the enzyme beta-galactosidase missing
  - These bacteria now could not use lactose as a food source
  - Hall then grew the bacteria on a lactose-containing medium, creating selection for bacteria that could use lactose as a food. . .

Can mutations ever be "good"?

- Not only did the bacteria recover the ability to break down lactose. . . they evolved two new control genes for it as well.
- These *evolved beta-galactosidase* (ebg) genes didn't "just appear out of nowhere". . .
  - The ebg genes are mutated versions of genes elsewhere in the genome, used for other functions
  - They're not very similar to the deleted genes—the new enzyme is only about 34% similar to the old one

Check out this critique and a rebuttal of the critique of Ball's experiments

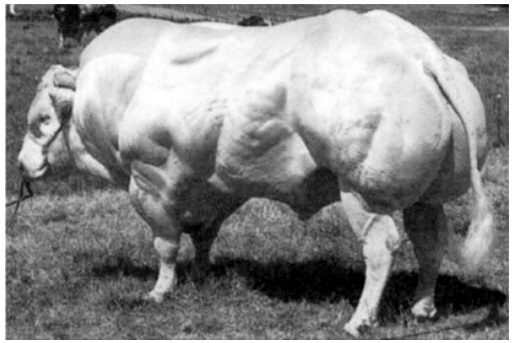
Additional experiments on bacteria confirm this basic principle: mutations in existing genes can and do produce new and functional genes with new features

- A 2001 study of artificially induced mutations in *E. coli* showed that as many as 12% were beneficial when the bacteria were grown on a new substrate
- A naturally occurring frameshift mutation in a Japanese population of *Flavobacterium* (K172), discovered in 1981, gave the bacteria the ability to digest nylon. . . which didn't *exist* before 1937. . .
- Resistance of HIV to human immune system is driven by mutations—the virus literally "out-evolves" the immune system

This just in (June 2004): A toddler in Germany is reported to have two copies of a mutation in the gene for *myostatin*, which blocks muscle growth. The child has muscles twice as large as normal. (Read the original article here. . .)

Predictably, the body-building industry has been capitalizing on this. . . you can already buy nutritional supplements that allegedly block the production of myostatin, and so they will pump you up. . .

Naturally occurring mutations in myostatin genes cause "double-muscling" in certain breeds of cattle, such as this Belgian Blue bull. (More here.)



Natural mutation rates

- The frequency of mutations varies between organisms, between genes in one organism, between different parts of the same gene, and even between different nucleotide positions. . .
  - Bacteria and viruses: typical observed mutation rates of 10^{-6} to 10^{-9} mutations per gene per replication
  - Humans: Clinically significant mutations are observed in about 10^{-4} - 10^{-5} gametes per gene; similar numbers have been observed in corn

Mutational biases

- Transitions are about twice as common as transversions
  - Why? Because of the geometry of the DNA molecule.
- Silent mutations (e.g. third-position) are much more frequent than replacement mutations (those that cause an amino acid substitution)
  - Why? Probably because silent mutations are "selectively neutral." Replacement mutations may *happen* at the same rate as silent ones—but selection "screens them out"

Mutational biases

- Unequal crossing over is most commonly observed in areas where a single sequence is repeated
  - Example: The human *centromere* consists of many repeats of a 171-bp sequence
  - Repeat number is highly variable, probably from unequal crossing over at meiosis
- Finally, some genes may block other genes from being passed on, causing violations of Mendelian rules—this is *transmission distortion*

Natural mutation rates

- Cairns and colleagues (1988) showed, using *E. coli,* that stressful conditions (starvation by growth on a food source that the bacteria couldn't use) seemed to *cause* the "right" mutations to enable the bacteria to use the food source
- This is the *adaptive mutagenesis* hypothesis, and it sounds almost Lamarckian!
  - If correct, it would imply that mutations aren't "random", because a cell can produce those mutations that it needs
- New interpretation: Stress increases the overall mutation rate, but doesn't make "good" mutations more likely
  - Other sources of selection can also affect the mutation rate, partly by acting on the DNA repair genes themselves