Bis2A_Singer_Lipids, carbohydrates and nucleic acids

Lipids

Lipids are a diverse group of hydrophobic compounds that include molecules like fats, oils, waxes, phospholipids, and steroids. Most lipids are at their core hydrocarbons, molecules that include many nonpolar carbon-carbon or carbon-hydrogen bonds. The abundance of nonpolar functional groups give lipids a degree of hydrophobic ("water fearing") character and most lipids have low solubility in water. Depending on their physical properties (encoded by their chemical structure), lipids can serve many functions in biological systems including energy storage, insulation, barrier formation, cellular signaling. The diversity of lipid molecules and their range of biological activities are perhaps surprisingly large to most new students of biology. Let's start by developing a core understanding of this class of biomolecules.

Fats and oils

A common fat molecule or **triglyceride**. These types of molecules are hydrophobic and, while they have many functions, are probably best known for their roles in body fat and plant oils. A triglyceride molecule derived from two types of molecular components—a polar "head" group and a nonpolar "tail" group. The "head" group of a triglyceride is derived from a single glycerol molecule. Glycerol, a carbohydrate, is composed of three carbons, five hydrogens, and three hydroxyl (-OH) functional groups. The nonpolar **fatty acid** "tail" group comprises three hydrocarbons (a functional group composed of C-H bonds) that also have a polar carboxyl functional group (hence the term "fatty acid"—the carboxyl group is acidic at most biologically relevant pHs). The number of carbons in the fatty acid may range from 4–36; Most common are those containing 12–18 carbons.
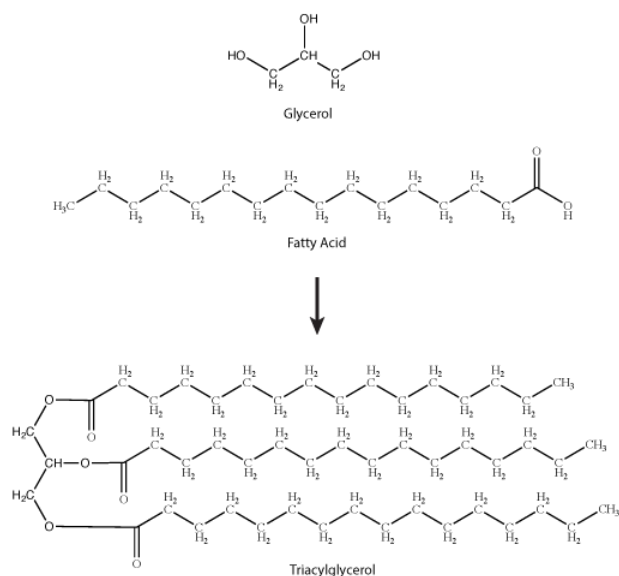
Figure 1. *Triacylglycerol is formed by the joining of three fatty acids to a glycerol backbone in a dehydration reaction. Three molecules of water are released in the process. Attribution: Marc T. Facciotti (own work).*

The models of the triglycerides shown above depict the <u>relative</u> positions of the atoms in the molecule. If you Google for images of triglycerides you will find some models that show the phospholipid tails in different positions from those depicted above. Using your intuition, can you give an opinion for which model you think is a more correct representation of real life? Why?
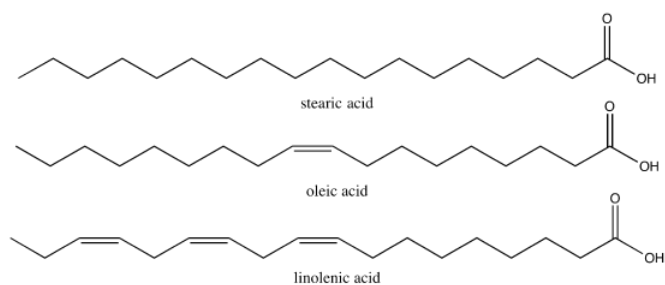

Figure 2. *Stearic acid is a common saturated fatty acid; oleic acid and linolenic acid are common unsaturated fatty acids. Attribution: Marc T. Facciotti (own work)*

Natural fats like butter, canola oil, etc., are composed mostly of triglycerides. The physical properties of these different fats vary depending on two factors:

1. The number of carbons in the hydrocarbon chains;
2. The number of desaturations, or double bonds, in the hydrocarbon chains.

