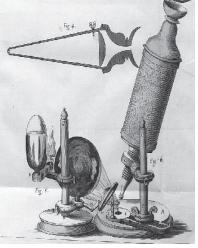
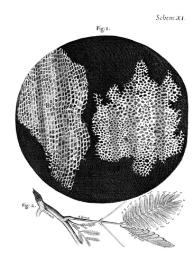
# **CHAPTER 1: HOW DID WE FIND OUT ABOUT CELLS?**

There was a time in the not-too-distant past when not a single person on earth knew that cells existed. Galileo, who used lenses to view distant planets, knew nothing of cells. It was in the decades following Galileo (the late 1600s) that someone figured out how to use lenses to make very small things visible. Two lenses were used, one at each end of a tube, forming a *compound microscope*.

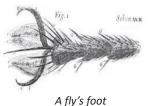
Englishman Robert Hooke (1635-1703) was probably the first person to observe cells. One day he sliced an extremely thin piece of cork and put it under his microscope. What did he see? Rows and rows of little box-like shapes that reminded him of the tiny rooms, or *cells*, in monasteries (where monks live). Today we don't use the word "cell" when referring to a room, except when we talk about prison cells. But in Hooke's day the word "cell" was commonly used for a small room, so it was natural for him to use the word "cell" to describe these little compartments he saw in the cork. He didn't really know what these cells were made of or how they functioned, but the name he gave them has been used ever since.



Hooke's compound scope



The famous cork cells



Hooke eventually wrote a book called Micrographia telling about his amazing microscopic discoveries. He drew pictures of cells, parts of insects, hairs, specks of dirt and many other things that fascinated him. He discovered that no matter how sharp he made the point of a needle, the end of it still looked dull when viewed under his microscope! The only objects that still looked sharp when viewed under magnification were the tiny claws on the ends of insects' legs and the almost invisible "hairs" he found on the stems and leaves of plants.

Hooke was a brilliant man. He was also a surveyor, an architect, an astronomer and a physicist. He was working on the principles of motion and gravity at the same time that Isaac Newton was. He didn't really want to go down in history as the man who named cells. He would rather have been known for one of his other achievements: figuring out the laws of gravity and motion, helping to re-design London after the fire of 1666, or proposing the wave theory of light. But as history would have it, most people know him as the man who gave us the word "cell."





Hooke without his wig

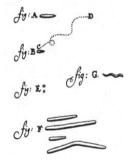
Hooke in a wig



Then along came Antoni van Leeuwenhoek (LAY-ven-hook), who lived his whole life in the Dutch town of Delft. He bought a copy of Hooke's Micrographia while on a trip to England in 1665, the only time in his life that he left Holland. Not long after reading Micrographia, Leeuwenhoek began making single-lens microscopes the likes of which have never been equaled. Leeuwenhoek perfected the art of making tiny lenses, but was careful to keep his technique a secret. He never wrote down his method, so we can only guess what he did. Modern glass making experts are fairly sure that Leeuwenhoek probably heated a glass rod and stretched it until it was a thin string. Then he would take



the very thin strand of glass and put it back into the flame and let the end melt until it formed a tiny round ball. This tiny round ball would be trimmed off and used as his lens. Other lens crafters of his day would spend hours grinding and polishing their lenses to get them into the right shape. Leeuwenhoek just took advantage of the natural physics of hot glass. He could make these tiny glass beads fairly quickly and easily; he managed to make over 500 of these little microscopes while keeping up with a full-time job as a cloth merchant. He mounted his lenses in silver panels and attached a screw mechanism on one side. With this simple magnifier, he was able to achieve magnification of at least 300 times larger than life size.



Leeuwenhoek observed bacteria

Leeuwenhoek was an incredibly patient person. He would sit for hours watching the specimens he had mounted on his microscope. He watched long enough to be able to observe the behavior and life cycles of microorganisms. He observed the microscopic food chain and knew what each little "animalcule" would eat. He saw eggs hatch. He saw blood cells circulate inside tiny circulatory systems. He observed sperm cells swimming. Once he

kept a colony of fleas in a pouch inside his sock (to keep their eggs warm) and every hour or so he would check on them to see what changes had occurred. He spent several decades reporting all his findings to the Royal Society in London. At first, his descriptions of bizarre invisible creatures were almost too much to believe.

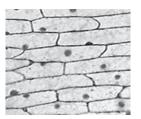
The Royal Society had to send some of their members to visit Leeuwenhoek to verify that what he was saying was true, and he wasn't just imagining his microscopic "zoo." The visitors from the Royal Society looked through the little microscopes and were amazed to see exactly what Leeuwenhoek had written about. From then on, Leeuwenhoek's reports were treated as valid science. Prominent scientists and politicians began visiting Leeuwenhoek. Peter the Great of Russia put Delft on his European travel itinerary so that he could see Leeuwenhoek's little animalcules. Today, Leeuwenhoek is generally considered to be the "father" of modern microscopy.



The man in "The Geographer" by Verneer is probably Antoni van Leeuwenhoek.

In the early 1800s, a Scottish botanist named Robert Brown made the next advances in our understanding of cells. Brown didn't have to make his own microscopes; by this time there were technicians who specialized in making optical devices such as microscopes. Since Brown was a botanist, it was plant cells he observed. He noticed that inside every cell there was a dark blobby thing. He called this the **nucleus** but he didn't have a clue what it did. Today we know that the nucleus contains the cell's DNA.

In 1827, Brown made another important microscopic discovery. While observing pollen grains under his microscope, he noticed that tiny particles inside the pollen grains were vibrating. He wondered if these particles were alive, since they were inside a plant cell. He tried a similar experiment with dust particles and saw the dust particles moving in the same way. He knew the dust particles were not alive, so he concluded that the motion must be due to a law of physics, not biology. He was right. Molecules are in constant motion and often collide. It is these molecular collisions that cause tiny particles to look like they are moving. We call this motion **Brownian motion**, after Robert Brown.



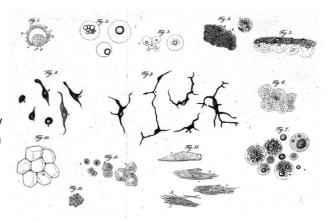




As an interesting historical side note, an ancient Greek named Lucretius was actually the first person to conceive of the idea of Brownian motion. In 60 BC, almost 2,000 years before Brown was born, Lucretius said this:

Observe the dust particles in sunbeams. You will see a multitude of tiny particles moving in a multitude of ways. Their motion is an indicator of underlying movements of matter that are hidden from our sight. It originates with the atoms which move of themselves. Their collisions set in motion slightly larger particles, and so the movement mounts up from the atoms and gradually emerges to the level of our senses, so that those particles we see in sunbeams are moved by blows that remain invisible. In 1837, a German scientist named Theodor Schwann developed a theory that we now call "cell theory." Schwann came to realize that all living things are made up of cells that are very similar in basic structure. He also observed that cells only came from other cells. Cells could not come out of nowhere. This sounds obvious to us, but until Schwann's time many people still believed that living things could just suddenly appear. They saw flies appear seemingly out of nowhere when fruit or meat spoiled. Most people did not know that the flies had hatched from eggs because fly eggs are too small to see.

This is a drawing that Schwann made of different types of plant and anaimal cells he observed under his microscope.



Schwann had a friend named Matthias Schleiden who was also a botanist. Together, they figured out that the nucleus played some role in cell division. They also observed the cytoplasm (fluid) inside the cell and saw that the organelles inside the cells moved around. Schleiden is considered to be the co-founder of *cell theory*, along with Schwann. Cell theory says that cells can only come from other cells—they can't just pop into existence from nothing or from inorganic materials. (Ironically, Schleiden also accepted the theory of evolution, which suggested that cells did originally come from inorganic materials. He believed a theory that contracted his theory?)

By the late 1800s, many different types of cells had been observed. There were fairly accurate pictures of plant cells, animal cells, single-celled organisms such as protozoa and bacteria. The big question now was how cells worked inside. Scientists knew that cells had some little "organelles" inside of them, but no one really knew what they did. The most obvious organelles were the nucleus (present in all cells) and chloroplasts (found only in plant cells). The chloroplasts were easy to spot because they were green. Other little spots and dots could be seen floating around inside the cell, but even the highest power on their microscopes could not enlarge them enough so that they could be studied. Another problem was that some of the little organelles were almost transparent. How can you study something you can hardly see?

A major breakthrough came when cell scientists learned how to stain cells before putting them under the microscope. The most famous "stain scientist" was Hans Christian Gram from Denmark. His technique of staining bacteria cells is still used today and bears his name: *the Gram stain*. This stain will be absorbed by some kinds of bacteria but not by others. This helps to identify what kind of bacteria you are working with. Other stain experts developed stains that would penetrate the nucleus or other organelles, making them highly visible so they could be studied more easily. Then an Austrian scientist named *Camillo Golgi* discovered how to use a silver compound to stain nerve cells. His stains made possible many discoveries about nerve cells and how the nervous system works. Golgi's most famous discovery was another type of organelle found in almost all cells: the *Golgi apparatus* (or Golgi body).



An electron microscope from the 1930s

Then cell science "hit a wall," so to speak. Even the very best microscopes in the world could not magnify something beyond about 1000 times. Scientists knew that many mysteries of the cell would not be discovered until there was a way to achieve magnifications beyond 1000. Then, in the mid 1900s, a completely new type of microscope was invented: the *electron microscope*.

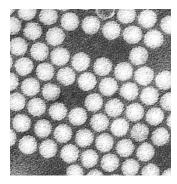
Regular microscopes use light and lenses to make things look larger. Electron microscopes work on an entirely different principle; they use electrons instead of light. Electrons from a tungsten filament are "fired" at the sample being studied, and the electrons either go through it (in the case of transmission electron microscopes, or TEM) or they bounce off at various angles (in the case of scanning electron microscopes, or SEM). In both TEM and SEM, the electrons then hit a screen to form a visible image. Pictures from electron microscopes, which are known as *micrographs*, are always in black and white. Color requires light, and electron microscopes don't use light. Colored micrographs are made by adding the color afterward. They use computer programs to adjust the graphics, just like you might use a program like Photoshop<sup>®</sup>.



An SEM microscope opened up to show you the vacuum chamber where the sample goes

Modern electron microscopes can provide images that are up to a million times larger than life. That's large enough to be able to see even the tiniest parts of the cell. However, electron microscopes have a big drawback. The samples being studied must be put into a vacuum chamber where there is not a single molecule of air (like outer space). Living cells need air. so basically, only dead specimens can be studied. The specimens can be killed and preserved only minutes before loading them into the machine, but nothing alive and moving can be viewed. Usually, the specimens have to be prepared by spraying them with an ultra-thin layer of gold, or some other metal. This means that you can't sit and watch little critters moving around under an electron microscope like you can with a regular (compound) microscope. You can't watch

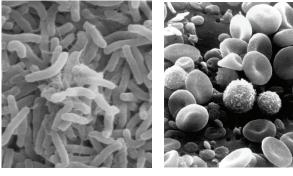
as a cell eats or grows or divides. You only get one picture of a cell at one moment in its life. Cell scientists must collect lots and lots of still pictures, then use "detective skills" to draw conclusions based on comparing all the pictures. Sometimes scientists can think of a way to test their theories about cells by "tagging" particular molecules with radioactive or fluorescent dyes that will show up on the screen. In the next chapter, we'll read about a cell part that was discovered in this way.



viruses



a single-celled organism



bacteria

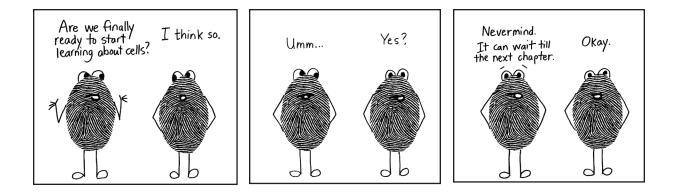
blood cells

#### **TEM images look flat**



Images produced by TEM microscopes look flat. The electrons pass throug the sample in much the same way that light passes through samples on a regular (compound) microscope. This type of image can be very good for studying the insides of cells. SEM electron microscopes produce 3D images. SEMs let you see textures and shapes. It takes both types of images to give us enough information to be able to understand what a cell is really like. Scientific illustrators try to create pictures that combine information gained from both types of images. Books about cells often contain many images made by scientific illustrators.

Electron microscopes are used for more than just biology. They can be used in the fields of material science (metals, crystals and ceramics), nanotechnology, chemistry, and forensics. They have become an essential tool for many branches of science.



<u>Comprehension self-check</u> If you can't think of the answer, go back and read that part of the chapter again until you find the answer. If you need to check your answers, check the answer key.

