1: THE WATER MOLECULE

Water is essential to life. Our bodies are 60 to 70 percent water. (Younger people tend to have more water, and older people have less.) If you removed all the water from our bodies, we'd be nothing but a small pile of dry, dusty minerals.

Water is made of one oxygen atom and two hydrogen atoms. The hydrogens stay attached to the oxygen because they are sharing electrons. Oxygen would like to gain two electrons (it has six in its outer shell but would like to have eight) so it works out very well if two hydrogens come over and share their electrons. This type of bond (sharing electrons) is called a ***covalent bond***. In general, non-metal atoms (such as carbon, nitrogen, and oxygen) form covalent bonds.

Atoms at the top of the Periodic Table obey what is called the "Octet Rule." They want to have 8 electrons in their outer shell. (If you would like a review activity about electrons shells and orbitals, try the "Quick and Easy Atom-izer" posted at www.ellenjmchenry.com; click on free downloads, then on chemistry.) Ideally, an atom with only 2 electrons in its outer shell will try to pair up with an atom that has 6 electrons in its outer shell. Between the two of them they will have 8, fulfilling the Octet Rule. It doesn't always work out this perfectly. Sometimes atoms have to "double share" to make things work out. For example, the oxygen in the air we breathe forms O_2 molecules. Each oxygen atom has 6 electrons in its outer shell and wants 2 more. They each give the other a pair of electrons, forming a ***double bond***. It's not a covalent bond where everything adds up to eight, but it seems to work well enough for the O_2 molecule. Oxygen molecules can even take on a third oxygen temporarily, forming ozone, O_3.

Chemists have actually been able to measure the angle at which the hydrogen atoms sit on the oxygen atom, and found it to be about 104 degrees (meaning geometry degrees, not heat). The placement of the hydrogens makes the molecule look a bit comical to us; it has been compared to a teddy bear, or to Mickey Mouse or Kermit the Frog.

Water molecules are constantly vibrating. The hydrogens go in and out, closer to and further from the oxygen. They also tumble around, bumping into each other like bumper cars at an amusement park. The faster they move, the more heat there is. Slower activity goes along with decreased temperatures. (Try the online interactive demo posted as an activity for this lesson. It lets you increase and decrease the movement of the molecules and see what happens.)

The oxygen atom is bigger than the hydrogen atoms. The oxygen atom has 8 protons, whereas the hydrogens have just one. This gives the oxygen a huge advantage when it comes to controlling the 8 electrons they are all sharing. The oxygen's large nucleus attracts those electrons strongly and keeps them circulating around it most of the time. Those poor hydrogens get an electron whizzing around them once in a while, but the electrons spend more time around the oxygen atom. This causes the entire molecule to become slightly unbalanced, so to speak. If you imagine the molecule to look like a teddy bear head, the chin of the bear becomes more negative because of the constant presence of the electrons, which carry a negative charge. The bear's ears, those hydrogens, are essentially made of nothing but a proton, and since protons carry a positive charge, the ear side of the molecule is more positive. This difference in charge between the two sides makes the molecule ***polar***. Polarity is when a molecule is more negative on one side and more positive on the other. Polarity is what gives water so many of its amazing qualities, such as being able to dissolve so many substances. We'll meet the concept of polarity again in future lessons. It is very important.

Hydrogen atoms sometimes leave their water molecules. This means that at any given time, there are some H's and some OH's floating around. We call these partial molecules ***ions*****.** An ion is an electrically unbalanced atom or molecule, with more electrons than protons or more protons than electrons. When a hydrogen atom leaves its water molecule, it leaves its electron behind. Without its electron, hydrogen becomes nothing but a proton. In a normal hydrogen atom there is one proton and one electron, so the positive and negative charges are equal. But a hydrogen ion has only one proton and zero electrons, so its overall electrical charge is +1. We can use the abbreviation H+ to represent a hydrogen ion. (You must always remember that the words "hydrogen ion" and "proton" can be used interchangeably since they are the same thing.)

In the case of OH, it has lost a proton (H+), so now it has one more electron than it does protons. Overall, it carries a negative (-) charge. We will therefore write it like this: OH-. The proper name of this molecule is the ***hydroxide ion***.

The strangest molecule in a drop of water has to be the ***hydronium ion***, H_3O. A hydrogen ion (a proton) goes and attaches itself to a regular molecule, turning H_20 into H_30. This does not work out so well, and one of the hydrogens immediately leaves, returning the molecule to normal water.

2: CARBON ATOMS and FATTY ACIDS

The carbon atom is like no other atom. It is so flexible in the ways that it can bond with other atoms, that it is the basis for thousands of molecules, many of which are found in living organisms. Starting with carbon, we can build sugars, proteins, fats, and nucleic acids —the essential molecules for life.

Carbon is element number 6 on the Periodic Table. This means it has 6 protons. Because it has 6 protons it also has 6 electrons. Of these 6 electrons, 2 fill the small inner shell and the remaining 4 occupy the outer shell. As you will remember, the outer shell would like to have 8 electrons in it, so carbon tries to bond with other atoms in order to gain 4 electrons. In other words, carbon has 4 places that it can bond to another atom.

The most basic carbon molecule is ***methane***: 1 carbon atom bonded to 4 hydrogen atoms. (The root "meth" means "one." The way you count carbon atoms isn't, "One, two, three, four," it's, "Meth, eth, prope, bute.") When we look at the electrical situation in this molecule, we see that the molecule is evenly balanced. The hydrogen atoms move around so that they are the maximum distance apart, evenly spaced around the carbon. We need to remember that hydrogens don't want to be right next to each other. Their positively charged protons don't like to be next to other positive charges. As they say, "Like charges repel, opposite charges attract." So the hydrogens space out evenly. This means that unlike water, methane does not have a positive and a negative side. All sides are the same. Methane is ***nonpolar***.

Another important feature of carbon is that it likes to bond to itself, making chains or rings. A 2-carbon chain is called ethane, a 3-carbon chain makes propane, and 4 is butane. You will perhaps recognize the words propane and butane and know them to be fuels we use in things like lighters and outdoor grills.

Methane is a very light molecule so it is a gas (at standard temperature and pressure). As the carbon chains get longer, the molecules get bigger and heavier. By the time we get to the 8-carbon chain called octane, we have a liquid. Octane is found in the gasoline (petrol) we put into cars. When carbon chains get to be really long they form solids such as wax. Plastics are also made of extremely long chains of carbon atoms, though sometimes other types of atoms are mixed in, too, such as chlorine in PVC (polyvinyl chloride).

Chemists use a short cut when drawing carbon chains. They draw only a zig-zag line. They know that at the point of each V there is a carbon atom. Since they all know this, they don't bother drawing it. They also assume, unless otherwise indicated, that there are hydrogens attached to the carbons in order to give each one its required 4 bonds. A carbon at the end of a chain will have 3 hydrogens and those in the middle will have 2.

The carbon chains found in our bodies are called ***fatty acids***. The chains are usually 12 to 18 carbons long, and they have a special group of atoms on one end. This group is called the ***carboxyl group***, or carboxylic acid, **COOH**. In the last lesson we briefly mentioned that a liquid with a lot of protons (hydrogen ions) in it will be acidic. In COOH, the H is not attached very well and can "fall off." Anything that creates loose H's is an acid. As we will see in the next lesson, this group has a special feature that will let us connect the carbon chain to other molecules, making larger structures. Just to confuse you, it will be the OH part of COOH that will fall off. However, this will not make the environment alkaline. The OH will immediately get picked up and joined to another atom to make a harmless substance.

The fatty part of a fatty acid is the carbon chain. We know that fats and oils are greasy and don't mix with water. Carbon chains are nonpolar so they don't have positive or negative sides that can attract water molecules. Other substances can dissolve fats, but not water. Water can only dissolve polar substances.

3: LIPIDS (part 1)

A fatty acid is a carbon chain with the COOH carboxyl group attached to one end. In this lesson we will see how fatty acids can be attached to a larger molecule, called glycerol.

Glycerol is a carbon-based structure, with a chain of 3 carbons at the center. The presence of 3 oxygen atoms makes it different from the carbon structures we saw in the previous lesson. Think of glycerol as a hanger, from which one, two, or three fatty acids can hang. The fatty acids hanging down from glycerol usually have from 12 to 20 carbon atoms.

To attach a fatty acid to a glycerol "hanger" you must take the OH off the COOH, leaving just CO. On the glycerol end, a hydrogen, H, is pulled off. The unhappy atoms who have an empty bond site dangling are the carbon on the fatty acid and the oxygen on the glycerol. The carbon and the oxygen and matched up and they bond to each other.

What happens to the OH and the H that were pulled off? They join together quite happily to form a molecule of water, H_20. This does not happen randomly, on its own, however. A little "machine" (an enzyme) does the attaching. As we will see in future lessons, enzymes are like little robots who do only one job. The enzyme at work here was designed to do this one task: join fatty acids to glycerol by popping off OH's and H's. This enzyme has an extremely long name that is almost impossible to remember even for an biochemist, so just knowing that an enzyme in involved is enough information for us.

This process has a name you will need to know; it's called ***dehydration synthesis***. (The word "synthesis" is from the Greek word for "make.") As it turns out, this is a common way of joining two molecules. Pull off an OH and an H and join the "ragged edges" you leave behind, making a water molecule in the process. The name might seem backwards. When we think of dehydration it's usually in the context of water evaporating and disappearing, not being made. Think of the word "dehydration" in this way: "de" means "from," and "hydro" means "water." You are using water to synthesize something. The end product is coming <u>from</u> the process of making <u>water</u>. This process can be reversed, too. Water can be used to separate two molecules. The water is broken into OH and H, and those ions are used to "plug" the ends of the two broken pieces.

A glycerol that has 3 fatty acids hanging on it is called a ***triglyceride***. ("Tri" is Greek for "three.") A triglyceride's fatty acids can be all the same, or they can be very different. Sometimes a glycerol will have only one fatty acid, so it will be called a ***monogylceride***. ("Mono" is Greek for "one.") A glycerol with 2 fatty acids would be a ***diglyceride***. ("Di" is Greek for "two.") Fatty acids that are not attached to a glycerol are called ***free fatty acids***.

Where does glycerol come from? The body can make it from glucuse sugar or it can use glycerols that come from the things we eat (fats from plants or animals). If glycerol needs to be manufactured from glucose, there are specialed enzyme "robots" that will perform this task. If glycerol is taken out of food, there are enzymes for that, too.

If a fatty acid has all the hydrogens it can possible hold, it is called ***saturated***. Saturated fats tend to be solid at room temperature and are most often found in animal products such as meat and butter. An unsaturated fat is a carbon chain that is missing some hydrogens. A place where two hydrogens are missing creates a double bond, which then causes as a slight bend in the chain. If the chain has only one double bond, it is called **monounsaturated**. If it has many double bonds and therefore many bends, it is called ***polyunsaturated***. ("Poly" is Greek for "many.")

Nutritionists are still debating whether it is better to consume saturated or unsatured fats. To complicate matters, there are ***trans fats*** where hydrogens have been artificially added, to break those double bonds, but the hydrogens end up on opposite sides of the molecule. ("Trans" means "across.") The trans fats tend to stick to the insides of our blood vessels and clog them up. Transfat are most often found in desserts and snack foods.

Fatty acids often have strange-sounding names such as myristoleic acid, sapeinic acids, vaccenic acids and caprulic acid. We won't be learning those. Fatty acids that are very common and also have decent names are lauric acid, (a short one with only 12 carbons and found in coconuts and palms), and palmitic acid with its 16 carbon chain (found in palms). Ther is a whole group of fatty acids that all have 18 carbons, though the number of double bonds varies. Stearic acid has not couble bonds so it is completely saturated. It is found in great aboundance in animal fat, particularly in the fat inside bones (which is where it gets its name). Oleic acid has one double bond and is found in great abundance in olive oil. The "ol" at the beginning of each word (olive and oleic) helps us to remember the connection. Linoleic acid has two double bonds in its chain and is found in flax (from which ***lin****en* is made). Alpha-linolenic acid has three double bonds and is found in nuts and seeds. Why all the fuss about double bonds? Those double bonds cause the chain to have bends or "kinks" in it. This alteration of the shape causes it to behave differently in cells.

Omega-3 fatty acids have a double bond starting at the third carbon from the end. ("Omega" means "last"). Omega-6 fatty acids have a double bond starting at the carbon sixth from the end. Our diets should contain more omega-3 fats and less omega-6 fats. Unfortunately, the modern diet has these reversed. Omega-3 fats are found abundantly in fish oil.

Our bodies can make some fatty acids. The ones we must get from food are called Essential Fatty Acids (EFAs).

4: LIPIDS (part 2: phospholipids)

When lipids are joined to phosphate molecules they form a large molecule called a ***phospholipid***. Phospholipids are one of the key building blocks of cells. As we will see in lesson 5, they will form the outside layer of cells, and also of many smaller cell parts called organelles.

A phospholipid molecule is made of a glycerol hanger that is holding on to two fatty acids and a phosphate. A phosphate is made of 1 atom of phosphorus and 4 atoms of oxygen.

Phosphorus can make 5 bonds. (The Periodic Table can help you determine how many bonds an atom wants to make. The atoms in the first column (Li, Na, etc.) all have one extra electron in their outer shell, so they want to make one bond. The second column atoms all have 2 electrons in their outer shell so they are good for 2 bonds. The third column has 3, and so on. Phosphorus is in the fifth column, so it can make 5 bonds.) Since there are only 4 oxygen atoms in this molecule, one lucky oxygen atom will get a double bond. The other oxygen atoms have one bond with phosphorus, but are also holding on to an extra electron, which will give the molecule an overall electrical charge of negative 3. We can write PO_4^{3-}. This molecule is a ***polyatomic ion***. Simple ions are made of one atom. Polyatomic ions are made of more than one atom. (By the way, don't let the word "ion" confuse you. It is common for students to have trouble remembering what an ion is. If you think of an ion as broken molecule, that's sort of right. Ions have had electrons added or taken away, ruining their original neutrality.)

The phosphate ion is best explained by looking at phosphoric acid, H_3PO_4. In this molecule, the oxygens have their two bonds, one with phosphorus and one with a hydrogen. Hydrogen atoms, as we have seen, have the bad habit of easily wandering off. When they leave, however, the oxygen atoms insist on keeping the electrons. You'd think that would make a hydrogen want to stay, but no, it goes off as nothing but a proton. (This makes the surrounding environment acidic. That's what acids do — they donate protons.) If all 3 hydrogens are gone, you have a phosphate ion.

One oxygen of the phosphate ion is bonded to the third hanger on the glycerol. One oxygen has a double bond and just sits there. One oxygen hangs off unbonded, and the fourth oxygen is usually attached to another molecule which can be labeled R. An R group is the variable part of a molecule. R could be any one of a number of different options. We don't need to know any specific molecules for R in this case. We will just write an R and leave it at that.

Two of glycerol's hangers are connected to fatty acids. There are many possibilities for what type of fatty acids these might be, but we are going to draw two special fatty acids: **EPA** and **DHA**. EPA stands for **e**icosa**p**entaenoic **a**cid, and DHA stands for **d**ocosa**h**exaenoic **a**cid. (That's why we calle them EPA and DHA. EPA has 20 carbon atoms and 5 double bonds. DHA has 22 carbons and 6 double bonds. The double bonds cause bends that make the molecules look almost like circles. EPA and DHA are especially valuable in some types of cells, such as nerve cells. They seem to have the ability to keep other molecules from getting too tangled. (This will make more sense a few lessons from now when we make membranes.) These fatty acids are found in other places, too, not just in phospholipids. They are important ingredients in messenger molecules, for instance. They help to stop inflammation.

The most important thing to know about a phospholipid molecule is that the head portion is ***hydrophilic,*** or "water loving," and the tails are ***hydrophobic***, or "water hating." This is a hugely important fact in biochemistry.

Carbon is a very flexible atom; besides being able to form long chains, it can also make rings. One of the most basic rings is called benzene. This is not a molecule found in your body (well, hopefully not), but it is a good example of a carbon ring. Carbon rings are often in the shape of a hexagon or a pentagon.

