Tuesday, February 5th

Today's Agenda:

1. Turn in pedigree assignment
2. Quiz!
3. KWL for mutations
4. Intro to mutations

Quiz!

Cystic Fibrosis is a human hereditary condition in which there is an abnormally thick mucus that blocks ducts, especially in the pancreas and lungs. Cystic fibrosis is due to a recessive gene, "b". A couple who are planning to marry are concerned about their chances of having a Cystic Fibrosis child because both the man's sister and the woman's brother had it. Both of them are phenotypically normal.

a. What are the genotypes of the man's parents? The woman's parents?

a. What is the man's genotype? The woman's?

b. Could this couple have a Cystic Fibrosis child? Why or why not? Explain using a Punnett square

c. Draw a pedigree including the man and woman's parents, the man and woman themselves, and any possible children they can have. Make sure to use the symbols discussed in class!

Quiz!

Huntington's disease is a human hereditary condition in which certain nerve cells waste away, leading to loss of coordination and cognitive abilities. Huntington's disease is caused by a dominant gene, "H". A couple who are planning to marry are concerned about their chances of their child having Huntington's disease because the man's father and sister had it as well as both woman's mother, father, and brother. Both the man and woman are phenotypically normal.

a. What are the genotypes of the man's parents? The woman's parents?

b. What is the man's genotype? The woman's?

c. Could this couple have a child with Huntington's disease? Why or why not? Explain and include a Punnett square.

d. Draw a pedigree including the man and woman's parents, the man and woman themselves, and any possible children they can have. **Make sure to use the symbols discussed in class!**

IMPORTANT NOTE

If you are unhappy with your quiz score, you will have up to a week after it is returned to re-take it, and you will be given the average of your two scores.

You **CANNOT** re-take the quiz during class time. You **CAN** take it during advisory, lunch, or after school.

Introduction to Mutations

What is a mutation?

A mutation is a permanent, random change in DNA

How can mutations happen?
>> They can be caused by replication errors (meaning the thing copying the DNA makes a mistake)
>> They can be caused by mutagens (things that cause mutations). Some common mutagens include cigarette smoke and UV light (that's why they always say to use suntan lotion!)

What mutations ARE NOT

Why are mutation important?

We have just studied how different traits are passed from one generation to a next.

>>Different forms of inheritance (and the randomness of heredity) give an individual a unique appearance

>>HOWEVER for different traits to be there in the first place we need **mutations**.

>> Remember– mutations don't only affect traits… they can affect ANY part of a living organism

For a mutation to cause changes in a species, the changes must be passed on to future generations (or else it will just stop with you).

>>That is, a mutation must exist in the sex cells (meaning the set of DNA that your offspring will inherit). They must be heritable

Think about this unrealistic example: What if you spontaneously develop the ability to fly, but your children can't inherit the trait? Thinking BIOLOGICALLY, your adaptation has no effect on future generations. 100 years from now, it doesn't matter that you could fly because nobody in the future will be able to either.

The same line of thinking is true if you don't have any children. Maybe you somehow mutate and have a really good immune system that can fight any infection, but you don't have any children. Nobody will have the trait in the future because you didn't pass it on for anyone else to have!

Are all mutations bad?

NO! In fact, most mutations don't cause a noticeable change in the functioning of your proteins! (We'll get there….)

>>Note that this fact gives us an important advantage in biological research

Some quick math…..

The human genome contains ~3.3×10^9 (3,300,000,000) base pairs of nucleotides

>> (This:  1.1 billion times over)

>>The mutation rate is an estimated 1.1×10^{-8} per base per generation (meaning a specific base has a 0.000000011% chance of undergoing a mutation within your lifetime)

>>So, your genome (set of DNA) will accumulate roughly 36 totally random mutations!

>> ($36/(3.3 \times 10^9)$ is only a 0.00000001% (1×10^{-8}) change in your DNA

So why aren't you dead?