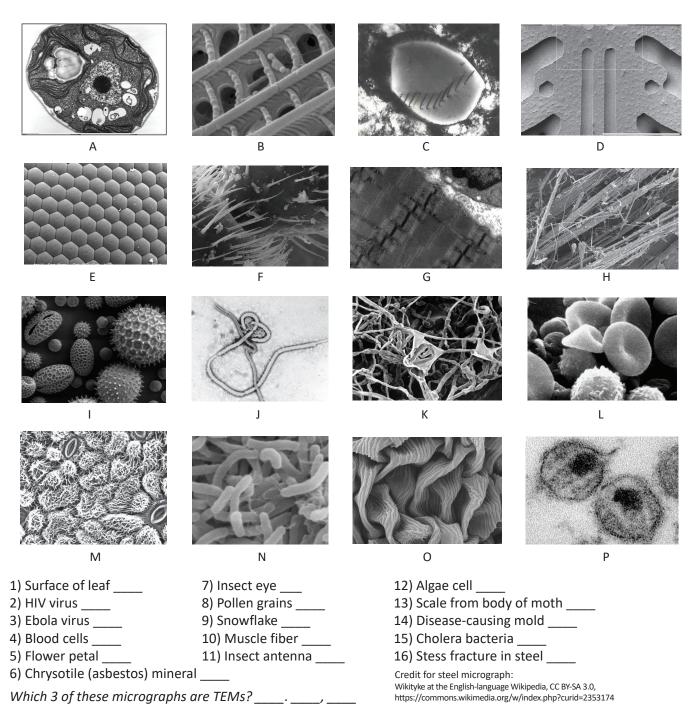
- The first person to ever see a cell was:
   a) Galileo
   b) Hooke
   c) Lucretius
   d) Leeuwenhoek
- 2) Which one of these did Hooke NOT do?
  a) develop theories about gravity and motion
  c) help to redesign London
  b) propose a wave theory of light
  d) develop cell theory
- 3) About how many microscopes did Leeuwenhoek make?a) less than 10b) about 100c) about 500d) millions
- 4) TRUE or FALSE? The Royal Society immediately made Leeuwenhoek a member, as soon as they read his descriptions of "animalcules."
- 5) What is Brownian motion?
  - a) a physical phenomenon caused by the constant motion of molecules
  - b) the movement of dust particles in air c) a biological phenomenon found only in living things
  - d) the movement of cells under the microscope
- 6) When was the idea of tiny invisible particles (atoms) first proposed?a) 60 BCb) 600 ADc) 1827d) early 1900s
- 7) TRUE or FALSE? Schwann and Schleiden proved that life could come from nonliving things.
- 8) TRUE or FALSE? By the late 1800s, scientists had seen many different types of cells.
- 9) TRUE or FALSE? Many cells, and their inner parts, are transparent.
- 10) What is the most noticeable object found inside a cell?a) Golgi bodyb) nucleusc) DNAd) cytoplasm
- 11) Who has a staining method named after him?a) Antoni Leeuwenhoekb) Theodor Schwannc) Camillo Golgid) Hans Christian Gram
- 12) The staining method named referred to in question 9 is used to stain \_\_\_\_\_\_.
- 13) What is the maximum magnification you can get with most ordinary (compound) microscopes?a) 100xb) 500xc) 1000xd) 100,000x
- 14) TRUE or FALSE? TEM images look 3D.
- 15) TRUE or FALSE? Electron microscopes can let you watch a cell as it divides.
- 16) For electron microscopy, what do the specimens have to be in?a) a vacuum b) suspended animation c) a frozen state d) high temperature environment
- 17) TRUE or FALSE? There is a special kind of electron microscopy that can show you both a flat image and a 3D image at the same time.

18) What does SEM stand for? \_\_\_\_\_ \_\_\_\_\_ \_\_\_\_\_\_

- 19) What metal is common used to spray samples that will be observed with electron microscopes? \_\_\_\_\_
- 20) TRUE or FALSE? Electron microscopes are used exclusively for biology.

### Activity 1.1: Just for fun-can you guess what these are?

Here are some SEM and TEM micrographs. Try to figure out what they are. (Answers are in the answer key.)

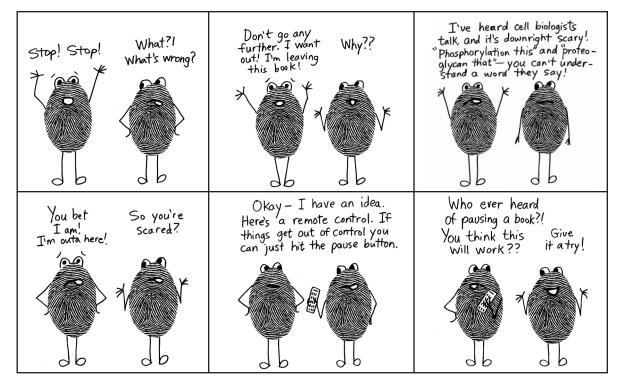


#### Activity 1.2: Watch some supplemental videos on the Cells playlist

This curriculum has a YouTube playlist. Go to www.youtube.com/TheBasementWorkshop. The Cells playlist might not be visible at first glance. Sometimes you have to click on "See all playlists" and then click on arrows to advance the list to see all the titles. The playlist is made of videos posted by various people around the world, and they have the right to take down the videos at any time, so occasionally there will be a blank spot. The author of this book tries to keep the playlist updated, but it is not possible to check it daily or even weekly. The videos that do appear on this list have been previewed by the author so they don't contain anything offensive and they hopefully aren't too boring. YouTube does not provide a way to label the videos to indicate which chapter they go with, but the will be in approximately the right order, so you can go down the list as you read the book.

# **CHAPTER 2: THE CELL MEMBRANE**

So now that we know a little bit about how cells were discovered, let's start learning about what cells are made of and how their insides work. We'll start with the outer surface, the *plasma membrane*.

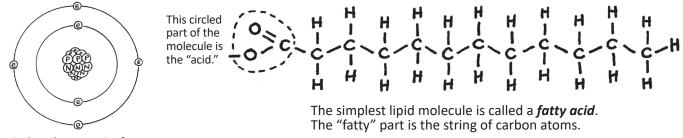


Okay, we're ready now?

Let's look at the outside of the cell first. The outer layer of a cell is called the *membrane*, or, to be more precise, the *plasma membrane*. (Don't worry about the word "plasma." We'll get to that later.) In plant cells there is an extra layer outside the membrane—a thick coating made of tough *cellulose*. Bacteria, also, sometimes have thick outer walls. However, underneath those thick walls there is still a thin membrane. The membrane is so thin that it would take 10,000 of them stacked on top of each other to be as thick as a sheet of paper. It's barely visible even with one of those high-power electron microscopes, because it's only two molecules thick! The molecules that form a cell membrane are called *phospholipids*.

### WAIT! DON'T PAUSE THE BOOK!

Let's look at this word and figure out what it means. The second part of the word, *lipid*, means "fat." You know what fats are—those white streaks in your meat, the vegetable oil you use to fry your potatoes, the cream on top of fresh milk, even the grease that builds up on your scalp if you don't shampoo your hair for a few days. Lipids are greasy and oily and don't mix with water. If we look at one molecule of grease or fat, we'll see that it is made of a chain of carbon atoms with hydrogen atoms attached.

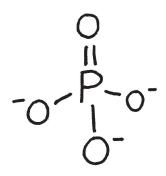


Drawing entire atoms is too difficult. In this book, we are going to simply use a letter to represent an atom. C is carbon, H is hydrogen, O is oxygen. If you want to know more about atoms and how they join together to make molecules, check out "The Elements" book by Ellen McHenry.

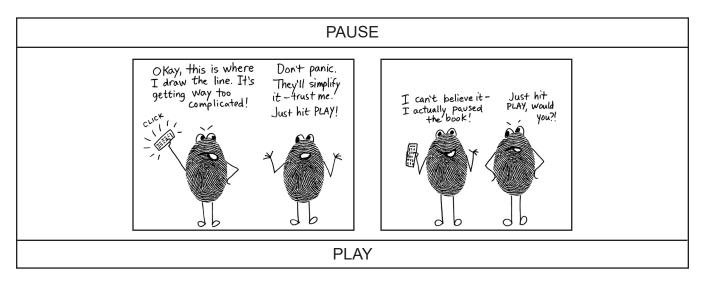
A single carbon atom is often drawn like this. Atoms have layers of electrons orbiting a nucleus made of protons and neutrons.

**Phospho** is short for "phosphate." A phosphate molecule is made of four oxygen atoms attached to an atom of phosphorus, P. (Phosphorus is a fascinating element that can glow in the dark and is found in matches and fluorescent light bulbs, but it is also found in many biological molecules, including phospholipids. We'll be meeting phosphorus again in future chapters.)

Phosphorus atoms can make five bonds. Imagine phosphorus has having five arms so that it can shake or clasp hands with five people all at once. Oxygen atoms can make only two bonds. They are more like you, having two arms. In phosphate, one oxygen atoms does a double handshake and uses two of phosphorus's five bonds. The three other oxygen atoms make one bond with phosphorus, but have



their other "arm" unattached to anything. This is indicated by that minus sign next to them. (The minus sign represents a free electron that can make a bond.) Phosphate is written like this:  $PO_4^{3-}$ . The "4" tells you how many oxygen atoms there are. The "3-" tells you how many dangling, unattached arms there are.



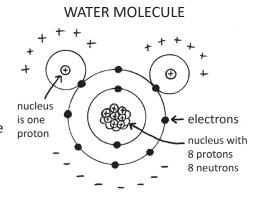
For our study of cell membranes, the most important difference between the phosphates and lipids is their reaction to water molecules. Phosphates are said to love water. Yes, scientists really do use the term "love," but they say it in Greek. They combine the Greek word for water, "hydro," with the Greek word for love, "philia" to make the word "hydrophilic," meaning water-loving.

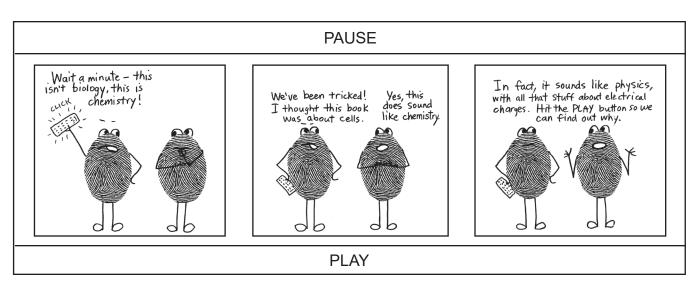
Lipids, on the other hand, "hate" water molecules. They are said to be "hydrophobic." The Greek word "phobia" means "fear," so perhaps they feel more fear than hatred? It is silly, of course, to say that molecules can love or hate or fear or have any other emotion. So, if molecules aren't actually loving or hating, what makes them react the way they do to water molecules? Let's look at a water molecule to find out.

A water molecule consists of an oxygen atom holding on to two hydrogen atoms. Remember, oxygen has two "arms" and can hold on to two atoms. Hydrogen atoms are very small and have only one "arm" with which to make a bond. The water molecule is a pretty happy molecule, since each atom is making the number of bonds that it wants to make. However, it does have one issue. The oxygen atom is much larger, with a nucleus that is 16 times larger than a hydrogen's nucleus. The eight protons in the oxygen's nucleus have a very strong

pull on the eight electrons that are being shared between the oxygen and the hydrogens. The result is that the electrons spend more time going around the oxygen than they do the hydrogens. The presence of the negatively charged electrons around the oxygen atom makes the molecule electrically lopsided. The side without the hydrogen atoms is slightly negative, and side where the hydrogens attach is slightly positive.

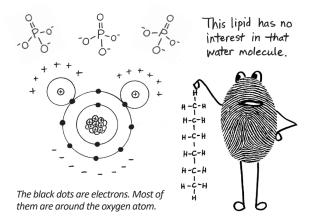
All molecules that are electrically lopsided are called **polar** molecules. "Polar" means that something has two ends, or sides, that are different. (Sometimes we think of the world "polar" as meaning "cold," because the north and south poles of the earth are located where it is cold, but the real meaning of "polar" is "opposite.")



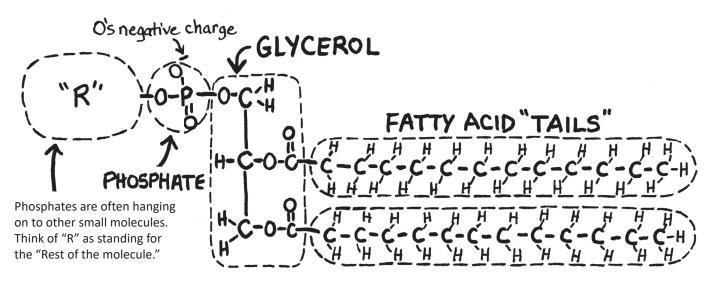


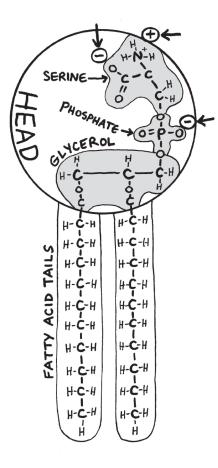
Chemistry is the foundation on which biology rests. The answers to many biology questions involve chemistry. And yes, chemistry is largely about the electrical interactions between atoms. So, in a way, biology boils down to physics. Let's continue on and see what role polarity plays in a membrane.