The first factor influences how these molecules interact with each other and with water, while the second factor dramatically

influences their shape. Introducing a double bond causes a "kink" in the otherwise relatively "straight" hydrocarbon, depicted in a slightly exaggerated was in Figure 3.

Based on what you can understand from this brief description, propose a rationale—in your own words—to explain why butter is solid at room temperature while vegetable oil is liquid.

Here is an additional piece of information that could help you answer question: butter has a greater percentage of longer and saturated hydrocarbons in its triglycerides than does vegetable oil.
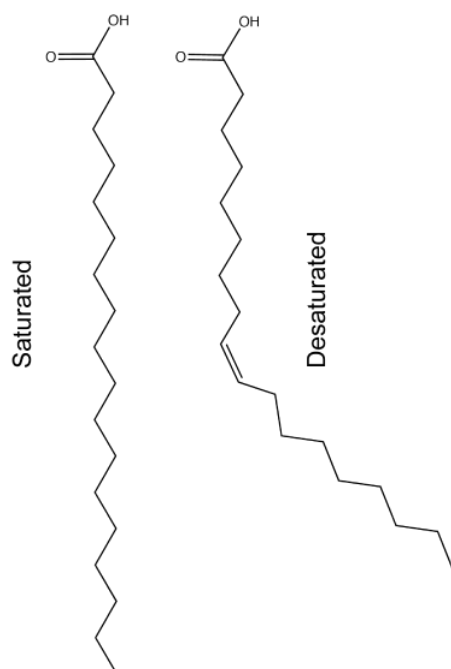

Figure 3. *The straight saturated fatty acid versus the "bent"/"kinked" unsaturated fatty acid. Attribution: Marc T. Facciotti (own work)*

Real-Life connection:

Ever thought about how lipids are important to vision? Read more here.

Sterols

Steroids are lipids with a fused ring structure. Although they do not resemble the other lipids discussed here, they are designated as lipids because they are also largely composed of carbons and hydrogens, are hydrophobic, and are insoluble in water. All steroids have four linked carbon rings. Many steroids also have the -OH functional group which puts them in the alcohol classification of sterols. Several steroids, like cholesterol, have a short tail. Cholesterol is the most common steroid. It is mainly synthesized in the liver and is the precursor to many steroid hormones such as testosterone. It is also the precursor to Vitamin D and of bile salts

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which help in the [emulsification](#) of fats and their subsequent absorption by cells. Although cholesterol is often spoken of in negative terms, it is necessary for the proper functioning of many animal cells, particularly in its role as a component of the plasma membrane where it is known to modulate membrane structure, organization, and fluidity.
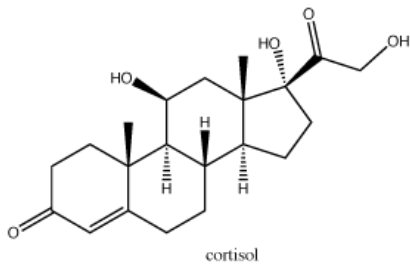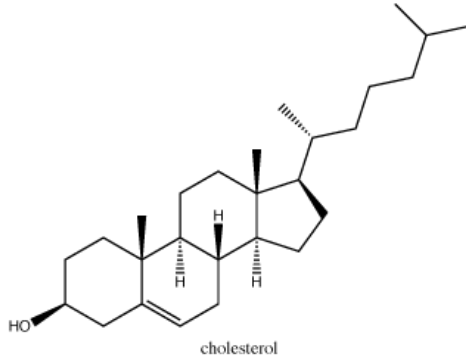