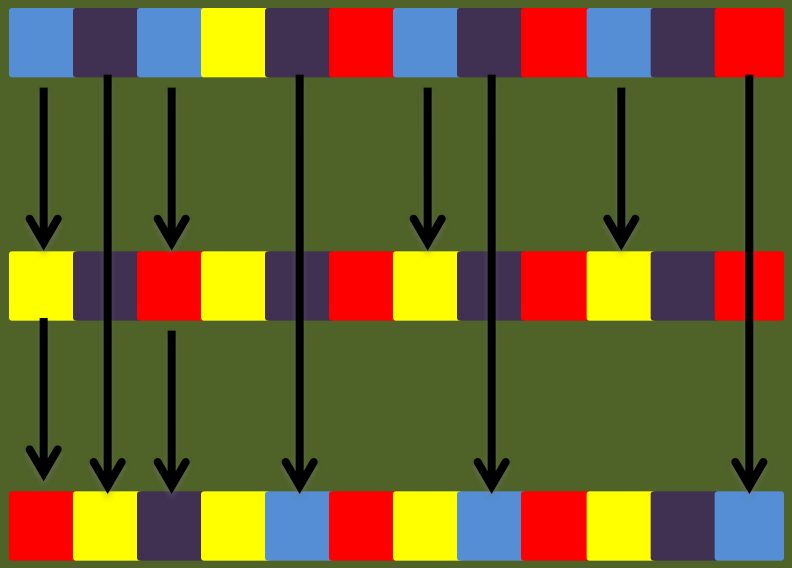
A lot of your DNA is so-called "junk DNA " because it does not code for anything.

EQ: Why might it be a good thing to have this "Junk DNA"?

>> Mutations tend to accumulate in this "junk DNA"

>> If we assume that the mutations occur in a clock-like manner (meaning in fixed, predictable intervals), we can compare the junk DNA of two species and estimate their relatedness!

Mutations as a way to track evolutionary change



Dogs and cats are mammals, they are more closely related to each other than to snakes, which are reptiles

This may seem trivial, but it is EXTREMELY useful when comparing two species that *seem* closely related but in reality aren't

Walrus

Manatee

Walruses (Walri?) are more closely related to Bears than to Manatees

…Or when two species seem completely unrelated but are closer than you'd think…

Important things to remember

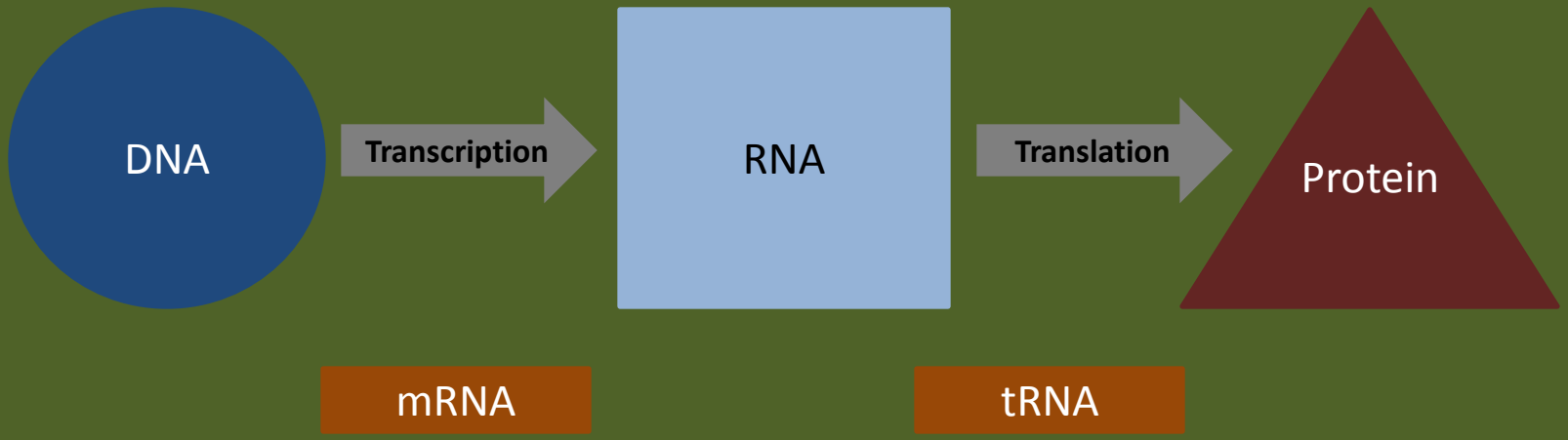
>>DNA codes for genes

>>Genes create proteins

>>Proteins are the “machines” that make everything in your body work

Let's put that another way…

DNA is transcribed to RNA then translated to proteins (word soup– how can we remember this?)