Cholesterol is made of four carbon rings with some extra atoms attached. It is a natural body substance, and as we will soon see, it is found in and around phospholipid molecules. It can tuck in amongst the fatty acid tails. Cholesterol is not a harmful substance; it is a natural and necessary component found in all body cells. Too much of anything can be bad, so, indeed, a very high level of cholesterol is not good for you. On the other hand, too little is not healthy, either.

5: MEMBRANES (part 1)

If you could throw a whole bunch of phospholipid molecules into a bucket of water, the water-hating tails would go into a panic and try to find a way to get away from the water molecules. The tails would all congregate together, to make an area that was water-free. More and more molecules would join in until a sphere had formed. A sphere is the most efficient, compact shape they could form. A simple. single-layer sphere of phospholipids is called a ***micelle***. We will see these in a future lesson. (A micelle is shown and discussed in the video lesson, but not drawn as part of this lesson.)

Another way the phospholipids could arrange themselves is into a double layer, with all the tails turned inward. A double layer of phospholipid molecules is called a ***phospholipid bilayer.*** This term is used quite frequently in cell biology. The phospholipid bilayer is the basic structure of a cell membrane. It separates the inside from the outside. Most cell organelles are also surrounded by a phospholipid bilayer.

A simple phospholipid sphere can be called a ***liposome***. "Lipo" is Greek for "fat," and "soma" is Greek for "body." We will look at three cell parts that have the structure of a liposome.

An empty liposome can be called a ***vacuole***. "Vacuus" is Latin for "empty." Vacuoles can contain water or air.

A ***vesicle*** is basically a vacuole that has stuff inside of it. Cells use vesicles like we use plastic or paper bags. Anything that needs to be stored, or transported across the cell, can be put into a vesicle "bag." Sometimes vesicles filled with certain substances (food, fats, chemicals) are given fancy names, rather than just being called a vesicle. We'll see some of these in future lessons.

A ***lysosome*** is a very special kind of liposome. It contains digestive enzymes, so it is a bit like a stomach. Things that need to be broken down and recycled (old cell parts, or even bacteria) are put into a lysosome. The digestive enzymes are able to tear them apart and turn them into simple proteins, sugars, and other molecules that cells can use. It's like destroying a Lego sculpture and using the parts to build something else. The word "lys" means "to dissolve or break apart." Lysosomes can contain as many as 50 different kinds of enzymes. Each enzyme does only one job.

Scientists used to think that if a lysosome burst, the cell would die because the enzymes would get out and go around digesting all the cell parts. (Enzymes are not smart. They don't know what they are supposed to digest. They digest anything in their path.) Then they discovered that the environment inside a lysosome prevents this from happening. The digestive enzymes need an acidic environment to be able to function. Little proton pumps in the membrane of the lysosome bring protons inside. An environment with lots of protons floating around will be acidic. When the lysosome bursts, the enzymes do escape, but they suddenly find themselves in an environment that is neutral, not acidic. Therefore they stop functioning (or at least slow way down).

NOTE: Lysosomes do participate in cell death (apoptosis or necrosis, which we will discuss in future lessons) and are sometimes "given instructions" to digest cell parts, but under normal circumstances lysosomes don't endanger their cells.

6: MEMBRANES (part 2)

ALL cells are surrounded by a membrane. Even plants cells, with their thick cell wall made of cellulose, still have a membrane under that wall. And what is that membrane made of? Phospholipid bilayer, of course. The membrane separates the inside from the outside; kind of obvious, perhaps, but a concept often emphasized in high school texts. Once "inside" and "outside" have been established, the cell now needs a way to bring things in and send things out. The cell will need to bring in nutrients and other helpful molecules, and will need to send manufactured products to other cells and to get rid of wastes. There are a number of different methods of getting things across the membrane, depending on the size and chemical properties of the materials being transported. The first thing to consider is whether these methods use energy or not.

We use the word "transport" to describe the process of crossing the membrane. We add the word "passive" to describe transport that does not require any energy. So ***passive transport*** is crossing the membrane without using energy.

PASSIVE TRANSPORT: There are two types of passive transport. They both use the principle of ***diffusion***, so we need to discuss that first. Diffusion comes from a Greek word meaning "to spread out." Diffusion is what happens when you open a bottle of something very smelly in a closed room. At first, people standing at the far end of the room can't smell anything. Then, as time goes on, the smell spreads and fills the room. Soon all areas of the room are equally smelly. Diffusion is the movement of molecules from where there are more of them to where there are less of them. The "goal" of the molecules is to end up equally distributed everywhere. The molecules will keep moving after this, but they will remain equally distributed. In our example, the smelly molecules did not have anything blocking them from moving around so we were not too surprised that they could fill the room.

If we had put a paper wall across the middle of the room and sealed all the edges, this would have made it more difficult for the smelly molecules to fill the room, but not impossible if the molecules were small enough to go through the microscopic holes in the paper. A paper wall isn't going to stop a smell like gasoline, for instance. This shows us that diffusion can still happen across a barrier if the chemistry is right. Water would also be able to get across our paper wall but not quite as quickly. Barriers that allow things to pass right through are called ***permeable***. (So why have them in the first place, right?) Barriers that allow only some things to pass through are ***semi-permeable***. Cell membranes fall into the category of semi-permeable, but an even better word would be ***selectively permeable*** because cells can select some things to come in and other things to stay outside. Again, these words mean exactly what they say, so it should not be hard to remember them.

Now that we know what diffusion is, we can learn the two types of passive transport. They are **1) *simple diffusion*** and **2) *facilitated diffusion***. Simple diffusion is often just called diffusion without the word simple in front of it. However, it might be easier to remember these terms if their format is the same. The brain likes pairs and groups and always looks for similarities, so we can help out brains remember if we cooperate and try to group things logically. The visual layout of the drawing will help you, also. Passive on the left, active on the right, with the types listed below.

Simple diffusion: Some things can diffuse right through the phospholipid membrane. If the concentration of that type of molecule is greater outside the cell than inside, the molecule will diffuse in. What kind of molecule will be able to do this? As you might guess, it would have to be small. Size is important. What about chemical properties? Look at the phospholipid bilayer. Which area is thicker—the head area or the tail area? The tails are very long, so the lipid layer in the middle is much thicker. This means that any molecule passing through will have most of its journey be through the fatty, non-polar area. Overall, this means that **fat-friendly, non-polar molecules** stand a better chance of getting through the bilayer than water-friendly, polar ones. Examples of small, fat-friendly molecules that can diffuse through the membrane are **vitamins A, D, E and K, and steroids**. These vitamins are often called the "fat-soluble" vitamins. Their molecular structure includes rings of carbons, like we saw in cholesterol, so they get along very well with the cholesterol molecules that sit in and among the fatty tails. They have no trouble slipping through. Steroids are also based on rings of carbon. In fact, your body turns cholesterol into steroid molecules (and also into vitamin D). Cholesterol isn't a poison; it is an essential molecule you can't live without. The steroids made from cholesterol include estrogen, testosterone, and anti-inflammatory steroids.

Oxygen and carbon dioxide are small and are non-polar so they can use simple diffusion, too. They are very numerous and must get across quickly, so it is good that they can just cross on their own. If they had to wait for a molecular gate to open, this would cause a chemical traffic jam for sure!

Water used to be on the list of molecules that use simple diffusion, but now that has been called into question. It is true that even though **water** is polar, the molecules are very small and they do indeed often slip through the membrane to the other side. The "pull" of diffusion (wanting to be where there are less of them) will sometimes be enough to get them through. However, we now know that even though water does sometimes diffuse through, the molecules prefer to go through a channel that we will discuss on the next page.

Facilitated diffusion: The word "facilitate" means "to make easier." In faciliated diffusion we find some molecules that can diffuse if they have just a little bit of help. Molecules that are not-so-small, or are polar, can't slip through that fatty middle layer of tails. There's just no way they are getting through that "We hate water and polarity" zone. They need some kind of tunnel that they can go through. The tunnels are often called "channel proteins." (There isn't one officially correct name for these channels. Some authors call them more complicated names, like "transmembrane integral proteins." We're going to stick with "channel proteins.") You don't know exactly what a protein is yet, but we'll go ahead and use that word since you are familiar with it. The key word is "channel." These channels provide a way for small polar or electrically charged molecules to diffuse in and out of the cell. Now we can go back to discussing water.

A) ***Aquaporins*:** Until 1992, it was thought that water simply diffused into cells. This is true to some degree. It's not impossible for a water molecule to get through the membrane. However, the journey is not easy. Scientists began to suspect that water was getting through another way but they did not know how. Then an American scientist named Peter Agre discovered a protein channel that he named ***aquaporin***. It's a pore that lets "aqua" (water) through. This discovery was so important that he received the nobel prize in 2003. (Just think of all the textbooks that had to be rewritten!) Aquaporins are channels that let water, and only water, diffuse in and out of the membrane. As Agre's team studied aquaporins they found out that there are many different kinds, depending on the cell type. Some aquaporins are found only in brain cells, other in eye or skin cells. You'll learn a little more about aquaporin in one of the activities that goes with this lesson.

At this point, we need throw another vocabulary word at you. You may already know this word; it shows up in botany and physics books, too. When water diffuses through a membrane, we don't call it diffusion — we call it ***osmosis***. We might guess that "osmos" means "water" in another language, but it doesn't. "Osmos" is Greek for "push." Water looks like it is pushing through the membrane? The person who named it apparently seemed to think so. Even though it doesn't mean "water," thinking of water when you see "osmo" is still a good idea. Most science words that start with "osmo" have something to do with water.

As long as we are throwing vocabulary words at you, we might as well go ahead and cover the last major diffusion term that you need to know. The action of going from where there are more of them (a higher concentration) to where there are less of them (a lesser concentration) is often called "following the ***concentration gradient***." Sometimes biologists will say that the molecules go "***down the concentration gradient***." You know what concentration means. Let's look at the word "gradient." The word "grade" is used by landscapers to describe the steepness of a hill. The grade of a hill is given in degrees (of geometry, not temperature). A gentle slope might be 3 degrees; a steep one would be 30 degrees. The word "grade" can also be used as a verb. Landscapers will "grade" the dirt around a house so that it goes downhill, away from the house. (This helps to keep rain water out of the basement.) So when you see the term "concentration gradient," don't panic. Just think of grading dirt so that water flows DOWN the slope and away from the house. The key word is DOWN. Molecules go DOWN their concentration gradient, from places of high concentration to places of lower concentration. When you see the word "gradient," think of a slope where things role from high places to low places. Think of rolling DOWN a hill. High to low, high to low.

It's actually not a hard a concept, despite the fact that the term "concentration gradient" sounds like it might be difficult. You will see this term used all the time in biology books, so it is best not to be scared of it!

B) *Ion channels*: Another example of facilitated diffusion is the ***ion channel***. An ion channel is designed to let only one type of ion get through. The most common types of ion channels are for sodium (Na^+), potassium (K^+), chlorine (Cl^-) and calcium (Ca^{2+}). Ion channels tend to look like two funnels stuck together at their narrow ends. The wide top and bottom are described as "water-filled." The narrow part in the middle is very small indeed, perhaps only one or two atoms wide. The channels can be constantly open or they can be "gated," meaning that they only allow ions through when certain conditions exist. Gates can act as a triggering mechanisms, allowing a sudden influx of ions that will cause a whole series cellular events.

Gated channels come in many kinds. Some respond to light (cells in the eye), temperature (skin cells), or pressure (skin cells). Some are triggered by messenger molecules coming from outside. The gated channels in your nerve cells are triggered by differences in electrical voltage. There are about 300 different types of ion channels present in most cell membranes. (That's 300 types, not 300 total.) The most important thing to know about ion channels is that they do <u>not</u> require energy to operate. They are passive, not using energy.

One particular type of channel needs special mention—the channel that transports **glucose** sugar molecules into cells. This channel relies on shape. Glucose molecules look like a hexagonal ring. When a glucose molecule goes into the channel, it is like a key fitting into a lock. The shape clicks in place. When it clicks in, this automatically causes the channel to change shape so that the glucose drops out the bottom and into the cell. With glucose gone, the shape returns to normal.

<u>ACTIVE TRANSPORT</u>: Active transport requires energy. Your body is full of tiny molecular re-chargeable batteries. The most well-known is called **ATP**. We'll take a closer look at ATP in a future lesson. Chances are good that you've heard of ATP already, so you won't be in too much suspense till then. Right now all you need to know is that ATP stands for "adenosine triphosphate" and that it is like a rechargeable battery for your cell. The molecule has three phosphates, and the third one can be popped on and off. When it is popped off, energy is released. Phosphates have all kinds of uses in the cell, but this is the most famous one. ATP provides energy of cellular work.

Two other (slightly less famous) rechargeable molecules are ***NADH*** and ***FADH***. You don't need to know what those letters stand for. (But for those of you who are curious, NADH stands for Nicotinamide Adenine Dinucleotide.) These molecules carry electrons to ion pumps. There are some very important ion pumps in your cells that depend on these molecules to deliver high-energy electrons. We will see them again during the lesson on what goes on inside a mitochondria.

We are going to look at three kinds of active transport: ***ion pumps, endocytosis and exocytosis***.

Ion pumps: These look similar in structure to ion channels. They cross the entire bilayer, and have an entry or exit at each end. Recently, researchers have found even more similarities and in future years you might be reading about their discoveries. The most important difference between them is that the pumps are going "***against the concentration gradient***." Water goes downhill, with gravity. Pumps can pump it back up, against gravity. But pumps need the energy of your arm or a motor to make them go. Ion pumps use ATP energy. There are places at the bottom of the pumps where ATP molecules attach and release their third phosphate. Details about this energy and how it is used by the pump are beyond the scope of this course. (Very quickly you get into quantum physics!) Ion pumps are found in plant cells, too, not just animal cells. The process of photosynthesis relies heavily on ion pumps. We'll also see ion pumps as a major feature of cellular respiration in a future lesson.

The most famous ion pump is the sodium-potassium pump located in the membrane of nerve cells. It pumps sodium out of the cell and potassium into the cell. The ions would not naturally go in this direction, because this is against their concentration gradient. Huge numbers of the ions build up on one side of the membrane, then they are let back in very suddenly when the gates of their ion channels open. (There are separate channels for sodium and potassium.) A pump and two channels work together, so to speak.

Endocytosis: "Endo" means "in," and "cyto" means "cell." So endocytosis just means going inside the cell. Endocytosis is used to take in very large things. In a future lesson, we'll meet immune system cells that take in all kinds of things, including bacteria. There is a special name for when a cell takes in just a tiny amount of something. This is called ***pinocytosis***. It is often described as cells "drinking or sipping." We will see cells doing this when we study the cells that line the insides of blood vessels and capillaries.

The best way to learn about endocytosis is to watch an animation of it. (Watch those supplemental videos on the YouTube channel.) An indent starts to form in the membrane, and it becomes deeper and deeper. The particle gets trapped inside this pocket. The pocket goes so deep that it starts to close off and pull away from the membrane. The pocket breaks away from the membrane and becomes a vesicle with the particle inside. This vesicle can be transported to where it is needed in the cell.

Exocytosis: "Ex" means "out" so exocytosis means things moving to outside the cell. Exocytosis is the opposite of endocytosis. When the cell wants to send something out, it puts it into a vesicle then send the vesicle to merge with the membrane. When the vesicle touches the membrane, it become part of it. The vesicle turns into a deep pocket which becomes more and more shallow until there is nothing left. The particle that was inside the vesicle now finds itself outside the membrane. Some cells of your body produce molecules that are needed by cells all over the body. These molecules exit the cell by exocytosis, and go into the blood so that they can circulate throughout the body.

7: MEMBRANES (part 3)

The plasma membrane of a cell is a busy place. Not only does it have many channels and pumps, it also is able to send and receive many kinds of molecular messages. The arrangement of these items in and around the plasma membrane is called the "fluid mosaic model." The word "fluid" tells us that it is not hard or solid, but flowing and changeable. All the phospholipids are able to move around, so the embedded proteins are also able to move. (Imagine a bathtub full of ping pong balls, with other objects floating among the balls.) The word "mosaic" refers to the art form where small colored tiles are used to make a picture. Artists' pictures of membranes often remind of a colorful mosaic image.