cholesterol

cortisol

Figure 4. *Cholesterol is a modified lipid molecule that is synthesized by animal cells and is a key structural element in cellular membranes. Cortisol is a hormone (signaling molecule) that is often released in response to stress. Attribution: Marc T. Facciotti (own work)*
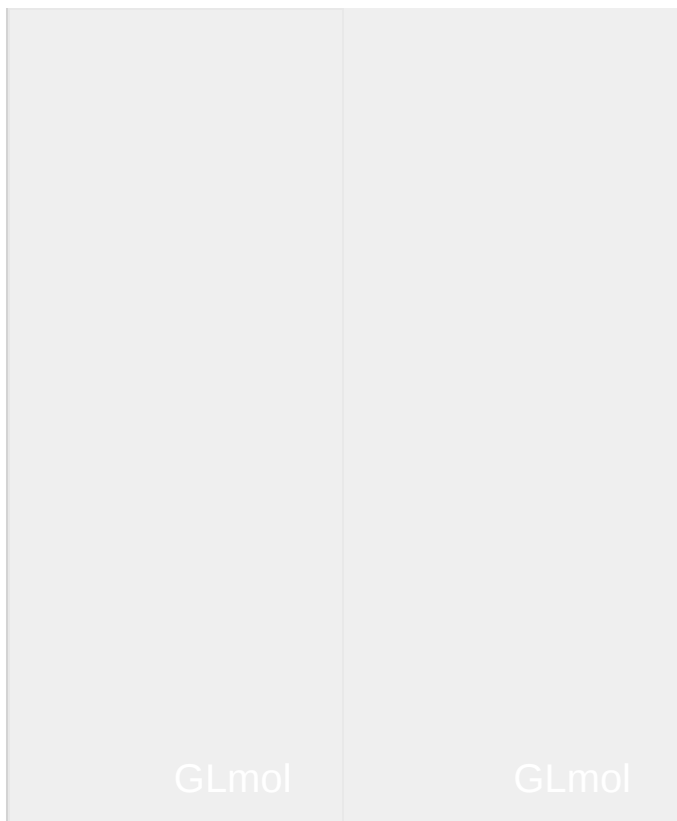
Cholesterol	Cortisol

Phospholipids

Phospholipids are major constituents of the cell membrane, the outermost layer of cells. Like fats, they are composed of fatty acid chains attached to a glycerol molecule. Unlike the triacylglycerols, phospholipids have two fatty acid tails and a phosphate group attached to the sugar. Phospholipid are therefore **amphipathic** molecules, meaning it they have a hydrophobic part and a hydrophilic part. The two fatty acid chains extending from the glycerol are hydrophobic and cannot interact with water, whereas the phosphate-containing head group is hydrophilic and interacts with water. Can you identify the functional groups on the phospholipid below that give each part of the phospholipid its properties?

