BIO 180

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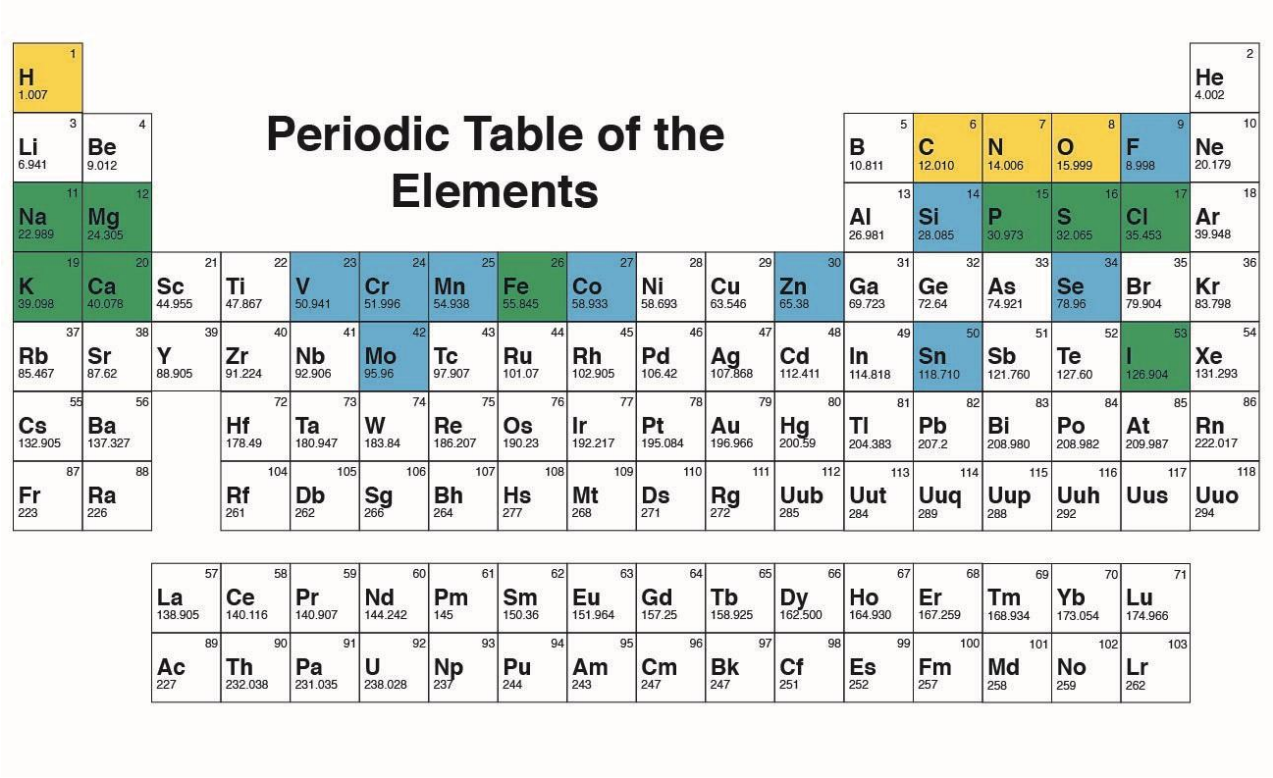
UNIT 1

INORGANIC CHEMISTRY

1.1

Matter

All living and non-living things are composed of **matter**. Using one of its most simple definitions, “Matter is anything that occupies space and has **mass”.** Mass is simply the amount of matter that an object contains. Matter is composed of **elements**. Elements are substances that cannot be broken down into simpler materials by ordinary chemical processes. Some common elements that you have probably heard of are carbon, hydrogen, oxygen, and nitrogen. The building blocks for elements are atoms, which we will discuss in more detail later. In nature, there are 92 naturally occurring elements. In addition to these natural occurring elements, 26 “new” elements have been artificially produced. Based on their chemical properties, these elements can be organized into what is referred to as the **periodic table of the elements**. We will refer to this table frequently as we discuss the basic chemistry of the elements.



Periodic Table of the Elements, created by BYU-I student Hannah Crowder, Spring 2011

The figure above is a “Periodic Table of the Elements.” The elements highlighted in yellow make up 96% of living matter namely **Carbon** (C), **Hydrogen** (H), **Oxygen** (O) and **Nitrogen** (N). The nine elements highlighted in green: Phosphorus (P), Sodium (Na), Potassium (K), Calcium (Ca), Magnesium (Mg), Sulfur (S), Chlorine (Cl), Iron (Fe), and Iodine (I) are considered major essential elements for living matter. The elements highlighted in blue, Vanadium (V), Chromium (Cr), Manganese (Mn), Cobalt (Co), Molybdenum (Mo), Zinc (Zn), Silicon (Si), Fluorine (F), Selenium (Se) and Tin (Sn) are considered minor or trace essential elements for living matter. Major elements are simply found in higher

concentrations in body systems than the minor elements. They are considered essential because the must be consumed and are “essential” for biochemical processes.

Notice that each element is represented by a 1 or 2 letter symbol. Often, these symbols are the first letter or letters in the name of the element: **H** for hydrogen, **C** for carbon, and **He** for helium. Occasionally, however, the symbols represent the Latin name for the element; hence, the symbol for sodium is **Na** for the Latin Natrium, and the symbol for Potassium is **K** for the Latin Kalium.

Subatomic Particles
Radioisotopes

1.1.1

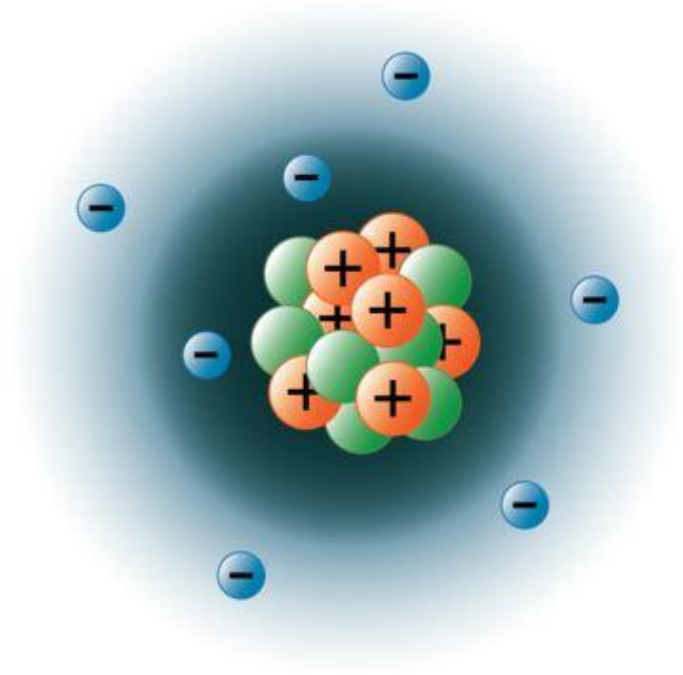
Subatomic Particles

All elements are composed of extremely small particles of matter called **atoms**. We can define an atom as the simplest particle of an element that still has the chemical properties of that element. Chemical properties include the physical state of the element during standard conditions (gas, liquid, or solid), the types of bonds the element can form, how it reacts with other elements, etc. For example, all carbon atoms have the same chemical properties.

Physicists have succeeded in blasting atoms apart into dozens of different sub-atomic particles; however, only three of them are stable. These stable sub-atomic particles are the **protons**, **neutrons,** and **electrons**. Protons are particles that are positively charged, have mass, and are in the center (or nucleus) of that atom. Neutrons also have mass and are located in the nucleus but have not charge. Neutrons bind with protons in a way that helps stabilize the nucleus. Too many or too few neutrons may result in an atomic nucleus that is unstable and may decay to form other elements. We refer to these types of unstable atoms as being **radioactive**. Although the mass of the neutron is slightly greater than that of a proton, we can assign both the relative mass of 1 (1 atomic mass unit or amu). We use the atomic mass unit because the actual weight of a proton is 1.67×10^{-24} grams. The AMU is measured in **Daltons**, named after John Dalton who mathematically showed that a unit Dalton is approximately equal to the molar mass of the same element in grams per mole (1AMU = 1 Dalton).

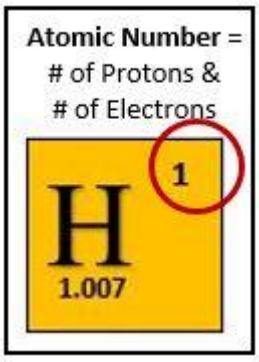
Neutrons and protons constitute almost all of an atom's mass. The third type of stable particle is the electron. Electrons have a negative charge but are extremely small and have a mass only 1/1850 that of a proton or neutron. They are so small that, for practical purposes, they do not contribute to the mass of the atom, thus are assigned a 0 for their amu. Electrons move around the nucleus at tremendously high speeds traveling near the speed of light. Although we often describe electrons as residing in orbits that circle the nucleus, like planets orbiting the sun, modern physics teaches us that this model is incorrect. These "orbitals" are areas in space around the nucleus where the electrons will be located most of the time. This area is often referred to as the electron "cloud." True, it is still a specific area, but it is a bit more amorphous (without a clearly defined shape or form) than a spherical orbit. For simplicity, however, we often think of these as satellite-like circular orbitals. The image below represents our current model of a nitrogen atom.

The nitrogen nucleus contains 7 protons (orange) and 7 neutrons (green). The shaded areas around the nucleus represent the electron orbitals (clouds). Electrons (blue) will be found somewhere within these orbitals. (Note: the image is not drawn to scale. It has been suggested that if the nucleus were the size of a basketball, the electrons would be about *six kilometers or 3¾ miles* away!)



Nitrogen Atom. *Image created by BYU-I student Hannah Crowder Fall 2013*

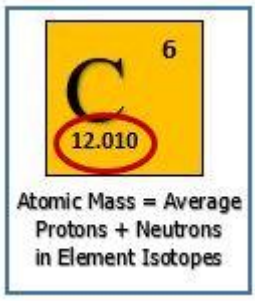
Atomic Number



Take a look at the periodic table again and notice the number at the top of each box. This number is the **atomic number** and is unique for each element. For example, the atomic number for hydrogen is 1, indicating it has 1 proton. No other element has an atomic number of 1. For carbon, the atomic number is 6 and, again, no other element has an atomic number of 6. The significance of the atomic number is that it tells us the number of protons in the nucleus of each element. Therefore, all hydrogen atoms have 1 proton (which is why the term hydrogen ion is sometimes used as a substitute for the word proton), and all carbon atoms have 6 protons. *Note: if you change the number of protons, you change the actual element.* In addition, since atoms have a neutral charge, the atomic number also tells us the number of electrons in the atom. In chemical notation, the atomic number for an element is expressed as a subscript preceding the symbol for the element. For example, carbon would be expressed as $_{6}C$.

Mass Number (Atomic Mass)

The **mass number** of an atom, as the name implies, tells the total mass of the atom. Since the mass of an electron is extremely small (negligible), it isn't used in the computation of the mass number. Also, recall that the mass of each proton, as well as each neutron, is 1 atomic mass unit. Therefore, the mass number is the sum of the protons and neutrons in the atom.

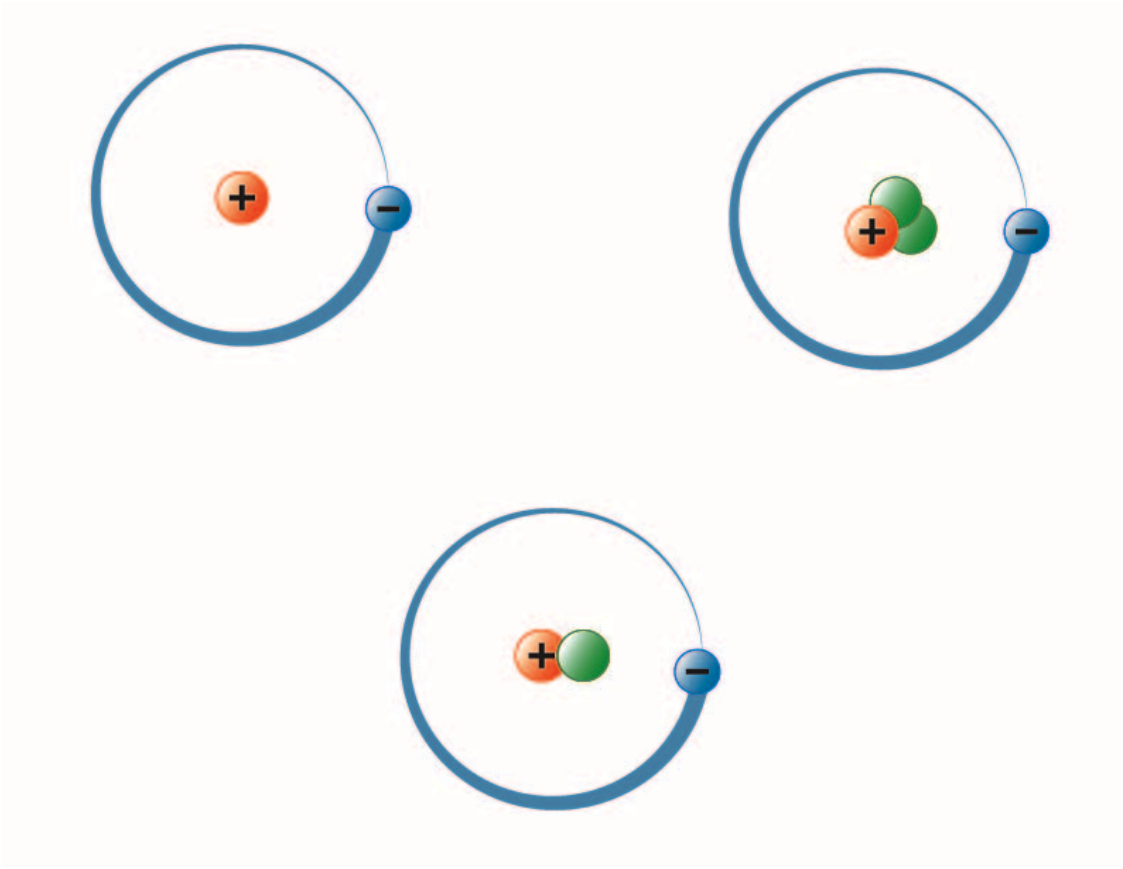


Since the mass number is the number of protons plus the number of neutrons and the atomic number is the number of protons, you can find the number of neutrons by simply subtracting the atomic number from the mass number. As an example, suppose we have an element with

an atomic number of 8 and a mass number of 17. From this information, you can deduce that this element has 8 protons, 8 electrons, and 9 neutrons (17-8=9).

Now, let's throw you a curve ball. As mentioned above, all atoms of a given element have the same number of protons (atomic number). However, different atoms of a given element may have *different* numbers of neutrons. When this happens, we call these elements **isotopes**. For example, there are three isotopes of hydrogen. The most common isotope comprising 99.98% of all hydrogen atoms has a mass number of 1. It, therefore, is composed of one proton, no neutrons, and one electron. The other less abundant isotopes of hydrogen have mass numbers of 2 and 3, respectively. These isotopes differ in the number of neutrons in their nuclei, but all three have one proton and one electron. There are naturally occurring isotopes of every element, each having its own unique mass number. In chemical notation, the mass number for a given isotope is expressed as a superscript preceding the symbol for the element. The three isotopes for hydrogen would be expressed as ^{1}H, ^{2}H, and ^{3}H.

Since each element is composed of several isotopes, one question that arises is "what is the actual mass of a given element?" Again, if you look at the periodic table above, you will notice a number in the bottom of each box. This is the atomic weight for the element. For example, the atomic weight of hydrogen is 1.00794 amu. This number was derived by computing the average mass of the 3 isotopes of hydrogen. Since ^{1}H is the most abundant isotope of hydrogen, it makes sense that the average atomic weight for hydrogen is very close to the atomic mass of ^{1}H.



Isotopes of Hydrogen. *Image created by BYU-I student Hannah Crowder Fall 2013*
The image above represents the three isotopes of hydrogen. The most common (upper left) has one proton and no neutrons in the nucleus. Deuterium (bottom) has one proton and one neutron, and Tritium (upper right) has one proton and two neutrons.

1.1.2

Radioisotopes

1.1.2 Radioisotopes

Some isotopes are unstable (have excess nuclear energy) and emit neutrons, protons, and electrons in order to try and attain a more stable atomic configuration. Excess energy can be emitted in three ways: gamma particles, alpha particles, or beta particles. When this emission energy happens, the isotope becomes a **radioisotope** and is said to be **radioactive**. These radioactive emissions are considered ionizing radiation because they have enough energy to knock off electrons from other atoms. Additionally, these emissions are also referred to as decay. The chart below shows additional details about emitted particles.

Radioactive particle	**Composition**	**Atomic number**	**Mass number**	**Human barrier penetration**	**Effective shielding**
Alpha	2 protons 2 neutrons	2	4	Skin deep	Clothes
Beta	High energy electron	1	No effect	Subcutaneous (below skin)	Plexiglass
Gamma	High energy photon	1	No effect	Any internal tissue	Lead plates

Radioisotopes are used extensively in biology. Consider these biological applications:

Radioactive Tracers: Since radioisotope structures are nearly identical to their nonradioactive isotopes, they are treated the same by living organisms. This means that for normal processes like photosynthesis or glycogen, synthesis it is easy to visualize what cells and what processes these cells are using to incorporate the isotope.

Diagnosis, Treatment, and Research: Isotopes that are emitting gamma radiation can be infused into the blood and then used to visualize internal structures as they move through them. In some cases, radioactive isotopes can be injected directly into the tumor with the hope that the emitted particles will destroy unwanted tumor cells.

Food Preservation: Certain forms of radiation can kill bacteria or fungi to sterilize food or can even be used to control the ripening time of stored fruit and vegetables.

Industry: Radioisotopes can be used to check the integrity of welds, to detect leaks, or to check the degree of water corrosion on metals.

Radiocarbon Dating: Even though radioisotopes try to become more stable by emitting subatomic particles, this emission happens at a very predictable rate. The discovery of radioactivity led to the development of one of the most powerful methods of absolute dating: radiometric dating. This predictability of decay is the basis of radio-dating, with the most famous radioisotope being carbon-14 (^{14}C). ^{14}C occurs naturally in our atmosphere when an atom of nitrogen is hit by a cosmic ray. Sounds like something out of Star Trek! A cosmic ray is a high-energy proton or neutron or both, originating from the sun or some other galaxy energy source, that moves through space at nearly the speed of light. If that ray strikes a nitrogen atom, the high-impact collision between one of these neutrons and the nucleus of a ^{14}N, results in a proton being knocked out of the nucleus and the addition of neutrons. About 10,000 trillion atoms of ^{14}C are formed in the atmosphere every second.

Now for the cool part! As stated above, carbon is one of the four elements that make up 96% of living matter. Thus, throughout the life of an organism it will incorporate carbon from the atmosphere into its living matter. That incorporation will be equal to the levels that are found in the atmosphere. When an organism dies, the amount of ^{14}C that it incorporates stops. Since ^{14}C is unstable it will start to "decay" back towards its original and more stable form of ^{14}N. In the case of ^{14}C, it takes about 5,730 years for half of the ^{14}C to decay back to ^{14}N. This decay rate is called its **half-life**. Half-lives occur as exponential decays and range from 10^{-6} seconds to 10^{10} years! Half-lives can be determined using the following formula:

$$N=N_o e^{-0.693T/T_{1/2}}$$

N is equal to the amount of radioactivity after time (t). N_o is the amount of starting radioactivity, T is the amount of time left for the starting material to decay, $T^{1/2}$ is the half-life the radioisotope and e is the natural log.

Conceptually, what this means is that if we assume that ^{14}C levels have always been produced at a constant rate, then our current atmospheric levels of ^{14}C are the same concentration that was present when the organism in question died. With that assumption in hand, we can simply look at the ratio between the amount of ^{14}C in a dead organism (i.e., wooly mammoth) with that of the current atmospheric levels and calculate an approximate date (age) as to when the organism died. Since ^{14}C has a relatively short half-life, there is still quite a bit in the atmosphere but once something dies, the maximum date that can be obtained is about 60,000 years ago. Past that date, the ^{14}C has almost completely decayed and levels are so small that they become undetectable to our measuring devices.

The issue with carbon dating can be found in the assumption that ^{14}C levels have always been constant throughout time. That is an impossible question to answer. To validate the dating scientists, use a variety of other methods. For example, it is a well-known fact that the ages of tree samples can be determined by counting the rings. These ring comparisons are then compared to the radiocarbon dating method. **Note: The oldest tree to date was accidentally cut down… but the tree rings showed it to be over 5000 years old!* Additionally, ^{14}C dating methods are compared to minerals that do not allow isotope atoms into their crystal structures during formation (minerals are much easier to date). Finally, dating methods are compared to isochron methods. Isochron dating is applied to date certain events, such as crystallization, metamorphism, or shock events in the history of rocks. It is good practice in science, and social media information, to verify answers through multiple sources and/or techniques.

1.2

Electron Configurations

The key factor determining the chemical properties of each element is the configuration of its electrons. Likewise, the energy associated with atoms and molecules is a function of their electrons. Think of the atom; it has a positively charged nucleus with negatively charged electrons orbiting the nucleus. Just like the opposite poles of a magnet, oppositely charged particles attract each other. Because of these attractive forces, it requires energy to pull them apart. In an atom, electrons can be moved further away from the nucleus but only if energy of some form is applied (usually light). Likewise, when electrons move closer to the nucleus, energy can be released. To illustrate, consider the idea of fluorescent glow sticks. If your glow stick starts to fade, you can shine light on it to "charge" the stick, and then, when the lights are turned off, your stick will glow or fluoresce. How does this work? Light, which is a type of electromagnetic radiation has energy that can be used to push electrons into orbitals further from the nucleus. When the light is turned off, the electrons "fall" back down into a lower orbital, releasing energy (**fluorescence**) which causes the stick to glow in the dark. Likewise, in the atmosphere when an electron is hit by a photon of light it absorbs (**absorbance**) the energy and moves to a higher state (electron starts moving faster; called **excitation**). Electrons then jump around the atom as they gain or lose (**relaxation**) energy releasing or gaining energy as packets of energy called photons.

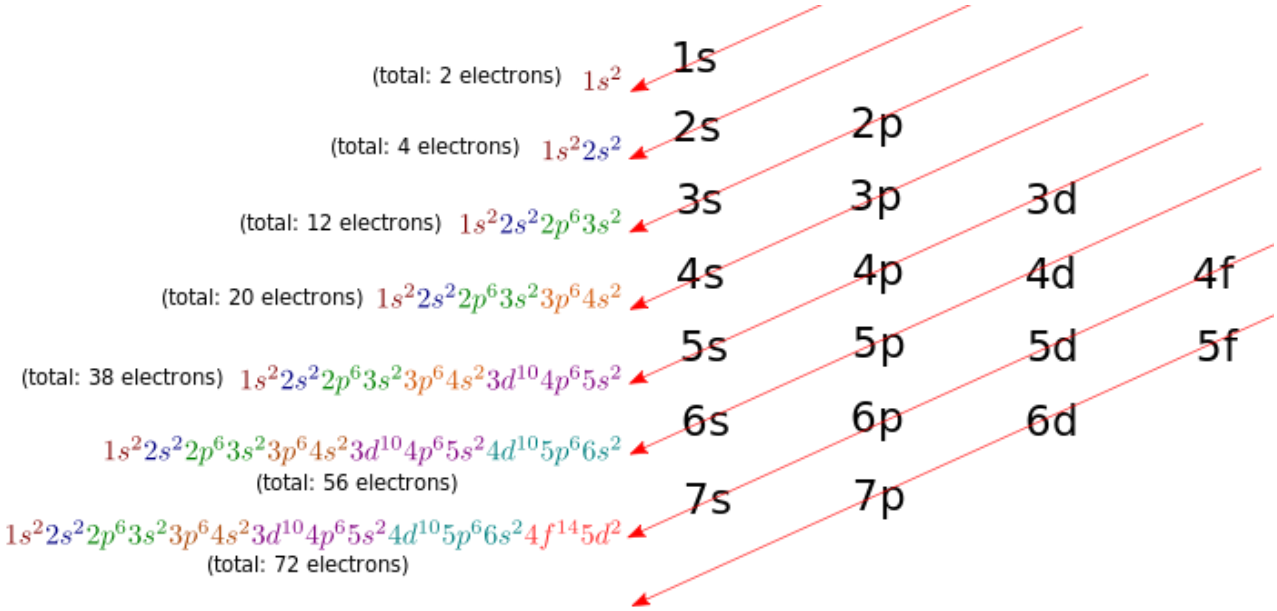
Note. Electromagnetic energy is a type of traveling energy, in the form of wavelengths such as gamma rays, x-rays, ultraviolet and visible light, infrared, microwave and radio waves. Each type of electromagnetic energy is defined by its wavelength with small wavelengths carrying more energy.

As was mentioned above, the electrons of the atom are in **orbitals.** From our discussion above, we learned that the energy associated with the electrons in an atom is a function of its position or distance from the nucleus. Therefore, electrons in orbitals close to the nucleus possess less energy than electrons in orbitals that are further away from the nucleus. Another important property of orbitals is that each orbital can hold a maximum of 2 electrons. Based on the amount of energy in each orbital, they are arranged into what are referred to as **electron shells** or **energy shells (first postulated by Niels Bohr; 1885 – 1962),** which contain one or more orbitals. The shell model is a very useful tool to help visualize and predict how one atom might react with another atom in a given situation (next section), but like most models in biology, when it comes to "real life" the model does not actually predict how electrons are distributed around the nucleus. In reality, electrons behave less like orbiting planets and more like waves. Thus, if you want to get really technical, the orbital model is a better predictive model that tries to "predict" where an electron is most likely to be by following its orbital "wave" path. This predictive model breaks orbital paths down into four subshells designated by the letters **s**, **p**, **d** and **f**. All of the electrons in a given electron shell have the same amount of energy and are designated by a number and the symbol "n". Thus, 1n would represent the first energy or electron shell closest to the nucleus . To summarize, electron shells (1n, 2n, 3n, etc.) are representative of the amount of energy that electrons have, with increasing shell numbers having increased energy, and those energy shells containing subshells (s, p, d, f). Each subshell represents the path of the orbitals that are contain in it, with each orbital holding up to 2 electrons.

To accommodate the electrons in the largest of the naturally occurring elements, seven electron shells (7n) are required. The first shell can only accommodate one orbital, designated as the s orbital; thus, the maximum number of

electrons in the first electron shell is two. The second shell contains four orbitals (one s and one p subshell) and can, therefore, accommodate eight electrons each. Shell 3n has s (1 orbital), p (three orbitals) and d (five orbitals) subshells allowing for 18 electrons. Shell 4n has s, p, d and f (seven orbitals) subshells and can accommodate 32 electrons.

It has also been observed that atoms appear to be more stable when they have eight electrons in their outer shell (not including the first shell), this is known as the **octet rule.** The outer shell is also called the **valence** shell. One other important fact is that as electrons are added to electron shells, they occupy the innermost shells first before filling the outer shells. It's like parking spaces at Walmart; those closest to the store fill first, and once they are filled, shoppers have no choice but to park in spaces further away. For example, hydrogen has one electron which is located in the first (innermost) electron shell. This can be explained as an **electron configuration** and is designated as $1s^1$ (1 representing the electron shell, and s the subshell). The superscript 1 indicates one electron within the 1s orbital. Helium has two electrons, both in the first energy shell so is designated as $1s^2$. All of the space in the first energy shell is now filled. Lithium has three electrons; two of them are in the first shell, and the third electron is in the second electron shell: $1s^2 2s^1$. Remember the 2n shell has 1 s and 1 p subshell orbitals, so the electrons fill the first s and then the one extra electron will fill the s of the 2nd shell. subshell orbitals, so the electrons fill the first s and then the one extra electron will fill the s of the 2nd shell.



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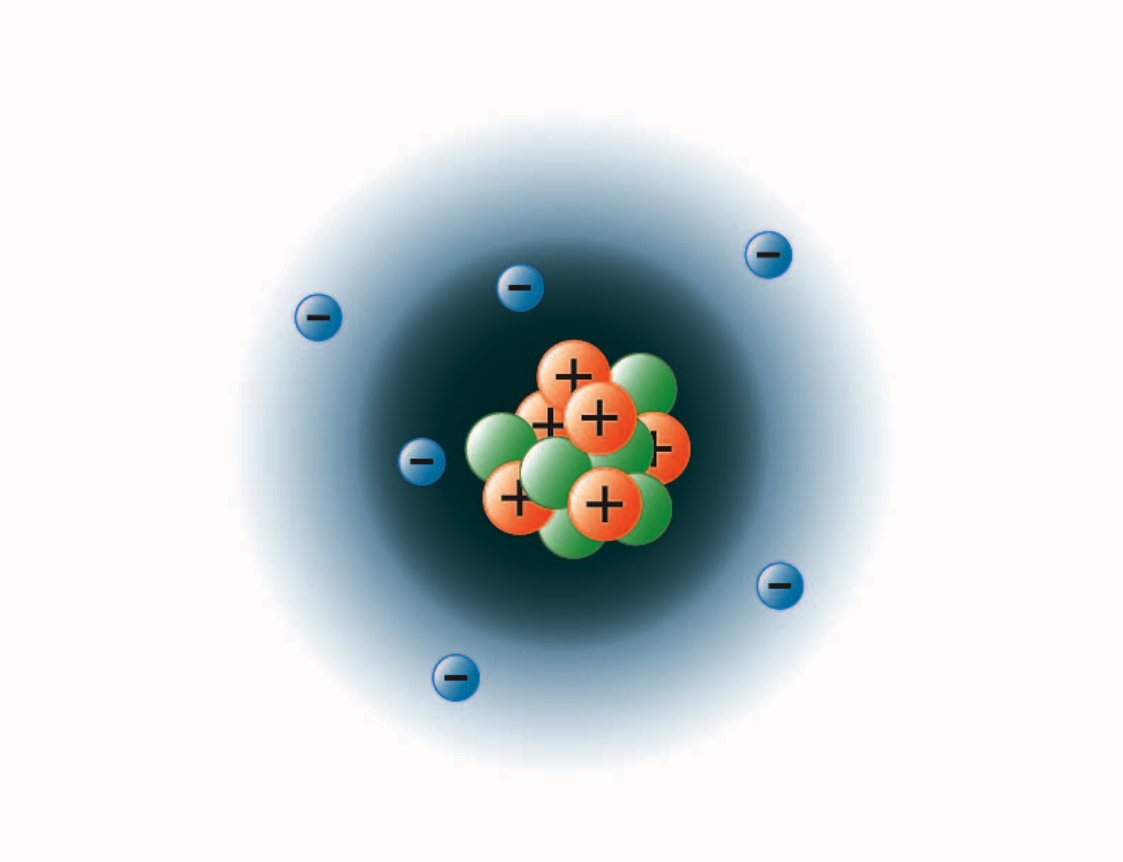
The reason that this is important to know is because **the chemical properties of an element are determined by the number of electrons in its outer electron shell**. We define the "outer electron shell" as the last shell that has electrons in it (valence), so for hydrogen, its outer electron shell would be the first shell, and for lithium, its outer shell would be the second shell. Each of these elements has one electron in its outer shell, which means that they will have similar chemical properties.

Let's try an example. Oxygen has an atomic number of 8, which means it has 8 protons and 8 electrons. How many electrons are there in the outer electron shell of oxygen? The first two electrons will go into the first shell, leaving six to go into the second shell. Therefore, the outer electron shell for oxygen is the second shell, and it has six electrons in it ($1s^2 2s^2 2p^4$).



Carbon Atom: *Image created by BYU-I student Hannah Crowder Fall 2013*
The image above represents the electron configuration for carbon. Carbon has an atomic number of 6, hence 6 electrons. The first two electrons fill the first shell (dark blue), and the next four are in the second shell (light blue).

Chemical Reactions

1.2.1

Chemical Reactions

Close examination of the periodic table will show that the atoms of all of the elements in the last column of the table (i.e., helium, neon, argon, etc.) have eight electrons in their outer shells (with the exception of helium). Therefore, their outer electron shells are full. These elements are known as the noble gases, they are all stable, meaning that they do not react with other elements and are given the name **noble** gases. The octet rule states that if there are eight electrons in the outer electron shell, the element is stable. The atoms of all of the other elements have vacancies in their outer electron shells and will react with other atoms to fill their outer shells. At the broadest level, this process is described using chemical reactions.

In a chemical reaction, the substances used to start the reaction are called **reactants** and the resultant substances following the reaction are called **products**. To describe the reaction visually, we use a chemical equation (similar to a mathematical equation) where the reactants are on the left side of the equation and the products on the right side. Instead of an equal sign we use an arrow. The arrow allows us more flexibility to describe the direction of the equation as oftentimes the products can go back towards the reactants. Chemical reactions that proceed in only one direction are called **irreversible** reactions, while chemical reactions that can run in either direction are called **reversible** reactions. Reversible chemical reactions are dependent upon a principle called **LeChatlier's** principle which states that the system will proceed in a direction that minimizes the amount of change. In other words, it will process in whichever way will bring the system back into homeostatic equilibrium or homeostasis. For example, if we add a reactant or remove a product the equation will go towards the products (right) and if we add product or remove a reactant the equation will drive towards the reactants (left). It is important to understand that homeostatic equilibrium does not mean equal parts of reactants and products, because every chemical reaction has a different equilibrium point with some favoring reactants and some favoring products. This concept is described as the **equilibrium constant (K)** which is equal to the concentration of products over the concentration of reactants at equilibrium. If K = 1, then there are equal amounts of products and reactants. A K-value less than 1 would indicate more reactants than products and a K value above 1 would favor products over reactants at equilibrium.

1.3

Chemical Bonds

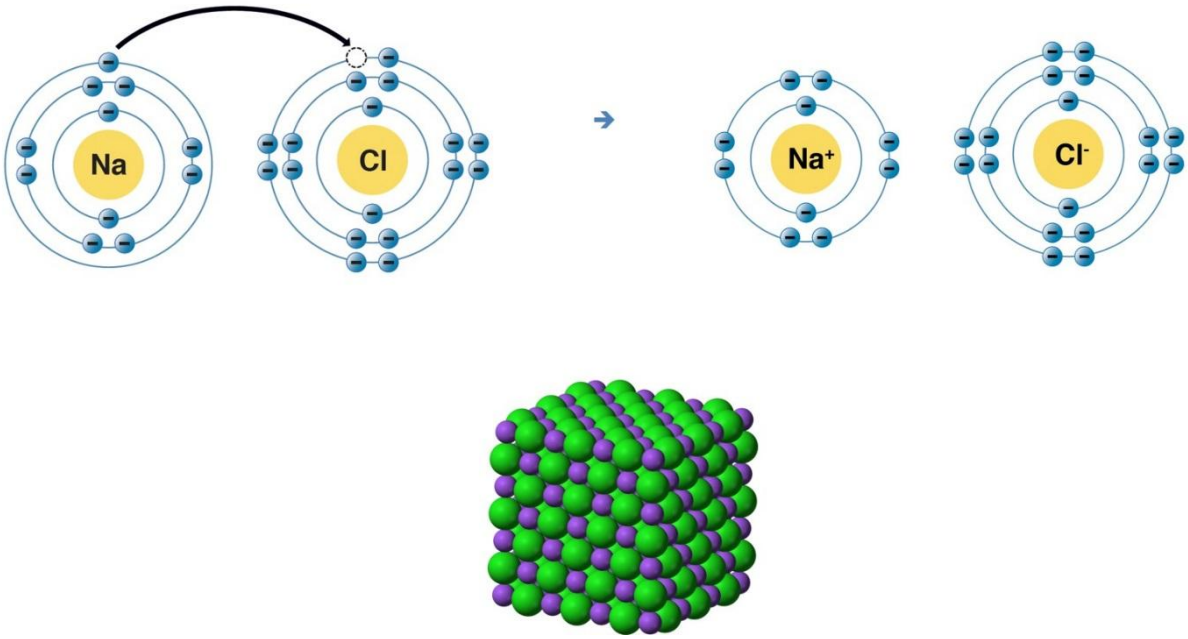
The sections below describe some of the important processes by which atoms become stable. The processes that result in the filling of the outer electron shells result in the formation of chemical bonds. In some cases, this involves the formation of molecules. **Molecules** are two or more atoms held together by the sharing of electrons (described below). Molecules composed of more than one type of element can also be called **compounds**. Hence, H_2 (same element) is a molecule, and H_2O (different elements) is both a molecule and a compound.

1.3.1

Ionic Bonds

To explain how ionic bonds form, we will use common table salt, NaCl, as an example. Sodium has an atomic number of 11; hence, sodium has one electron in its outer electron shell. Chlorine, on the other hand, has an atomic number of 17 and has seven electrons in its outer shell. When these two elements react, sodium gives the one electron in its outer shell to chlorine. Sodium now has eight electrons in its outer shell and is stable. However, the result of losing one electron leaves sodium with one more proton than electron, and therefore, it is now an **ion** with an electrical charge of +1. An ion is an atom that has a net + or – charge. Ions that have a net positive charge are called **cations**. Chlorine picked up one electron, and in the process, has become an ion with a -1 charge (one more electron than proton). Ions that have a net negative charge are called **anions** (think of the term anion as an acronym standing for **a n**egative **ion**). The opposite charges on these ions create an attraction that will hold them together. We refer to this attraction as an **ionic bond**. The figure below shows the formation of sodium and chloride ions. By changing the electron configurations of these two elements, their chemical properties have been drastically changed. In terms of strength, this bond is incredibly strong unless placed in water. Biological life requires NaCl (Na^+ and Cl^-) for proper functions, but both sodium and chlorine with different electron configurations can be lethal. Chlorine gas, Cl_2, is a deadly poison, and elemental sodium (no charge) is a metal that ignites when placed in water. This emphasizes the significance of the statement above that the chemical properties of an element are determined by its electron configuration.

It is also important to note that ionic bonds do not form distinct one-to-one attractions between ions, so technically, ionic bonds do not form molecules. Instead, they form crystalline structures in which each anion is attracted to all of the cations near it, and each cation is attracted to all of the anions near it. Even so, you may still read or hear NaCl being referred to as a molecule/compound.



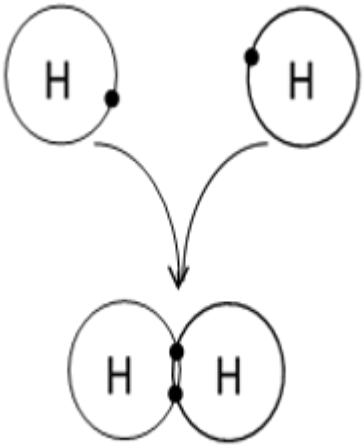
NaCl Crystal Ionic Bonds: *Image created by BYU-I student Hannah Crowder Fall 2013*

In the image above, the upper left portion represents the formation of an ionic bond. Sodium gives up one electron and becomes a positively charged sodium ion. In the process, its outer electron shell now has eight electrons. Chlorine gains one electron and becomes a negatively charged chloride ion with eight electrons in its outer shell. Upper Right—the negatively charged chloride ions are attracted to the positively charged sodium ions, forming an ionic bond. Bottom—Sodium Chloride crystal. Each sodium ion (purple) is attracted by all of the chloride ions (green) that surround it, and each chloride ion is attracted by all of the sodium ions that surround it.

1.3.2

Covalent Bonds

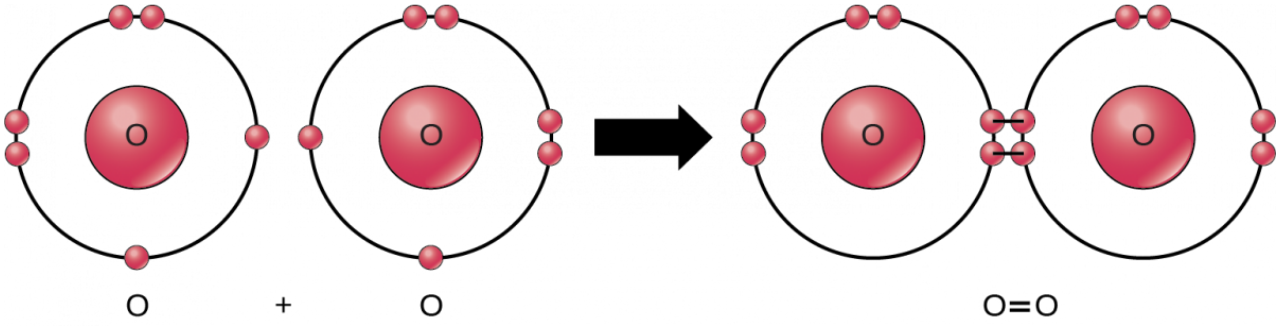
Another way that atoms can fill their outer electron shells is to share electrons. For example, hydrogen has an atomic number of 1 and, therefore, has 1 electron in its outer electron shell. To fill this shell, hydrogen needs one more electron (recall that the first electron shell will hold a maximum of two electrons). One way of filling this shell would be for two hydrogen atoms to unite to form a molecule by sharing electrons with each other. This type of bond, formed by sharing electrons, is called a **covalent bond** . Covalent bonding is highly dependent on a property called **electronegativity** , which is a measure of the tendency of an atom to attract a bonding pair of electrons. Units for electronegativity are measured using the Pauling scale (strongest 4.0 to weakest 0.7). An atom with a higher electronegativity value will more strongly attract electrons to covalent bond with. The chemical shorthand for a covalent bond is simply a dash. Therefore, the molecule represented in Figure 6 could be expressed as H-H, with the dash representing the shared electrons. Note that the equal sharing of electrons does not cause either atom to have unequal numbers of electrons and protons; hence, there is no net – or + charge. Equal sharing occurs when the atoms have the same, or close to the same, electronegativity because they have the same attraction for electrons. Also, unlike ionic bonds, which form crystals, covalent bonds create an intimate relationship between the two atoms. That is, these two atoms are linked directly to each other. You could think of ionic bonds as a group date or hanging out and a covalent bond as marriage. The image below represents a covalent bond between two hydrogen atoms.



Hydrogen Covalent Bond: *Image created by MG Fall 2013*

Covalent bonds can also be formed by the sharing of more than one pair of electrons. For example, oxygen has an atomic number of 8 with 6 electrons in its outer electron shell. Two oxygen atoms will combine to form oxygen gas, O_2, by sharing two pairs of electrons, thus completing the outer shell of both oxygen atoms. We refer to this as a **double covalent bond** and represent it by two dashes, O=O, with each dash again representing a pair of shared electrons. Once bonds move from single to double, they lose the ability to rotate around the bond. It should be noted that triple covalent

bonds are also possible by sharing three pairs of electrons. However, in the compounds we will be studying, none have **triple covalent bonds.**



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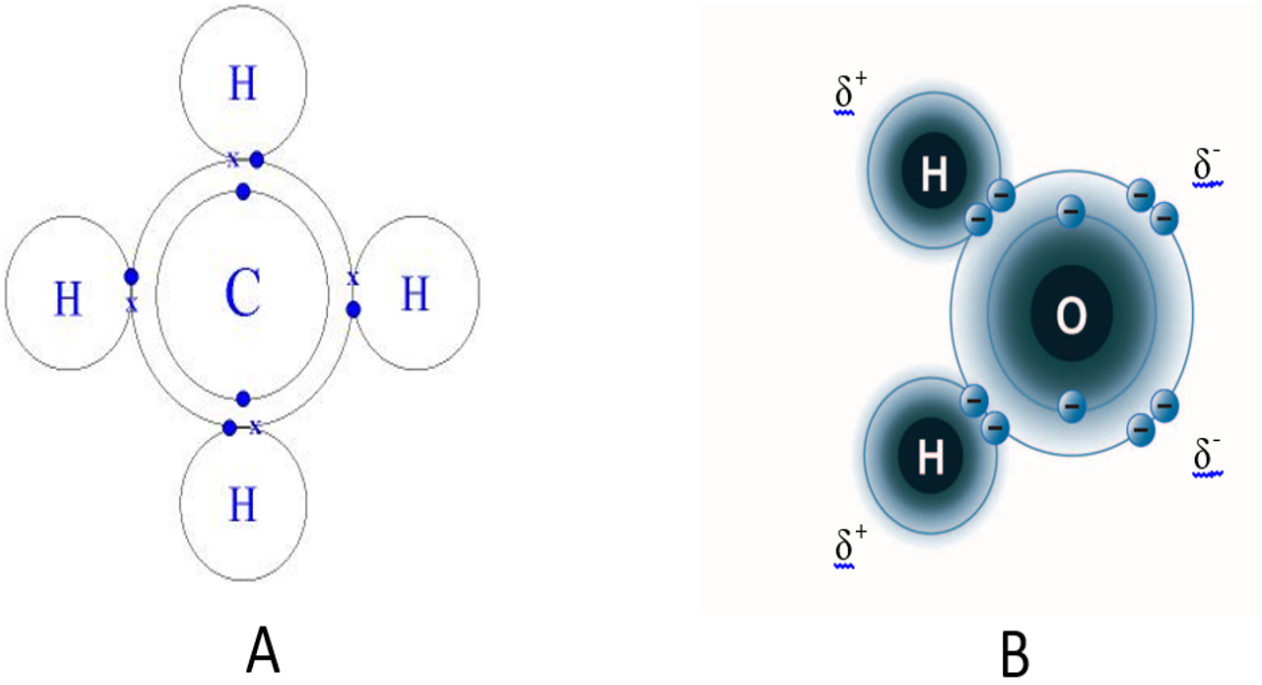
Depending on the atoms involved in the covalent bonds, the electrons can either be shared equally, or the electrons may spend more time with one partner than the other, resulting in unequal sharing of electrons. Two molecules are shown in the figure below. Methane is the image on the left and is a gas that is composed of one carbon and four hydrogen atoms. In this molecule, the electrons are equally shared between the carbon and each hydrogen (their electronegativities are very close), forming **non-polar covalent bonds** . Because all the bonds in the molecule are non-polar, this molecule is a non-polar molecule. The other image on the right is water. In this molecule, the negatively charged electrons are more strongly attracted to the oxygen (because of its increased electronegativity) and, hence, spend more time with the oxygen than with the hydrogen. This creates a molecule with bonds that have a slight negative charge at one end (the oxygen end) and a slight positive charge at the other end (the hydrogen end). Since the molecule is made up of bonds that have oppositely charged ends, we refer to these types of bonds as a **polar covalent bond** . Because all the bonds in the molecule are polar, water is a polar molecule. Note that the total charge on the molecule is 0, but the ends are partially charged. Polar covalent bonds and ionic bonds are similar, in that electrons are pulled away from one atom and pushed towards the other. The difference is that with ionic bonds, the electrons are completely removed from one atom, forming the cation, and captured by the other atom, forming the anion.



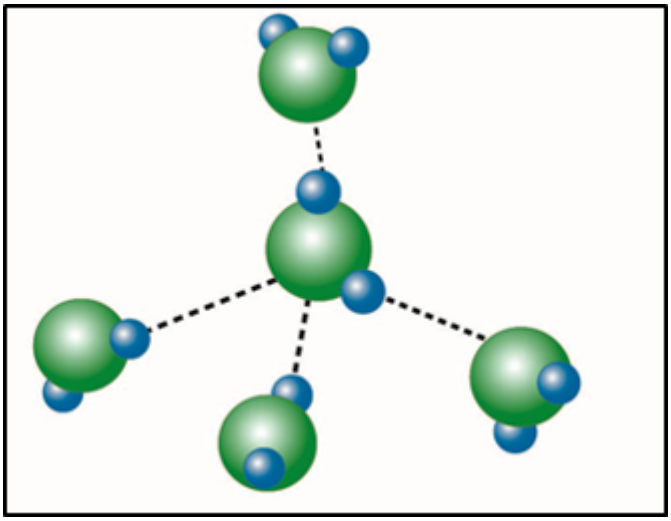
A: Methane gas – Non-polar covalent bond; B: Water molecule – Polar Covalent Bond.
Image created by BYU-I student Hannah Crowder Fall 2013

UNIT 2

INTERMOLECULAR FORCES, WATER, AND ACIDS AND BASES

2.1

Hydrogen Bonds



Hydrogen Bond: *Image created by BYU-I student Hannah Crowder Fall 2013.*

One other interaction of importance in biological systems is called the **hydrogen bond**. This is not a bond that forms molecules or ionic crystals; rather, it is an interaction between molecules containing polar covalent bonds. Because of this, it is referred to as an **intermolecular force** or an attraction between two molecules. Hydrogen bonds can only occur between molecules containing polar covalent bonds and are a result of attractions between the oppositely charged ends of these molecules called **electrostatic** attraction. Note that hydrogen bonds and ionic bonds are similar. The difference is that ionic bonds are created by attractions between oppositely charged ions, while hydrogen bonds are attractions between oppositely charged ends of polar covalent molecules. Although hydrogen bonds are very weak compared to the other bonds we have discussed, they play important roles in many of the compounds we will be studying in this class. For example, most of the important characteristics of water are due to its ability to form hydrogen bonds with itself and other polar molecules. Likewise, the complex structures of proteins and nucleic acids rely heavily on hydrogen bonding.

Another weak bond, like hydrogen bonding, occurs from an interaction called a **Van Der Waal**. This interaction can occur between any two or more molecules (polar and nonpolar) and is dependent on very small fluctuations in electron densities surrounding an atom. The interactions are extremely weak and require the molecules to be very close to one another.

Water
Chemical Characteristics of Water

2.1.1

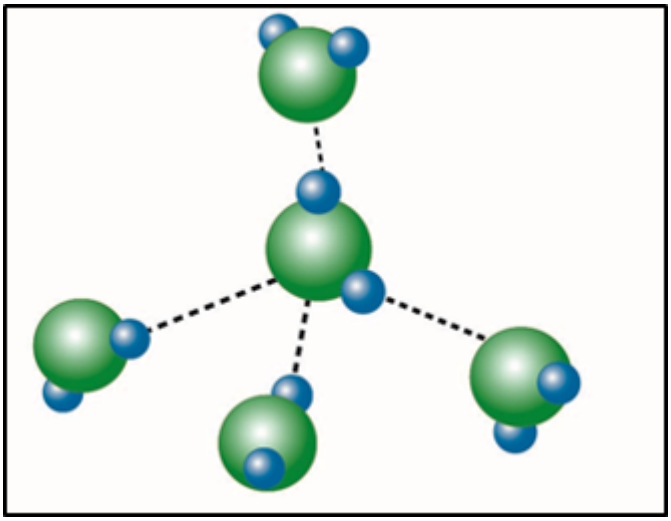
Water

If someone asked what the most important molecule for life is, hopefully most of us would say water. Although a close second must be chocolate! Whenever there is speculation of life on other planets, the question always arises: Is there water on the planet? What is so special about water? What makes it essential for life? Wouldn't some other fluid work as well? These are some of the questions that we will attempt to answer in this section.

2.1.2

Chemical Characteristics of Water

Recall that the water molecule, H_2O, is held together by **polar covalent bonds**. Since the oxygen attracts the electrons in the covalent bonds more strongly than the hydrogen do, the oxygen end of the molecule has a slight negative charge while the hydrogen ends of the molecule have a slight positive charge. Also, recall that molecules composed of polar covalent bonds can participate in weak interactions with other polar molecules through hydrogen bonding. The figure below shows how water molecules form hydrogen bonds with each other. Each water molecule has the potential to form a maximum of four hydrogen bonds with other water molecules. Most of the characteristics of water that we will be talking about are the result of the polar nature of the water molecule and its ability to form hydrogen bonds with itself and other polar molecules. Remember that hydrogen bonds are very weak interactions and can be formed and broken relatively easily. However, as with all bonds, energy is required to break bonds, and energy is released when new bonds are formed. It is the number of these bonds that determine the physical state of the water. For example, in the solid state, each water molecule forms hydrogen bonds with four other molecules, resulting in the formation of a stable, crystal structure known as ice. In the liquid state, each water molecule forms fewer than four bonds (on average 3.4), which are continually rearranging. Water becomes steam when there is enough energy to break all of the hydrogen bonds between water molecules, and they can escape in the form of a gas.



Hydrogen Bonds of Water Molecules: *Image created by BYU-I student Hannah Crowder Fall 2013*
The image above shows hydrogen bonds between water molecules in the solid state. In the liquid state, hydrogen bonds are constantly rearranging (breaking and reforming with other molecules) which allows more movement of the molecules. To our eyes and experience this liquid state can "flow".

Temperature Stabilization

The amount of energy in the form of heat that must be added to or taken from a substance in order to change its temperature is called the **heat capacity** of the substance. Water has a very high heat capacity. In fact, we define the calorie as based on the heat capacity of water. (One calorie is the amount of heat energy necessary to raise the

temperature of 1 gram of water 1° Celsius. Note: when reporting the calorie content of food, calorie is written with a capital C. These “big” calories are actually kilocalories or 1000 calories.) Likewise, 1 calorie of energy must be taken away from water to lower the temperature of 1 gram of water by 1° Celsius. Compare this to the heat capacity of air, which is 0.24 calories per gram. This high heat capacity is due to the hydrogen bonds between the water molecules. Temperature is a measure of the total kinetic energy (motion) of a material. Before the water molecules can start moving faster, the hydrogen bonds between the molecules must be broken, which requires the input of energy. Therefore, much of the energy (heat) is used to break the bonds rather than increase the temperature (movement) of the water molecules. By the same token, when heat is removed and the water molecules begin to slow down, new hydrogen bonds form, releasing energy, which helps prevent a big drop in temperature.

Another property of water is its high **heat of vaporization**. This means that in order to convert water from a liquid to a gas, it requires the input of relatively large amounts of energy to increase the movement of the water molecules enough for them to break free from the water molecules around them. As these water molecules move faster and faster, they eventually will have enough energy to completely break away from the liquid and will be converted to a gas (water vapor). When the fastest moving molecules break free, their kinetic energy goes with them, removing heat. This is the basis for the cooling effect of the evaporation of sweat from human skin or off the tongue of a panting animal.

Adhesion, Cohesion and Lubrication

Water is able to stick to other polar substances. This property is referred to as **adhesion**. An excellent example of the importance of this property in the body involves the lungs. A thin layer of water between the outer surface of the lungs and the walls of the thoracic cavity “glues” the lungs to the walls and prevents them from collapsing. **Cohesion** is the sticking together of water molecules. This property prevents the blood from separating as it moves through the blood vessels. Finally, water can act as a lubricant and is found in areas of the body where structures are required to slide past each other. For example, synovial joints (knee, shoulder, ankle, etc.) have a thin layer of water (synovial fluid) between the opposing structures, allowing them to easily slide past one another as the joint moves.