Transcription:

Key player: mRNA (messenger RNA)

Just writing down what the DNA tells it to
BUT it changes T to U (DNA is ATCG, RNA is ACG)

Transcription as in transcribe or scribe (someone who writes something down)

Translation

Key player: tRNA (transfer RNA)

Takes the RNA and turns it into a protein
Changes the nucleotides (AUCG) to proteins (amino acids)

It translates the nucleotides into a different form (language)– that is, proteins

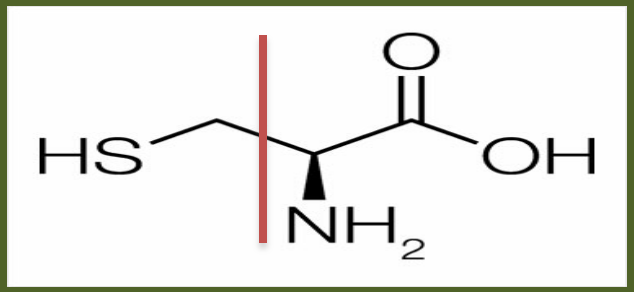
Okay… RNA is made based on what DNA tells it to write down

…Then the protein is made from what the RNA tells it to make

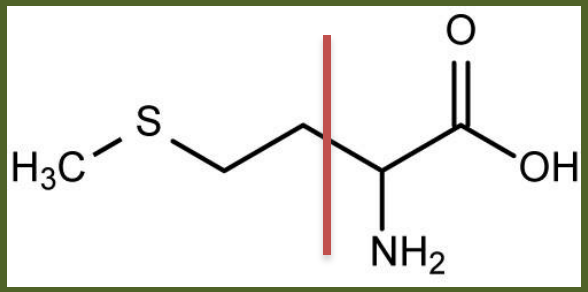
First, what are proteins?

Proteins are large biological molecules (i.e. macromolecules) that perform a wide range of functions

Proteins are made up of smaller building blocks known as amino acids
>> There are 20 amino acids, each with a *slightly* different composition.



Cysteine



Methionine

Proteins as machines?
What does it mean?

Some Important proteins and their jobs

>>**Hemoglobin**: In blood cells. Transports oxygen throughout your body

>>**Antibodies**: Detect harmful invaders and signal to other cells to kill them

>>**ATP synthase**: A molecular motor that spins and helps create ATP (a cell's primary energy source)

>>**Actin** and **Myosin**: What muscles are made of. These allow you to move (which is pretty important)

>>**DNA polymerase**: Allows your DNA to be replicated

>>**Hormones**: Signal to (relatively) distant parts of your body to do something (note proteins make up only one class of hormones, the other is made up of steroids)

ALL enzymes are proteins. What do enzymes do?

If there is a problem with the DNA (i.e. a mutation), the RNA is going to be wrong as well. Then, the protein is going to be wrong.

So how can such a small change cause an ENTIRE protein to be ruined?

Analogy

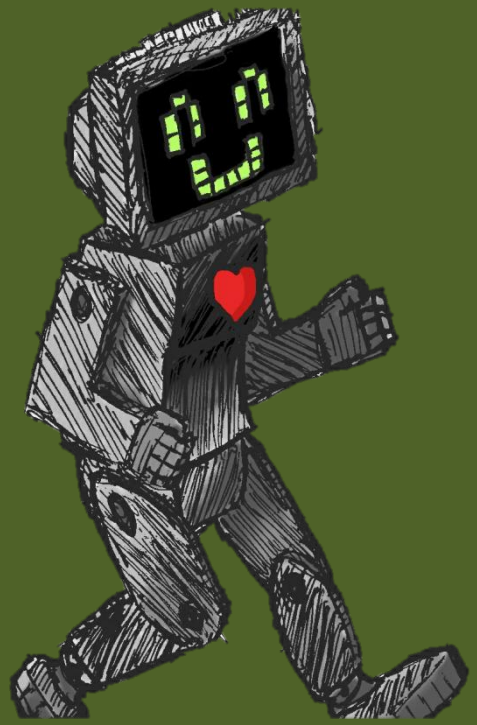
Analogy: DNA is the instruction manual to build a robot

>YOU are the DNA polymerase (an enzyme; the thing that reads DNA and makes a copy of it)

