**Genetic Mutations**

There are many different ways that DNA can be changed, resulting in different types of mutation. Here is a quick summary of a few of these:

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| Substitution | http://evolution.berkeley.edu/evolibrary/images/dot_clear.gif | **Substitution**A substitution is a mutation that exchanges one base for another (i.e., a change in a single "chemical letter" such as switching an A to a G). Such a substitution could:1. change a codon to one that encodes a different amino acid and cause a small change in the protein produced. For example, [sickle cell anemia](http://evolution.berkeley.edu/evolibrary/glossary/glossary_popup.php?word=sickle+cell+anemia) is caused by a substitution in the beta-hemoglobin gene, which alters a single amino acid in the protein produced.
2. change a codon to one that encodes the same amino acid and causes no change in the protein produced. These are called silent mutations.
3. change an amino-acid-coding codon to a single "stop" codon and cause an incomplete protein. This can have serious effects since the incomplete protein probably won't function.
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| insertion | http://evolution.berkeley.edu/evolibrary/images/dot_clear.gif | **Insertion**Insertions are mutations in which extra base pairs are inserted into a new place in the DNA. |
| http://evolution.berkeley.edu/evolibrary/images/dot_clear.gif |
| deletion | http://evolution.berkeley.edu/evolibrary/images/dot_clear.gif | **Deletion**Deletions are mutations in which a section of DNA is lost, or deleted. |
| http://evolution.berkeley.edu/evolibrary/images/dot_clear.gif |
| frameshift | http://evolution.berkeley.edu/evolibrary/images/dot_clear.gif | **Frameshift**Since protein-coding DNA is divided into codons three bases long, insertions and deletions can alter a gene so that its message is no longer correctly analyzed. These changes are called frameshifts.For example, consider the sentence, "The fat cat sat." Each word represents a codon. If we delete the first letter and analyze the sentence in the same way, it doesn't make sense.In frameshifts, a similar error occurs at the DNA level, causing the codons to be parsed incorrectly. This usually generates truncated proteins that are as useless as "hef atc ats at" is uninformative.There are other types of mutations as well, but this short list should give you an idea of the possibilities. |

**Causes of Mutations**

Mutations happen for several reasons.

**1. DNA fails to copy accurately**
Most of the mutations that we think matter to evolution are "naturally-occurring." For example, when a cell divides, it makes a copy of its DNA — and sometimes the copy is not quite perfect. That small difference from the original DNA sequence is a mutation.



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| **2. External influences can create mutations**Mutations can also be caused by exposure to specific chemicals or radiation. These agents cause the DNA to break down. This is not necessarily unnatural — even in the most isolated and pristine environments, DNA breaks down. Nevertheless, when the cell repairs the DNA, it might not do a perfect job of the repair. So the cell would end up with DNA slightly different than the original DNA and hence, a mutation. |

**Effects of Mutations**

Since all cells in our body contain DNA, there are lots of places for mutations to occur; however, some mutations cannot be passed on to offspring and do not matter for evolution. [Somatic mutations](http://evolution.berkeley.edu/evolibrary/glossary/glossary_popup.php?word=somatic+mutation) occur in non-reproductive cells and won't be passed onto offspring.

The only mutations that matter to large-scale evolution are those that can be passed on to offspring. These occur in reproductive cells like eggs and sperm and are called [germ line mutations](http://evolution.berkeley.edu/evolibrary/glossary/glossary_popup.php?word=germ+line+mutation).

Some regions of DNA control other genes, determining when and where other genes are turned "on". Mutations in these parts of the genome can substantially change the way the organism is built.

Many organisms have powerful control genes that determine how the body is laid out. For example, [*Hox* genes](http://evolution.berkeley.edu/evolibrary/glossary/glossary_popup.php?word=%3Ci%3EHox%3C%2Fi%3E+gene) are found in many animals (including flies and humans) and designate where the head goes and which regions of the body grow appendages. Such master control genes help direct the building of body "units," such as segments, limbs, and eyes. So evolving a major change in basic body layout may not be so unlikely; it may simply require a change in a Hox gene and the favor of [natural selection](http://evolution.berkeley.edu/evolibrary/glossary/glossary_popup.php?word=natural+selection).

**Sickle Cell Anemia**

Sickle cell anemia is a genetic disease with severe symptoms, including pain and anemia. The disease is caused by a mutated version of the gene that helps make hemoglobin — a protein that carries oxygen in red blood cells. People with two copies of the sickle cell gene have the disease. People who carry only one copy of the sickle cell gene do not have the disease, but may pass the gene on to their children.

The mutations that cause sickle cell anemia have been extensively studied and demonstrate how the effects of mutations can be traced from the DNA level up to the level of the whole organism. Consider someone carrying only one copy of the gene. She does not have the disease, but the gene that she carries still affects her, her cells, and her proteins:

1. **There are effects at the DNA level**



1. **There are effects at the protein level**



Normal hemoglobin (left) and hemoglobin in sickled red blood cells (right) look different; the mutation in the DNA slightly changes the shape of the hemoglobin molecule, allowing it to clump together.