We've already learned about some of the things you will find in a plasma membrane: channels and pumps. Aquaporins are also there, but we're going to be non-specific in our drawing and just put in a generic channel and pump (they could be anything). Proteins like channels that go all the way through the membrane are called ***transmembrane proteins***. "Trans" means "across." These proteins go across the membrane. (Don't worry about what the word "protein" means exactly—we'll get to that in the next lesson.) There are also proteins that go only half way in, and proteins that stick to the inside or outside and don't go in at all. Proteins that go in, either halfway or all the way across are called ***integral proteins***. (So all transmembrane proteins are integral proteins, but not all integrals are transmembrane.) Proteins that don't go inside at all are called ***peripheral***. "Peri" means "around or outside."
Our integral protein here looks like it has a hook attached to it. There are proteins that do function like little hooks.

One of the most interesting transmembrane proteins is ***Flippase***. Finally, a name that is easy and makes sense! Flippases can flip phospholipids from the top to the bottom, or vice versa. (The one that flips bottom to top is often called "Floppase.") Why would this be necessary? Several reasons, but the easiest to understand is that during the process of endocytosis a new circle of membrane is being formed. Imagine a vesicle as a running track. The inside lane is shorter than the outside lane. If you put balls along the lanes, you would need more balls for the outside lane because it is longer. In the same way, there will need to be more phospholipids on the outside layer of the vesicle than the inside because the outer layer is larger. As soon as endocytosis starts, Flippase begins flipping phospholipids over, to prepare for this new geometry. Brilliant!

There are many ***receptors*** on the outside of plasma membranes. Receptors receive messages in the form of special molecules. Each receptors has a unique shape so only one kind of message molecule will fit. If a message comes along and snaps into place, then chemical changes will take place inside the cell.

Some proteins have sugar chains attached to them. Because they have sugars as part of their structure, they are called ***glycoproteins***. "Glyco" is Greek for "sugar." Cells use glucose molecules for more than just energy. Short strings of sugars are used as tags or labels. These chains are called ***oligosaccharides***. "Oligo" is Greek for "few," and "sacchar" is Latin for "sugar." (The English word "sugar" came from the Latin "sacchar.") Oligosaccharides are used inside the cell, also, often as "mailing labels" directing where things such as vesicles should be taken. The arrangement of the sugar molecules contains information.

Every cell the body has an "ID tag" called ***MHC1***. We will meet this molecule again when we study the immune system. In those lessons you'll learn all about MHC1. For now, you just need to know it exists and that its job is to label that cell as belonging to the body. When roving immune cells come to inspect, they will look for that tag.

Transmembrane proteins have a middle section that is hydrophobic. This is how they stay in the membrane. In our drawing, the protein's hydrophobic region looks like a spring.

Some floating proteins must work together to do a job. If they drifted apart in the fluid mosaic, they would not be able to work together, so they need to be kept near each other. This is accomplished by a ***lipid raft***. The raft is an area with extra cholesterol and other fatty molecules. The lipids stick everything in that area together, so the proteins can't float away. The raft can drift around, but the proteins will all stay put inside the raft. Lipid rafts are especially important in nerve cells and in immune system cells.

8: PROTEINS (part 1)

We've already looked at a number of things that are made of proteins. All the "gadgets" in the plasma membrane, such as ion pumps, aquaporin channels, and receptors, are made of proteins. Now it is time to find out what a protein is.

The basic unit of all proteins is the ***amino acid***. The word "amino" refers to this group of atoms: NH_2. The presence of ***nitrogen*** is primarily what makes proteins different from lipids. Nitrogen is number 7 on the Periodic Table, so this means it has 5 electrons in its outer shell. The first two are hidden in the small inner shell, so only the last 5 are in the outer shell. This means that nitrogen wants to make 3 bonds. (5+3=8)

The word "acid" refers to a group we've already met: COOH. If we combine these two groups, we get an amino acid. Like lipids, amino acids are built around carbon. At the core of the amino acid is a carbon atom. Attached to the four bonding sites of that carbon are: 1) the amine group, NH_2 2) the acid group, COOH 3) a hydrogen, H 4) the "wild card" R group Remember that R stands for the **R**est of the molecule. (It really stands for "radical," but "rest" works just as well and is much easier to understand.) There are several dozen possibilities for what R could be. We will look at just five of them in the next lesson.

We can't forget that molecules are not flat. They have a 3D shape. What would happen if we switched the positions of the amine group and the carboxyl group, "flip-flopping" them? The new molecule would contain the very same atoms, so its chemistry would be the same. The flip-flopped molecule, however, would be the mirror image of the original. We could call the original one the "left-handed" molecule and the mirror image would be "right-handed." To help us imagine the difference between left and right handed molecules, we should think of a pair of gloves. The gloves are mirror images of each other and seem identical. However, if you try to put a right-handed glove onto your left hand, it doesn't work so well. In biology, the shape of a molecule is vitally important. Many cellular processes are based on shape. It turns out that right-handed molecules will not make usable proteins for any form of life. All proteins in your body and in every living thing on the planet are made from left-handed amino acids. Life is left-handed. Left-handed proteins are designated by the letter "L" and right-handed ones by the letter "D." (You can use the fact that "dexter" is Latin for "right" to help you remember that D is the right-handed form.)

The correct name for "handedness" is ***chirality***. "Chiro" is Greek for "hand." (Chiropractors manipulate your spine with their hands. Bats are classified as Chiroptera, meaning "hand wings.") The importance of chirality was first seriously recognized in the early 1960s when a drug called Thalidomide was given to pregnant women to prevent nausea. The medicine contained equal amounts of the left and right handed versions of the molecule. Unfortunately, one of them was harmful to developing fetuses and thousands of babies were born without arms and legs. (Recently it has been determined that even if you eliminate the harmful version, the human body will convert the harmless version into the harmful version.) Another example of a molecule where chirality is important is the sweetener Aspartame. One version of the molecule is sweet, the other is bitter. Asparatme is controversial, but not because of its chirality. Penicillin, ibuprofen and DNA are also chiral molecules, but their chirality is not an issue that causes problems.

9: PROTEINS (part 2)

Proteins are chains of amino acids. Think of a long bead necklace; amino acids are like the beads. The bond that holds amino acids together is called a ***peptide bond***. The peptide bond is created using a process we are familiar with: ***dehydration synthesis***. The OH on the COOH is removed on the carboxyl group, and one of the Hs is removed on the amine group. The OH is connected to the H to make H_2O. The C and the N are stuck together with a very firm peptide bond. ("Pep" means protein.) The peptide bond is not very flexible and can't rotate. The other parts of the molecule can rotate a bit, and will adjust their position depending upon what situation they find themselves in. More on this in the next lesson.

When two amino acids are joined, we call this a ***dipeptide***. Three amino make a tripeptide. Many aminos in a long chain are called a ***polypeptide***. Polypeptides can be as short as 4 aminos or as long as 4,000. Amino acids are most often represented by circles, sometimes with a three-letter abbreviation written on them. The abbreviations are usually the first three letters of their names.

There are only 20 amino acids in the human body. (These aminos are also found in other forms of life.) Remember, they are all left-handed aminos. Some amino acids are said to be ***essential***, meaning your body can't manufacture them. You have to get these from the foods you eat. The other are ***non-essential*** because your cells can make them (often from other aminos). There are 9 essential aminos and 11 non-essential.

The R group determines the chemical characteristics of each amino acid. Aminos can be hydrophilic or hydrophobic (polar or non-polar). They can carry an electric charge or they can be neutral. They can be acidic or basic. Some contain extra elements such as sulfur. The nature of each amino acids is what enables long polypeptides to fold into specific shapes.

Let's look at glycine, valine, lysine, glutamic acid and cysteine.

Glycine is the smallest and simplest of the aminos. The R group is simply an H. Because glycine is so small, it is useful in proteins that are wound tightly, such as collagen. Its main feature is its size.

Valine is an example of an amino that is hydrophobic. This is easy to predict when you see that the R group is made of carbons and hydrogens, looking very much like a short fatty acid. The difference between valine and a fatty acid is that valine's carbons branch apart, forming a V. Valine is very hydrophobic (non-polar) and will always be found on the inside of a large protein, trying to hide from water molecules. A group of hydrophobic aminos will bend the polypeptide chain so that they can be together, forming a hydrophobic region. This will help to determine the overall shape that the polypeptide makes. (More on this in lesson 10.) Valine is also the amino acid that your body can use to make glucose for energy.

Lysine is one of the essential amino acids that you must get from food. Good sources of lysine include milk, meat, fish, eggs and beans. Lysine is hydrophilic (polar), basic (alkaline), and also is ionized, meaning it carries an electrical charge. Lysine has (NH_3^{+1}) as its R group. Nitrogen only really needs two H's so the third one can easily be replaced with something else. Lysine is used in strategic places where tiny molecular switches are needed, such as on the spools around which DNA is wound. Molecular "tags" can be popped on and off lysine, signaling the spool to tighten or loosen. Two examples of molecular tags are the methyl group, CH_3, and the acetyl group, $COCH_3$.

Glutamic acid is the official name of this amino acid, although it is often known as ***glutamate***. As you might guess from the word "acid" in its name, it has the carboxyl group as its R group. As we've mentioned before, that H on the end of COOH comes off very easily, so that the COOH is very often just COO^-. When this happens, glutamic acid is then called glutamate. So basically glutamic acid and glutamate are the same thing, but the acid version still has its COOH intact. However, the body's natural pH encourages the H to fall off, so for all practical purposes, this amino exists in the body as glutamate. So you can call it either one. Right now we will switch to calling it glutamate so that you will understand a video on the playlist. One of glutamate's most important jobs is to allow nerve cells to transfer electrical signals. Both glutamate and glycine must bind to the top of an ion channel in the nerve cell's plasma membrane. When they bind to the receptors on the ion channel, this allows a sudden influx of calcium ions. The sudden influx of ions is what helps to generate the electrical signal in the cell.

When glutamate is produced artificially and a sodium (Na) atom is added, you get ***monosodium glutamate, MSG***. This substance is used as a food additive to make the food taste better. MSG affects your sensory nerve cells, not the food. Your cells are excited and told to send more signals to the brain. Wow, your brain gets the message that the food tastes better! Unfortunately, the glutamate in MSG is the right-handed D form, not the left-handed L form. This may or may not be the reason that MSG causes health problems for so many people. It could also be that artificial glutamate floods the body with too much glutamate all at one time. MSG is very controversial, just like Aspartame is. Some people don't have any problems with it; others have terrible reactions to it.

Cysteine has a sulfur atom as its R group. (Sulfur needs two bonds, so it has an H attached to it.) Sulfur is an element that allows substances to form cross links. Charles Goodyear discovered this when he discovered how to vulcanize rubber. His rubber recipe was horrible until tried adding sulfur. The addition of sulfur allowed the chains of rubber molecules to form cross links, like rungs on a ladder, so that the substance became very sturdy, even in extreme heat and cold. In the body, there are also substances that need to be cross-linked and tough, so they use a lot of cysteine in their structure. An example of a protein high in cysteine is insulin.

10: PROTEINS (part 3)

The two most important things to remember about proteins are:

1) Proteins are made of amino acids.
2) The shape of a protein is what allows it to do its job.

This lesson will show you how a polypeptide chain will coil, bend, and fold to create a unique 3D shape. There are three levels of organization in this folding process, plus a fourth that some large proteins have. (We will see similar layers of organization when we look at DNA.)

1) ***Primary structure***: This is the sequence of amino acids. Since amino acids have different "personalities" the order in which the aminos occur will determine how it folds up.

2) ***Secondary structure***: There are basically two secondary shapes: the alpha helix and the beta sheet. In the alpha helix, the polypeptide coils tightly to look like an old-fashioned telephone cord. In the beta sheet, the chain bends back and forth like a paper fan, sometimes with multiple strips lining up to make a wider sheet. (Other formations include turns, loops and random coils.) Hydrogen bonding between the H that is bonded to the N, and the O that is double-bonded to the C, allows these formations to hold their shapes.

We saw hydrogen bonding between water molecules when the positive and negative sides were attracted. Here we have something similar, with oxygen acting like an "electron hog," holding the electrons a little bit longer than carbon does. (The correct term is "electro-negativity." Oxygen is more "electronegative.") The poor H has a nucleus consisting of only one proton, so it is no match for nitrogen when it comes to attracting the electrons. Therefore the H nucleus (a proton) sits by itself a fair amount of the time, making that side of the molecule more positive than negative. The negative and positive areas are attracted to each other and they form an association that is strong enough to let the helices and beta sheets hold their shape.

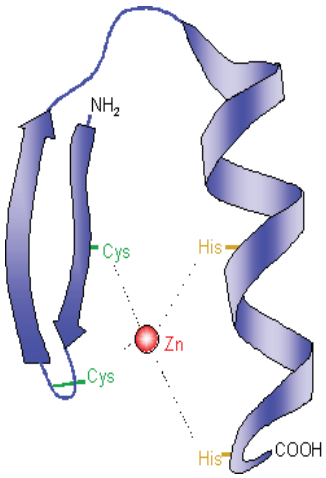
3) ***Tertiary structure***: Polypeptides can have sections curled into helices or bent into beta sheets, but the entire chain also folds up into a 3D shape. A simple and memorable tertiary shape made of nothing but beta sheets is the beta barrel. These proteins make good channels and portals in membranes. Aquaporin is made of nothing but helices. Another 3D shape that has a memorable name is the "zinc finger." Zinc fingers are used in proteins that grab and hold DNA. (For those of you who love trivia, the aminos that hold the zinc atom are 2 cysteines and 2 histidines.)

Amino acids that are hydrophobic will all try to gather together on the inside as the protein folds, creating a hydrophobic zone. The hydrophilic aminos like to be on the outside edges. Various other interactions occur between positive and negative areas. Besides alpha helices and beta sheets, you will find loops, turns, and random coils.

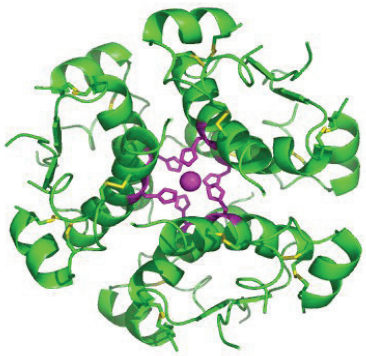
4) ***Quaternary structure***: This is when several individual proteins get together and form a large shape. Ex: hemoglobin

beta barrel

zinc finger



insulin also has a zinc atom (center)



11: PROTEINS (part 4)

Many cell parts and body parts are made of protein. It's like wood or steel—a building material that is strong and can be used in a variety of ways. This page is a brief visual catalog of cellular (and ***extracellular***, meaning outside of cells) "gadgets" that are made of protein. It is very helpful to think of these cells parts as biological equivalents to non-biolgocial items we are already familiar with.

The cell's plasma membrane has lots of embedded gadgets, as we've already seen. We've got ***channels*** (or we could call them tunnels or portals), ***pumps***, ***hooks***, ***anchors***, ***receptors*** ("mailboxes"), ***messages*** ("letters"), and ***motors.*** We'll meet this particular motor in a future lesson.

Inside the cell we will meet cables and ropes. The largest cable is called a ***microtubule***. Even though it is the largest, it is still small, so it still qualifies as "micro." Microtubules are hollow and they criss-cross the inside of the cell, attached to each end. This network of cables is called the ***cytoskeleton*** and it allows the cell to maintain its shape. In the case of ***motile*** cells (those that can move on their own, like amebas), the cytoskeleton is what causes the movement. The microtubule is made of small units of a protein called ***tubulin***. The microtubules can be made longer by the addition of tubulin units on the end. The tubulin units "self assemble," that is, they don't need an enzyme robot to do the assembly. The units just snap into place automatically. There are trigger molecules that get the process started by taking off an "end cap." When the end cap is removed, tubulins will start snapping into place and will continue to do so until an end cap is put back on again. This process happens very quickly. Millions of units can snap on in a few seconds. If you watch an ameba crawl along, you can see how fast the microtubules can lengthen.