Chemical Reactions

All of the thousands of chemical reactions taking place in our bodies require water. This is because in order to react, the chemicals must be in a watery solution. Water also participates directly in many of the important reactions taking place in the body.

2.2

Water and Aqueous Solutions

As mentioned above, before chemicals can react in chemical reactions, they must be in solution. As it turns out, water is an excellent solvent. A **solvent** is a dissolving agent and is the liquid portion of a solution. The molecules that dissolve in the solvent are called the **solutes**. Therefore, in a solution of salt (NaCl) and water, the water is the solvent, and the sodium and chloride are the solutes. A solution in which water is the solvent is called an **aqueous solution**. Although water is an excellent solvent, not everything dissolves readily in water. Materials that dissolve well in water are said to be **hydrophilic** (hydro- = water; -phil- = love), and those that do not dissolve readily are said to be **hydrophobic** (phobia = fear). Usually, if we know the chemical nature of a solute, we can predict how readily it will dissolve in water. For example, compounds that are bound together by ionic bonds tend to be hydrophilic and dissolve readily. The secret is the ability of the polar water molecules to surround the ions and pull them out of the crystal. When the ions are pulled apart in this manner, we say the compound has become dissociated or ionized. The dissociated ions in the solution are referred to as **electrolytes**. Important electrolytes for life include Na^+, K^+, Ca^{2+}, Cl^-, HCO_3^-, H^+, and Mg^{2+}. These ions participate in many important physiological processes such as nerve impulse conduction, muscle contraction, and regulating water balance.

In addition to ionic compounds, compounds bound together with polar covalent bonds also tend to be hydrophilic. Sucrose, or table sugar ($C_{12}H_{22}O_{11}$), is a good example of a polar compound that readily dissolves in water, forming an aqueous solution. However, when polar covalent molecules dissolve in water, they do not ionize or separate into smaller particles like ionic compounds do.

Compounds bound together with nonpolar covalent bonds tend to be hydrophobic and do not dissolve readily in water. This is because there are no charged or polar parts to interact with the polar water molecules. Fats and oils are good examples of compounds that are hydrophobic.

One of the most important structures in cells is the biological membrane. These membranes are stabilized by the hydrophobic and hydrophilic interactions of some special compounds that we will study later.

Solute Concentration

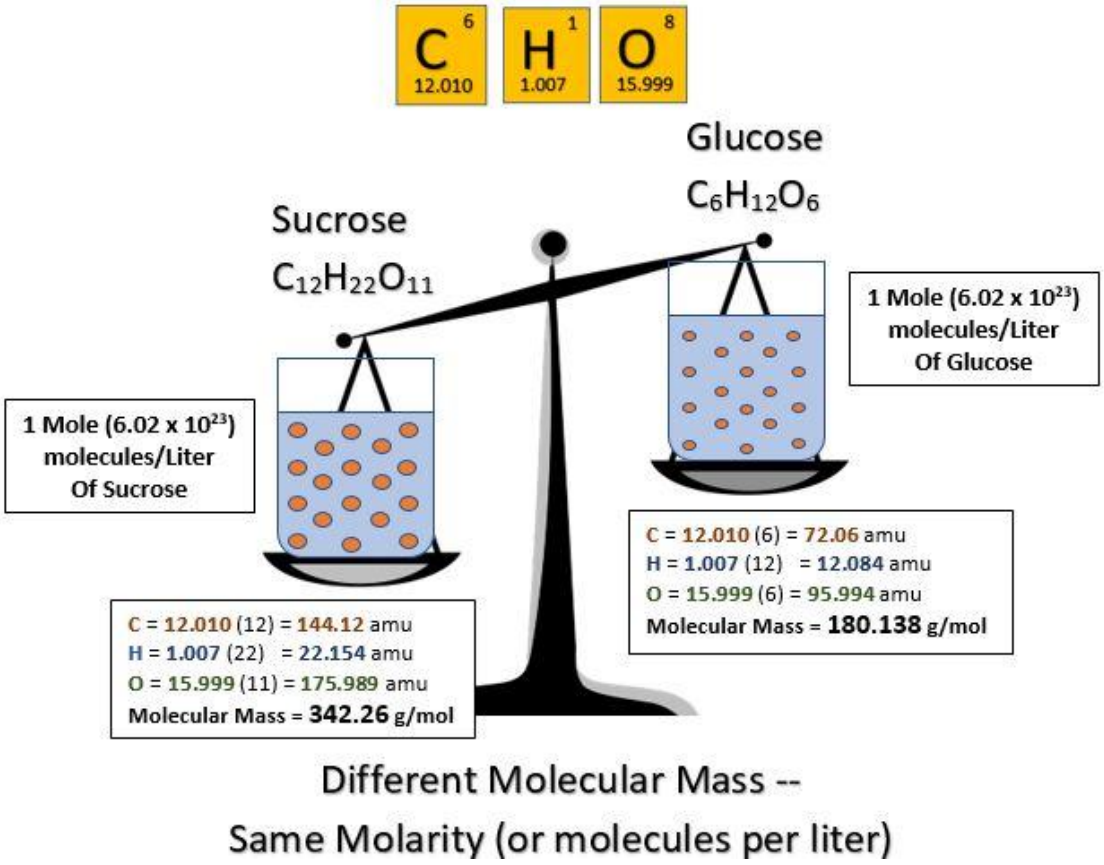
It is often important to know the concentration of the solute in a solution. Some common ways of expressing concentration are straightforward. For example, the normal fasting glucose concentration in human blood is approximately 90 mg glucose per 100 ml of blood. This would be written as 90 mg/dl (dl stands for deciliter or 1/10 of a liter). Another fairly simple method is to express the concentration of the solute in a **percent solution**. This method expresses the concentration as grams of solute per 100 ml of solvent. For example, the normal concentration of NaCl in human blood is 0.9%. This means that there is 0.9 g of NaCl per 100 ml of blood plasma. Both of these methods are fairly easy to visualize. However, they are not very precise. A less obvious but more precise method is to express the concentration as the **molarity** of the solution. Let's see if we can walk through what this means. First of all, the term *molarity* means **moles** of solute per liter of solution. So, the next question is, what the heck is a mole?

To begin, a mole is a unit of measurement. In order to understand what is meant by "unit of measurement," let's start with something you are familiar with, the dozen. We are tempted to ask, "Where in the world did that word come from,

and why does it signify the value of 12?" The value of 12 is a unique number because of the early observations of the cycles of the moon, which led to the proposed twelve-month cycle of a year. After a gradual shorting of the Latin word for twelve, "duodecim", the English derivation of this word became the word dozen—a grouped quantity, signifying the value of twelve. Why group things? For starters, it is easier to go to the store and buy 12 dozen eggs than it is to individually count out 144 eggs. Units of measurements allow us to conveniently talk about large numbers at an understandable level. The concept of unit measurement is absolutely essential when it comes to counting atoms.

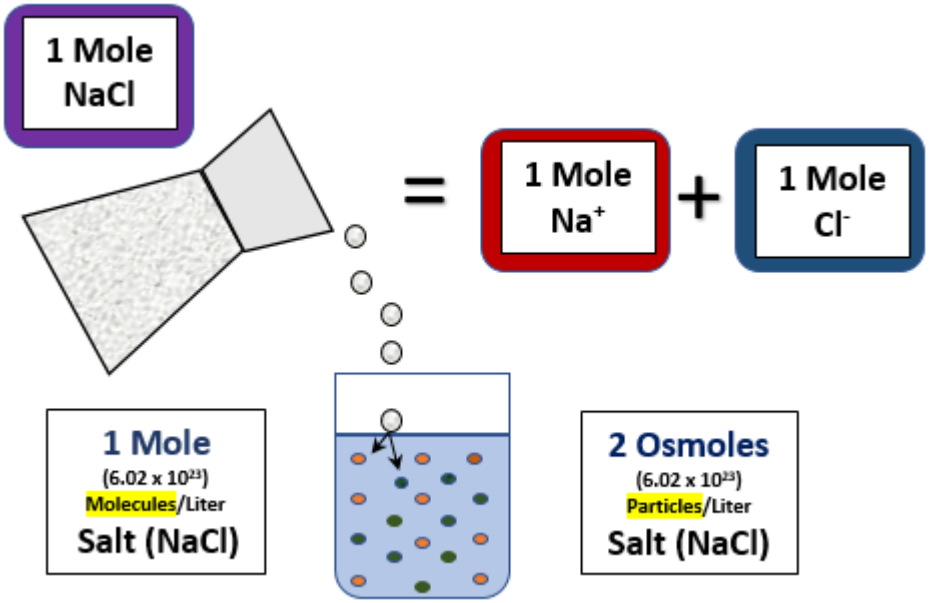
Since it is nearly impossible for us to measure 12 atoms, we need to use an understandable unit of measurement. A universally recognized unit of measurement for atoms (or molecules) is the mole (abbreviated mol). Just like one dozen is equivalent to 12, it has been determined that one mole is equivalent to 6.02×10^{23} atoms. The number is called Avogadro's number and is named after the famous scientist, Amedeo Avogadro (1776-1856). Just how big is a mole? If we were to go to a store and buy a bunch of eggs equivalent to the number of molecules in a mole, we could fill the volume of the earth approximately 40 times! Thankfully, molecules are much smaller than eggs; in fact, a mole of sucrose (table sugar) weighs only 342 grams and would barely fill the volume of a tennis ball. The difference, of course, is the size of the atoms that make up the sucrose molecule. So, how did we determine that 342 grams of sucrose contain Avogadro's number of molecules? First, we need to determine the **molecular mass** of sucrose. To do this, we take the atomic mass of each atom in the compound and add them together. For example, the formula for sucrose is $C_{12}H_{22}O_{11}$. The atomic mass of carbon is 12, and there are 12 carbon atoms in sucrose, so 12 x 12 = 144. The atomic mass of hydrogen is 1, and there are 22 hydrogen atoms in sucrose, so 22 x 1 = 22. Finally, the atomic mass of oxygen is 16, and there are 11 oxygen atoms in sucrose, so 11 x 16 = 176. When we add these together, we get 144 + 22 + 176 = 342. Therefore, the molecular mass of sucrose is 342 (we have rounded the atomic masses to the nearest whole number to make the computations easier). The units for this weight are atomic mass units (amu). Therefore, one sucrose molecule weighs 342 amu and one mole of sucruose weighs 342 grams.

This is much too small of a mass to weigh out on any existing scale (recall that one amu is approximately the mass of a proton or a neutron). However, we can easily weight out 342 g of sucrose. The amu total for a molecule expressed in grams is equal to one mole of that molecule. If we take that amount of sucrose (342 g) and add water until we have one liter of solution, we will have a one molar solution of sucrose. So, in a one molar solution of sucrose, we have 342 g, one mole, or 6.02×10^{23} molecules in one liter of solution. The advantage of expressing concentrations in molarity is that it is an expression that lets us compare the number of molecules in the solutions. For example, a one molar solution of sucrose (molecular mass = 342) and a one molar solution of glucose (molecular mass = 180) will have exactly the same number of molecules per liter of solution even though the molecules are different in size, and we may have added different masses of each.



Molarity & Molecular Mass: *Image created by T. Orton Summer 2017*

One other expression of concentration that is often useful is **Osmolarity**, which, as you can probably guess, is **Osmoles** per liter. This is a lot like molarity except that molarity is 6.02 x 10^{23} *molecules* per liter, whereas osmolarity is 6.02 x 10^{23} *particles* per liter. At first, it may seem like molecules and particles are the same thing. However, if a solute dissociates (comes apart) when dissolved, you end up with more than one particle per molecule. Take NaCl (salt) for example. When you dissolve one mole of salt in water, each molecule splits in two, so you end up with 2 x (6.02 x 10^{23} particles) in the solution. Hence, a one molar NaCl solution would be a two osmolar NaCl solution (NaCl is a molecule, and Na^+ and Cl^+ are particles). **Note: the actual osmolar NaCl solution is 1.6 because complete dissociation doesn't actually occur, but this will take on more significance when we talk about osmosis later in the course.*



Osmolarity: *Image created by T. Orton Summer 2017*

2.3

Acids, Bases, pH, and Buffers

Recall that the bonds that bind the oxygen and hydrogen together in water are polar covalent bonds and that covalent compounds typically do not dissociate. However, the polarity of water allows it to form hydrogen bonds with other water molecules in which the negative (oxygen) end of one water molecule is attracted to the positive (hydrogen) end of another water molecule. Although this is a weak attraction, occasionally, the oxygen of one water molecule is able to steal the hydrogen from another water molecule, splitting the water molecules into ions. When this happens, it results in the formation of a hydrogen ion (H^+) and a hydroxide ion (OH^-). Realize that in pure water, very few water molecules split —about 1 out of every 554,000,000 (who counted?). We can write the equation for this process like this:

$$H_2O \longleftrightarrow H^+ + OH^-$$

Note that as with all chemical reactions, the reactants and products are in equilibrium, and if that equilibrium is disturbed, the reaction will proceed until a new equilibrium is reached, hence the two-headed arrow in the equation (←→).

2.3.1

Acids and Bases

In pure water at 25^{o} C, the concentration of H^+ is always equal to the concentration of OH^-. Both have a concentration of 1.0 x 10^{-7} Molar. (Placing the symbol for a chemical in brackets [H^+] is chemical shorthand for "concentration of." Therefore, [H^+] is read "the concentration of hydrogen ion.") If we add a substance that results in an increase in [H^+], we say that substance is an **acid**. If we add a substance that results in a decrease in [H^+], we say that substance is a **base**. An acid is any substance that, when added to an aqueous solution, increases the [H^+] of the solution, and a base is any substance that, when added to an aqueous solution, decreases the [H^+] of the solution. A common acid, for example, is hydrochloric acid, HCl. When HCl reacts with water, it dissociates into an H^+ and a chloride ion (Cl^-), thus increasing the [H^+]. HCl is considered a strong acid because when placed in water, it completely dissociates into its two ions.

$$\mathbf{HCl \longrightarrow H^+ + Cl^-}$$

A weak acid, such as **acetic acid** (CH_3COOH), dissociates into H^+ and CH_3COO^- (acetate). However, most remains intact as acetic acid, and there is a chemical equilibrium between the CH_3COOH and the $H^+ + CH_3COO^-$. The **conjugate base** is the name given to the now unprotonated compound (acetate). Thus, the disassociation of acetic acid (weak acid) produces acetate (conjugate base) and a hydrogen ion:

$$\mathbf{CH_3COOH \longleftrightarrow H^+ + CH_3COO^-}$$

An example of a base is ammonia (NH_3), which will combine with H^+ to form an ammonium ion (NH_4^+), thus removing H^+ from the solution.

$$\mathbf{NH_3 + H^+ \longrightarrow NH_4^+}$$

Another common base is sodium hydroxide (NaOH). How is this a base? When it dissolves, it dissociates into a sodium ion (Na^+) and OH^-, no change in [H^+], right? However, the OH^- will combine with H^+ to form water, thus removing H^+ from the solution.

$$\mathbf{NaOH \longrightarrow Na^+ + OH^-}$$

$$\mathbf{H^+ + OH^- \longrightarrow H_2O}$$

2.3.2

pH

Why do we care about the $[H^+]$ anyway? What is special about this particular ion? Well, it turns out that either too much or too little H^+ can cause serious problems to chemical reactions. We use the terms acidic and basic to describe these conditions. If the $[H^+]$ of the solution is greater than 1.0×10^{-7}, we say the solution is **acidic**, and if the $[H^+]$ is less than 1.0×10^{-7}, we say the solution is **basic**.

Because the $[H^+]$ is so important and because it is rather cumbersome to say things like, "the $[H^+]$ of the fluid is 1.0×10^{-7} Molar," chemists have developed a shorthand to express the $[H^+]$. This shorthand expresses the $[H^+]$ as the **pH** of the solution. The pH of a solution is the **negative logarithm of the $[H^+]$** (concentration expressed as moles per liter, M). So, if the $[H^+]$ is 1.0×10^{-7} M, the pH of that solution would be 7 ($-\log 10^{-7}$ is $-(-7)$ or 7). Since this is the pH in which the $[H^+]$ and $[OH^-]$ are equal, we say that this is a **neutral solution**. When using pH, one thing that is a little confusing is that as the $[H^+]$ of a solution goes up, the pH goes down. Suppose that a solution has a $[H^+]$ of 1.0×10^{-6} M. The pH of the solution would be 6, but since the math behind pH is log base 10, the change in pH from 7 to a pH of 6 represents a 10-fold increase in hydrogen ions. Moving from a pH of 7 to pH of 5 represents a 100-fold increase. Thus, an **acidic solution** is any solution with a pH<7. Likewise, any solution that has a pH>7 is a **basic solution**. Below is an image that shows the pH of some common solutions.

pH	Examples of solutions
0	Battery acid, strong hydrofluoric acid
1	Hydrochloric acid secreted by stomach lining
2	Lemon juice, gastric acid, vinegar
3	Grapefruit juice, orange juice, soda
4	Tomato juice, acid rain
5	Soft drinking water, black coffee
6	Urine, saliva
7	"Pure" water
8	Sea water
9	Baking soda
10	Great Salt Lake, milk of magnesia
11	Ammonia solution
12	Soapy water
13	Bleach, oven cleaner
14	Liquid drain cleaner

pH Scale and Examples. *Downloaded from Wikimedia Commons Fall 2014; Author: OpenStax College; License: Creative Commons Attribution 3.0 Unported license.*

So, there are two important lessons from this; the lower the pH, the higher the $[H^+]$, and a change in pH of one unit (7 to 6 for example) is a 10-fold change in $[H^+]$.

2.3.3

Buffers

Because it is essential for many chemical reactions that pH is maintained within a narrow range, biological system employ various **buffer systems**. Buffers are chemicals that tend to *resist* changes in ph. Note that buffers do not *prevent* changes; they *resist* changes. Let's see if we can figure out how this works.

The determination as to whether something will be weak or strong (acid/base) is dependent upon a value called the **Ka** or **disassociation constant**. A Ka value is calculated from the ratio of the products to the reactants at equilibrium (Ka = [products/reactants]). For example, the Ka of acetic acid is 1.73×10^{-5}. In fact, the Ka values for all weak acids are all very small so we employ the same logic as that of pH and use the negative log which means we use the letter p. Thus, the **pKa** for acetic acid is 4.73. Also, like the pH system, strong acids will have very low pKa values while weak acids will have higher pKa values.

A typical buffer system is composed of a weak acid and the conjugate base of that acid. Remember, weak acids are those that do not dissociate completely but reach an equilibrium between the reactants and the products of the reaction. An important buffer system is the bicarbonate buffer system. The components of this system are shown below.

$$H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

Carbonic Acid Hydrogen Ion Bicarbonate Ion

In this case, the carbonic acid is the weak acid, and the bicarbonate ion is its conjugate base. The entire reaction is in equilibrium. If the equilibrium is disrupted by the addition of more hydrogen ions, the reaction will proceed to the left until equilibrium is restored. When it proceeds to the left, some of the excess hydrogen ions will combine with bicarbonate forming carbonic acid, hence removing some of the excess hydrogen ions from the solution. Essentially, the buffer has "soaked up" some of the extra hydrogen ions, thus preventing a large change in pH.

Another way of thinking of this system is to assume it behaves like a teeter-totter. If we have equal weights on each side, the teeter-totter is balanced (in equilibrium). If we add excess weight to one side (excess hydrogen ions), it will be out of balance. The only way to restore balance (equilibrium) is to move some of the excess weight to the opposite side until the teeter-totter is balanced again (equilibrium restored). Obviously, in this simple example, we realize that we cannot move all of the added weight to the opposite side because it would again be out of balance, but if *some* of the excess weight is moved to the other side, balance can be restored. Like the teeter-totter, when extra hydrogen ions are added, not all can be combined with bicarbonate, so there will still be a few more hydrogen ions than at the beginning (this is why buffers *resist* pH changes instead of *prevent* changes in pH). The pH will decrease, but not nearly as much as it would have if all added hydrogen ions were allowed to remain without being buffered. We could use the same analogy to see what happens when hydrogen ions are removed from the solution by the addition of a base. Since the

equation is again out of equilibrium, the reaction will proceed to the right (dissociation of carbonic acid) until some of the hydrogen ions have been replaced. Again, there will be a slight increase in pH, but not nearly as great as would happen in the absence of the buffer.

An important buffer rule is that buffer systems work best at a pH that is near the pKa for the system.

In 1908 two researchers developed an equation that predicts the resultant pH of a given buffer system, the equation is named after them and is called the Henderson-Hasselbalch equation.

(Henderson-Hasselbalch equation)

$$pH = pK_a + \log \frac{[A^-]}{[HA]}$$

In this equation A^- is the concentration of conjugate base and HA is the amount of weak acid. If we know the pKa of the buffer, we can then calculate the resultant pH of the solution. Alternatively, if we know the among of HA, A^- and the pH (and remember our math log rules!) we can calculate the pKa of the weak acid.

UNIT 3

CARBOHYDRATES

3.1

Carbon

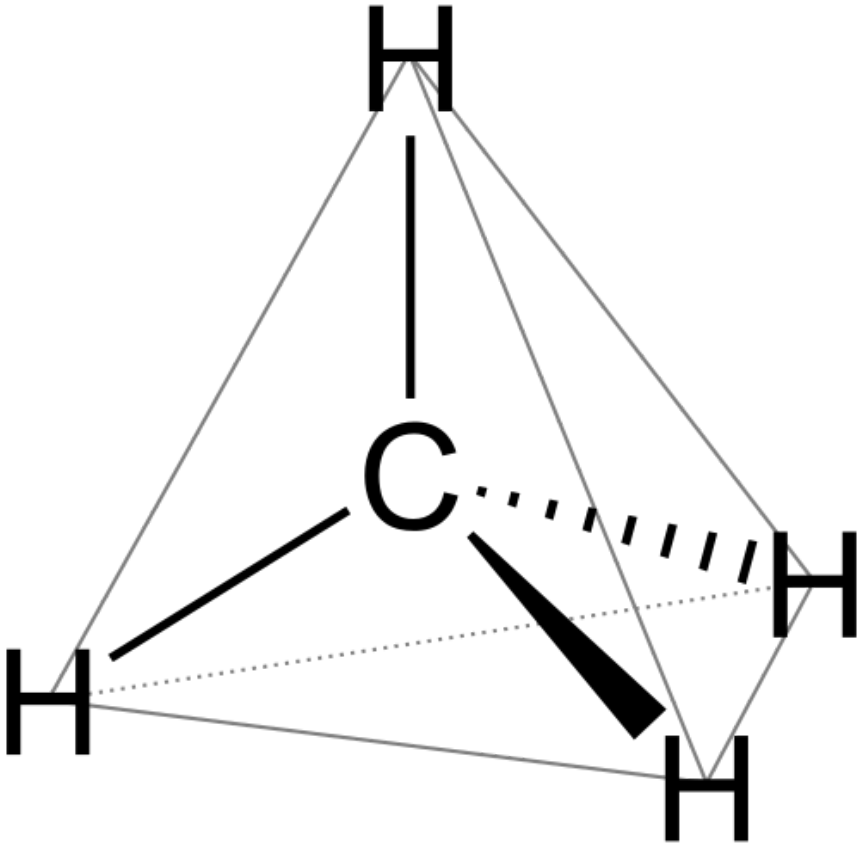
There are roughly 92 naturally occurring elements on earth, but only four make up about 96% of all living organisms: oxygen, carbon, hydrogen and nitrogen. These elements combine to form life-sustaining biomolecules, which can be divided into four major groups of macromolecules: carbohydrates, lipids, proteins, and nucleic acids. Carbohydrates, proteins, and lipids are used by cells as the building blocks for cells and for energy, while nucleic acids are the basis of genetic material (DNA and RNA). There is one shared characteristic among all these macromolecules in that they all contain carbon. In fact, the definition of organic chemistry is "*the chemistry of carbon compounds*." Why carbon? Because carbon has the perfect electron distribution (4 valence electrons) to form covalent bonds with as many as four different atoms at one time. This makes carbon very versatile, a characteristic that will be explored in more detail below.

3.1.1

Hydrocarbons

TEXT HERE

When carbon forms bonds with just hydrogen we call the structure a hydrocarbon. The simplest hydrocarbon is composed of four single bonded hydrogen atoms surrounding a center carbon and is called methane (CH_4). Since covalent bonds store lots of energy, hydrocarbons are often used as fuel, an example being the propane in your barbeque grill. In addition, to maximize structural stability, the electron orbitals cause methane to exist in a three-dimensional shape called a tetrahedron with bonds spaced as far apart as possible, in this case exactly 109.5˚ apart, and four triangular faces. The three-dimensional shapes of various hydrocarbons dictate how they function within the macromolecule. Shapes are typically straight chains or rings or combinations of both.

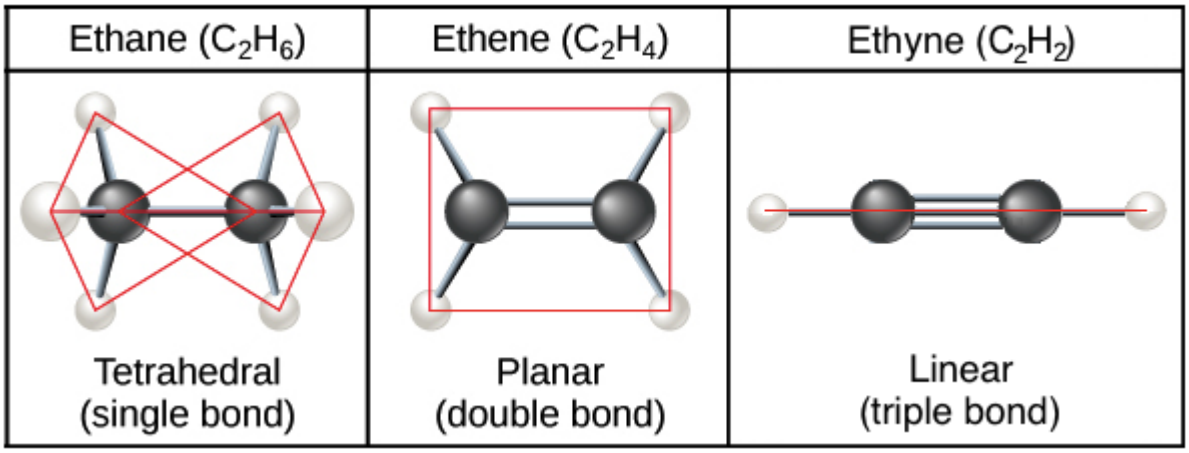


By Hbf878 CCO 1.0

Hydrocarbon Chains and Rings

As already stated, some hydrocarbons exist as linear chains also called **aliphatic** . The geometry of the chain is affected by the number of single, double, or triple covalent bonds which in turn effects the overall shape of the molecule they are

incorporated in. Single bonds allow carbons to rotate around the axis of the bond, double bonds force planar structures and triple bonds linear structures. For example, consider the three hydrocarbons ethane, ethene, and ethyne. Note the prefix “eth-“ which always signifies a two carbon hydrocarbon. The suffixes of “-ane,” “-ene,” and “-yne” indicate a single bond, double, or triple bond respectively, between the two carbons. Thus, like methane, ethane will have a tetrahedral shape because there is a single bond between the two carbons (allows for rotation) and each are surrounded by three hydrogens. The hydrogen will try and space out as far as possible creating a tetrahedral three-dimensional shape. Ethene has a double bond between the carbons and only two hydrogen atoms connected to each carbon. Thus, the shape becomes flat or planar because the two carbon atoms are locked in place (can’t rotate). Finally, Ethyne has three bonds and each carbon only one hydrogen making the structure linear. The same model follows for the prefix of three carbon hydrocarbons “prop-“(propane, propene, propyne) and the prefix of four carbon hydrocarbons “but-“ (butane, butene, butyne).



Hydrocarbons that are not linear but instead form benzene rings are called **aromatic**. Benzene rings are closed rings of carbon atoms that may or may not contain double bonds. Rings can be formed with five or six carbon atoms. Rings are incorporated in many of the macromolecule structures.

3.1.2

Isomers

How atoms are placed within organic molecules (three-dimensional structure/chemical bonds) determines the overall function of the molecule. Interestingly, some molecules can have the exact same number and types of atoms (i.e., chemical formula) but those atoms can be arranged completely differently, dramatically changing function. In this case, we called these molecules **isomers**. There are two types of isomers: **structural isomers** and **stereoisomers**. Stereoisomers can be further subdivided into **geometric isomers**, **enantiomers** and **diastereomers**.

Structural Isomerism

Structural isomers, also called *constitutional isomers*, have the same molecular formula but with different arrangements of atoms. For example, butane and isobutene both contain four carbons and ten hydrogens (C_4H_{10}) but because of their structural differences, butane is an explosive fuel property and isobutane is a propellant ("cold" properties) used as a refrigerant. We call them structural isomers because they have a different pattern of covalent bonding. In butane all the carbons form a single chain, but the carbons in isobutene form a branched chain.

Stereoisomers

Stereoisomers have the same number of atoms and bonds, but they differ in how their atoms are oriented around one or mor carbons. Often, they look very similar, but if you were to try and stack them on top of each other they would not fit, a phenomenon that is called non-super imposable structures.

Geometric isomers

Geometric isomers also have the same molecular formula and the same pattern of covalent bonding but differ in how atoms are spaced around a double covalent bond, especially in a carbon-to-carbon double bond. For example, consider the molecule butene (C_4H_8). In the molecule butene the two methyl groups (CH_3) can be located on same side as the double bond (**cis configuration**) or opposite sides (**trans configuration**). The cis arrangement makes the molecule bend since the two methyl groups act to "repel" each other, whereas in the trans configuration the molecule will be more linear as the two methyl groups "balance" each other.

Enantiomers

When two molecules' atoms are arranged in the exact opposite way, so that they actually look the same in the mirror, we call them enantiomers. To be an enantiomer the atoms swap positions around a central carbon called an **asymmetric carbon**. At this point you may be thinking: "How on earth did anyone in the right mind figure this stuff out when they can't even see them!?" Well, in the case of enantiomers scientists used the properties of light. Apparently, when you shine light at structures that are invisible to the naked eye, light rotates, and rotating light is something that can be seen. Thus, even though a molecule has the same molecular formula, swapping positions with different groups of atoms to create a mirror image can drastically affect how light rotates through it. The term mirror image refers to the result of the swapping groups of atoms (**functional groups; see below**) around a center carbon and can be captured in one concept

called **chirality**. For example, a metal rod would not be considered chiral because its appearance in a mirror would look the same. However, consider the threads on a screw. Rotating the threads to the right would appear as if you were rotating the screw to the left in the mirror, this effect could be described as chiral.

In chemistry, a chiral molecule can exist in two forms, described as non-superimposable mirror images, and these two forms are called enantiomers. Non-superimposable mean that if you tried to stack images of the two molecules on top of each other they would not line up. Consider your hands, they are mirror images of each other but they do not stack on top of each other. Pairs of enantiomers will rotate light either clockwise (to the right) or counterclockwise (to the left). Initially, clockwise rotations (right) were described as dextrorotary (d) and counterclockwise rotation (left) as levorotary (l). This nomenclature evolved to the capitol D and capitol L system. Once a structure has been identified, determining which way light will rotate is determined using the Cahn-Ingold-Prelog (CIP) system which uses R (clockwise) and S (counterclockwise) nomenclature. The CIP system assigns priority based on atomic numbers to help determine the rotation (I > Br > Cl > S > P > F > O > N > C > H).

Diastereomers

The final group of stereoisomers are diastereomers which are very similar to enantiomers except that they contain more than one asymmetric carbon. This property makes it impossible for them to form mirror images.

3.2

Functional Groups

The term functional group refers to the groupings of atoms within molecules. Functional groups determine the specific chemical properties of the molecules and as explained above, the rotation of light. The understanding of functional groups is pivotal to being able to understand the functions of the four major macromolecules: carbohydrates, lipids, proteins, and nucleic acids. Functional groups in macromolecules are usually attached to carbon backbones in different places, and each macromolecule group has unique sets of functional groups. Some of the most important functional groups are identified below in the table.

Functional Group Name	Structure	Polarity	Properties and Features	Compound names	Macromolecule example
Alkyl		Nonpolar	Hydrophobic, Vander Waals interactions	Hydrocarbons	Lipids
Hydroxyl		Polar	Soluble in water	Alcohols	Carbohydrates
Carbonyl		Polar	Soluble in water	Aldehydes or ketones	Nucleic acids, carbohydrates
Carboxyl		Ionic	Soluble in water, acidic	Carboxylic acids	Lipids, amino acids
Amino		Ionic	Soluble, basic	Amines	Amino acids, nucleic acids
Sulfhydryl		Weak polar	Disulfide bonds	Thiols	Amino acids
Phosphate		Ionic	Soluble in water, acidic, energetic	Phosphoric acids	Lipids, nucleic acids
Amide		Polar	Soluble in water, peptide bonds, not acidic	Amides	Amino acids

Polymers

In addition to the formation of isomers, functional groups also allow for similar molecules called monomers to bond together and form more complex structures called polymers. Some of the important macromolecules in biology that are polymer carbohydrates such as glycogen and starch, nucleic acids, and proteins. Lipids are not considered polymers. The synthesis or breakdown of polymers occurs through dehydration reactions or hydration reactions (hydrolysis) respectively. As polymers are synthesized from monomers, specific functional groups from one monomer will lose a -H and a corresponding functional group on another monomer will lose an -OH. As H^+ and OH^- ions are lost, they will combine to form water (H_2O) and their loss is replaced with a new covalent bond between the two monomers. For this reason, this synthesis reaction is called dehydration synthesis. In contrast, when polymers are broken down, water molecules are split to yield a -H and an -OH and those ions are "put back on" each specific monomer which acts to replace the covalent bond between the two monomers which causes them to break apart. This process is called hydrolysis.

3.3

Carbohydrates

Carbohydrates are the most abundant of the biomolecules. If we were to identify the most important carbohydrate molecule on the planet, in terms of its ability to sustain life, we would undoubtedly select the monosaccharide glucose. Without glucose, nearly all animal life as we know it could not exist.

Carbohydrates can be classified into 4 major subtypes: **monosaccharides, disaccharides, oligosaccharides** and **polysaccharides**. These classifications are based on both the size and function of the molecule. The name "saccharide" is derived from Greek; it means “sugar.” Monosaccharides are the simplest form of carbohydrates and are composed of a single molecule or subunit. The disaccharides are composed of two monosaccharides linked together, while oligosaccharides are composed of between 3 and 20 monosaccharides and polysaccharides consist of hundreds or thousands of monosaccharides linked together. We will now examine each of these types of carbohydrates.

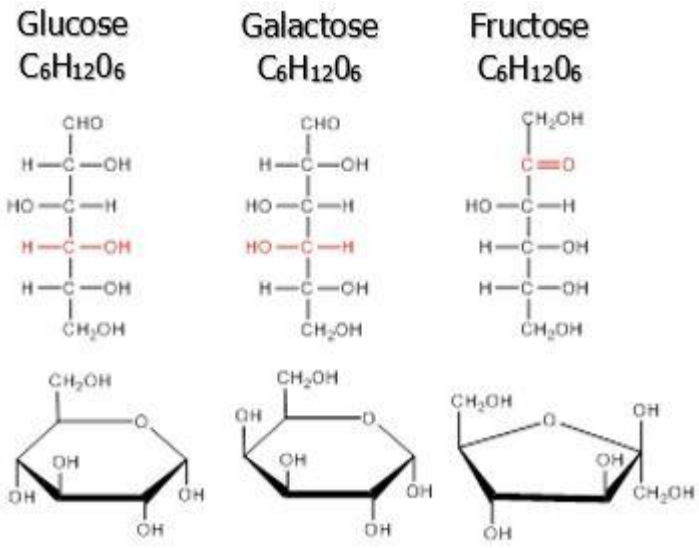
- Monosaccharides
- Disaccharides
- Polysaccharides
- Oligosaccharides

3.3.1

Monosaccharides

Monosaccharides (mono = one, saccharide = sugar) are the basic subunits of carbohydrates. They contain from 3–7 carbons and have the general formula of $(CH_2O)_n$ where n ranges from 3–7 (5 or 6 being the most common). For example, if n = 6, the formula for the monosaccharide would be $C_6H_{12}O_6$. Please note that the ratio of carbon to water (H_2O) is 1:1 in a monosaccharide, giving credence to the name carbohydrate. Note also that monosaccharides contain a significant amount of oxygen. Carbohydrates have the highest oxygen to carbon ratio of any of the important organic molecules. Monosaccharides contain multiple hydroxyl functional groups and always on carbonyl functional group. These oxygens can increase the solubility of carbohydrates in water (due to the increased number of polar covalent bonds).

Common monosaccharides include **glucose, fructose, galactose, ribose, and deoxyribose**. Notice that the name of each of these sugars ends with the suffix -ose. This suffix, -ose, means full, specifically full of oxygen. The names of most sugars will end with this suffix. The structures of three common dietary monosaccharides are shown in the figure below. Note that the molecules can exist in two different forms. When they are in a dry or powdered state, they exist as a linear molecule (top), but when dissolved in water, they adopt a ringed form with oxygen being one of the members of the ring (bottom).

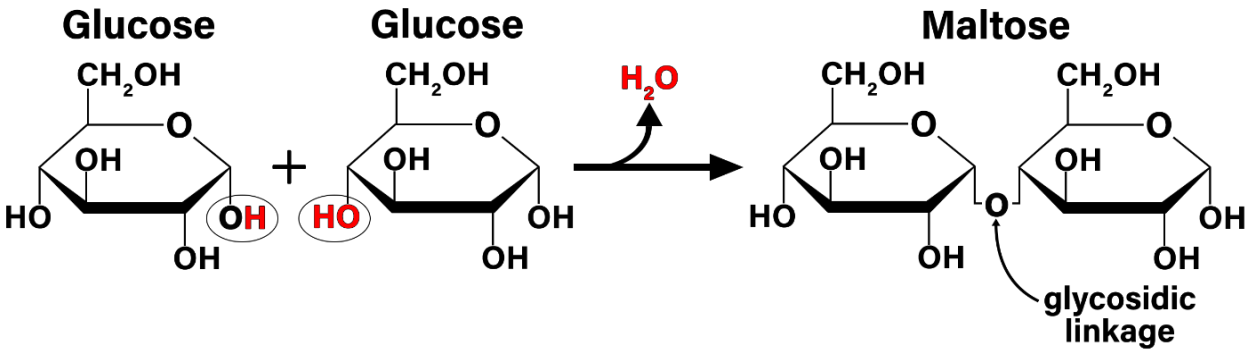


Linear and Ring Structure of Isomers of $C_6H_{12}O_6$. *Image created by MG 2013*

3.3.2

Disaccharides

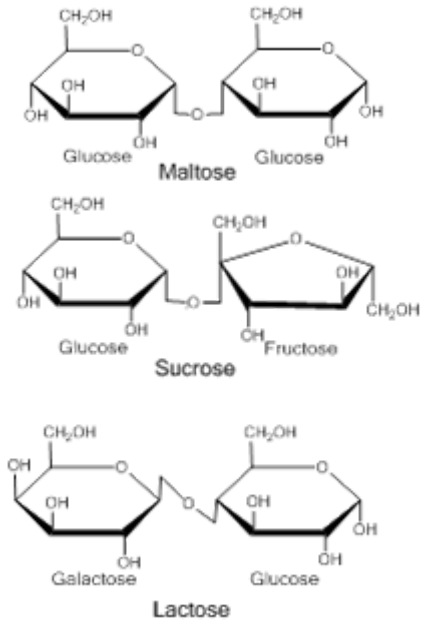
Disaccharides (Di = two, saccharide = sugar) are formed when two monosaccharide molecules are joined together covalently (glycosidic linkage) through a dehydration reaction. Glycosidic linkages occur from dehydration reactions of two hydroxyl groups, one of which is **anomeric** carbon, or the carbon associated with the carbonyl group. In the linear structure of glucose, the carbon with the carbonyl group is the anomeric carbon which becomes the carbon #1 (chiral center carbon) of the ring shape. Another way to find the anomeric carbon is to locate the one carbon that has two oxygen atoms attached to it.



Dehydration Synthesis Reaction Showing the Formation of Maltose.
Image by BYU-Idaho professor Spring 2021

The image above shows a dehydration synthesis reaction. The reactive hydroxyl groups (-OH) are circled. The hydrogens and oxygen that will be removed to form water are colored red. The resulting linkage is called a glycosidic linkage.

There are three important disaccharides that we will discuss: **sucrose, lactose, and maltose**. In all three of these disaccharides, glucose is one of the monosaccharides that make them up. The figure below shows the structure of these disaccharides, and the table below outlines their characteristics.



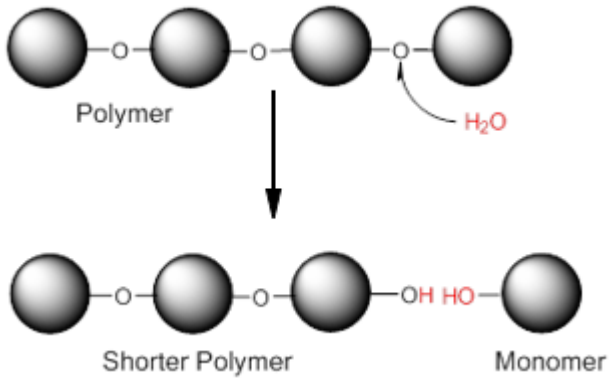
Disaccharide Structure: *Image created by MG, 2013*

The image above shows the structures of the three common dietary disaccharides. All contain glucose as one of their subunits. The difference between the three is the second subunit.

Table: Characteristics of three common disaccharides.

Name	Combined Monosaccharides	Nutritional Information
Sucrose	Glucose + Fructose	The most common dietary disaccharide. Naturally found in beets, cane sugar, brown sugar, maple syrup, and honey. You know it as table sugar.
Lactose	Glucose + Galactose	Found in dairy products. This is the least sweet of the disaccharides.
Maltose	Glucose + Glucose	Found in foods including breakfast cereals, germinating seeds, and beer.

Only monosaccharides can be absorbed from the digestive tract into the blood. Therefore, in order to enter the body, disaccharides must first be broken down (or digested) into their monosaccharide subunits. In the small intestine, there are specific enzymes for each of these disaccharides: **sucrase** to digest sucrose, **lactase** to digest lactose, and **maltase** to digest maltose. The reaction for digestion is essentially the reverse of the dehydration synthesis reaction (i.e. water is added back into the bond to break it). This type of reaction is called a **hydrolysis reaction**. Because disaccharides are easily digested and quickly absorbed into the blood, they, along with the monosaccharides, are often referred to as the **simple sugars**.



Hydrolysis Reaction. *Image created by BYU-I Student Hannah Crowder, 2013*

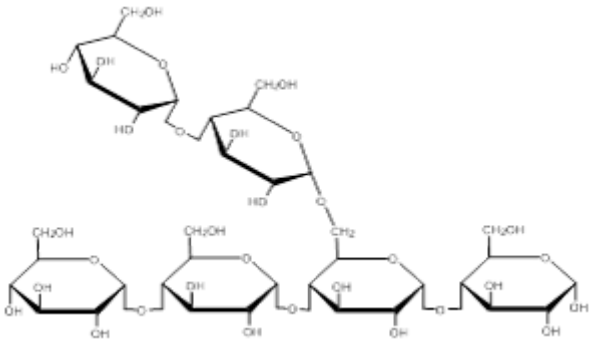
The image above shows a hydrolysis reaction. Bonds between the monomers in a polymer can be broken by the enzymatic addition of water to the bonds. Monomers can be defined as a single molecule that can bind to other molecules to form a polymer.

3.3.3

Polysaccharides

Polysaccharides are long chains of monosaccharide subunits linked together through dehydration synthesis reactions. Typically, these chains contain hundreds to thousands of monosaccharides linked together through glycosidic linkages. Because of their length, polysaccharides are considered **complex carbohydrates**., Polysaccharides can be classified into two categories based on their function as either energy storage or anatomical structure. When monosaccharides form rings they adopt one of two possible orientations. The first orientation involves the anomeric carbon hydroxyl group being located below the ring called the **alpha** orientation. The other orientation involves the hydroxyl group on the anomeric carbon being above the ring called the **beta** orientation. Storage polysaccharides are made from alpha monomers with glycosidic linkages at the anomeric carbon and the 4^{th} or 6^{th} carbon of the other monomer (alpha 1-4, alpha 1-6). Alpha 1-4 bonds are linear whereas alpha 1-6 bonds form branches. Structural polysaccharides are made from the beta monomers with glycosidic linkage occurring at the anomeric carbon and 4^{th} carbon of the other monomer (beta 1-4).

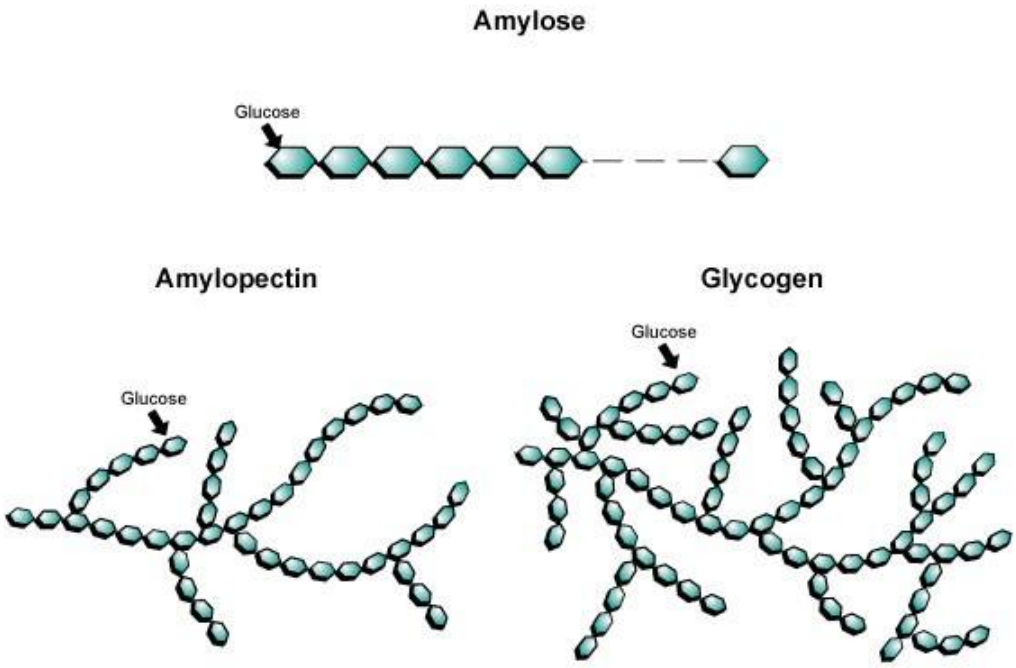
Storage polysaccharides: Storage polysaccharides include starch and glycogen. Plants and animals store sugar for energy use in the form of glycogen (animals) and starch (plants). **Starch** is a large polymer of glucose subunits and may be branched (alpha 1-6) or linear (alpha 1-4). **Amylose** is a long, unbranched chain of glucose subunits. **Amylopectin,** on the other hand, has a branched structure (see figure below). In mammals, it is the proportion of each form of starch in a particular food that determines the food's ability to be digested. Foods with a large amount of amylopectin are digested and absorbed rapidly because of the many branches, which facilitates hydrolysis. Foods that have higher levels of amylose break down at a slower rate. Some examples of starches include seeds, grains, corn, beans, potatoes, and rice.



Branched Polysaccharide Amylopectin: *Image created by MG, 2013*

The image above shows branching in a polysaccharide molecule. Branching allows increased enzymatic breakdown and faster digestion.

Glycogen is the storage form of carbohydrates in animals. Glycogen, like starch, is a polymer of glucose subunits. It is similar in structure to amylopectin, but it is even more highly branched. The branched structure of glycogen allows for easy breakdown by enzymes to release the glucose, so it can be utilized for energy.



Amylose, Amylopectin & Glycogen Structure. *Image created by BYU-I student Hannah Crowder, 2013*

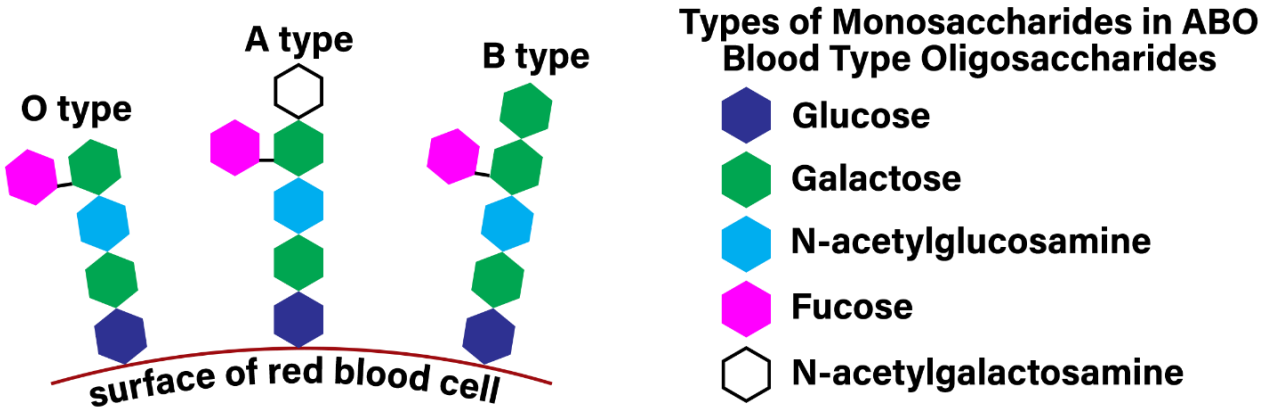
This image above shows different degrees of branching in amylose, amylopectin, and glycogen.

Structural polysaccharides: **Cellulose** is an important structural molecule in plants. Cellulose is a polymer of glucose but is assembled using different glycosidic linkages (beta 1-4). Most animals do not contain enzymes that can break beta 1- 4 bonds. These bonds are found in cellulose (fiber), however, certain types of bacteria can breakdown the bonds. Cows or animals that eat grass (high in fiber) have large amounts of bacteria in different chambers of their stomachs that help them break down the fiber to usable sources of monosaccharides.

3.3.4

Oligosaccharides

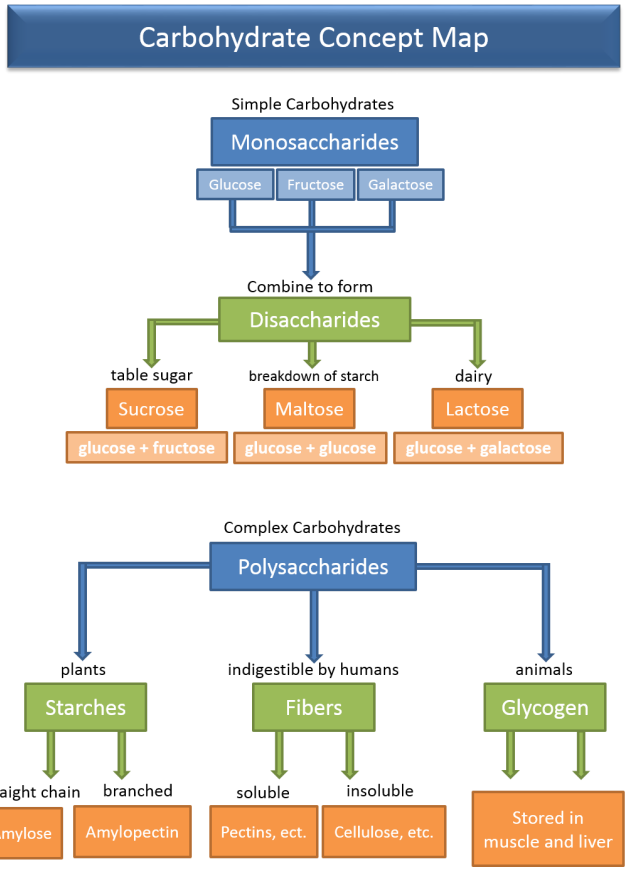
Oligosaccharides differ from polysaccharides primarily in their function. Oligosaccharides range in length from a few monosaccharides up to 100 or more. In humans, most oligosaccharides are between 5-30 monosaccharides in length. These sugars can be linear or branched and are made of a diverse pool of monosaccharides. The diversity in shape and composition facilitates their primary role as cell signaling molecules. Attached to the outer cell membrane, oligosaccharides aid in cell identification and function. A familiar example is blood type. A, B, and O blood types are all designated by a type of oligosaccharide found on the surface of red blood cells (see image below).



ABO blood types are identifiable by different oligosaccharides on the surface of red blood cells.
Image by BYU-Idaho professor Spring 2021

This image shows the different oligosaccharides expressed on the surface of red blood cells that contribute to blood type. These oligosaccharides are branched and are made of 5 different monosaccharides.

In summary, the Dietary Carbohydrate Concept Map shown below ties together the major relationship between and most common examples of monosaccharides, disaccharides and polysaccharides.