You may have heard the phrase, "Opposites attract." The context in which you heard the phrase might not have been physics, but the origin of this saying is rooted in physics. Positive and negative charges attract. The reason why this is true can only be explained by studying quantum physics, which is far beyond the scope of this book. All we need to know is that those dangling minus signs on molecules will want to be close to a molecule, or a part of a molecule, that has a positive charge. Those minus signs on the phosphate will be attracted to the positive side of a water molecule. But what about lipid molecules? If you look at the fatty acid that our friend is holding, you can see that there aren't any minus or plus signs around it. Therefore it doesn't interact with water molecules.



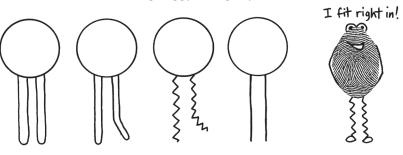
And, now, finally, we are ready to look at a phospholipid molecule. The name tells us that it is a phosphate connected to a lipid (a fatty acid carbon chain). A little clump of atoms called **glycerol** (GLISS-er-ol) holds them together. Glycerol is like a 2-sided clip that can hold on to both a phosphate and two carbon chains.





This is the most complicated phospholipid diagram you will see in this book. It shows that the "head" area is made of a glycerol, a phosphate, and another small molecule (here we see a simple protein called "serine"). The head isn't really round, but we can imagine that these odd-shaped molecules are contained in a circular area. The arrows are pointing to the electrical charges of the head area. We see two negative charges, and one positive charge, so the negative charges win by one. The overall charge of this head is (-1). This negative charge will be attracted to a water molecule's positive side. Some phospholipid heads have one positive and one negative charge, which makes them electrically neutral. They are still considered "hydrophilic" molecules, though, even without a negative charge.

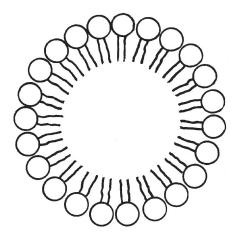
Now that we've seen the complete structure of a phospholipid molecule, we are going to learn a helpful shortcut. We'll need to draw lots of these molecules to make a cell membrane, and it's obvious that this molecule is far too complicated to draw repeatedly. Scientists use a simple diagram that is easily recognizable as a phospholipid. The tails can be thick or thin, and are sometimes zig-zaggy or slightly bent.

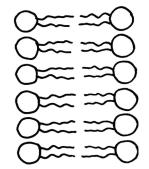


Now that we can easily draw a lot of phospholipids, we are ready to see how they behave as a group. What would happen if you took a bunch of these phospholipids and tossed them into a bucket of water? The heads would feel quite at home among the water molecules because they are hydrophilic, loving water. The hydrophobic tails, however, would be freaking out. It would be a nightmare for them to be surrounded by water molecules. They would need to cooperate to create a "NO WATER" zone where they can feel comfortable and safe. This is accomplished by having the phospholipids create a sphere where the tails are all pointing to the inside.

This shape is called a *micelle* (mie-SELL). (Though shown as a circle in this diagram, a micelle is actually a sphere.)

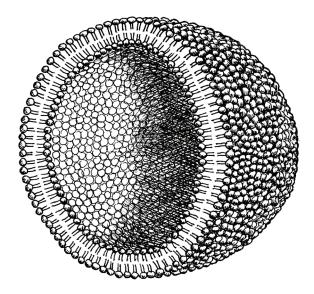
BONUS INFO: Micelles are found throughout your body, especially in your blood. They allow hydrophobic molecules (such as digested fats and some vitamins) to be transported in the bloodstream. Since blood is 90% water, the bloodstream is a very uncomfortable place for a molecule that hates water! The hydrophobic molecule hide inside the micelle.

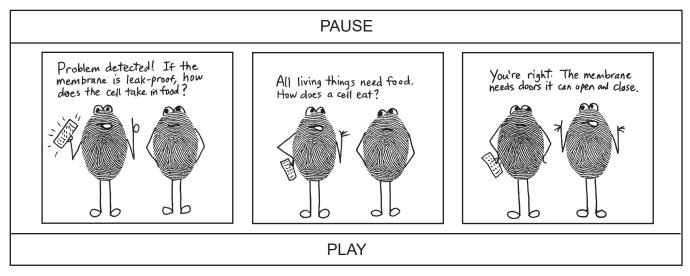




Another arrangement that phospholipids can make is called a *bi-layer*. ("Bi" means "two.") This shape is sort of what you would get if you took a micelle and flattened it. The diagram here on the left shows the phospholipids lined up perfectly, with the tails of one molecule exactly opposite the tails of another. In reality, they don't always line up so perfectly. (Notice the optical illusion: a white line down the middle.) If we had a large, three-dimensional sheet of bi-layer we might be able to fold it in such as way that it formed a hollow sphere. If we use hundreds, or perhaps even thousands, of phospholipid molecules, we can make a sizable sphere. Look at the cut-away edge. Can you see all the individual phospholipid molecules lined up tail to tail, forming a bi-layer? If we had not cut the sphere in half, you would not be able to see the tails. The surface of the sphere would look like a "sea" of balls.

Now we have a nice, tight, almost leak-proof ball. Very small molecules, such as oxygen or carbon dioxide, might sneak through the cracks, but large molecules don't stand a chance of getting through. This is what the outer layer, or *plasma membrane*, of a cell is made of. Most of the organelles inside a cell are also wrapped in a bi-layer membrane. Additionally, the cell makes and uses spheres like this for storing things, almost as if they were plastic bags.



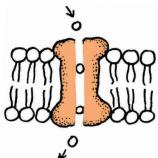


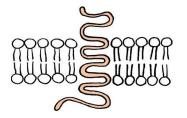
Yes, the membrane needs doors and portals that it can control. Now that we understand the structure of the membrane itself, we can look at the microscopic "gadgets" that are in it.

Many of the structures that are embedded in a cell's membrane are made of **protein**. They are called (no surprise here) **membrane-bound proteins**. In future chapters we'll learn what proteins are made of and see how the cell manufactures them. For now, we are just going to take a brief survey of the general types of proteins we find and the jobs they do. Membrane-bound proteins can be found on the outside, on the inside, or going all the way through membrane.

Proteins that go all the way through the membrane are called *transmembrane proteins*. ("Trans" is Latin for "across.") They act as **tunnels**, or **portals**, letting some types of molecules pass through and keeping others out. A cell wants to take in food molecules (sugars, fats, proteins) and get rid of waste molecules. It might also want to take in a chemical message sent by another cell. Some transmembrane proteins act like **pumps**, pushing water or salt molecules in or out of the cell.

Another type of transmembrane protein acts like a **switch**. When you flip a light switch, it moves internal parts that are hidden in the wall, and the





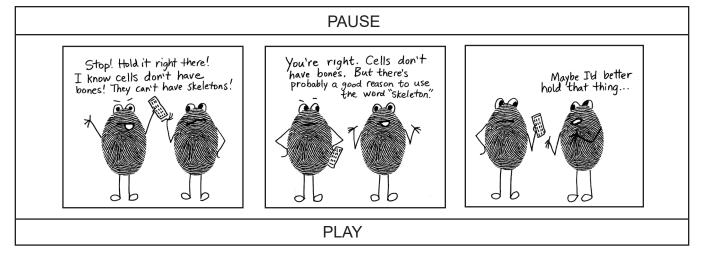
result is that electricity flows into a light bulb. A cell has biological switches with an external part that can be triggered by something in the cell's environment, and an internal part that reacts to the stimulus and makes a change inside the cell. Proteins attached to the outer surface of the cell are properly called *peripheral membrane proteins*. (Peripheral means "on the outside.") Here are some examples of jobs they might do:

1) Act as a **flag**, identifying the cell as belonging to the organism it is part of, so that it doesn't get attacked by immune system cells who are out looking for foreign invaders. Cells don't have eyes and can't see; they rely on their sense of touch to identify things around them. Immune system cells feel the surface of any cell that crosses their path. If they feel this ID flag, they know not to attack the cell. If this flag isn't there, the battle is on!

2) Act as a **mailbox**, receiving messages from other cells. Cells are usually part of a larger organism and they must all work together to keep themselves alive. They communicate by sending chemical messages to each other. These messenger molecules have a particular shape that will only fit into a receptor that has a complimentary shape, like a key into a lock.

3) Act as an **anchoring hook**, allowing the cell to stick to other cells. These proteins can grab and hold on to the corresponding anchor proteins of other cells. Some anchoring mechanisms are designed to hold the cells tightly together. Other mechanisms allow for a looser, more flexible attachment. The anchoring hooks between skin cells (shown here) are called **desmosomes**. Desmosomes allow your skin to be very strong yet very flexible.

The proteins on the inner side of the membrane most often function as a place to attach things to, sort of like a hook or clip stuck into a wall. The most common cell part that needs to be anchored to the membrane is the cell's skeleton.

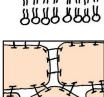


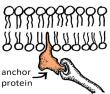
We'll learn about the cell's skeleton in the next chapter. No, cells don't have bones; but they do have rafts...

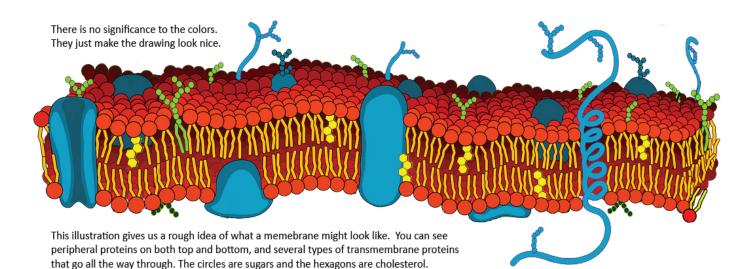
Some cell processes require more than one of the protein structures that are embedded in the membrane. Think of how many tools a carpenter needs to build something. All the tools and materials must be right there within reach so that he can do his job. Imagine if the carpenter's tools kept wandering off all the time because the floor was in constant motion. He turns around to grab the saw and it's not there. He must go and search for it, and by the time he gets back his lumber is missing. And when he is ready to nail something, his hammer is gone. He spends all his time trying to keep his tools in one place and never actually gets the job done. Fortunately, this would never happen because we live in a world where gravity and friction keep objects (on flat surfaces) firmly in place.

The surface of a membrane, however, is quite unlike the firm floors on which we place our furniture and our tools. The phospholipids are not tied together and are probably in constant motion. How much they move is still being researched, but most scientists think that the membrane forms what they call a *fluid mosaic*. The word "mosaic" is used by artists to describe a picture or pattern that is formed by many small objects such as colored pebbles or pieces of colored glass. The word "fluid" means "in motion." (Imagine a small pond completely covered by floating ping-pong balls. A ball would not be able to travel across the pond but would still be able to shift its position quite a bit.)

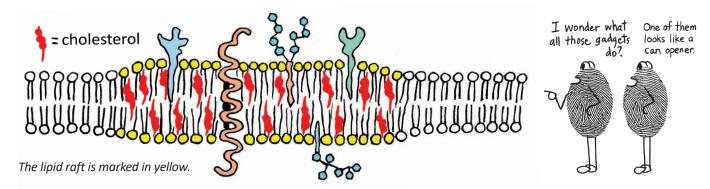


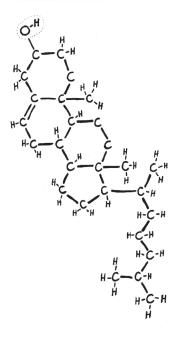






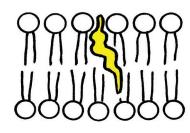
If the phospholipids in the membrane can shift their position and move about, this creates a problem for structures that must work together. How will they stay together so they can work together? One answer is to secure all of them into a structure called a *lipid raft*. The raft is made of a certain type of phospholipid that is very good at sticking to another molecule that is present in all membranes: *cholesterol*. You may have heard the word "cholesterol" used during a discussion about foods that are bad for you. Cholesterol is a lipid molecule that your body makes, but you can also consume it in your diet. It is most often found in food that contain animal fats. Eating too much cholesterol can sometimes be a problem, but the molecule itself is not "bad." Cholesterol helps to hold fatty acid tails together. Lipid rafts are areas that contain many cholesterol molecules. The protein structures embedded in these rafts stay in place. The rafts themselves seem to be able to move about, but the movement of the entire raft does not interfere with the ability of the protein structures to do their job. (Imagine a clump of those floating ping-pong balls that are glued together.)



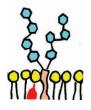


The cholesterol molecule is a member of a group of molecules that are based on hexagonal (6-sided) rings of carbon atoms. Other members of this group include vitamin D, and hormones such as testosterone, estradiol, progesterone, and cortisol. (You don't need to remember these names.)

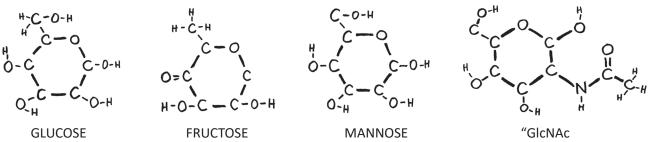
You can see that the cholesterol molecule has three hexagonal rings of carbon, one pentagon, and a "tail" of carbons that reminds us of a fatty acid. The entire molecule, except for the O-H part at the top, wants to be tucked into the fatty acid tails of the phospholipids. The O-H is hydrophilic like the heads, so it stays as closes to the heads as it can. Since this molecule is so complicated, you'll see a variety of short-cuts, some of them with neat hexagons, and others very blobby.