This network of microtubules, the cytoskeleton, also functions as a road system. There are proteins that act like vehicles, driving along these microtubule highways. Or perhaps a better analogy would be to imagine the microtubules as tightropes in a circus, with acrobats walking on them, sometimes while carrying objects larger than themselves. The proteins that travel along microtubules look like they have legs and feet, and their motion looks very much like walking. In video animations of these walking proteins, the microtubules underneath their "feet" often look very thin, more like tightropes than like roads or sidewalks.

Microtubules also form the basic structure of ***flagella*** and ***cilia***. Flagella are whip-like tails found on motile (moving) cells such as bacteria, protozoans, and sperm cells in both plants and animals . Cilia look more like tiny hairs than like tails, thus, the name "cilia" which means "hairs". Cilia are found in great numbers on some cells, where they beat back and forth, moving in unison. Some cells, such as bacteria and protozoans use cilia to move, and other cells, such as those in your trachea, use cilia to sweep their surface clean. We even find ciliated cells in the fallopian tubes of females, sweeping egg cells along. For both flagella and cilia, tiny "motors" at their bases pull on the protein cables, causing them to move.

The medium-sized cables are called ***intermediate filaments***. They look a bit like a braided rope. There are many different types of intermediate filaments, the most well-known being ***keratin***. One type of keratin (***hard keratin***) is tough and relatively stretchy and is used to form hair and nails. (In animals, scales and horns are also made of hard keratin.) ***Soft keratin*** is found in skin cells and helps to make skin waterproof. Other types of intermediate filaments (not keratins) occur as part of the cytoskeleton and act as strengthening cables. Unlike microtubules, intermediate filaments can't help the cell move; they simply provide structure.

The smallest cables are called ***microfilaments***. They are made of only two strands, so they are super thin. The strands are made of a protein called ***actin***, which is found in great abundance in all cells, but especially in muscle cells where they interact with other proteins in such a way that your muscles contract. Microfilaments can't help the cell move (like microtubules can) but they are responsible for changing the shape of the cell. For example, when a cell reproduces by splitting in half, the microfilaments are what carry out the action of splitting.

Enzymes are proteins that act as "scissors" or "staplers." The things they join or separate are called ***substrates***. The scissor-like enzymes are the little robot molecules whose job it is to tear things apart. Our digestive processes rely heavily on these destructive enzymes which tear apart food molecules and reduce them to individual molecules that our bodies can then use. Other enzymes are designed for joining things together. We already met one of these when we talked about dehydration synthesis. Constructive ("stapler") enzymes are required for most cellular processes. And don't forget that they are specific to their jobs—an enzyme can only do ONE thing. An enzyme that can build a particular type of protein can't also build other proteins, and it certainly can't build lipids or sugars.

Often, an enzyme is described as something that ***speeds up reactions***. The reaction might, just maybe, take place given enough time, but the enzyme goes in and does the job quickly and efficiently. Enzymes, like all workers, work best in certain environmental conditions. Some people like to keep their office toasty warm, others like their rooms on the cool side. Some people like to have music playing while they work, others do not. Enzymes have environmental preferences, too. Some like it hot, some like it cold. Some like to be in an acidic environment; others like alkaline. And just like some people need help (secretaries, support staff), some enzymes are dependent on other molecules to help them do their job. These helper molecules are called ***coenzymes***. ("Co" means "with.") Usually the coenzymes fits into a special slot in the main enzyme, to help create the correct shape needed for the job.

Proteins can be used to make "vehicles" that can carry other molecules. We've already mentioned the ***motor proteins***. The correct name for this protein is ***kinesin***. ("Kine" is Greek for "motion," and also appears in the word "cinema.") They look like they have little legs and feet and they do something very similar to walking as they travel along the microtubule cables. (Note, however, that their "feet" are actually called "heads.") Their job is to carry loads, often heavy and large loads, from one place to another. We've talked about vesicles traveling around the cell or moving out to the membrane, but we've not said how. This is how. Motor proteins can also drag entire organelles across the cell. If the load is too large, several kinesins will join together and cooperate.

Kinesins (motor proteins) travel in one direction, usually starting from the center and going toward the outside. They know what direction to travel because microtubules are polar. Kinesins will go toward the positive end. A different type of motor protein is required to go the other way. These "reverse direction" motor proteins are called ***dyneins***. (Dyneins are also responsible for the motion of cilia.) Motor proteins that can go both ways do exist but are rare. When a motor protein reaches the end of the microtubule, it releases its cargo then gets off the microtubule. It jumps off and floats back to the starting point. Then it is ready to reattach to another microtubule, take on new cargo, and begin a new journey.

Some cells use proteins to manufacture transportation devices that can be likened to boats because they float along in the bloodstream. Why do we need boats in our blood? Blood is mostly water, which is polar. When a hydrophobic molecule needs to be transported via the blood, it will refuse to get in unless it is safely enclosed in a "vehicle" of some kind. Just think— if you are afraid of water but need to cross a river, would you swim or ride in a boat? Same concept applies to molecules. The most common protein boat you'll find in blood is called ***albumin***. (This word looks similar to albumen, which you find in egg whites. Notice that the egg word has an "e" instead of an "i.") Albumins account for half of the proteins found in blood. Albumins can carry free fatty acids, hormones, ions, calcium, broken pieces of hemoglobin that are in the midst of being recycled, and also some prescription drugs such as the blood thinner ***warafin*** (which we will meet again in a later lesson). Albumins do another job, besides transport things. Their very presence in the blood works to regulate osmosis as water diffuses in and out of the blood. Albumins help to maintain proper blood pressure.

The last major category is "tags." We've seen how sugars can also be used as tags, both inside the cell and at the surface. Protein tags are specifically used as "flags" to mark foreign invaders. These tags can be called ***gamma globulins***, ***immunoglobulins***, or ***antibodies***. All three words are correct and can be used interchangeably. They are Y-shaped, with the upper part designed to stick to the foreign invader, and the base part designed to stick to a cell membrane if need be. Some float around freely and others stick to the outside of a cell. Each Y has a unique shape and can stick to only one type of invader. Your body makes millions of differently shaped antibodies, hoping that a small percentage of them will actually be useful.

YOU WILL NEED THIS STRIP FOR LESSON 52. Don't cut it off right now-- wait until you get to lesson 52.

CUT OFF THIS BOTTOM SECTION ALONG DOTTED LINE

Here are patterns for two action potential sliders. You'll only need one, but the extra is provided in case of multiple students, or in case you make a mistake and need an extra. The blank rectangles fold around the axon (make sure they are loose enough to slide). The action potential rectangle is glued on top. (The video will show you how to assemble them.)

12: CARBOHYDRATES

Carbohydrates, as the name implies, are a mixture of carbon and water ("hydra"). This means that their chemical formula will include the elements carbon, hydrogen and oxygen. Just like proteins have a basic building block (amino acids), carbohydrates also have basic unit: monosaccharides. ***Monosaccharide*** is a fancy word for "single sugar." (Remember, "mono" means "one," and "sacchar" means "sugar.") However, they are usually called simple sugars instead of single sugars. The three simple sugars we will look at in this lesson are ***glucose, fructose and galactose***. All three have the same chemical formula: $C_6H_{12}O_6$. The only thing that is different is the arrangement of the atoms.

Glucose (from "gluco" or "glyco" both meaning "sugar") is the most abundant and most useful sugar molecule in your body. It's the one we'll see again and again in this course. Glucose is the molecule that is "burned" as fuel in the energy-producing processes inside your cells. Glucose also shows up as a structural element in glycoproteins and glycolipids and in these forms is often found attached to the outside of cells. Strings of glucose are used by cells almost like mailing labels, tagging proteins for delivery.

Fructose is found in fruits. It tastes much sweeter than glucose. Your liver has to work hard to break it down, though, and can only do so at a certain rate. High-fructose corn syrup, a sweetener used in candy and carbonated drinks, overloads the liver with too much fructose and can cause long-term health problems. The amount of fructose found in natural fruits is fine. It would be hard to overwork your liver by eating too many apples and bananas.

Galactose got its name from the Greek word "galaxias," meaning "milky one," referring to the Milky Way in the night sky. So the words "galaxy" and "galactose" are related. The first person in history to study galactose was Louis Pasteur in 1856. Galactose is most abundantly found in milk, where is it attached to a molecule of fructose. Like glucose, galactose can also be used by the body as a structural component. For example, you find galactose in the "tags" on the outsides of red blood cells, marking them as type A, B or O.

The arrangement of the atoms in a molecule is extremely important, as we saw in the case of amino acids where the mirror image molecule is useless (or harmful) to the body even though the atoms are identical. Sugars can also be right or left-handed, and though our bodies are made exclusively of left-handed aminos, they use right-handed sugars. Left-handed sugars can't be digested. The little enzyme robots that take apart right-handed sugars can't operate on left-handed ones. In the last years of the 20th century, food chemists discovered a way to convert galactose to its left-handed form, which they named ***tagatose***. The patent for making tagatose was passed around among several European food companies until someone found a way to make it inexpensively in great volumes. Tagatose began to be marketed in the USA in 2003. Brand names include Naturlose, PreSweet, and Tagatesse.

When you join two simple sugars together, using ***dehydration synthesis***, you get a ***disaccharide***. The most well-known disaccharide is ***sucrose***, or "table sugar." The enzyme that cuts the bond between the glucose and the fructose is called ***sucrase***. Notice how the sugar ends in "-ose" and the enzyme ends in "-ase." (***Sucralose*** is an adpated form of sucrose. Not only are the atoms rearranged, but three chlorine atoms are also added. Food chemists say that it tastes 600 times sweeter than sucrose. The brand name "Splenda" is sucralose. Though the FDA says that it is perfectly safe, YouTube is full of videos claiming otherwise.)

Another common disaccharide is ***lactose***. This is the sugar found in milk. We already learned that galactose is one of milk's simple sugars; the other is glucose. Lactose is a galactose bonded to a glucose. The enzyme that can tear apart this bond is called ***lactase***. Some people lose the ability to make this enzyme as they get older, and they become "lactose intolerant."

When you join many simple sugars together you get a ***polysaccharide***. Two types of polysaccharides that you are very familiar with are ***starch and cellulose***. A third, ***glycogen***, is less familiar because it is inside your body where you can't see it.

Starch is what we call a long string of glucose molecules. These strings can have several thousand glucose molecules in them. Starches are made by plants and are stored in seeds and roots. Food items high in starch include wheat, oats, rice, corn, beans, potatoes and carrots. Notice how the glucose molecules are arranged in a starch. The "flags" on the glucose molecules are all pointing the same direction. This configuration is easy for your digestive system to deal with because you have enzymes designed to tear apart those chemical bonds.

Cellulose is similar to starch, but has the glucose "flags" in alternating directions. This small difference in molecular structure makes a big difference in physical characteristics. Cellulose is made by plants to be used in their tough cell walls. It is fibrous and dense and is the stuff that leaves and stems are made of. Most animal bodies don't make the right enzymes for breaking down cellulose. So why can cows live on nothing but grass? They have a gut full of bacteria that digest cellulose. Cows (and all herbivores) rely on bacteria to digest their food for them. Without the bacteria, they would starve. In humans, most of the cellulose we eat (leaves, stems) passes through our system undigested. This is not really such a bad thing, though. We need "bulk" in our intestines to keep things moving along. We do have some bacteria in our gut, though, and they do munch on our spinach and broccoli a bit. Keeping the friendly, vegetarian bacteria happy helps to keep the population of bad bacteria low.

Glycogen is a type of polysaccharide made by our bodies as a way to store glucose. After we eat, the glucose level in our blood goes way up and if it stays high this causes major health problems. The hormone ***insulin*** is released by the pancreas and it signals the enzyme ***glycogen synthase*** to start collecting glucose molecules out of the blood and begin stringing them together. These strings then get stored mainly in the liver and in the muscles. When the level of blood glucose begins to fall too low, these strings come out of storage and the glucose molecules are clipped off and put back into the blood.

13: HOW PROTEINS ARE MADE (part 1: TRANSLATION)

We've been fairly thorough in our discussion of proteins so far. We've gone into detail about the atomic structure of amino acids, what R groups are made of, how polypeptides fold into helices and beta sheets, and how proteins fold into complex shapes. We skipped over one very important detail, however. The arrangement of the amino acids on the polypeptide chain is critically important. The order in which the amino acids occur will determine every quality that protein will have. If even one amino acid were to be added or deleted, it might cause the protein to be useless or even hazardous. The sequence of the amino acids is vitally important. So how do the amino acids get lined up in the correct order?

We are going to present the answer by working backwards. First, we'll see a polypeptide being assembled by a tiny "factory" called a ribosome. Then we'll find out where the ribosome's instructions came from. We'll eventually end up at the source of all cellular information: the DNA In the nucleus.

Ribosomes are the "factories" that make polypeptides. Though they might look like it, they are NOT protein gadgets. Well, they do have a little bit of protein in them, but not enough to call them protein gadgets. Ribosomes are mostly made of ***RNA,*** or ***ribonucleic acid***. (RNA is sort of like one half of DNA. We'll study RNA in more depth in the next lesson.) The RNA strands are twisted into a complex shape (similar to a protein's tertiary shape). Ribosomes are made of two sections: a ***large subunit*** and a ***small subunit***. These subunits float around separately if they are not actively engaged in making a polypeptide.

Ribosomes "read" a strip of coded information that is also made of RNA. This strip is called ***messenger RNA*** (***mRNA***). The mRNA tells the sequence of amino acids for a particular polypeptide. There are "letters" in this code that correspond to the different types of amino acids. (We will see this in the next lesson.) The mRNA "tape" goes in one side, is read in the middle, and comes out the other side. When it is finished, the mRNA can be used again to make another identical polypeptide. The ends of the tape are different, and biochemists keept track of which end is which by using the numbers 5 and 3. They use"prime" marks that look like apostrophes after the numbers, so that the leading end, the one that is read first, is called 5' (five prime), and the end that gets read last is 3' (three prime).

Amino acids are brought to the ribosome by little "taxis" that are also made of RNA. The taxis are called ***transfer RNA*** (***tRNA***). It is fairly easy to remember what tRNA does, because tRNA actually looks a bit like the letter T, which is the first letter in the words "taxi" and "transfer." The tRNAs carry amino acids very much like taxis carry passengers. On the other end of the tRNA (the end that does not attach to an amino acid) is a special site called the ***anticodon***. Each anticodon will match a corresponding site on the mRNA called a ***codon***. (We'll learn about codons in the next lesson. A codon is a secret code for an amino acid.) As the mRNA slides through the ribosome, the codons on the mRNA will determine which aminos will be brought by the tRNAs.

The ribosomes have "parking places" for the tRNA taxis. The first two are called A and P, and the last one is E for Exit. The mRNA coded tape slides along underneath these sites, exposing the codes, one by one, under the A site. The mRNA waits until a matching tRNA comes along and parks in the A site. That tRNA then moves to the P site, allowing a new tRNA to occupy the A site. As a tRNA moves from the A to the P site, it transfers its amino acid to the bottom of the growing peptide chain. After successfully attaching its amino to the chain, it sits briefly on the Exit site, then leaves. This continues until the end of the mRNA tape is reached. When finished, all the parts separate.

The new polypeptide then folds up, often with the help of chaperone proteins. Some chaperones are designed to "spell check" or "shape check" and if the protein does not pass inspection, it will be sent to a shredding machine and the amino acids will be recycled.

It's interesting to think about the fact that the chaperone proteins are made of the same stuff they are folding (protein) and were therefore also made by ribosomes. So who folded the chaperones—other chaperones? And who folded those other chaperons? And then who folded the chaperones that folded the chaperones? We see a cycle that must continue, unbroken, with no room for mutations or gradual change.

All cells have ribosomes, even bacteria cells. The antibiotic called ***erythromycin*** kills bacteria by blocking the active sites of their ribosomes. The erythromycin molecules stick in the P site so that the tRNAs can't move out of the A site. This means that the bacteria will not be able to manufacture the proteins that it needs to survive. Thus, the bacteria dies.