>You have all the tools and materials to build the robot

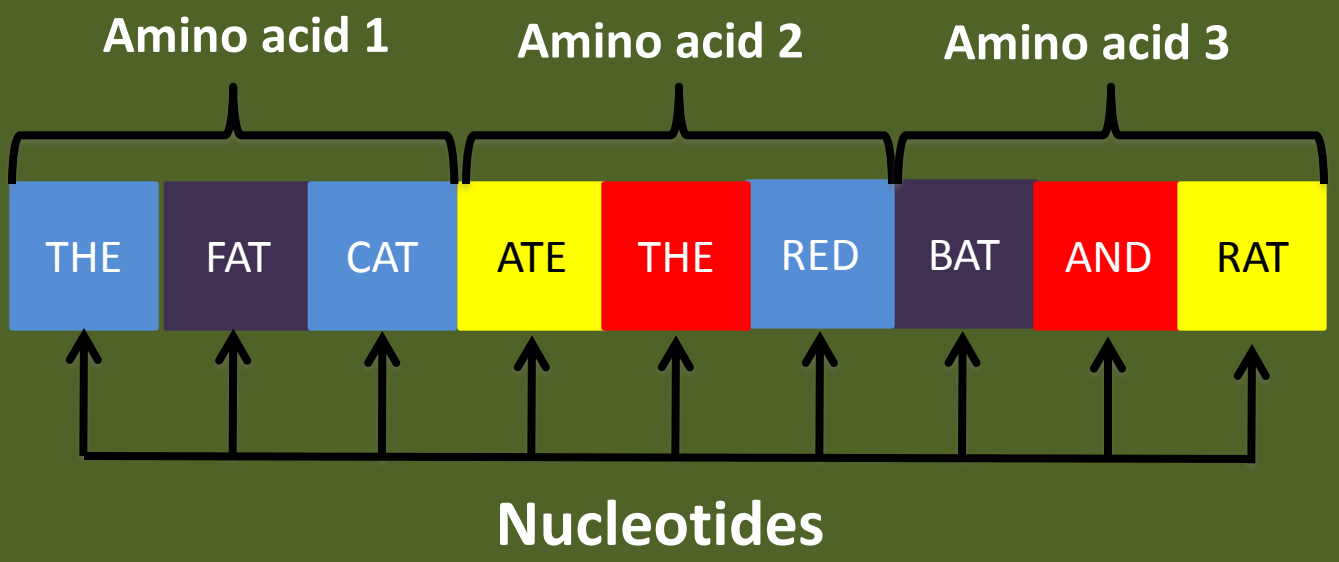
>Even with all the right tools and materials, without the right directions you'll make something other than an exact copy of the robot (of course!)

>>Your robot probably won't work properly, but maybe somehow it works better



tRNA reads mRNA in groups of 3

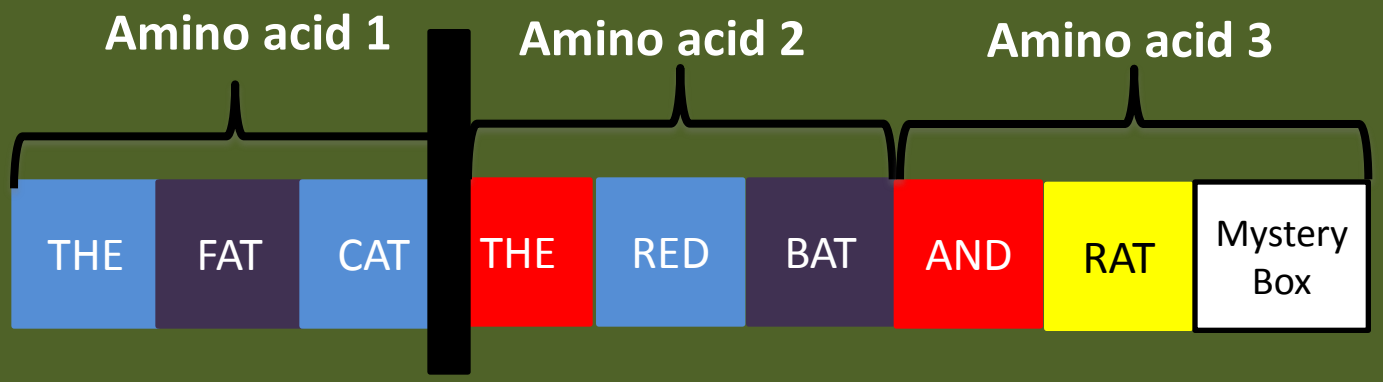
These groups of 3 are known as “codons”
Each codons tells the tRNA which amino acid to attach next



So… What happens if a SINGLE nucleotide is taken out?