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| http://evolution.berkeley.edu/evolibrary/images/dot_clear.gif | red blood cells |
| http://evolution.berkeley.edu/evolibrary/images/dot_clear.gif |
| http://evolution.berkeley.edu/evolibrary/images/dot_clear.gif | sickle cells |
| http://evolution.berkeley.edu/evolibrary/images/dot_clear.gif |
|  |  |
| http://evolution.berkeley.edu/evolibrary/images/dot_clear.gif | Normal red blood cells (top) and sickle cells (bottom) |
| http://evolution.berkeley.edu/evolibrary/images/dot_clear.gif |
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1. **There are effects at the cellular level**
When red blood cells carrying mutant hemoglobin are deprived of oxygen, they become "sickle-shaped" instead of the usual round shape (see picture). This shape can sometimes interrupt blood flow.
2. **There are negative effects at the whole organism level**
Under conditions such as high elevation and intense exercise, a carrier of the sickle cell allele may occasionally show symptoms such as pain and fatigue.
3. **There are positive effects at the whole organism level**
Carriers of the sickle cell allele are resistant to malaria, because the parasites that cause this disease are killed inside sickle-shaped blood cells.

This is a chain of causation. What happens at the DNA level propagates up to the level of the complete organism. This example illustrates how a single mutation can have a large effect, in this case, both a positive and a negative one. But in many cases, evolutionary change is based on the accumulation of many mutations, each having a small effect. Whether the mutations are large or small, however, the same chain of causation applies: changes at the DNA level spread up to the phenotype.

**Questions**

1. **What are the types of genetic mutation and define them.**
2. **What causes gene mutations?**
3. [**\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**](http://evolution.berkeley.edu/evolibrary/glossary/glossary_popup.php?word=somatic+mutation) occur in non-reproductive cells and won't be passed onto offspring.
4. Mutations that matter to large-scale evolution are those that can be passed on to **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**
5. These occur in reproductive cells like eggs and sperm and are called **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**
6. [*\_\_\_\_\_\_\_\_\_*genes](http://evolution.berkeley.edu/evolibrary/glossary/glossary_popup.php?word=%3Ci%3EHox%3C%2Fi%3E+gene) are found in many animals, and designate where the head goes and which regions of the body grow appendages.
7. **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** is a genetic disease with severe symptoms, including pain and anemia. The disease is caused by a mutated version of the gene that helps make hemoglobin.
8. People who carry only **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** of the sickle cell gene do not have the disease, but may pass the gene on to their children.
9. The mutation in the DNA slightly changes the **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** of the hemoglobin molecule, allowing it to clump together.
10. A negative effect of the disease is:
11. A positive effects of the disease is:
12. **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** is based on the accumulation of many mutations, each having a small effect.
13. Whether the mutations are large or small, however, the same chain of causation applies: changes at the DNA level spread up to the **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**
14. Look at the following sequence: **THE FAT CAT ATE THE RAT.**
	1. Delete the first H and regroup the letters in groups of three (write out the new groups of three).
	2. Does the sentence still make sense?
	3. What type of mutation is this?
15. Below is the DNA base sequence for the normal protein for normal hemoglobin and the base sequence for (abnormal) sickle cell hemoglobin:

**Normal gene: GGG CTT CTT TTT**

**Sickle gene: GGG CAT CTT TTT**

* 1. Transcribe and translate the normal and sickle cell DNA sequences above.

**mRNA codon sequence**

normal:

sickle:

**amino acids coded**

normal:

sickle:

* 1. What kind of a gene mutation is this? Support your answer.
	2. If the base sequence read GGG CTT CTT TTC instead…
		1. Would this result in functional hemoglobin? Explain.

**Answer Key**

1. **What are the types of genetic mutation and define them.**

**Substitution**
A substitution is a mutation that exchanges one base for another

**Insertion**
Insertions are mutations in which extra base pairs are inserted into a new place in the DNA.

**Deletion**
Deletions are mutations in which a section of DNA is lost, or deleted.

**Frameshift**
Since protein-coding DNA is divided into codons three bases long, insertions and deletions can alter a gene so that its message is no longer correctly analyzed. These changes are called frameshifts.

1. **What causes gene mutations?**
	1. **DNA fails to copy accurately**
	2. **External influences can create mutations**: Mutations can also be caused by exposure to specific chemicals or radiation.
2. [**Somatic mutations**](http://evolution.berkeley.edu/evolibrary/glossary/glossary_popup.php?word=somatic+mutation) occur in non-reproductive cells and won't be passed onto offspring.
3. Mutations that matter to large-scale evolution are those that can be passed on to **offspring.**
4. These occur in reproductive cells like eggs and sperm and are called [**germ line mutations**](http://evolution.berkeley.edu/evolibrary/glossary/glossary_popup.php?word=germ+line+mutation)**.**
5. [***Hox***genes](http://evolution.berkeley.edu/evolibrary/glossary/glossary_popup.php?word=%3Ci%3EHox%3C%2Fi%3E+gene) are found in many animals, and designate where the head goes and which regions of the body grow appendages.
6. **Sickle cell anemia** is a genetic disease with severe symptoms, including pain and anemia. The disease is caused by a mutated version of the gene that helps make hemoglobin.
7. People who carry only **one copy** of the sickle cell gene do not have the disease, but may pass the gene on to their children.
8. The mutation in the DNA slightly changes the **shape** of the hemoglobin molecule, allowing it to clump together.
9. **A negative effect of the disease is**: Under conditions such as high elevation and intense exercise, a carrier of the sickle cell allele may occasionally show symptoms such as pain and fatigue.
10. **A positive effects of the diseaseis:** Carriers of the sickle cell allele are resistant to malaria, because the parasites that cause this disease are killed inside sickle-shaped blood cells.
11. **Evolutionary change** is based on the accumulation of many mutations, each having a small effect.
12. Whether the mutations are large or small, however, the same chain of causation applies: changes at the DNA level spread up to the **phenotype.**
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normal:

sickle:

**amino acids coded**

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