14: HOW PROTEINS ARE MADE (part 2: RNA)

Now we are going to find out exactly what RNA is. RNA is an abbreviation for **r**ibo**n**ucleic **a**cid. "Ribo" is short for "ribose." ***Ribose*** is classified as a simple sugar, but has only 5 carbon atoms, so its formula is $C_5H_{10}O_5$. The other simple sugars we learned about all had 6 carbons ($C_6H_{12}O_6$). The basic structure of ribose is a pentagon, so it looks similar to fructose. The "nucleic" part of the name refers to the nucleus, which is mainly where RNA is made. (DNA is also a nucleic acid.) The "acid" part of the name refers to the phosphate group that is attached to the molecule. (You'll remember that the phosphate ion used to be H_3PO_4, phosphoric acid. The H's went running off as protons, leaving their electrons behind.)

When you combine a ribose sugar, a phosphate ion, and something called a ***base*** (more on this in a minute) you get a molecule called a ***nucleotide***. Nucleotides are the individual units that string together to make RNA and DNA.

The phosphate ion functions sort of like glue, or maybe a paper clip or a staple, and holds the ribose sugars together. The pattern is: ribose, phosphate, ribose, phosphate, ribose, phosphate, etc. Since ribose is a simple sugar, this string is often called the "sugar-phosphate backbone" of the molecule.

The ribose's job is to hold on to a molecule called a ***base***. There are five different types of bases, three of which are common to both RNA and DNA, and two that are found in just one or the other. The common bases are: ***adenine, cytosine and guanine***. ***Thymine*** is found only in DNA and ***uracil*** is found only in RNA. Thymine and uracil are very similar, with thymine being basically a uracil with a CH_3 added to it. CH_3 has a special name: the **methyl** group. (Remember, "meth" means "one" when you count carbons.) This methyl group must be added when the base is used in DNA in order to make DNA less likely to tear apart at that point. In RNA, it is better not to have that methyl group there.

The bases contain several nitrogen atoms, so sometimes they are called ***nitrogenous*** *(nie-TRODGE-en-us)* bases, meaning "nitrogen-containing." The bases pair up with each other in a predictable way: A with T (or U), and C with G. In DNA they are always paired up in this way. In RNA they only pair up at certain times, such as when DNA is being copied or when tRNAs are matching up with mRNA.

RNA is a long chain of nucleotides. The order of the nucleotides is critically important, because they code for amino acids. Each set of three nucleotides forms a trio called a ***codon***. It's easy to remember what a codon does because the word "codon" looks like the word "code."

A codon codes for an amino acid. The bases A, C, G and U provide 64 possible codons, which is more than enough since there are only 20 amino acids. Some amino acids have more than one code. Lysine has two codes: AAA and AAG. Valine, one of the hydrophobic aminos, has four codes: GUU, GUC, GUA, and GUG.

Some codons don't code for any amino acid. For example, UAG, UGA and UAA mean "stop." To signal "start" the codon AUG is used. This codon codes for the amino acid ***methionine***. Therefore, methionine is always the first amino acid in every polypeptide.

Amino Acids			Codons
Alanine	Ala	A	GCA GCC GCG GCU
Cysteine	Cys	C	UGC UGU
Aspartic acid	Asp	D	GAC GAU
Glutamic acid	Glu	E	GAA GAG
Phenylalanine	Phe	F	UUC UUU
Glycine	Gly	G	GGA GGC GGG GGU
Histidine	His	H	CAC CAU
Isoleucine	Ile	I	AUA AUC AUU
Lysine	Lys	K	AAA AAG
Leucine	Leu	L	UUA UUG CUA CUC CUG CUU
Methionine	Met	M	AUG
Asparagine	Asn	N	AAC AAU
Proline	Pro	P	CCA CCC CCG CCU
Glutamine	Gln	Q	CAA CAG
Arginine	Arg	R	AGA AGG CGA CGC CGG CGU
Serine	Ser	S	AGC AGU UCA UCC UCG UCU
Threonine	Thr	T	ACA ACC ACG ACU
Valine	Val	V	GUA GUC GUG GUU
Tryptophan	Trp	W	UGG
Tyrosine	Tyr	Y	UAC UAU

Transfer RNA (tRNA) needs to be mentioned again at this point. One end of tRNA holds the amino acids. The other end has an ***anticodon***. "Anti" can mean "against" or "opposite." In this case, "opposite" is a good translation because the anticodon contains the opposite match for each of mRNA's codons. The bases come in pairs. C and G are matches, and A matches with U in RNA. The anticodon for AAA would be UUU; for AUG it would be UAC; for GCA it would be CGU. So as the mRNA slides through the ribosome, a codon is exposed right under that A parking space. When a codon is right under the A site, that is when a tRNA with the correct anticodon will come over and match up. If the mRNA codon AUG is exposed, then a tRNA that has the anticodon UAC will come over and match up. The UAC tRNA will be carrying the amino acid methionine.

RNA is found in several places in a cell. We've seen most of these already. Messenger RNA (mRNA) is used by ribosomes to make proteins. Ribosomal RNA (rRNA) is the RNA that ribosomes are made of. Transfer RNA (tRNA) is used as a taxi for amino acids, bringing them to the ribosomes to be hooked together to form polypeptides. MicroRNA (miRNA) comes in very short pieces and is used to control which parts of DNA get used. miRNA can "shut down" the production of a protein by binding to the area of DNA that has the instructions for how to make it. This is part of epigenetics and we'll learn more about it in a future lesson.

15: HOW PROTEINS ARE MADE (part 3: Transcription)

We have approached this topic in the opposite direction from most book and video presentations. We looked at proteins first, then began working backwards, step by step, to see where they came from. You'll need to follow up this lesson with some video animations showing the process in the "forward" direction. Animations usually start in the nucleus with DNA, then show mRNA being made, then show translation in a ribosome. However, it's good to look at this process from many directions, so that your learning is not a matter of mere memorization but of understanding.

Messenger RNA is a copy of one small section of DNA. DNA is often described as the "library" of the cell, containing all the information a cell will ever need. In fact, it contains a lot of information the cell will never need. Every cell in the body has a complete set of DNA. Therefore, a skin cell has information about how to be a lung cell or a liver cell, but this extra information is permanently locked up, never to be used. The DNA library is so vital to the health of the cell that it never leaves the safety of the nucleus. The membrane around the nucleus is twice as thick as the outer membrane of the cell. This ***nuclear envelope*** is made of two phospholipid bilayers. The envelope has holes in it, to let things come in and out. These holes are specialized ***pores*** designed to regulate the traffic of molecules in and out of the nucleus, including mRNA.

If you look at a cell under a microscopic, and the cell has been stained so that the nucleus shows up very well, you will see that there is a dark spot inside the nucleus. This is called the ***nucleolus***. This is a place where the DNA is particularly dense. In this area you will also find lots of RNA, because the nucleolus is where ribosomes are made. There are also some proteins being manufactured in this area, mostly associated with the ribosomes. You'd have a lot of loose nucleotides floating around, too. We'll soon see why.

DNA is similar to RNA, but there are four main differences:

1) DNA is a double helix, having two strands. RNA is a single helix, having one strand.
2) DNA has **T**hymine; RNA has **U**racil.
3) DNA has ***deoxyribose***; RNA has ***ribose***. ("Deoxy" means "missing an oxygen.")
4) DNA is found only in the nucleus; RNA is found in all parts of cell.

Since DNA cannot leave the nucleus, whenever a piece of information is needed outside the nucleus, a messenger must be sent out. Messenger RNA is an exact copy of a small section of DNA. (mRNA can be thousands of nucleotides long, but since DNA has billions of nucleotides, a few thousand seems like a small number.) You might be able to guess that a special gadget is required to copy this information from the DNA. This gadget is called ***RNA polymerase***. Polymerase can be broken into "poly," which means "many," and "mer," which means "individual unit," and "ase," which means "enzyme." All molecules ending in "ase" are protein gadgets. This one acts like both a scissor (or zipper) and a stapler. It makes a "polymer" from nucleotides.

RNA polymerase snaps on to a section of DNA, reading some special codes (written with A, T, C and G) that allow it to identify the correct section to copy. Then the DNA goes into the polymerase machine where it meets a splitter that separates the two strands. DNA is easy to split because the two helices are held together only by hydrogen bonding, which is fairly weak. In our picture, the top strand is the one that is being copied. If the RNA was copied directly from the correct strand, it would then be a reverse copy, with A's instead of T's and C's instead of G's. This would mess up the protein manufacturing. So to get a correct copy that makes sense to the ribosome, the opposite strand of DNA must be copied. Sometimes this strand is called the ***antisense*** (or nonsense) strand. It is the reverse of the strand you want to copy. When you copy it with RNA, you get a correct, "sense" strand. (Don't forget, when the mRNA copies it, uracil is used to replace thymine. Uracil is thymine without a CH_3 group.)

Nucleotides go streaming into the polymerase through a special funnel-like opening. When they meet the antisense strand of DNA, they begin to match themselves up. A strand of RNA begins to form. As it gets longer, it exits the polymerase. This new strand of RNA is not ready to be used yet. It is called ***pre-mRNA*** because it must be processed before it can leave the nucleus.

The first end to come out is called the 5' ("five prime") end. Scientists have to keep track of the ends of RNA and DNA because they are not the same. There is a front and back, so to speak. The front end is called 5' and the back end is called 3'. As soon as the 5' end comes out, a special cap is put onto it by a little enzyme robot designed to do that job. The cap ends with a G and a ***methyl tag***, CH_3. (Remember, "meth" means "one" when you count carbons. "Meth-, eth-, prop-, but-" means "1, 2, 3, 4.") You will see methyl tags again soon. They keep sections of DNA zipped shut, and are therefore a key to cell differentiation and epigenetics. The lagging end that comes out last (the 3' end) gets a tail put onto it. The tail is called the ***poly(A) tail*** because it is made of a long string of A's. AAAAAAAA... etc.

There is one last step in the preparation of mRNA. There are sections that must be snipped out. The information does not come in one long piece, but in little pieces with "filler" sections in between. The necessary pieces are called ***exons*** and the extra filler pieces are called ***introns***. An RNA gadget called a ***spliceosome*** comes along and pinches the introns into a loop, then snips them off. The snipped ends are glued back together, so that, when finished, you have a long line of exons with no introns left. (Don't think of the introns as "junk." They play a necessary role. If you got rid of them, DNA would get really messed up.) After the introns are gone and the cap and tail are stuck on, the mRNA leaves the nucleus and is ready to meet a ribosome.

16: PROKARYOTES (part 1)

We've got enough cell parts now to make a cell—but not a human cell. The only type of cell we can draw is a bacterium; but that fits in well with our study of the human body because humans are full of bacteria. For every one human cell in your body, there are ten bacterial cells. Estimates on the number of cells in a human body range from 15 trillion to 70 trillion. Many sources say about 37 trillion. Using the 37 trillion figure, that means you have 370 trillion bacterial cells inside of you, or on your skin. As long as the many species stay in balance, you remain healthy.

Bacteria are classified as ***prokaryotes.*** ("Karyo" means "nut or kernel," referring to the nucleus.) Prokaryotes ***do not have a true nucleus***. They have DNA, but they do not have a nuclear envelope around it. Another related group of organisms, the ***archaea***, are also classified as prokaryotes. Archaea used to be classified as bacteria. When scientists began examining bacterial DNA, they found that some types of bacteria had their DNA wound on little spools and some did not. The ones with the little spools were moved to a new group and given a new name: "archaea," meaning "old." You have both kinds of prokaryotes in your intestines. Some types of archaea produce methane gas, a partial explanation of where all that air and gas in your intestines comes from.

There are many types of bacteria. We will start by drawing something that represents what all bacteria have in common. It's labeled as a "basic" bacteria. This is a no-frills model, without any of the special features that many bacteria have. We will look at some of the special features after we see what they all have in common.

Bacteria are cells, and therefore must have a plasma membrane. However, unlike our cells, bacterial cells also have a cell wall outside of the membrane. The cell wall is made of a substance called ***peptidoglycan***. "Peptid" means "protein," and "glyc" means "sugar." It was mentioned in a previous lesson that sugars can be used as structural elements, not just as food. The cell wall is made of long strings of sugar molecules held together by protein cables. The cables that hang down are made of just four amino acids: alanine, glutamate, lysine and another alanine. We've already met glutamate and lysine.

Alanine has been called the most boring amino acid because it doesn't have a strong "personality." Its R group is the methyl group, CH_3. (Yes, the methyl group is showing up again already!) Although CH_3 is non-polar and therefore technically hydrophobic, it's small enough in comparison to the whole alanine molecule that it does not affect the amino's "personality" very much. Alanine does not act either hydrophobic or hydrophilic. It also does not carry an electrical charge It basically minds its own business and gets along well with everyone. Perhaps you know someone with alanine's personality? In some situations that's exactly what you want. Alanine shows up at some point in most proteins. About 8% of the amino acids in your body are alanine.

In this situation, alanine's job is to hang on to a sugar molecule or a glycine cable. The cables that run horizontally, parallel to the plasma membrane, are made of five gylcine amino acids. (Glycine is the smallest amino, with only an H as its R group.) There are also long molecules that act like molecular ropes, attaching the sugar layers from top to bottom and anchoring it to the plasma membrane. These long molecules have phosphate "hooks" at intervals. Phosphates, [PO_4's] are good at hanging onto sugar molecules, as we can see in DNA and RNA.

Bacterial cells have little enzyme robots that do jobs, just like our cells do. One particular enzyme attaches the glycine cables to the alanine cables. This enzyme can be prevented from doing its job by ***penicillin*** and other "cillin" antibiotics. The penicillin molecule interferes with the active site on the enzyme so it can't do its job. Without those cross-linking glycine cables, the bacteria's cell wall falls apart and the cell dies.

Bacteria do not have a true nucleus, but they do have DNA. Their DNA is circular, but the circle is so large that it folds and crumples into a lump. This central clump of DNA is called its ***genomic DNA***. A genome is a complete set of DNA— all the instructions the cell will ever need. We need to use the word "genomic" in order to distinguish this DNA from other DNA in the cell. Bacteria also have small circles of DNA called ***plasmids***. These are just bits of "bonus" information that might help the cell survive in certain situations. For example, resistance to antibiotics is often found as DNA code on plasmids. Bacteria can share this "bonus" information with other cells of it species by a process called ***conjugation***. In this process, a plasmid is transferred from one bacteria to another via a small tunnel that grows between the two cells. The donor cell makes a copy of the plasmid DNA and sends this strip through the tunnel to the recipient cell. The strip of DNA can then form a circle, and the recipient cell now has a new plasmid.

Bacteria must have ***ribosomes***. They've got enzymes, such as that enzyme that attaches the glycine cables, and enzymes (as well as all other protein gadgets) are made by ribosomes. They also have a ***cytoskeleton***, though it is not exactly the same as the cytoskeleton of an animal cell. Textbooks used to say that bacteria did not have a cytoskeleton, but this has been corrected as more research has revealed that they do indeed have their own bacterial version of a cytoskeleton. Some bacteria have gas-filled ***vacuoles*** that help them float or move. The watery fluid that fills the cell is called ***cytosol***. Cytosol is made of water, minerals, salts, sugars and enzymes. Sometimes there are particles such as oil droplets or mineral crystals floating around in the cytosol. These particles are called ***inclusions***. The word ***cytoplasm*** can be easily confused with the word cytosol. The cytoplasm is the cytosol plus the organelles floating in it, such as the ribosomes. In a human cell, the cytoplasm is basically everything outside of the nucleus.

The word ***morphology*** means "shape." Or, more correctly, "study of shape," because "-ology" means "study of." Fortunately, bacterial shapes are easy to draw.