> **Note**
>
> Note in Figure 5 that the phosphate group has an R group linked to one of the oxygen atoms. R is a variable commonly used in these types of diagrams to show some other atom or molecule bound at that position. That part of the molecule can be different in different phospholipids—and will impart some different chemistry to the whole molecule. At the moment, however, you are responsible for being able to recognize this type of molecule (no matter what the R group is) because of the common core elements—the glycerol backbone, the phosphate group, and the two hydrocarbon tails.
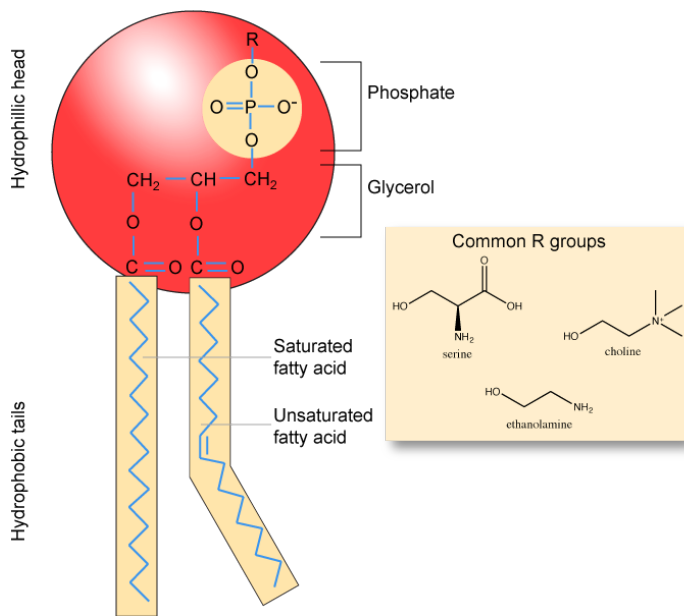
Figure 5. *A phospholipid is a molecule with two fatty acids and a modified phosphate group attached to a glycerol backbone. The phosphate may be modified by the addition of charged or polar chemical groups. Several chemical R groups may modify the phosphate. Choline, serine, and ethanolamine are shown here. These attach to the phosphate group at the position labeled R via their hydroxyl groups.*
Attribution: Marc T. Facciotti (own work).
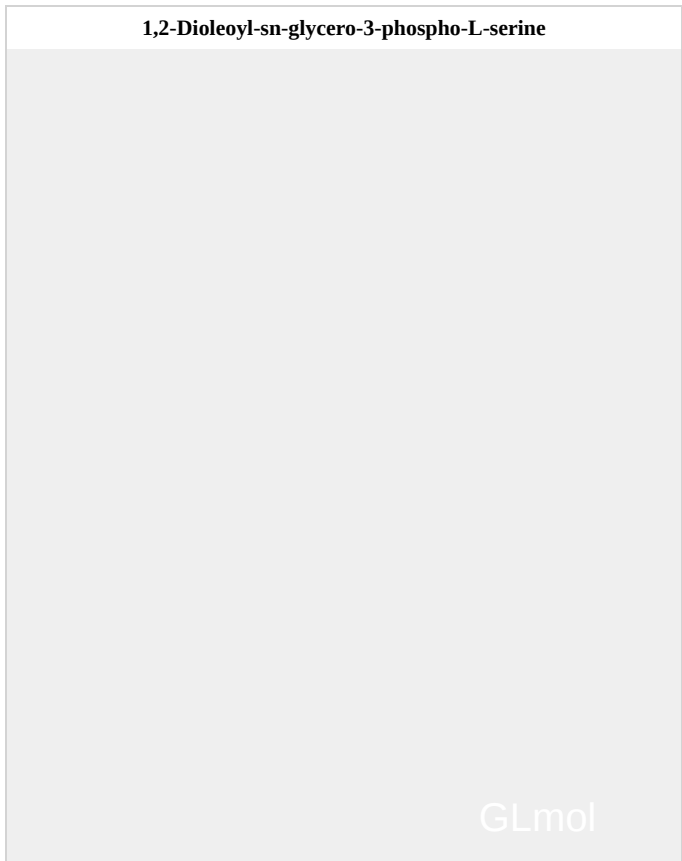
1,2-Dioleoyl-sn-glycero-3-phospho-L-serine