Great Question!

This is known as a deletion. What happens to our message when a base is deleted?



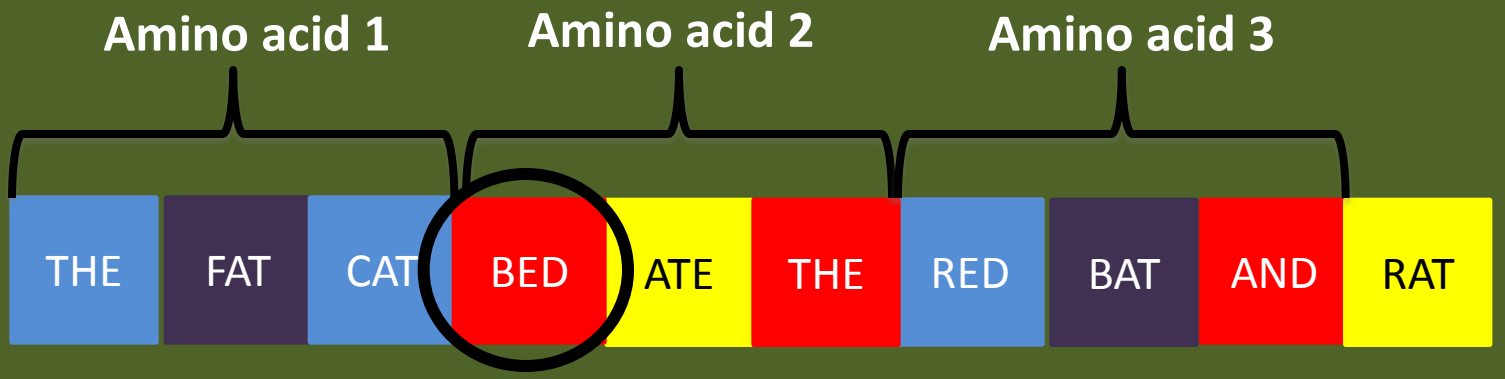
Not only do we not know what the fat cat did, but we have a "mystery box" to deal with.

Instead of amino acid 2 reading "ATE THE RED", it now reads "THE RED BAT"– if a tRNA were reading this, it would put in a totally different amino acid!

So… What happens if a SINGLE nucleotide is added?

Another great question!

This is known as an insertion. What happens to our message when a nucleotide is inserted?



What happened? How can a cat bed eat a bat and rat?

Instead of amino acid 2 coding for "ATE THE RED", it now codes for "BED ATE THE". Again, a tRNA would put in a different amino acid!

When nucleotide(s) is/are inserted or deleted, we shift the whole reading frame of our DNA
>> In other words, the whole codon gets messed up.

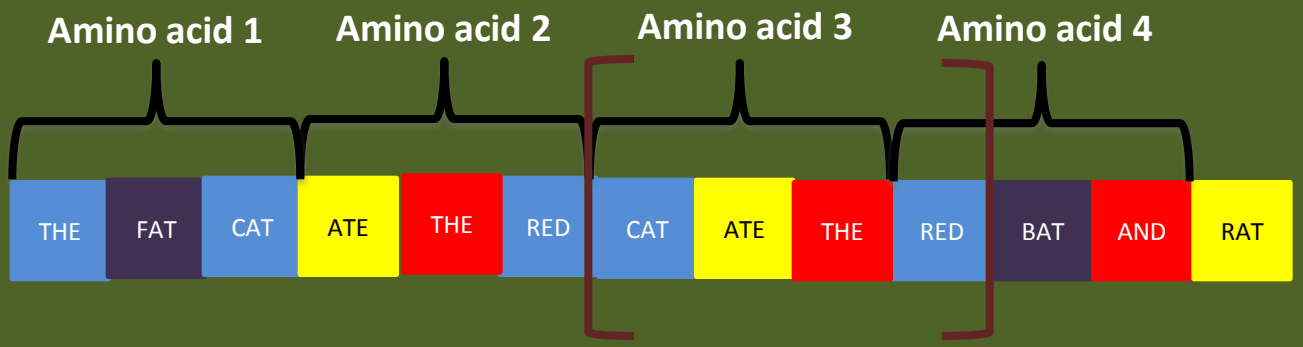
These mutations are known as frameshift mutations (makes sense, right?)
>> A lot of times, biologists will refer to insertions or deletions simply as "indels"

When we have a frameshift mutation, anything downstream (i.e. after) the mutation will be off track

What happens if a MULTIPLE nucleotides are added?

This is unlikely to happen at the same spot (remember that mutations are highly unlikely anyways)… what is more common, though, is when sections of DNA are replicated.

This type of mutation is known as a duplication



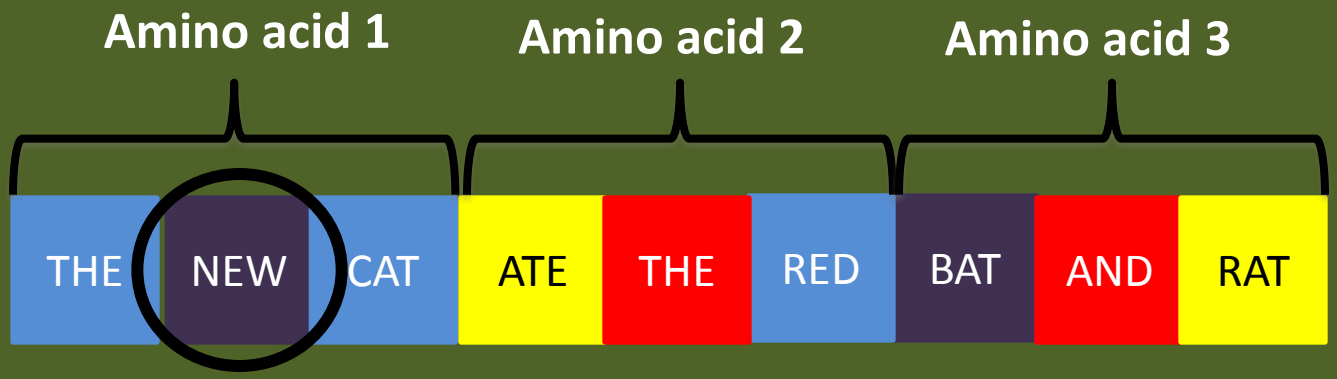
Notice that not only do we have an additional codon (our BAT AND RAT amino acid is now CAT ATE THE), but also our reading frame is out of sync

>>Note: if a multiple of 3 is added, we still keep our reading frame

What other kinds of mutations are there?

A nucleotide can be substituted for a different nucleotide

This is known as a substitution mutation

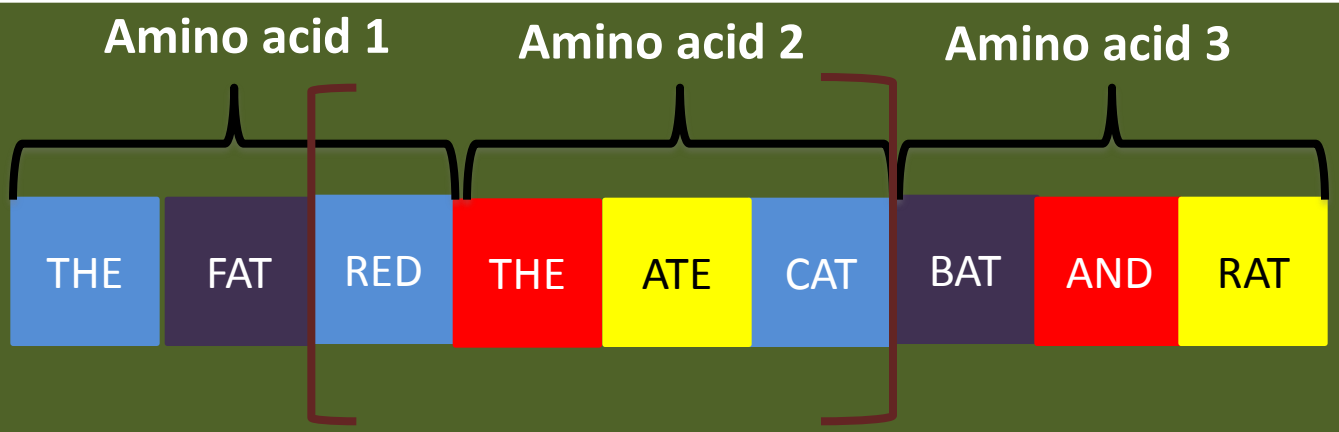


In this case, we changed "FAT" to "NEW".

Notice that the reading frame stays in tact for amino acids 2 and 3

Inversions

In this case, a chunk of DNA is taken out, flipped around, and put back



Between the brackets, our message is gibberish.