- The ***cocci*** *(cock-eye, or cocks-eye)* are little spheres.
- ***Diplococci*** are two spheres stuck together.
- The ***bacilli*** *(ba-sill-eye)* look like little rods or sticks, though some are stubby and rounded on the ends.
- ***Vibrio*** are C-shaped. (The most well-known vibrio is ***cholera***, an intestinal disease that often strikes after natural disasters like earthquakes, as drinking water is contaminated.)
- ***Streptococcus*** looks like a long chain. The illness we call strep throat is caused by one species of streptococcus, but there are many other species, too.
- ***Staphylococcus*** looks like a bunch of grapes. There are many species of staphylococci, but the one that gets most of the public's attention is *Staphylocuccus aureus*, the one that causes "staph" infections on the skin. (S. aureus is part of our natural bacterial population and does not cause harm as long as it is kept in check by other species of bacteria.)
- The ***spirilli*** *(spir-ill-eye)* are spiral-shaped and often have a flagella at each end of their bodies. They can look squiggly as they move, but their bodies are not actually flexible. Spirilli are less common that the cocci and bacilli, but can be found in watery places like sewers.
- Unlike the spirilli, the ***spirochetes*** *(spi-ro-keets)* are flexible and can really bend around as they move. This is mainly due to their inner flagellum. They can spiral their way right through soft tissue (such as the connective tissue in our joints). The most famous spiriochete is the one that causes Lyme Disease.

Some bacteria have ***fimbriae*** *(fim-bree-eye)*. These hair-like structures help the bacteria to hold on to surfaces, including our cells. Some bacteria have additional hair-like things called ***pili*** *(pie-lie)*. These have several functions. They help the bacteria stick to surfaces. They can help the bacteria by acting like grappling hooks. The bacteria can toss out a few pili and the ends will stick to the surface out in front of the bacteria; then it retracts the pili so that its cell body is moved forward. It then repeats the process, throwing the pili out again and then pulling its body to close the gap. A special pilus can also be used for conjugation. This type is often called a conjugation pilus or a sex pilus. The pilus is extended in order to grab a passing bacteria. The trapped bacteria is then "reeled in" until it is almost touching. The pilus then acts as a transfer tube, allowing the plasmid DNA to be passed from donor to recipient, as we discussed on the previous page.

NOTE: Scientists are not in agreement as to whether fimbriae and pili are the same thing. Some insist that they are different and give good reasons for thinking so. Other scientists don't see any difference and use the words interchangeably. This is good to know as you read books and websites on this topic. Be aware that the word "pili" might be used to describe what we have defined as fimbriae.

Bacteria are not part of human anatomy, but they are part of our physiology. Bacteria form a vital portion of our internal ecosystem and they affect our digestion and nutrition, our immune responses, and sometimes even our mental health. In the past, doctors and medical researchers did not realize the importance of bacteria in our bodies. Now they are beginning to understand how critically important it is, and some researchers have begun to catalog the ***human microbiome***, a list of all the microorganisms (including fungi, protozoans and viruses, too) normally found in and on humans. Medical care of the 21st century will increasingly be focused on maintaining a healthy microbiome.

17: PROKARYOTES (part 2)

The word ***motility*** means movement. Bacteria motility is most commonly the result of one or more flagella, but there are also a few other ways they can move, such as making internal air bubbles that float them to the surface if they are in water. Some bacteria, that don't live in water, can glide using a slippery slime make of sugars (polysaccharides). Scientists speculate that the slime is extruded out the back and acts as a very slow jet engine causing an equal and opposite reaction that propels the bacteria forward, albeit extremely slowly.

Most often, bacteria rely on flagella for movement. Flagella are made of microtubules. At the base, where it attaches to the cell wall, there is a tiny protein gadget motor that spins the flagella around at speeds up to 200 rotations per second. Flagella are similar to cilia, a feature often found on unicellular protozoans but also found on some human cells. Cilia beat back and forth, creating a coordinated waving motion. Flagella beat in circles, acting more like an outboard motor.

Some bacteria have only one flagellum. The cell can still move backward and forward, however, because the direction of the flagellum's rotation can be reversed. Other bacteria have a clump of flagella instead of just one. Some have a flagella at each end. Perhaps the strangest arrangement is the all-over look, where there are so many flagella that the bacteria starts to look hairy. Bacteria with multiple flagella can spread them out and vibrate them in such a way that they do a "tumbling" motion, which helps them to turn and go in a different direction. Spirochetes have an inner flagellum, set between an inner and outer membrane. This geometry allows the spirochete to flex and twist, allowing it to "swim" through soft body tissue such as skin and cartilage. Whatever type of motility a bacteria has, it is used to go toward sources of food and away from things that would harm them.

Bacteria can be classified several ways. One is by shape, as we have seen. This is important for some purposes, but not for applying antibiotic medicines. When you need to get rid of harmful bacteria in your body, you must know which medicines will be most effective. ***Pathologists*** (doctors who study diseases) want to know about the bacteria's biochemistry. The most important testing procedure is called the ***Gram stain***. The results of this test will give you information about a bacteria's outer coating. Some bacteria have a thick layer of peptidoglycan, as we saw in the previous drawing. These bacteria will turn purple when the Gram stain method is applied. The peptidoglycan layer will soak up a lot of purple stain. Bacteria that turn purple with Gram staining are called ***Gram positive***.

Other bacteria have a much thinner peptidoglycan layer and have an additional outer membrane. These bacteria don't have enough peptidoglycan to turn purple, but will hold a reddish-pink stain. Bacteria that turn pink with Gram staining are called Gram negative. The names "Gram positive" and "Gram negative" don't mean "good" and "bad." There are good and bad bacteria in both categories. And from the bacteria's point of view, they are just trying to survive, which to them is always good.

Gram negative bacteria also usually have an additional feature that causes problems for their hosts. They have toxic sugars sticking up from their outer membrane. These toxins can be a problem even if the bacteria has died. In fact, if you kill off these bacteria too rapidly your body can be overwhelmed with trying to get rid of all the toxins. Your liver can only process toxins at a certain rate. The sick feeling (fever, aches, nausea) you get from an overload of these toxins is called the ***Herxheimer reaction***.

Some bacteria have yet another outer layer called a ***capsule***. The capsule is made of sugars (polysaccharides) and is very soft and sticky; it is often called the ***slime layer***. Having a slime layer is a big advantage for a bacteria. It prevents the cell from drying out, it helps it to stick to surfaces, and it makes it much harder for our immune cells to eat and digest it.

The archaea used to be classified as bacteria. Basically they are bacteria. They look and act like bacteria. The only reason they now get their own kingdom is because of some minor differences. Regular bacteria are now called ***eubacteria***, *(yu-bacteria)* meaning "true" bacteria. Here are some differences between archaea and eubacteria:

1) The protein structure of archaea RNA polymerase (the thing that makes mRNA) is slightly different from eubacteria.

2) The archaea ribosome has a slightly different structure and can't read eubacteria DNA code that tells where to start.

3) The phospholipids in the archaea plasma membrane have their fatty acids attached differently. This difference makes it possible to have a molecule with heads on both ends, so that there is no need for two molecules to make a bilayer. (Imagine joining the tails of all those phospholipids in our bilayer pictures.) This makes a very tough plasma membrane—one that can survive extreme conditions such as boiling hot or extremely salty.

4) Archaea cell walls are not made of peptidoglycan. Their walls are made of sugars, proteins and various combinations of those, sometimes looking very much like peptidoglycan, but not close enough for chemists to use the term "peptidoglycan."

5) Archaea DNA is wound around little spools made of protein balls called ***histones***. Plant and animal cells also have their DNA wound on histone spools. Eubacteria do not have histones.

For better or for worse, depending upon the situation, archaea will react differently to antibiotics than eubacteria will. We've seen how two types of antibiotics work: erythromycin and penicillin. Erythromycin attacks bacterial ribosomes at their P site, and penicillin attacks peptidoglycan cell walls. Archaea are not susceptible to either of these medicines because their ribosomes and cell walls are different from those of eubacteria.

18: ATP and GLYCOLYSIS

Living things need energy. In this lesson we will begin to learn about cellular energy and see the first step in breaking down glucose to release its energy. But first, let's take a look at something that is not alive and therefore does not need energy. Viruses are often confused with bacteria. We use the word "germ" to describe anything that makes us sick. Many people are not aware of how different bacteria and viruses are.

A ***virus*** is basically nothing more than a piece of DNA or RNA wrapped in a protein shell. Sometimes there is an extra layer made of phospholipid membrane. Protein hooks are often attached to this lipid layer. The hooks have a particular shape that will match receptors on the outside of the cells they attack. This means that a virus that invades skin cells probably won't be able to get into stomach cells. Viral diseases of fish or reptiles are not a threat to humans because the viral protein hooks only match the receptors on fish cells or reptile cells. Viruses called bacteriophages can only attack bacteria cells. (It's funny to think that bacteria can come down with viruses!)

A virus does not have ribosomes so it cannot make proteins. In order to manufacture its protein coat and its protein hooks, it needs to borrow the ribosomes of a living cell. The cell's ribosomes follow the instructions written in the viral DNA or RNA and they manufacture viral proteins. These parts assemble into thousands of new viruses and they fill the cell until it bursts. Then each new virus goes and attacks another cell.

Viruses are not considered to be living organisms because they do not have the basic characteristics of all living things. Living things can grow, move, reproduce, respond to their environment, and use energy. Cellular energy will be the theme of the rest of this lesson.

ATP is a tiny molecule that can store energy. ***ATP*** stands for ***adenosine triphosphate***. Adenosine is an adenine connected to a ribose. If you add a phosphate to adenosine you get adenosine monophosphate, ***AMP***. (Notice how similar this is to the nucleotide that includes adenine.) If you add another phosphate you get adenosine diphosphate, ***ADP***. A third phosphate brings you to adenosine triphosphate. This third phosphate is what stores and releases energy. The phosphates carry a negative charge so they don't want to be next to each other. They act like a compressed spring, storing energy. When the third phosphate pops off, energy is released and you are left with ADP plus a single phosphate. That phosphate can be put back on so that ADP gets recharged and goes back to being ATP. Recharging ATP requires energy, just like recharging a battery does. In lesson 20 we will meet an enzyme gadget that is very efficient at recharging ATPs.

Glucose is the primary molecule from which our bodies derive energy. If all the energy in glucose were released at once, it would be too much for our cells to handle. They'd explode. Glucose must be torn apart very slowly, with a series of very small steps. The process of ***glycolysis*** is the first part of releasing the energy locked up in the chemical bonds of the molecule. "Glyco" means "glucose," and "lysis" means "break apart." Glycolysis will break glucose in half.

Glycolysis happens in the cytosol (cytoplasm) of the cell. No special organelle is needed. This is not true of many cell processes. Many of them only happen inside a particular location. Glycolysis happens anywhere and everywhere outside the nucleus.

There are ten steps in glycolysis. The first and third steps require a phosphate. The phosphates are used as part of the process of snipping the hexagon and turning it into a line. Then this chain of 6 carbons (with all their associated oxygens and hydrogens) is cut in half. In steps 6-10, 4 ATPs are recharged as well as 2 NADH molecules.

NADH is a "taxi" for high-energy electrons. It carries 2 electrons (and 1 proton) from glycolysis over to an assembly line that includes 3 proton pumps. The electrons will power the pumps and push protons across a membrane. (We'll look at this in lesson 20.) When the NADH taxi is empty it is called NAD^+. When it is carrying 2 electrons and 1 proton, it is called NADH. Like ATP, NADH can be used over and over again.

At the end of step 5, we have two 3-carbon molecules. Steps 6- 10 make small alterations to the molecules so that by the end of step 10 we have two identical 3-carbon molecules of ***pyruvate***. The pyruvates will go on to the next step where they'll get one of their carbons snipped off, leaving them as 2-carbon molecules. Then the 2-carbon molecules will begin a complicated process called the Krebs Cycle (or Citric Acid Cycle).

As we said, in steps 6-10 we have 4 ATPs being recharged, as well as 2 NADHs. Since we used 2 ATPs in the beginning of the process, our net gain of ATPs is 2. The most important thing that most books/teachers/ texts/tests want you to know about glycolysis is that it produces 2 ATPs and 2 NADHs. (Often, they only ask about ATPs.)

19: SPERM and MITOCHONDRIA

Male ***gametes*** (reproductive cells) are called ***sperm***. It's not just animals that make sperm — plants make them as well. Mosses and ferns make sperm that swim. Most plants, however, make non-motile sperm that must be carried by pollen grains. In animals, sperm are made continually and only have a life span of a few days. Mature male mammals make tens of millions of sperm every day (about 1000 per second). The male reproductive tract also makes fluid for the sperm to swim in, but that is outside the scope of this lesson.

A sperm has three body sections: a head, a midpiece and a tail called a ***flagellum***. The head is about 5 ***microns*** long, making sperm the smallest human cells. (Compare this to a coccus bacteria which is 1 micron in diameter. A micron (or micrometer) is 1/1000 of a millimeter.) The midpiece contains the ***centrioles*** and the ***mitochondria***, which are discussed below. The flagellum is about 50 microns long and has a central core called the ***axoneme***, which is made of microtubules. ATP energy is used at the base of the flagellum to make it go back and forth. The entire sperm, including the flagellum, is surrounded by plasma membrane.

The head contains the ***acrosome***, which has enzymes that will dissolve the outer portion of the egg, and a nucleus containing tightly packed DNA. The DNA contains 23 ***chromosomes,*** very long pieces of DNA. This is half the number of chromosomes required for a human cell (46), so gametes are called ***haploid*** cells. The human genome contains about 3 billion base pairs ("rungs" on the DNA "ladder.") Chromosomes are often shown looking like little sticks. That's not what we find here. Inside this nucleus, the DNA strands have been specially packaged for traveling.

A swimming sperm has one goal: get to the egg first, and enter it. Each sperm has this goal, but there are usually about 100 million of them competing against each other, so the odds of winning are pretty small. A sperm with the slightest defect won't even get close to the egg. Some sperm have unfortunate mutations such as two tails, or a head that is too large. The sperm have to be so perfect that even small disadvantages will cause them to be losers in the race. The DNA packed into the nucleus is bundled very tightly using special protein spools called ***protamines***. The protamines allow the DNA strands to get closer than they would ordinarily, and they also cause it to bundle into donut shapes called toroids, which are then stacked right next to each other. If the protamines aren't perfect, the DNA will be packed too loosely and this will cause the sperm to swim more slowly, losing the race. If you use Google image search with key words "sperm protamines" you will see many illustrations showing the spools and the toroids. (Regular DNA is wound on spools called histones. You might see these, as well.)

Since the sperm has a very particular purpose and a very short life span (less than a week), many organelles are not needed. For example, it is not going to need any ribosomes since it won't be making any proteins. The only organelle the sperm really needs are the mitochondria, which generate lots of ATP energy that can be used for making the flagellum whip back and forth. However, the sperm does have one other organelle: a pair of ***centrioles***.

Centrioles do two things: 1) they form flagella (and cilia), and 2) they act as a focal point for the creation of a spindle of microtubles used in cell division. In other words, centrioles allow a cell to divide. It's good that the sperm have these because, as far as we know, egg cells don't. Researchers think that it is likely that the centrioles in every cell of our bodies can be traced back to those original centrioles that came from the sperm of our fathers. Centrioles make duplicates of themselves before each cell division. By the time a baby is born, those original centrioles from the sperm will have made copies of themselves trillions of times! Centrioles are easy to overlook in sperm anatomy and are often not even shown in diagrams, yet they are essential to the creation of a new life.

The mitochondria are often called the "powerhouses" of the cell. It is inside these organelles that those pyruvate molecules are completely "burned" and ATP energy is generated. Sperm have about 100 mitochondria, but they are fused together (unlike those found in regular cells) and then shaped into a coil. We will consider the structure of a single mitochondrion.