Carbohydrate Concept Map: *Image created by BYU-I student Hannah Crowder, 2013*

UNIT 4

LIPIDS, NUCLEIC ACIDS, AND PROTEINS

4.1

Lipids

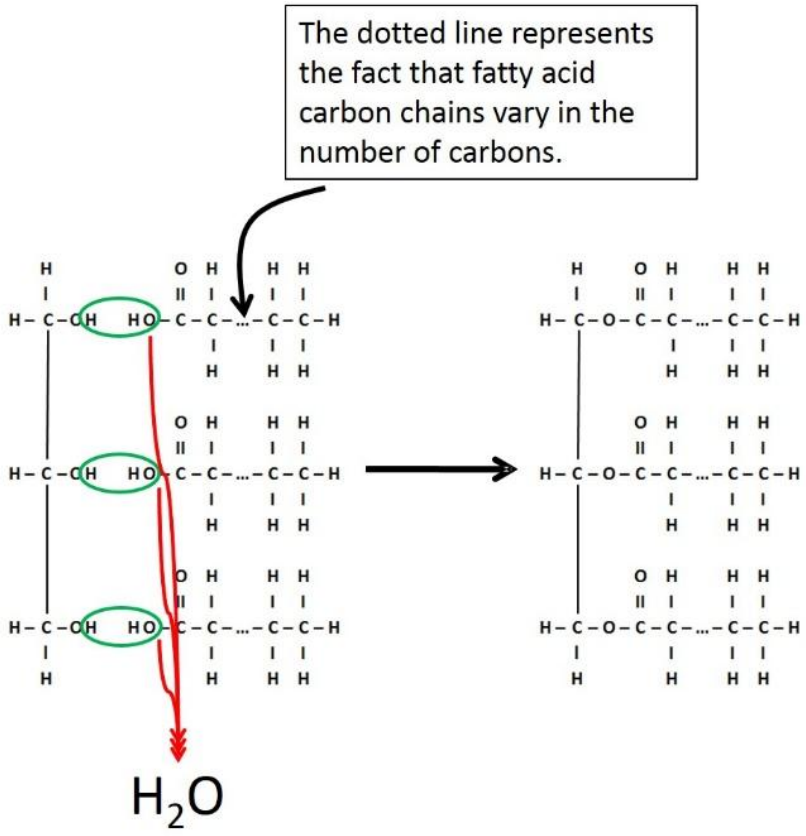
The Nature of Lipids

Lipids include a vast array of naturally occurring organic molecules. Lipids can be categorized as fats, oils, waxes, cholesterol, cell membranes, some pigments, some vitamins, and many other important compounds. Lipids are molecules that are insoluble in water. Among the many types of lipids, the terms "fat" and "oil" are probably the most familiar. **Fats** are generally solid at room temperature while **oils** are liquids. Here we will examine 3 primary classes of lipids: triglycerides, phospholipids, and steroid lipids.

4.1.1

Triglycerides

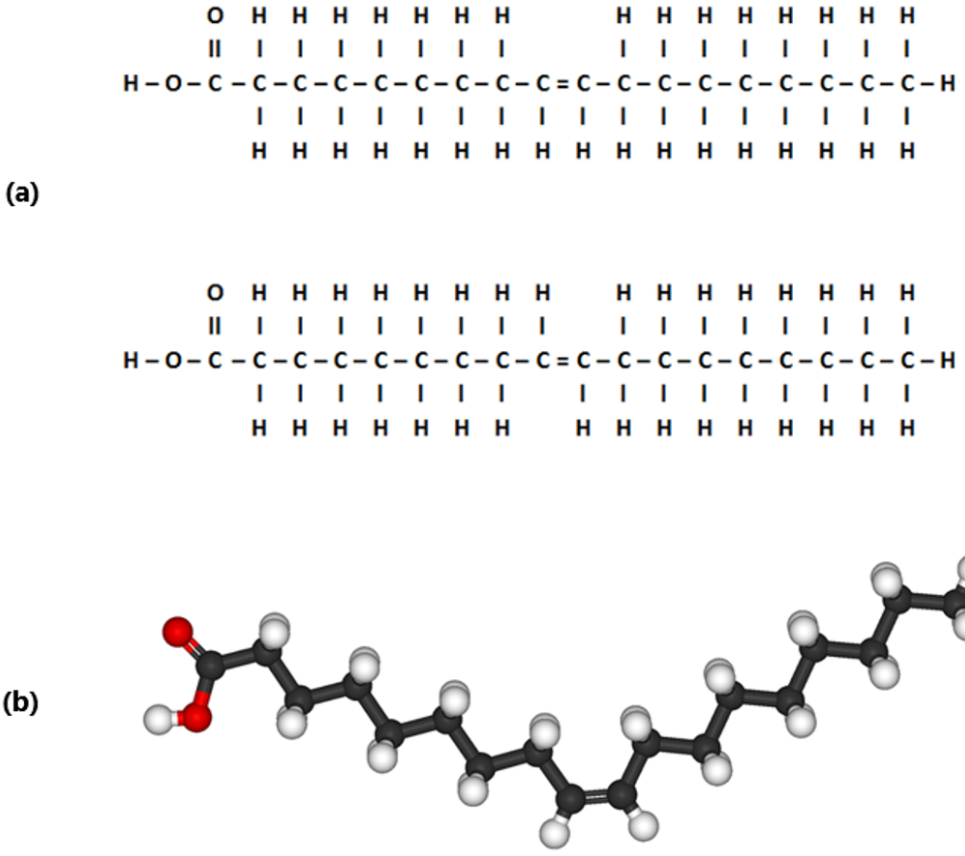
Triglycerides (also called triacylglycerol) constitute the major form of fat stored in plants and animals. Triglycerides are composed of two molecular building blocks: glycerol and fatty acids. Glycerol is a 3-carbon sugar alcohol. A triglyceride is formed by attaching a fatty acid to the hydroxyl group (-OH) of each of these 3 carbons of glycerol through a process called **esterification**. This reaction is a dehydration synthesis reaction (water is removed) and the resulting bond is called an **ester linkage** (see figure below).



Bonding of Three Glycerol and Fatty Acids by Dehydration Synthesis Reaction to Form Triglyceride.
Image created by JS at BYU-Idaho 2014

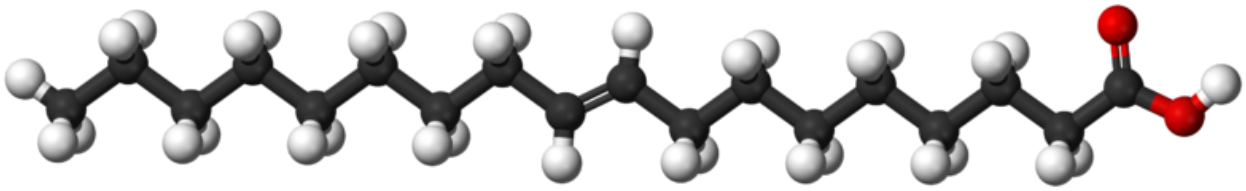
To understand the properties of a triglyceride, you must first understand the properties of fatty acids. **Fatty acids** are hydrocarbon chains with a carboxyl group (-COOH) at one end. The hydrocarbon chain consists of carbon-carbon and carbon-hydrogen bonds, which are non-polar covalent bonds and therefore **hydrophobic**. The carboxyl group at the beginning of the hydrocarbon chain is considered a weak acid because it can donate a proton at physiologic pH. Hence the name “fatty acid”.

Fatty acid chains can vary in length, as well as the number and type of carbon-carbon double bonds contained within the hydrocarbon chain. Fatty acid chains with no carbon-carbon double bonds are referred to as **saturated**. This means that every carbon-carbon bond in the chain is a single bond, which allows two hydrogen atoms to link to every carbon in the chain, except for the last carbon which is bonded to three hydrogen atoms. However, if a double bond occurs between two carbons in the hydrocarbon chain, then the carbon atoms connected by a double bond will each bond with one less hydrogen atom in order to maintain four bonds per carbon atom. As such, the hydrocarbon chain is no longer "saturated" with hydrogen atoms at every carbon. Therefore, an **unsaturated** fatty acid will contain one or more double bonds (see the image below).



(a) Cis & Trans Double Bond in Monounsaturated Fatty Acid; (b) Cis Double Bond in Unsaturated Fatty Acid.
Image created by JS at BYU-Idaho 2014: Modified File: Oleic-acid-3D-ball-&-stick.png; Author: Benjah-bmm27; Site: https://commons.wikimedia.org/wiki/File:Oleic-acid-3D-ball-%26-stick.png; License: Public Domain

Carbon-carbon double bonds significantly affect the behavior of the fatty acid. These double bonds can occur in one of two states: ***cis*** (same) or ***trans*** (across). The figure above shows a line drawing of two monounsaturated fatty acids. Note that the first molecule in illustration (a) has the hydrogen atoms extending from the carbon chain on the same side of the double bond. This is called a cis double bond. Note that the second molecule in illustration (a) is nearly identical except that the hydrogen atoms extend from the carbons at the double bond on opposite sides. This is called a trans double bond. Illustration (b) shows a 3D representation of the cis double bond in the unsaturated fatty acid chain. Notice how cis bonds bend or put a kink in the carbon chain.



Trans Double Bonds in Unsaturated Fatty Acid. *Title: File: Tridecylic-acid-3D-balls.png; Author: Jynto and Ben Mills; Site: https://commons.wikimedia.org/wiki/File:Tridecylic-acid-3D-balls.png; License: public domain*

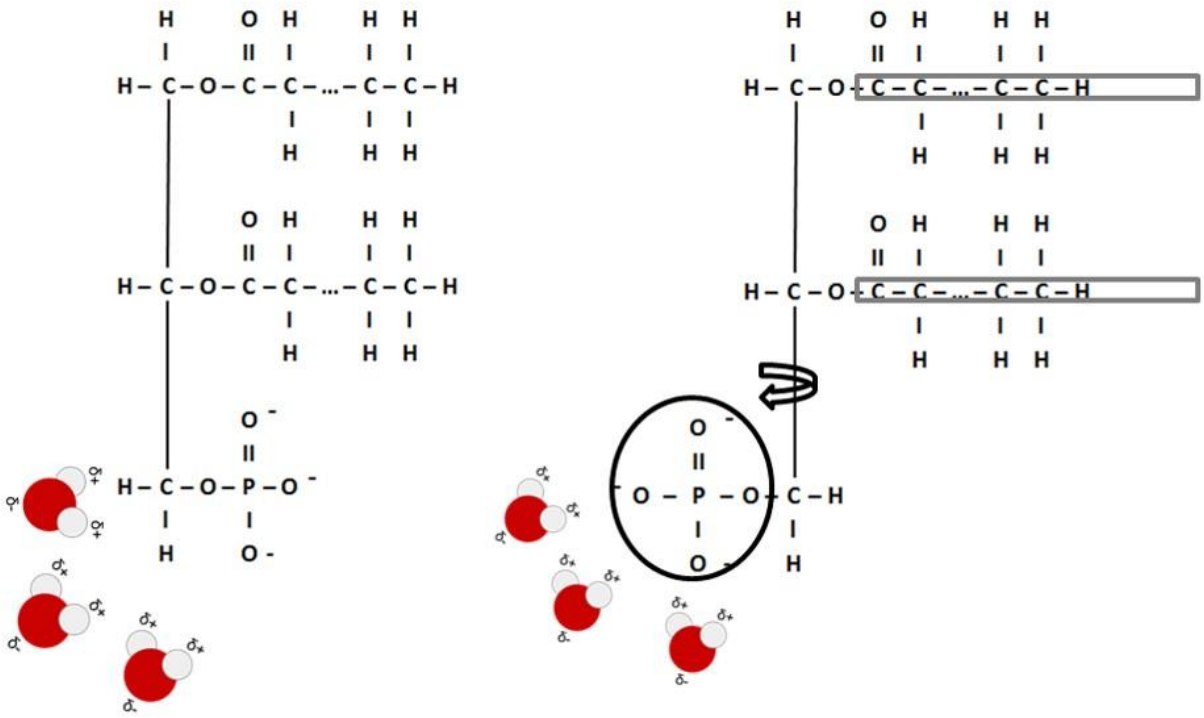
A fatty acid with one double bond is referred to as a **monounsaturated fat,** and fatty acids with two or more double bonds are **polyunsaturated fats**. All lipid containing foods have a specific mixture of saturated and unsaturated fatty acids. Because saturated fatty acids tend to be straight, they can pack together more tightly. The more tightly packed molecules of fat are more dense and more likely to be solid at room temperature. In contrast, unsaturated fats with cis bonds allow for a kinked or angled geometry that makes it more difficult to pack together, causing them to be a liquid at room temperature. Most naturally occurring unsaturated fats are cis fats.

Unsaturated fats with "Trans" bonds contain a geometry that resembles the straight line of a saturated fat. This geometry allows for trans unsaturated fats to pack together tightly enough that they will be found as a solid at room temperature. Products like Crisco and Margarine often have substantial quantities of "trans fats". Cis fats are the most common type found in nature, although there are some naturally occurring trans fats. Although trans fats are rare in nature they have appeared in the American diet as a product of oil processing. Food manufacturers take naturally occurring oils and use high pressures, high temperatures and hydrogen gas to artificially "hydrogenate" unsaturated fats, making them a creamy solid. A byproduct of this process is the formation fats with rearranged double bonds (trans fats). This type of fat is usually listed as "partially hydrogenated oil" in the food ingredients list. Food companies are interested in the "hydrogenation" of oils so that they might get fat that has the texture, flavor and chemistry necessary for many of the food products we enjoy (i.e. many pastries, puddings, sauces, creamers, and confectioneries). Unfortunately, this switch of hydrogen arrangement has been shown to increase the risk of coronary heart disease by altering LDL and HDL levels (discussed further below).

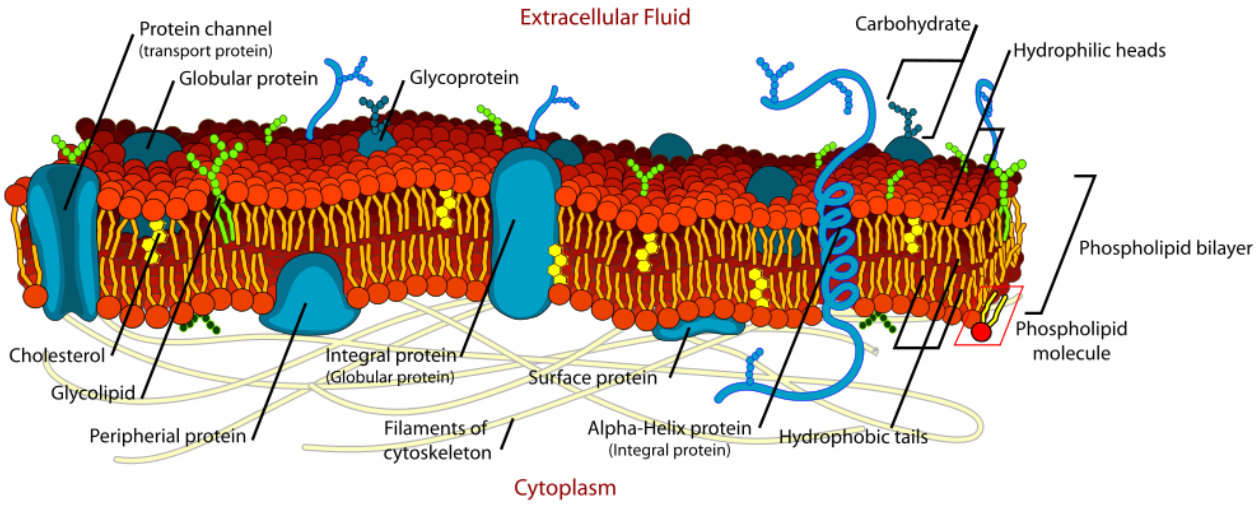
4.1.2

Phospholipids

A **phospholipid** is structurally similar to a triglyceride. However, one of the three fatty acids is substituted for a polar phosphate group (see image below). This creates a molecule that is hydrophilic on one end (the phosphate group) and hydrophobic on the other end (2 fatty acid tails). This type of molecule – hydrophobic on one end and hydrophilic on the other – is referred to as **amphipathic.** The amphipathic nature of phospholipids allows them to maintain the structural integrity of cell membranes and serves as a selectively permeable barrier that modulates movement of substances in and out of cells.



Phospholipid Structure Showing Polar Phosphate Group. *Image created by JS at BYU-Idaho 2014; modified File: Na+H2O.svg; Author: Taxman; Site: https://commons.wikimedia.org/wiki/File:Na%2BH2O.svg; License: Public Domain*
Because of their amphipathic nature, phospholipids spontaneously coalesce into spheres (called micelles) when placed in water. In like manner, a double layer of phospholipids, called a lipid bi-lipid layer, constitutes a cell membrane (see figure below).



Cell Membrane Detailed Diagram *File: Cell membrane detailed diagram en.svg; Author: LadyofHats Mariana Ruiz; Site: https://commons.wikimedia.org/wiki/File:Cell_membrane_detailed_diagram_en.svg; License: Public Domain*
In a cell membrane the polar heads of the phospholipids are oriented towards the aqueous cytoplasm and also towards the extracellular water. The fatty acid tails are oriented away from water but blend with each other. This configuration creates a barrier or boundary that separates the cytoplasm environment from the extracellular environment. Cell membranes also contain proteins and cholesterol (a steroid lipid) which aid in attachment and signaling, and also membrane integrity (see image above).

4.1.3

Steroids

A **steroid lipid** is a type of lipid that differs in structure from triglycerides and phospholipids. A steroid lipid consists of 4 hydrocarbon rings (3 hexamers and a pentamer) that are joined to each other (see image below). However, the solubility characteristics of steroids are like other lipids in that they are nonpolar (hydrophobic). The best known and most abundant steroid lipid is **cholesterol**. Cholesterol is very important for several reasons. First, it is required to build and maintain cellular membranes. Second, cholesterol is used to synthesize bile, an important component of digestive juices that helps in the digestion of fat. Third, cholesterol is also used to synthesize steroid hormones (see image below). Steroid hormones are critical for healthy growth and development of most biological tissues. Cholesterol is essential to all animal life, so we find that animals (including humans) have the ability to make this important molecule. Animals also ingest cholesterol.

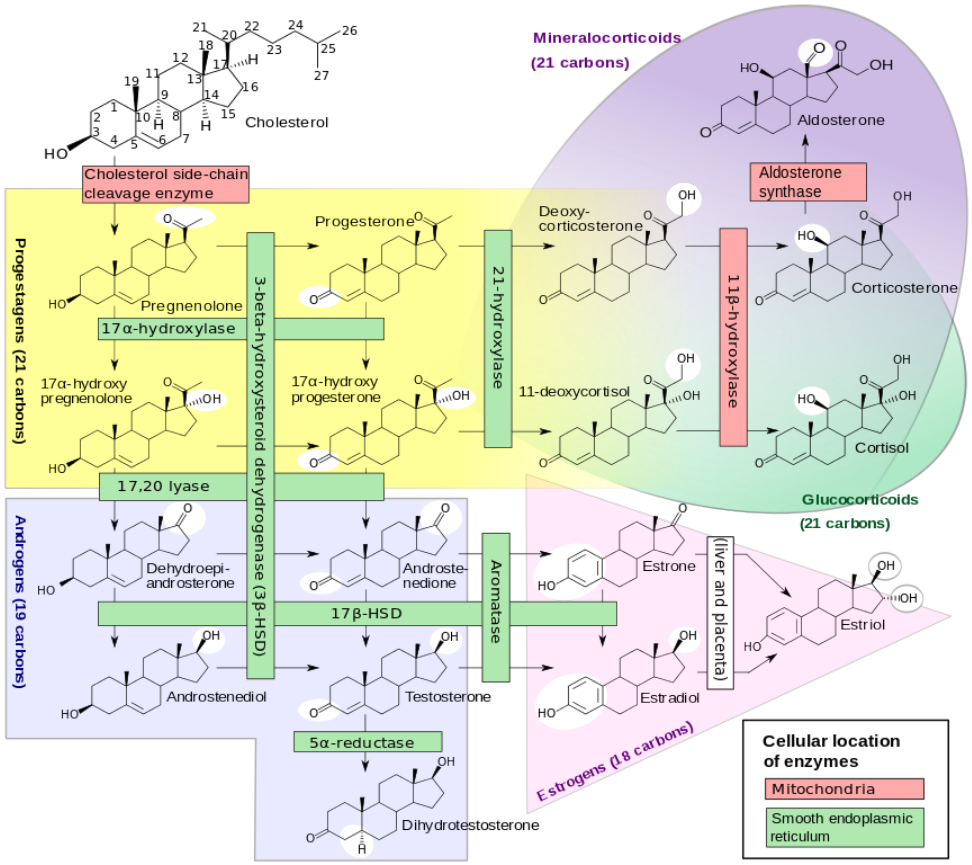
4.1.4

Lipoproteins

After ingestion, cholesterol and lipids are transported in the blood using micelle-like structures called **lipoproteins**. A micelle is a sphere consisting of a single layer of phospholipids. A lipoprotein is essentially a micelle with certain proteins embedded within the phospholipid monolayer. As the phospholipid hydrophobic tails orient toward the inside of the sphere, this hollow structure becomes a useful tool to transport lipids within its hydrophobic core. Cholesterol and triglycerides travel inside of these spheres and are shielded from the water.

You may have heard of these terms **HDL** and **LDL** before. These are two common lipoproteins that have gained a lot of attention as they appear to correlate with the risk of atherosclerosis development. Many brochures and websites refer to HDL as "Good Cholesterol" and LDL as "Bad Cholesterol."

In reality, there is no such thing as "good cholesterol" or "bad cholesterol." Cholesterol is simply a type of lipid that is necessary for life. It does not come as "bad" or "good." The idea of "good" and "bad" refer to the lipoproteins. LDL particles tend to accumulate in the walls of arteries. It is the overabundance of this LDL deposition that contributes to atherosclerosis, hence why it receives the term "bad." HDL or **H**igh-**D**ensity **L**ipoprotein is often called the "good cholesterol" because HDL particles help prevent atherosclerosis by extracting cholesterol from artery walls and disposing of it through biochemical reactions in the liver. Research has shown that lowering LDL cholesterol reduces the risk of heart attacks, strokes, and atherosclerosis.



***Steroideogenesis**. File: Steroidogenesis.svg; Author: Hoffmeier and Setters. Site: https://en.wikipedia.org/wiki/File:Steroidogenesis.svg; License: Creative Commons Attribution-Share Alike 3.0 Unported License.*

This figure shows man of the steroid hormones that are synthesized from cholesterol, including estrogen, progesterone, testosterone, and cortisol.

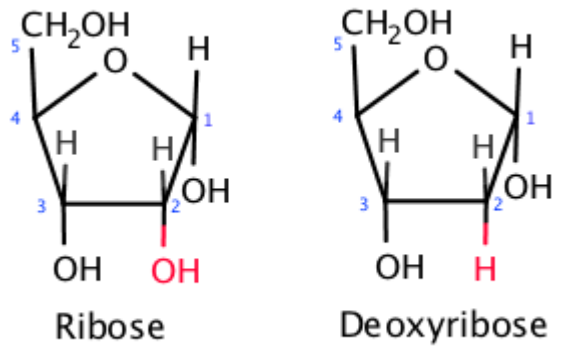
4.2

Nucleic Acids

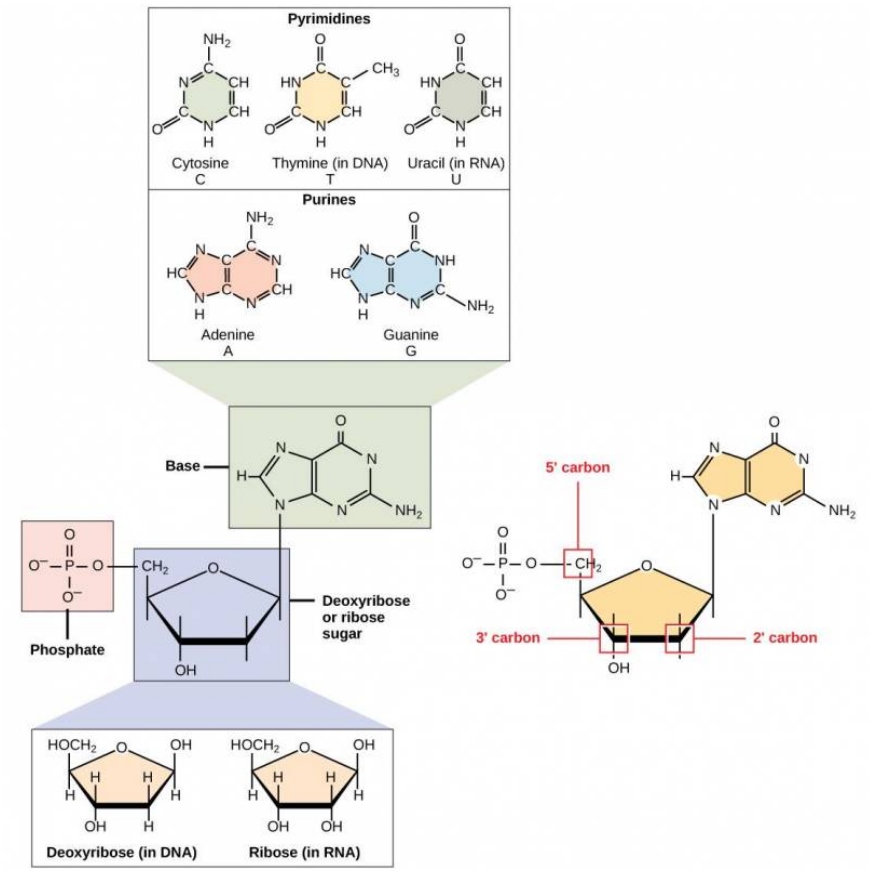
Nucleic acids can be categorized into deoxyribonucleic acid (**DNA**) and ribonucleic acid (**RNA**) both of which act to carry the genetic information essential to life. DNA is the genetic material common to all living organisms with slight variation between organism type. For example, in eukaryotic cells, DNA complexes with proteins called histones to make chromatin which then forms chromosomes that are stored in the nucleus. Chromosomes are the site of genes, which contain all the information necessary to make proteins. In contrast, prokaryotic DNA is less organized and found throughout the cytoplasm of the cell. If DNA is packaged in a nucleus, it never leaves, instead it communicates instructions to the rest of the cell via the other type of nucleic acid, RNA. RNA comes in multiple different subtypes like rRNA, tRNA, mRNA and microRNA.

Both types of nucleic acids are made of monomers called nucleotides. All nucleotides contain three components: a nitrogenous base, a pentose sugar, and a phosphate group. These components interact in a very specific way in that each nitrogenous base attaches to the sugar molecule, and each sugar molecule then attaches to one or more phosphate groups.

Nitrogenous bases: Nitrogenous bases contain carbon and nitrogen and are considered “bases” because they contain an amino group that can bind hydrogen. Nitrogenous bases come in five varieties: adenine, guanine, cytosine, thymine, and uracil. Additionally, nitrogenous bases are categorized as either purines or pyrimidines. Purines structures contain two nitrogen-carbon rings and pyrimidines have one nitrogen-carbon ring. Guanine and adenine are purines while cytosine, thymine and uracil are pyrimidines. Each base is abbreviated as follows: adenine (A), thymine (T), guanine (G), cytosine (C), and uracil (U). DNA contains A, T, G and C and RNA contains A, U, G and C.



By Miranda 19983$! CC BY-SA 4.0



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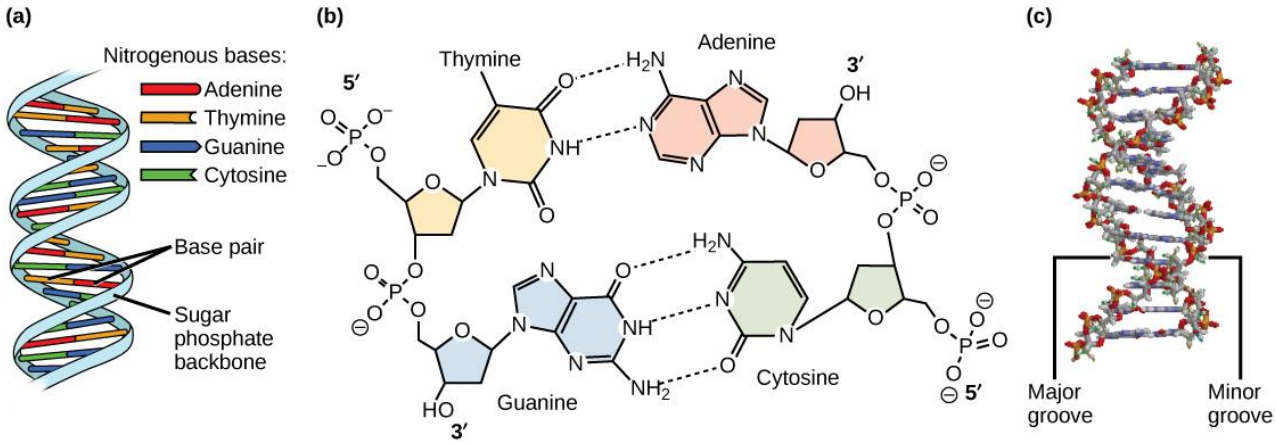
Pentose Sugar: The pentose sugar found in DNA is called deoxyribose and the pentose sugar found in RNA is ribose. The difference between the two sugars is whether they contain a hydroxyl or a hydrogen on the second carbon. Ribose contains a hydroxyl group and deoxyribose contains a hydrogen. Since pentose sugars are monosaccharides the most stable structure is "ring" shaped, and namely follows the conventional form of starting the number 1 carbon as the first carbon clockwise from oxygen. Thus, the carbon atoms are number 1,2,3,4, and 5 prime (i.e., one prime (1'), two prime (2'), etc).

Phosphate group: Phosphate groups are attached to the hydroxyl groups on carbon number five (5') and carbon number three (3') of different monomers to form polymers through phosphodiester linkages.

Once assembled, nucleic acids form long chains where the pentose and the phosphate phosphodiester linkages make up the backbone and the nitrogenous base extends out from the backbone chain. DNA exists as two chains interwoven around each other (double-helix structure) where the nitrogenous bases become stacked in the interior like steps on a spiral staircase. Hydrogen bonds stabilize the structure between the nitrogenous base and the two strands run in opposite directions so that the 5' carbon on one strand faces the 3' carbon of the matching strand. The backbones of DNA run antiparallel, meaning in opposite directions. In addition, only certain nucleotides can form hydrogen bonds with each other called pairing. For example, only A can pair with T (two hydrogen bonds form), and G with C (three hydrogen bonds form). Since hydrogen bonds are weaker bonds, the two strands can be pulled apart (unzipped) and put back together rather quickly. To summarize, strands run from 5' to 3' or from 3' to 5' and must be paired complementary to each other. Using only the nitrogenous base, if one strand ran 5' to 3'with nitrogenous bases lined up as ATTAGGCTG then the complementary strand would run 3' to 5' and the nitrogenous based would be lined up as TAATCCGAC. The order at which nitrogenous bases are lined up in a strand of DNA, much like how letters are lined up in this sentence, is the bases of the genetic code. For example, chromosome one is composed of 250 million base pairs (bp) and can be

read by cellular machinery similar to how we are reading this textbook. Since we understand the order of letters and how they are used to form words and then sentences we can then build ideas based on what we read.



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Central Dogma

4.2.1

Central Dogma

Strands of nucleic acids are the basis of information storage and carry all necessary instructions to make proteins. This idea is captured as the ***Central Dogma of Molecular* Biology**. At the most simplistic level the dogma explains how DNA makes RNA and how RNA makes protein. At a more specific level there are two major concepts of the central dogma listed below.

1. DNA contains all information necessary to make the macromolecule protein. This information is stored in the cell nucleus and carried out of the nucleus by RNA and delivered to ribosomes. Ribosomes are the factory that "translates" the instructions into a functional protein.

2. When the instructions are translated into a functional protein the process is called gene expression which can be divided into two stages: transcription and translation. Transcription is the process of converting DNA to RNA while translation is the process of delivering the message to the ribosome.

Note: Four types of RNA are utilized in this process: messenger RNA (mRNA), ribosomal RNA (rRNA), transfer RNA (tRNA), and microRNA (miRNA). mRNA is the carrier of information from the DNA. rRNA is the primary component of ribosomes and is thus directly involved in the process of protein synthesis. tRNA is an "adaptor" that serves as the link between the mRNA, the ribosomes and the individual amino acids needed to assemble proteins. Finally, microRNA can modulate gene expression, even "silencing" mRNAs before they arrive to the ribosome.

4.3

Proteins

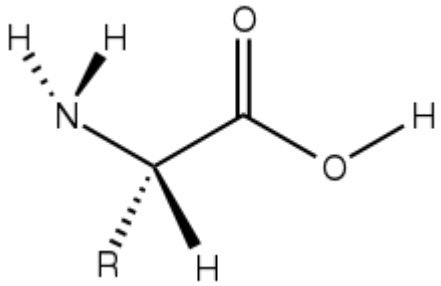
Of the four classes of biological molecules, the proteins are the most diverse in their functions. By some estimates, cells make more than 50,000 different proteins, with each protein having a specific job. With such diversity, what gives a protein its functionality and specificity? For proteins, form is function. In other words, the specific 3-dimensional shape of a protein is what allows it to do its job. Table 1 lists some of the major functions of proteins, but this list is not exhaustive. In fact, it is hard to think of any function in the body in which proteins are not integral.

Function	Example
Structure	Collagen in tendons and ligaments, Keratin in the nails and skin
Transport	Hemoglobin in the blood, Na^+, K^+-ATPase in cell membranes
Protection	Antibodies of the immune system
Movement	Actin and Myosin in muscles
Enzymes	Digestive enzymes in the small intestine (Lactase, Sucrase, Trypsin)
Receptors	Membrane proteins that respond to chemical messengers (insulin receptors)
Regulation	Chemical messengers: hormones, neurotransmitters, cytokines

4.3.1

Amino Acids

Amino acids, defined as simply as possible, are organic molecules that contain two functional groups: a carboxyl group (-COOH) and an amino group (-NH_2) and a side chain (R group). The side chain is specific to each amino acid and determines the function of the amino acid.The most common type of amino acid is known as the α-amino acid so named because the amino group and the carboxyl group are bonded to the same carbon.The center carbon of an α-amino acid is a car boxylic acid (an organic acid that contains a carboxyl group). *Note: *not every amino acid has the amino and carboxyl groups bound to the same carbon (ie, Y-aminobutyric acid; GABA), but the most common amino acids (n = 20), encoded by the human body, are all α-amino acids*.



Most amino acids rotate light (optically active) with exception of glycine, which has a single hydrogen atom at its R group, making it look the same in the mirror despite rotation (achiral).

Despite all this explanation of optical rotations, all chiral amino acids in eukaryotes are L-amino acids and follow priority rules for an S absolute configuration, with one exception, the exception being cysteine. Cysteine is still an L-amino acid but with an R configuration because even though the side chain is in the same location as other amino acids, the chain contains Sulphur which has a higher priority than Oxygen.

4.3.2

Amino Acid Structure

As stated previously, organization and classification of amino acids is a helpful way to understand and keep track of the different amino acids. Important factors to consider for classification include charge, hydrophilicity or hydrophobicity, size and functional groups (i.e. side chains or R groups). Once the amino acids are incorporated into proteins these factors will influence protein structure, protein-protein interaction, and functionality. The most popular way of organization is to do a structural classification based on the side chains (R-groups). **Note: each identified amino acid (bold) will be followed with the three and one letter symbols)*

Nonpolar, Nonaromatic side chains

Of the twenty amino acids, seven of them fall into this class: Glycine, alanine, valine, leucine, isoleucine, methionine, and proline. **Glycine** (Gly, G), the achiral amino acid already discussed, has a single hydrogen atom as a side chain making it the smallest amino acid and very flexible in its functions. **Alanine** (Ala, A), **Valine** (Val, V), **Leucine** (Leu, L), and **Isoleucine** (Ile, L) have alkyl side chains (*contains only carbon and hydrogen atoms, which are arranged in a chain*) containing one to four carbons. **Methionine** (Met, M) is one of only two amino acids that contains sulfur in the side chain. **Proline** (Pro, P) is a unique amino acid in that it is cyclic. The other 19 amino acids have the amino group attached only to the center carbon (α-carbon), but in proline, the nitrogen from the amino group becomes incorporated in the side chain and results in a conformation resembling a five membered ring. This arrangement makes proline particularly “picky” on how it can be incorporated into other structures (proteins).

Aromatic Side Chains

Three amino acids have aromatic side chains (unsaturated ring of atoms) that are uncharged. Tryptophan, phenylalanine, and tyrosine. **Tryptophan** (Trp, W) has a double ring that contains a nitrogen atom. The side chain of **Phenylalanine** (Phe, F) is a benzyl (benzene rings and an additional CH_2 group) while adding an OH group to phenylalanine makes **Tyrosine** (Tyr, Y). The OH group also make tyrosine polar.

Polar Side Chains (non-aromatic)

Five amino acids have polar side chains: serine, threonine, asparagine, glutamine and cysteine. **Serine** (Ser, S) and **Threonine** (Thr, T) each contain OH groups which influence their polarity and hydrogen bonding capacity. **Asparagine** (Asn, N) and **Glutamine** (Gln, Q) contain amide side chains (RC(=O)NR'R", where R, R', and R" represent organic groups or hydrogen atoms). Amide side chains are stable enough that they do not gain or lose protons during pH changes. The last amino acid in this group is **Cysteine** (Cys, C) which contains a thiol group in it side chain (SH). The large nature of the sulfur group makes it less electronegative (weaker bond) and susceptible to oxidation (loss of electrons). The sulfur group also allows cysteine to form covalent disulfide bonds to other cysteine residues.

Negatively Charged Side Chains (Anionic side chains)

Two amino acids have negative charges on their side chains under physiologic pH (7.4). These amino acids are **Aspartate** (Asp, D) and **Glutamate** (Glu, E). Although often called acids (i.e. aspartic acid and glutamic acid) they actually act as bases, accepting hydrogen in almost all cases.

Positively Charged Side Chains (Cationic side chains)

The remaining amino acids have side chains that contain positively charged nitrogen atoms; lysine, arginine and histidine. **Lysine** (Lys, K) has one amino group while **Arginine** (Arg, R) has three nitrogen atoms. **Histidine** (His, H) contains an aromatic ring with two nitrogen atoms (imidazole).

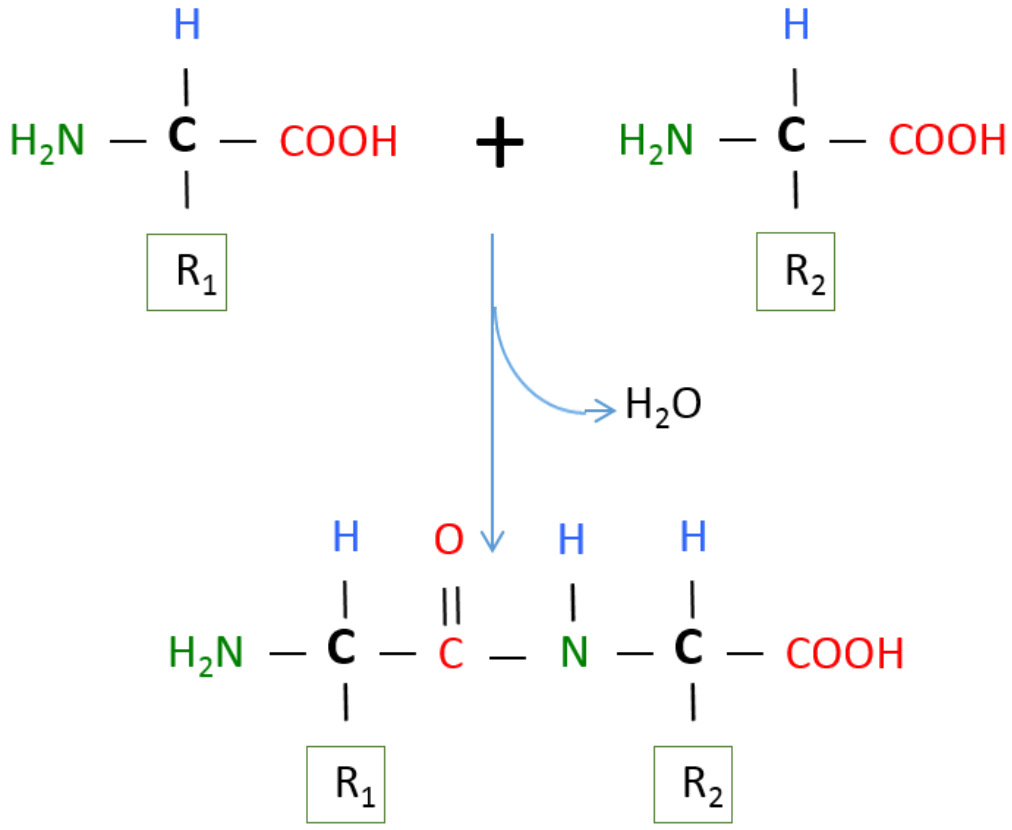
Amino acids as Acids and Bases

The structure of amino acids makes them some of them function as weak acids or weak bases. These structural components are the carboxy and amino groups as well as some of the functional groups (R-group). Since some amino acids can either accept a proton or donate a proton they can be referred to as **amphoteric** (having dual nature). Additionally, when some amino acids are placed in water at neutral pH, the amino and carboxy groups can become charged (NH_3^+ and CO_2^-) giving them the property of a dipole ion called a **zwitterion**.

4.3.3

Peptide Bonds and Polypeptides

Proteins are polymers of amino acids. Like all of the polymers we have discussed so far, amino acids are linked together via **dehydration (condensation) synthesis reactions.** The bond that is formed between the amino acids is called a **peptide bond**. The figure below shows how these bonds are formed. In this simple example, we would call the resultant polymer a **dipeptide**. Small peptides are designated tripeptides, tetrapeptides, pentapeptides, etc. The generic term **polypeptide** is used to designate many amino acids linked together. The terms polypeptide and protein are often used interchangeably. A polypeptide chain has at its beginning an unbound amino group and is given the name **amino- or N-terminus**, while the other end of the chain is called **carboxyl- or C-Terminus**.



***Peptide Bond formed through Dehydration Synthesis of Amino Acids.** Image created by MG BYU-I; 2013.*

The image above represents a dehydration synthesis reaction between two amino acids to form a peptide bond. Peptide bonds form between the carboxyl group of one amino acid and the amine group of another.

Almost all living things contain proteins made from 20 amino acids. The human liver is a pretty effective amino acid factory and can synthesize 11 of the 20 amino acids. However, nine amino acids are **essential amino acids**. If they are

not consumed, there won't be enough of the necessary supplies available when new proteins need to be produced. These essential amino acids are histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine.

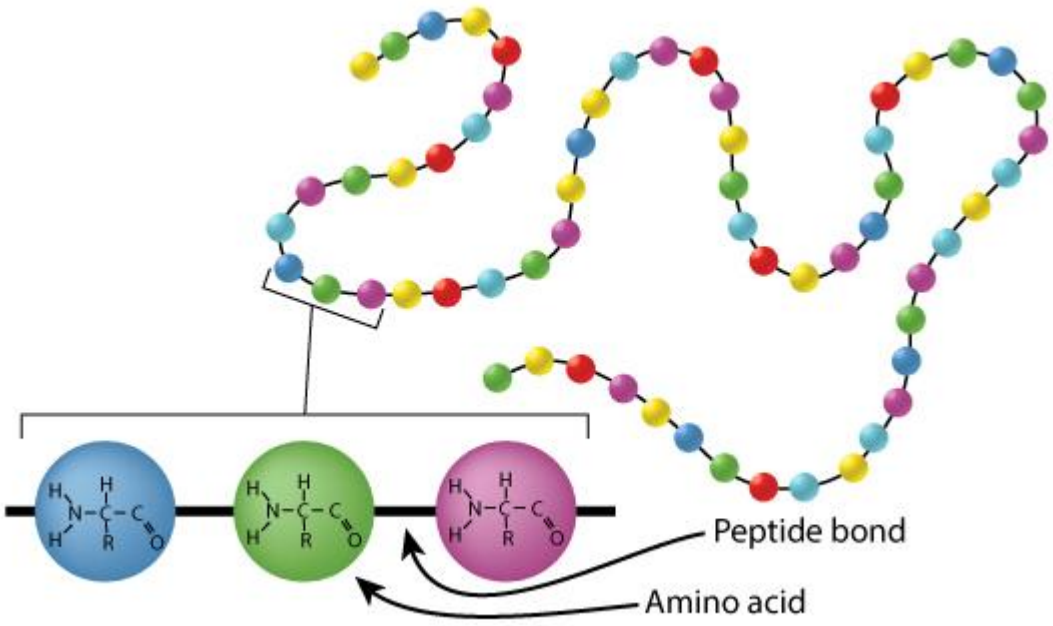
4.3.4

Protein Structure

By now, you should be starting to realize the importance of proteins; they are critical to the proper functioning of various life systems. What is it about proteins that allow them to perform all of these different tasks? The answer to this question can be summed up in three words: shape, shape, and shape. As mentioned earlier, form (shape) equals function. As you can imagine from the many functions of proteins, they have very complex shapes. If we think of proteins as cars, we all quickly understand that the wheels on the bottom of the car and a steering wheel to guide the car are very important standard equipment. Similarly, if our protein doesn't have the right parts in the right places with each component properly connected together, the protein will function about as well as a car that has been put through an auto crusher. In studying the shape of proteins, biochemists have dissected and broken them down into four levels of complexity or structure. Keeping with the car analogy, if we really wanted to dissect a car and determine how it works, we could take it apart all the way down to the nuts and bolts and then reassemble it again. Biochemists do the same thing to proteins to try and understand how proteins work. The first level would be analogous to the “parts” level. As we move from the first to the fourth level of structure, the preceding level adds to the next. For example, you cannot have secondary structure without a primary structure.

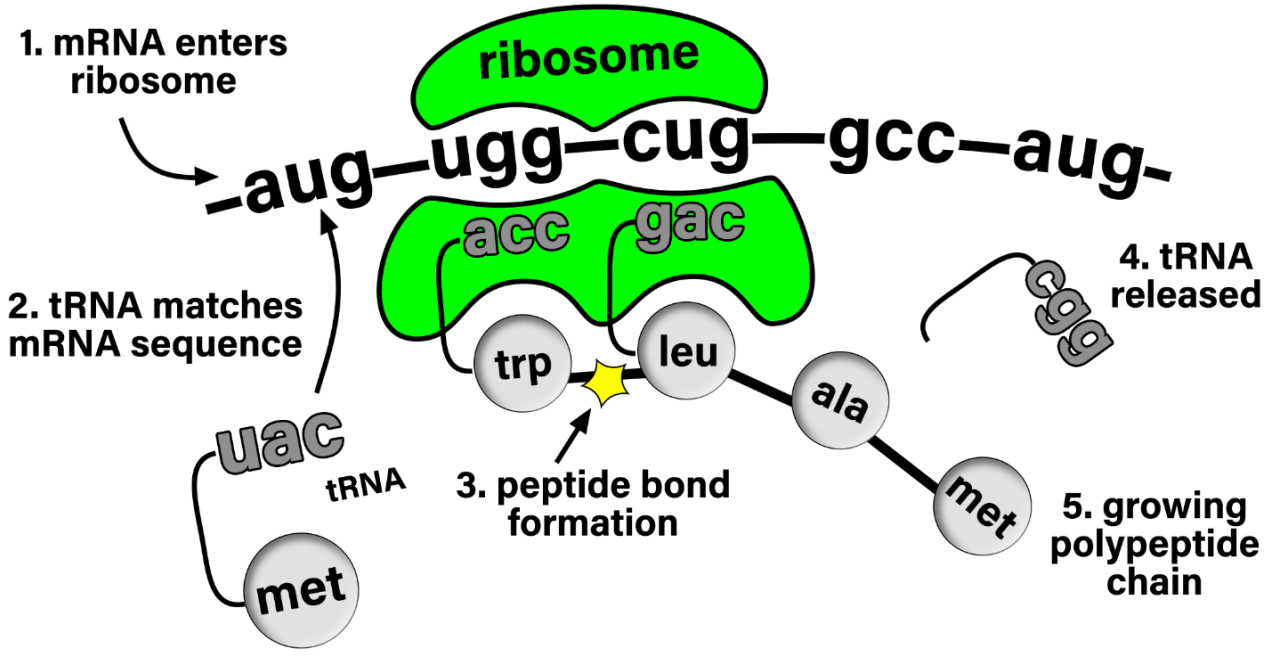
Primary Structure (First Level)

The primary structure of the protein is the sequence of the amino acids in its polypeptide chain. If proteins were popcorn stringers made to decorate a Christmas tree, the primary structure of a protein is the sequence in which various shapes and varieties of popcorn are strung together. The primary structure of a protein is maintained by ***covalent peptide bonds*** connecting the amino acids together. Insulin, the first protein to be sequenced, contains the following 110 amino acid primary sequence: malwmrllpl lallalwgpd paaafvnqhl cgshlvealy lvcgergffy tpktrreaed lqvgqvelgg gpgagslqpl alegslqkrg iveqcctsic slyqlenycn. Each letter is specific for 1 of the 20 amino acids.



Primary Protein Structure: Insulin Polypeptide Chain linked by Covalent Peptide Bonds.
Image by BYU-Idaho student Nate Shoemaker Spring 2016

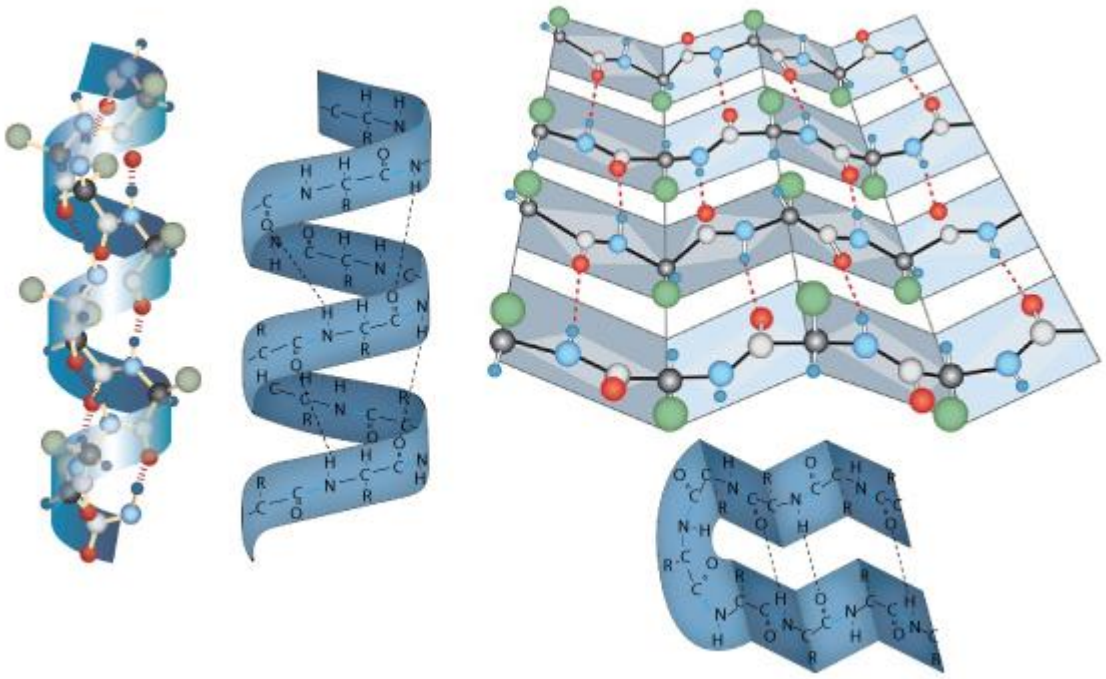
The image above represents the primary structure of a protein (a chain of amino acids). As you might expect, the sequence of the amino acids in the polypeptide chain is crucial for the proper functioning of the protein. Importantly, how does the cell know the right order in which to connect the amino acids? The original code is found in the DNA (deoxyribonucleic acid) housed in the nucleus of the cell. When a specific protein needs to be made, a segment of DNA called a gene is first copied in a process called transcription. This copy is called messenger RNA (mRNA). The mRNA strand exits the nucleus and attaches to a ribosome, a specialized organelle within the cell that interprets the code contained in the mRNA, recruits the appropriate amino acid, and catalyzes the formation of the peptide bond that links amino acids together. The process is called translation and results in a growing polypeptide chain (see figure below).



Protein Translation. The mRNA feeds through the ribosome which helps match the appropriate tRNA carrying its respective amino acid. The ribosome then catalyzes the formation of a peptide bond between amino acids to create a polypeptide chain.
Image by BYU-Idaho professor Spring 2021
If there is a mutation in the DNA then the amino acid sequence may be altered and the function of the protein can be affected. Many known genetic diseases in humans, such as cystic fibrosis, sickle cell anemia, albinism, etc., are due to mutations that result in alterations in the primary structures of proteins, which then, in turn, cause alterations in the other levels of protein folding: secondary, tertiary, and possibly quaternary structure.

Secondary Structure

The *secondary structure* of proteins involves twisting or folding polypeptides into highly regular sub-structures. Whereas the primary structure of a protein is pretty much two-dimensional, the secondary structure of proteins begins the very important three-dimensional configuration of proteins.

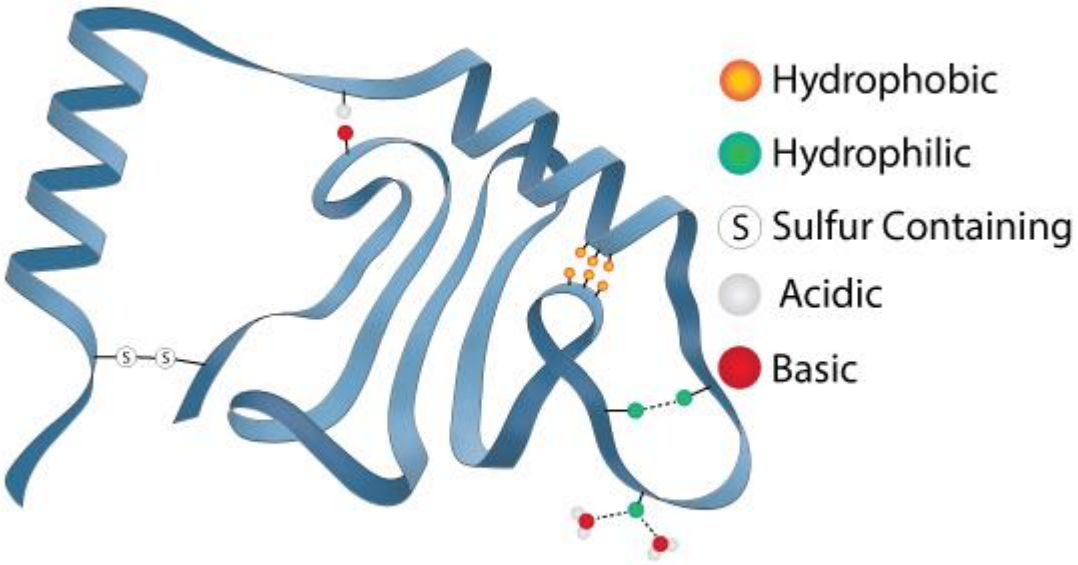


Secondary Protein Structure: Alpha Helix and Beta Pleated Sheet linked by Hydrogen Bonds.
Image drawn by BYU-Idaho student Nate Shoemaker Spring 2016

The two types of secondary structure are the **alpha helix** (think "slinky" as shown in the left picture just above) and the **beta pleated sheet,** or simply pleated sheet (shown to the right in the image above; think about one of those folded cardboard windshield guards that can be placed on the inside of your car's windshield on a hot day so the inside of your car doesn't end up with a temperature approximately that of the interior of our sun). The secondary structure of proteins is a result of the sequence of amino acids in the primary structure and is maintained by **hydrogen bonds**. These hydrogen bods occur along the protein backbone, independent of R-group side chains. Some proteins, like collagen, are almost entirely alpha helix, while others, like silk, are a mostly pleated sheet. Other proteins can have short segments of alpha helix and/or pleated sheet in their structure.