In the presence of water, some phospholipids will spontaneously arrange themselves into a micelle (Figure 6). The lipids arrange such that their polar groups are on the outside of the micelle, and the nonpolar tails are on the inside. Under other conditions, a lipid bilayer can also form. This structure, only a few nanometers thick, is composed of two opposing layers of phospholipids such that all the hydrophobic tails align face-to-face in the center of the bilayer and are surrounded by the hydrophilic head groups. A phospholipid bilayer forms as the basic structure of most cell membranes and are responsible for the dynamic nature of the plasma membrane.
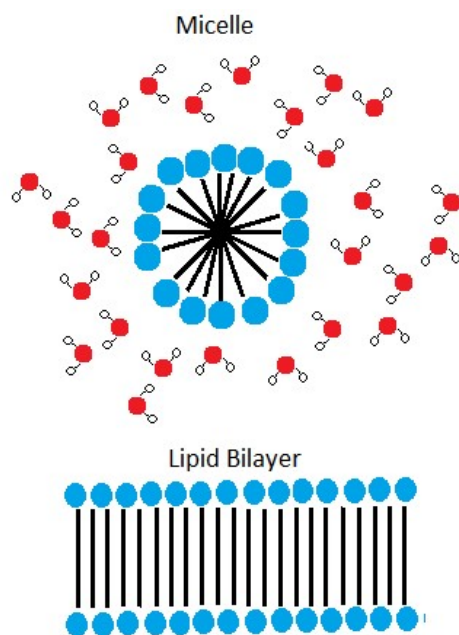

Figure 6. *In the presence of water, some phospholipids will spontaneously arrange themselves into a micelle. Source: Created by Erin Easlon (own work)*

As mentioned above, if you were to take some pure phospholipids and drop them into water that some phospholipid would spontaneously form into micelles. This sounds like a process that an Energy Story could describe. Go back to the Energy Story rubric and see if you can try to create an Energy Story for this process — I expect that the steps involving the description of energy might be difficult at this point (we'll come back to that later) but you should be able to do at least the first three steps.

We discuss the phospholipid membrane in a later module. It is important to remember the chemical properties associated with the functional groups in the phospholipid to understand the function of the cell membrane.

Carbohydrates

Carbohydrates are one of the four main classes of macromolecules that make up all cells and are an essential part of our diet; grains, fruits, and vegetables are all natural sources. While we may be most

familiar with the role carbohydrates play in nutrition, they also have a variety of other essential functions in humans, animals, plants, and bacteria. In this section, we will discuss and review basic concepts of carbohydrate structure and nomenclature, and a variety of functions they play in cells.

Molecular structures

In their simplest form, **carbohydrates** can be represented by the stoichiometric formula $(CH_2O)_n$, where n is the number of carbons in the molecule. For simple carbohydrates, the ratio of carbon-to-hydrogen-to-oxygen in the molecule is 1:2:1. This formula also explains the origin of the term "carbohydrate": the components are carbon ("carbo") and the components of water ("hydrate"). Simple carbohydrates are classified into three subtypes: monosaccharides, disaccharides, and polysaccharides, which will be discussed below. While simple carbohydrates fall nicely into this 1:2:1 ratio, carbohydrates can also be structurally more complex. For example, many carbohydrates contain functional groups (remember them from our basic discussion about chemistry) besides the obvious hydroxyl. For example, carbohydrates can have phosphates or amino groups substituted at a variety of sites within the molecule. These functional groups can provide additional properties to the molecule and will alter its overall function. However, even with these types of substitutions, the basic overall structure of the carbohydrate is retained and easily identified.

Nomenclature

One issue with carbohydrate chemistry is the nomenclature. Here are a few quick and simple rules:

1. Simple carbohydrates, such as glucose, lactose, or dextrose, end with an "-ose."
2. Simple carbohydrates can be classified based on the number of carbon atoms in the molecule, as with triose (three carbons), pentose (five carbons), or hexose (six carbons).
3. Simple carbohydrates can be classified based on the functional group found in the molecule, i.e ketose (contains a ketone) or aldose (contains an aldehyde).
4. Polysaccharides are often organized by the number of sugar molecules in the chain, such as in a monosaccharide, disaccharide, or trisaccharide.

For a short video on carbohydrate classification, see the 10-minute Khan Academy video by clicking here.