Before we end this chapter, there's one last feature of the membrane that must be mentioned. If you looked carefully at the illustrations on the previous page, you may have noticed strings of little circles or hexagons. They represent sugar molecules. As funny as it might sound, cells are "sugar coated."



The smallest and simplest sugar molecules are hexagonal in shape and made of carbon, oxygen and hydrogen atoms. (The last one is a special sugar that include a nitrogen atom.)



(You might be wondering where "table sugar" fits into this scheme. Table sugar, or "sucrose", is made of a glucose molecule attached to a fructose molecule. Your digestive system breaks them apart and puts them into your blood. Your cells take in the glucose molecules and then break them apart to harvest energy.)

Sugars can be used as a source of energy, but your cells can also use sugars for many other purposes. Just like wood can be either burned for energy or used to make furniture, sugars can also be either "burned" for energy or used to build things. The sugars that the cell uses to build things include these simple sugars shown above, but also include more complicated variations. It isn't necessary for us to go into the chemistry of these more complicated sugars to appreciate what they do. Here are some examples of ways that various sugar-based molecules are used by cells. (Let's called them by their official name: *glycans.* The root "glyc-" means "sugar.")

**1)** Glycans can function as "**mailing labels**," helping manufactured parts to get to their destination inside the cell. (We will mention this again in the chapter on Golgi bodies.)

**2)** Your red blood cells have short glycans sticking out of their membranes, and, depending on what the string looks like, your blood will be "typed" as **A**, **B**, **AB**, **or O**. (There are other blood types, as well, though we don't hear much about them because a mismatch is not life-threatening like the ABO types.)

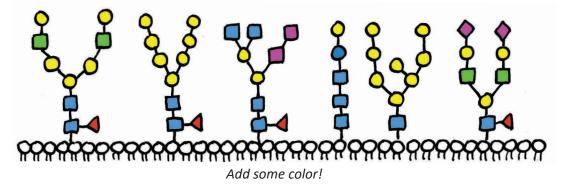
**3)** A sugar called "O-GlcNAc" is a key player in **cell division**. Scientists used to think that cell division (the cell cycle) was controlled by proteins called cyclins. Then new research revealed that these proteins were being controlled by glycans, especially O-GlcNAc. Too much of this sugar was as bad as too little—either way, things went terribly wrong when the cell duplicated itself. A new cell might end up with two nuclei, or with a wrinkled, weird-looking nucleus where all the DNA was crumpled on one side.

**4)** A dense coat of glycans can act as a **protective coating**. Bacterial cells are the most striking example of this "sugar-coating," but all cells make at least some protective sugars. One way this protection can happen is by "hiding" the cell's peripheral proteins from the natural, protein-dissolving chemicals that roam throughout the body looking for bits of protein "garbage" that need to be recycled.

5) Certain glycans on key molecules help to control the growth of embryos.

6) Glycans can act as **clips** that hold molecules in a storage area, so the molecules will be ready to go if the need arises.

7) The cells of our immune system use a "sugar code," using glycans to communicate with each other.



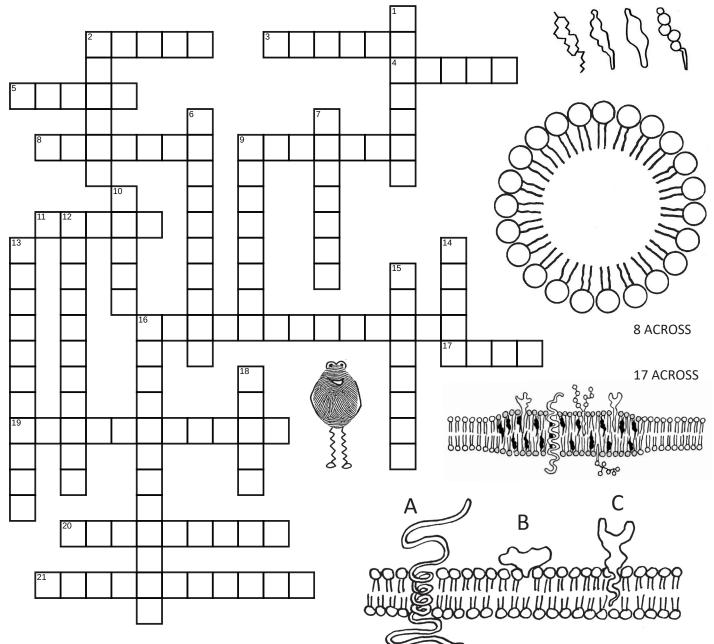
Diagrams always give you a key to let you know which shapes represent which types of sugars. For example, here we have squares for GlcNAc, circles for mannose, diamonds for glucose. Don't forget to check the "Cells" YouTube playlist for animations of what you just read!

# <u>Comprehension self-check</u> If you can't think of the answer, go back and read that part of the chapter again until you find the answer. If you need to check your answers, check the answer key.

- 1) The word "lipid" means: a) protein b) fat c) sugar d) membrane 2) The most natural shape for a group of phospholipid molecules to make is: a) flat surface b) ball c) long line d) cytoskeleton 3) How many bonds (to other atoms) can an oxygen atom make? \_\_\_\_\_ (Look at the water molecule, for example.) 4) How many bonds can a phosphorus atom make? \_\_\_\_\_ (You can count the lines coming out of it.) 5) What does glycerol do in the phospholipid molecule? a) keep the phosphate and the lipid together b) push the phosphate toward water c) push the lipid away from water d) allow the cell to stick to other cells 6) Which hates water? a) the phosphate head b) the lipid tail 7) Where would you find a membrane-bound protein? a) all the way through the membrane b) stuck to the inside of the membrane c) stuck to the outside of the membrane d) all of the above 8) Which of these elements would you NOT find in a phospholipid molecule? a) carbon b) potassium c) nitrogen d) hydrogen e) oxygen f) phosphorus 9) Which one of these would you NOT find as part of a phospholipid molecule? a) glycerol b) fatty acids c) water d) phosphate e) serine 10) TRUE or FALSE? Micelles are made and used in your body to transport fats through the blood. 11) TRUE or FALSE? A micelle is a made of a bi-layer of phospholipids. 12) TRUE or FALSE? The only place you find phospholipid bi-layers is the outer layer of a cell. 13) TRUE or FALSE? Tiny molecules, such as oxygen, O<sub>2</sub>, might be able to go through a phospholipid bi-layer, but larger molecules cannot. 14) TRUE or FALSE? The correct name for the outer membrane of a cell is the "plasma membrane." 15) Which one of these is *least likely* to be an example of a transmembrane protein function? b) portal c) anchor d) pump a) tunnel 16) What happens to cells that do not have an ID flag on their surface? a) Nothing. b) They take one from another cell. c) They are killed by immune system cells. 17) Which one of these is NOT a function that a protein on the outside of the membrane might perform? b) act as a mailbox to receive messages a) act as an ID flag c) act as an anchor for the cytoskeleton fibers d) act as an anchor for "cables" that attach to other cells 18) The word "mosaic" means: a) a moving picture b) pattern made with tiny pieces c) surface layer 19) This substance is found through the membrane but is particularly concentrated in lipid rafts: a) cholesterol b) phosphate c) glycerol d) water e) phospholipids 20) Which one of these is something that sugars do NOT do?
  - a) act as protective coating around the cell b) allow cells to communicate c) control growth d) act as mailing labels for product made insdie the cell e) act as channels that allow molecule to enter cell

## ACTIVITY 2.1 Review crossword puzzle





#### ACROSS:

2) Glucose and fructose are examples of \_\_\_\_\_ molecules.3) The appearance and texture of cell membranes is often described as a fluid \_\_\_\_\_.

- 4) The person who gave us the name "cells."
- 5) The scientific name for fat is \_\_\_\_\_.
- 8) A <u>single</u> layer of phospholipids forming a ball shape.
- 9) Sugars most often take this 6-sided geometric shape.
- 11) Sugar tags known as A, B and O are found on \_\_\_\_\_ cells.

16) Proteins that go all the way through a membrane are called \_\_\_\_\_\_ proteins.

17) An area of membrane dense with cholesterol that keeps phospholipids and proteins together is called a \_\_\_\_\_.

- 19) This molecule has 3 hexagonal rings and a tail made of a string of carbons, and helps to keep phospholipids together.20) This molecule is made of 1 phosphorus and 4 oxygens.
- 21) A molecule that "hates" water and won't interact with it.

### DOWN:

- 1) This scientist worked with Schleiden to develop "cell theory."
- 2) Protein A, shown above, probably acts as a \_\_\_\_\_.
- 6) Protein B, shown above, is a \_\_\_\_\_ protein.
- 7) Protein C, shown above, probably acts like a \_\_\_\_\_.
- 9) Cholesterol is similar to both vitamin D, and a group of molecules called \_\_\_\_\_.

10) Water is a \_\_\_\_\_ molecule because electrons spend more time circulating around the oxygen atom.

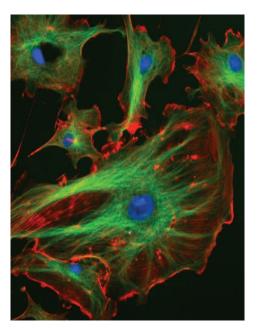
- 12) This scientist is called the "father of microscopy."
- 13) Sugar codes can allow immune system cells to \_\_\_\_\_.
- 14) One oxygen atom and 2 hydrogens make \_\_\_\_\_.
- 15) This type of electron microscope gives us 3D images.
- 16) This type of electron microscope gives us flat images.
- 18) This scientist gave us the word "nucleus."

# **CHAPTER 3: THE CYTOSKELETON AND MOTOR PROTEINS**

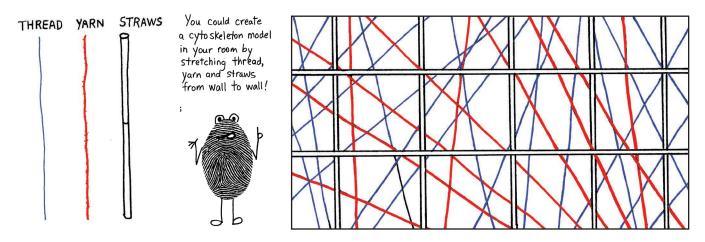
Inside their membranes, cells are filled with a watery fluid called *cytosol*. The word "cyto" means "cell," and the ending "-sol" is short for "solution." The term *cytoplasm* is also used to describe the watery insides of a cell, but this term includes not only the fluid but also small things that are floating around in it. It can seem like these words mean the same thing because science writers use them almost interchangeably. To be fair, in many cases it doesn't really matter which word the writer chooses because either word will fit the meaning of the sentence. A helpful analogy might be to think of a can of soup. If the can is the membrane, the soup is the cytoplasm. If the soup is chicken noodle, it has noodles and bits of chicken floating in broth. The word 'cytosol" would correspond to the broth. The words "soup" and "broth" are very similar, but we can use the more specific word "broth" when we want to talk about only the liquid element of the soup, not the things floating in it. In many conversations, the word "soup" is good enough and we don't have to be any more specific than that.

In 1903, a Russian scientist proposed that cells must have some kind of network inside that helps them keep their shape. He reasoned that if cells were nothing but a bag of liquid, they would be too easily flattened. The cells he saw in his microscope were anything but flat. This proposed network of fibers was nothing but a theory until the 1970s, when scientists discovered a way to detect fibers too thin to be seen under a microscope. Trying to see these filaments in the cytosol is like trying to see fishing line underwater. Both are transparent, and the fishing line is very thin. (That's the whole idea—the fish can't see it!)

The breakthrough came in the 1970s. Someone discovered a natural molecule (antibody) that would stick to these invisible fibers. This natural molecule could be stained with fluorescent dyes that glowed green or red. If you put these stained molecules into a cell, they would stick to the fibers and make them show up as brightly colored lines. The images produced in these experiments were stunning. They showed organized networks of filaments, like a three-dimensional system of roads and highways. It was obvious that this network of fibers acted as a structural support, so it was named the **cytoskeleton**.



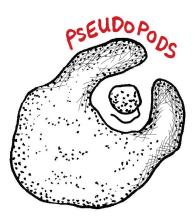
With further research, scientists discovered that the cytoskeleton not only helps the cell to maintain its shape, but also functions as a transportation system. It really does act like a system of roads and highways. The roads come in three sizes: small, medium and large. The scientists who discovered them gave them these names: *microfilaments, intermediate filaments and microtubules*. If we were to make a model of a cytoskeleton we might use thread, yarn, and drinking straws to represent these fibers.



The smallest ones, the *microfilaments* (the thread in our model) are made of protein molecules called *actin*, so the filaments are also known as *actin filaments*.



The microfilaments are very important to the overall shape of the cell, and can also help the cell to change its shape. If a cell wants to move, it quickly builds a whole bunch of new microfilaments in that direction. The cell can build these at the rate of thousands per second. As the new microfilaments are built, they push the flexible membrane outward. Cytoplasm flows along with the microfilaments. Together they create what is called a **pseudopod**, or "false foot." (Can you see the tiny microfilament lines in the pseudopods in this diagram?) We have white blood cells in our bodies that form pseudopods in order to surround and capture bacteria and viruses. Single-celled organisms like the ameba (old spelling: amoeba) also use pseudopods to move through their environment. In fact, this type of movement is often called "ameboid motion." The balls represent little units of actin protein. More about protein later in the book.





Microfilaments are also very important when it is time for the cell to reproduce by splitting itself in half. The microfilaments cause the cell to "pinch" in the middle, in preparation for the splitting process.

In some types of cells, such as muscle cells, we find actin filaments being used as a track along which another protein, *myosin*, can travel. The interaction between actin

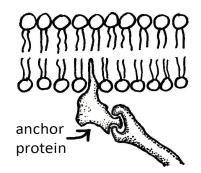
and myosin is what allows you to move your muscles. Most anatomy courses cover this topic quite thoroughly, so we'll just give it a brief mention in the last chapter when we look at various types of cells.

The medium-sized *intermediate filaments* (the yarn in our model) are especially abundant in nerve cells, skin cells, and muscle cells. They form a stretchy lattice inside the cell that help to give it strength. In skin cells, an intermediate filament called *keratin* forms a very strong, stretchy network that gives skin its flexibility and durability. It adheres to several types of anchor proteins in the membrane. One type allows skin cells to make strong connections to each other.

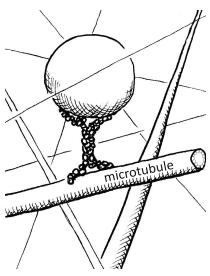
What would happen if something went wrong with the manufacturing process and the cell accidentally made these protein anchors the wrong shape? The intermediate filaments would not stay anchored. When this happens in muscle cells, it can cause a condition called muscular dystrophy. A person with this condition has very weak muscles. When intermediate filaments (keratins) in skin cells are the wrong shape, it causes life-threatening skin diseases.

The largest filaments, the *microtubules* (the drinking straws in our model), really do look like tubes. These tubes are the "highways" that the cell uses to move things about. What does a cell need to move?

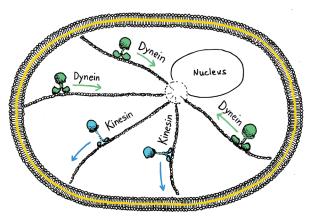
Some of the cell's organelles act like little factories and make proteins, fats and enzymes for their own use or to ship out to other cells. These products are then "packaged" into vesicles made of phospholipid membrane. The packages can't move on their own, so something has to take them to where they need to go. When it was discovered how this transport happens, scientists could hardly believe their eyes—they saw little proteins with "feet" that were "walking" along the microtubule roads! These **motor proteins** move like tightrope walkers at a circus, putting one foot in front of the other along the narrow rope. They carry their cargo as if it was a huge sack resting on their shoulders. How the motor proteins know where to go is still being studied.



The shapes of the anchor proteins match the ends of the filaments a bit like like jigsaw puzzle pieces that fit together.

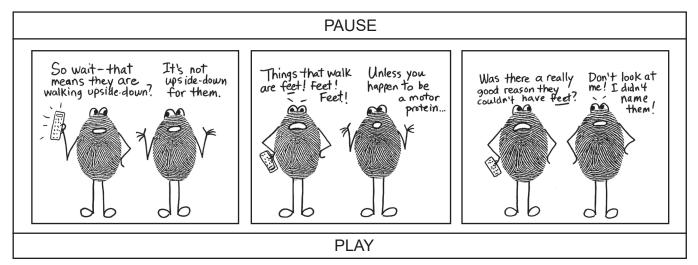


There are several types of motor proteins. The ones that are most abundant (and therefore the most studied) are called *kinesin* (*kin-EE-sun*) and *dynein* (*DIE-nin*). As a general rule, they seem to "walk" in only one direction. Kinesin carries things away from the central nucleus and towards the outer membrane. Dynein goes the opposite way, carrying things from the outside towards the center. When they get to the end of the line and have fulfilled their mission, they often drop off the tubule and eventually float back towards their starting point. Then they receive new instructions and are off on another mission. They probably won't attach to the same tubule they used for the previous mission. Their missions can be as short as a few seconds or as long as a few minutes. If a kinesin and dynein run



into each other, one of them will probably fall off, or dynein might side step long enough to let kinesin pass.

Now, here comes the tricky part. The things that look like feet on a motor protein are actually called *heads*. And the things that look like its hands (holding the load) are actually called its *tails*.

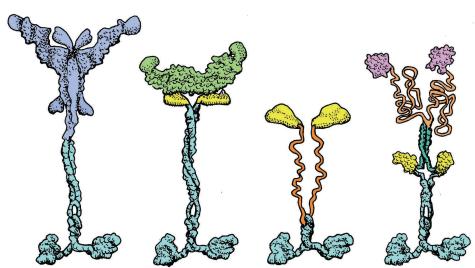


Yes, it is unfortunate. Sorry. But let's learn a little more about these heads and tails.

The shape and structure of motor protein heads is pretty standard because they all have to walk along the same tubule roads. Their tails can be quite different, though, because a particular shape is needed to connect to a particular type of cargo. The part

particular type of cargo. The part of a motor protein that connects to the cargo is called the **binding site**. (This term is also used for the place on each head that touches the microtubule.) So far, scientists have identified about 40 types of cargo binding sites. This picture shows four different kinesins. The one on the left is considered "standard" (the most common kinesin) and the others are variations.

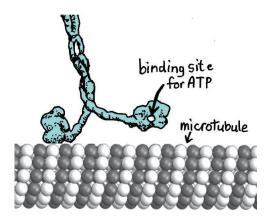
Make sure you watch the recommended videos listed at the end of this chapter so you can see these guys in action!



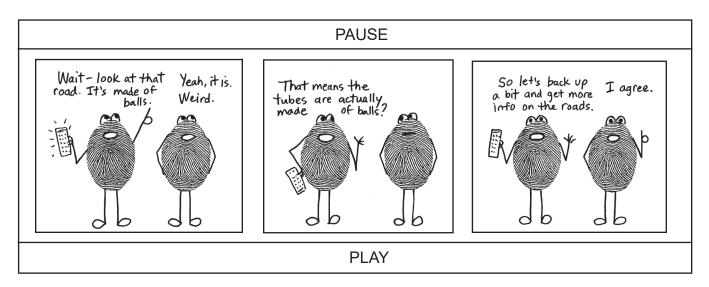
Notice that the heads (feet) all look the same. The tails (top) are specialized for different cargo. They don't have any natural color, but scientists often add color to diagrams.

With each step a motor protein takes, it will use a tiny energy molecule called ATP, which we will study in the next chapter. These steps occur very quickly, much faster than you can walk. One researcher saw a motor protein talking 100 steps per second. This would be like you running as fast as a car on a highway! They can also carry loads much larger than themselves, the equivalent of you towing a house. For exceptionally large cargo, several motor proteins can work together.

When a motor protein wears out (after only a day of action) it will be taken apart and its parts recycled, as if it was a used car. There are tiny factories inside the cell that are constantly using the atoms and molecules from the old motor proteins (and from other recycled cell parts) to make new ones.

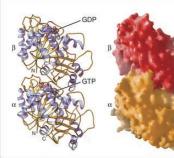


How important are these motor proteins to the life of a cell? Well, just imagine what would happen to your town or city if many of the cars and trucks stopped working. Mail might not get delivered, food would not be shipped to grocery stores, hospital workers might be stuck at home, and construction materials might never arrive at construction sites. Everyone in the town or city would be eventually be affected by the failure of the transportation system. When things go wrong with a cell's transport system, the result is often a very serious disease.



Microtubules are made of tiny individual units of protein called *tubulin*. (As mentioned previously, we'll learn exactly what protein is in a later chapter.) There are two types of tubulin: *alpha* tubulin and *beta* tubulin. You will see the words "alpha" and "beta" used a lot in biology. They are Greek words for the letters A and B.

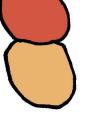
One alpha and one beta tubulin snap together to make a pair that stays together. There is a special word for a pair of molecules, a word that is easy to pronounce and to spell: *dimer*. ("Di" is Greek for "two.") The cytosol of the cell is FULL of these tubulin dimers. They are simply everywhere!



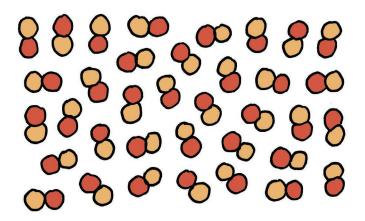
Most accurate drawing of tubulin.

Slightly simplified way

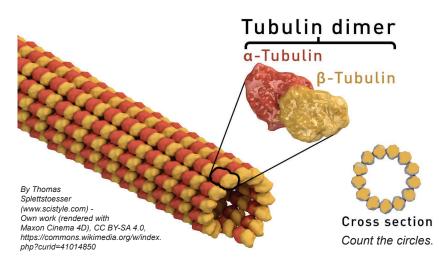
to draw it.



Simple enough for us to draw!



When two dimers bump into each other, they can stick together if a tiny molecule called GTP is present. GTP is similar to ATP, the energy molecule that motor proteins use. GTP fits into a little pocket in the tubulin molecule. When it sticks, it changes the shape of the dimer just slightly, making it a little more straight. Once it has been

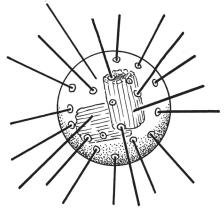


straightened, the tubulin dimer will be able to stick to other dimers. When there are many straightened dimers, they will forms long lines, then the lines will stick together to form sheets. The sheets will curl up to form tubes. (Video animations can show you this process in action. Be sure to check out the videos on the Cells playlist, or search for some on your own.)

Often there are "helper proteins" in the area, too, that will come alongside the forming tubes and help to add more dimers to the growing ("positive") end.

If we look at the end of a tubule, we can count exactly how many dimers it takes to form the tube: 13. Isn't that an odd number to find in something biological? Although it is one of the Fibonacci numbers (1, 2, 3, 5, 8, 13, 21, 34, 55, etc.) it only shows up occasionally in a flowering plant.

Microtubules are not scattered randomly around the cell. Like a welldesigned city, the cell's roadways are very organized. There is a central "hub" for the microtubules, like a railway station from which all the train tracks branch out. This central station is called the *centrosome*. ("Som" or "soma" is Greek for "body," but it is often used in the same way that we use the word "thing.") The centrosome is also called the *microtubule organizing center* of the cell. It is made of two *centrioles* surrounded by a blob of protein gel. The little places where the microtubules are attached are cone-shaped structures (made of another type of tubulin) that acts like a foundation platform on which a microtubule can start to grow. The attached ends of a tubule are called the "negative" ends. Dynein walks towards them.

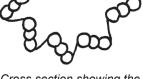


If we take a close-up look at those barrelshaped centrioles inside the centrosome, we can see that they are made of microtubules arranged in a very precise pattern. Three microtubules get bundled together in a straight line. Then nine of these flat bundles are arranged into a circle. Some thin protein fibers hold them in place.

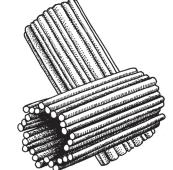
Notice that the centrioles are perpendicular to each other, making an "L" shape. They always stay in this position.

Don't pause the book—we are almost done learning about the cytoskeleton! Before we end the chapter, however, we need to mention two other important jobs that microtubules do, besides their role as a road system: they help a cell to make a copy of itself, and can form

All living organisms must be able to grow, and growth occurs through the process of cell division. Cells are able to split in half, forming two identical copies of themselves. During this duplication process, the cell must make a second copy of its DNA. (We'll learn about DNA in a future chapter, but you probably already know that DNA is like a library, containing all the information the cell will ever need.) The two sets of DNA must be pulled apart and taken to opposite sides of the cell so that when the split occurs, each side will have a full set of DNA.

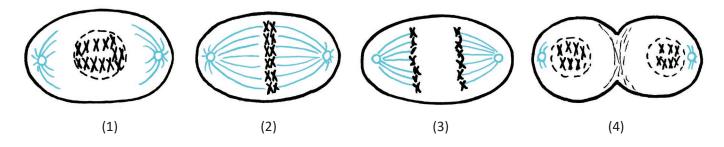


Cross section showing the "end view" of the centriole

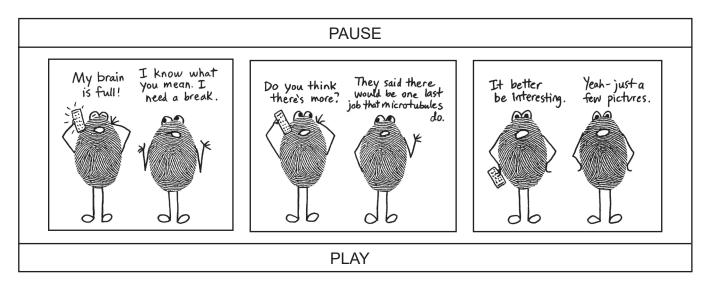


First, the cell duplicates its centrosome so now it has two of them. The centrosomes go to opposite sides of the cell, as shown in diagram (1). Meanwhile, the DNA duplicates itself inside the nucleus. During the duplication process, the DNA coils up into long sticks called chromosomes. The covering around the nucleus dissolves so that the chromosomes are sitting out in the open in the middle of the cell. The rest of the diagrams have all the other cell parts removed so that we can focus only on what happens to the chromosomes.