Tertiary Structure

The tertiary structure of a protein is the overall folding of the polypeptide chain and represents a protein's final 3-dimensional shape. In contrast to secondary structure, tertiary structure can be stabilized by multiple types of bonds (covalent, ionic, hydrogen) and hydrophobic/hydrophilic interactions as dictated by the amino acid R-group side chains.

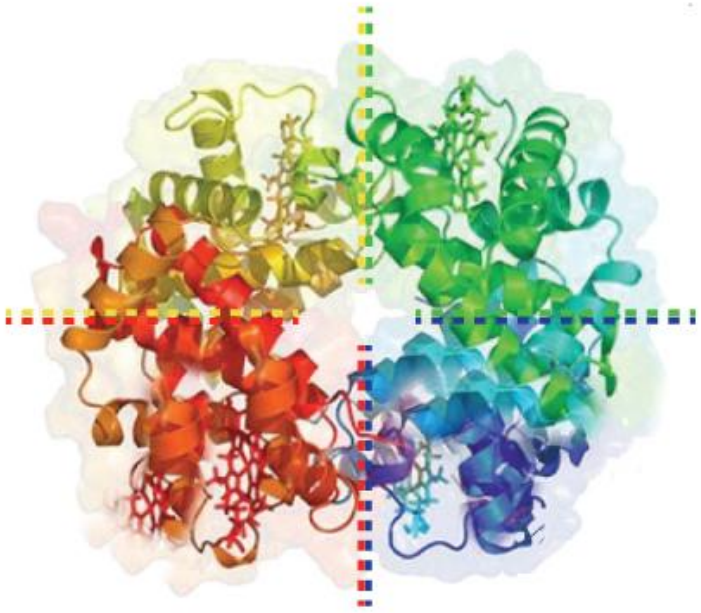


Tertiary Protein Structure: Hydrophilic & Hydrophobic R Groups bound by Hydrogen Bonds, Ionic Bonds Impacted by pH, and Covalent Disulfide Bonds. *Image drawn by BYU-Idaho student Nate Shoemaker 2016*

For example, R-groups that act as weak acids and bases can donate or accept protons. This can create positive and negative charges on the amino acids that will create ionic attraction. Certainly, pH can affect how these attractions between acidic and basic R groups occur. This helps explain why radical changes in pH can cause the structures of proteins to fall apart and ruin the protein's ability to function. One very important and very strong tertiary structure bond is a covalent bond that occurs between R groups on cysteine residues. These R-groups contain sulfur, which can interact with other sulfurs to form a disulfide bridge. The loss of a protein's 3-dimensional shape is called denaturing the protein.

Quaternary Structure

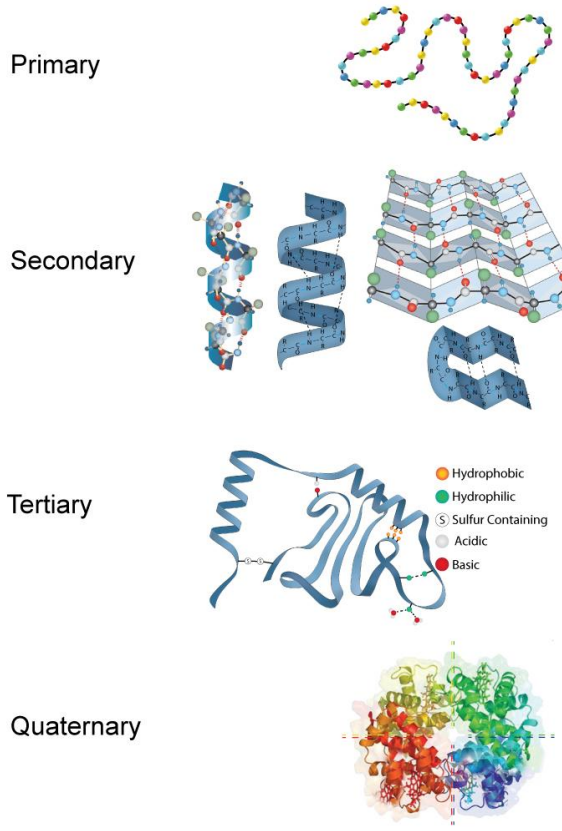
Sometimes multiple protein subunits work together to perform a specific function. Quaternary structure describes the number and arrangement of multiple polypeptide chains coming together to form a functional multi-protein complex. Not all proteins assume a quaternary structure. Only proteins composed of more than one polypeptide chain have quaternary structure. As an example, the protein in the picture below has four polypeptide chains that work together to form one functional protein called hemoglobin.



Quaternary Protein Structure: Four Polypeptide Chains Forming One Protein.
Image developed by BYU-Idaho student Nate Shoemaker Spring 2016

Hemoglobin is found in the red blood cells of humans and has the job of carrying oxygen throughout the body. There are two alpha and two beta chains that make up hemoglobin. You may have heard of sickle cell anemia. This genetic disease is caused by a mutation that results in a change to just one amino acid in the primary structure of the beta chains. This small change is enough to cause a significant alteration to the quaternary structure of hemoglobin, resulting in an abnormal sickle shape. This alteration affects hemoglobin's ability to function correctly, resulting in multiple pathological symptoms.

This next image below is just a summary that shows all the levels of protein structure in one image. You can see how each level leads to a more complex development of a very specific three-dimensional protein.



Four Levels of Protein Structures. *Image developed by BYU-Idaho student Nate Shoemaker Spring 2016*

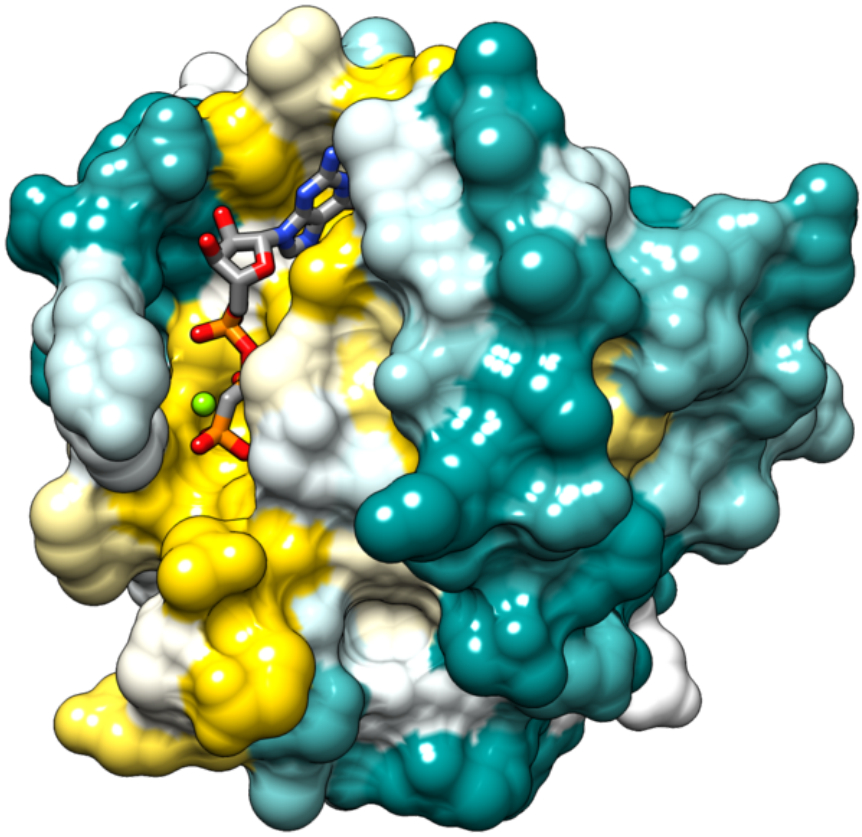
4.3.5

Classes of Proteins

There are two major classes or types of proteins: **globular** and **fibrous proteins**. Globular means *globe-like*. Hemoglobin is a good example of a globular protein. Globular proteins are quite fragile and can be inactivated (**denatured**) by things like heat (think of the protein albumin in an egg white when you fry it), organic solvents, or strong ionic solutions.

Fibrous proteins are much stronger and tougher. As the name implies, these proteins are more like ropes or cables. Fibrous proteins give the body structural support and help it resist mechanical stress. Common examples of body structures containing fibrous proteins include bone, cartilage, tendons (which anchor muscles to bones), ligaments (which anchor bones to other bones), and capsules around our internal organs.

The two images below show the molecular image representations of a globular (first) and a fibrous protein (second).



Globular Protein. *File: Hras surface colored by conservation.png; Author: Elaine Meng;*
Site: https://books.byui.edu/-nhlb;
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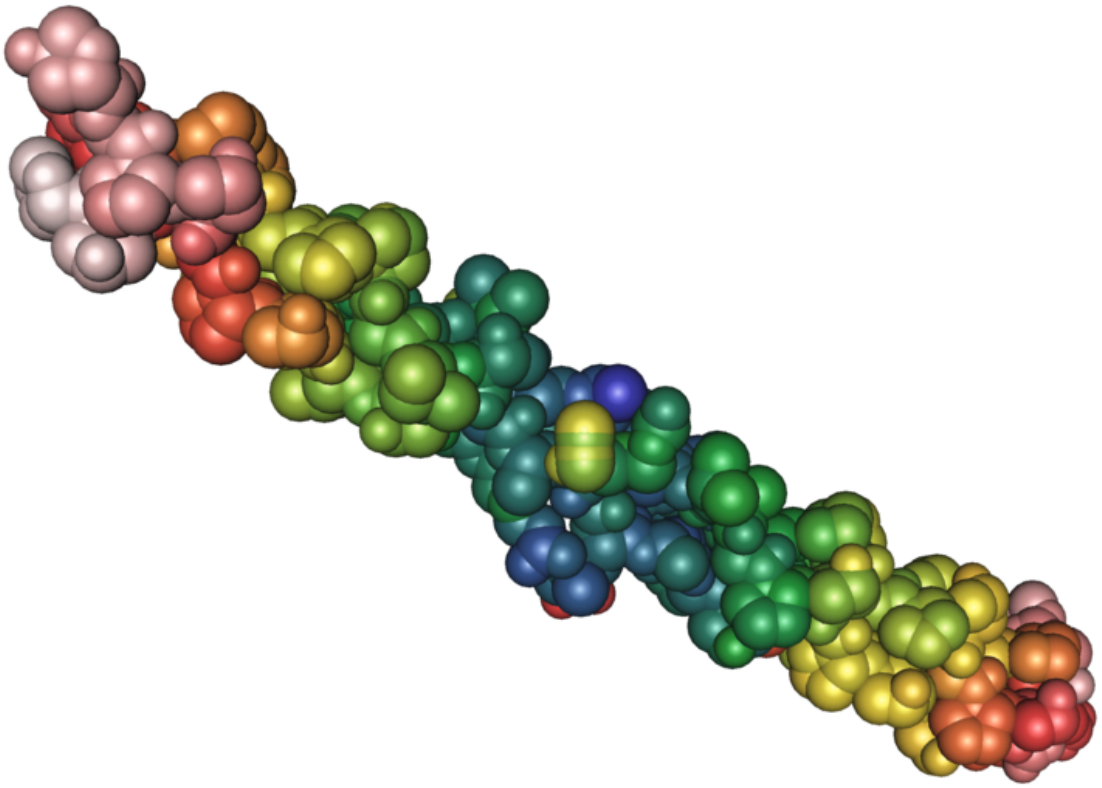

Fibrous Protein. *File:1bkv collagen 02.png; Author: Nevit Dilmen;*
Site: https://books.byui.edu/-RGFQ;
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4.3.6

Enzymes

One of the most diverse and important class of proteins is that of enzymes. An enzyme's purpose is basically to speed up the rate of a chemical reaction. Enzymes accomplish this by decreasing the activation energy needed to start the process. As an example, consider a wooden stick just thin enough to be broken in half if you exert all of your strength. Now, take that stick and place it in a vice or a press and start compressing the stick until it is just about to break. Under this pressure, how much energy is required to break the stick now? With just a flick of your finger the stick breaks. Enzymes, like this press, are used to lower the amount of energy required to initiate a chemical reaction. Regarding enzyme function, consider the following points:

1. Enzymes are not used up or consumed during the chemical reaction. In other words, a single enzyme can serve as a catalyst for multiple reactions.
2. Enzymes are quite specific, so a single enzyme is able to catalyze a reaction between certain reactants (substrates) but not others, which is why we need so many different enzymes. An example that you are familiar with is converting a common disaccharide, sucrose, to two monosaccharides, glucose and fructose. The enzyme that is involved in this reaction would be unable to convert the disaccharide lactose to the monosaccharides glucose and galactose.
3. Enzymes are often named for the substrates on which they act. Thus, the enzymes involved in the reactions above would be sucrase and lactase respectively. Notice that the suffix –ase is added to the name of the substrate.
4. An enzyme's shape governs its function. Each enzyme has an active site where only certain molecules (substrates) can bind. When the substrates bind to the active sites, the enzymes catalyze the chemical reaction, and they are released as a new product.
5. Enzymes are sensitive to changes in temperature and pH. One way to speed up chemical reactions is to turn up the heat but increasing temperature too much can alter or even destroy cells. Enzymes in the human body function optimally between 35–40° C (95–104° F). They also function best at around a neutral pH level, with a range typically between six and eight. If we change the temperature or pH to values outside the optimum, the enzymes may change shape and lose their function.
6. Enzymes may require "helper" substances to catalyze chemical reactions. These helpers are termed cofactors or coenzymes. Cofactors are inorganic substances such as zinc or iron. Coenzymes are organic molecules like vitamins.

UNIT 5

CELL MEMBRANES-STRUCTURE AND CELL FUNCTION

5.1

Structure of the Cell Membrane

One of the challenges faced by all living things, be they amoebae or humans, is to separate their internal environment from the external environment. Critical nutrients must get into the cells, and waste must get out. To make matters more complex, cells need to be able to regulate that movement, letting the materials cross sometimes and preventing them from crossing at others. Another challenge is finding a way for cells to communicate with each other. The solution to these challenges lies in the properties of the cell membrane (also called the **plasma membrane**). This delicate structure is essential to the life of cells. When the membrane loses its ability to carry out these processes, the cell dies.

5.1.1

Fluid Mosaic Model of the Membrane

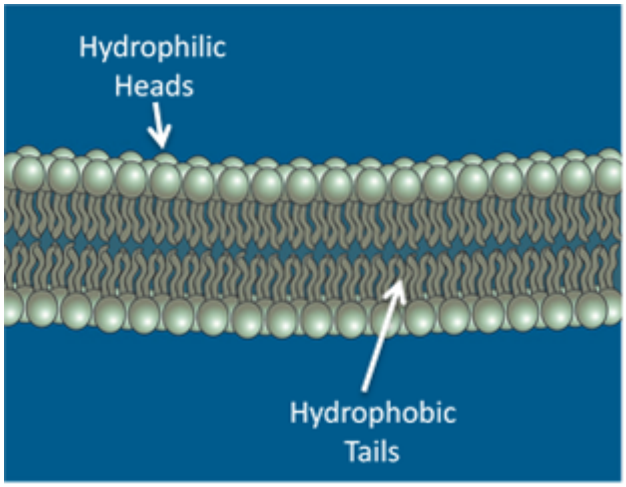
The plasma membrane is more than just a sack to hold the contents of the cell. It plays an important role in cellular function and the maintenance of homeostasis. One obvious function is to regulate what enters and leaves the cell. This process is highly coordinated and very specific. In addition, the cell membrane responds to countless chemical messengers in ways that alter the activity of the cell. As we discuss the structure of the plasma membrane, keep in mind that this description also applies to other membranes that are components of intracellular organelles.

Our modern model of the cell membrane is called the **Fluid Mosaic Model** *of the Cell Membrane*. The word *fluid* implies that the membrane is constantly changing and moving. Indeed, it is not a static structure but one that changes depending on cellular need and environment. The term *mosaic* conjures up an image of numerous small and different pieces. Indeed, the membrane contains many different components including lipids, proteins, and carbohydrates.

5.1.2

Membrane Phospholipids

A key component of the membrane is a double layer of phospholipids, the **phospholipid bilayer**. This bilayer forms the scaffolding into which the other components of the membrane are housed. This bilayer has a central hydrophobic region and two outer hydrophilic sections (**amphipathic**), one facing the aqueous interior of the cell and one facing the aqueous extracellular space (see figure below). Recall phospholipids are composed of a hydrophilic head containing a phosphate group and two hydrophobic tails composed of long chain fatty acids.



Phospholipid Bilayer. *Image created by BYU-IU student, Hannah Crowder 2013*
In water, phospholipids can form a bilayer. The hydrophobic fatty acid tails turn away from the water, and the hydrophilic phosphate heads turn towards the water.

The hydrophobic core of the membrane creates a barrier, preventing hydrophilic substances, such as ions and large polar molecules, from moving across the membrane. Hydrophobic (lipid soluble or lipophilic) materials, on the other hand, typically move readily across the membrane. Because some things easily pass through the membrane and others do not, we describe the membrane as being **selectively permeable**. Lipids within the membrane can rotate (spin) and move across each other within a leaflet, but typically cannot flip-flop unless an enzyme is present called flipase (finally a name that makes sense!). Each separate bilayer can be described as a leaflet with the terms inner and outer. The outer and inner leaflets differ in the type of phospholipids and components that they contain. Additional leaflet names are as follows:

Extracellular leaflet = Outer leaflet of plasma membrane

Cytosolic Leaflet= Inner leaflet of plasma membrane and Outer leaflet of organelles

Luminal Leaflet = Inner leaflet of organelles

In addition to the phospholipids, another important lipid found in membranes is **cholesterol**. Cholesterol is a hydrophobic molecule and resides among the fatty acid tails of the phospholipid bilayer. As mentioned above, the membrane exhibits fluidity, allowing movement of components within the membrane. Cholesterol plays an important role in regulating the fluidity of the membrane across a range of temperatures the body is exposed to. At high temperatures, cholesterol enhances the interactions between phospholipid fatty acids and prevents destabilization and melting of the membrane. At low temperatures, cholesterol prevents phospholipid tail groups from interacting too strongly with each other, a condition which would otherwise stiffen the membrane and decrease fluidity. Thus, without cholesterol the membrane might be compromised leading to impaired cellular function. Together, phospholipids and cholesterol comprise nearly 50% of the membrane.

5.1.3

Membrane fluidity

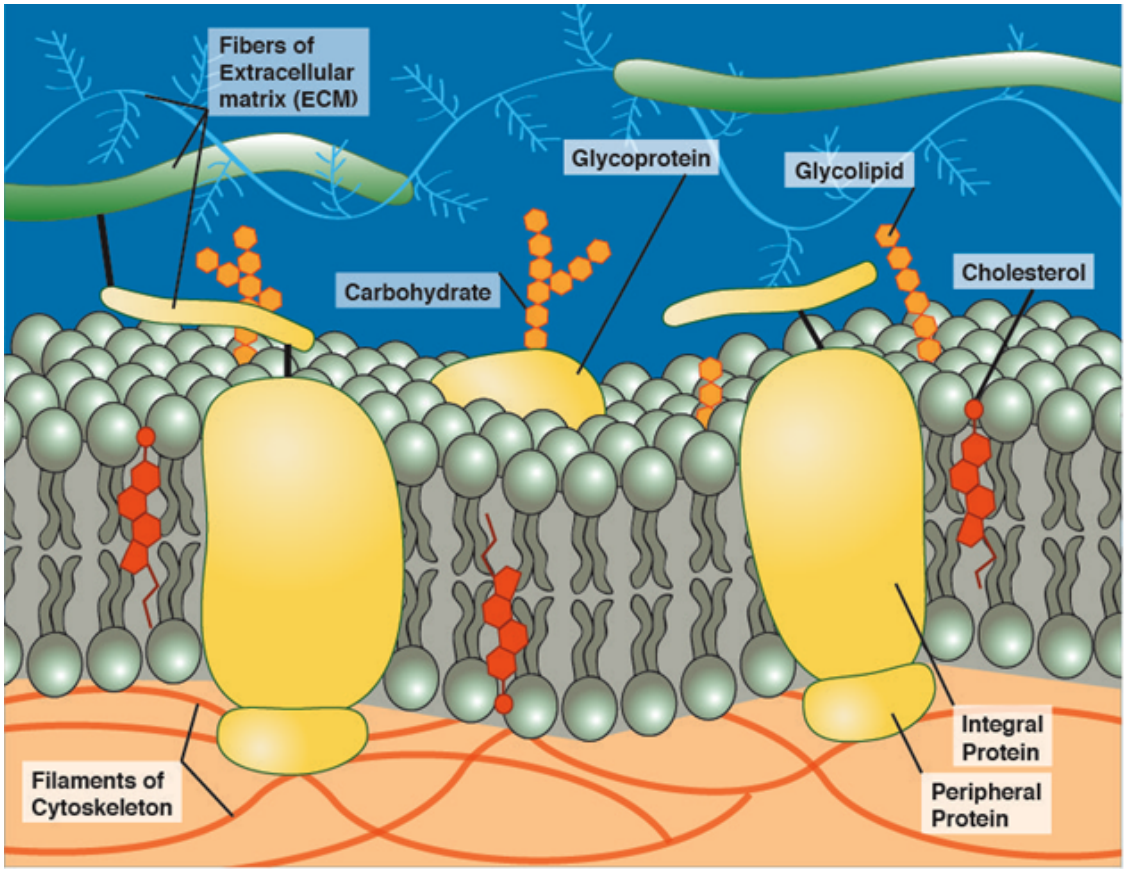
The amount of lipids and how they are “packed” within the membrane can have a major impact on the viscosity or fluidity of a given membrane. The biggest impact on membrane fluidity is the type of fatty acids (saturated or unsaturated) found in the phospholipid structure. Saturated fatty acids lack double bonds and are therefore linear which allow them to be packed more tightly thereby decreasing fluidity. Unsaturated fatty acids contain one double bond which kinks the chain forcing fatty acids to spread out thereby increasing fluidity. Other factors that change membrane fluidity include cholesterol (explained above) and temperature (explained above).

Note: Fluorescent Recovery After Photobleaching (FRAP) – is an experiment used to test the fluidity of membranes. To use this technique a membrane phospholipid or protein (explained below) is chemically tagged with a light sensitive dye. The light sensitive dyes are then bleached (destroyed) using a focused light beam. The cell is then observed to see how long it takes for the bleached region to diffuse away. The diffusion time is then used to equate a fluidity value of the membrane.

5.1.4

Membrane Proteins

Making up about another 50% of the membrane are the membrane proteins. The figure below demonstrates the relationship of the membrane proteins with the phospholipid bilayer. Note that some of the proteins are found only on the inner or outer surface of the membrane. These are called **peripheral or extrinsic proteins** because they do not extend through the membrane. One function of the peripheral proteins is to attach the membrane to the cytoskeletal proteins inside the cell or to proteins of the extracellular matrix. Peripheral proteins can bind to other proteins or lipids within the bilayer. When a protein binds directly to lipids it is called **amphitropic**. The integration of proteins within the bilayer causes the protein to have unique folding patterns which can alter (enhance) function.

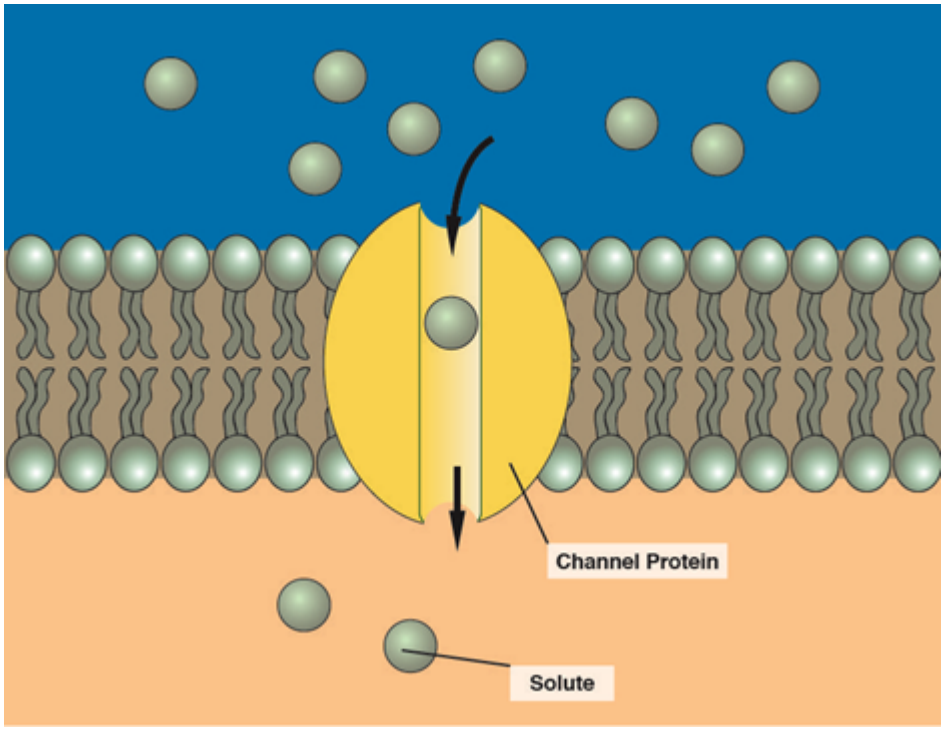


Cell Membrane Model: Relationship of Lipids, Proteins & Carbohydrates.
Image created by BYU student, Hannah Crowder 2013

Other proteins pass all the way through the membrane. These proteins are called **integral or transmembrane proteins** and have segments that associate with the hydrophobic region of the membrane that most often contain alpha helical structures. These integral proteins perform several important functions in the cell. Based on their functions, these integral proteins can be grouped into the following categories:

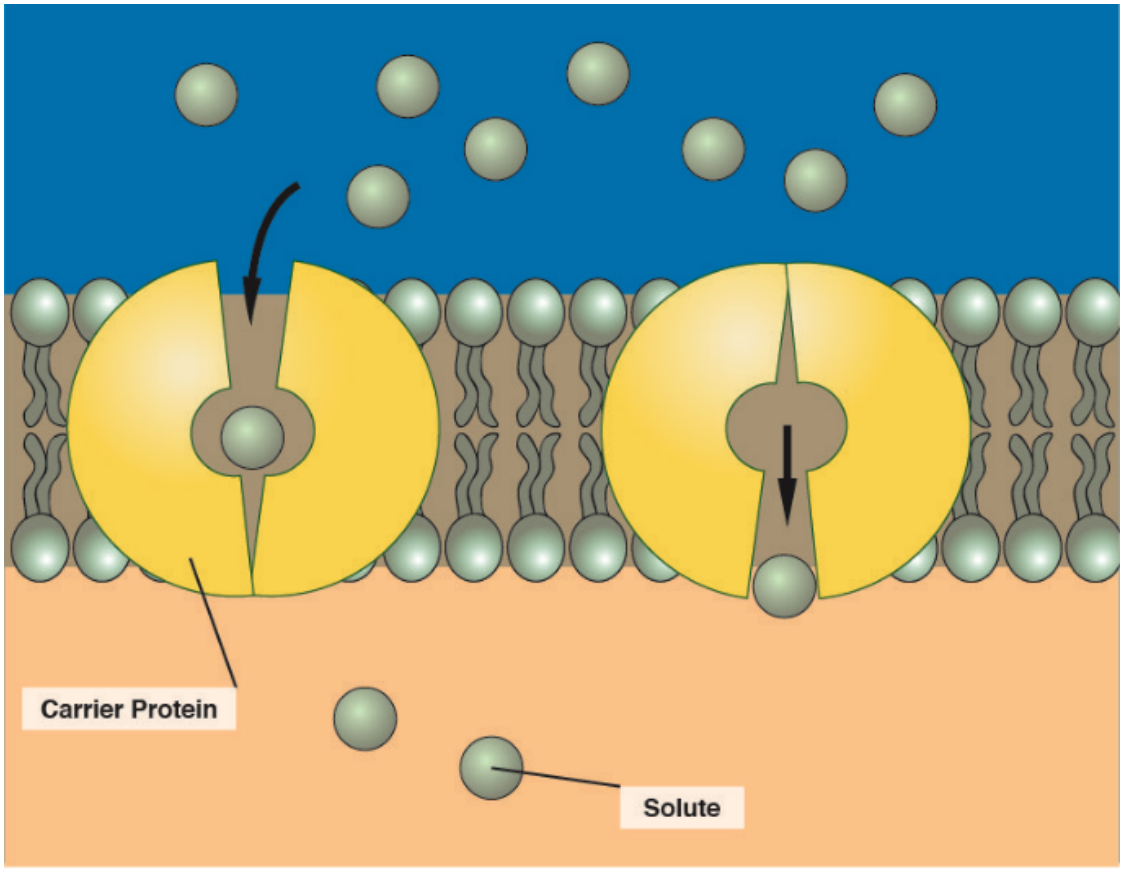
Transport Proteins

Integral proteins can act as transporters that facilitate the movement of compounds across the membrane. One type of transport protein, called **channels,** form a 'tunnel' for hydrophilic materials, such as ions and even water to cross the membrane. These channel proteins are usually gated; like a door, they allow substances to cross only when they are open.



Channel proteins allow solutes, such as ions, to move across the membrane.
Image created by BYU student, Hannah Crowder 2013

Carrier proteins are another type of transport protein. Carriers have sites that bind to specific solutes. For example, one type of carrier binds with glucose, while another carrier binds to urea. Once the solute binds, the carrier protein changes shape, allowing the solute to move across the membrane. Imagine a revolving door. As these doors turn (change shape), they are open to either the inside of the building or to the outside but never to both at the same time. You can enter a revolving door from the outside of a room and move the door until it is open to the inside of the room. At no time in this process was the door open to both sides at the same time. This is how carrier proteins work. Carrier proteins bind to solutes and then move them across the membrane by changing shape.



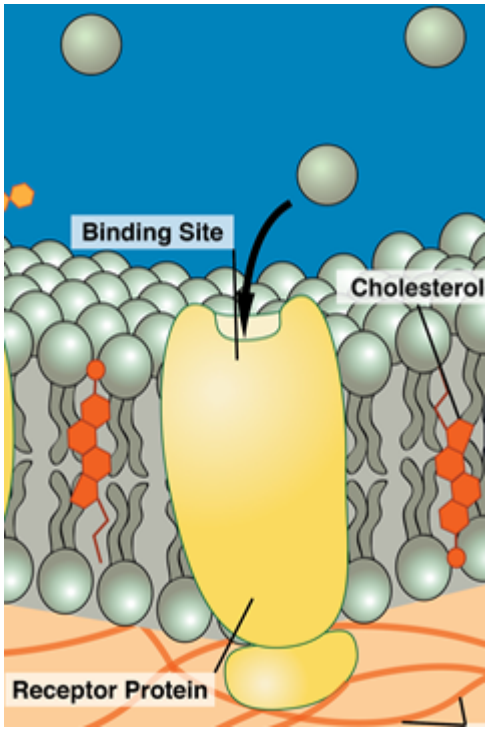
Carrier Proteins. *Image created by BYU student, Hannah Crowder 2013*

Enzymes

Integral membrane proteins can function as enzymes, catalyzing important chemical reactions. The enzyme, lactase, which digests the disaccharide lactose in the small intestine is an integral membrane protein in the cells that line the lumen of the duodenum. The discomfort associated with lactose intolerance is caused by having insufficient amounts of this enzyme in the body.

Receptor Proteins

Integral proteins may act as receptor proteins and allow the cell to respond to extracellular chemical messengers which regulate the activity of the cell. When a chemical signal (also known as a ligand) binds to its specific receptor protein, it transmits a signal to the inside of the cell through a shape change in its transmembrane protein structure. This shape change will then activate or inhibit intracellular events that result in altered cell function.



Receptor Protein. *Image created by BYU student, Hannah Crowder 2013*

Attachment Proteins

Integral proteins are involved in attaching cells to each other, as well as to the extracellular matrix and to intracellular structural proteins. Often, a peripheral protein functions as a link between the integral proteins and the structural proteins or the extracellular matrix. These attachments can confer tissue strength and shape.

Marker Proteins

These proteins allow cells to identify one another. Functions of these marker proteins include the ability of sperm cells to recognize the oocyte during fertilization, as well as the ability of immune cells to distinguish between “self” cells and foreign cells.

5.1.5

Carbohydrates

In addition to lipids and proteins, the membranes also contain carbohydrates. These are short-chained polysaccharides (oligosaccharides) that attach to the proteins and lipids on the extracellular layer of the membrane. If attached to a protein, they are called **glycoproteins,** and if attached to a lipid, they are called **glycolipids**. One function of these oligosaccharides bound to membrane proteins or lipids is to form additional cell markers. Human blood types (A, B, AB, or O), for example, are determined by glycoproteins expressed on red blood cells. *Note: Human blood groups are determined by a sphingolipid oligosaccharide. The branched chain common in all groups is Glc-Gal-GalNAc-Gal-Fuc. Type A has an additional GalNAc; B has an additional Gal: and O has no additions*.

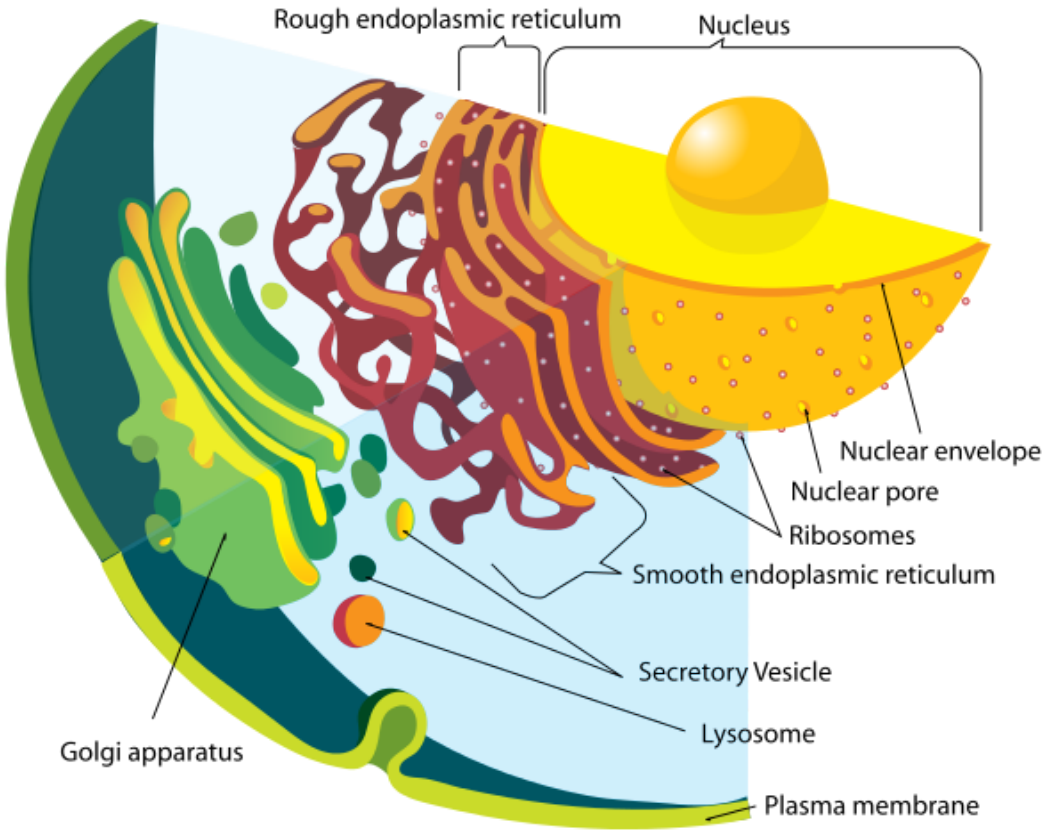
Additionally, some cells, such as the apical surface of epithelial cells, have a dense layer of glycoproteins referred to as the **glycocalyx**. The glycocalyx has been implicated in cell recognition during development, adherence of cells to each other, and playing a role in the permeability of the membranes.

5.2

Cell Structures

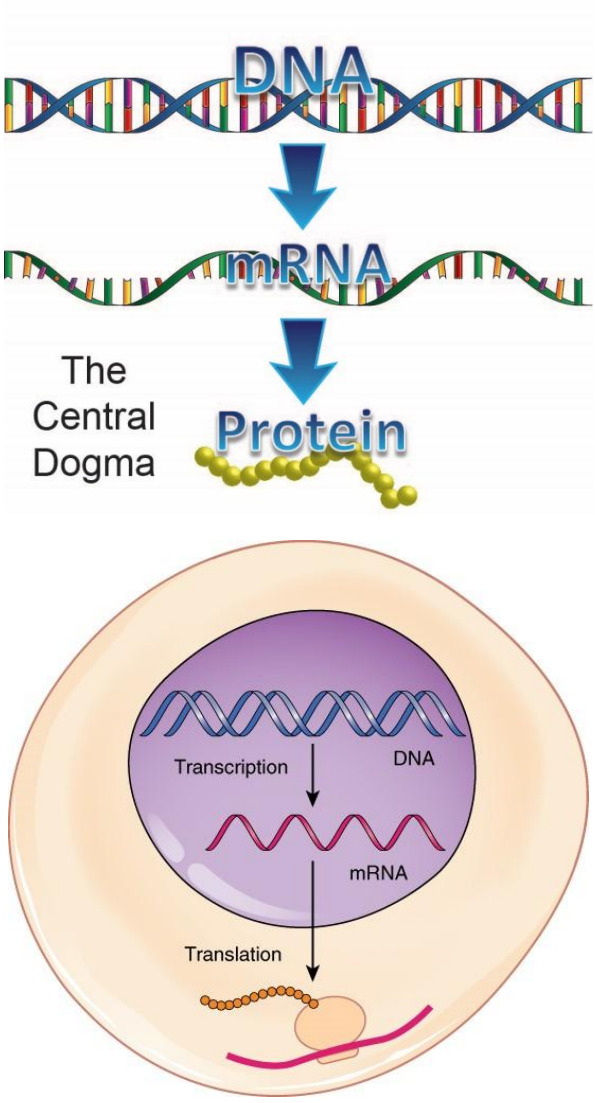
As technology progressed to the point of peering deeper and deeper into the world of the cell, it became apparent that the cell cytoplasm, when viewed under a light microscope, was full of even smaller intracellular structures. The structures are collectively called cellular organelles.

To help illustrate the function of many of these organelles, let us consider the secretion of insulin by beta cells in the pancreas. In order to secrete insulin, the cell must first make it. This process starts in the cell **nucleus**. The nucleus houses the genetic material (DNA) of a human cell and provides a location for **DNA transcription** (the copying of DNA). Importantly, the nucleus is surrounded by two distinct lipid bilayer membranes. The outer membrane belongs to the **endomembrane system** (made up of the nuclear envelope, the endoplasmic reticulum, the golgi apparatus, lysosomes, the plasma membrane, and most vacuoles and vesicles).



Endomembrane System Diagram. *Title: File: Endomembrane system diagram en.svg; Mariana Ruiz LadyofHats; Site: http://en.wikipedia.org/wiki/File:Endomembrane_system_diagram_en.svg; License: Public Domain.*

The production and secretion of insulin helps illustrate the coordinated efforts of the organelles in this system. Within the nucleus, the insulin gene is *transcribed* from DNA to RNA and then further processed into messenger RNA or mRNA. This mRNA is then transported out of the nucleus to **ribosomes** docked to the surface of the **endoplasmic reticulum** (ER). The ER is divided into two components: the rough ER and the smooth ER. The rough ER is named "rough" because it is studded with ribosomes, which create a bumpy surface when viewed under an electron microscope. The function of the ribosome is to perform **translation** (the use of mRNA as a template to synthesize protein). The ribosome is specifically suited to interpret the mRNA nucleotide acid code and assign the appropriate amino acid in the creation of a polypeptide chain. This is the first step of making a protein.



Central Dogma of Biology - DNA Transcription to Translation. File:0328 Transcription-translation Summary.jpg; Author: OpenStax College; Site:http://commons.wikimedia.org/wiki/File:0328_Transcription-translation_Summary.jpg; License: This file is licensed under the Creative Commons Attribution 3.0 Unported license.

Within the rough ER, the nascent (immature) insulin protein is folded into primary, secondary, and tertiary structures. It is then transported to the **Golgi apparatus**. The Golgi apparatus is the location for processing and sorting (think of a giant UPS mail warehouse). Within the Golgi, the nascent insulin is further processed into mature (functional) insulin and packaged into secretory vesicles. These vesicles (now full of insulin) bud off the Golgi and are transported, via microtubules, to the **plasma membrane** where they await the proper signal for secretion. Secretion occurs as the vesicle fuses with the **plasma membrane**, expelling its contents into the extracellular space in a process known as exocytosis.

Now that you understand the process of how cells can create and secrete insulin let us now examine the roles of each of these organelles in greater detail.

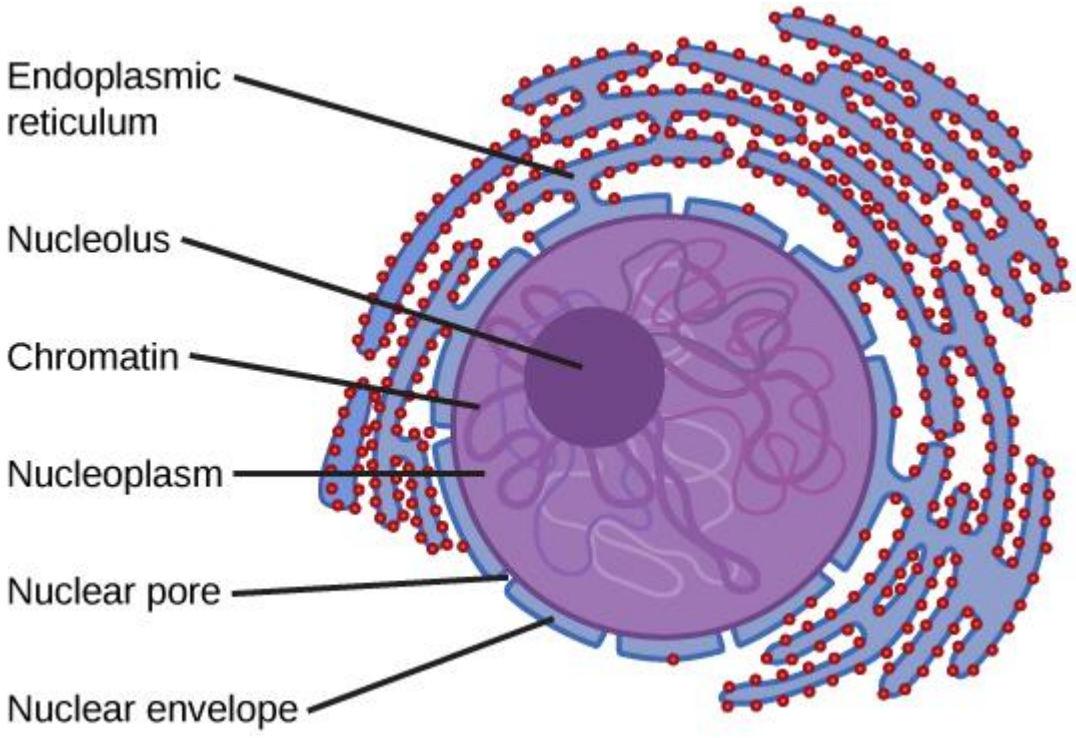
*It should be noted that two major cell types exist, **prokaryotic** and **eukaryotic**. Prokaryotic cells far out number eukaryotic cells, but eukaryotic cells are larger so that the collective mass between the two is about equal. Eukaryotic cells typically contain membrane bound organelles and as such will be used first to discuss the functions of organelles.*

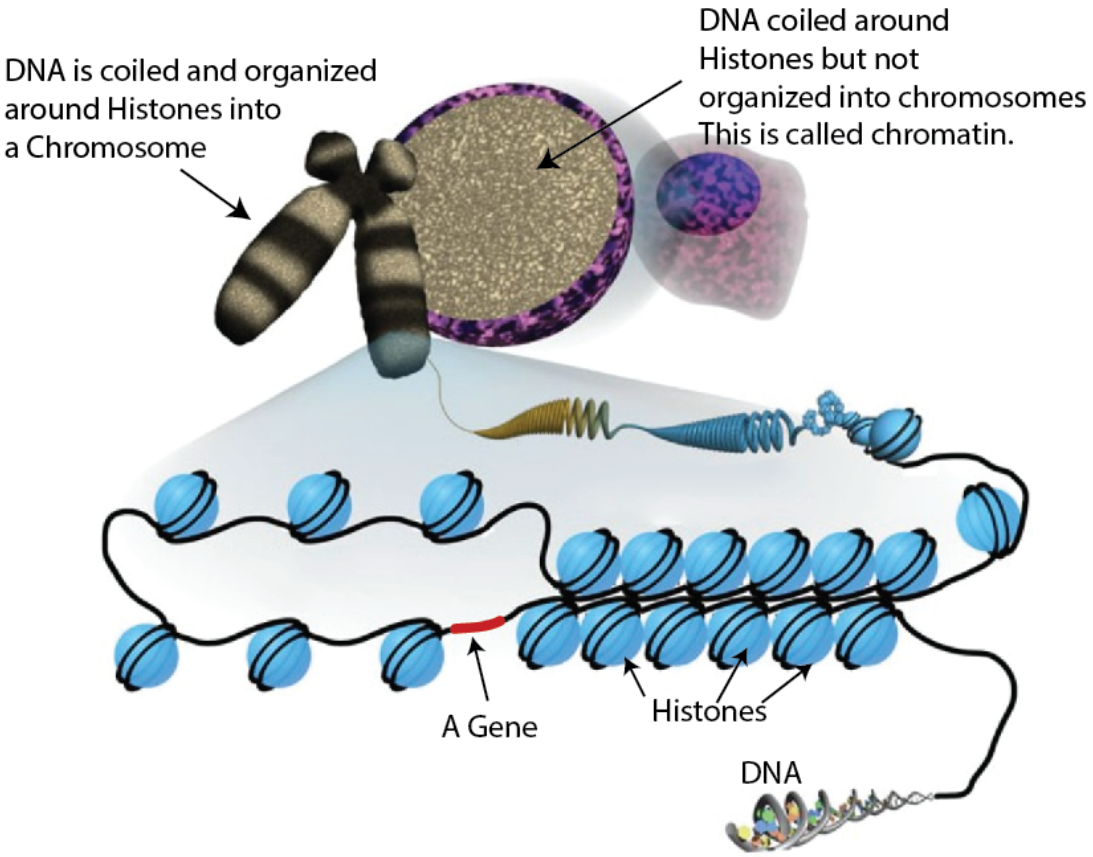
The Cell Nucleus
The Endoplasmic Reticulum
The Golgi Apparatus
Lysosomes, Proteasomes, and Peroxisomes
Vacuoles
The Mitochondrion
Chloroplasts

5.2.1

The Cell Nucleus

The nucleus is surrounded by a double membrane bound structure (**nuclear envelope**) that serves to isolate the nuclear contents from the cellular cytoplasm. This nuclear envelope is dispersed during mitosis and meiosis as the cell prepares to divide. The outer membrane of the nuclear envelope is continuous with the membranes of the rough endoplasmic reticulum. The inner membrane makes the border to isolate the nucleus. The space between the two membranes is continuous with the space (lumen) inside the endoplasmic reticulum, except at various points where the two membranes are connected by specialized structures known as **nuclear pores** . The nuclear pores serve as transport pathways between the interior of the nucleus and the cytoplasm. The nucleus contains the genetic material (genes) that are organized into long double stranded molecules called DNA. DNA are tightly bound to proteins called histones to form chromatin, which is finally organized into chromosomes.





DNA Structure: Gene, Histones, Chromatin & Chromosomes. Modified image - Title: File: Sha-Boyer-Fig1-CCBy3.0.jpg; Author: unknown; Site: https://books.byui.edu/-FjMn;
License: This work is licensed under the Creative Commons Attribution 3.0License.

The **nucleolus** is a region of the nucleus responsible for the synthesis of ribosomes. This region is made of DNA, RNA, and proteins. Gene messages are copied from the DNA as single strands of RNA, which are further processed into what we call “messenger RNA” (or mRNA) and sent out of the nucleus through the nuclear pores. The mRNA interacts with ribosomes to produce a specific protein. Many genetic mutations result in errors, making the associated proteins non-functional. The nucleus also functions to maintain control and integrity over the genes. The genes, in turn, regulate the activity of the cells. Thus, the nucleus is the control center of the cell.

5.2.2

The Endoplasmic Reticulum

As mentioned previously, the endoplasmic reticulum has a rough component and a smooth component. The **rough endoplasmic reticulum** is associated with ribosomes that constantly bind and unbind to the membrane. Ribosomes bind to the endoplasmic reticulum after they interact with an mRNA strand from the nucleus. The ribosomes "read" the mRNA strand and produce the specific protein associated with the code and secrete it into the lumen of the rough endoplasmic reticulum. The newly produced proteins are then folded and prepared for transport to the Golgi complex where they will complete processing prior to being utilized outside of the cell. The **smooth endoplasmic reticulum** synthesizes lipids, phospholipids, and steroids. In addition, it aids in the breakdown of carbohydrates and steroids. The membrane of the endoplasmic reticulum contains proteins that move Ca^{++} into the structure for storage and thus plays an important role in regulating cellular calcium ion concentrations.

5.2.3

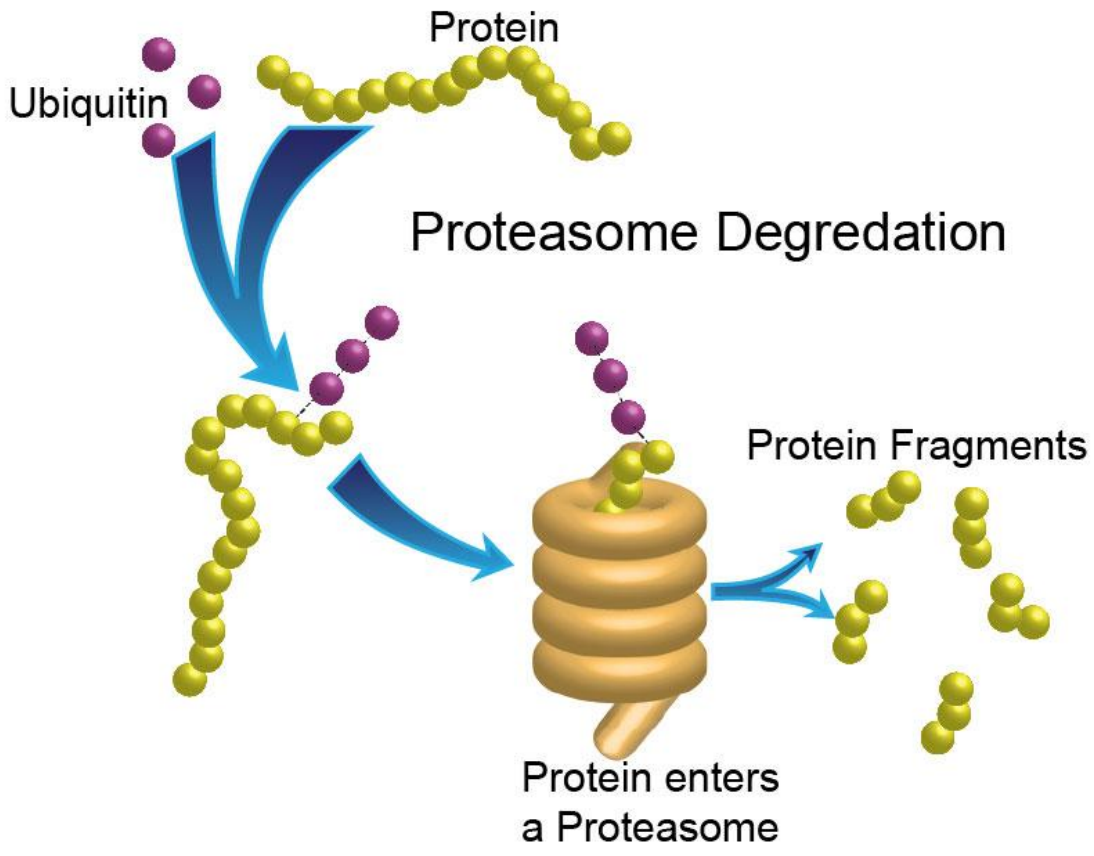
The Golgi Apparatus

The Golgi apparatus is named after the person that discovered it; an Italian physician named Camillo Golgi who discovered the organelle in 1897. Like the endoplasmic reticulum, the Golgi apparatus is an organized structure of phospholipid membrane that are essentially flattened stacks of 5-12 distinct compartments. The compartments of the Golgi body are involved in further processing of proteins that were first made in the rough endoplasmic reticulum. Membrane bound vesicles that arise from the Golgi are distributed to various locations within the cell. The Golgi apparatus is particularly important in the processing of proteins that are destined for secretion outside of the cell. Proteins are sent to the Golgi apparatus from the rough endoplasmic reticulum through transport vesicles that move on the "highway" network of the cell, the cytoskeleton (discussed below). The Golgi apparatus is primarily associated with proteins but also serves in the transport of lipids around the cell and the creation of lysosomes. Perhaps the best analogy for the Golgi apparatus would be that of the post office of the cell.

5.2.4

Lysosomes, Proteasomes, and Peroxisomes

As mentioned, **lysosomes** are also part of the endomembrane system. Lysosomes are specialized vesicles that bud off of the Golgi apparatus. A lysosome uses a pump within its membrane to transport high concentrations of H^+ into its lumen, thus lowering the internal pH. The acidic environment of the lysosome allows it to break down macromolecules (such as proteins). Other organelles involved in recycling used or unneeded materials include **proteasomes** and **peroxisomes**. When a cell wants to quickly reduce the amount of a given protein, it can tag that protein with a specific signal (called ubiquitin) that sends that protein to the proteasome for degradation. The peroxisome is responsible for detoxifying harmful substances that may enter the cell by using hydrogen peroxide (H_2O_2). Peroxisomes are also involved in some metabolic reactions.