Monosaccharides

Monosaccharides ("mono-" = one; "sacchar-" = sweet) are simple sugars; the most common is glucose. In monosaccharides, the number of carbons usually ranges from three to seven. If the sugar has an aldehyde group (the functional group with the structure R-CHO), it is known as an aldose; if it has a ketone group (the

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functional group with the structure RC(=O)R'), it is known as a ketose.
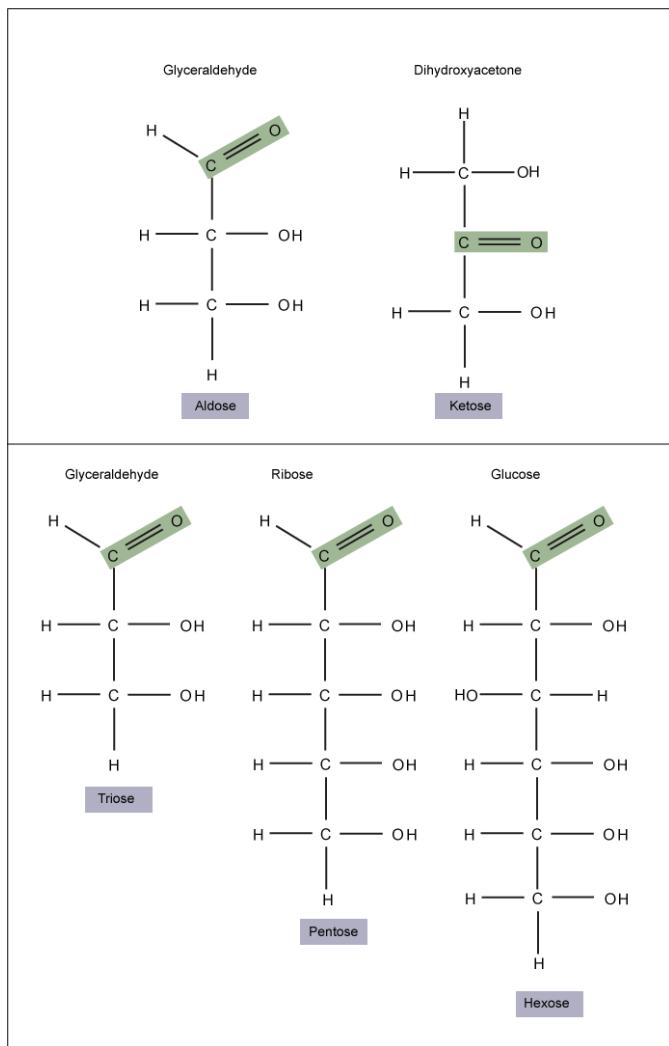

Figure 1. *Monosaccharides are classified based on the position of their carbonyl group and the number of carbons in the backbone. Aldoses have a carbonyl group (indicated in green) at the end of the carbon chain and ketoses have a carbonyl group in the middle of the carbon chain. Trioses, pentoses, and hexoses have three, five, and six carbons in their backbones, respectively. Attribution: Marc T. Facciotti (own work).*

Glucose versus galactose

Galactose (part of lactose, or milk sugar) and **glucose** (found in sucrose, glucose disaccharride) are other common monosaccharides. The chemical formula for glucose and galactose is $C_6H_{12}O_6$; both are hexoses, but the arrangements of the hydrogens and hydroxyl groups are different at position C_4. Because of this small difference, they differ structurally and chemically and are known as chemical isomers because of the different arrangement of functional groups around the asymmetric carbon; both of these monosaccharides have more than one asymmetric carbon (compare the structures in the figure below).

Fructose versus both glucose and galactose

A second comparison can be made when looking at glucose, galactose, and **fructose** (the second carbohydrate that with glucose makes up the disaccharide sucrose and is a common sugar found in fruit). All three are hexoses; however, there is a major structural difference between glucose and galactose versus fructose: the carbon that contains the **carbonyl** (C=O).

In glucose and galactose, the carbonyl group is on the C_1 carbon, forming an **aldehyde** group. In fructose, the carbonyl group is on the C_2 carbon, forming a **ketone** group. The former sugars are called **aldoses** based on the aldehyde group that is formed; the latter is designated as a **ketose** based on the ketone group. