

Mutations

Mutation is a change in **DNA**, the hereditary material of life. An organism's DNA affects how it looks, how it behaves, and its physiology—all aspects of its life. So a change in an organism's DNA can cause changes in all aspects of its life.

Mutations are random.

Mutations can be beneficial, neutral, or harmful for the organism, but mutations do not “try” to supply what the organism “needs.” In this respect, mutations are random—whether a particular mutation happens or not is unrelated to how useful that mutation would be.

Not all mutations matter to evolution.

Since all cells in our body contain DNA, there are lots of places for mutations to occur; however, not all mutations matter for evolution. Somatic mutations occur in non-reproductive cells and won't be passed onto offspring.

For example, the golden color on half of this Red Delicious apple was caused by a somatic mutation. The seeds of this apple do not carry the mutation.

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**.

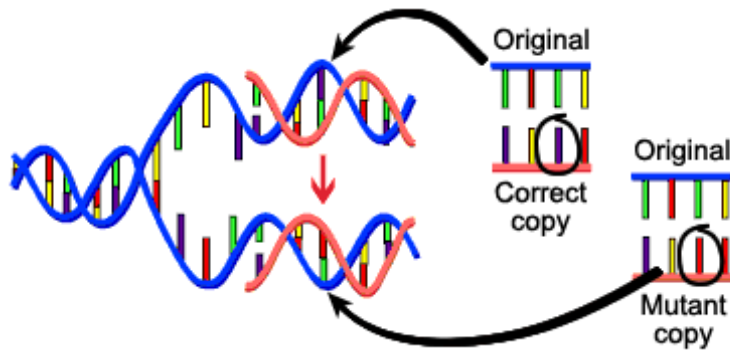
A single germ line mutation can have a range of effects:

The 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.



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.

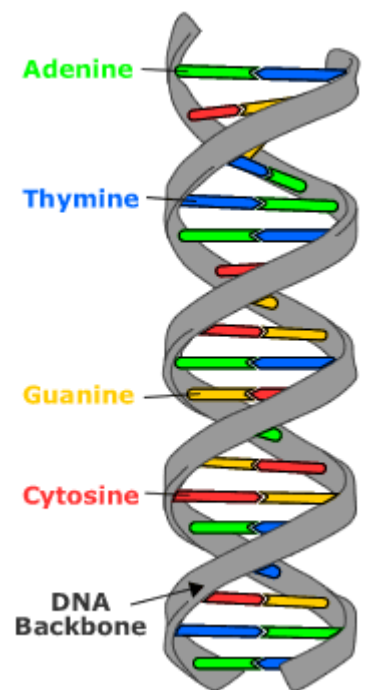
Reviewing DNA

Your **DNA** contains a set of instructions for building a human. These instructions are inscribed in the structure of the DNA molecule through a genetic code. It works like this:

DNA is made of a long sequence of smaller units strung together. There are four basic types of unit: A, T, G, and C. These letters represent the type of **base** each unit carries: adenine, thymine, guanine, and cytosine.

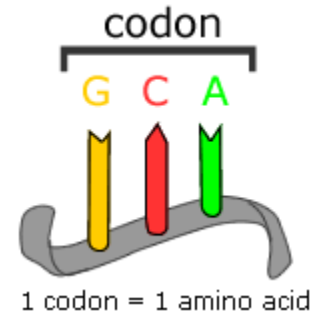
The sequence of these bases encodes instructions. Some parts of your DNA are control centers for turning **genes** on and off, some parts have no function, and some parts have a function that we don't understand yet. Other parts of your DNA are genes that carry the instructions for making **proteins**—which are long chains of **amino acids**. These proteins help build an organism.

Protein-coding DNA can be divided into **codons**—sets of three bases that specify an amino acid or signal the end of the protein. Codons are



identified by the bases that make them up—in the example at right, GCA, for guanine, cytosine, and adenine. The cellular machinery uses these instructions to assemble a string of corresponding amino acids (one amino acid for each three bases). The amino acid that corresponds to “GCA” is called alanine; there are twenty different amino acids synthesized this way in humans. “Stop” codons signify the end of the newly built protein.

The completed protein is then released to do its job in the cell.



Types of Mutations

Knowing a few basic types of mutations can help you understand why some mutations have major effects and some may have no effect at all.

At chromosomal level: e.g. numerical abnormality (increase or decrease in number) and/or structural abnormality.

Large gene mutations: e.g. deletion of entire gene or big insertions etc...

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** 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.

CTGGAG
CTGGGG

Insertion

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

CTGGAG
CTGGTGGAG

Deletion

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

CTGGAG
CTAG

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 parsed. 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 parse the sentence in the same way, it doesn’t make sense.

~~T~~he fat cat sat
hef atc ats at

In frameshifts, a similar error occurs at the DNA level, causing the codons to be parsed incorrectly. This usually generates proteins that are as useless as single “hef atc ats at” is uninformative.

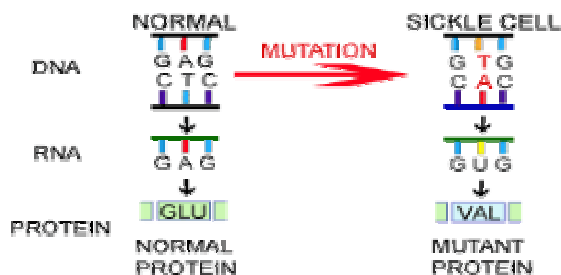
There are other types of mutations as well, but this short list should give you an idea of the possibilities.

A Case Study: Sickle Cell Anemia (1 of 2)

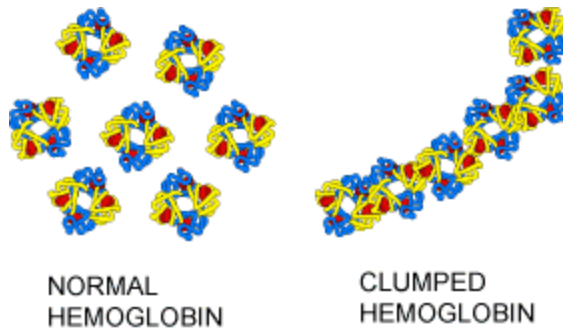
Sickle cell anemia is a genetic disease with severe symptoms, including pain and anemia. The disease is caused by a mutated version of the **gene** that helps make hemoglobin—a **protein** that carries oxygen in red blood cells. People with two copies of the sickle cell gene have the disease. People 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.



2. 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 changes the shape of the hemoglobin molecule, allowing it to clump together.

3. 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.



4. 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.

5. 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 propagate up to the **phenotype**.

Phenotype

“FEE-noh-TYPE”

the physical features of an organism. Phenotype may refer to any aspect of an organism's morphology, behavior, or physiology. An organism's phenotype is affected by its

Mutation

“myoo-TAY-shun”

a change in a DNA sequence, usually occurring because of errors in replication or repair. Mutation is the ultimate source of genetic variation. Changes in the composition of genome due to recombination alone are not considered mutations since recombination alone just changes which genes are united in the same genome but does not alter the sequence of those genes.