Proteasome Degradation. *Original image drawn by BYU-I Biology Department Jan 2015*

5.2.5

Vacuoles

Vacuoles are organelles primarily found in plants and fungi, although the organelle is also found in some animals and bacteria. Vacuole function is more difficult to categorize because the function varies between organisms and even cells. Still the general properties of vacuoles include containment of waste products, water storage (helps to maintain pressure), pH balance, exocytosis, and holding vesicle for various proteins. Vacuoles can also be used in the process of phagocytosis.

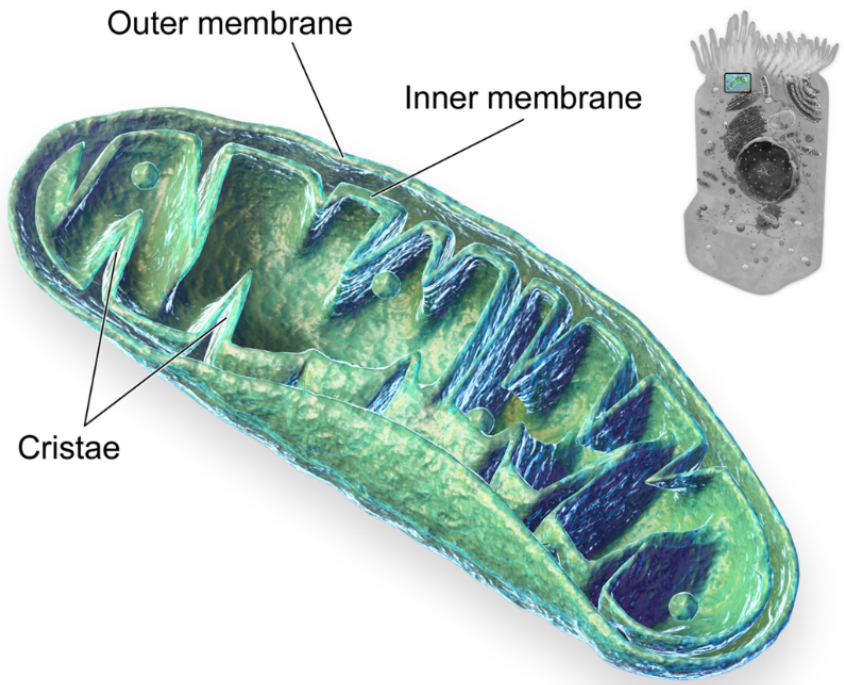
5.2.6

The Mitochondrion

The mitochondrion (or mitochondria in the plural form) is usually described as the “power plant” because it generates the energy (in the form of adenosine triphosphate or ATP) required for normal cellular function. Like the nucleus, mitochondria also have two membranes, which are critical for its function in energy production (further detail will be given later as we study metabolism). Also, like the nucleus, the mitochondrion has its own set of DNA with its own set of genes. Mitochondria are very important in metabolism and they can be stimulated to synthesize proteins from its DNA and even divide and create more mitochondria when metabolic demands increase (this happens with exercise training). The mitochondrion is composed of an outer and an inner membrane (a balloon within a balloon) that gives five distinct structural components.

1. The outer mitochondrial membrane
2. The intramembranous space (space between outer and inner membranes)
3. The inner mitochondrial membrane
4. Cristae (foldings of the inner membrane)
5. The matrix (space of the interior of the mitochondrion)

Each region is associated with a particular function as it relates to mitochondrial activity. The number of mitochondria per cell varies widely with more than 2000 per cell in liver cells and down to zero for red blood cells.



Mitochondria

***Mitochondria**. File: Blausen 0644 Mitochondria.png; Author: Blausen.com staff. "Blausen gallery 2014". Wikiversity Journal of Medicine. DOI:10.15347/wjm/2014.010. ISSN 20018762; License: Creative Commons Attribution 3.0 Unported license.*
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5.2.7

Chloroplasts

Chloroplasts are organelles found mostly in plants and function as the site of photosynthesis. Chloroplasts contain pigments called chlorophyll which can capture photon energy from the sun and convert that energy into chemical energy to produce food in the form of sugars. Water and carbon dioxide are substrates that are used in photosynthesis, along with the captured light energy, to produce sugar and oxygen. The process is divided into two stages: the light reactions (water is split to produce oxygen) and the dark reactions or Calvin cycle (builds sugar molecules from carbon dioxide). Chloroplasts have three membrane systems: the outer membrane, the inner membrane, and the thylakoid membrane. Between the inner and outer membrane is a space called the stroma. The thylakoid membrane system floats in a gel-like fluid located in the stroma and is the site of photosynthesis.

5.3

The Cytoskeleton

The cytoskeleton, as the name implies, is the structural component of the cell and is composed of a network of proteins that are constantly destroyed, renewed, and newly built. The cytoskeleton functions in maintaining the cell shape, resisting deformation, movement both inside (transport of vesicles within) and migratory movement, cell signaling, endocytosis and exocytosis, and cell division. The cytoskeleton is composed of three major filaments: **microfilaments**, **intermediate filaments**, and **microtubules filaments**.

Microfilaments are the thinnest (7nm) of the cellular filaments and are composed of long chains of protein monomers called G-actin. They can generate force by adding monomers that cause the growing strand to push against barriers like the cell membrane. Other proteins, like myosin, can move along the track and pull against it, generating contractile forces in all cells, which is especially important in muscle cells. These structures are very dynamic in that they are constantly growing and shrinking, and they do son in a very directional manner.

Intermediate filaments are stronger than micro filaments and thus help maintain the cell shape. The filaments serve as anchors for other organelles; they also serve as cell-to-cell junctions. Intermediate filaments are also used in helping to maintain the shape of the nucleus. Intermediate filaments are the most stable of all three filaments, are the most diverse, and exits at diameters around 10nm.

Microtubules are the largest of all filaments (25nm), with a hollow structure made up of protein monomers called *tubulin*, which wind like a spiraling staircase. Microtubules are closely associated with an organizing center called the **centrosome and motor proteins called kinesins (proteins that move away from centrosome) and dyneins (proteins that move toward the centrosome)**. Microtubule networks serve as "highways" for the transport of vesicles and are important for specialized movements like the swirling tail of sperm cells or the flagellum of bacteria. They also play a crucial role during cell division where they function to pull apart and segregate individual chromosomes. Like microfilaments, microtubules are dynamic, constantly growing and shrinking.

UNIT 6

PROKARYOTES AND VIRUSES

6.1

Prokaryotes

Up to this point we have been talking about organelles associated with Eukaryotic cells but will now shift our attention to prokaryotic cells which are single celled organisms that lack nuclei and membrane bound organelles. Prokaryotes can be separated into two domains: **bacteria** and **archaea**. As a reference, organisms with a nucleus are placed into the third domain, Eukaryota. For those who study the origin of life, the prokaryote is hypothesized to have started before the eukaryotes.

Prokaryotes also lack membrane bound organelles like mitochondria, endoplasmic reticuli, Golgi apparati etc., however some prokaryotes appear to have compartments formed by protein shells or carbohydrate-enclosed microcompartments. Prokaryotes do contain vacuoles and a cytoskeleton; the most prominent part of the cytoskeleton being arranged into a structure called the **flagellum**. The flagellum is a long, whip-like structure that helps the prokaryote move, although the structure is not always present. Other cytoskeleton structures include **fimbriae** (numerous short appendages used to adhere) and the **sex pili** (protein-based tubes that pull cells together to transfer DNA). In addition to the cell membrane, some prokaryotes (bacteria) also contain a cell wall which is an outer covering that gives the cell shape and protection. Cell walls are comprised of polysaccharide chains that are cross-linked together by short polypeptides, and together the structure forms a **peptidoglycan**. Cell walls differ slightly between groups of bacteria and this difference can be seen through a technique called gram staining. Gram staining involves the application of two dyes; red safranin (stains all cells) and crystal violet (gets trapped in peptidoglycan walls). This technique revealed two categories of bacteria, a **Gram-Positive** group and a **Gram-Negative** group. If a cell is gram-positive it means that the peptidoglycan cell wall was very thick and the crystal violet remained “stuck” despite several washings, leaving the cell a purple color (safranin + crystal violet). If a cell is gram-negative it means that the cell was thin, so that the crystal violet washed out, leaving the cell pink (from the safranin). This categorization is very important when it comes to antibiotics because knowing the composition of the cell wall determines which antibiotic is likely to work or not. Some bacteria can secrete additional polysaccharides that surround the cell wall forming a **capsule** that allows the cell to adhere to surfaces and help prevent dehydration. A common capsule type is called a **slime layer**.

Prokaryotic Morphology and Reproduction

6.1.1

Prokaryotic Morphology and Reproduction

Prokaryotic cells can be identified by one of four shapes:

Cocci – spherical

Bacilli – cylindrical or rod shaped

Spiral – twisted rod

Vibrio – shaped like a comma

Prokaryotes reproduce through a process called asexual reproduction, primarily through a process called **binary fission** (the division of a single entity into two parts). The process results into two daughter cells with identical DNA, each being a clone to the parent cells. The reproductive rates are very high with cells doubling every 1-3 hours or 20 min in comes species like *E. coli*. In addition, the high reproductive rates come with a high error rate when it comes to copying the DNA. This high error rate is referred to has **mutation**. Most of the time mutation causes high rates of death, but every once and while, a mutation proves beneficial to the organism (more fit), improving its survival. In this case, the new "mutated" bacteria outcompete the other less adapted bacteria and a new strain takes over. Sounds just like an X-men movie! Growth is regulated by the conditions of growth such as nutrient supply, space, predation, and competition with other organisms. If conditions are bad, some prokaryotes can from endospores, which are extremely tough desiccated shells full of DNA, ribosomes and dipicolinic acid, the latter being necessary to maintain dormancy. These endospores can survive very difficult conditions such as extreme temperatures, pH, and even UV exposure for decades. When conditions return to optimal, the endospores will rehydrate and start growing again.

With no defined nucleus, the DNA is still found in given areas or regions called the **nucleoid.** DNA is organized into a single circular chromosome. Additionally, some pieces of shorter circular DNA called **plasmids** exist in bacteria cells, these plasmids often contain genes that improve survival (i.e., antibiotic resistance). Thus, with high mutation rates and unique plasmids that both improve survival rates, its no wonder that bacteria and humans exist in a kind of "arms race" to see who can defeat the other first!

The most important part of any reproductive process is the transfer of DNA and in prokaryotes have developed three unique ways to transfer DNA: **transduction**, **conjugation**, and **transformation**.

Transduction is defined as the process through which foreign DNA is introduced into a cell. Transduction does not require physical contact, instead DNA is transferred between bacteria by viruses called **bacteriophages**. Like humans, bacteria also share viruses, and these viruses can take over some of the DNA machinery turning the cells into mini virus production factories. The discovery that bacteriophages can insert "foreign" DNA into bacterial DNA led to the new discipline called genetic engineering.

Conjugation is the process that uses pili to pull two bacteria together and exchange plasmids. This allows unique genes to be transferred from on bacterium to another. The first plasmid discovered was named the fertility factor (F-sex factor or F-plasmid). Scientists now understand what gives the F-factor its unique property to be transferred and have since

used that property to insert different genes into bacteria. For example, the gene for human insulin was inserted into a genetically modified plasmid and then conjugated into a bacteria cell which then began to divide rapidly and produce human insulin!

Transformation is a “built-in” mechanism that some bacteria have that allows them to incorporate DNA from the outside. This typically happens when bacteria experience starvation and are thus “looking” for ways to increase their survival. Taking in foreign DNA comes with all kinds of risk, but, like mutation, every once a while the attempt works, giving a new advantage to the bacteria.

6.2

Viruses

Viruses are infectious agents that can only replicate inside another living organism. All forms of life have been known to be susceptible to viral infection and viruses have been found in almost every ecosystem on earth. Viruses have one objective, take over a section of the DNA of a host cell by inserting new DNA that contains the instructions to make more virus. Once infected, the cell is "forced" to produce thousands of copies of the original virus which can then be released to infect new cells. Viruses that exist outside of host cells are called **virions**. Virions are composed of a protein coat called the **capsid** that surrounds genetic material. The genetic material exists as four different types: double stranded DNA (chicken pox), single stranded DNA (uncommon), double stranded RNA (uncommon) and single stranded RNA (most common, i.e., common cold). Virions are small, typically one-hundredth the size of a bacterial cell and over one hundred thousand bacteria can fit into the area of the period at the end of this sentence! Talk about small and simple bringing about great means! Capsids are often surrounded by a lipid bilayer called the **viral envelope**. Since the viral envelope is lipid based, like host cells, it is used to evade detection and to interact with cell recognition proteins, tricking the host cell into letting the virus enter. For example, the virus responsible for COVID19 enters cells through the ACE2 receptor, found primarily in lung, kidney, olfactory and taste cells, and placental tissues. Some viruses will even package necessary enzymes for replication inside their viral envelopes. There is still great debate as to whether viruses should be considered life and there is still debate on where viruses originated. Perhaps the best definition is that they are "organisms at the edge of life."

Viruses can spread from host cell to host cell in many ways, but the most common seems to be through **vectors**. Vectors can be anything from insects to droplets from coughing and sneezing to food and water, to sexual contact. How well a virus infects a host is called its host range. Some viruses have very narrow host ranges and other much broader. Fortunately, viral infections lead to immune responses that are usually very effective at eliminating the virus, the exceptions being viruses that cause HIV/AIDS, HPV (human papillomavirus), and hepatitis.

Viruses do not grow by cell division of binary fission, instead the use the host cell machinery to make thousands upon thousands of copies of themselves. Although some variation exists, there seems to some common stages in the "life" cycle of a virus.

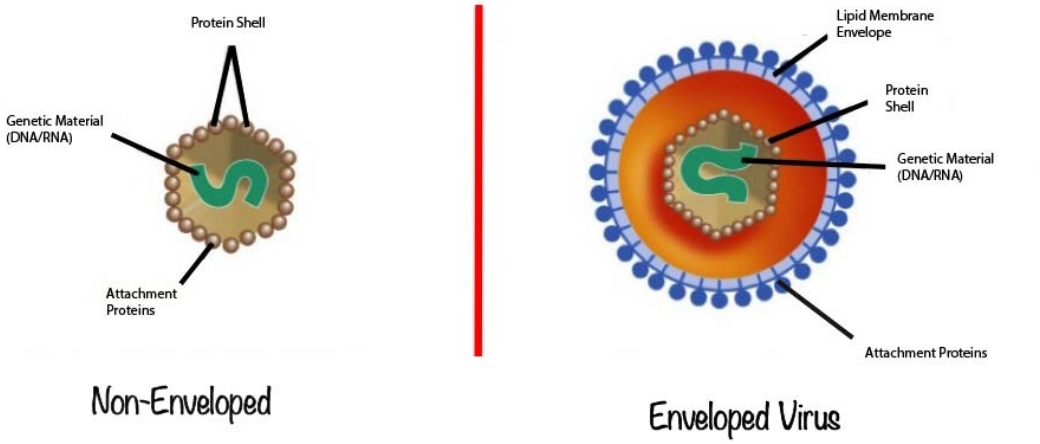
Attachment. Attachment is the interaction between the viral capsid or envelope with specific receptors on the host cell. As stated previously, how specific this interaction determines the host range of the virus. Successful attachment allows the virus to enter the host cell.

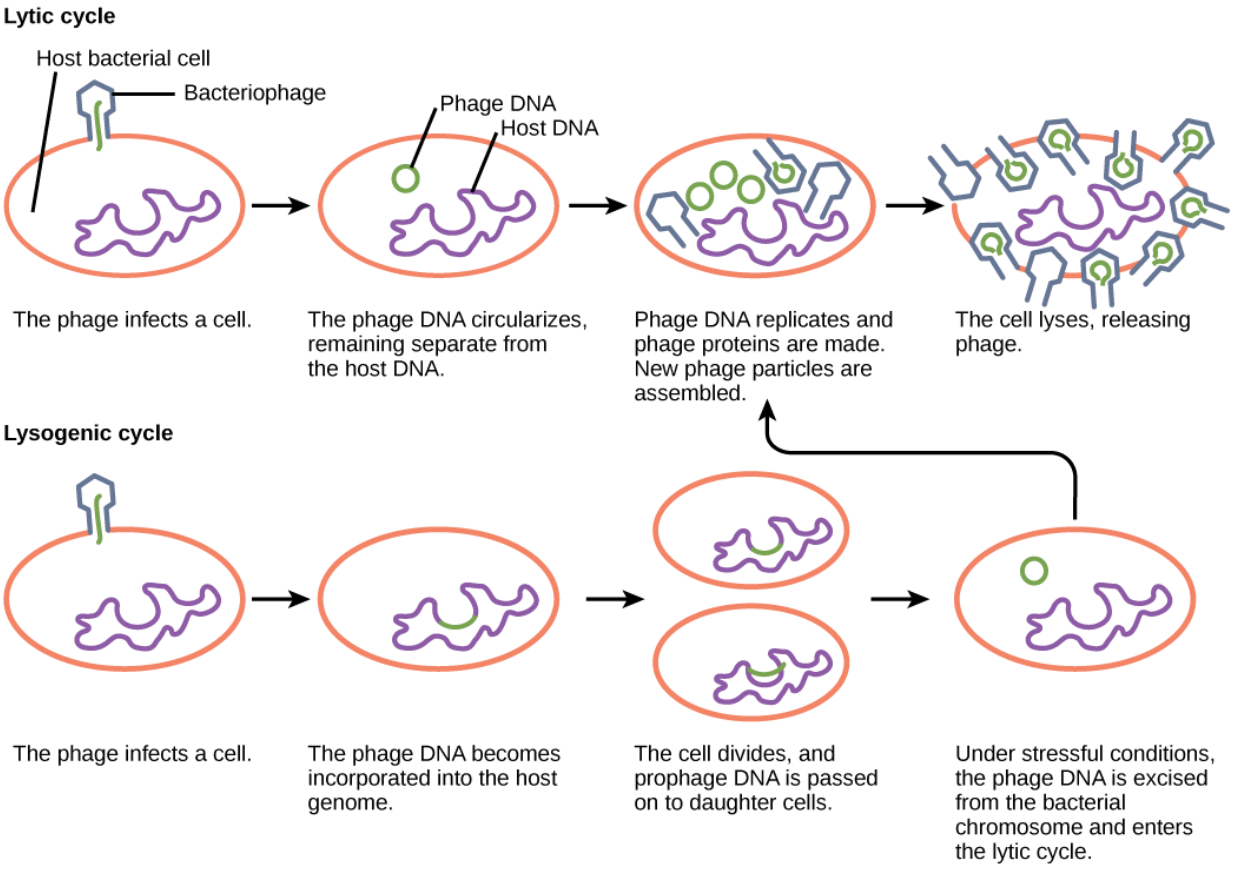
Penetration. Penetration describes how a virus enters the host cell either though receptor mediated endocytosis or membrane fusion. Because plants have ridged cell walls, viruses typically can only penetrate if the cell wall has undergone some sort of damage. Still, some viruses have evolved a strategy to inject their DNA across the cell wall, leaving the capsule intact and stuck to the cell wall. The result of penetration is the releasing of the viral genetic material into the host cell.

Replication. With successful penetration, the viral nucleic acids are incorporated into the host cell DNA, and viral components are then produced and assembled. How the assembled virus is released is determined by whether the virus induces a lytic or lysogenic cycle. In the lysogenic cycle the viral DNA is spliced into the host DNA but then pauses

before synthesis and assembly. This spliced DNA is called a provirus or prophage and the DNA is continually transferred each time the host cell replicates but the virus “waits” for a later time for synthesis and assembly. In the case of the HIV virus, in some humans the virus may lay dormant. The lytic cycle can be activated at any time due to sunlight, stress, etc. and this cycle results in the production of hundreds of thousands of viruses that end up lysing or rupturing the cell. The lytic cycle and the lysogenic cycle are not totally independent from each other. When a virus is synthesized, assembled, and released from the host immediately after the DNA incorporation, that is a purely lytic cycle. When there is a pause between the incorporation of DNA and the start of assembly (for host replication), that is a lysogenic cycle followed by the lytic cycle. Some viruses have even evolved the ability to make viral envelopes that can be released via exocytosis without rupturing the host cell membrane. Incorporation in the host DNA varies as to the type of viral genetic material that was introduced. The DNA viruses must make their way to the nucleus and use the host cells DNA and RNA machinery, or, in the case of very large viruses, they bring their own machinery. RNA viruses replicate in the cytoplasm, and they bring with them the necessary replicating enzymes. Of these enzymes, the best studied are called reverse transcribing enzymes or **reverse transcriptase**, which converts the RNA into DNA that can then be incorporated into the host DNA.

Since viruses become so integrated into the host cell, they can be difficult to eliminate using toxic drugs because the drug also destroys the host cells. The most effective approaches to viral disease have been vaccinations. Most vaccines contain live, but weakened forms of the virus in question, that do not cause the disease but still allow the body to recognize and build immunity. These viruses are called attenuated viruses. Although not perfect, their uses still have nearly eradicated viral diseases such as polio, measles, mumps, rubella, and smallpox. The COVID19 virus vaccine introduces an exciting discovery that has changed the effectiveness of vaccines. Instead of using an attenuated virus, the COVID19 vaccine used mRNA that was specifically designed for COVID19. In brief, once injected (and similar to natural viral infections), the engineered mRNA makes it way to the cells where it instructs the cell to make a harmless protein called a spike protein. The mRNA is quickly removed by the cells and the synthesized spike protein is placed at the surface of the cells. Our own immune system then recognizes the spike proteins and builds up an immunity. Thus, the body is prepped for any virus that displays the same spike protein (COVID19) and quickly eliminates the threat. This discovery allows for quick and precise vaccine immunity and will most likely prove extremely beneficial as new and more virulent viruses enter the population.





UNIT 7

ENERGY BALANCE

7.1

Energy Cycle, ATP, and Electron Carriers

Survival of living organisms depends on the ability to harvest energy from their surroundings and then convert that energy to forms that can carry out cellular processes. Energy can be found in our physical world in many different forms, some of which include electrical energy, light energy, heat energy, and even the energy of motion. **Thermodynamics** is the study of the relations between heat, work, temperature, and energy. The study of thermodynamics has two governing scientific laws. The first law states that – Energy cannot be created or destroyed and the second law states that – No energy transfer is 100% efficient, instead some energy is lost to **entropy**, a form that is the least useable for organisms.

At the broadest level, energy can be organized into one of two categories, **kinetic** and **potential** energy. Objects in motion (electrons, moving cars, or air molecules) all have kinetic energy, while objects not in motion (parked car) have potential energy. Since energy is defined as the ability of an object to do work, both moving (kinetic), and nonmoving objects (potential) possess energy. It might seem a bit odd to categorize nonmoving objects as having energy, but it is precisely this concept of potential energy that allows cells to exist. In the case of biological cells, it is the potential energy stored in the chemical bonds that hold molecules together that sustain life. This type of potential energy that exists in chemical bonds is called **chemical energy**. As macromolecules are synthesized from simpler molecules, they store chemical energy in their newly formed bonds through **anabolic pathways**. Then when these same macromolecules are broken down back to their simpler forms, they release the stored chemical energy through **catabolic pathways**.

Bioenergetics is the study of how energy is transferred through the chemical reactions of living systems. Cells are always breaking and making bonds. Every time a bond is broken, energy is released and every time a bond is made energy is required in forming that bond. Keep in mind that whenever we see a reaction that involves the synthesis of new molecules, we call this an **Anabolic** reaction. **Catabolic** reactions occur when molecules are broken down into smaller and smaller parts. Several catabolic reactions occur in cells to break sugars, proteins, and lipids down into smaller and smaller parts until finally the C-H bonds have been processed to allow the energy in such bonds to be used in the form of ATP to do work.

The energy transfer between breaking and making bonds is quantified with a measurement called **free energy** or **Gibbs free energy** (**G**) named after Josiah Gibbs who developed the measurement. Gibbs free energy attempts to quantify the amount of useable energy that is left over after a chemical reaction. Recall, that the second law of thermodynamics states that no reaction is 100% effective, and some energy is lost through **entropy** which is unusable. Thus, Gibbs free energy gives an estimate of only the energy available after entropy for a given chemical reaction. This energy exchange is called the delta G (ΔG). Therefore, to calculate ΔG the total energy of a system called enthalpy (ΔH) is subtracted from entropy (ΔS). Since temperature is a very big factor in energy exchange, we also include temperature (T; in degrees Kelvin) in the ΔG calculation and make assumptions that pH and pressure are constant.

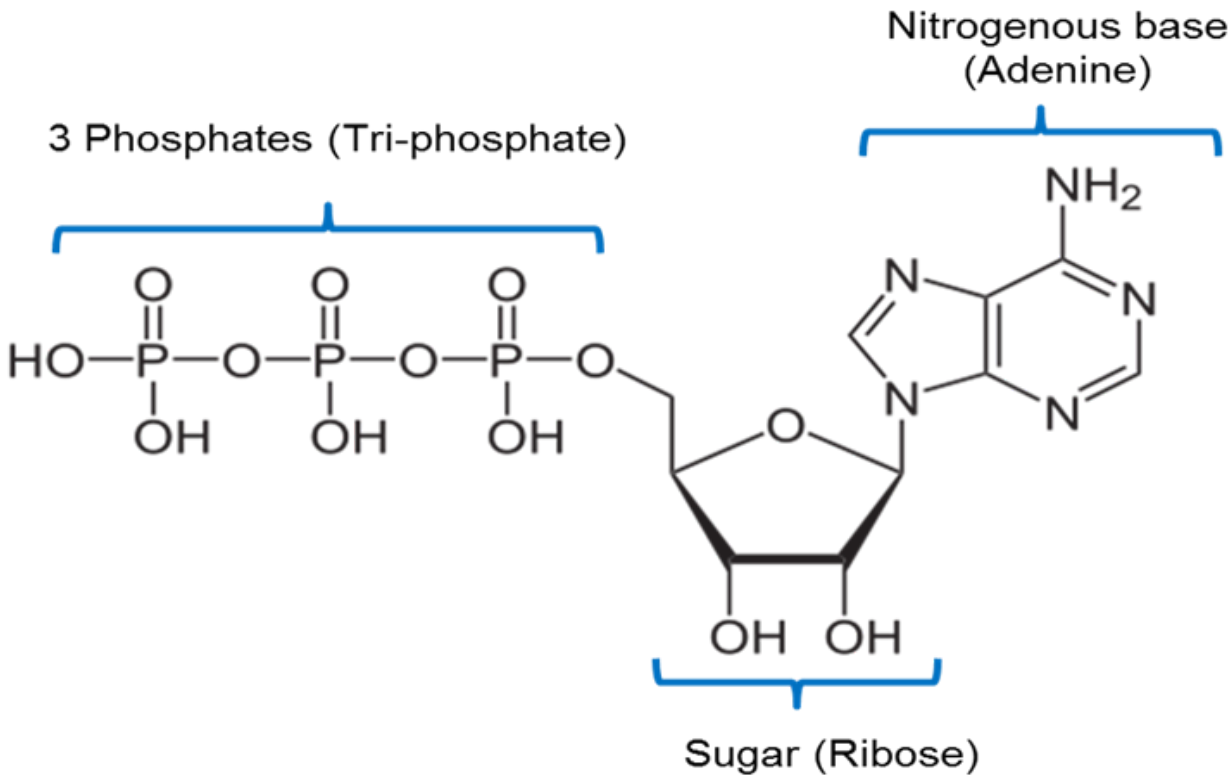
$$\Delta G = \Delta H - T\Delta S$$

The units will include the measure of energy (kilojoules or kilocalories) per the amount of chemical reactants (mol). Using the ΔG calculation for a give chemical reaction reveals two kinds of reactions: **exergonic** or **endergonic**. Exergonic means that energy is being released during the reaction. Stated more specifically, the products have less energy than the reactants and the ΔG will be less than zero or negative. These reactions occur spontaneously which means that if two reactants are placed together, they will eventually make a product, even though technically, they do require energy to get started. Sometimes these reactions occur quickly and sometimes slowly, but they will eventually make the product. In contrast, endergonic reactions require the input of large amounts of energy so that the products will have more energy than the reactants and the ΔG will then be greater than zero or positive. These reactions will not occur without the addition of more energy. Combining all the terms thus far, anabolic processes that build complex molecules (glucose to glycogen) are endergonic reactions, and catabolic processes (glycogen to glucose) are exergonic.

Perhaps no other molecule in biology demonstrates the importance of endergonic and exergonic better than the molecule adenosine triphosphate (**ATP**). In terms of cellular energy, ATP could be considered currency! The molecule of ATP consists of the nucleoside adenosine bound to three phosphate groups. When ATP is combined with water the resultant hydrolysis reaction can yield -7.3 kcal/mol for the loss of one phosphate or -10.9 kcal/mol with the loss of two phosphates.

$ATP + H_2O \rightarrow ADP + Pi \quad \Delta G^\circ = -7.3 \text{ kcal/mol}$

$ATP + H_2O \rightarrow AMP + PPi \quad \Delta G^\circ = -10.9 \text{ kcal/mol}$



***Chemical Structure of ATP**. Image created by JS at BYU Idaho Fall 2013.*

The chemical reaction is considered exergonic because the resultant products (ADP and one inorganic phosphate (Pi) have lower free energy than the initial reactants (ATP and water). The free energy can then be used for cellular work. In fact, the molecule ATP is very unstable, "spontaneously" converting to ADP and Pi and constantly releasing energy as heat unless harnessed by other proteins.

Most endergonic or exergonic reactions are reversible, releasing energy in one direction and consuming energy in the other direction. Since exergonic reactions are spontaneous, in a closed system, the ultimate direction would always favor the exergonic direction. Fortunately for living organisms, the system is open, with constant supplies of energy. Thus, all living organisms are in a constant uphill battle to try and keep the direction of reactions equal, requiring constant supplies of energy. The amount of energy needed to start reactions, both endergonic and exergonic, is known as the **activation energy**. A common source of energy for the initial "push" to start the reaction is heat energy. Heating up a system will increase the energy available and speed up the process. The higher the activation energy, the slower the reaction will occur and the more heat energy it will need to get it started. In many systems, the activation energy is too high to be overcome with heat energy alone (this is good, so things don't just spontaneously start), instead they require the use of a **catalyst** to help facilitate the process, thereby indirectly lowering the activation energy.

7.2

Enzymes

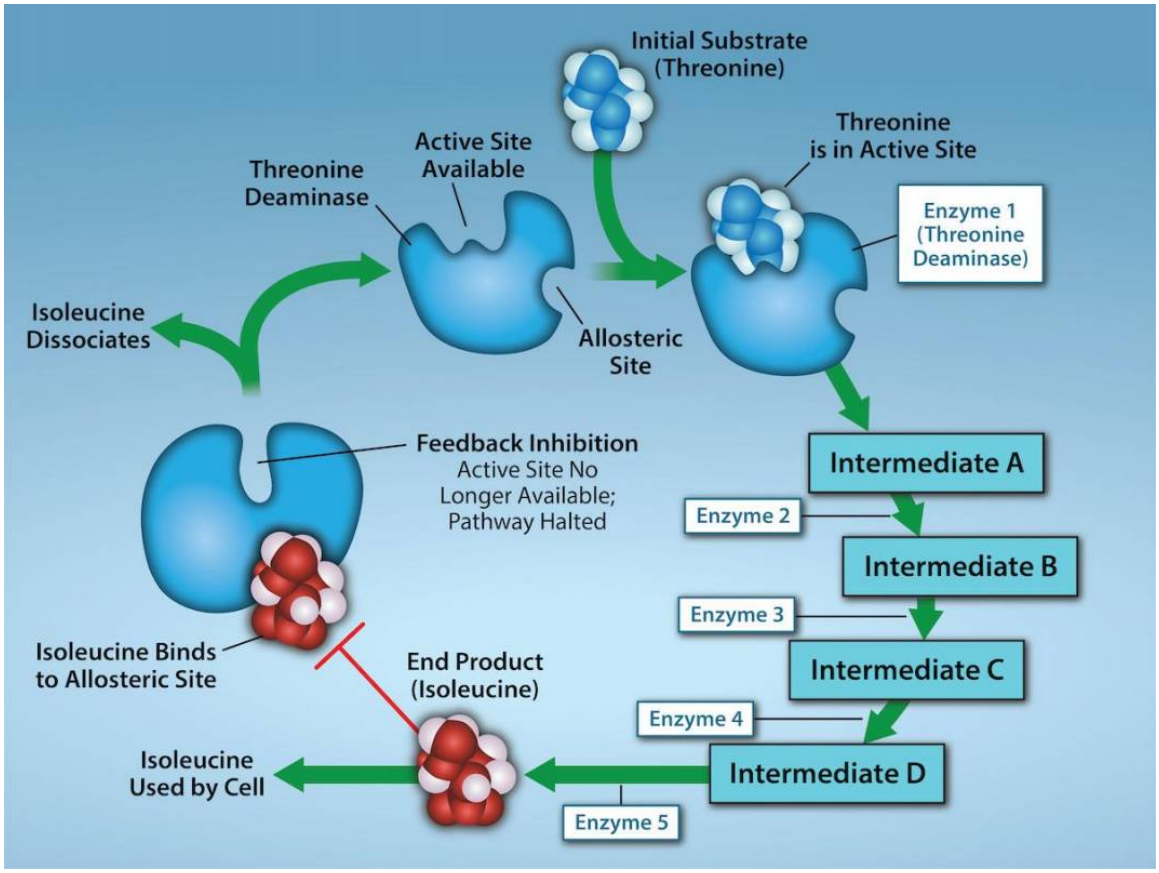
Biological molecules that act as catalysts for biochemical reactions are called **enzymes**, and almost all enzymes are proteins. Enzymes lower the activation energy by binding to the reactants in such a way that the shape of the molecules are changed enough to destabilize the bonds. A destabilized bond is easier to break or make, thus requiring less heat energy to get the process started. Enzymes don't actually change the ΔG, they simply reduce the activation energy needed to start the reaction process.

Reactants that bind to enzymes are called **substrates** and the location at which they bind is called the enzymes **active site**. In fact, enzymes are name after the substrate and designated with a suffix -**ase** (ATPase, Lactase, etc.) Active sites are created by unique combinations of amino acids and their side chains. Since side chains of amino acids can be acidic, basic, hydrophilic, hydrophobic, positively, or negatively charged, binding sites can be very specific to a particular substrate, in fact, enzymes are defined by their unique specificity towards substrates. However, this uniqueness also comes with very little wiggle room if environmental conditions change (i.e., temperature, pH), which can greatly alter enzyme effectiveness. Still, the enzyme-substrate complex is designed specifically to lower the activation energy which can involve: promoting reactions by bringing certain substrates closer together, creating proper environments like acidic, basic, polar, or non-polar, altering arrangements of bonds to facilitate bond breaking or bond forming, and even providing additional needed substrates like ions or certain chemical groups. After the enzyme helps to catalyze the chemical reaction, the products are released and the enzyme is ready for more substrate, with the enzyme essentially remaining unchanged by the reaction.

7.2.1

Enzyme Regulation

Since activation energy is such an important part to chemical reactions, and since enzymes play an integral part in lowering activation energies, it would make sense that cells have evolved complex mechanisms to regulate enzyme activity. Enzymes can be regulated in ways that increase or decrease their activity. One regulatory pathway is through the use of inhibitor molecules. An inhibitor molecule looks and acts very similarly to the actual substrate but when it binds to the active site it is not catalyzed, instead it simply blocks the binding site. This regulatory function is called **competitive inhibition** . Sometimes molecules can bind to an enzyme in a place that is not the active site, but the binding nevertheless alters that active site in a way the affects binding of the substrate. This is called **noncompetitive inhibition** . Both types of inhibition are effective, but competitive inhibitors are less effective because if the concentration of substrate is increased it can "out compete" the inhibitor molecule for the active site. Additionally, competitive inhibitors can affect the initial rate of enzyme activation



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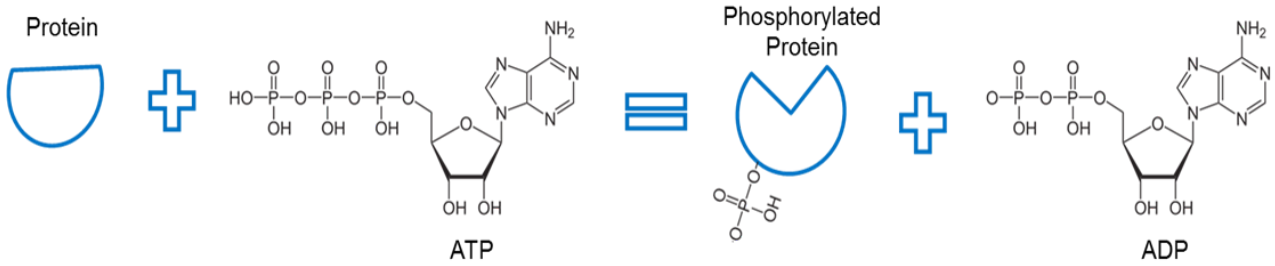
but have little effect on the maximal rate (due to competition of substrate). Noncompetitive inhibitors affect both the initial and maximal rate because they are not in competition with the substrate; if present, they always alter the

enzyme's active site and no amount of increased substrate can change that. Noncompetitive inhibitors that alter the active site by binding elsewhere on the protein are also called **allosteric inhibitors** . In contrast, there are also molecules called **allosteric activators** which are molecules that bind to an enzyme to a location away from the active site, but this binding alters the protein slightly, increasing the affinity of the binding site for the substrate. Sometimes, the allosteric inhibitor or activator is the molecule produced by the enzymatic reaction. In this case, the biochemical reaction acts as a **feedback system** to regulate enzyme function, either speeding up or slowing down the reaction. Product feedback regulation is a primary pathway in regulating the amount of ATP produced in the cell. Since ATP is quite unstable, producing too much of it would be wasteful. Therefore, ATP serves as an allosteric inhibitor, while ADP (which is representative of low ATP) serves as an Allosteric activator.

Allosteric activators can be categorized into molecules called **cofactors** and **coenzymes** . Cofactors are often inorganic ions like iron (Fe^{++}) or magnesium (Mg^{++}) or even zinc (ZN^{++}). Cofactors are often integrated into the final product of the biochemical reaction. Coenzymes, as their name suggests, are "helpers" for the enzyme. A good example of coenzymes are vitamins (i.e., Vitamins A, D, E, K, C, folic acid, and B vitamins).

Enzymes activity can also be regulated by other enzymes through phosphorylation. Covalently adding a phosphate to an enzyme can increase activation or can inactivate the enzyme. Enzymes that add phosphates are called **kinases** and enzymes that remove phosphates are called **phosphatases** .



***Phosphorylation.** Image created by JS at BYU-Idaho Fall 2013.*

7.2.2

Metabolism

Metabolism refers to all the catabolic and anabolic processes that a cell is engaged in.

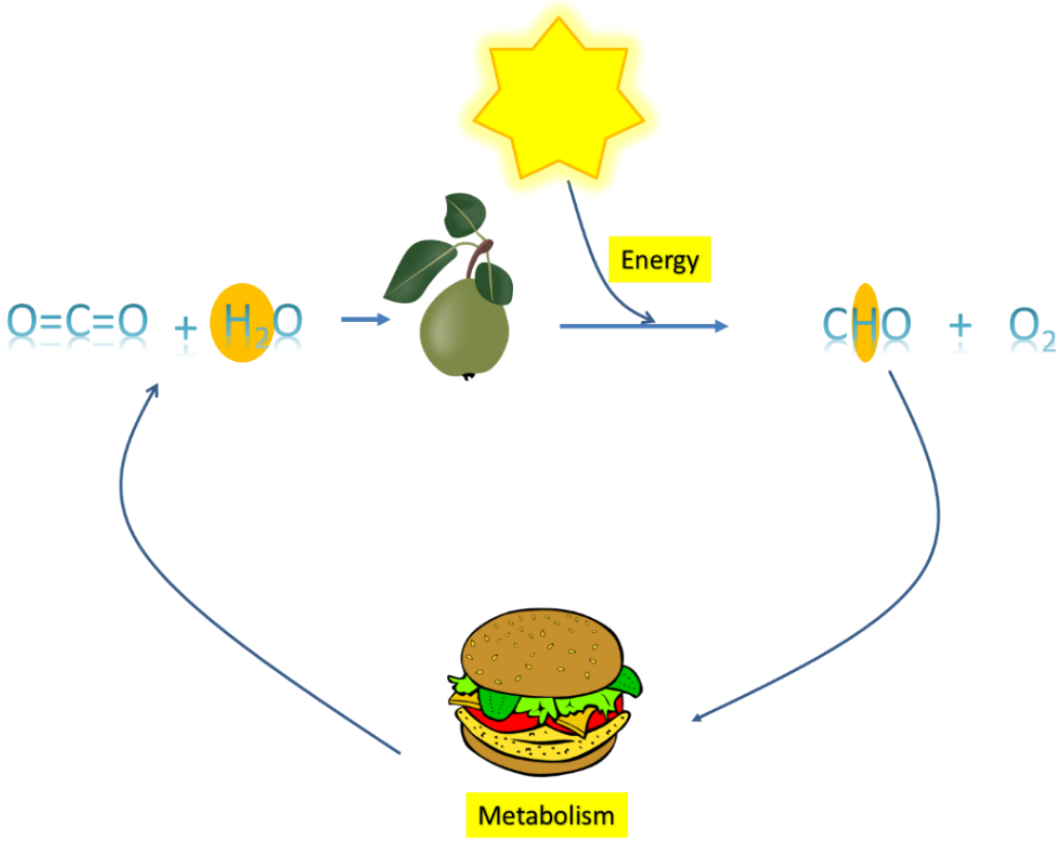
Metabolism in its most simplified "big picture" description is largely a story of chemical bonds, more specifically the electrons in these bonds. You probably recall that electrons are a subatomic particle with a negative charge. Electrons also move with considerable energy and speed as they find themselves drawn to protons. So, what if we could take some high energy electrons and store them somewhere. Later, when we wanted to harvest some of the electron energy to do some work, we could go get them. This is kind of how a battery works. Smart people have figured out how to store high energy electrons and when we want these electrons to do something (like flow through a flashlight filament) we can get them and use them. Living things also use high energy electrons to power the processes of biology.

On planet earth, the primary source of energy is the sun. This energy is called solar energy. You can feel some of this energy when you go out on a warm day. Solar energy is absorbed by plants and when a plant gets solar energy it uses this energy to excite electrons.

An electron in a bond between oxygen and hydrogen has a certain amount of energy. An electron in a bond between carbon and hydrogen has even a greater amount of energy. When sunlight strikes a plant, the solar energy is used to break an oxygen-hydrogen bond and then create a carbon-hydrogen bond. In this very incredible and complex process called photosynthesis, plants use water as the source of oxygen-hydrogen bonds and carbon dioxide (CO_2) serves as the source of carbon that will accept a hydrogen with its newly energized electron. Whenever an atom receives more electrons, the atom has been **reduced,** and whenever an atom loses electrons, the atom has been **oxidized**. In the case of photosynthesis, CO_2 is reduced, and H_2O is oxidized.

Let's summarize to this point. Plants take CO_2 and H_2O, and then capture solar energy to excite some electrons in H_2O and then transfer the excited electrons to a C-H bond, increase the energy of that bond. Reduced CO_2 can be transformed into a variety of molecules with different numbers of C-H bonds that include the macromolecules (i.e., sugars, lipids and proteins). The structures of these macromolecules reveal lots of C-H bonds. From the broadest sense, plants create a kind of "battery." The carbon-hydrogen bonds formed by plants can exist for a long time as sugars, lipids and proteins. If the high energy electrons are allowed to go back and form an O-H bond, energy will have to be released. This is what metabolism is all about. Cells can facilitate the transfer of high energy electrons in C-H bonds back to O-H bonds and use the energy that is released as work.

This process is called the energy cycle. Organisms consume C-H bonds in the form of carbohydrates, lipids and proteins. Cells then "process" the C-H bonds in a way that allows the high energy electrons back onto Oxygen. Energy is released that energy is used to run cell processes. Also, if you note in figure 1, CO_2 and H_2O are created again when high energy electrons return to oxygen. Plants use the CO_2, and the H_2O and the cycle continues.



Energy Cycle. *Image created by JS at BYU Idaho. Clipart from clker.com; License Public Domain;*

The main metabolic processes that create energy in cells are Glycolysis (the breakdown of sugars), the Citric Acid Cycle (cellular respiration), the Electron Transport Chain (where ATP is created due to the transfer of electrons and protons along the membrane of the mitochondria during cellular respiration), Lipolysis and Beta Oxidation (the breakdown of fats), and Protein Metabolism. Since energy exchange is all about electrons, what follows will be a brief description of molecules categorized as electron carriers and how they contribute to each of the metabolic processes described above.

7.2.3

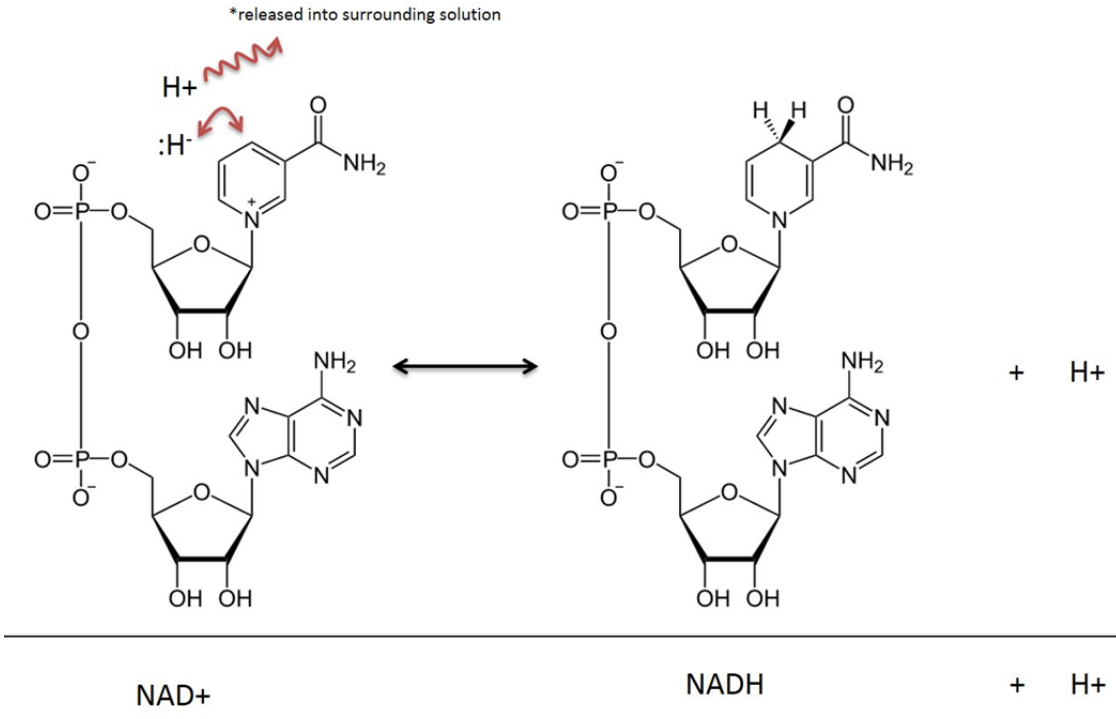
Electron Carriers (NAD and FAD)

Nicotinamide Adenine Dinucleotide (NAD) and **Flavin Adenine Dinucleotide** (FAD) are coenzymes involved in reversible oxidation and reduction reactions. It is often stated that these compounds are electron carriers because they accept electrons (become reduced) during catabolic steps in the breakdown of organic molecules such as carbohydrates and lipids. Then, these reduced coenzymes can donate these electrons to some other biochemical reaction normally involved in a process that is anabolic (like the synthesis of ATP).

NAD^+ / NADH

Nicotinamide Adenine Dinucleotide in its oxidized state is called **NAD^+**, after being reduced (or accepting electrons), it is referred to as **NADH.** *Note: the + in the NAD^+ doesn't refer to the overall charge on the molecule, but just the fact that it is without electrons and will accept a hydride*. The coenzyme vitamin Niacin (also called B3) is used to derive this compound. Niacin provides the organic ring structure that will directly participate in the transfer of a hydrogen atom and 2 electrons. NAD^+ is often found in conjunction with a "d*ehydrogenase*" enzyme. A dehydrogenase reaction removes two hydrogen atoms; one as a hydride ($:H^-$) (*a hydride is a hydrogen atom with 2 electrons*) and one as a hydrogen cation (H^+) (*and of course, a hydrogen cation has no electrons*). The hydride bonds with NAD^+ and creates a reduced compound of Nicotinamide Adenine Dinucleotide (NADH). The second hydrogen atom (H^+) is released into solution.

As you examine the reactions for metabolism, look for reactions that yield NADH. NADH will be important as it will deliver the hydrogens and electrons that it picks up to biochemical processes that can use the electrons and hydrogens to make ATP.

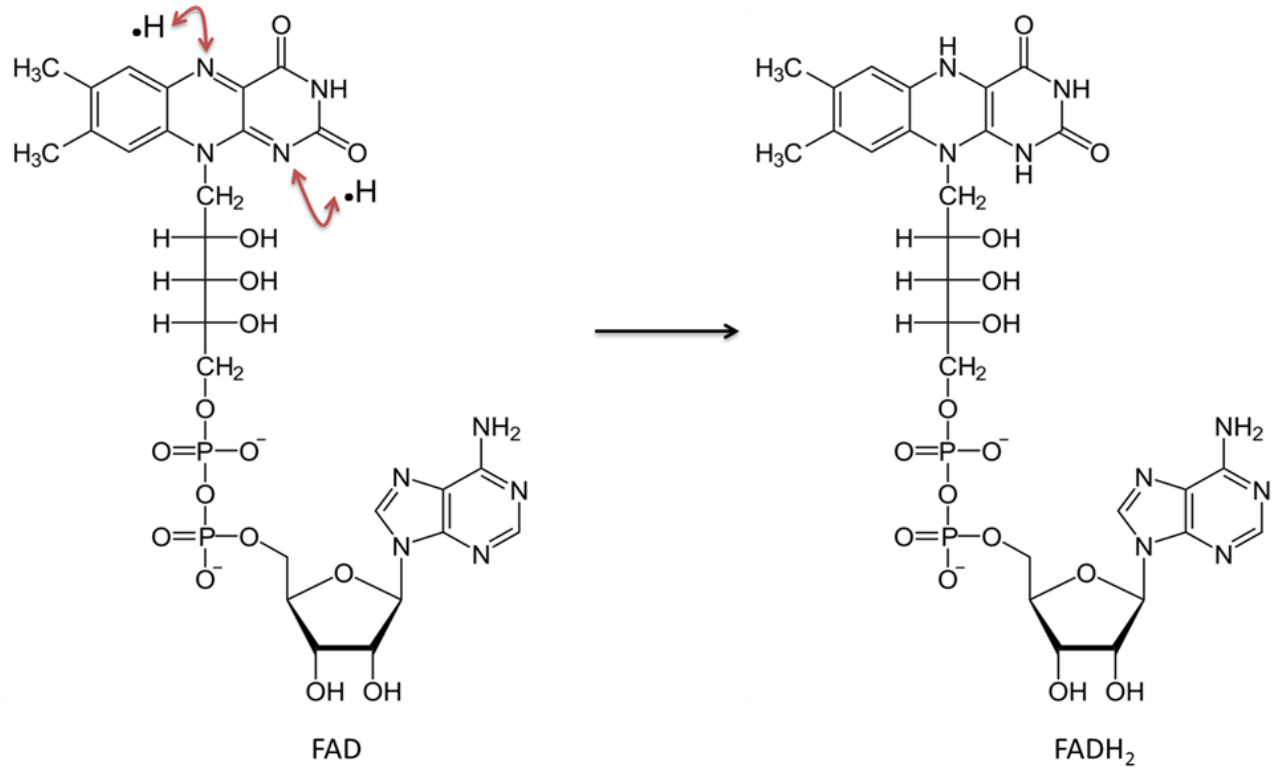


NAD⁺ Reduction to NADH + H⁺. *Image created by JS at BYU-Idaho Fall 2013.*

In metabolic reactions that involve NAD, two hydrogen atoms and two electrons are removed from a substrate and transferred to NAD^+. NAD^+ accepts a hydride ion (a hydrogen with 2 electrons) and becomes Nicotinamide Adenine Dinucleotide in the reduced form (NADH). The hydrogen cation that is also captured in the reaction is released into the surrounding solution. Remember that this reaction is reversible. In the explanation of reactions that occur in Metabolism, it is common to ignore the H^+ released into solution and this text will depict the outcome of NAD reduction as simply NADH, rather than NADH + H^+.

FAD / $FADH_2$

Flavin adenine dinucleotide in its oxidized state is called FAD. After being reduced, it is called $FADH_2$. The coenzyme vitamin, riboflavin (or B2) is used to derive this compound. Riboflavin provides the ring structures that will directly participate in the transfer of two hydrogen atoms (each with one electron this time). Similar to NAD, FAD works in association with a "*dehydrogenase*" enzyme. The reaction removes two hydrogen atoms: each a proton with one electron. Both hydrogen atoms bond with FAD. This reaction does not release an H^+ into solution like the reduction of NAD does.



FAD Conversion to $FADH_2$. *Image created by JS at BYU Idaho F2013.*

Flavin adenine dinucleotide in the oxidized form (FAD) accepts two hydrogen atoms (each with one electron) and becomes $FADH_2$.

As you examine the reactions for metabolism, look for a reaction that yields $FADH_2$. Like NADH, $FADH_2$ will be important as it will deliver hydrogens and electrons to biochemical processes that can use the electrons and hydrogens to make ATP.

7.4

Reduction-Oxidation Reactions (Redox)

Reduction-oxidation or “redox” reactions are a way to describe the transfer of electrons from one molecular intermediate to another. They are often discussed as half reactions like the oxidation half reaction or the reduction half reaction. Reduction occurs when atoms gain one or more electrons during the reaction which adds a negative charge to the atom. Adding a negative charge (electron) decreases the **oxidation number** and removing a negative charge (oxidation) increase the oxidation number. The oxidation number of an atom is the charge that the atom would have if the compound was composed of ions. Here are a few rules, the oxidation number of an atom is zero if the atoms all come from the same element. Thus, the atoms in O_2 all have an oxidation number of 0. The oxidation number of an ion is equal to the charge of the ion. For the Na^+ ion the oxidation number would be +1 and for Cl^- it would be -1. Hydrogen is a bit tricky because the oxidation number is +1 if hydrogen in combined with nonmetals (H_2O) and -1 if hydrogen is combined with a metal (CaH_2).

