Genetic Variation

Variation is the key to the persistence of a population or a species in a changing environment.
Although adaptive variation can originate in a population as it exposed to a new condition, experimental evidence shows that adaptive variation exists in populations prior to exposure.
In the second experiment, **Joshua and Esther Lederberg** used **replica plating** to determine if penicillin resistance in bacterial colonies was present before exposure to penicillin or only arose after exposure to penicillin. They cultured nonresistant bacteria and then exposed them to penicillin. Their technique allowed them to determine if the original colonies from which the resistant bacteria were derived were resistant before exposure to penicillin.

Their results showed that resistance did not arise during exposure to penicillin. Resistance arose in the culture before exposure to penicillin.
Variation is the result of a change in the DNA of a single organism – a mutation.

**Mutation** - the alteration of a region of DNA or chromosome; and altered state of a region of DNA or chromosome

<table>
<thead>
<tr>
<th>Original sequence:</th>
<th>Direction of transcription</th>
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<tbody>
<tr>
<td>DNA:</td>
<td>RNA:</td>
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<tr>
<td>AGA</td>
<td>UCU</td>
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<tr>
<td>TGG</td>
<td>ACU</td>
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<tr>
<td>CGG</td>
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<tr>
<td>TTT</td>
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<tr>
<td>GCA</td>
<td>CGU</td>
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<td></td>
<td>Protein:</td>
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<tr>
<td></td>
<td>Ser</td>
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<tr>
<td></td>
<td>Thr</td>
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<tr>
<td></td>
<td>Ala</td>
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<td></td>
<td>Lys</td>
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<td></td>
<td>Arg</td>
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</tbody>
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**Base pair substitutions**

- **Transition** (A → G)
  - GGA → TGA
  - CCC → ACU
  - Pro → Thr
- **Transversion** (A → T)
  - TGA → TGA
  - ACU → ACU
  - Thr → Thr

**Frameshifts**

- **Insertion (T)**
  - UCA → UCA
  - Ser → Tyr
  - Alu → Cys
  - Glu → Thr
- **…followed by deletion (T)**
  - AGT → ATGA
  - UCA → UCA
  - Ser → Ser

Most changes in DNA do not result in improvements.
Mutations and Fitness

Most mutations have little or no effect on fitness. A few are beneficial and a few are very deleterious.
Examples of mutations:

**Sickle-cell anemia** - a single base pair substitution that results in a single amino acid change in the β chain of Hb

**Precocious puberty** - a single amino acid change in the gene for the receptor for luteinizing hormone results in males that show signs of puberty as early as age 4.

**Cystic fibrosis** - a fatal disease that occurs in 1 in every 2500 births among northern Europeans is due to a mutation in a chloride ion channel protein. Different mutations account for the same condition: a deletion of 3 base pairs results in the deletion of a single amino acid, a conversion of an arginine codon into a stop codon, an alteration in a splicing enzyme has resulted in the deletion of an exon from the mRNA transcribed from the gene.

**Retinitis pigmentosa** - a degenerative disease of the retina - can be caused by mutations in at least 8 different genes.
**Hemophilia** - caused by mutations in two different genes for blood clotting proteins. The mutations can be base pair substitutions, small deletions, small duplications. Twenty percent of the cases of hemophilia A are caused by an inversion of a long sequence of bases within one of the genes.

**Huntington’s disease** - a fatal neurological disorder - is due to an excessive number of repeats of the sequence CAG - normal forms of the genes have 10 to 30 repeats, mutants have more than 75

Although most mutations are have deleterious effects on the encoded protein some have beneficial effects and have been important in evolution
**FOXP2** - encodes a transcription factor - mutations in this gene can cause severe speech and language disorders. Humans differ from chimpanzees at two base pairs that result in nonsynonymous amino acid changes. The amount of change in this gene is unusually high relative to synonymous changes in the gene suggesting the gene may have been important in the evolution of human speech abilities.
Rates of mutation of individual base pairs are low but when summed over the entire genome the effect is considerable.

With 1.6 mutations per sexual generation in the effective genome, a population of 1 million humans will have 1.6 million new mutations in each generation. Although most will be deleterious or neutral, if only a small fraction were beneficial there would be considerable raw material for evolution.
The effects of a mutation can vary among environments.

An allele that increases fitness in a cool environment may decrease fitness in a warm environment.

The sickle-cell allele confers high fitness to the heterozygote where malaria is common but is neutral in heterozygotes where malaria is not common.

Experiments with *Drosophila* showed that a mildly deleterious allele became up to 10 times more deleterious when populations were crowded and had fewer resources.

Thus, many alleles that have little or no effect on fitness in the current environment may be beneficial or harmful if the environment changes. For example, alleles for pesticide or antibiotic resistance may have little effect on fitness until the agent is applied. The same is likely true for many other mutations.
The effects of slightly beneficial mutations in different genes can be combined to produce more adaptive combinations.

Mutations in different individuals can be combined quickly in sexual species.

In asexual species combination of mutations depends upon multiple independent mutations within a genetic lineage.

Sex allows much faster adaptation through the rapid combination of slightly beneficial mutations.