The mitochondrion has an oddly shaped "bag" in its interior. The bag has lots of folds and creases (called ***cristae***) which allow a lot of surface area to be packed into a small space. The "fabric" that this bag is made of is something you are very familiar with: plasma membrane (phospholipid bilayer). The fluid inside this bag is called the ***matrix***. The word matrix is very common in biology and means "a central area." The matrix is similar to the fluid of the cytoplasm, with lots of tiny molecules floating in it, such as oxygen, carbon dioxide, minerals, phosphates, pyruvates, tRNAs, nucleotides, and many enzymes that do various jobs. Also inside the matrix are rings of DNA called ***mitochondrial DNA (mtDNA)***. These rings have 37 genes that code for proteins that the mitochondrion will need frequently. (A ***gene*** is a strip [or compilation of several strips] of DNA that codes for one protein.) The mtDNA also has codes for tRNAs and ribosome parts. The mitochondrion still needs to access the DNA in the nucleus, though, because the mtDNA does not hold all the necessary information, only some of it. Why these particular genes (the ones on the mtDNA) are found inside the mitochondria is still a mystery. The mtDNA is inherited predominantly from the mother, which makes it useful for tracing family ancestries. MtDNA mutates faster than the ***genomic DNA*** (in the nucleus), making it ideal for studying genetic changes in the human genome over time.

Pyruvates are taken into the matrix, where they go through the ***Krebs Cycle*** (named after its discoverer, Hans Krebs), also known as the ***Citric Acid Cycle***. (You can use either name; it's your choice. I chose "Krebs" because it is easier to remember.) The Krebs Cycle recharges electron carriers that will be used in the ***Electron Transport Chain***. The ETC is made of three pumps, several shuttles, and a motor, and is found embedded in the plasma membrane of the matrix.

20: The KREBS CYCLE and the ELECTRON TRANSPORT CHAIN

Pyruvate molecules are transported into the mitochondrion through channel (portal) proteins. Once inside, they enter the matrix through a special channel that does two jobs. (The channel is not actually shown.) First, an enzyme "scissor" snips off one of the three carbons. This carbon has two oxygens attached to it, so it goes floating off as carbon dioxide, CO_2. The carbon dioxide will go to your lungs to be exhaled. Next, an enzyme "scissor" attaches a molecule called Coenzyme A to the remaining two carbon atoms. This makes a molecule called ***acetyl-CoA*** *(ah-SEE-till-co-A)*. Acetyl-CoA is a very important molecule, despite the fact that you have probably never heard of it. Just like a piece of wood can be used either to build something, or to be burned as fuel, acetyl-CoA can be "burned" in the Krebs Cycle, or it can be used in other places in the cell to build various parts. This step, forming acetyl-CoA, doesn't have a cool name like the Krebs Cycle does. It usually just gets called the "pre-step," since "pre" means "before." The technically correct name is "pyruvate oxidation." Though it is not one of the 8 steps in the cycle, it is still often considered to be part of the cycle.

NOTE: The Krebs Cycle isn't really a circle. It consists of various chemical processes, which are going on all over the place all the time. However, in order to understand the chemistry, it is very helpful to draw a diagram that looks like a circle.

Acetyl-CoA's are attached to a 4-carbon molecule to create a 6-carbon molecule called ***citric acid***. Many scientists prefer to call the Krebs Cycle the ***Citric Acid Cycle***, naming it after the molecule formed in the first step. The citric acid then has two carbons snipped off and releases (once again) a carbon dioxide. The most important thing to know about the cycle is what energy molecules it produces. Out of the Krebs Cycle come 3 NADH, 1 GTP (which is converted to ATP), and 1 **$FADH_2$**. The $FADH_2$ is another taxi for high-energy electrons; its function is similar to NADH. By the time the cycle is complete, you are back to having the same 4-carbon molecule you started with, and it is ready to accept another acetyl-CoA. (The two carbons that get snipped off during the cycle are not the ones that come in on the acetyl-CoA. Those two carbons go to the back of the molecule, so to speak, and get moved up each time the cycle goes around. So after two turns of the cycle, those carbons that came in on acetyl-CoA will have moved up enough so that they will be the ones that get snipped off during the next cycle.
At the end of the Krebs Cycle, the original glucose molecule is finally gone. NADH and $FADH_2$, now contain high-energy electrons that will be carried to the Electron Transport Chain.

The ETC is a series of protein gadgets, including three pumps, a few shuttles and a large motor. (The motor at the end is what will generate the ATPs.) NADH goes over to the first pump in the chain and donates its two electrons. The electrons go into the pump and cause 4 protons to be pumped up from the matrix, out into the inter-membrane space above. A shuttle then takes the electrons to the next pump. $FADH_2$ is a supplemental shuttle between the first two pumps. It brings its electrons to a protein between the first two pumps. The electrons go through the second and third pumps, causing each one to pump protons up and out. By the time the electrons exit the third pump their energy is used up and they need to be discarded. The two "tired" electrons are matched up with two protons to form two hydrogen atoms, which are then attached to an oxygen atom to make water, H_2O. It is important to remember that oxygen is final "electron acceptor" at the end of this chain. The oxygen comes from the air you breathe.

NOTE: You should also be familiar with the term ***oxidative phophorylation***. "Oxidative" means that oxygen is used, and "phosphorylation" means "adding a phosphate." Phosphorylation means "adding a phosphate." This happens as the ATP synthase machine pops the third phosphate onto ADP. This is a mechanical process, with the ADP and the phosphate going into those beater-looking things, being pressed together, and then coming back out as ATP.

In the end, ***each glucose molecule makes a maximum of 36 ATP's***. The count is often given as ***32-36***, depending on how you count molecules in all the cycles, and depending on whether the pumps are operating at 100% efficiency.

Mitochondrial diseases are caused by defects in the molecular machinery inside the mitochondria. About 1 in 4000 babies will be born with a mitochondrial disease (more common than all childhood cancers combined). How many things could go wrong inside a mitochondrion? A lot, as you can see. Mistakes in coding for proteins could cause the shapes of the portals, pumps, motors or shuttles to change, such that they could not function properly. It would take only a small mistake in the DNA, perhaps even just one base (A, T, C, G) to mess up the shape of the protein. The mistakes could be in either the mtDNA or the genomic DNA found in the nucleus of the cell. Each mitochondrial disorder is named after the part that is broken. Since the problem originates in the DNA, there is no cure. Doctors just try to ease symptoms. Perhaps some day they'll figure out how to restore the correct sequence to the DNA.

Even without mitochondria, cells would still be able to make some ATP's using glycolysis, but this would not be enough to adequately power the cell. Without lots of ATPs, cells can't function properly because ATPs are needed for every cell activity. Cells would eventually die. Mitochondrial disorders can range from mild to very severe. In the most severe cases, babies die shortly after birth. Mitochondrial problems probably account for at least some of the cases of Sudden Infant Death Syndrome (SIDS). In moderate cases, the children live into their teen years, but with much suffering. They can have a range of problems, including seizures, blindness, deafness, diabetes, muscle weakness, liver and kidney disease, and brain problems. When mitochondrial disease is mild, the symptoms might not show up until the person is well into adulthood.

DRAWING 21: THE OVUM and FERTILIZATION

In drawing 19 we met the smallest human cell. Now we meet the largest: the ***ovum*** (egg). The ovum is about 200 microns (.2 mm) which is so large you can almost see it without a microscope. You wouldn't be able to see any detail, of course. It would look like a tiny dot, smaller than the period at the end of this sentence.

The ovum starts out in the ovary as a cell called a primary oocyte. By the time a baby girl is born, she has already produced all the eggs she will ever have (on the order of a million). By the time she is a teenager, the number of egg cells has decreased by half that number, and then through the middle of her life, the number of eggs drops steadily. However, there are still plenty left, and one egg each month is released from the ovary. It travels down the fallopian tube to the uterus. A future drawing will give more details about this process. Here in this drawing we will just look at the ovum itself.

The ovum is surrounded by a layer of protective cells called the ***corona radiata*** (named for the sun's corona). These cells have been surrounding the ovum for a very long time. In fact, there used to be a lot more, but when the ovum left the ovary, only a few layers of these cells managed to stick close enough to be able to go along for the ride down the fallopian tube. These cells have nourished the egg for years. This is mainly to protect the ovum's DNA from damage. The normal metabolic processes that go on inside cells can produce dangerous by-products (free radicals) that can bounce around inside the cell and damage DNA if they happen to run into it. Cells have ways of dealing with this damage and are constantly making repairs, but if a few body cells die.. oh well, there are millions more like it. Not so with an egg cell; there's a lot at stake here! This DNA will rise to a whole new human being. Damage here can be fatal. So to keep the environment safe inside the ovum, those nourishing cells do all the metabolic work and the ovum sits there, pampered and lazy, letting the corona cells do all the work of feeding her and keeping the cell neat and clean.

Inside the corona radiata is the ***zona pellucida***. The word "lucid" there in the middle means "clear." This layer is clear and jelly-like. Later is will harden, but right now it is soft. Then comes the plasma membrane. Inside the membrane we find cytoplasm, a watery goo in which many things float around: mitochondria, ribosomes, enzymes, fats, proteins, minerals, ions, and dissolved gases such as oxygen and carbon dioxide. An ovum has about a million mitochondria, ready and waiting to start churning out ATPs if and when the egg joins with a sperm and begins to form an embryo. The egg's mitochondria will use the fats in the cytoplasm, chopping them up into acetyl-CoA's and burning them in the Krebs Cycle to make energy for the ETC which will generate ATPs. The cytoplasm contains enough energy to keep the embryo going until it can implant itself into the mother's uterus and begin drawing upon her supply of glucose.

The ovum has a nucleus with 46 chromosomes. It will need to reduce down to 23 chromosomes before it joins with the sperm's 23. If the ovum's nucleus retained all 46 and then joined with the sperm's 23, it would have one-and-a-half times the normal amount and we would call this situation "triploid." Haploid (N) means half the correct number, diploid (2N) means the correct number, triploid (3N) is 1.5 times too many, and tetraploid (4N) means having twice the correct number. Some organisms are okay with having more or less than the diploid number. Moss plants and male bees are haploid (N), seedless watermelons are triploid (3N), goldfish and salmon are tetraploid (4N), and wheat plants can be tetraploid or hexaploid (6N). The Ugandan clawed frog is the record-holder at dodecaploid (12N)! However, in most cases, if an organism gets too many chromosomes, it does not survive. These are very unusual examples. If a human embryo gets more than 46 chromosomes, it either dies or is born with serious problems. (Note: Each species has its own correct number of chromosomes. The least number on record is a certain type of ant with only 6. The highest is a species of butterfly with 268 chromosomes. There is not a detectable pattern as to which species have how many.)

Gametes (eggs and sperm) are produced by a process called ***meiosis***. In meiosis, a primary cell divides, then divides again. These two divisions yield four haploid cells, three of which will be discarded. These discards are called ***polar bodies***. The ovum has already been through the first part of meiosis, and the first two discarded cells (polar bodies) are still visible at the outside rim. They will just dissolve and disappear. Now the nucleus is waiting for its final division. If a sperm enters, those 46 will split and 23 of them will be discarded as a third polar body. If no sperm enters, the entire egg will die. It will then be flushed out during menstruation.

Notice that the nucleus has a ***nucleolus***. Remember, this is a section of dense DNA that manufactures ribosomes. It will become very active if the ovum in fertilized.

As the sperm approach the ovum, they must force their way into and through both the corona radiata and the zona pellucida. They are aided by the enzymes in the acrosome, which can dissolve the zona pellucida. The ovum secretes chemicals that aid this process, too. Some researchers say they've seen the ovum stay in this state (with sperm burrowing in) for several hours. The action of the sperm flagella cause the ovum to rotate slowly, like a Ferris wheel. It must be an amazing sight!

Right outside the ovum's membrane are little protein receptors that act like finish line buttons at the end of a swimming pool. Like swimmers in a race, the sperm will announce their arrival at the finish line by hitting one of these protein buttons. And like the buttons in a swimming pool, they are wired to allow only one winner, and once a button is hit, the others are disabled in a split second. When a sperm makes contact with a receptor protein, immediate changes take place. First, there is an instantaneous electrical change across the membrane, preventing the binding of any other sperm. However, this electrical change doesn't last very long, so the ovum triggers its secondary "security system." The vesicles that are waiting right inside the membrane fuse with the membrane (exocytosis), spilling their chemical contents into the zona pellucida, causing it to become hard and impenetrable. This hardened shell will stay around the embryo for about a week (at which point the embryo will have to "hatch" out of it!).

Meanwhile, the winning sperm's membrane is fusing with the ovum's membrane, allowing the sperm's nucleus, centrioles, mitochondria and even the axoneme to enter the ovum. The sperm's 23 chromosomes then join with the egg's 23, making a new cell called a ***zygote***. The sperm's centrioles will allow the zygote to make its first division (mitosis).

22: THE ZYGOTE

In this drawing, we finally achieve our goal of making a human cell. As soon as the sperm nucleus fuses with the ovum nucleus, a complete cell is formed. This cell is ***totipotent***, meaning "all powerful." It can turn into ANY cell, not only body cells but placenta cells and umbilical cord cells, as well. We can't forget how important these supporting parts are. Although you discarded your placenta when you were born, it was once part of you. It's an odd thought, but every cell of the placenta and the umbilical cord contained a full set of your DNA.

In reality, a newly formed zygote would be a bit more complicated than this. As soon as the sperm nucleus enters, those polar bodies are expelled as the ovum completes meiosis. And while that is happening, the cell is also beginning its first division using a process called mitosis, which we will look at in the next lesson. Here we have a simplified zygote cell that has not yet started dividing. Actually, this diagram is more of a generic (average) cell, not specifically a zygote cell.

NUCLEUS: This is where the full set of DNA instructions is kept. Most of the time, when the cell is not dividing, the DNA looks like a pile of spaghetti and is called ***chromatin***. When the cell goes to divide, the chromatin will organize into bundles called ***chromosomes***. The nucleus is surrounded by a double layer of phospholipid membrane and has many pores.

NUCLEOLUS: This is a particularly dense part of the nuclear DNA and under the microscope it looks like a dark spot. This is where ribosomes are made. There are many copies of these instructions , so many ribosomes can be made quickly.

NUCLEAR PORES: The nucleus has over 3000 pores which control what goes in and out. The pore isn't just a hole; it is a complex protein gadget (called the ***pore complex***). The pore has several rings, some filaments, and a basket. The inner ring can open and close so that only the necessary molecules can move in and out. (One molecule that needs to get out is mRNA.)

RECEPTORS and PORTALS: The cell is covered with protein gadgets, many of them ***receptors*** that receive messages from other cells, and ***portals*** that control the flow of various molecules, including nutrients and ions.

MHC1: One of the proteins stuck to the outside of the cell is MHC1, which functions as an identification tag, telling other cells that this cell is part of the body and is not a foreign invader. (M= Major, H= Histocompatibility, C= Complex)

CENTROSOME: This is a blob of protein goo with two barrel-shaped centrioles inside. The most important thing to know is that the centrosome is responsible for making the spindle at the beginning of mitosis (as we shall see in lesson 23). Centrioles also seem to be responsible for making cilia and flagella. (Cilia are found on cells lining the trachea.)

SMOOTH ER: Smooth endoplasmic reticulum is a network of tubes right outside the nucleus. In fact, it is attached to the nucleus's outer membrane. They often say that the ER is "continuous" with the nuclear membrane, which means it is attached to it (or is part of it). Smooth ER does not have any ribosomes attached to it. Its primary function is to make phospholipids that can replenish the membrane. It can also make steroid hormones and it can store calcium (especially in muscle cells). It has other minor functions, depending on what type of cell it is in.

ROUGH ER: Rough endoplasmic reticulum is also a network of tubes. It is identical to smooth ER except that it has lots of ribosomes attached to it. The ribosomes are what make it look "rough." The ribosomes feed their polypeptide chains into the rough ER so that they can be wrapped in membrane, forming a vesicle. Often, these vesicles leave the rough ER and go to a Golgi body for further processing.

RIBOSOMES: These are the only organelles that are not "membrane bound" (surrounded by membrane). Ribosomes are made mostly of RNA with just a few small protein bits added in. They come in two halves: the large and small subunits. Ribsomes make proteins of all kinds using mRNA instructions.

GOLGI BODY: It can also be called the ***Golgi apparatus***. Its structure is similar to the ER, as it is made of hollow tubes and "pancakes" of phospholipid membrane. The side facing the ER (the "cis" side) receives vesicles from the rough ER. The proteins enter the Golgi and have various tags (often sugars) added to them. Many of the extra tags act like labels telling where the proteins are supposed to go. For this reason, the Golgi is often called the "post office" of the cell. Then the vesicles exit the far side (the "trans" side) and go off to wherever they are headed. No one is sure how the Golgi is able to keep its enzymes inside, because the "pancakes" are constantly shifting. (Videos of the Golgi can show this shifting process.)