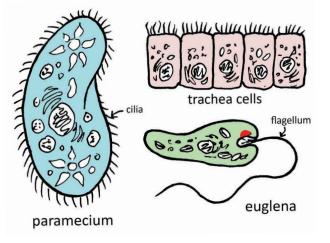
The two sets of chromosomes must be separated and pulled to opposite sides of the cell. In diagram (2), we see the centrosomes form a shape called a *spindle*, which in made from microtubules and looks a bit like an American football. In the middle of the spindle, the microtubules attach to the chromosomes. The microtubules then begin to pull the chromosomes apart, as shown in diagram (3). The pulling is caused by the microtubules beginning to disassemble themselves so they get shorter and shorter. Finally, the two sets of chromosomes are completely separated and arrive at opposite ends of the cell, as shown in diagram (4). The cell is now ready to split in the middle and form two independent cells. Microfilaments will help do the pinching in the middle.



We will study this more in a later chapter. The main point we need to learn now is that microtubules play an important role in cell division by forming a spindle that pulls chromosomes apart.



Microtubules are used in some specialized cells to make things that look like hairs or tails. The hairs are called *cilia* and the tails are called *flagella*. These structures allow the cell to move by acting like paddles (cilia) or propellers (flagella). Cilia are used by single-celled animals like the paramecium, but are also found in our own bodies in the cells that line our trachea (the tube that goes down into our lungs). Flagella are used by many single-celled animals, but are also found in sperm cells made by most living organisms.



# Can you remember what you read? If you can't think of the answer, go back and read that part of the chapter again until you find the answer.

1) What is the fluid inside a cell called? or
2) Which one is made of a protein called actin? a) microtubules b) microfilaments c) intermediate filaments
<ul> <li>3) Which one of these (as far as we know) is NOT something a microfilament might do?</li> <li>a) cause a muscle fiber to move b) act like a road for motor proteins</li> <li>c) help a cell to divide in half d) allow the cell to move using pseudopods</li> </ul>
4) TRUE or FALSE? The only cells that move using "ameboid" motion are single-celled organisms like the ameba.
<ul><li>5) Which one of these is attached to the membrane using anchor proteins in the membrane?</li><li>a) microfilaments</li><li>b) intermediate filaments</li><li>c) microtubules</li><li>d) all of these</li><li>e) none of these</li></ul>
6) Which of these motor proteins walks outward, towards the edge of the cell? a) kinesin b) dynein
7) Which part of a motor protein touches the microtubule highways? a) tails b) feet c) heads
8) How long (as far as we know) is the lifetime of a motor protein? a) days b) weeks c) months d) years
<ul> <li>9) How fast (as far as we know) can a motor protein travel?</li> <li>a) one step per second</li> <li>b) one step per minute</li> <li>c) 100 steps per second</li> <li>d) 100 steps per minute</li> </ul>
10) What tiny energy molecule does a motor protein need in order to move? (three letters)
<ul> <li>11) Which one of these does the cytoskeleton NOT do?</li> <li>a) form new phospholipid membranes</li> <li>b) help the cell maintain its shape</li> <li>c) transport things across the cytoplasm</li> <li>d) form pseudopods</li> </ul>
12) The protein unit that microtubules are made of is called: t
13) A pair of molecules that is bound together is called a d
14) How many protein units are need to form a microtubule circle? a) 8 b) 9 c) 11 d) 12 e) 13
15) Which of these word roots means "body"? a) cyto b) soma c) pseudo d) pod
16) A centrosome is made of two in a blob of protein gel.
<ul><li>17) What does the centrosome do? a) acts as a gathering point for all the proteins floating around the cell</li><li>b) builds microtubules c) organizes microtubules d) All of these e) b and c</li></ul>
<ul><li>18) What does the spindle do? a) pulls chromosomes apart b) makes centrosomes</li><li>c) gives shape to the cell d) duplicates chromosomes</li></ul>
<ul><li>19) Which type of fibers help the cell to pinch in the middle and form two new cells?</li><li>a) microfilaments</li><li>b) intermediate filaments</li><li>c) microtubules</li></ul>
<ul><li>20) Microtubules are used by specialized cells to make structures (cilia and flagella) that allow them to:</li><li>a) divide in half</li><li>b) be identified by other cells</li><li>c) use oxygen</li><li>d) move</li></ul>

## ACTIVITY 3.1 "Must-watch" videos

NOTE: The original posters of the videos can decide to take down their videos. In some cases, someone else will put the video back up again, but the address will have changed. Check the Cells playlist for these videos, but if they are not there, try searching for them using key words.

### 1) "A Day in the Life of a Motor Protein"

This video has over a million views on YouTube. (If you can't access YouTube, check for it on other videos streaming services.) A biology lab at the University of Utrecht, in the Netherlands, put together an informative and marvelously funny animated film about kinesin and dynein. The cell in which these particular motor proteins live is a nerve cell, so the film starts out with a little information about this type of cell.

#### 2) "The workhorse of the cell: Kinesin"

This video also has a lot of views, so it should pop right up in a search. The animation is fabulous and will bring to life everything you read about kinesins in this chapter.

#### 3) "White blood cell chases a bacteria"

Another video with millions of views and posted from multiple sources. White blood cells use their cytoskeleton to change their shape very quickly. In this video clip you can see a white blood cell chasing some bacteria. It does catch one at the end.

WHILE YOU ARE AT THE PLAYLIST, CONSIDER WATCHING THE OTHER VIDEOS ABOUT THE CYTOSKELETON.

## ACTIVITY 3.2 Kinesin vs. Dynein strategy game

This is a two player game. It takes only a few minutes to play. The point of playing the game is to reinforce the fact that motor proteins go in only one direction. **Kinesin** (*kin-EE-sin*) goes away from the nucleus, and dynein (*die-nin*) goes towards it. The board represents a cell with a very simple microtubule arrangement.

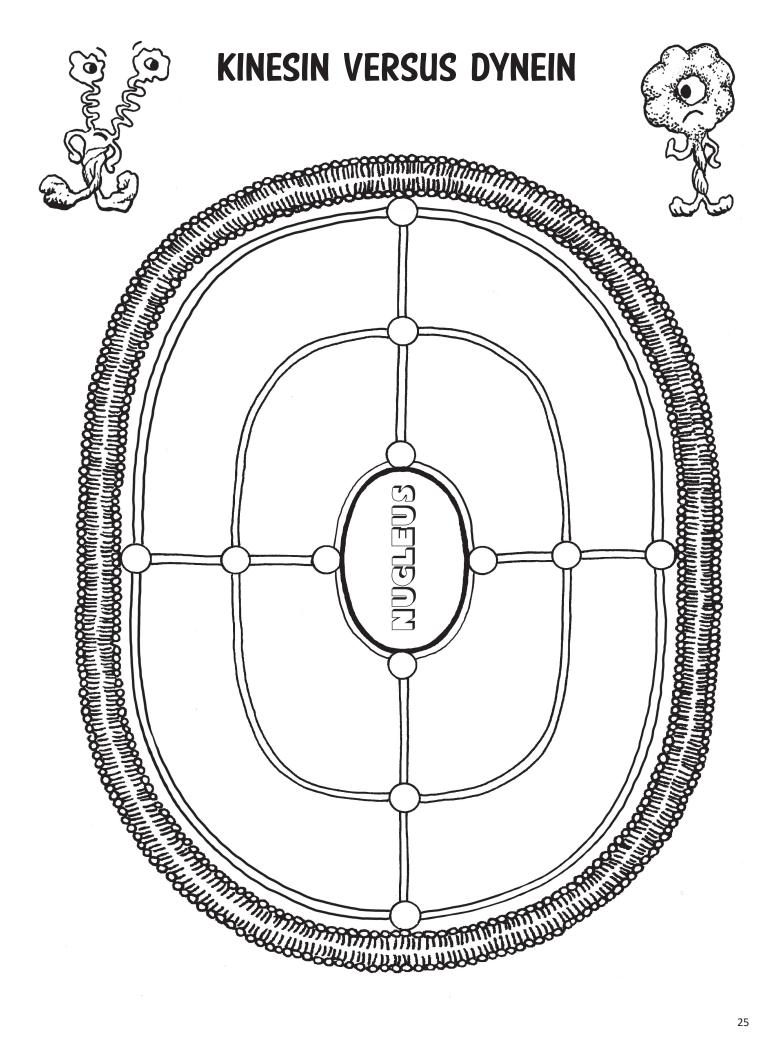
You will need eight coins. Mark four of them with the letter K, and the other four with the letter D. You can use a permanent marker, or you could write the letters on paper circles and tape them on. If you have "sticky notes," you could cut pieces from the sticky strip of the note. (Using coins will give the tokens some weight so that if someone coughs or sneezes, the tokens won't blow off the board.)

Put the K tokens on the circles that are close to the nucleus. The goal of the K player will be to get the tokens out to the circles near the plasma membrane.

Put the D tokens on the circles that are close to the outer membrane. The goal of the D player will be to get all the token into the circles close to the nucleus.

Players will take turns making a move. The K pieces can ONLY go either <u>away</u> from the nucleus, or side to side, around the circle that they are currently on. The D pieces can ONLY go either <u>towards</u> the nucleus or side to side, around the circle that they are currently on. Players MUST make a move on each turn. Remember, the tokens can't go "backwards." Once they have advanced to another ring, they can't go back. They can go around that ring, but they can't go back to the previous one they were on.

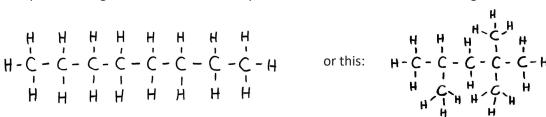
The first player to get all their tokens to their destination wins the round.



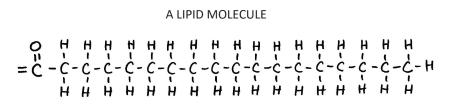
# **CHAPTER 4: ATP AND THE MITOCHONDRIA**

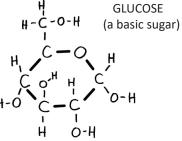
Cells use a lot of energy. It takes energy for those motor proteins to walk along the cytoskeleton highway. It takes energy to build molecules. It takes energy to create pseudopods. Everything the cell does requires energy. Where do your cells get energy? The process begins with the food you eat. You know that your food is digested in your stomach and intestines, so that its molecules can be absorbed into your blood and distributed to your cells. But exactly how do your cells process the food molecules and harvest energy from them?

Surprisingly, human bodies are not that different from cars. Engines that run on gasoline use combustion to break apart the long carbon chains found in petroleum molecules. A molecule of gasoline looks something like this:



Both of these molecules have eight carbons with hydrogens attached to them. Compare these gasoline molecules with two types of molecules your body uses for energy: fat and sugar:





This is actually the lipid tail from our phospholipid molecule.

The similarity is striking, isn't it? All of these molecules are basically strings or clumps of carbon atoms with hydrogens attached to them. The edible molecules have a few oxygens thrown into the mix, too.

Basically, our food is not that different from gasoline. The way an engine gets energy out of a fuel molecule is to apply a spark to it, causing it to explode. The explosion happens inside a metal cylinder that contains a movable piston. The motion of the piston is then transferred, by various shafts and gears, to

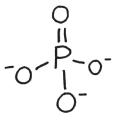


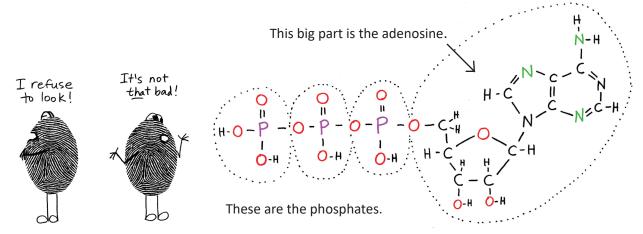
Can you see how this explains why plants we eat can also be used to make `biofuel" for cars?

the wheels. The chemical waste products created by this explosion are carbon dioxide and water (plus some miscellaneous carbon chain molecules that somehow escaped being torn apart). Both carbon dioxide and water come out the exhaust pipe. Do you want to guess what waste products your body creates as it "burns" your food? Yep, carbon dioxide and water!