Notice, however, that right after the mutation, the message remains in tact! (we still have BAT AND RAT). That is, our reading frame after the inversion is fine

Side note: Mutations that affect a single nucleotide are known as point mutations.

There are three (3) kinds of point mutations:

>> Insertions
>>Deletions
>>Substitutions

So why is this such a huge problem?

Remember the proteins we just talked about before?

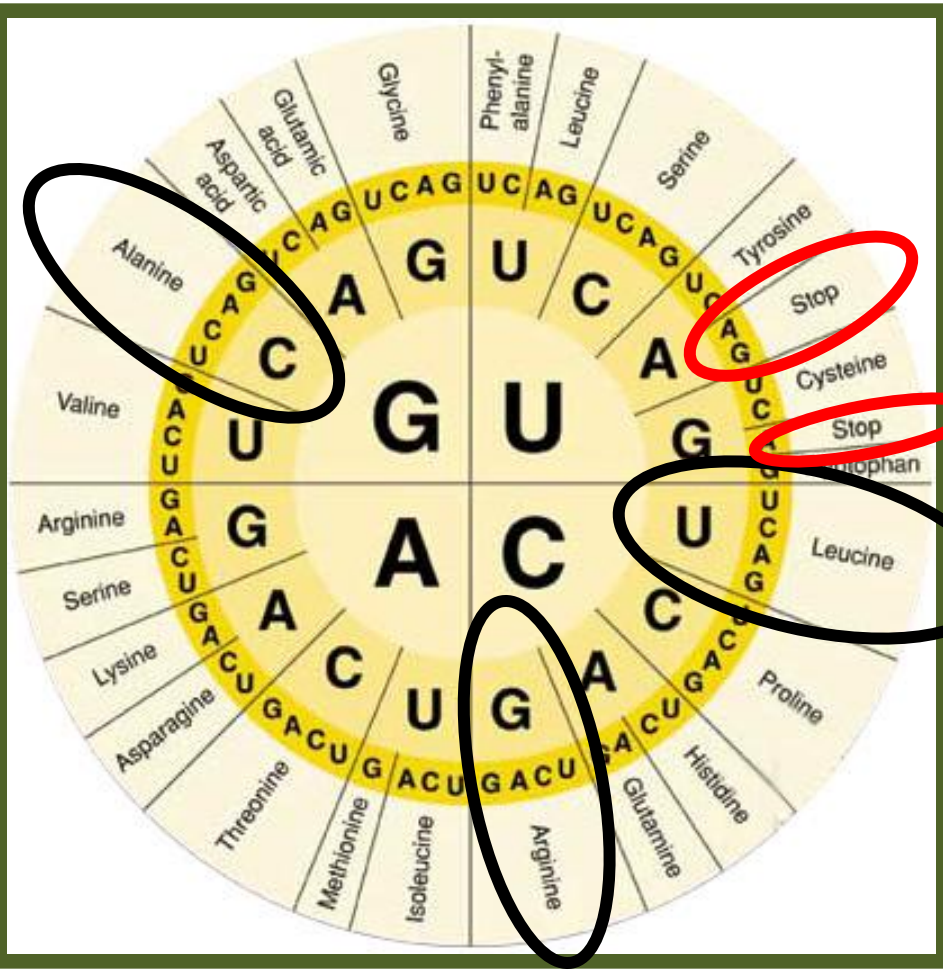
Hemoglobin	574 amino acids (1722 nucleotides)
Antibodies	1322-1534 amino acids (3966-4062 nucleotides)
ATP synthase	2062 amino acids (6486 nucleotides)
Actin and myosin	Highly variable
DNA polymerase	335 amino acids (1005 nucleotides)

Is all lost?