Thus, a half reaction for a reduction reaction may look something like this:

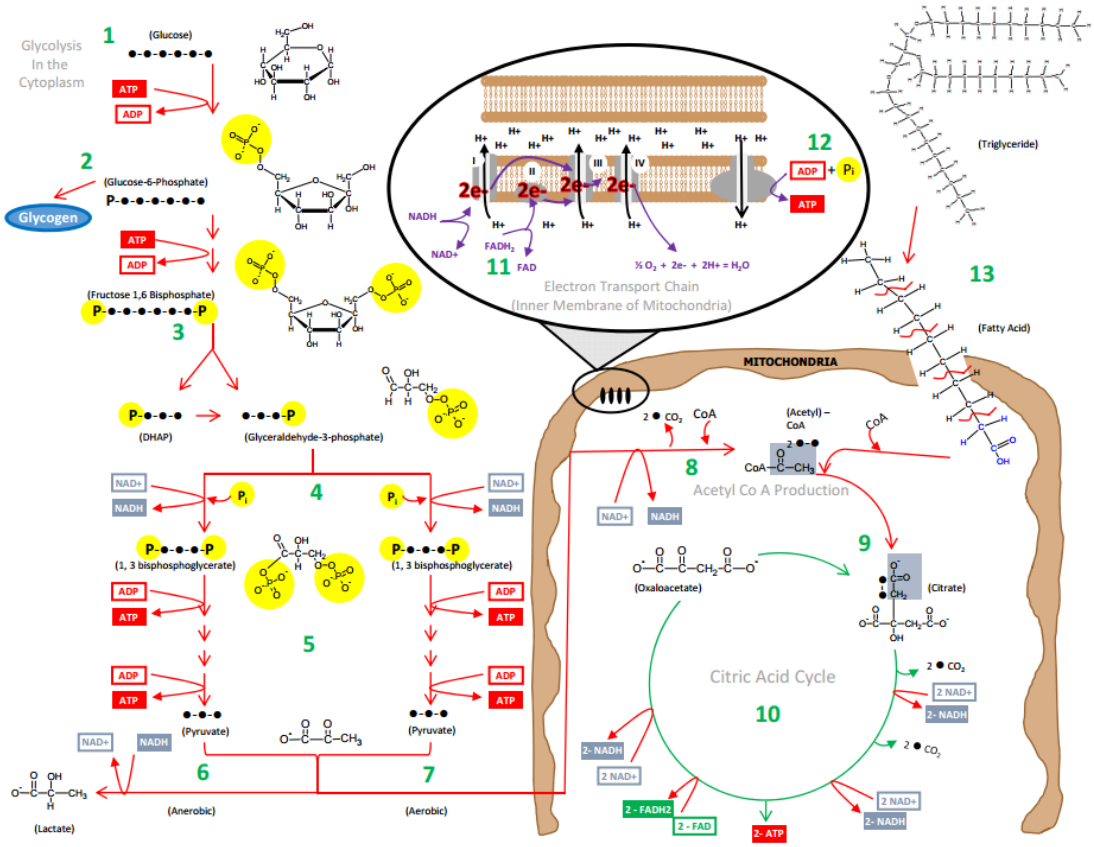
$Cu^{2+} \rightarrow Cu$

In this example, the initial oxidation number of 2+ for copper is reduced to zero. Cu^{2+} will be called the **oxidizing agent** because it is the one getting reduced.

A half reaction for oxidation happens when an atom loses one or more electrons during the chemical reaction so that its oxidation number increases.

$Zn \rightarrow Zn^{2+}$

In this example, the initial oxidation number of 0 for zinc is oxidized to 2+. Zn will be called the **reducing agent** because it is the one getting oxidized.



The "Big Picture" of Metabolism: Glycolysis, Citric Acid (Krebs) Cycle, Electron Transport Chain, Beta Oxidation and Lipolysis.

Image created at BYU-Idaho by JS 2010

***You can find a detailed description of each metabolic process shown in this image at the end of each section below.**

You can also download this image and the complete summary at this link: Metabolism Summary.

UNIT 8

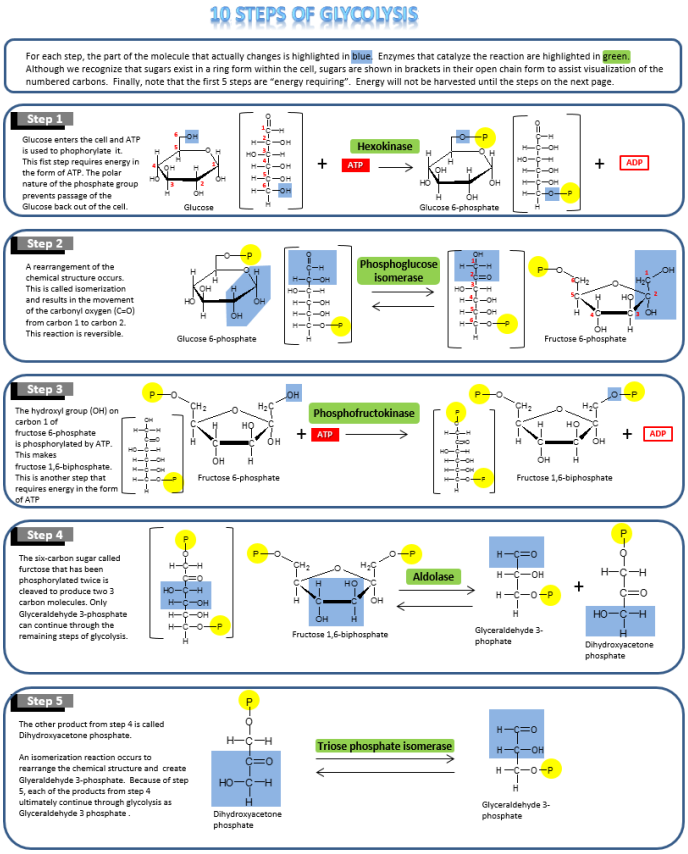
GLYCOLYSIS AND CITRIC ACID CYCLE

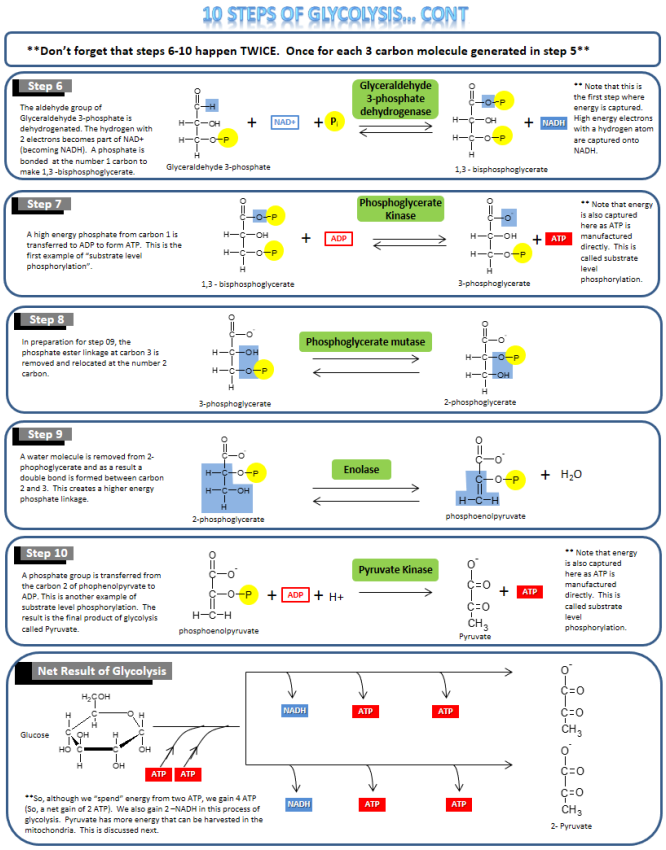
8.1

Glycolysis

Glycolysis literally means the breakdown of sugar (Glyc = sugar or sweet and Lysis = to cut or loosen). Glycolysis occurs in the cytoplasm of the cell. In short, glycolysis takes 1 glucose molecule of 6 carbons and makes two 3 carbon molecules called pyruvate. In the process, electrons and hydrogen atoms are captured by NAD^+. Any energy liberated will be released as heat or captured as ATP or NADH.

Molecule	**Net Yield through Glycolysis**
ATP	2
NADH	2
Pyruvate	2

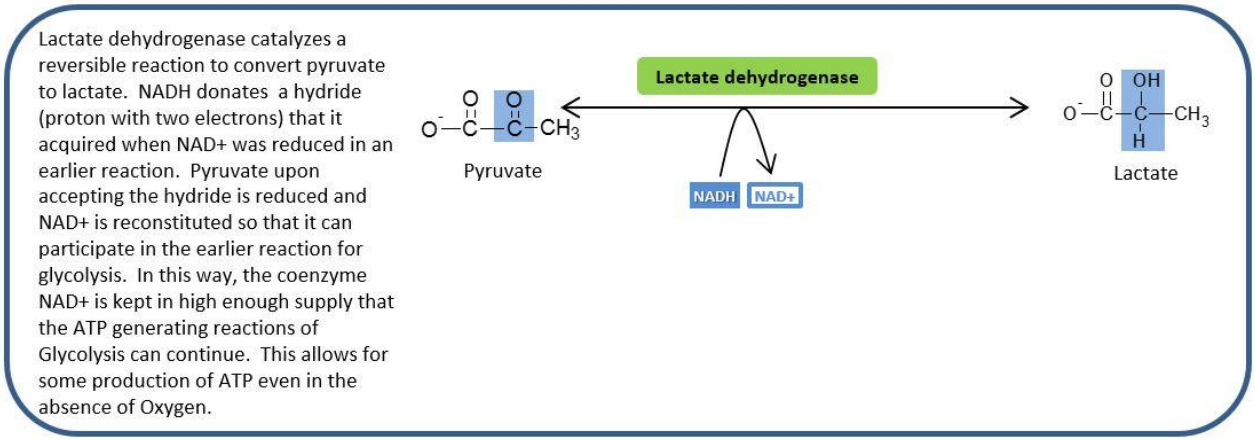




Anaerobic and Aerobic Use of Pyruvate

Anaerobic

The last step of glycolysis results in two 3-carbon molecules, called pyruvate. The fate of pyruvate depends on the availability of oxygen and whether the organism has mitochondria. If oxygen is available, then pyruvate is shuttled into the mitochondria and continues through several more biochemical reactions called the "Citric Acid Cycle." This is called **aerobic metabolism**. If oxygen is not available in sufficient quantity to the cell, then pyruvate goes through a reduction reaction that, depending on the organism, results in the production of Lactate or alcohol (**fermentation**). This is called **anaerobic metabolism**.

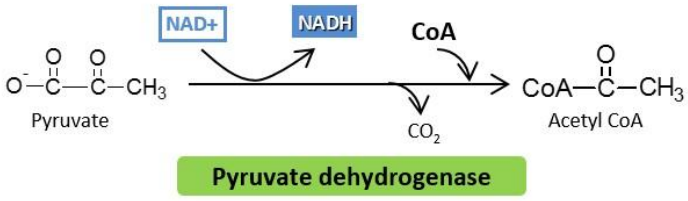


Anaerobic Metabolism: Pyruvate Reduction to Lactase. *Image created by JS at BYU-Idaho Fall 2013.*

Aerobic

When there is enough oxygen available to the cell, pyruvate crosses the mitochondrial membrane and is quickly converted to Acetyl CoA (a 2-cabon molecule). During this process, one molecule of CO_2 is released. Acetyl CoA enters the Citric Acid Cycle where CoA is removed, and the acetate is added to a 4-carbon molecule to make a 6 carbon molecule called "Citric Acid." As the biochemical steps of the Citric Acid Cycle continue, 2 more carbons are lost as CO_2 and so ultimately all the carbons of pyruvate are lost as CO_2. After 2 pyruvates complete the citric acid cycle, all the carbons of the original Glucose molecule have been released as CO_2.

The reaction to the right occurs in the matrix of the mitochondria. Pyruvate is the end product of glycolysis (which occurs in the cytoplasm). Pyruvate is moved into the mitochondria where it reacts with the enzyme "Pyruvate dehydrogenase". The result of this reaction is the loss of a carbon from the 3 carbon pyruvate (lost in the form of CO_2). Also, Coenzyme A is attached to the remaining two carbons. The two carbon molecule remaining after CO_2 is lost is called acetate. When acetate is joined to CoA, it is called Acetyl CoA. Acetyl CoA will be used in the first step of the citric acid cycle.



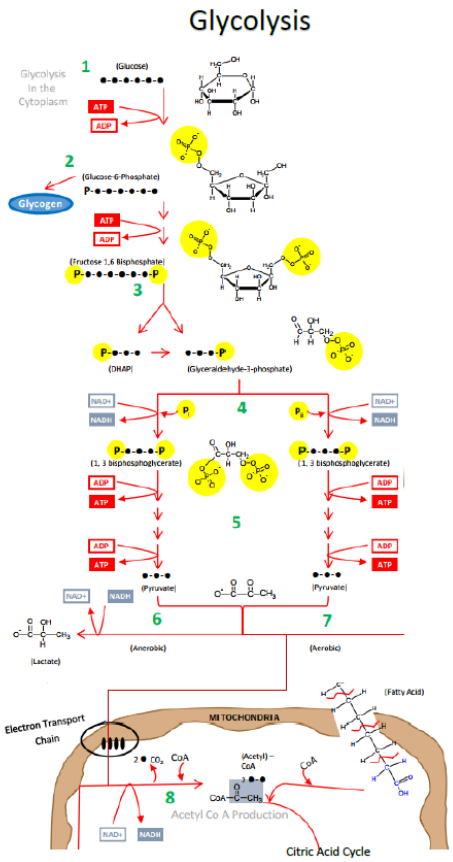
Conversion of Pyruvate to Acetyl CoA. *Image created by JS at BYU Idaho F2013.*

The image above shows the conversion of Pyruvate to Acetyl CoA occurs in the mitochondria and results in the loss of a Carbon as CO_2 and the creation of Acetyl CoA.

8.2

Metabolism Summary Part 1: Glycolysis

Below is an image of the process of Glycolysis magnified from the Metabolism Summary image you saw in 8.1. A summary follows for the process of Glycolysis that you have just read about. The green numbers in the image correlate with each of the steps listed below:



Glycolysis, from the "Big Picture" of Metabolism:
Glycolysis, Citric Acid (Krebs) Cycle, Electron Transport Chain, Beta Oxidation and Lipolysis.
Image created at BYU-Idaho by JS 2010

1 Glucose enters a cell and is quickly phosphorylated (meaning a phosphate group is added to the glucose molecule) on the 6th carbon by ATP. This "traps" the glucose in the cell as the charged phosphate group changes the way glucose fits in a glucose transport protein (GLUT). Glucose with a phosphate attached is too large and polar to escape by passive diffusion through a bi-lipid membrane layer.

2 If the enzyme "glycogen synthase" is available, and the cell has enough energy that it does not necessarily need the glucose to make ATP, then this newly phosphorylated glucose may be attached to a chain of glucose molecules called

glycogen. This is a very important pathway in animals because later, when blood sugar begins to drop, glucose will be cleaved from glycogen and the phosphate may be removed for the glucose to be put back into the blood to bolster blood sugar levels. These processes called **glycogenesis** (glycogen synthesis) and **glycogenolysis** (glycogen break down) occur in muscle cells and in liver cells.

3 A phosphorylated glucose that does not become part of the stored glycogen will undergo a conformational change and become fructose. The fructose molecule has another phosphate attached to it from ATP. At this point, two ATP molecules have been invested. This double phosphorylated 6 carbon fructose is now primed to be divided into two 3-carbon sugars – each with one phosphate attached. The remaining glycolytic reactions will now happen twice because there are two 3-carbon molecules called Glyceraldehyde-3-phosphate.

4 The energy available in the glucose molecule is found in the form of "chemical energy". This energy exists in the C-H bonds – or more specifically within the electrons that constitute the carbon – hydrogen bonds. The dehydrogenase enzyme in step 4 will remove two hydrogens (2 protons and 2 electrons, or a proton and a hydride) from Glyceraldehyde-3-phosphate. Oxidized **Nicotinamide Adenine Dinucleotide (NAD^+)** accepts and bonds with one of the protons and both of the electrons. The other proton does not bond with the NAD^+ but will be found nearby. This may be written as: $H^- + H^+ + NAD^+ \rightarrow NADH + H^+$.

Because NAD^+ acquires 2 new electrons, we say that NAD^+ is reduced. The 3 carbon molecule that the protons and electrons were removed from is oxidized. This is an example of a redox reaction. For simplification, the reduced form of NAD^+ will be referred to as NADH (instead of $NADH + H^+$).

Think of NAD^+ as an electron carrier. It is like an empty taxi cab. It comes in and parks near the "dehydrogenase" enzyme and as the reaction occurs, NAD^+ acquires 2 high energy electrons and a proton as passengers. This "taxi" becomes occupied and will be referred to as NADH. Later, we will see that these new "passengers" will need to be dropped off for other metabolic reactions to proceed. When NADH unloads its "passengers" NAD^+ is reconstituted and becomes available to go back and participate in reactions again. Without NAD^+ involvement, the dehydrogenase enzyme would not be able to complete the reaction and glycolysis would stop at that point. Notice that if glycolysis stopped, ATP would not be generated in glycolysis because the ATP generation steps are yet to come. It is important to have enough NAD^+ around to keep the reactions going.

Another important effect of the dehydrogenase reaction in step 4 is that an inorganic phosphate (Pi) ends up being bonded to the 3-carbon molecule from step 3 resulting in two 3 carbon molecules called 1,3 bisphosphoglycerate.

5 In step 5 there are several biochemical reactions that ultimately accomplish one very important outcome – **Substrate-Level Phosphorylation**. In glycolysis, Substrate-Level Phosphorylation is the transfer of a phosphate group from a 3-carbon organic molecule to ADP. This reconstitutes ATP which can be used in other important energy consuming processes of the cell. Substrate-Level Phosphorylation is different from Oxidative Phosphorylation which will be discussed in Step 12.

Notice that because there are two 3-carbon molecules to donate phosphate groups, 4 ATP molecules will be generated. For every glucose molecule in glycolysis, 4 ATP are made. However, 2 ATP are required at the beginning steps of glycolysis, so the net production of ATP in glycolysis is 2 New ATP for every glucose molecule.

6 The two 3-carbon molecules left after Substrate-Level Phosphorylation are called pyruvate. **Pyruvate** is the end product of glycolysis. The fate of pyruvate will depend on whether there is enough oxygen available to the cell or not.

If a hypoxic (meaning that oxygen is deficient) condition exists, then a dehydrogenase enzyme will perform a reaction that is actually the reverse of what we saw in step 4. A hydrogen ion and 2 electrons will be removed from NADH and put onto pyruvate. This causes pyruvate to become **lactate**.

You might be asking why this conversion of pyruvate to lactate is even necessary. Remember that the reactions of step 4 are not possible without NAD^+. If we continually made NADH and had no way to reconstitute or recycle back NAD^+,

then we would soon have to stop glycolysis and wait until more NAD^+ became available. Since none of the ATP producing steps of glycolysis can happen until NAD^+ arrives, we would not be making ATP which could kill the cell. Making lactate is a quick way to free up NAD^+ to go back to step 4 and allow the Substrate-Level Phosphorylation reactions to take place. This is called **Anaerobic Metabolism**. Anaerobic metabolism is very fast, but not very efficient (not a lot of ATP per glucose molecule). In organisms that lack mitochondria, electrons from NADH are donated instead to acetaldehyde to create alcohol and regenerate NAD^+. For example, in yeast cells, this process is essential in producing wine/beer and bread.

7 If Oxygen is available then pyruvate is transported to the mitochondria. Pyruvate moves across the two mitochondrial membranes and a whole new sequence of metabolic steps proceed in the mitochondrial matrix. The culmination of all the metabolic reactions in the cytoplasm and the matrix of the mitochondria are called **Aerobic Metabolism**. It is called aerobic because oxygen is used in step 11. Aerobic Metabolism results in much more ATP than were produced by glycolysis alone.

8.3

Citric Acid Cycle

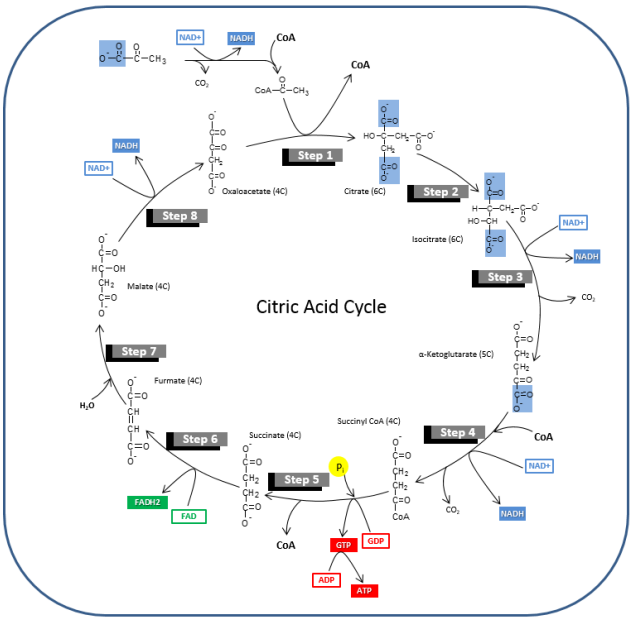
The Citric Acid Cycle is also called the "Tricarboxylic Acid Cycle (TCA) and the "Krebs Cycle." This cycle is a series of biochemical reactions that completes the catabolic pathway for the Glucose molecule that started glycolysis. Energy from the Citric Acid Cycle is captured by electron carriers (NAD and FAD). Also, ATP is generated at one of the steps in this cycle.

After the completion of this phase of metabolism, the following molecules and ATP are made as a byproduct:

Molecule	**Net Yield through Glycolysis**
ATP	2
NADH	6
Pyruvate	2

Below is a more detailed figure showing the citric acid cycle. Keep in mind that this is per glucose molecule. Two pyruvate are produced per glucose so the Krebs cycle will run twice per molecule of glucose.

FIGURE 9 - 8 STEPS OF THE CITRIC ACID CYCLE

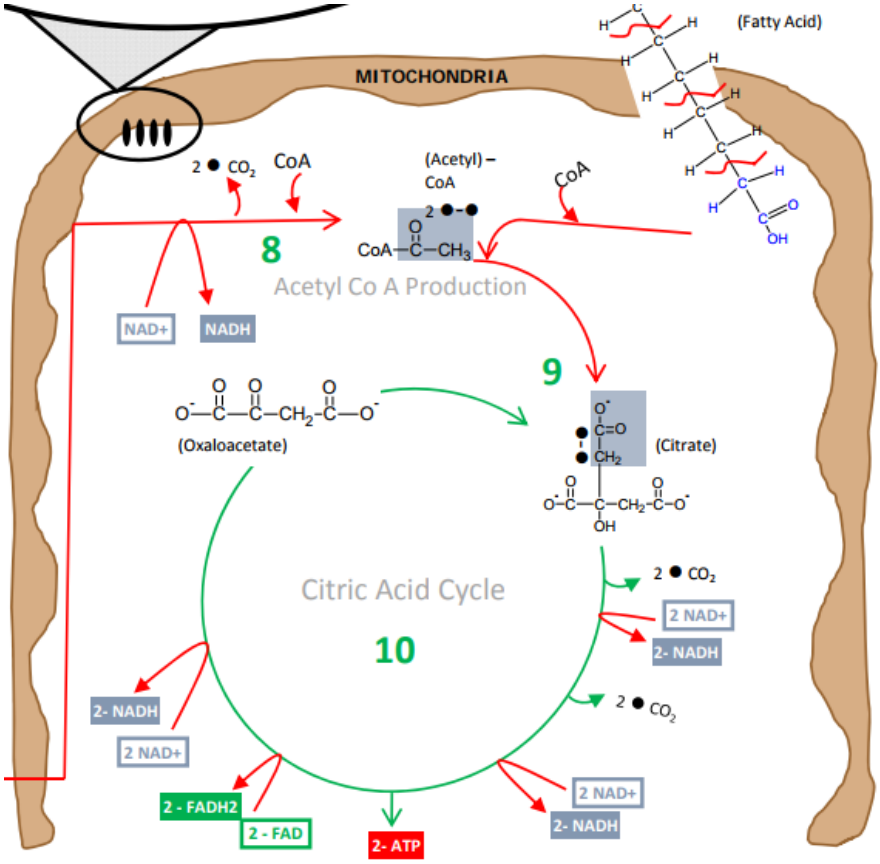


The figure above represents the Citric Acid Cycle (also called the "Krebs Cycle"). The part of the molecule that becomes carbon dioxide is highlighted in a blue box. Notice that a 4 carbon molecule called Oxaloacetate picks up 2 more carbons when it is joined with an acetyl group from Acetyl CoA. Through the beginning steps of the cycle, 2 carbons are lost as carbon dioxide and the molecule is again restored to a 4 carbon state, ready to pick up another acetyl group.

The details of the eight steps above are shown in the following pages. This time, the part of the molecule that undergoes a change is highlighted in blue and the name of the enzyme that catalyzes the reaction is in a green box.

Metabolism Summary Part 2: Citric Acid Cycle

Below is an image of the process of the Citric Acid (Krebs) Cycle magnified from the Metabolism Summary. A continuation of our summary on metabolism follows below for the Citric Acid Cycle up until we reach the Electron Transport Chain where we will return to get the detailed information on this process first before continuing with our summary on all of the processes of metabolism. The green numbers in the image correlate with each of the steps listed below:



Citric Acid (Krebs) Cycle, from the "Big Picture" of Metabolism: Glycolysis, Citric Acid (Krebs) Cycle, Electron Transport Chain, Beta Oxidation and Lipolysis. *Image created at BYU-Idaho by JS 2010*

8 Steps 8-12 complete the story of aerobic metabolism of glucose. After pyruvate is transported into the mitochondria, another dehydrogenase enzyme (actually a very large enzyme complex) will accomplish several things. It will remove 2 protons and 2 electrons from pyruvate. This creates NADH (actually 2 NADHs because there are 2 pyruvates). Also, the reaction results in the loss of a carbon and two oxygen atoms (released as CO_2) from pyruvate. Finally, the remaining 2 carbon molecule is attached to Coenzyme A.

Coenzyme A (often referred to as simply CoA) is derived from pantothenic acid (Vitamin B5). **Acetyl CoA** is the name used for the product of the reaction in step 8. The "Acetyl" prefix specifically refers to the 2-carbon group that is being transported by the CoA. Black dots in the summary figure help us keep track of the carbons that originated from the glucose molecule way back at the beginning of glycolysis. Notice that ultimately all the black dots are released as CO_2 so that the metabolism of glucose leaves us with no accumulation of carbons in the cell. Acetyl CoA will enter and participate in the reactions of the Citric Acid Cycle.

9 Step 9 represents the activities of the **Citric Acid (or Krebs) Cycle**. The Citric Acid Cycle involves a lot of steps.

10 The important things to remember about the Citric Acid Cycle are…

1. A 4-carbon molecule called oxaloacetate combines with the acetyl (2 carbon) group of Acetyl CoA (which came from glucose or fatty acids or possibly even some of the amino acids). This will yield a 6-carbon molecule called citric acid. Citric acid will be changed and manipulated as this 6-carbon molecule ends up recycled back to oxaloacetate – thus the term “Citric Acid Cycle”.
2. During the reactions of the citric acid cycle, CO_2 will be lost twice. This means that if you are counting, you will realize that every carbon of the original Glucose or Fat is ultimately lost as CO_2. This is the reason complex organisms need to breathe continuously.
3. Hydrogens with electrons are transferred to NAD^+. This creates 6 NADH molecules.
4. FAD is reduced to $FADH_2$. This yields 2 $FADH_2$ molecules.
5. Substrate-Level Phosphorylation will yield an ATP for each turn of the Citric Acid Cycle (or 2 total for each glucose).

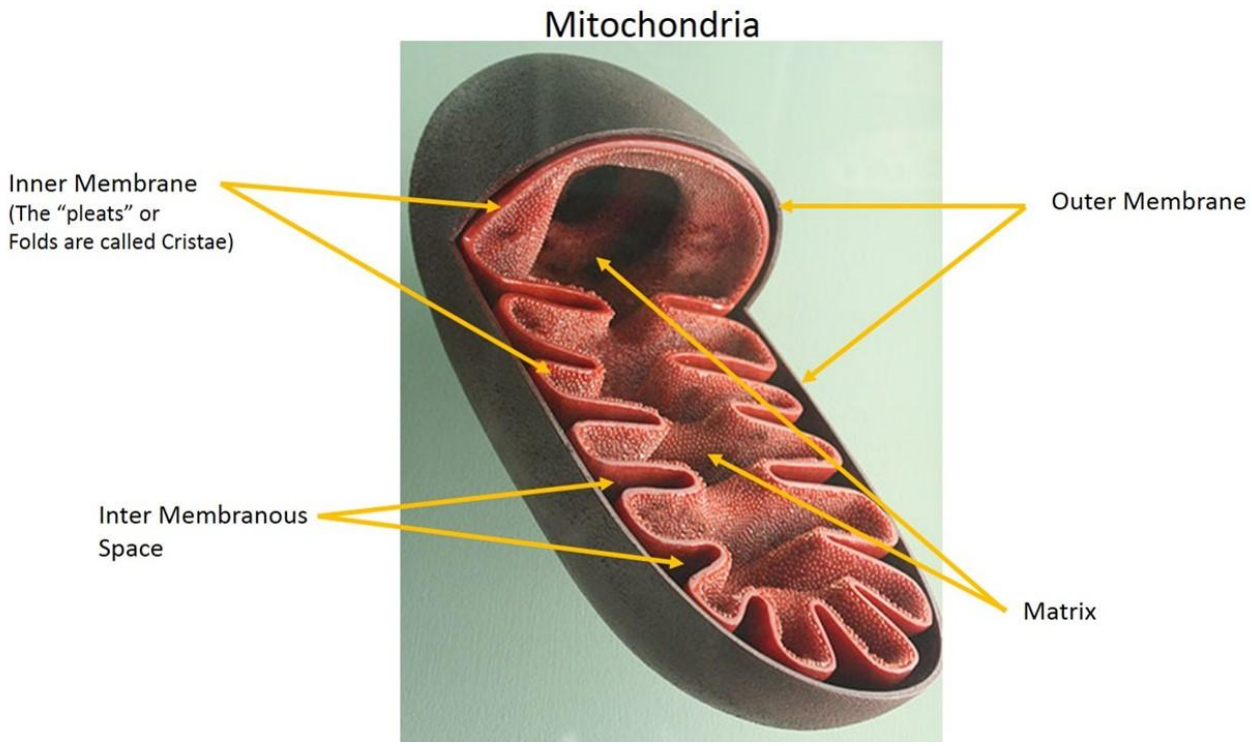
UNIT 9

ELECTRON TRANSPORT CHAIN

9.1

Electron Transport Chain (Oxidative Phosphorylation)

The Electron Transport Chain is responsible for the synthesis of most of the ATP in the cell. In order to understand how the electron transport chain works, it is critical that you have a good understanding of what the mitochondria are and how it is organized.



Mitochondria, a double membrane organelle inside the cell. *Image derived from File: Überseemuseum Bremen 2009 237.JPG; Author: Sterilgutassistentin.*
Site: https://books.byui.edu/-cgKk*;*
License: GNU General Public License as published by the Free Software Foundation

The Mitochondria have an inner and an outer membrane. The inner membrane folds in and out on itself and these folds are called Cristae. Cristae increase the total surface area of the inner membrane. The center of the mitochondrion is called the matrix and is analogous to the cytoplasm of a cell. The Electron Transport Chain reactions take place on the inner membrane.

The term, electron transport refers to the proteins on the inner membrane of the mitochondria that will take hydrogen

atoms and electrons from NADH and $FADH_2$ and then ultimately use the energy in the electrons to make ATP. Recall that NAD^+ and FAD picked up high energy electrons and hydrogens from C-H bonds in glycolysis (from the cytoplasm) and the citric acid cycle (in the matrix of the mitochondria).

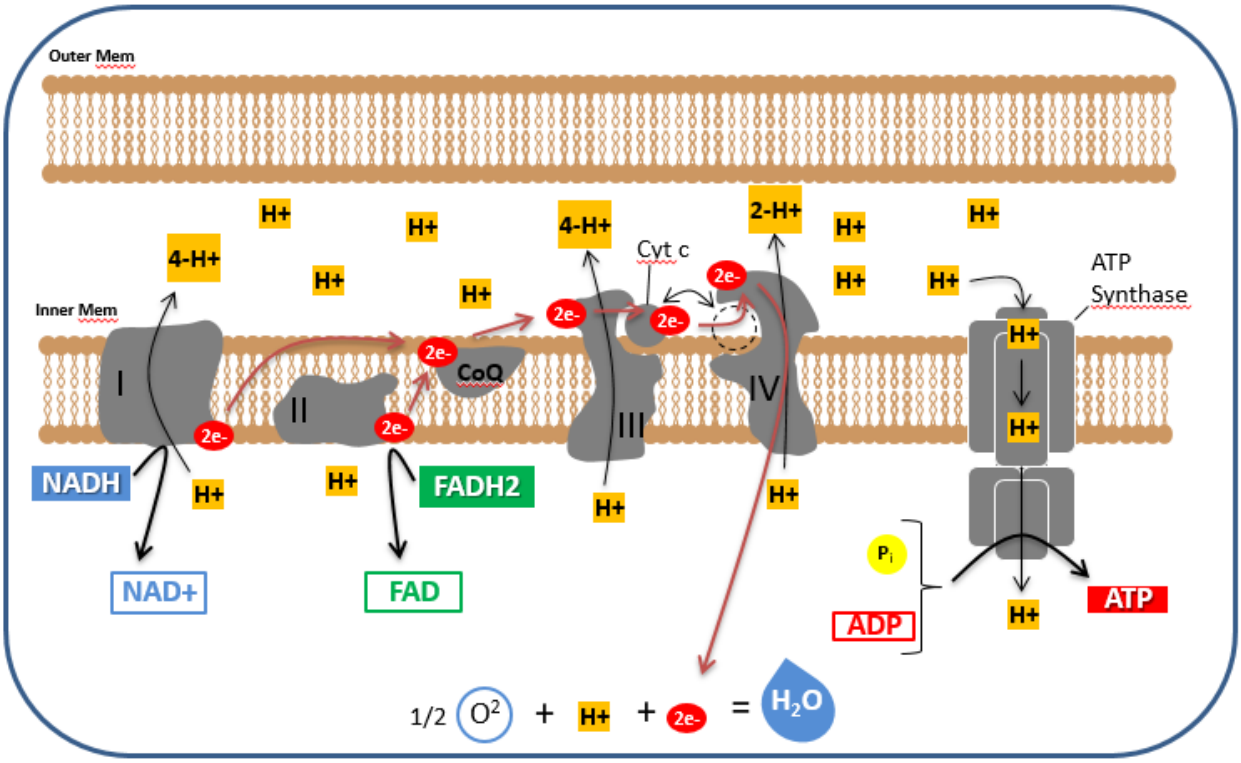
In the inner membrane of the mitochondrion is a series of protein complexes that will receive the electrons and pass them from one complex to another. NADH passes 2 high energy electrons onto a protein complex (**Complex I**) in the inner membrane of the mitochondria. This complex is called *NADH dehydrogenase*. *NADH dehydrogenase* does two things. First, it accepts a pair of high energy electrons from NADH. Second, it uses some of the energy from these electrons to undergo a conformational change. This conformational change is associated with the movement of $4H^+$ ions from the mitochondrial matrix to the intermembranous space (the space between the inner and outer membranes of the mitochondria). Next, these two new electrons on Complex I are moved to Coenzyme Q (**CoQ**). Coenzyme Q is also called *ubiquinone*. CoQ will pass these electrons straight to complex III. **Note: the flow of electrons is either 1,3,4 for NADH or 2,3,4 for $FADH_2$ and complex II doesn't pump protons. For these reasons, we get more energy from NADH than $FADH_2$.*

$FADH_2$ also passes a pair of high energy electrons to a protein complex (**Complex II**), also called *Succinate dehydrogenase*. Complex II accepts the electrons but does not go through any conformational change that is associated with the movement of H^+ ions. However, Complex II does pass the electrons to **CoQ** just like Complex I did. **CoQ** is a mobile shuttle that moves easily through the membrane and is able to relocate and react with **Complex III**. Complex III has a long name (*Coenzyme Q-Cytochrome c Oxidoreductase*). Complex III also goes by the name *Cytochrome bc_1 Complex.* Complex III will undergo a conformational change that is associated with the movement of $4H^+$ ions from the mitochondrial matrix to the intermembranous space. The two electrons are then moved from Complex III to Cytochrome C (**Cyt c**). **Cyt c** another mobile shuttle that is a soluble protein in the intermembranous space that moves easily along the membrane and reacts with **Complex IV**. Complex IV, also called *Cytochrome c Oxidase*, uses some of the electron energy to undergo a conformational change that is associated with the movement of 2 H^+ ions from the mitochondrial matrix to the intermembranous space. Oxygen receives the 2 electrons from Complex IV and reacts with H^+ available in the surrounding fluid to make H_2O or water.

A review of figure 11 below reveals that one NADH results in the movement of 10 H^+ ions from the mitochondrial matrix to the intermembranous space. One $FADH_2$ results in the active transport of 6 H^+ ions. The important message in all of this is that electron energy is used to transport H^+ ions to the intermembranous space and this sets up an electrochemical gradient that favors the movement of H^+ ions back into the matrix. This is allowed to happen through another protein complex called **ATP synthase**. The diffusion of H^+ ions through ATP synthase is called "**chemiosmosis.**"

ATP synthase is made up of two main components referred to FO and F1 regions. Protons flow through the FO regions (carousel) and cause rotation of the F1 region (stalk). The F1 region is made of α, β, γ, and δ subunits. The rotation of F1 causes the subunits to come in contact and change between three conformations. In conformation one, ADP and Pi can bind with high affinity. In conformation two, ADP and Pi increase binding that they are essentially "smashed" together to that ATP can be formed. In conformation three ATP is released. This process is called **Oxidative Phosphorylation**.

For each pair of electrons that move from Complex I to Complex IV, about 2.5 ATP can be produced. For each pair of electrons that move from Complex II to Complex IV, about 1.5 ATP can be produced. Therefore, if we round up, it is often stated that each NADH yields 3 ATP while each $FADH_2$ will yield 2 ATP.



Electron Transport Chain. *Image created by JS at BYU Idaho F2013.*

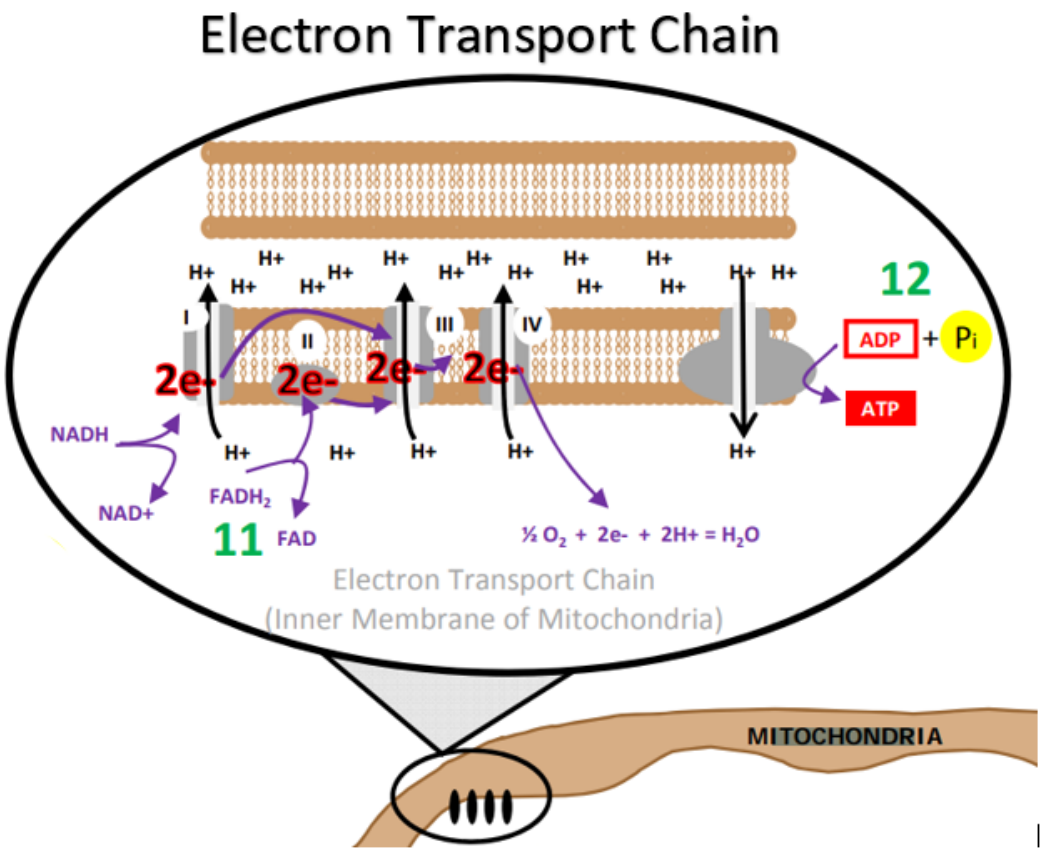
The image above illustrates the Electron Transport Chain. The protein complexes on the inner mitochondrial membrane use high energy electrons from NADH and FAD_2 to move H^+ ions to the intermembranous space. The H^+ concentration gradient is then used to make ATP through the enzyme complex called ATP Synthase. Oxygen is the final electron acceptor and becomes water.

A quick recap of what has happened so far might go like this: Electrons and hydrogen ions were harvested from the C-H bonds of glucose. These high energy electrons with hydrogen are carried from the reactions of glycolysis and the citric acid cycle to the electron transport chain on the inner membrane of the mitochondria. The electron transport chain takes these high energy electrons and gradually "uses" the energy to pump hydrogen ions into the intermembranous space. As the energy in the electrons is used, the electrons don't have enough energy to form a C-H bond anymore, but they can form an O-H bond. Thus, oxygen comes along and accepts the electrons and hydrogen to form water. The cycle is complete, and water can once again be used by a plant somewhere to participate in the photosynthetic reactions that will excite O-H bond electrons again. The hydrogen ions that have been pumped into the intermembranous space are allowed to flow down their electrochemical gradient through ATP synthase. ATP is generated as a result and ATP is used to run the many molecular processes in cells.

Glucose is not the only molecule with C-H bond energy to use in metabolic reactions. Lipids and Proteins are also metabolized by cells.

Metabolism Summary Part 3: Electron Transport Chain

We will continue with our summary of the metabolic process using the Electron Transport Chain process magnified from the “Metabolism Summary” image. (Green numbers from summary correlate with green numbers on the image below.)



Electron Transport Chain, from the "Big Picture" of Metabolism:
Glycolysis, Citric Acid (Krebs) Cycle, Electron Transport Chain, Beta Oxidation and Lipolysis.
Image created at BYU-Idaho by JS 2010

11 NADH is carrying a proton and 2 high energy electrons that need to be "dropped off". $FADH_2$ is also carrying high energy electrons and a couple of protons. These electron "carriers" are able to donate these electrons to an enzyme complex found in the inner mitochondrial membrane. Think of the "**electron transport chain**" as a bucket brigade. A series of proteins pass 2 electrons from one to another. Sometimes when the electrons are passed, a little bit of the energy from the electrons is used to induce a conformational change in some of the protein structures. This conformational change results in the transport of protons from the inside of the mitochondria to the intermembranous space (the space between the inner and outer mitochondrial membranes). Also, some of the energy released as the electrons move through the electron transport chain is given off as heat. NADH donates to the electrons to the electron transport chain at complex I and $FADH_2$ donates electrons at complex II. There are more protons pumped from electrons moving down the transport chain from complex I than from complex II. For this reason, NADH yields more ATP ultimately than $FADH_2$. Whether from NADH or $FADH_2$, any donated electrons will move down the transport chain to the last electron acceptor and cannot go back to previous components of the chain.

Oxygen accepts the electrons from the last protein complex (complex IV) of the chain. As oxygen accepts the electrons, the oxygen becomes reactive and capable of forming a covalent bond with two protons and water is formed (H_2O). Oxygen is the final electron acceptor.

Notice that NADH becomes NAD^+ at the beginning of the electron transport chain. Also, $FADH_2$ becomes FAD. This recycles these electron carriers such that they can be used again in earlier metabolic reactions. This has been mentioned, but it is worth mentioning again. Without NAD^+, reactions that use NAD^+ cannot occur.

12 In step 11, we learned that as high energy electrons passed down the chain of protein acceptors, energy was used to move H^+ ions into the intermembranous space. This generates a proton gradient. This means that there will be a

higher concentration of protons in the intermembranous space than there is inside the mitochondrial matrix. This proton gradient represents “potential energy” because the protons will try to flow down their gradient if a passageway opens and allows such movement.

Step 12 represents the idea sometimes referred to as **chemiosmosis**. This is a term that refers to the fact that protons tend to flow down their gradient through a selective protein channel. This protein channel, called ATP-Synthase is a very intricate and specialized molecular machine. This protein literally turns as the protons come through it and this kinetic energy is used to bring ADP and inorganic phosphate together so that ATP is created. The synthesis of ATP through chemiosmosis is referred to as **Oxidative Phosphorylation**.

While glycolysis gives us 2 ATP per glucose molecule, the electron transport chain gives us approximately 34 ATP per glucose molecule. We say “approximately” because it is difficult to say exactly how many ATP we get. This is because some ATP is used to shuttle molecules in and out of the mitochondria and there is likely some “leaking” that occurs when protons from the intermembranous space accidentally escape by some other way than through the ATP synthase enzyme complex. However, it is generally accepted that aerobic metabolism yield between 18 and 19 times more ATP than anaerobic metabolism. From a thermodynamic perspective 686 kcal of energy are released and 432 kcal of that energy are captured in ATP. Showing an efficiency of 63% energy while the rest (37%) is lost as heat.

Molecule	**Conversion Rate to ATP**	**ATP Yield through Electron Transport**
2 NADH from Glycolysis 2 NADH from Pyruvate Oxidation 6 NADH from Citric Acid Cycle	3 ATP / NADH	6 ATP 6 ATP 18 ATP
2 FADH from Citric Acid Cycle	2 ATP /FADH	4 ATP
Net Total from Electron Transport		**34 ATP**
Net Total from Glycolysis + Citric Acid Cycle (Remember 2 ATP used to start glycolysis)		4 - 2 + 2 = 4 ATP
Total ATP from the complete aerobic metabolism of one glucose molecule		**~38 ATP (minus some loss)**

9.2

Lipid and Protein Metabolism

Lipid Metabolism

9.2.1

Lipid Metabolism

Lipid catabolism (or **lipolysis**) refers to the process of triglycerides being broken down into glycerol and 3 fatty acids. Glycerol enters the glycolytic pathways and can be used to make a pyruvate. Fatty acids enter the mitochondria and are used to generate Acetyl CoA that can be used in the citric acid cycle.

Beta oxidation is the term used to describe a series of reactions that break down a fatty acid into 2 carbon acetyl groups which are associated with Coenzyme A (see figure 12). The 2-carbons on the carboxyl end of the fatty acid are cleaved, then combined with CoA to from an acetyl CoA. Each time an acetyl CoA is generated from a fatty acid, the fatty acid re-enters the Beta oxidation biochemical pathways to remove the next 2 carbon fragment. This occurs until the entire fatty acid chain has been broken down in this way. Each time a beta oxidation cycle occurs, NADH and $FADH_2$ are generated. Also, each time an acetyl CoA from beta oxidation goes through the Citric Acid Cycle, 3 NADH, 1 $FADH_2$ and 1 ATP are generated. Since a fatty acid is many carbons long (most often found in lengths of 16 or 18 carbons), many acetyl CoA molecules can be acquired from a triglyceride molecule. Enough ATP is made from all the NADH and $FADH_2$ that it becomes clear that fat molecules give us more ATP per gram than glucose molecules.

Lipogenesis is the term used to describe the process of making new fat. Fatty acid chains can be synthesized by combining Acetyl groups which adds carbons to a growing fatty acid chain. It is almost like Beta oxidation in reverse, but the reactions use different enzymes and occur in a different place. While beta oxidation occurs in the matrix of the mitochondria, lipogenesis occurs in the cytoplasm of cells (mostly in the liver and adipocytes). Cells that synthesize fat have an enzyme complex made up of about 7 protein enzymes called **Fatty Acid Synthase**. When cells have excess glucose, there arises an excess of Acetyl CoA molecules. This upregulates lipogenesis and explains how diets high in sugar can cause increased adipose tissue.

Clinical Pearl: Ketoacidosis *is a complication that occurs when cells only metabolize fat. In animals, this may occur in times of excessive dieting, fasting, or malnutrition. In humans, the most common cause of ketoacidosis is Type I Diabetes. In type I diabetes, there is no endogenous insulin, and sugar cannot get into the fat and muscle cells which make up the largest percentage of body tissue by volume and weight. This means that these cells will catabolize predominately fat for ATP production (fat does not require insulin to get into cells). As increasing amounts of fat molecules are broken down through beta oxidation, accumulation of acetate and acetyl CoA may occur as the Citric Acid Cycle reaches a limit on how many acetyl CoA molecules it can take in at the first biochemical step. These two carbon products begin to spontaneously react with each other and produce 4 carbon molecules referred to as ketone bodies. The three most common ketone bodies are* ***acetone****,* ***acetoacetate,*** *and* ***beta-hydroxybutyrate****. These molecules are acidic and in high quantities can lower the pH of the blood. Also, acetone is volatile and can escape through the lungs and give a particular smell to a person's exhaled breath. The smell has been described as being similar to fingernail polish remover (which contains acetone).*

Fatty acids must be "activated" before they are transported into the mitochondria. Activation involves the attachment of Coenzyme (CoA). The result is a fatty acid derivative called Fatty acyl-CoA. Fatty acyl-CoA goes through a series of steps illustrated below. This process is called beta oxidation, which suggests that the molecule will be oxidized at the beta carbon and then cleaved to yield Acetyl CoA (last step below). The Acetyl group is highlighted in blue in the figure below. The alpha (α) and beta (ß) carbons are labeled on the fatty acid. Notice that after Acetyl CoA is produced, the α

and ß carbons for the next cycle are illustrated in gray. Palmitoleic acid has 16 carbons, is one of the most common fatty acids in animals and is the fatty acid used in this illustration. However, fatty acids can be any length with the most common ones between 14 and 18 carbons long. Complete beta oxidation of palmitoleic acids yields 8 Acetyl CoA molecules that can metabolize further in the citric acid cycle. The enzymes that catalyze each step are depicted in green boxes.

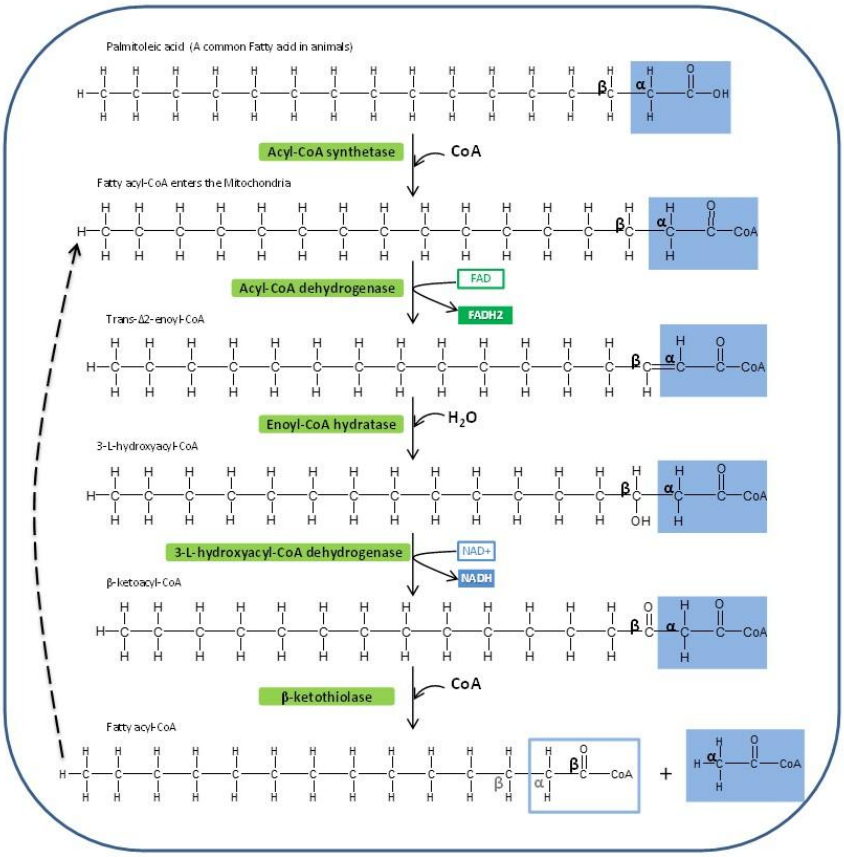
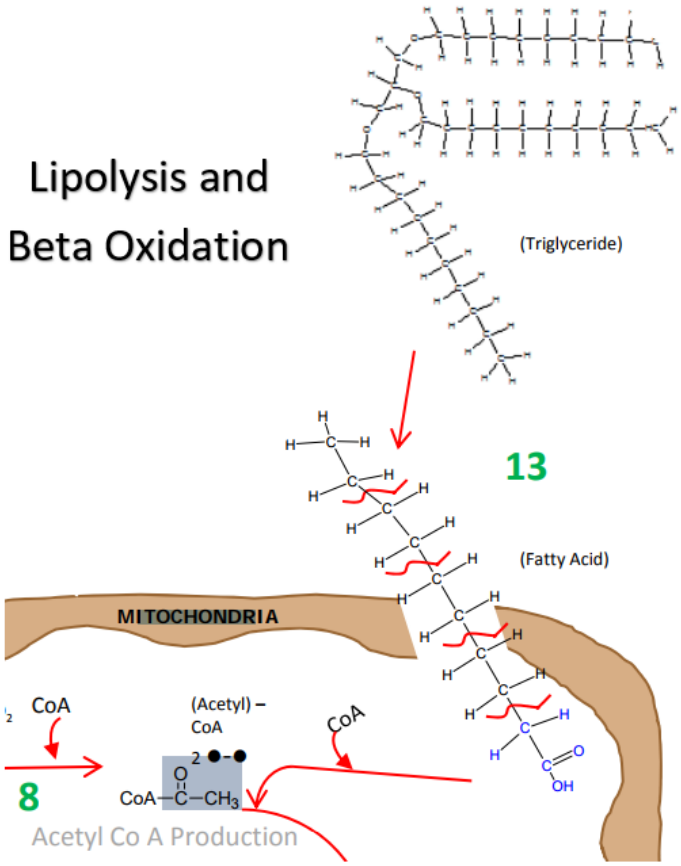


Image created by JS at BYU-Idaho Fall 2013.

Metabolism Summary Part 4: Beta Oxidation and Lipolysis:

Below is the final installment of the Metabolism Summary:



Lipolysis and Beta Oxidation, from the "Big Picture" of Metabolism:
Glycolysis, Citric Acid (Krebs) Cycle, Electron Transport Chain, Beta Oxidation and Lipolysis.
Image created at BYU-Idaho by JS 2010

13 Fat can also be used to make ATP. The metabolism of fat is called Beta Oxidation. Triglycerides are dismantled into glycerol and fatty acids. The glycerol can be converted into Glyceraldehyde-3-phosphate and then it completes the glycolytic reactions. The fatty acids are transported into the Mitochondria. Once in the Mitochondrial matrix, fatty acids are dismantled 2 carbons at a time and each 2-carbon piece is converted to Acetyl CoA. Acetyl CoA enters the Citric Acid Cycle. A single triglyceride molecule can ultimately yield a lot more Acetyl CoA than a glucose molecule. So, we say that fat is much more energy dense than sugar because we get more ATP per gram of fat than we do with sugar. However, notice that the end product of Beta oxidation is Acetyl CoA (not pyruvate). So, anaerobic metabolism is not possible with fat metabolism. Fat can only be burned if there is enough oxygen available to the cell.

9.3

Protein Metabolism

So far, this reading has focused on the metabolism of sugars and fats. Indeed, sugars and fats make up most organic molecules processed as fuel in cells. However, proteins can be metabolized to make ATP as well. Proteins are responsible for most of the structure and function in tissues, so animals wouldn't want to metabolize them too extensively. In fact, animals employ several regulatory mechanisms to spare proteins from metabolism. When proteins undergo catabolism, they are broken down into individual amino acids. Amino acids differ with respect to the "R group. The "R" group will determine where in the metabolic cycles that the amino acid products will enter. Notice in figure 13 that there are several metabolic entry points for amino acids in the biochemical pathways we have discussed.

Gluconeogenesis

The conversion of pyruvate to acetyl CoA is an irreversible reaction. This means that when fatty acids are metabolized to form acetyl CoA, it is not possible to turn the acetyl CoA back to pyruvate or any earlier glycolytic product. Also, acetyl CoA is 2 carbons long and 2 carbons are lost in the early reactions of the Citric Acid Cycle. For both reasons, it is not possible to use fatty acids to make glucose. To make glucose from scratch (Gluconeogenesis), cells must use a substrate that is not acetyl CoA and will not go through CO_2 expelling steps. In the figure below, we see that some amino acids can enter the metabolic pathways in places that meet these requirements. Therefore, amino acids are the best choice for a raw material to make glucose. When amino acids enter the metabolic pathways for the purpose of making glucose, the reactions of glycolysis more or less run-in reverse to synthesize a new glucose molecule. The liver is particularly good at doing this. Gluconeogenesis is stimulated by hormones that are released when blood sugars become low.

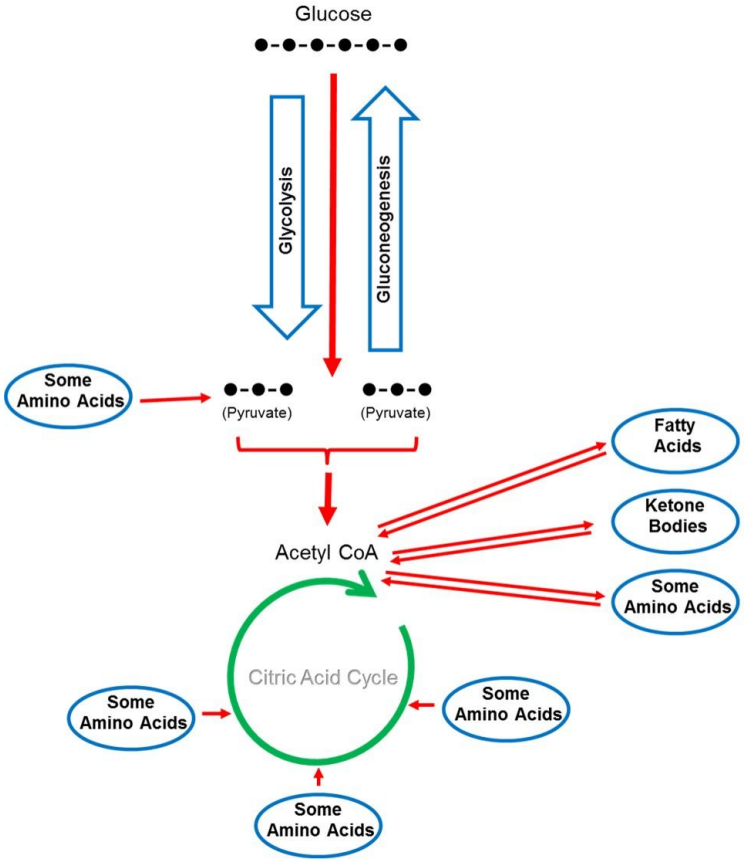


Image created by JS at BYU-Idaho Fall 2013.

This illustration shows the metabolic entry point of carbohydrates, fatty acids, and amino acids (from proteins). Notice that many of the reactions are reversible.

UNIT 10

PHOTOSYSNTHESIS

10.1

Photosynthesis

Now that we have managed to learn about harvesting energy from electrons, let's spend some time learning in more detail how the energy was trapped in the electrons in the first place. The process of capturing energy from the sun to energize electrons and then store them in covalent bonds is called **photosynthesis**. Interesting, unless broken down and released, that energy can be stored indefinitely. For example, consider fossil fuel energy (coal, natural gas) that is being harvested from products 100s of millions of years old. There are not a lot of organisms capable of capturing sun energy to harness it. Organisms that fit into this category are called **autotrophs** and consist of plants, algae, and a few bacteria (and maybe Celestial beings!). Autotrophs, in particular photoautotrophs, can literally produce food from the sun! The rest of the world's organisms fit into the category called **heterotrophs** because they rely on captured energy from the autotrophs to survive.

Photoautotrophs use specialized structures during photosynthesis, some that capture CO_2 and H_2O and then release O_2 called **stomata**, and some that capture light energy called **chlorophyll**. The stomata are small openings, typically on the underside of leaves (minimizes water loss), that are surrounded by cells that respond to osmotic changes. These cells will shrink or swell, depending on osmotic conditions, which in turn regulates the pore size of the stomata. Chlorophyll is a pigment molecule located in structures called thylakoid membranes of the chloroplast (an organelle found within the plant cell). Like mitochondria, chloroplasts have a double membrane (outer and inner leaflets) and sandwiched between the two layers are the thylakoid structures (stacked discs) with the embedded chlorophyll pigment. The chlorophyll pigment has the ability to absorb light energy and convert that energy into chemical energy.

What then, is light energy?

10.1.1

Light Energy

Light energy is part of electromagnetic radiation where visible light is a very small portion of that spectrum. The nature of electromagnetic radiation is often described as a wave. For example, the color of light that animals perceive is based on the wavelength of the light waves. Light waves contain discrete packets of light energy called photons. The shorter the wavelength, the greater the energy. Hence, gamma waves have very short wavelengths and contain large amounts of energy while radio waves have very long wavelengths but relatively small amounts of energy. The portion of the spectrum of electromagnetic radiation that animals perceive is referred to as the visible spectrum and includes light with wavelengths between 380 (violet) and 700 nm (red).

When light strikes an object, one of three things will happen. If the object is transparent the light is transmitted, meaning it will pass through the object. However, if the object is not transparent the light will either be absorbed, or it will be reflected. The color that is perceived by the human eye is due to the light that is being reflected off it. Objects that appear black absorb all the light that is striking them while objects that appear white reflect all of the light that is striking them.

10.1.2

Photosynthetic pigments

Organic pigments like chlorophyll can only absorb light wavelengths in the visible spectrum. Wavelengths shorter than 380nm contain too much energy and would tear molecules apart, whereas wavelengths longer than 700nm would not contain enough energy to raise an electron to another orbital. Different pigments are required to absorb the different wavelengths of light. If a pigment is unable to absorb a given wavelength it will reflect it instead, giving the characteristic corresponding color (i.e., green). Photosynthetic pigments are found in two major classes: **chlorophylls** and **carotenoids**. In turn, each class contains subclasses. For example, chlorophylls exist in five subclasses: a, b, c, d and bacteriochlorophyll, but only a and b are found in plants. Carotenoids have many more subclasses as can be observed by the array of different colored fruits. Carotenoids absorb blue to green light wavelengths (reflect reds) while chlorophylls absorb blue to red wavelengths (reflect green).

10.1.3

Photosynthesis summarized

Before we introduce the complexity of photosynthesis, let's try a "big picture" summary approach. The ultimate goal of photosynthesis is to store converted light energy (sun) into stable chemical energy (chemical bonds). Light "sun" energy will be initially captured by light absorbing pigments (chlorophyll) in the form of excited electrons. Those excited electrons possess lots of absorbed energy which needs to be captured. The capturing will occur by sending the electrons through an "electron transport chain" where protein complexes will use that energy to split water, resulting in free H^+ and O atoms. The H^+ ions will then be pumped "uphill" into a small space (thylakoid space). This is very similar to what happened in the mitochondria during aerobic respiration, but now this electron transport chain is found in another organelle called the chloroplast.

Not all the energy will be used to pump H^+ ions, some of the energized electrons will be placed on H^+ ions and then stuck to a molecule of $NADP^+$ to form NADPH (NAPDH functions exactly the same as NADH). Thus, the hydrogen atoms that are split from water will have a dual role, some will be used to directly bind excited electrons and then bind to $NADP^+$ and others will be used to run the ATP synthase enzyme and make ATP. Thus, light energy (excited electrons) will successfully be converted to chemical energy in the covalent bonds of NADPH and as potential energy in phosphate bonds of ATP. This process will be called the light **dependent** reaction.

The problem is that both forms of the chemical energy bonds (ATP and NADPH) are very unstable so we must convert those bonds to more stable forms (carbohydrates). To make a carbohydrate we will need three things, carbon (CO_2), water, and the newly trapped energy (ATP and NADPH) which we will do in the light **independent** reactions. Seems simple right? Well, let's take a deeper dive below!

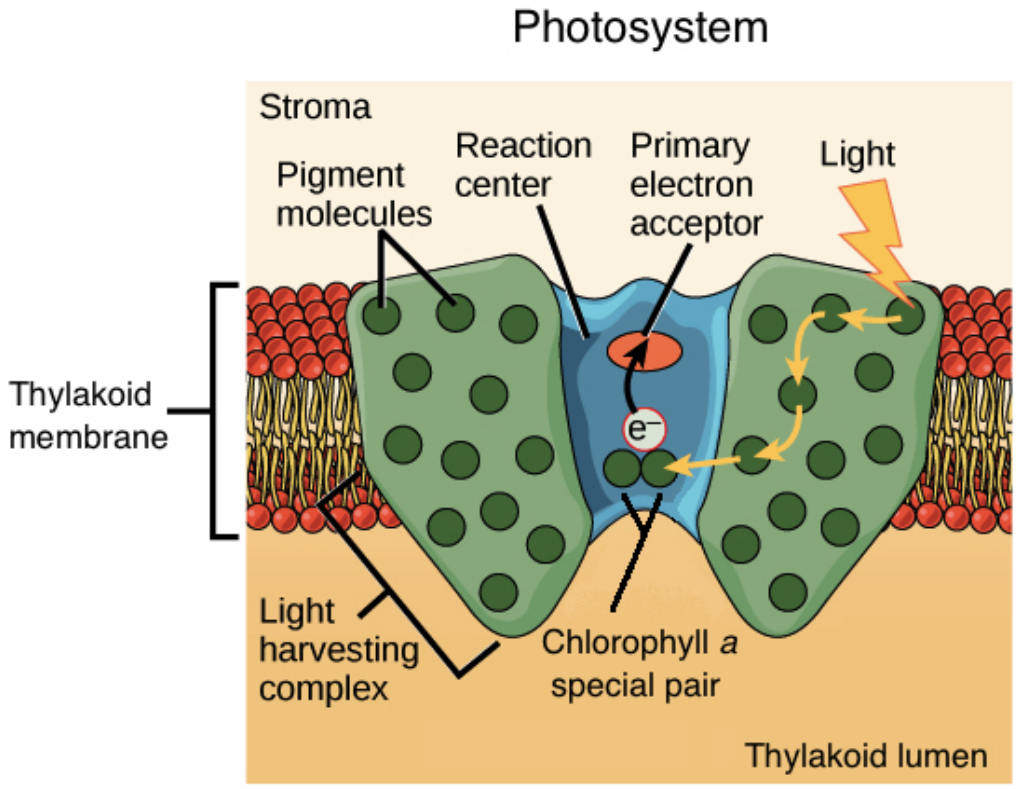
10.2

Light dependent reactions

As stated, the light dependent reactions are designed to convert light energy into chemical energy which they trap in NADPH or ATP molecules. This “trapping” occurs in unique complexes called photosystems (PS), designated as **PSI** and **PSII** , and consist of a pigment and a reaction center. Both complexes have the same structure of antenna proteins that surround the reaction center and bind chlorophyll pigments. The photosystems are classified by the maximal absorption wavelengths of visible light (**PSI = 700nm** ; **PSII = 680nm**). The two complexes differ in what they oxidize and what they reduce.

Absorbed light (photon) excites the chlorophyll molecules into a more excited state and that energy is then transferred from chlorophyll to chlorophyll until the energy level becomes suited for the reaction center. Within the reaction center are chlorophyll (a) molecules that are oxidized by the incoming energy as that light energy is converted to an excited electron. The reaction center of PSII (also called P680) will deliver its excited (high energy) electrons through an electron transport chain to PSI (also called P700). The transport of the electron through the transport chain proteins causes the electron to lose energy. This “lost” energy is recaptured and used to split water, which creates H^+ ions for translocation into the thylakoid space and to replace the loss of the electron from P680. The accumulation of the H^+ ions will be used to synthesize ATP through ATP synthase just like we saw in the mitochondria.

By the time the electron arrives at PSI it has lost the majority of its energy but can be re-excited by PSI through the absorption of another photon. That re-energized electron is sent to the reaction center, combined with a H^+ ion, and then attached to $NADP^+$ to form NADPH (reduction). The two complexes work to produce NADPH and ATP at very similar rates.



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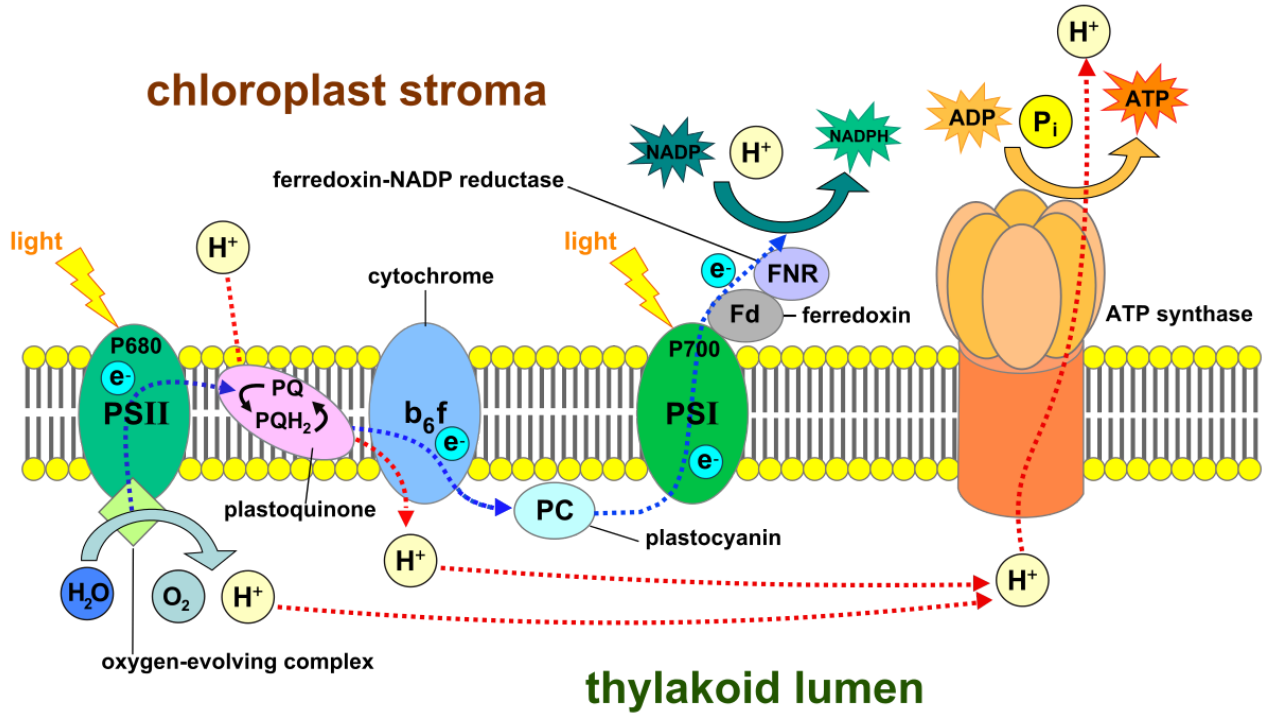

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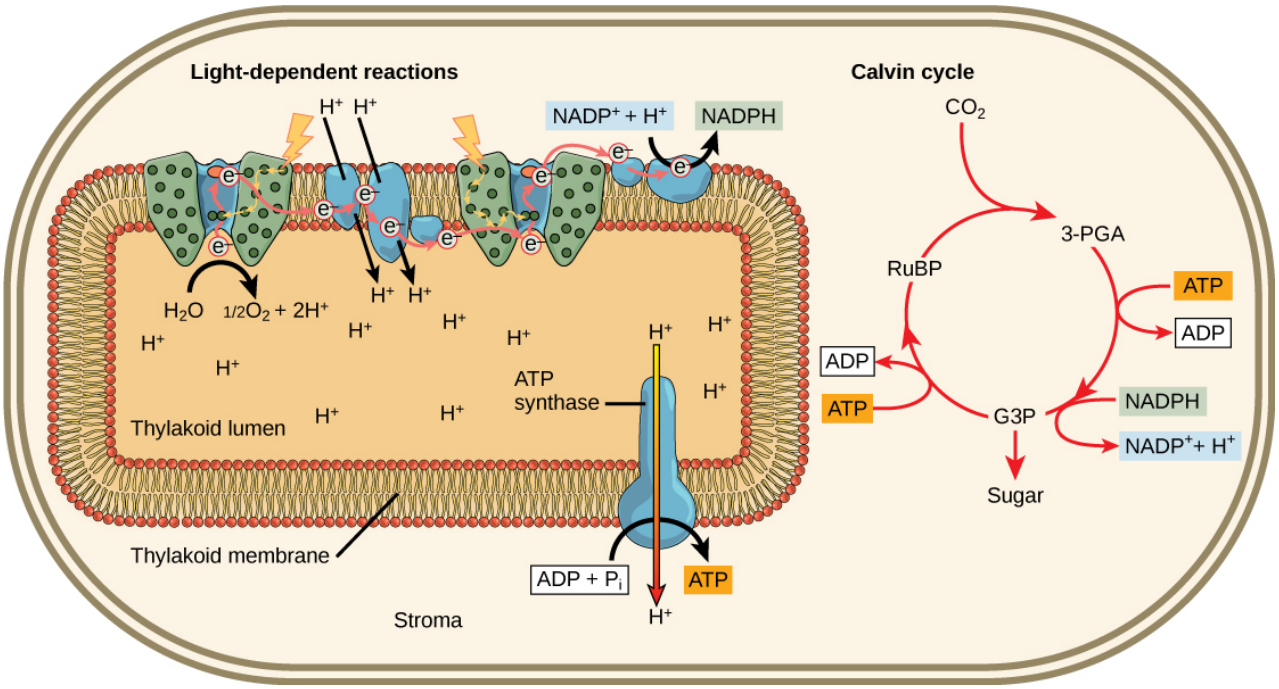


10.3

Light independent reaction or the Calvin Cycle

Once light energy has been converted to the chemical energy and stored in ATP or NADPH molecules, cells will need to move the stored energy into more stable forms of storage like carbohydrates. Interestingly, energy stored as ATP or NADPH will last only millionth of seconds, whereas energy in carbohydrate form will last millions of years! The transfer of chemical energy from temporary storage to long term storage occurs in the light independent reactions and is called the Calvin cycle. In brief, CO_2 will enter the Calvin cycle and leave as sugar (carbohydrate). The Calvin cycle becomes a story about carbons and recycling and can be thought of occurring in three stages.

Stage 1: Carbon Fixation

Stage 1 employs an enzyme called Ribulose-1,5-bisphosphate carboxylase-oxygenase (**RuBisCO**) which can take CO_2 and incorporate it into a five-carbon molecule called ribulose 1,5-bisphosphate (**RuBP**) to form a highly unstable six carbon molecule. The six-carbon intermediate is cleaved immediately to form two 3-carbon molecules of 3-phosphoglycric acid (3-PGA).

Stage 2: Reduction

In stage 2, each 3-PGA molecule receives a phosphate group from ATP and is reduced using electrons from NADPH to form one molecule of glyceraldehyde 3-phosphate (**G3P**) and the other 3-PGA molecule will be used to regenerate RuBP (stage 3). G3P will eventually react to form monosaccharides and then polysaccharides. Since only one molecule of carbon can be incorporated at a time (stage 1), and because glucose contains six carbons, the cycle will need to be run six times to get enough G3P to make one glucose molecule.

Stage 3: Regeneration

In stage 3, we need to regenerate RuBP, the five-carbon molecule that starts the whole process. Again, because we can only incorporate one carbon at a time from CO_2, it takes multiple turns of the Calvin cycle to get enough intermediates. The same is true for replacing RuBP. Let's try to track the carbons and see if we can follow the regeneration step. If we run through the Calvin cycle six times, we will have accumulated 36 carbons. More specifically, RuBP is a five-carbon molecule that becomes six when CO_2 is incorporated on it. Thus, with each turn, we use six carbons, but only one of the carbons is a "new" carbon that we can use for glucose. Running the Calvin cycle six times will generate six "new" carbons but 30 "old" carbons. Those 30 old carbons will be used to replace RuBP (30 carbons/5 = 6).

The generation of glucose from G3P is essentially glycolysis but in reverse. In glycolysis we split a 6-carbon molecule to make two three carbon molecules along with NADH and ATP. In photosynthesis we take two 3 carbon molecules along with NADPH and ATP and make a 6-carbon molecule. This back and forth of making and breaking glucose is the basis of life!

UNIT 11

CELLULAR TRANSPORT AND CELLULAR SIGNALING

11.1

Fluid Compartments

The cell is the functional unit of the body, but it cannot survive outside of an environment of water, nor without its most important structure, the biological membrane. This membrane effectively separates water in the body into two distinct fluid compartments, the **intracellular fluid** compartment (ICF) and the **extracellular fluid** compartment (ECF). Water movement is an essential characteristic of life, a phenomenon called **osmosis**. Movement of water between the ICF and ECF must occur through cell membranes that are essentially impermeable to water. Thus, the movement occurs through special protein water channels called **aquaporins** and is driven by **osmotic pressure gradients**. The pressure gradients are determined by the molecules or ions dissolved in the water. These molecules and ions (**solutes**) exist in a state of **chemical disequilibrium**, which means they are not equally distributed between the ICF and ECF (see figure below).

Osmosis
Diffusion of Solutes

11.1.1

Osmosis

By definition, osmosis is the diffusion of water through a **selectively permeable** membrane from an area of high-water potential (low solute concentration) to and area of low water potential (high solute concentration). Therefore, for osmosis to occur the membrane must be permeable to water but impermeable to the solute, and the concentration of the solute must be different on the two sides of the membrane. Water will move from the side with lower solute concentration to the side with higher solute concentration until the concentrations are equal or until some external force prevents further movement of water. This is a passive process, in that no energy expenditure is required for the movement of water. If the solute concentration in the extracellular fluid is lower than the solute concentration in the cell, water moves into the cell, and the cell will swell.

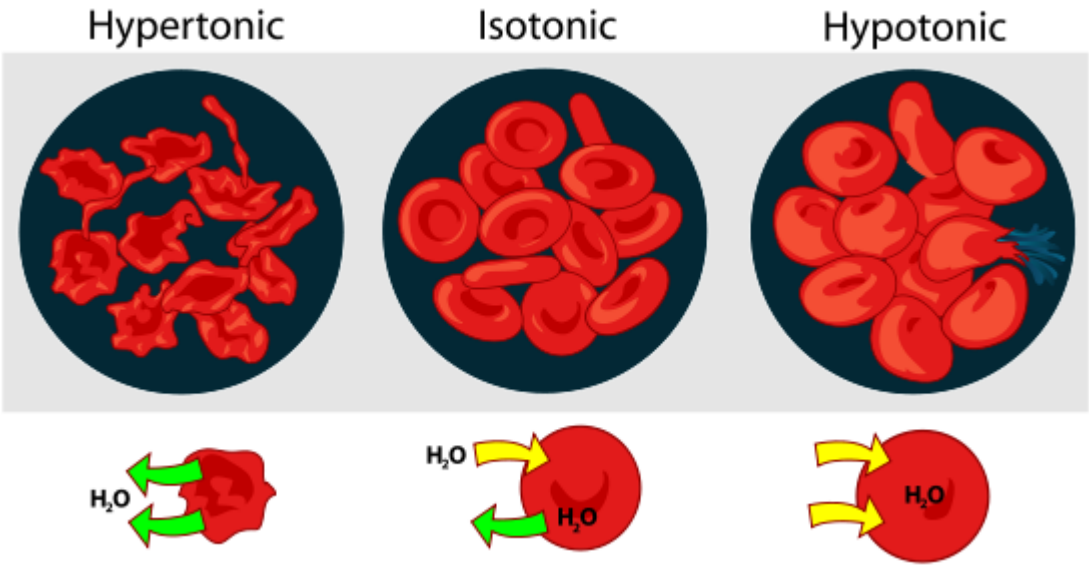
Before we can explain why cells shrink or expand when placed in a certain kind of solution, we first need to discuss the difference between osmolarity and tonicity. Osmolarity represents the number of moles of *particles* per liter of solution, while molarity represents the number of moles of *molecules* per liter of solution. Why do we have these different ways of expressing concentration? We have to change the units because different substances behave differently in solution. For example, when NaCl is dissolved in water it breaks apart into Na^+ and Cl^- ions (this is a characteristic of substances held together by ionic bonds). Thus, the number of particles double when NaCl is added to water when compared to dry NaCl. Consequently, a *1 molar* solution of NaCl (molecules) would be a *2 osmolar* solution (particles) (*technically it would be a 1.6 osmolar solution as there is not complete dissociation of the two atoms*). Glucose is different. Glucose does not break apart in water because the atoms are covalently bonded. Therefore, a 1 molar solution of glucose will also be a 1 osmolar solution. Osmolarity is a useful term because now we can use words to describe solutions: such as *isosmotic*, which means, "two solutions have the same number of particles;" *hyperosmotic*, which means, "one solution is more concentrated than the other;" or *hyposmotic*, which means, "One solution is less concentrated than the other." Notice how we use three different prefixes to help us describe the nature of the solution: *iso* means "same," *hyper* means "more," and *hypo* means "less." (Note: Osmolarity takes into account all of the particles in the solution. Therefore, if you have a liter of solution containing one mole of glucose and one mole of NaCl, you will have a *three osmolar* solution.)

Perhaps the most important concept when talking about solutions and how they affect cells is **tonicity**. "Tone" means "firmness or stretch", so the term Tonicity is a term used to describe how a solution affects the firmness or stretching of a cell when it is placed into a solution. Why are cells affected by different solutions? The answer lies in the behavior of particles with regard to diffusion. Particles will tend to diffuse from areas of high concentration to areas of lower concentration to reach equilibrium (diffusion). However, if the membrane is not permeable to the particles, then instead of particles diffusing, water will move through aquaporins in the cell membrane to reach equilibrium. Additionally, at equilibrium, the osmolarities of the two solutions will be the same. When water moves out of a cell, the cell shrinks; likewise, when water moves into a cell, the cell swells. Thus, if we place a cell into an isotonic solution, the cell shape will not change because the solutions are already in equilibrium, so there will be no net movement of water or solutes across the membrane. In other words, isotonic solutions have the same concentration of osmotically active particles (osmotically active particles are non-permeable particles) as are found in the cell. If the cell swells, we say that the solution was hypotonic, and if the cell shrinks (crenates), we say the solution was hypertonic.

Remember, fluids and ions inside the cell (intracellular fluid) and fluids and ions outside the cell (extracellular fluid) will always move to equilibrium, either by movement of solutes (ions) if they can cross the membrane or by the movement of water if the solutes cannot cross

Here is another way to think of osmolarity and tonicity. Osmolarity can be used to compare the concentration of solutes in two solutions. It can also be used to compare the concentration of the solutes in a solution with those in the cell before equilibrium is achieved. Tonicity is used to describe what effect the solution has on the cell. Osmolarity does not take into account the nature of the solutes, while tonicity is dependent upon the concentration of the *nonpermeable* solutes.

The figure below shows what happens to red blood cells when they are placed into hypertonic, isotonic, or hypotonic solutions.



Osmotic Pressure on Blood Cells Diagram. Title: File: Osmotic pressure on blood cells diagram.svg; Author: LadyofHats; Site: https://commons.wikimedia.org/wiki/File:Osmotic_pressure_on_blood_cells_diagram.svg; License: Public Domain

When placed in a hypertonic solution, red blood cells will shrink or crenate. When placed in an isotonic solution, there will be no change in volume, and when placed in a hypotonic solution, red blood cells will swell. If the concentration of the solution is great enough inside the cell, the cells will swell and even burst (lyse).

The link below shows what happens to a wilted plant when it is placed into a hypotonic solution.

https://books.byui.edu/-vip

Let's try one more example. Consider a solution that is composed of a 0.9% NaCl solution mixed with a 5% dextrose solution. Both solutions are considered isosmotic to the cell, but when added together, they become double the concentration of the cell. Thus, this solution would be considered hyperosmotic. If we place a cell into this solution, what will happen? To answer this question, let's talk about tonicity. Now, when talking about tonicity we need to consider the nature of the particles. NaCl is considered nonpenetrating (nonpermeable), while dextrose is considered penetrating (permeable). Once a cell is added to the solution, the dextrose will immediately move down its concentration gradient into the cell and "disappear" until all that is left will be the 0.9% NaCl. Thus, even though this solution was hyperosmotic to begin with, it becomes isotonic with respect to its interactions with the cell. At equilibrium, the cell will not change shape.

To check understanding, complete the table below by filling in the missing column items with regard to osmolarity and tonicity. Use the terms *iso*, *hypo*, and *hyper* to complete the table.

SOLUTION	OSMOLARITY	TONICITY
0.9 % saline		
5% dextrose		
5% dextrose + 0.9% saline		
0.45% saline		
5% dextrose + 0.45% saline		

Here are the answers for the table above. Be sure you understand why the answers are what they are.

SOLUTION	**OSMOLARITY**	**TONICITY**
0.9% saline	Isosmotic	Isotonic
5% dextrose	Isosmotic	Hypotonic
5% dextrose + 0.9% saline	Hyperosmotic	Isotonic
0.45% saline	Hyposmotic	Hypotonic
5% dextrose + 0.45% saline	Hyperosmotic	Hypotonic

11.1.2

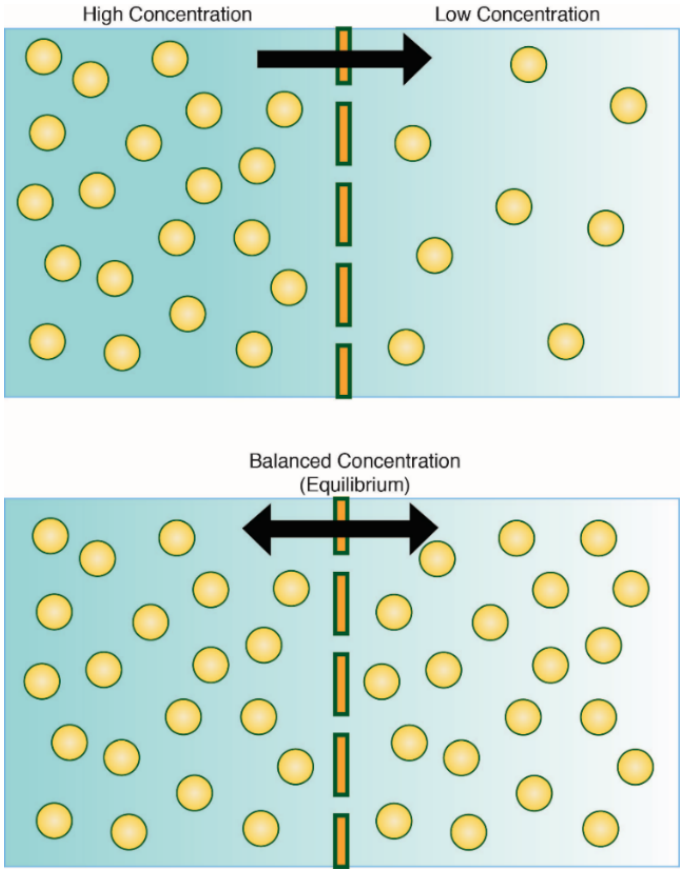
Diffusion of Solutes

Because the hydrophobic core of cell membranes creates a barrier, preventing hydrophilic substances, such as ions, water, and large polar molecules, from moving across the membrane, the membrane makes use of proteins to facilitate movement of most solutes and water. Processes that move substances (solutes) across membranes can be grouped into two general categories based on whether the process requires an input of cellular energy or not. If no energy input is required for the transport, then we say particles move via a **passive transport process**. On the other hand, if the process requires cellular energy, usually in the form of ATP, then it is an **active transport process**.

Simple Diffusion

Diffusion is a process that results from the fact that molecules are constantly in a state of random movement. All molecules, including solids, liquids and gases are in continuous motion. This motion causes collisions between neighboring molecules, thus altering directions and creating a state of "random" motion. This random motion can be further altered by temperature, with increases in temperature stimulating a more rapid random movement. If there is an initial, unequal distribution of the molecules (i.e., more concentrated in one area than another), the constant random movement and collisions cause them to eventually become equally distributed. This process of gradual movement from where they are more concentrated to where they are less concentrated is called ***diffusion***. We refer to the concentration difference as the **concentration gradient**.

Therefore, substances diffuse down their concentration gradients (from high to low concentration). Once the molecules are evenly distributed, we say that we have reached a state of **diffusion equilibrium,** and even though the molecules are still moving, there is no longer any net change in concentration. You can observe this phenomenon by carefully placing a drop of food coloring into a glass of water. The dye gradually moves through the liquid until it is evenly dispersed in the water. If the material in question can pass through the cell membrane without the aid of a membrane protein, we refer to the process as **simple diffusion**. Solutes that cross the membrane by simple diffusion tend to be hydrophobic. Examples of substances that cross the membrane by simple diffusion are the gasses CO_2 and O_2.



Simple Diffusion: Process of Moving from High to Low Concentration to Reach Equilibrium.
Image created by BYU-Idaho student, Hannah Crowder 2013.
The top panel shows the diffusion of solute from left (high concentration) to the right (low concentration) until an equilibrium is established. Once a diffusion equilibrium exists, there will no longer be any net movement of solute (lower panel).

Factors That Affect the Rate of Diffusion

The speed at which a molecule moves across a membrane depends in part on the mass, or molecular weight, of the molecule. The higher the mass, the slower the molecule will diffuse (rate is proportional to $1/MW^{1/2}$). Another factor that affects the rate of diffusion across the membrane is the solubility of the substance. Nonpolar substances, such as oxygen, carbon dioxide, steroids, and fatty acids will diffuse rapidly, while polar substances, having a much lower solubility in the membrane phospholipids, move through slowly, or not at all. Ions, such as Na^+ and Cl^-, tend to diffuse across a membrane rather rapidly. The diffusion rate across a membrane is proportional to the area of the membrane and to the difference in concentration of the diffusing substance on the two sides of the membrane. This relationship can be demonstrated by Fick's first law of diffusion, which states that:

$$J = -DA(\Delta C/\Delta X)$$

J = net rate of diffusion in moles or grams per unit time

D = diffusion coefficient of the diffusing solute in the membrane (this coefficient takes into account the size of the substance as well as its solubility in the membrane)

A = surface area of the membrane

ΔC = concentration difference across the membrane

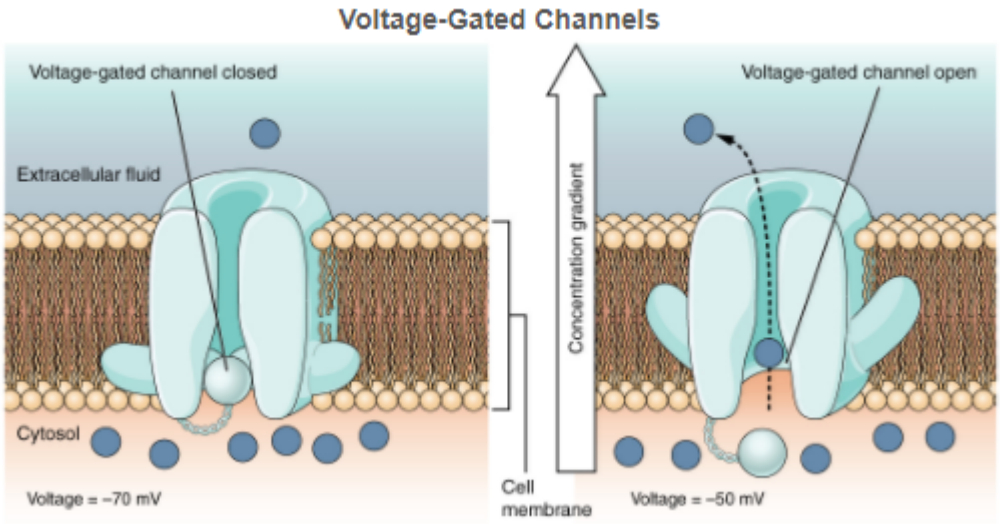
ΔX = thickness of the membrane. Diffusion is quite rapid over short distances but gets slower the further it goes. The time it takes for something to diffuse is proportional to the square of the distance. Therefore, if it takes one second to diffuse one centimeter, it will take 100 seconds to diffuse 10 cm and 10,000 seconds to diffuse 100 cm. So, to go 100 times further takes 10,000 times longer. Diffusion is quite sufficient to cross the thin cell membrane, but to travel long distances by diffusion would be very slow. Therefore, organisms have developed other mechanisms, like circulatory systems, for moving substances long distances.

11.2

Facilitated Diffusion

Facilitated Diffusion represents the movement of substances across the membrane that are too big and/or too polar to pass through the membrane. This type of movement is mediated by integral membrane proteins called transport proteins. Unlike simple diffusion, this process of diffusion exhibits saturation, and its rate is directly related to the concentration of specific transport proteins within the membrane. In addition, this type of transport, like simple diffusion, does not require an input of energy. Facilitated diffusion can occur in two different ways, through channel proteins and carrier proteins.

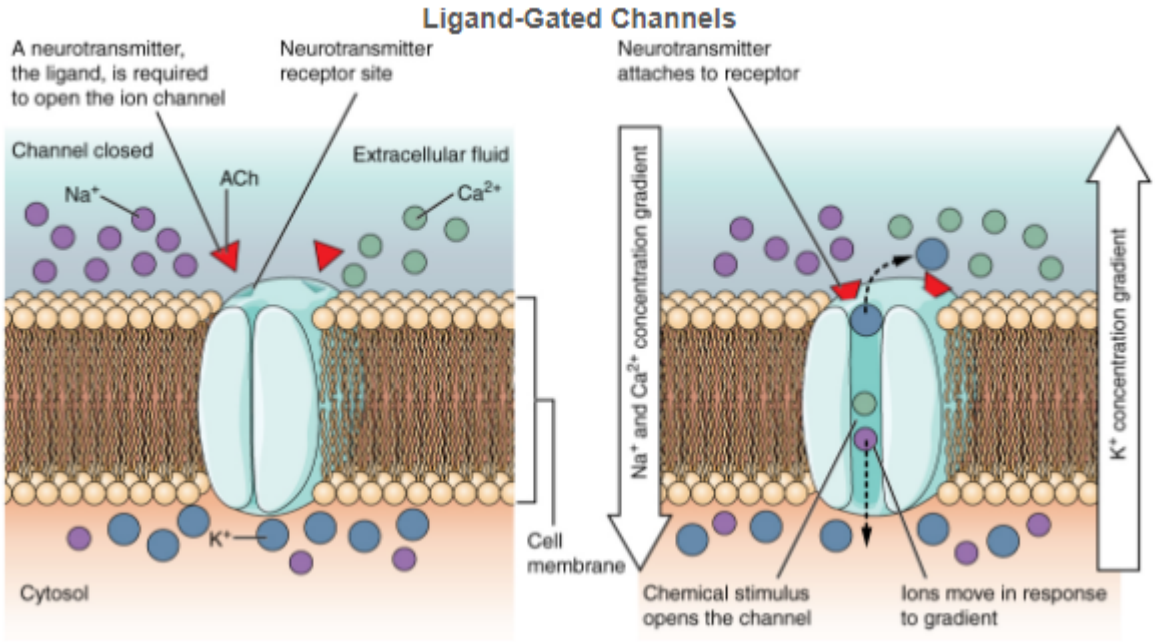
Channel proteins resemble fluid filled tubes through which the solutes can move down their concentration gradients across the membrane. These channels are often responsible for helping ions, such as Na^+, K^+, Ca^{2+}, and Cl^-, cross the membranes. Even though they are open tubes, they often only allow very specific ions to pass through them. For instance, a K^+ channel may allow K^+ to pass through but not Na^+ or Cl^-. This is due to the presence of a **selectivity filter** that selects for hydrated or dehydrated states of the specific ion. These channels are often gated (they have doors or gates that can be opened or closed). Depending on the channel, these gates may respond to voltage differences across the membrane (**voltage-gated channels**), specific signal molecules (**ligand-gated channels**), or even stretching or compressing of the membrane (**mechanically-gated channels**).



Voltage Gated Channel. *Author: OpenStax College; Site: https://books.byui.edu/-yThl License: Licensed under a Creative Commons Attribution 4.0 License*

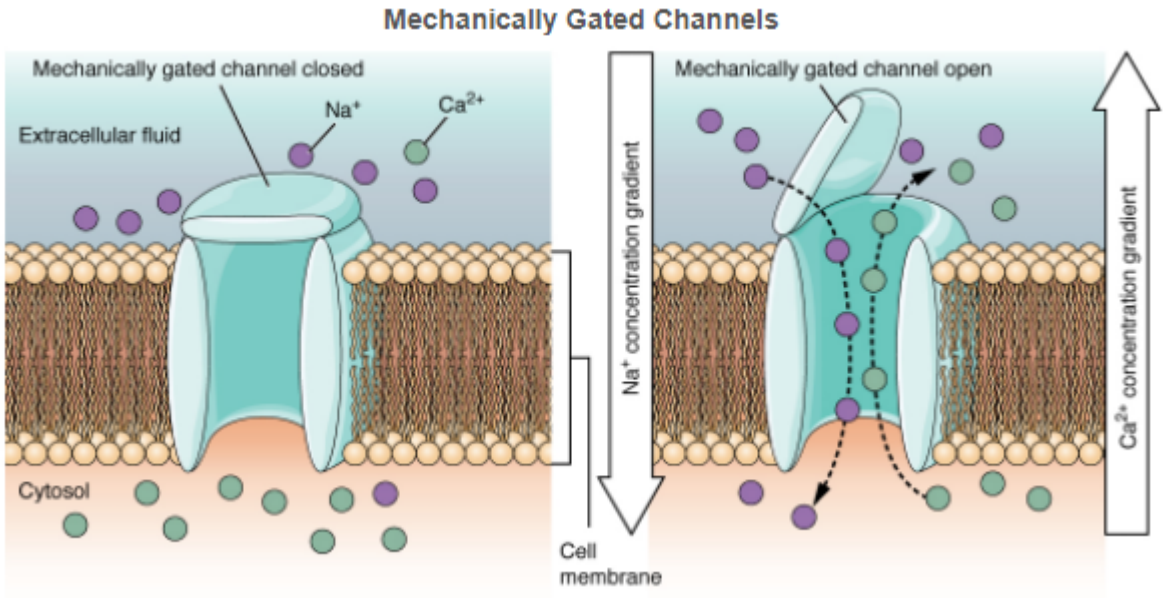
Voltage-gated channels (shown above) open when membrane voltage changes. The concentration of ions in the intracellular fluid creates the voltage. Amino acids in the protein transporter are sensitive to charge and cause the channel to open for a specific ion.

In ligand-gated channels the pore opens to ions when the ligand binds to a specific location on the extracellular surface of the channel protein. Acetylcholine is the ligand shown in the example below.



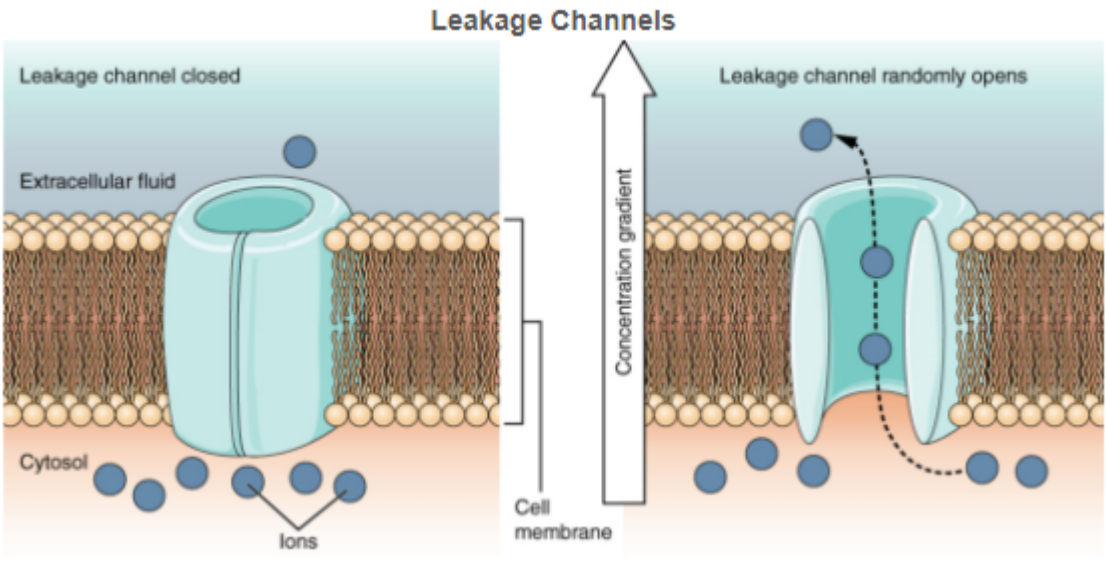
Ligand-Gated Channels. *Author: OpenStax College; Site: https://books.byui.edu/-dfk License: Licensed under a Creative Commons Attribution 4.0 License*

When a mechanical change happens such as pressure, touch, or a change in temperature mechanically gated channels open.



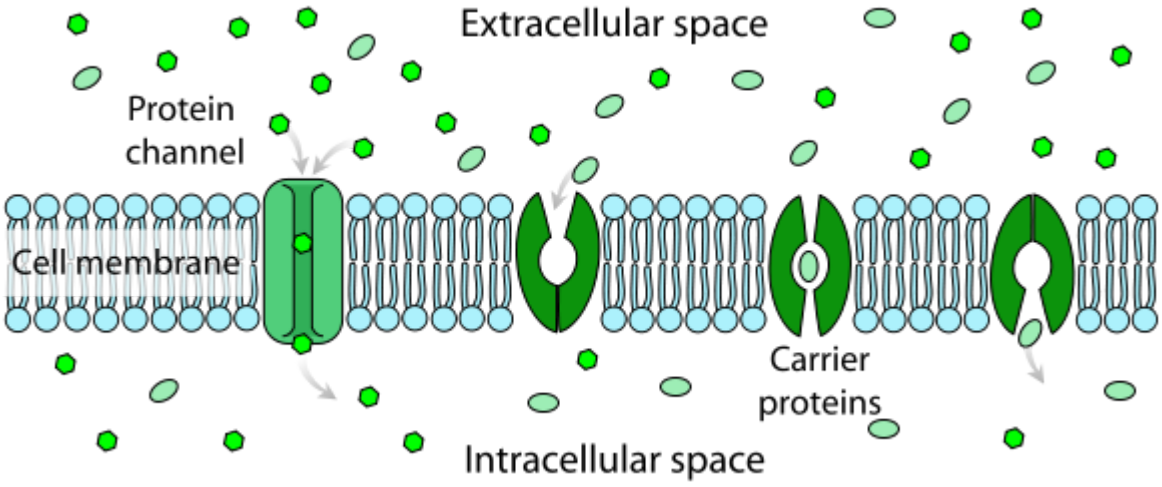
Mechanical-Gated Channels. *Author: OpenStax College; Site: https://books.byui.edu/-ULoF License: Licensed under a Creative Commons Attribution 4.0 License*

Another example of a gated channel protein is the K^+ **leak channel** which opens and closes intrinsically and contributes to the cell's electrical potential.



Leak Channel. Author: *OpenStax College; Site: https://books.byui.edu/-Mpz License: Licensed under a Creative Commons Attribution 4.0 License*

The second type of facilitated diffusion utilizes **carrier proteins** in the membrane and is known as carrier-mediated transport. Unlike the channel proteins, these carriers do not open to both sides of the membrane simultaneously. Instead, they bind to a specific solute on one side of the membrane. This binding causes the carrier to change shape, which moves the solute to the other side of the membrane (think of a revolving door).



Carrier Proteins. *By LadyofHats Mariana Ruiz Villarreal [Public domain], via Wikimedia Commons*

Like the channel proteins, these carriers can be very specific in the solute they transport since the solute must bind to a receptor site that is designed to fit a specific solute. Another interesting characteristic of these carriers is, like all channel proteins, that they have a maximum rate of transport and can thus become **saturated** if the solute concentration is high enough.

Active Transport
Primary Active Transport

Secondary Active Transport
Bulk Transport

11.2.1

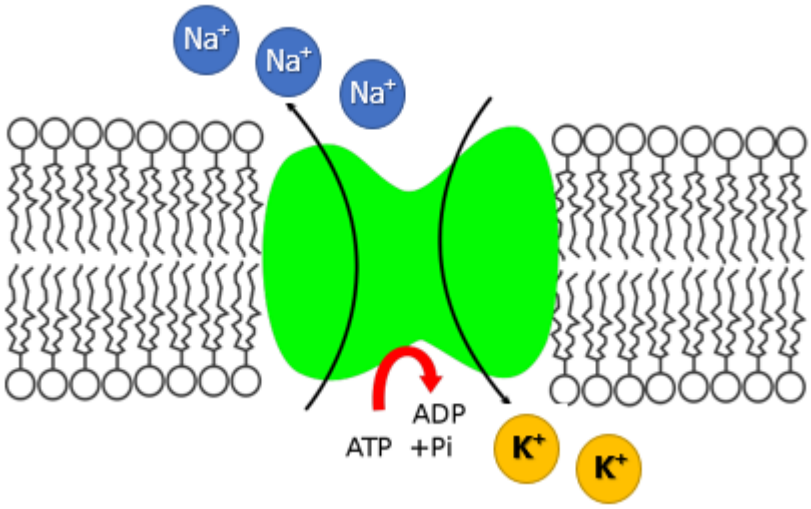
Active Transport

To this point, the transport processes we have discussed have all been passive processes in which the solute, or the water, movement has been down a concentration gradient with no input of energy required. However, there are times when it is important for the cell to be able to move solutes against their concentration gradient. Just like moving water from the first to the top floor of a high-rise building, these processes require an energy source. Processes that require energy are called **active transport** processes.

11.2.2

Primary Active Transport

Primary active transport can move solutes, such as ions, against their concentration gradient. This process requires a carrier protein that is much like the proteins involved in carrier-mediated diffusion mentioned above. However, in this case, the carrier has a site for the binding of ATP, which provides the energy to move the solute against its gradient. These transport systems can move one or multiple ions across the membrane. One of the most important active transport systems is the **Na-K ATPase** (see figure below). This system moves sodium out of the cell and moves potassium into the cell. Each cycle of the pump moves three sodium ions out of and two potassium ions into the cell. The Na-K ATPase pump exists in two different conformational states: an E1 form, where the binding sites for the ions face intracellularly and an E2 form, where the binding sites face the extracellularly.



Sodium Potassium- ATPase pumps. Image created at BYU-Idaho by MG 2013

Three Na^+ ions are moved out of the cell in exchange for two K^+ ions with the aid of ATP. In addition to the Na-K ATPase pump other types of ATPase pumps exist as well, these include the H-K pump, Ca pump (SERCA), H pump, and MDR (multidrug- resistance transporters).

11.2.3

Secondary Active Transport

Like primary active transport, secondary active transport also moves solutes against their concentration gradients. However, with secondary active transport, ATP is not directly involved in the pumping of the solute. Instead, this process uses the energy stored in concentration gradients to move the solute. Since sodium is always in higher concentration outside of the cell (due to primary active transport), the sodium gradient is often used to power secondary active transport. In this process, the carrier protein has a binding site for the solute to be transported, as well as a binding site for sodium. Once both solutes have bound, sodium moves down its concentration gradient and moves into the cell, much like what happens with carrier-mediated diffusion, and in the process pulls another solute into the cell (**symport**) or moves another solute out of the cell (**antiport**), against its concentration gradient. Several organic molecules are transported across membranes by this process, such as glucose and amino acids. ATP energy is required to generate the sodium concentration gradient but is not directly involved in moving the desired solute across the membrane, hence the designation as *secondary active transport*.