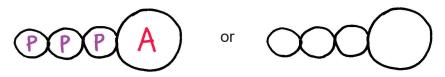
Now, you'd be in big trouble if your body used sparks and rapid combustion to get the energy out of your food. You wouldn't survive past your first meal. Instead, your body uses a very gradual method, a process that involves numerous small steps, so that there is never a harmful release of too much energy all at once. Your body breaks down the large energy molecules into smaller and smaller molecules, and finally into molecules so small that they are safe for a cell to use. The tiny energy unit that a cell uses is called **ATP**.

ATP is short for "<u>a</u>denosine <u>t</u>ri-<u>p</u>hosphate." (*a-DEN-o-zine*) The word "tri" tells you that there are three of something. Does the word "phosphate" look familiar? (If it doesn't, you might want to go back and read chapter 2 again.) A phosphate is a phosphorus atom with some oxygens attached to it. "Tri-phosphate" means that the ATP molecule has three of these phosphates. What about the adenosine part? Well... we'll show you what it looks like, but some of you may want to close your eyes because this looks a bit complicated.



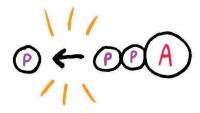


This molecule is way too complicated for scientists to draw every time they want to show ATP. So instead, they just draw it as circles, with one big circle representing the adenosine and three little circles for the phosphates. Often, they don't even put the letters in. Scientists just recognize this shape as ATP.

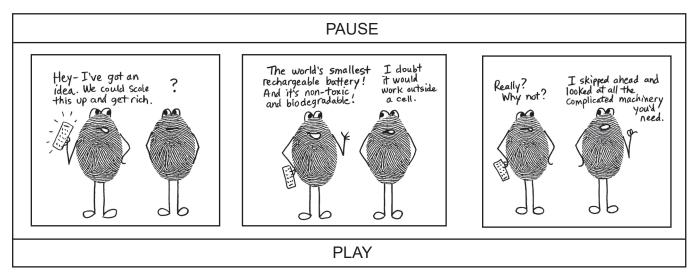


The way ATP releases energy is by popping off the phosphate on the end. There is energy stored in the bond

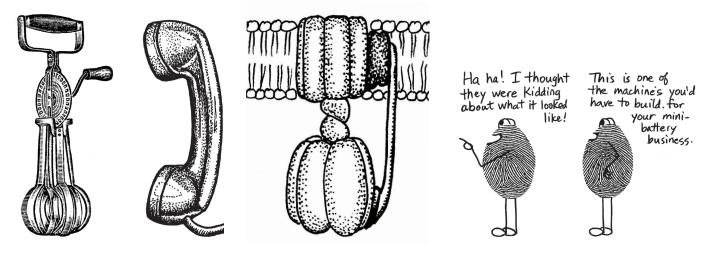
that keeps that third phosphate on, and when it comes off, energy is released. Once the third phosphate is gone, the molecule is no longer called ATP because it no longer has three phosphates. It is now *ADP*: adenosine <u>di</u>-phosphate. (You might wonder why ATP can't pop off its other two phosphates and provide three energy units instead of just one. The short, over-simplified answer is that those two other phosphates don't come off easily.) For the ATP molecule to be "recharged," the third phosphate must be put back on, and putting it back on takes



energy. That's where your food comes in. The energy from your food is used to pop that third phosphate back onto ADP and recharge it into ATP. The primary reason your body needs food calories is for recharging ATPs. Once the ATPs are made, they can float around freely inside the cell, available to any cell art that needs them.

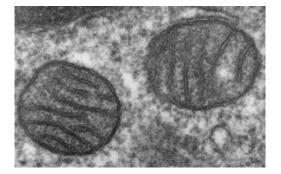


Cells have little recharging "machines" specially designed to put those third phosphates back onto ADP, turning them back into ATP. The scientific word for "make" is "*synthesize*." So scientists (who love Latin and Greek words) decided to name this machine *ATP synthase*. (The "-ase" on the end of the word is the ending they always use for this type of protein. It's sort of like a last name.) This little machine looks like a cross between an old-fashioned telephone and an old-fashioned egg beater.



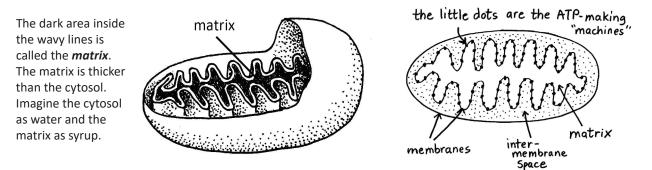
The ATP synthase machine sits in the middle of a phospholipid membrane, held in place by the phospholipid molecules. As we will see, this machine is very similar to a motor, except that it runs on protons, not electrons. The electricity that comes out of the outlets in our walls is made of a continuous stream of moving electrons. ATP synthase uses a stream of moving protons. (We usually find protons locked inside the nucleus of an atom, but here we will see some floating around in the cytoplasm.) A stream of protons will travel through the ATP synthase machine and cause that lumpy "rotor" on the bottom to turn. -

There is more to say about how this little machine works, but first, let's find out exactly where it is located. It's <u>not</u> in the outer membrane of the cell. It's in a special membrane inside organelles called *mitochondria*.



Every cell has at least one mitochondrion, and some cells, such as those found in our liver, have thousands of mitochondria. In this micrograph (a photograph taken with a microscope) we see two mitochondria from a cell taken from the lung tissue of a mammal (probably a lab rat or mouse). The dark circle around the outside of the mitochondria is a phospholipid membrane. Because the mitochondria are "bound" around the outside by a membrane, they are called **membrane-bound organelles**. In future chapters we will meet other membrane-bound organelles.

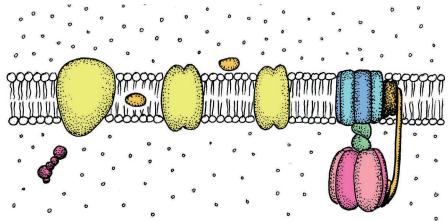
When we look at a diagram of a mitochondrion, we might be a bit confused because it doesn't seem to match the micrograph pictures. In the micrographs, we see stripes. In diagrams, we see a plump, wiggly structure.



The diagram on the left shows a "cut-away" view, revealing the inner structure. The diagram on the right is a cross section, or slice, taken right through the middle, as if the "knife" in the left hand drawing had kept on going and cut the top completely off. This view is less interesting to look at since it is flat, but it shows us where these little ATP synthase machines are located. They are embedded in a wavy, complicated-looking membrane. The area inside the membrane is called the *matrix*. The area outside the membrane is called the *intermembrane space* because it is "inter" (meaning "between") the matrix membrane and the outer membrane. The matrix membrane is made of exactly the same thing as the cell's outer membrane: a double layer of phospholipid molecules.

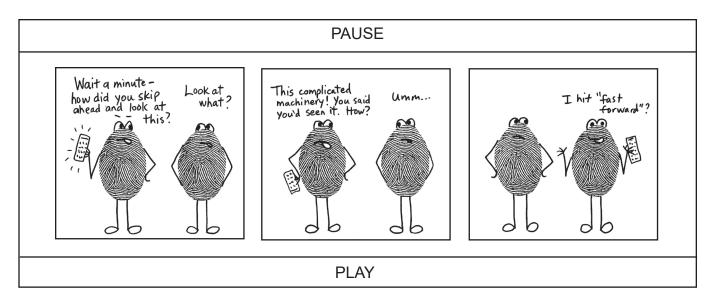
To learn more about what happens in the mitochondria, we will have to zoom in and take a very close-up view of the membrane surrounding the matrix.

In this diagram we can see that the ATP synthase machine isn't alone. You can see other little machines labeled as pumps, plus three tiny "carriers." (All the dots are protons.) This assembly line of machines is called the *electron transport chain*. This <u>chain</u> of machines <u>transports electrons</u> through the assembly line to power the pumps. The pumps pull protons from below the membrane and put them above it. Like people, molecules usually



Remember, these things don't really have any color. We add color to make them less boring.

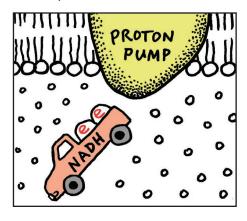
don't like to be in a place that is too crowded, so as soon as there are more protons above than below, the protons will want to go back down to where it is less crowded. The only way to go back down is through a channel in the ATP synthase machine. As they funnel down through the machine (headed for the less-crowded side of the membrane), they cause the "beaters" of the ATP synthase machine to rotate.



Before we continue with the details of how these machines work, let's do the overview one more time. The goal of this assembly line is to turn those beaters on the ATP synthase machine. The ATP synthase machine will be powered by protons going down through it. The protons will be able to go down through the machine because they were pumped up above the membrane by pumps. The pumps will be powered by electrons.

Okay, now for more details! To get things started, a pair of electrons is brought over to the assembly line by a molecule called NADH. Never mind what NADH means—all you need to know is that these electrons came from a process where sugars from food were digested. Think of NADH as a little pickup truck carrying two electrons. These electrons have a lot of energy and will be used to power the three proton pumps.

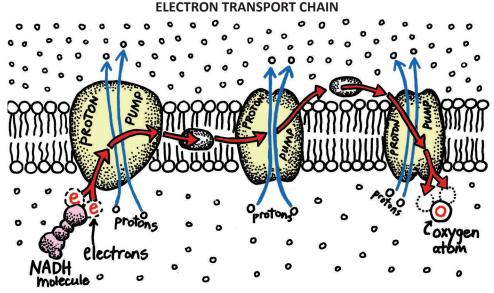
Now we will look at the whole assembly line again and add some arrows to show the path of the electrons.



The electrons will go through all three pumps, but will need to ride on a carrier molecule to get from pump to pump. You could think of these carriers as ferry boats or shuttle buses.

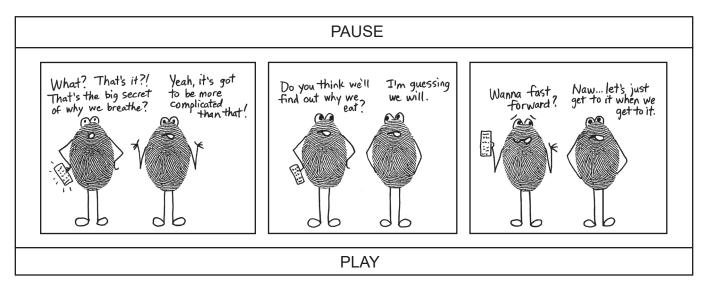
The electrons are headed for an oxygen atom waiting at the bottom of the third pump. This is their final destination.

Every time an electron goes through a pump, the pump pushes two protons from below the membrane up into the space above the membrane. As the electrons go through the pumps, their energy gets used up.

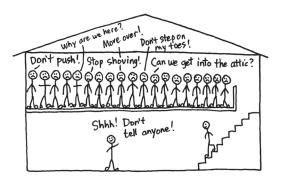


By the time they get to the third pump, the electrons have "slowed down" and lost much of their ability to do work. The fate of these "worn out" electrons is actually an important feature of this assembly line. It just so happens that there are oxygen atoms hanging out near the bottom of this third pump. An oxygen atom would love to turn itself into a water molecule; all it has to do is acquire two hydrogen atoms. A hydrogen atom is nothing more than an electron stuck to a proton. So all the oxygen has to do is grab two of those protons that are floating around, then take the two tired electrons as they come off the assembly line. The electrons stick to the protons to make hydrogen atoms and presto—a molecule of water ( $H_2O$ ) is made! Your body can use this water molecule for other cell processes, or it can get rid of it as waste. The water vapor in your breath when you exhale contains many water molecules that were made by this assembly line.

As strange as it may seem, the only reason you need to breathe is to provide oxygen molecules for the end of this electron transport chain. (If there aren't any oxygen atoms waiting near that third pump, your body immediately shuts down the assembly line.) Because this process is directly tied to breathing, it is called *cellular respiration*. It's the use of oxygen ("respiration") at the cellular level.



Now let's go back and follow the protons and see what happens to them. As the pumps push the protons up into the space above the membrane, the protons start to accumulate up there. Soon, there are more protons "upstairs" than "downstairs." Imagine someone who lives in a two-story house inviting about 50 friends to come and visit. During the visit, all 50 friends are required to go upstairs. First, it was too crowded downstairs, and now it is too crowded upstairs! Then someone is able to quietly sneak down the staircase. What a relief to be back downstairs—so much empty space! Then someone else comes downstairs. With only two friends downstairs, it



is still a relief to be in an uncrowded space. Then another friend comes down, then another, and another. When will they stop coming down? As soon as there are an equal number of friends upstairs and downstairs, there will be no advantage to going downstairs. Unless you force them to go down, (or tell them that a new batch of cookies has just come out of the oven downstairs), the migration downwards will stop because going down would mean going to a <u>more</u> crowded, not less crowded, space.

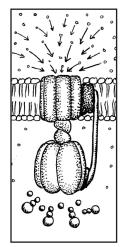
When atoms and molecules behave like this, going to a less crowded place, we call it *diffusion*. The ATP synthase machine takes advantage of the diffusion of protons. The synthase machine is like the staircase in our imaginary scenario, allowing the protons to sneak down to a less

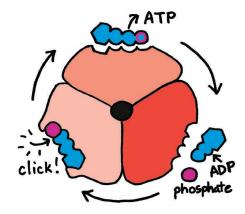
crowded place. (However, this analogy quickly breaks down because unlike the staircase, the ATP synthase machine can only be used to go down. To make our house analogy work, you would have to imagine one-way pumps going up through the floorboards, into the upstairs. Too weird.)