Remember that the amino acid code is somewhat redundant

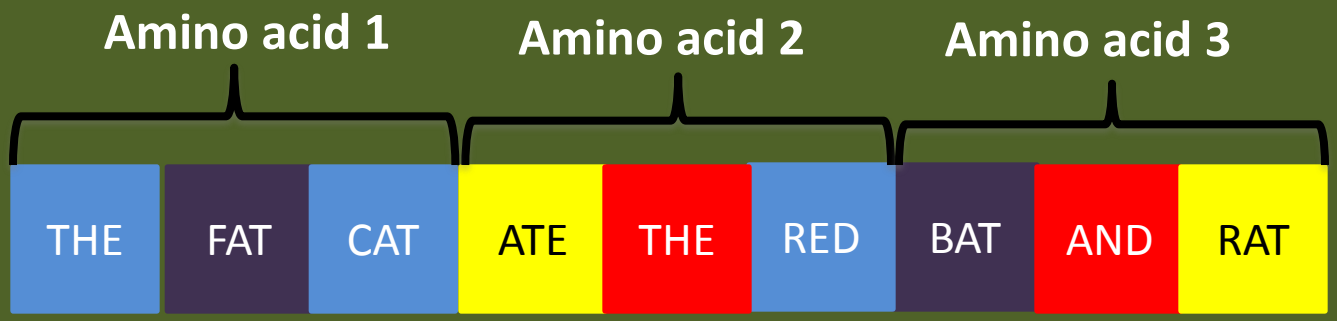
>>This means multiple codons (sequences of 3 nucleotides) *can* code for the SAME amino acid

The amino acid chart



Silent mutations

When there is a mutation that changes the nucleotide, but the codon is still read the same way and the same amino acid is placed in the growing protein



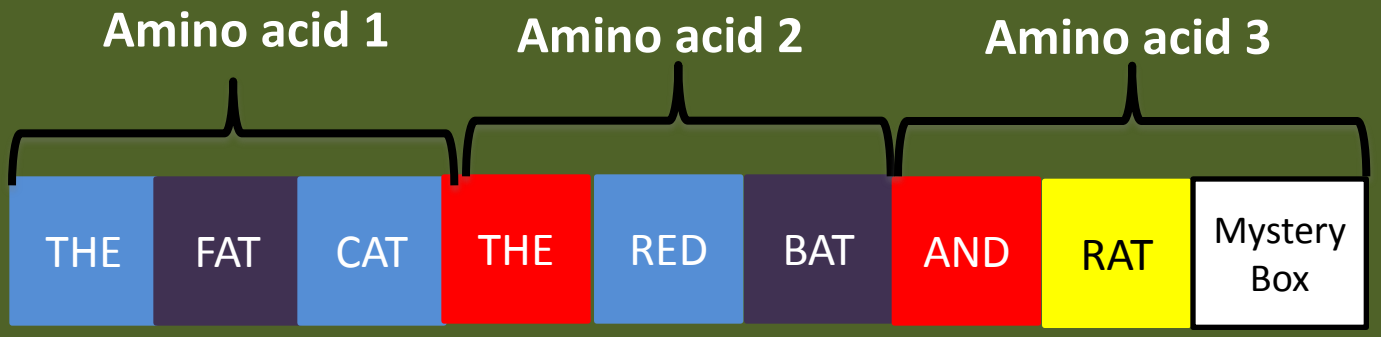
In this case, CAT was changed to CAT. At the end of the day nobody would know this mutation took place

Problems can arise, however, if you have multiple mutations near each other that can lead to a different amino acid being put in the protein

What is we're not that lucky?

Most of the examples we saw before are known as missense mutations

In a missense mutation, a different amino acid is added to the protein



Again, amino acid 2, 3, 4, 5, 6,…. Are going to be put off of their reading frame.

>>We are going to have different amino acids in place of the correct ones.

Nonsense mutations

Remember that we have three (3) different codons that are called “Stop codons”

>>These tell the tRNA that it has reached the end of its line. The protein is finished being made.

>> We can have a mutation in which the codon changes and tells the tRNA to prematurely stop translating the protein.

This is known as a nonsense mutation

The past two (2) mutations that I introduced are:

Missense mutations
&
Nonsense mutations

It's REALLY easy to get confused between these two.

They mutations aren't *that* much different, and the names are *really* similar

So how can we EASILY tell them apart?

Missense mutations:

When a nucleotide is changed and codes for a different amino acid

Nonsense mutations:

When a nucleotide is changed and codes for a STOP codon (tells the tRNA to stop making the protein)

In the case of a nonsense mutation, the tRNA is going along, translating the mRNA and creating the protein.

Suddenly, it sees a stop codon that is telling it the protein is finished.

The tRNA thinks to itself, “Stop here? That’s nonsense!” but it has to follow what the mRNA is telling it to do, so it stops anyways.

Questions, comments, concerns?

Exit ticket

1. What is a mutation?

2. What is the difference between a missense and nonsense mutation?

3. Which is worse, a point mutation or a frameshift mutation? Explain your answer.