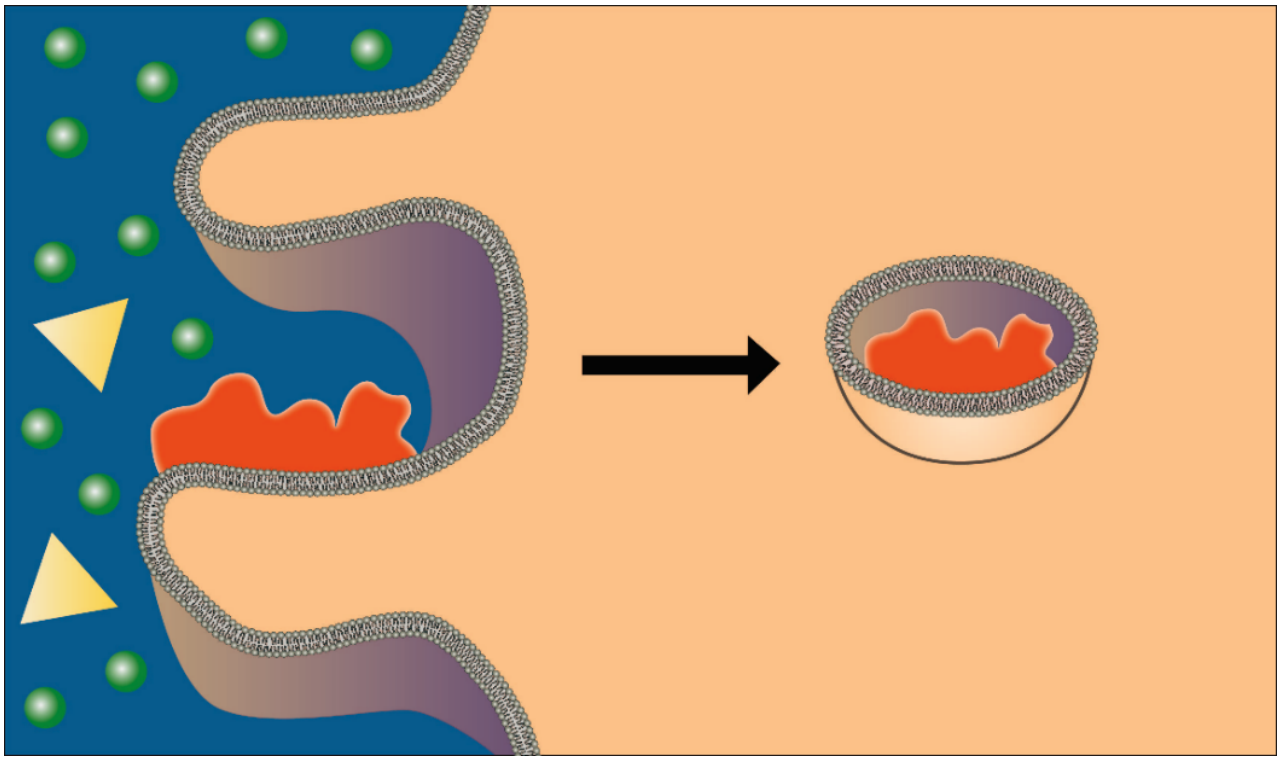
11.2.4

Bulk Transport

To this point, we have been talking about the movement of relatively small solutes across the cell membranes (i.e. ions and small organic molecules). There are instances, however, when it is necessary to move much larger materials across the membrane, like when a macrophage engulfs a bacterium or when larger amounts of a given material are released from a cell, such as the release of a hormone. These processes also require ATP and are, therefore, examples of active transport, but they move materials in a very different way.

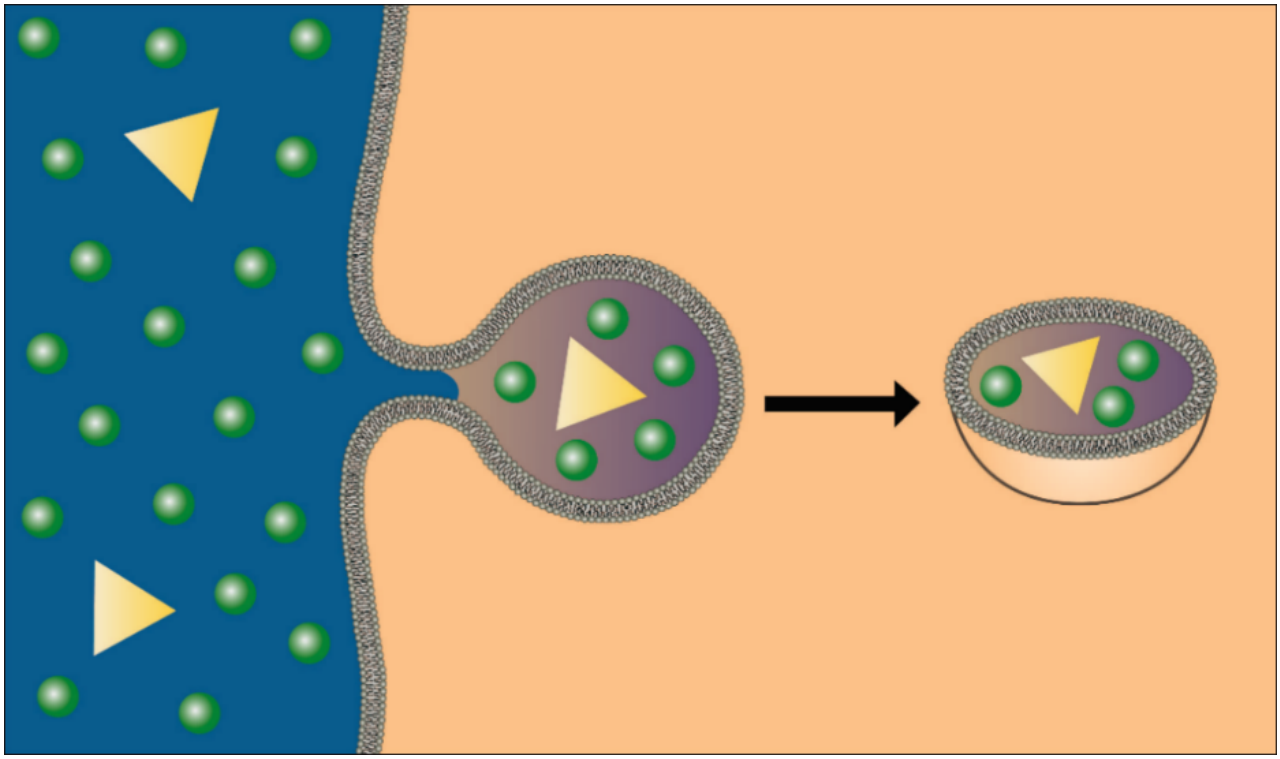
Endocytosis

Endocytosis is the bulk transport of materials into the cell. There are several types of endocytosis, and we will briefly explore each one. First, let's discuss **phagocytosis** (see figure below), which means *cell eating.* In this process, the cell sends extensions of its plasma membrane, called *pseudopodia*, out and around the particle to be phagocytized. As these **pseudopodia** surround the particle, they eventually fuse, creating a vesicle containing the particle.
This **phagosome** can then unite with a lysosome inside the cell, and the engulfed material can be digested for use within the cell.



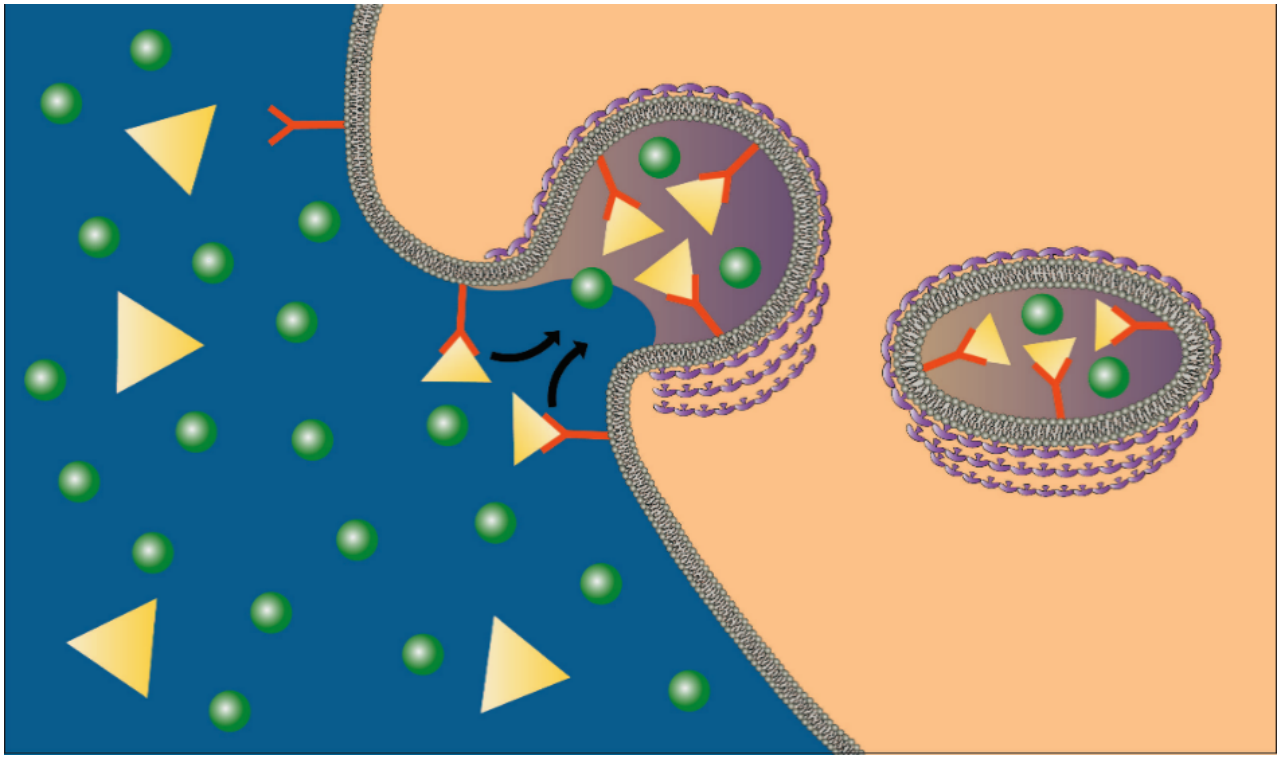
Phagocytosis. In phagocytosis (shown above), the cell membrane forms processes that surround and engulf a particle to be brought into the cell. Image created by BYU-Idaho student, Hannah Crowder, 2013.

A second type of endocytosis is **pinocytosis, which means** *cell drinking.* In this process, rather than send out pseudopodia, the cell membrane simply invaginates (forms a pocket) and engulfs anything in the fluid that is taken into the cell (see figure below). The cells are not interested in the water in the vesicles but any solutes that might be brought in. As you can imagine, this is not a very efficient way of bringing materials into the cell because it is nonspecific and brings whatever is in the fluid into the cell. It provides cells with a nonselective mechanism for sampling the extracellular environment. Thus, phagocytosis engulfs larger particles like bacteria or other microorganisms, and pinocytosis engulfs smaller particles/molecules such as endo/exotoxins released from bacteria or other molecules used for cell signaling.



Pinocytosis. In pinocytosis, the membrane forms an invagination (pocket) that pinches off, bringing into the cell the fluid in the pocket along with any solutes in the fluid. Image created by BYU-Idaho student, Hannah Crowder, 2013.

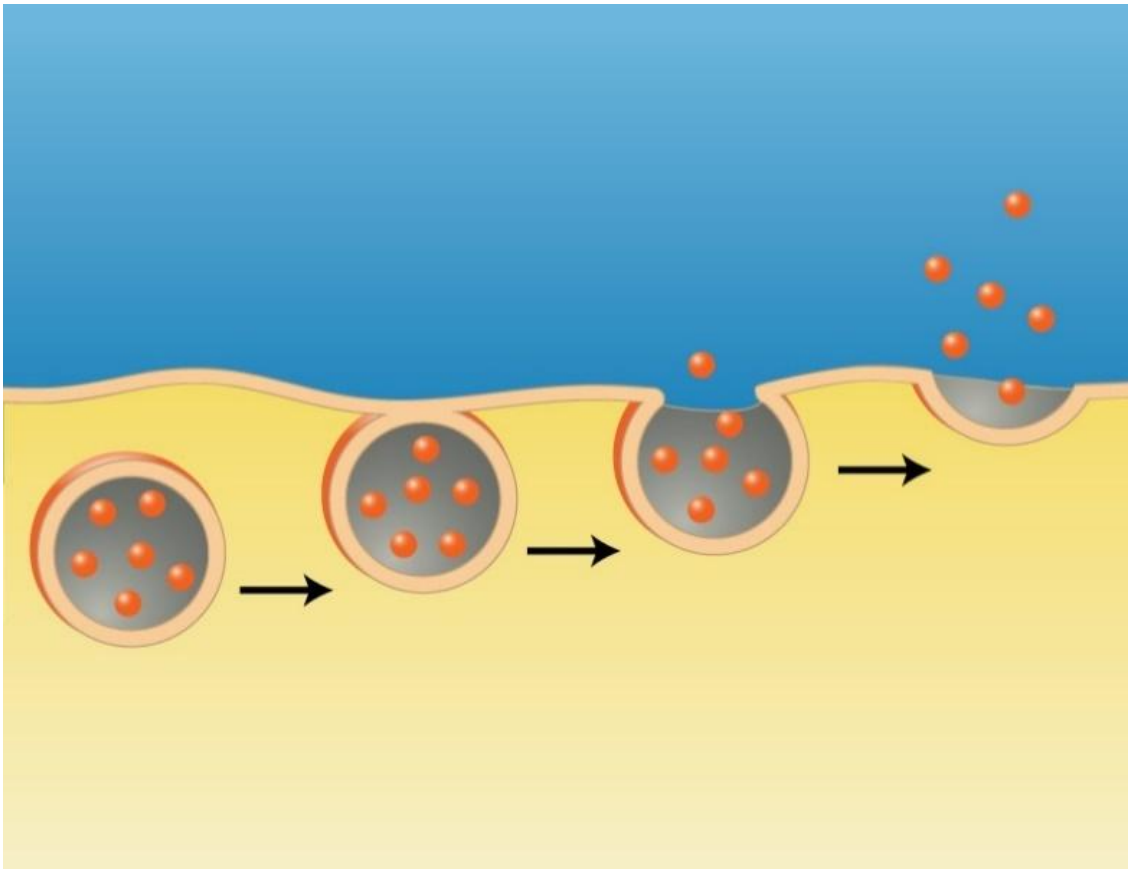
A much more efficient mechanism for bringing specific solutes into the cell is **receptor-mediated endocytosis**. As the name implies, this mechanism employs specific receptors that bind to the material (**ligand**) to be brought into the cell. Once the material binds, the receptor-ligand complex migrates to a specific area of the membrane, a clathrin-coated pit, which is then brought into the cell by a process like pinocytosis (see figure below). The advantage of receptor-mediated endocytosis is that it can engulf large amounts of a specific solute.



Receptor-Mediated Endocytosis. Image created by BYU-Idaho student, Hannah Crowder, 2013.

Exocytosis

Thus far, we have been discussing bulk transport, bringing material into the cell. There is also a need to export material from the cell into the extracellular fluid. This process is called **exocytosis**. The mechanism is essentially the reverse of endocytosis. **Secretory vesicles** filled with the material to be released migrate to the plasma membrane where the membrane of the vesicle fuses with and becomes a part of the plasma membrane (see figure below). The material that was in the vesicle suddenly finds itself outside of the cell. The usual signal that initiates this process is the entry of calcium ions into the cell. Recall that calcium is an extracellular ion, so there is a large diffusion gradient for calcium to move into the cell. The opening of gated calcium channels, allowing calcium to diffuse into the cell, initiates the exocytosis process.



Exocytosis. Image created by BYU-Idaho student, Hannah Crowder, 2013.

In exocytosis, secretory vesicles migrate to the cell membrane where the vesicular membranes fuse with the plasma membrane, releasing the vesicles' contents into the extracellular fluid.

11.3

Cell Signaling

In addition to regulating substances that come in and out of cells, it is also essential for cells to communicate (signal) with each other (Intercellular signaling) as well as with organelles withing themselves (intracellular signaling). Cell signaling molecules are called ligands and ligands can interact with proteins imbedded in cell membranes called receptors. This receptor/ligand interaction can be quite complex and is usually very specific.

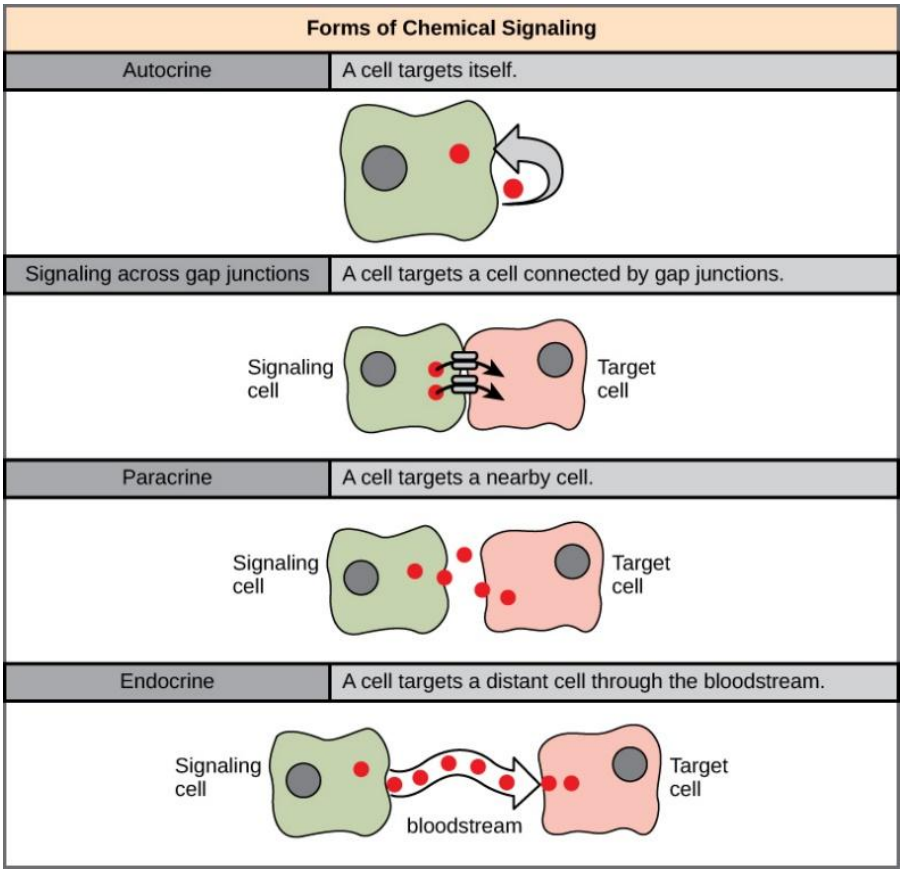
Cell Signaling Pathways
Receptor Interactions
G Protein-Coupled Receptor (GPCR)

11.3.1

Cell Signaling Pathways

To help simply and organize the different types of cell signaling pathways we will divide the process into four categories: autocrine, gap junction, paracrine, and endocrine signaling.

Endocrine, Autocrine, Paracrine Signaling.



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Autocrine Signaling

As the name implies, auto “self” refers to the action of a ligand on the same cell that secreted it or on another cell of the same type that produced the hormone. For example, a lymphocyte releases signals that affect itself as well as other lymphocytes. In the case of viral infections, cells can release ligands that signal itself to start to undergo a programmed death to kill the virus.

Gap Junction Signaling

Gap junctions are physical connections of proteins that span between plasma membranes of neighboring cells. These proteins act as channels that allow small ligands to diffuse rapidly between two cells. An example of this type of ligand would be ions like Ca^{++}, or Na^{+}. This allows for a rapid communication between the two cells. In some cases, gap junctions form as a network between all the cells of a given tissue system, making the whole system function as one giant network. Examples would be some plants and animal heart muscle.

Paracrine Signaling

Like autocrine signaling, paracrine signaling is a local but short distance signaling. In paracrine signaling, the ligand is released into the extracellular space and regulates nearby cells of a different type. This type of signaling does not last long, eliciting short but quick response. For example, endothelial cells send signals that regulate smooth muscle activity in the walls of a blood vessel.

Endocrine Signaling

Endocrine signaling can reach the farthest and is the longest lasting form of cellular signaling. Ligands that are part of the endocrine signaling pathways employ the use of circulatory systems to travel long distances to interact with receptors of target cells. Ligands release in this fashion are called hormones.

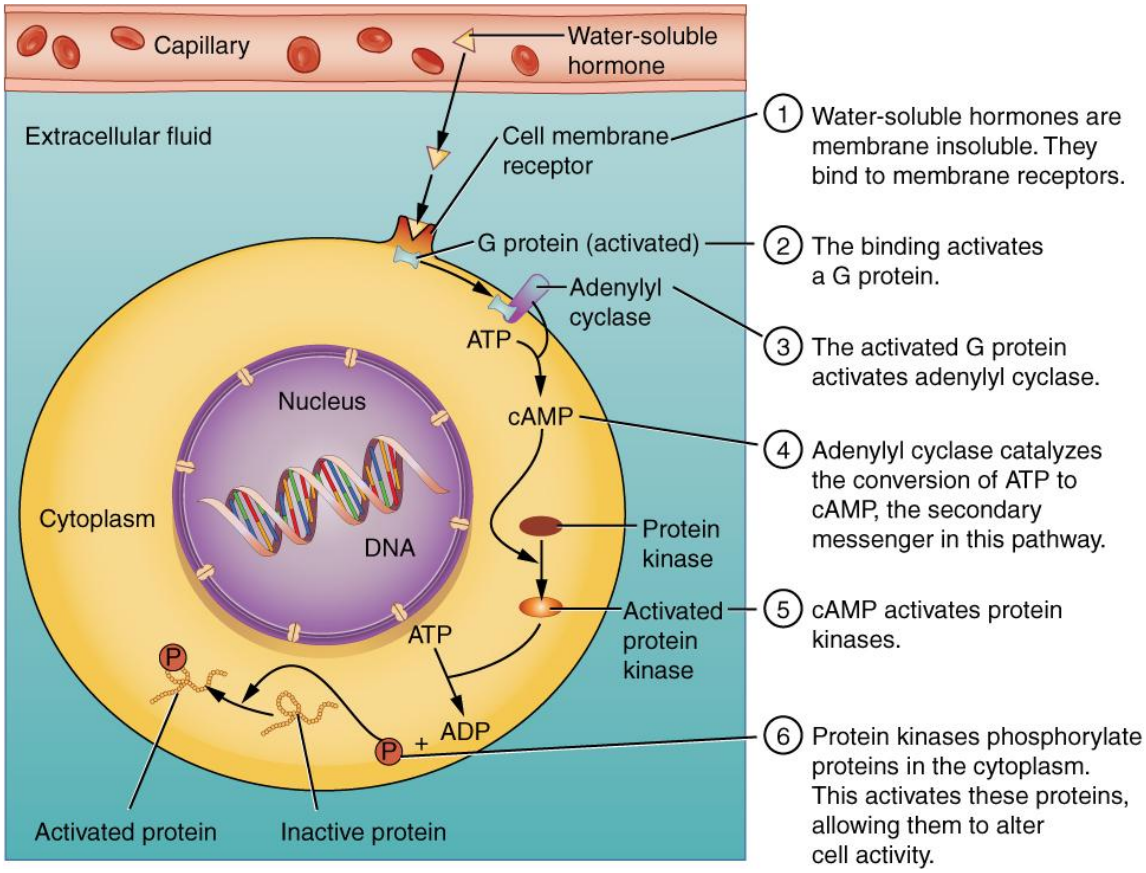
11.3.2

Receptor Interactions

Receptors that respond to ligands are found in three general locations:

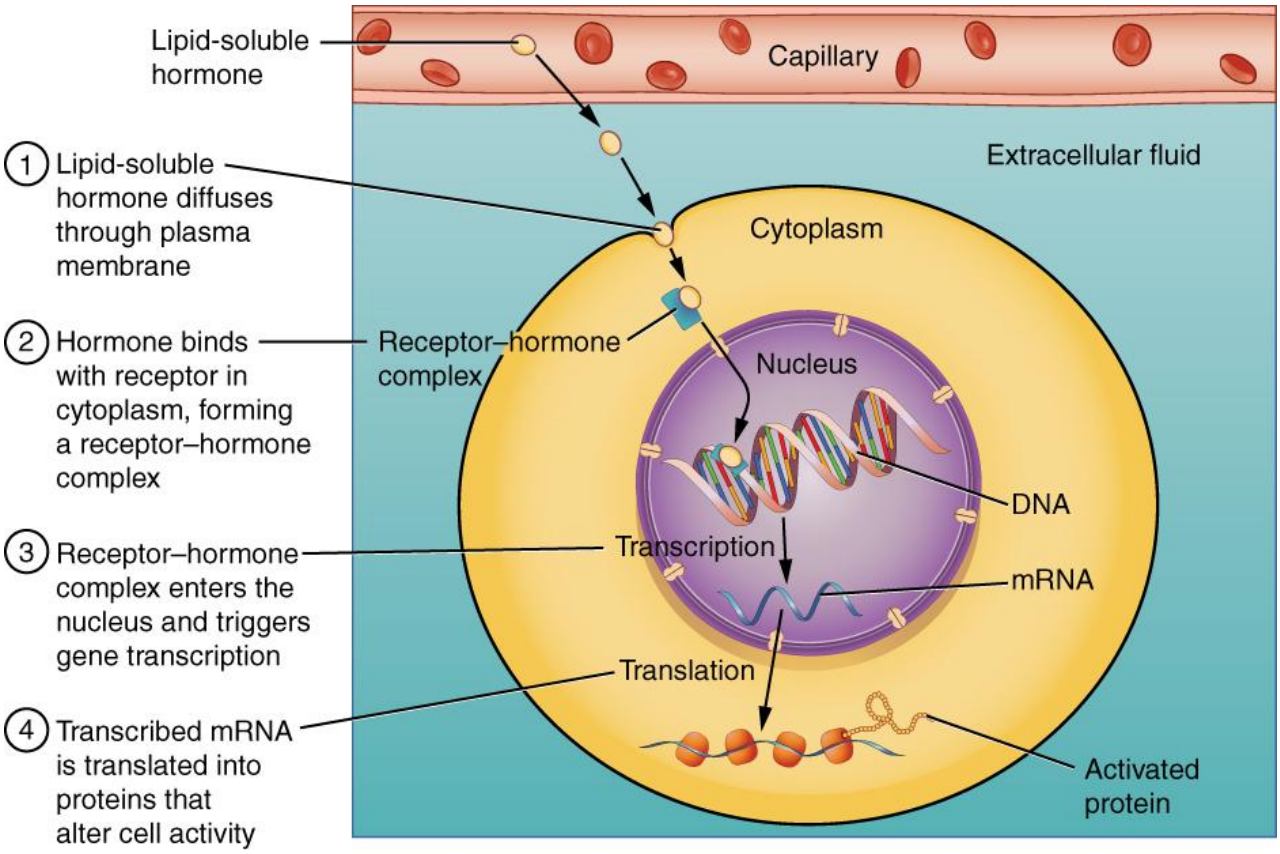
- On the plasma membrane
- In the cytosol of the cell
- In the nucleus.

Most plasma membrane receptors are **G-protein-coupled receptors** (discussed below). Other types include **receptor tyrosine kinases** and **receptor serine/threonine kinases.** Activation of these receptors leads to an intracellular cascade that produces second messengers like cAMP, cGMP, or inositol triphosphate (IP3). These second messengers activate other enzymes such as those that phosphorylate or dephosphorylate proteins. Adding a phosphate to an enzyme is like flipping a light switch, when the phosphate is attached to the enzyme it can become active and when the phosphate is removed it becomes inactive. The opposite can also be true where adding a phosphate can inactivate an enzyme and removing the phosphate would then activate the enzyme. Additionally, the second messenger may increase intracellular calcium. Calcium can also act as a messenger that turns on events in the cell.



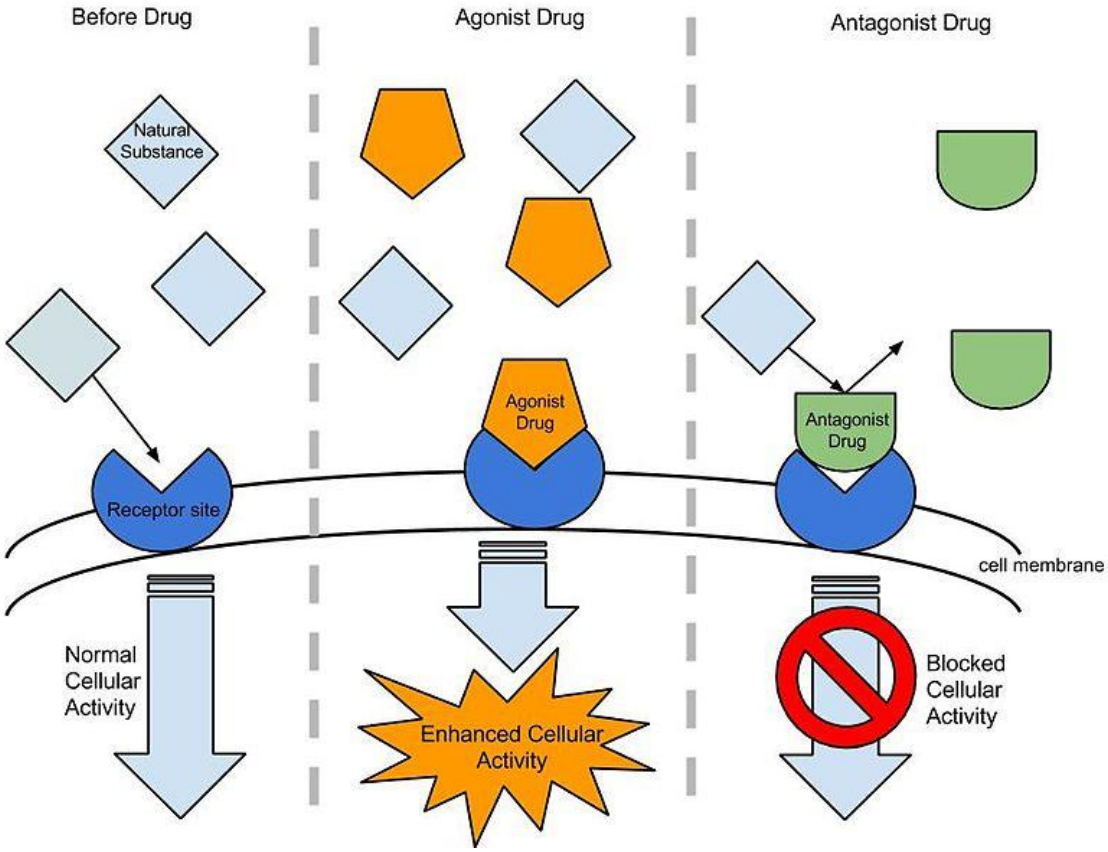
Water-Soluble (Hydrophilic or Amino Acid Derived) Hormone Receptors: G-protein-coupled receptors. Synthesized by cell receptors on cell surface. Examples include Insulin, Growth Hormone, and Epinephrine. *Author: OpenStax College; License: [CC BY 3.0 (http://creativecommons.org/licenses/by/3.0)], via Wikimedia Commons; Link: https://books.byui.edu/-YEuY*

Intracellular and nuclear receptors interact with DNA and affect mRNA synthesis. Nuclear receptors, or receptors on the nucleus of the cell, when activated stimulate transcription of various genes, resulting in the production of new proteins. The new proteins result in a change in the cell. Having different kinds of receptors such as membrane receptors and intracellular receptors accommodates both **hydrophilic** and **hydrophobic** ligands. Hydrophilic ligands easily dissolve in water, but do not easily enter the cell due to the phospholipid bilayer of the cell membrane and therefore act via membrane bound receptors, while nonpolar or hydrophobic ligands can easily cross the plasma membrane bind to cytosolic and nuclear receptors. In addition, membrane receptors typically induce short term and rapid responses, while intracellular receptors tend to produce slower but prolonged responses.



Lipid-Soluble (Hydrophobic or Cholesterol-derived) Steroid Hormone Receptors: Cytosolic and Nuclear Receptors. Synthesized inside the nucleus of the cell. Examples are Testosterone and Estrogen. *Author: By OpenStax College; License: [CC BY 3.0 (http://creativecommons.org/licenses/by/3.0)], via Wikimedia Commons; Link: https://books.byui.edu/-Hua*

It is truly the receptor, not the ligand that ultimately determines the cellular response. Most receptors are highly selective to their ligand, that is, even similar ligands don't bind to the receptor with the same affinity. The receptor recognizes subtle differences in ligand structure which allows the receptor to distinguish between ligands. This concept has allowed pharmaceutical companies to design drugs (analogs) that can interact with specific receptors to provide medicinal intervention. Drugs that bind to and stimulate a receptor are called **agonists**, while those that bind to a receptor and block its effects are called **antagonists**.



Agonist and Antagonist Ligands. Agonists fit hormone receptors and activate them. Antagonists occupy hormone receptors and do not activate them but block them from activation. *Author: By Dolleyj (Own work) [CC BY-SA 3.0 (https://creativecommons.org/licenses/by-sa/3.0)], via Wikimedia Commons Link: https://books.byui.edu/-zknP*

The specificity of receptors allows endocrine ligands to be released at any site and circulate throughout the system, but only affect the cells that contain the receptor for the ligand.

Receptor numbers are constantly being changed within a given cell, thus, depending on the number of receptors present, a cell may become less or more responsive to a given ligand. These receptor numbers can be regulated by ligands in a positive (**up-regulation**, more) or negative (**down-regulation**, less) manner.

11.3.3

G Protein-Coupled Receptor (GPCR)

The GPCR complex is composed of two units: a receptor protein that binds to the chemical signal (the ligand) and the G protein complex associated with the inner side of the membrane (i.e., a peripheral protein complex). The GPCR has a ligand binding site on the external surface and a G protein binding site on the internal surface. The G protein complex is composed of three subunits: the alpha, beta, and gamma subunits. The alpha subunit has a site that can bind **Guanosine Triphosphate (GTP)** or **Guanosine Diphosphate (GDP)**, hence the name **G protein**. In its inactive form, the G-alpha subunit is bound to GDP, and the three subunits (alpha, beta, and gamma) are bound together. When a ligand binds to the receptor on the surface of the cell, the G protein binding site changes shape, allowing the G protein to bind to the intracellular region of the receptor. This binding causes the G protein to then change shape, and the GDP exits the binding site on the alpha subunit and is replaced by a GTP from the cytoplasm. The binding of GTP causes the alpha subunit to separate from the other two subunits (beta/gamma dimer). Once separated, the alpha subunit (and sometimes the beta/gamma dimer) can then bind to and activate other proteins inside the cell. The mechanism of action is typically mediated by one of two enzymes: **adenylate cyclase** or **phospholipase C**. Cellular responses include activation of metabolic enzymes, opening or closing ion channels, turning on transporters, initiating gene transcription, regulating motility, regulating contractility, stimulating secretion, and even controlling memory. After a short period of time, the G-alpha subunit hydrolyzes the GTP into a GDP and phosphate, allowing it to reunite with the beta/gamma dimer, turning off the signal. To date, approximately 800 genes for G protein-coupled receptors have been identified.

Adenylate cyclase

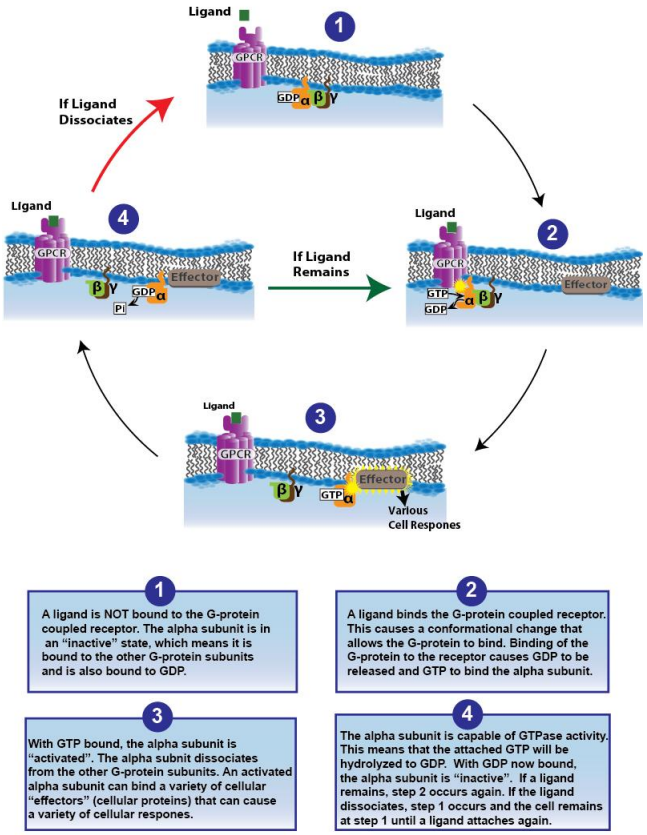
Activation of Adenylate cyclase results in the synthesis of a second messenger molecule called cyclic adenosine monophosphate (cAMP). The primary action of cAMP is to activate the enzyme protein kinase A (PKA). PKA phosphorylates serine and threonine residues of proteins which can lead to activation.

Phospholipase C

Activation of the phospholipase C results in the cleavage of a membrane phospholipid called Phosphatidylinositol bisphosphate (PIP2). This enzymatic cleavage yields two molecules: diacylglycerol (**DAG**) and inositol triphosphate (**IP3**). DAG remains in the membrane and activates another enzyme called protein kinase C (PKC) while IP3 diffuses into the cytoplasm and acts as a ligand for calcium channels on the endoplasmic reticulum.

Calcium

The ion calcium is a very common intracellular second messenger. Intracellular Ca^{++} levels are kept very low because of various secondary and primary active pumps. This is because Ca^{++} has potent effects on a variety of different protein activities. Muscle cell proteins are particularly sensitive to Ca^{++}.



Ligand Activation and G-Protein Effect. Image drawn by JS Fall 2014

UNIT 12

CELL DIVISION AND CANCER

12.1

Cell Division

Of all the pathways in cellular function, perhaps none other pathway is more tightly controlled than the pathways involved in cell growth and division. These processes are collectively called the **cell cycle**. Cell cycles differ between prokaryotic and eukaryotic cells, and between the gametes and somatic cells of more complex eukaryotes. The cell cycle in prokaryotes is called **binary fission**. In eukaryotic cells the processes of the cell cycle in somatic cells can be organized into two broad categories: **interphase** and **mitosis**. The gamete cell cycle is called **meiosis** and is a topic of Bio 181. Interphase represents cell growth and where DNA is replicated, mitosis represents cell division. Cells will cycle through interphase then mitosis and back to interphase. The most important result of the cell cycle is the replication (copying) and movement of the DNA. To help facilitate this movement, the vast array of DNA will be organized into structures called chromosomes.

12.1.1

Chromosomes

In eukaryotic cells, the majority of DNA is found within the nucleus and associated with proteins (**chromatin**) that will help the DNA condense into organized structures called chromosomes. In humans, the 3.2 billion nucleotides that make up DNA can be arranged into 46 chromosomal structures which in turn can be separated into 23 pairs (in males, 22 pairs and a mismatched sex chromosome pairing). This pairing is possible because of unique similarities in the DNA that come from the fact that half of the DNA comes from the mother (maternal) and the other half comes from the father (paternal). The similarities between the two sources of DNA are found within distinct sequences of nucleotides called **genes**. More specifically, DNA contains instructions (genes) to make the same types of proteins from two different sources (maternal and paternal). When the DNA condenses into chromosomes, maternal and paternal genes will arrange themselves in a particular order within a chromosome essentially creating a maternal and a paternal chromosome. Since the same types of genes from either source are arranged similarly, the chromosomal arrangement will be close to the same, because in some cases those gene sequences between maternal and paternal sources differ by only one nucleotide! Thus, maternal DNA gene sequences will arrange themselves into 23 chromosomes, and paternal DNA gene sequences will be arranged into 23 chromosomes in a very similar pattern so that the chromosomes can be paired. This pairing is known as **homologous** pairing. In males, although the X and Y sex chromosomes contain different genes, they pair as homologous chromosomes much like the two X chromosome pair in females. This pairing is also referred to as a set and sets of chromosomes are organized by the number of sets that a cell contains, a concept called **ploidy**. For example, if a cell contains one set of chromosomes (maternal only) it is called **haploid**. One set of chromosomes is represented by N. Since humans have two sets, one maternal set (N = 23 total chromosomes) and one paternal set (N = 23 total chromosomes), humans are **diploid** (2N) which means that the total number of chromosomes would be 46 where 2N = 46 and N = 23. Cells that contain complete sets of chromosomes are called **euploid** (2N) and cells with missing or additional chromosomes are called **aneuploid** (2N-1; Turner syndrome, 2N+1; Down syndrome, etc.). The N represents the number of sets, and the -1 or +1 represents a single chromosome missing or added.

12.1.2

Interphase

Interphase is longest part of the cell cycle and is subdivided into three growth phases: G1, S and G2 phases. The G1 stage stands for "GAP 1", the S for "Synthesis" and the G2 for “GAP 2”. During G1 the cell grows, but not from a size standpoint. This growth occurs at the biochemical level where the cell begins to accumulate building blocks in the form of proteins and energy sources in the form of carbohydrates. The S phase is marked by DNA growth. DNA is replicated to form identical pairs of chromosomes called **sister chromatids**. *Note: after replication cells are still diploid (2N) but in humans would now contain 92 total chromosomes (46 original + 46 exact copies). The S phase also marks the appearance of the centrosome, an organelle that will orchestrate the movement of the sister chromatids to that new cell. The G2 phase marks another surge in biochemical growth that replenishes used up proteins and energy from the previous phases. During G2 the cytoskeleton will start to be broken apart in preparation for cell division. Some cells will enter a G0 phase following the cell cycle which represents an inactive state which length varies by cell type, with some cells remaining in G0 permanently.

12.2

Mitosis

The mitotic phase of the cell cycle is divided into five subphases: prophase, prometaphase, metaphase, anaphase, and telophase. Mitosis represents that part of the cell cycle where the replicated chromosomes are separated into two identical nuclei. The purpose it to transfer the parent's cells genome into two daughter cells. The chromosomes were replicated (copied) in the S phase of interphase. Mitosis can be further broken up into a beginning phase (**karyokinesis** ; prophase, prometaphase, metaphase, anaphase, and telophase) and a later phase (**cytokinesis**).

Prophase . Prophase occurs after the G2 phase and is marked by the disappearance of the nucleolus, nucleus, and organelles such as the Golgi apparatus and the endoplasmic reticulum. The Golgi apparatus and the endoplasmic reticulum disappear by fragmenting and dispersion to the edges or periphery of the cell. The nucleus disappears because the nuclear envelope starts to dissociate into much smaller vesicles and the DNA (chromatin) fibers condense into discrete chromosomes. During prophase centrosomes can also be seen on opposite sides of the cell with extended microtubules between them. The microtubules are formed from tubulin monomers and occur at center of the cells with various tubules attached to chromosomes, and then motor proteins help push the centrosomes to opposite sides of the cell. Interestingly, plants do not appear to use centrosomes and microtubular spindles.

Prometaphase . The migration of the centrosomes along the microtubular complex to opposite poles causes a tension that aligns the chromosomes in the center of the cell. The center region is called the equatorial plane or the metaphase plate. Tension is generated because of structures called kinetochores. During prometaphase, kinetochore structures on microtubules search for and attach to kinetochore structures on chromosomes. Kinetochores are polar protein binding structures. These structures will form mitotic spindles. The attachment of two kinetochore protein structures induces a motor activity that uses ATP to crawl along tubules, pulling the microtubule toward each centrosome.

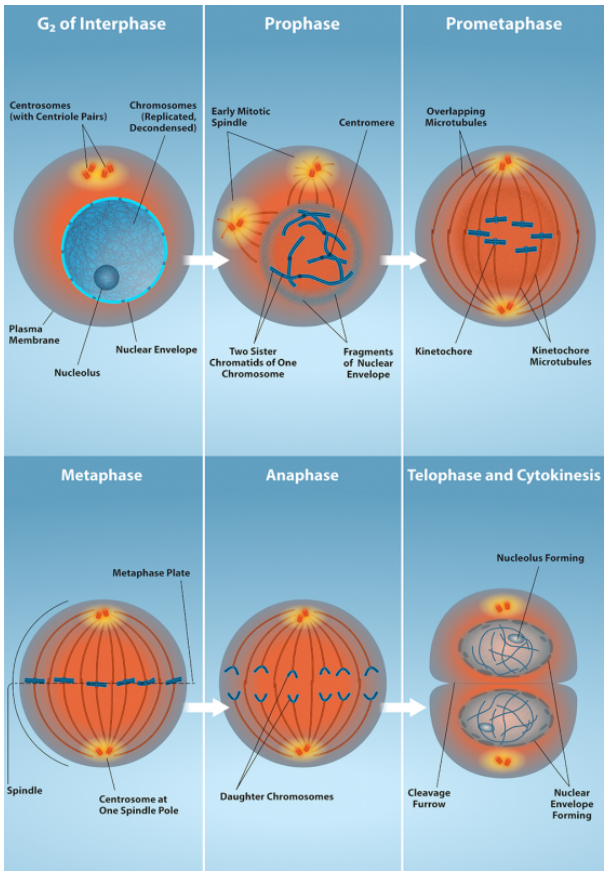
Metaphase . The pulling by the motor proteins on the spindles is most evident in metaphase. The pulling causes the chromosomes to align along the equatorial plate. Although not fully understood, cells have the ability to ensure that the kinetochores are properly attached and that the chromosomes are correctly aligned. This is referred to as the metaphase checkpoint and if deemed correct the cell will proceed to the next phase called anaphase, if not, division will stop. Check points are used throughout the cell cycle to stop the cell cycle if mistakes were made or if external conditions are not favorable for growth. Other checkpoints occur at the end of G1 and at the G2/M transition. The G1 checkpoint is based on environmental conditions, G2/M checkpoint is based on DNA conditions.

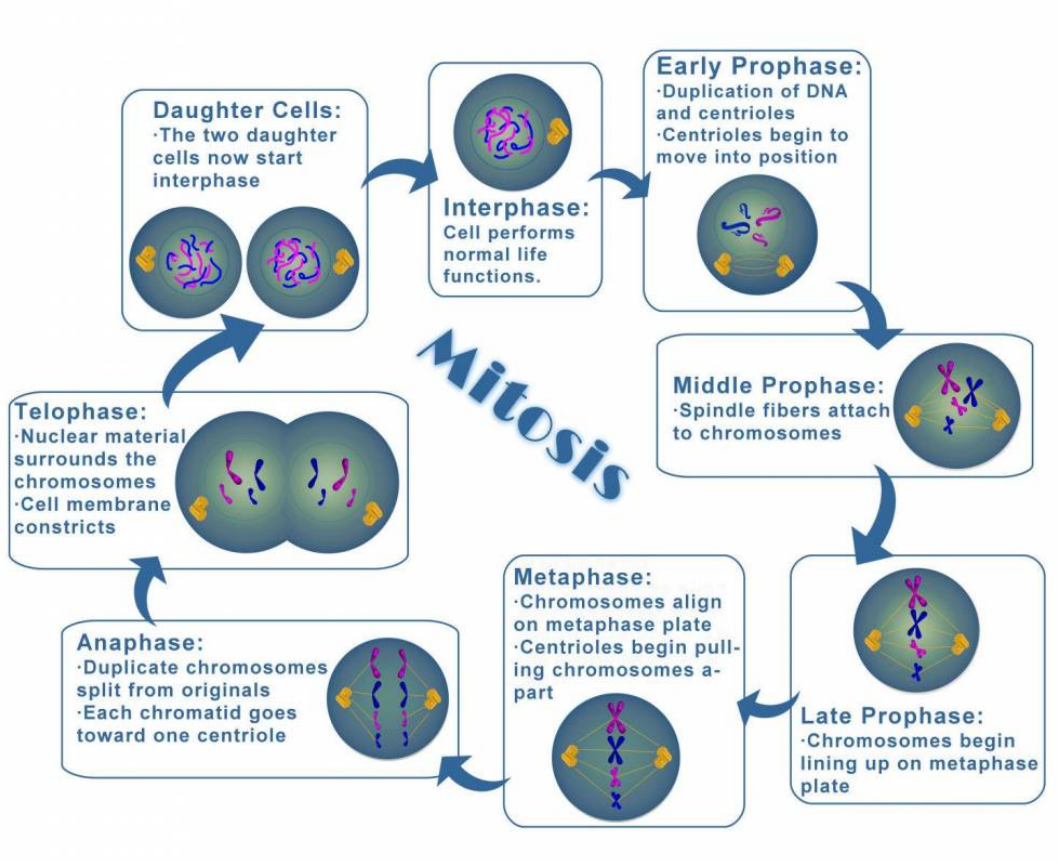
Anaphase . During anaphase the microtubules shorten so much that the sister chromatids start to pull apart. The chromatids can only come apart if the proteins that are linking them together (cohesion proteins) are cleaved. The pulling will also cause the cell to elongate as the sister chromatids are pulled to opposite sides of the cell in preparation to reform within a new nucleus.

Telophase . In telophase, the cell becomes maximally elongated and nuclear envelops begin to reform on each end. The nucleolus reappears and the chromosomes start to decondense. For a brief moment the cell has two nuclei, but the center will soon cleave, leaving two identical daughter cells during cytokinesis.

Cytokinesis . During cytokinesis the cells will cleave in half, forming two identical daughter cells. The cleavage site, located in the center of the cell, is called the cleavage furrow. Vesicles derived from the Golgi apparatus migrate to the middle of the cell and help in the cleavage by forming a contractile ring composed of actin filaments. The actin filaments will pull the cell inward, forming the cleavage furrow. Cytokinesis in plant cells, because of the cell wall, is a more complex process involving enzymes, structural proteins, and glucose molecules need to make a new cell wall and cleavage furrows are not present.

Mitosis





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Binary Fission

12.2.1

Binary Fission

Prokaryote cell division is asexual meaning that the DNA does not have maternal and paternal contributions. In fact, binary fission does not involve chromosomes, but the DNA is still replicated so that when the cell is pulled apart the original and the replicated DNA are separated. This means that the new cells are genetically identical unless errors during replication are made. This process is very fast, allowing prokaryote growth to double each division causing it to have a logarithmic growth cycle. For example, E. coli bacteria cells double every 20 minutes referred to as the **doubling time**. Doubling times varying between different prokaryotes and are dependent upon the availability of nutrients, space, temperature, etc.

12.3

Cancer

Control of cell growth is one of the most important functions for cells to regulate, but despite all the levels of control, errors can still occur, and those errors can result in uncontrolled cell growth, a condition called cancer. A major checkpoint occurs during replication of DNA during the S phase. Still, some errors can be passed on to daughter cells and depending on the type of error, it can result in a gene mutation. These mutations can be passed over and over with each replication, often amplifying the mistake. Mistakes associated with cell cycle control and repair mechanisms can result in uncontrolled cell growth and a tumor. Tumors can be classified as **benign**, **malignant**, or **metastatic** tumors. Benign tumors represent large masses of cells but seem to be somewhat under control of inhibiting factors and stay localized to their tissue type. A benign tumor is not considered cancerous. Malignant tumors start to invade surrounding tissue and since they lose the ability to be regulated, they also lose normal functioning capabilities. Metastatic tumors are like malignant tumors in that they no longer listen to control factors, but they also detach from their sites of origin and can travel to anywhere in the body and start a “new” tumor growth.

12.3.1

Regulating molecules of the Cell Cycle

Molecules that help regulate the cell cycle can be categorized into two groups: positive and negative regulators. Positive regulating molecules help promote movement from one phase to another while negative regulators stop progression. This regulation can occur directly by the molecules themselves or indirectly through a plethora of other pathways.

Positive Regulators. Proteins called cyclins and cylcin-dependent kinases (Cdks) are considered positive cell cycle regulators and act by phosphorylating other proteins. Cyclins are activated in a very predictable manner throughout the cell cycle. The primary form of regulation occurs by altering the concentration of the cyclin/Cdk ratios. As cyclin concentrations fluctuate according to timing events in the cell cycle, different complexes of cyclin/Cdk complexes form which result in different phosphorylation activities. It is the amount and activity of the cyclin/Cdk activities that signal the cell to continue to different phases.

Negative Regulators. There are three negative regulating proteins called retinoblastoma protein (Rb), p53, and p21. These proteins act primarily at the G1 checkpoint. P53 identifies damaged DNA and then stops the cycle and recruits repairing enzymes. If the damage is too extensive, P53 will instead start process that will lead to cell death called **apoptosis**. As the levels of p53 increase, p21 becomes triggered which reinforces the stopping of the cell cycle by inhibiting cyclin/Cdk complexes. The Rb protein monitors cell size because its activity is link to the cell growth. As cell size increases, the Rb protein becomes phosphorylated which inactivates it. When Rb is dephosphorylated, it is active and binds to and inhibits transcription factors. Transcription factors turn on specific genes allowing the production of proteins associated with the gene so if growth is going to continue the negative regulators must not be active.

12.3.2

Proto-oncogenes and Tumor suppressor Genes

Genes that contain instructions to make proteins that will become positive cell cycle regulators are called proto-oncogenes and the genes that contain instruction to make proteins that will become negative cell cycle regulators are called tumor suppressor genes. If a proto-oncogene experiences a mutation that renders the associated protein nonfunctional, the cell would be unlikely to complete the cycle, but a mutation that increases activity of the protein could result in increased cell growth. Likewise, mutated genes associated with negative cell cycle regulators that render the protein inactive are like removing the breaks from an automobile. Indeed, more than half of human tumors show mutated forms of p53 genes!