Another analogy that scientists sometimes use is a water reservoir and a water wheel. When the reservoir starts to overflow, the water goes over a spillway and down into the wheel. The mechanical motion of the turning wheel is then used to turn machinery that grinds grain or runs a saw. The ATP synthase machine is like the water wheel, and it really does turn. Those things on the bottom that look like egg beater blades actually rotate.



There are lots of ADP molecules floating around near the beaters, as well as individual phosphate molecules. Both ADP and phosphates will be taken up into the beaters. They snap into little pockets in the beaters that are exactly

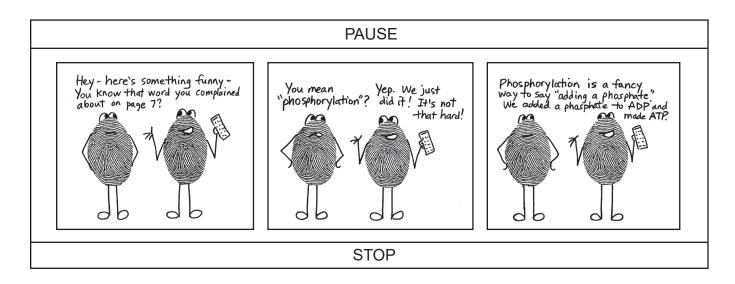




Bottom view of ATP synthase "beaters"

the right shape to hold one ADP and one phosphate. The turning motion of the beaters will squeeze them together and the phosphate will be pressed back onto the ADP, turning it into ATP. With the next turn of the beater, the ATP is released and falls out. The ATP is then ready to be used by any cell process that needs it.

The Wikipedia article on ATP synthase has a helpful animated graphic that shows the bottom view. You can watch ADP and phosphate going into a pocket, snapping together, then being released as ATP.



NOTE: You might want to watch the videos suggested in Activity #1 before answering these questions.

## If you can't remember these answers, go back and find them in the chapter.

1) What is the basic unit of energy used by cells? 2) Why can plants be made into fuel for vehicles? a) because plants contain petroleum b) because plants contain protein c) because plants contain strings of carbon atoms with hydrogens attached d) trick question — they can't 3) What is the molecule shown here? \_\_\_\_\_\_ 0 = P-0 4) TRUE or FALSE? Your body uses a slow form of combustion to burn your food. 5) What happens when the third phosphate is popped off ATP? a) a molecule of water is formed b) energy is released c) energy is used up d) a proton is released 6) The word "synthesize" means "to \_\_\_\_\_." 7) What is the inside of the mitochondria called? a) matrix b) membrane c) cytosol d) synthase 8) TRUE or FALSE? The electron transport chain assembly line sits in the outer membrane of the mitochondria. 9) What happens when electrons pass through the pumps in the ETC assembly line? a) ATP is formed b) water is formed c) two protons are pumped upward d) two electrons are pumped upward 10) What does the NADH molecule do? a) pumps protons b) shuttles electrons c) makes ATP 11) What is the ultimate goal of the electron transport chain assembly line? a) to make an oxygen atom happy b) to pump protons upwards c) to make you study science d) to recharge ATP molecules 12) TRUE or FALSE? Atoms and molecules like to be packed tightly together. 13) How many pumps are in the electron transport chain? 14) What happens to the electrons after they go through the third pump? a) They stick to an oxygen atom. b) They are pumped back into the matrix. c) They go down through the synthase machine. d) They escape through gaps in the membrane. 15) If you join an electron and a proton, what do you get? a) water b) hydrogen c) oxygen d) nothing 16) What is it called when a lot of something goes to a place where there is less of it? 17) TRUE or FALSE? The electron transport chain produces both ATP and water molecules. 18) What does the word root "di" mean? \_\_\_\_\_ 19) REVIEW: Which of these motor proteins walks outward, towards the edge of the cell? a) kinesin b) dynein 20) REVIEW: Which part of a motor protein touches the microtubule highways? a) tails b) feet c) heads

# ACTIVITY 4.1 "Must-watch" videos

#### 1) Animations showing the ATP synthase machine in action

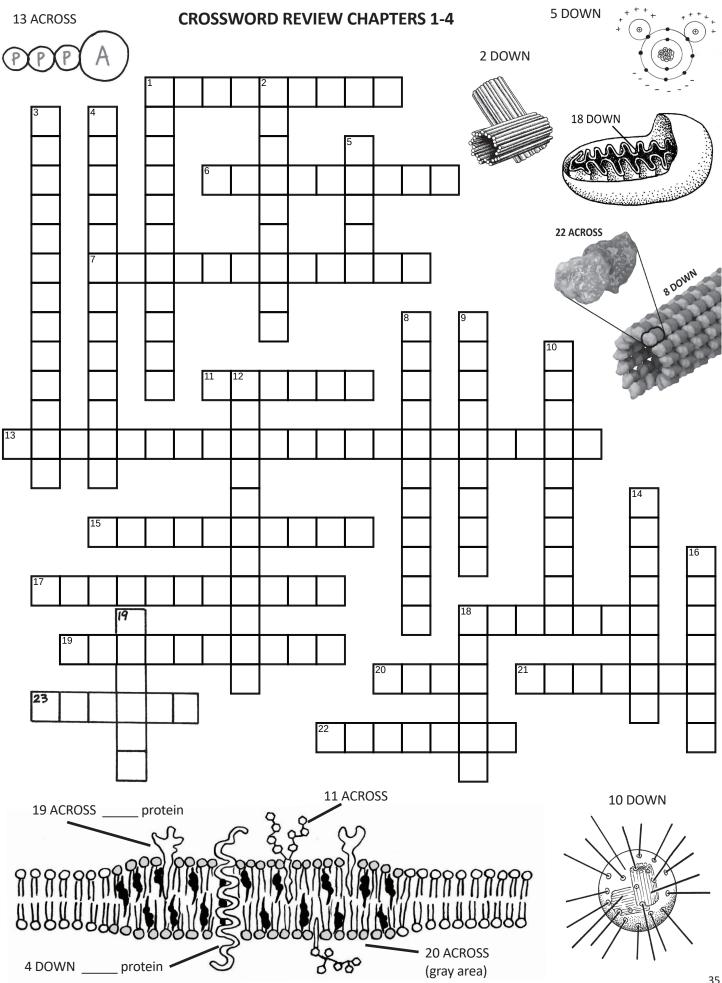
There should be several animations posted on the Cells youtube playlist. If they have disappeared, just use the search feature with key words "ATP synthase." If you don't want to use youtube, use these key words in your preferred video posting/streaming site.

### 2) Animations showing how the electron transport chain (ETC) works

You might hear the word "gradient" in some of these videos. A "gradient" means that there is an area of higher concentration and an area of lower concentration (like the upstairs and downstairs in our house analogy). Also, you might hear the term "hydrogen ion," which is another word for a proton. The word "ion" means any atom or molecule that carries an electrical charge. Protons are positively charged, so they are ions. Phosphate is also an ion because it carries a negative charge. A proton pump is a type of ion pump. Don't be too concerned about understanding every word of the narration. Just enjoy the animations and notice all the parts that we discussed in this chapter.

# **17 ACROSS 12 DOWN** 1 ACROSS 15 ACROSS 1 DOWN H O 23 ACROSS 0-H 16 DOWN 21 ACROSS 19 DOWN 18 ACROSS 3 DOWN **14 DOWN** 7 ACROSS 6 ACROSS 9 DOWN

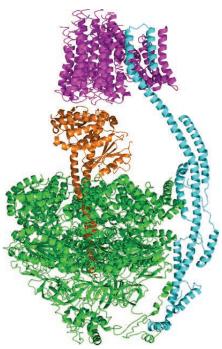
## ACTIVITY 4.2 Crossword puzzle with wordless clues



# ACTIVITY 4.3: What do these little cell parts really look like?

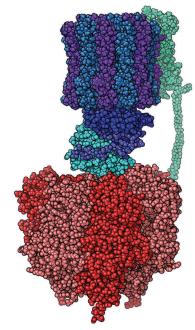
People who draw diagrams of cell processes are aware that the viewer can easily be overwhelmed by too much information. One way they can make diagrams less complicated is by simplifying the shapes of the little cellular machines. Our diagrams of the electron transport chain used very simplified shapes. What do these little pumps and shuttles really look like?

The ATP synthase machine is made of proteins curled up into a spiral shape called the *alpha helix*. We will learn more about this shape in the next chapter. No individual atoms are shown.



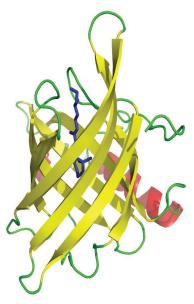
By BiochemEkaterina - Own work, CC BY-SA 4.0, https:// commons.wikimedia.org/w/index.php?curid=59979304

This is also ATP synthase. The artist has chosen to show the atoms as little balls. The spiral shapes are harder to see. The colors show you individual sections that fit together to make the whole machine.

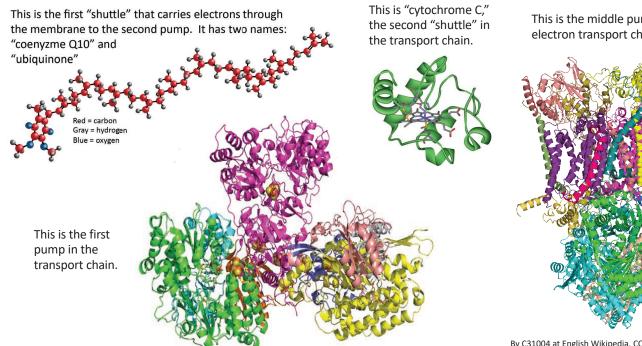


By Alex.X - enWiki (PDB.org for coordinate), CC BY-SA 3.0, https://commons.wikimedia.org/w/index. php?curid=1618502

This protein machine isn't in our chapter, but we are looking at it anyway because it shows you another common shape for transmembrane channels: the "beta barrel." (The yellow things are called "beta sheets.")

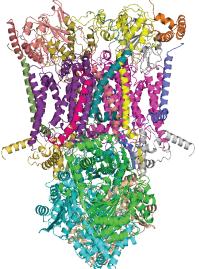


By Opabinia regalis - Self-created from PDB ID 1BRP using PyMol, CC BY-SA 3.0, https://commons. wikimedia.org/w/index.php?curid=1775129



By A2-33 - Own work, CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=41107517

This is the middle pump in the electron transport chain.



By C31004 at English Wikipedia, CC BY-SA 3.0, https:// commons.wikimedia.org/w/index.php?curid=24133439

# ANSWER KEY

#### CHAPTER 1:

1) b, 2) d, 3) c, 4) F, 5) a, 6) a, 7) F, 8) T, 9) T, 10) b, 11) d, 12) bacteria, 13) c, 14) F, 15) F 16) a, 17) F, 18) Scanning Electron Microscope, 19) gold, 20) F

#### Activity 1.1:

1) M, 2) P, 3) J, 4) L, 5) O, 6) H, 7) E, 8) I, 9) D, 10) G, 11) F, 12) A, 13) B, 14) K, 15) N, 16) C A, 6J and P are TEMs.

#### CHAPTER 2

1) b 2) b 3) 2 4) 5 5) a 6) b 7) d 8) b 9) c 10) T 11) F It is a single layer with tails pointing inward. 12) F You also find them surrounding organells and forming storage vessicles. 13) T 14) T 15) c 16) c 17) c 18) b 19) a 20) e

#### Crossword, page 16:

ACROSS: 2) sugar3) mosaid4) hooke5) lipid8) micelle9) hexagon11) blood16) transmembrane17) raft19) cholesterol20) phosphate21) hydrophobicDOWN:1) Schwann2) switch6) peripheral7) mailbox9) hormones10) polar12) Leeuwenhoek13) communicate14) water15) scanning16) transmission18) Brown

#### CHAPTER 3

1) cytoplasm or cytosol 2) b 3) b 4) F 5) b 6) a 7) c 8) a 9) c 10) ATP 11) a 12) tubulin 13) dimer 14) e 15) b 16) centrioles 17) e 18) a 19) a 20) d

#### CHAPTER 4

1) ATP 3) phosphate 6) make 8) F (matrix membrane!) 9) c 10) b 2) c 4) T 5) b 7) a 11) d 12) F 13) 3 15) b 16) diffusion 17) T 18) 2 19) a 14) a 20)c

#### 4.2 Crossword puzzle with picture clues

ACROSS: 1) cork cells7 mitochondria11) glycan13) adenosine triphosphate14) glycerol17) ATP synthase18) micelle19) peripheral20) raft21) glucose22) tubulin23) dyneinDOWN: 1) cholesterol2) centriole3) phospholipids4) transmembrane5) water6) fatty acid8) microtubule9) phosphate10) centrosome12) Leeuwenhoek16) nucleus18) matrix19) kinesin