MITOCHONDRIA: The site of the Krebs Cycle and the Electron Transport Chain (that make ATPs). The mitochondria contain a ring of DNA, mtDNA (mitochondrial DNA), that has information on how to make tRNA and parts for the E.T.C.

LYSOSOME: This is the recycler of the cell. It is a hollow ball made of membrane, very much like a vesicle. However, it is filled with enzymes that can break apart proteins and fats. It is often called the "stomach," the "trash can," or the "recycling center" of the cell. Without lysosomes, cellular garbage would pile up and poison the cell. ("Lys" means "break apart.")

PEROXISOMES: This organelle was not discovered until 1967. The peroxisomes contain enzymes that work to neutralize toxins that we take in (alcohol, for example) and also dangerous "free radicals" (molecules with extra electrons or oxygen atoms). A by-product of the neutralization process is ***hydrogen peroxide***, H_2O_2, which isn't exactly good for you, either. Therefore, they also contain an enzyme that neutralizes the H_2O_2. Liver cells contain a lot of peroxisomes. Peroxisomes also work to break down long chain fatty acids into medium length chains which then get sent over to the mitochondria to be chopped up into acetyl-CoAs. (You'll remember that acetly-CoAs are what the Krebs Cycle uses.) Peroxisomes have a few othe minor functions, but these two (dealing with toxins and chopping fatty acids) are the most important ones to remember.

CYTOSKELETON: This was discovered in the 1960s, but the motor proteins that travel along it were not discovered until the mid-1980s. The cytoskeleton is made of ***microtubules***, which are made of protein units called ***tubulin***.

23: MITOSIS

Mitosis is a word that has two definitions, one formal and the other informal. Informally, the word mitosis is used to mean the ordinary process of cell division. Cells are constantly dying and being replaced. When you injure your skin, for example, you must grow new skin cells to replace the damaged ones. The cells near the damaged area begin duplicating, making many copies of themselves, enough to fill in the damaged area. Regular body cells are called ***somatic*** cells. (Remember, "soma" is Greek for "body.") We need this term in order to make the distinction between body cells and the reproductive gamete cells. Only gametes go through meiosis. Regular somatic cells never use meiosis, only mitosis. In mitosis, you end up with two cells that both have 46 chromosomes. In meiosis, you end up with four cells that each have 23 chromosomes.

Formally and technically, the word mitosis means only one part of this duplicating process: the duplication of the nucleus. Our drawing will clearly show what is included in the technical definition of mitosis. However, even scientists and teachers who know perfectly well that mitosis is actually about the nucleus, will still use this word to describe the whole process of somatic cell division. There isn't really a word for the whole process, so "mitosis" has to do double duty!

The organelle that controls mitosis is the ***centrosome***. A centrosome is a pair of centrioles surrounded by a blob of protein goo. Centrosomes are often called "microtubule organizing centers" because they seem to be the focal point of the cytoskeleton network of microtubules. They are also the organelles that create cilia and flagella. Each cell has a centrosome that hangs out near the nucleus. When the cell wants to divide, one of the first things that happens is that the centrosome duplicates itself. The original centriole is always called the "mother" and the duplicate is called the "daughter." (The centriole that was the daughter in the original pair turns into a mother because it produces a daughter. The original mother stays a mother and also produces a daughter.) Then these two new centrosomes then go to opposite sides of the nucleus. The DNA inside the nucleus then duplicates, and all the resulting pairs of chromosomes then line up in the middle of the nucleus. The centrosomes start forming a spindle made of microtubules. The microtubules fasten themselves to the chromosomes (at a place in their middle called the kinetochore). When all is ready, the centrosomes contract those microtubules and pull the chromosome pairs apart. Each side of the cell ends up with a full set of chromosomes and one centrosome.

There are official names for the stages of mitosis as well as the stages of a cell's life when it is not dividing. When a cell is resting, just growing and enjoying cellular life, we say it is in i***nterphase***. ("Inter" means "between.") Some cells spend most of their existence in this phase. Nerve cells (neurons), for example, stop dividing by the end of infancy and then stay in interphase for the rest of your life. Other cells, such as skin cells, are constantly dividing and spend very little time resting.

Interphase can be divided into phases, too. The part of interphase where a cell is really and truly resting and not even thinking about mitosis is called the ***Gap 0 phase***, or just G_0 (G zero). (During G_0 the DNA in the nucleus looks like a pile of spaghetti, and is called ***chromatin***. Later, as part of mitosis, the chromatin will be arranged into ***chromosomes***.)

Gap 1, or G_1, is when the cell has decided it would like to expand and grow and probably go into mitosis. So during Gap 1, the cell makes lots of extra organelles, especially mitochondria that can give the energy necessary to divide. There must eventually be enough organelles for two complete cells.

Once the cell has enough organelles for two cells, it will enter the ***S phase***. The S stands for "synthesis," which means "to make." What is being made is DNA. Every chromosome (though at this point it is still a messy pile of chromatin) will duplicate itself. Now the nucleus will have a total of 92 chromosomes. Also, the centrosome duplicates itself during S phase.

The last part of interphase is called ***Gap 2***, or G_2. During this phase, the cell continues to make organelles and enzymes in preparation for mitosis. At various points in this cycle, there are "check points" where certain protein gadgets are given the task to check and make sure that everything is going well. If one of these little protein robots senses that there are not enough mitochondria, for example, it will send out a signal that means "do not begin mitosis yet." If these little gadgets are not working correctly, a cell might begin to divide when it shouldn't. This could lead to uncontrolled cell growth and the formation of a tumor. Cancer researchers are trying to figure out how to use these mitosis "policemen" to stop inappropriate cell growth.

When a cell is ready to divide, the first thing that happens is that the chromatin (those 92 chromosomes) get organized and go from looking like a pile of spaghetti to tightly organized little bundles called chromosomes. This phase is called ***prophase***. "Pro" means "first," so this is the first stage of mitosis. Also during this stage, the thick nuclear envelope begins to dissolve. The nucleus must dissolve in order to let the pairs of chromosomes go opposite directions.

The next phase is called ***metaphase***. The centrosomes begin to weave the spindle and the chromosomes line up in the middle. This is the easiest phase to find when looking at real cells.

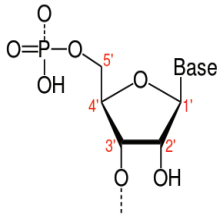
Then comes ***anaphase***, where the centrosomes tug on the chromosomes and split the pairs. Generally, anaphase is identified when the spindle has split and shrunk to where it looks more like a V (or A) on each side. It's hard to say when exactly prophase ends and anaphase begins. All you need to know is that if you are asked to find cells that are in anaphase, look for two V-shaped spindles. (It might be helpful to think of them as looking like the letter A instead of V, because the word "anaphase" begins with the letter A and you can use this as a mnemonic.) "Ana" means "opposite" so anaphase is when the chromosomes are in the process of going to opposite sides of the cell.

The last part of mitosis is ***telophase***. "Telo" means "far," so this is when the chromosomes are now on the far sides of the cell, far away from the middle. (A telescope is something you use to look at faraway objects.)

Notice that mitosis ends before the cell splits in half. Again, the technical meaning of the word mitosis is the division of the nucleus, not the whole cell. When the entire cell splits in half, this is called ***cytokinesis***. You know that "ctyo" means "cell," and "kine" means "motion." The root word "kine" shows up a lot in biology and has various shades of meaning. Here, the motion or action is the cell pinching in at the middle and then splitting to make two individual cells. While the split is happening, the new nuclei are busy re-growing a nuclear envelope. The DNA must not be exposed for longer than necessary. While the envelope is missing, the DNA is vulnerable. (This is another place where cancer treatments, especially radiation, can intervene and try to stop cell division.) These two new cells will then be in interphase, at the beginning of the cell cycle. They will grow for a while then possibly begin the process of mitosis again.

Let's take a close-up look at DNA replication. (Often, the word "replication" is used instead of "duplication," so we'll switch over to that word, but they mean the same thing.) First, the DNA must be unwound and unzipped. As you might guess, there is a specialized enzyme robot that does that job. Its name is ***helicase***, because it unzips the helix. Remember, the rungs on the DNA ladder are made of base pairs (A and T, C, and G) held together in the center by hydrogen bonding. Hydrogen bonding is the best bonding to use in a location where you want the molecules to stick together most of the time but still be able to be separated when necessary. (Remember, water molecules stay together by hydrogen bonding.) The helicase doesn't have to pull any molecules apart or undo any covalent bonds. Hydrogen bonds are relatively weak and easy to separate.

After the helicase unzips the DNA, another specialized robot enzyme called ***DNA polymerase*** is used to make a new matching strand of DNA. DNA polymerase is similar to RNA polymerase, but it does not use uracil. The polymerase runs along the DNA strand, reading the sequence of bases and forming a complimentary strand with the opposites, A with T, C with G. You can see in the picture that the result is two identical strands of DNA. However, there is one small problem that must be overcome.



Remember that DNA and RNA strands have a direction to them. Just like English must be read left to right, DNA and RNA are directional. We don't use left and right or up and down, we use the terms 5' (5 prime) and 3' (3 prime). The numbers 5 and 3 come from the numbering of the carbon atoms in the ribose molecule. This illustration shows how the carbons are numbered. They go clockwise, with number 1 being the first one after the oxygen atom. So number 3 ends up being the carbon that attaches to the phosphate below it, and carbon number 5 ends up being the one that attaches to the phosphate above it. If you imagine the molecule shown here as being just one part of a long string, the 5' end would above and the 3' end below. If you turned the string upside down, the 5' end would then be pointing down instead of up.

Why is this 5' and 3' stuff worth mentioning? Because one of these strands has a replication problem. The DNA polymerase enzyme can only go from a 3' end towards a 5' end. So for one of the strands, the polymerase enzyme slides along with no problems. This strand is called the ***leading strand***. The other strand is "backwards" for the enzyme and is called the ***lagging strand***. The enzyme must work on little sections of the lagging strand, constantly hopping back up to a new piece as it finishes the old one. Your drawing should have this motion indicated by arrows. Each little section of new DNA is called an ***Okazaki fragment***, after the scientist who discovered it. The Okazaki fragments must then be "glued" together by an enzyme called ***ligase***. Yet another specialized enzyme, ***primase***, is used to determine the starting point for each fragment. (It is interesting to think about the fact that these little enzyme task robots were made using the information encoded somewhere on the very DNA that they are duplicating!) Watching a few video animations of this whole process is very helpful.

After the DNA polymerase is done replicating the entire strand of DNA (millions of base pairs long) all the enzymes disengage and you've got two copies of the original. Does DNA polymerase ever make mistakes? Yes, all the time. There are specialized "spell checking" robots that go along checking the work that the polymerase did, and trying to fix mistakes. The process is amazingly accurate given how difficult the task is and how fast it has to occur. However, little mistakes are introduced every time this process happens. These tiny mistakes add up over a lifetime and in the end contribute to the aging process. Mistakes in the instructions for making organelles cause them to work less efficiently. A mistake in a very critical place could be the beginning of a degenerative disease. (Just think-- a mistake could occur in the DNA that codes for the spell checker enzymes themselves!)

24: EPIGENETIC MECHANISMS

A zygote is a cell that can become any type of cell. The DNA in the nucleus contains every bit of information that every type of cell will need for the entire lifetime of the organism. A fairly large portion of the DNA contains instructions for embryonic development. Once the body has fully formed, this information is no longer necessary and will be locked away permanently. Also, bodies change and grow over time. When children begin to turn into adults, their bodies will begin to make proteins they never made before.

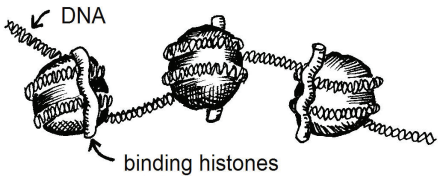
The nucleus has a way to control what sections of DNA can be opened at what times. The opening and closing of DNA is called ***epigenetics***. "Epi" means "outside of" (or "on top of") so epigenetics is on the outside of the genes. A gene is a piece of DNA that codes for one thing. The traditional understanding of a gene was a continuous strip of DNA, running along like a section from a bead necklace. New research has suggested that it is more complicated than this. A gene, even though it codes for one thing, (such as a particular protein), can be encoded as smaller sequences located in different places, not one continuous piece all in one place. The polymerase machinery has to copy the small sections then splice them together to make the mRNA. Or, a gene might be encoded in a continuous strip but using only every other base pair, or every third base pair. Genes have turned out to be a lot more complicated than anyone had imagined. However, it is okay to keep it simple for now and think of a gene as one strip, like a section snipped from a necklace.

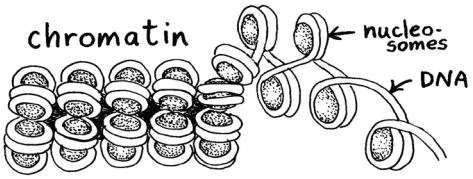
The most permanent way to close DNA is ***methylation***. The ***methyl*** group, CH_3, can be used like clip. The methyl clip fastens to cytosines that are almost opposite each other. We have to say "almost opposite" because, of course, cytosines can't be exactly opposite because they always match up with guanine across from them. However, if you have a C-G next to a G-C, the cytosines are close enough that a methyl clip can be placed on the cytosines. This clip prevents those polymerase machines from using the DNA to create RNA. If the polymerase "sled" tries to ride along the DNA, it gets stuck on these clips and has to stop. If the polymerase can't ride along that section of DNA, no mRNA will be made. If no mRNA can be made, no proteins will be made, and the gene has effectively been silenced.

These methyl clips are put on by special enzymes designed to do that job. They have to do this every time the DNA is replicated (during mitosis, for example). DNA replication is complicated enough, but all those little methyl tags have to be added, too!

Another way to prevent gene transcription is ***histone modification***. A ***histone*** is a protein gadget that acts like a spool. DNA is very long and thin and there is a lot of it in the nucleus. It might get hopelessly tangled if it were not for the ingenious way it is wound onto "spools" and then wound again into long chains. Eight "balls" called histones stick together to make one spool. Often, the entire spool is mistakenly called a histone. The spool is properly called a ***nucleosome***, but this word seems to be harder to remember than the word histone. Therefore, many people say "histone" when they mean "nucleosome." (We can say "histone spool" and we'll know we are talking about the whole spool, not just one histone.)

The histone spool (nucleosome) has DNA wound around it—145 to 147 base pairs in length, to be exact. There is also a protein gadget that acts like a clip to keep the DNA tightly wound. The clip (or "binding histone") is called H1.





When the DNA is tightly wound, the polymerases can't get in to read the DNA. The histones must allow the DNA to loosen and relax and come unwound a bit. There are little switches (not shown in these pictures, but shown in your drawing) that control the tightening and loosening. The switches look like strings, and can be activated by three different molecules:

1) methyl (CH_3) 2) acetyl ($COCH_3$) 3) phosphate (PO_4)

Acetyl tags make the spools stay open and let the DNA be transcribed. When a gene is actively being used, we say it is being ***expressed***. ("Gene expression" is a term you should know.) If the histones are "deacetylated" (acetyls are taken off) then we say that the gene has been "turned off." Methyls and phosphates work in a similar way.

Cells have a "Plan B" for stopping genes from being expressed. Even if the DNA is open and mRNA has already been made from the DNA, it is still not too late to prevent proteins from being made. The cell can manufacture a piece of ***microRNA***, or ***miRNA***, that will prevent that mRNA from being used. A piece of miRNA is very small, usually only 20 or 22 nucleotides long. It will match one place on the mRNA. The miRNA locks on to that place and sticks there permanently. If the mRNA tries to slide through a ribosome, the miRNA will stop it from doing so. It physically prevents the mRNA from sliding through. The mRNA becomes useless and is eventually chopped up and recycled. Thus, the gene is effectively silenced.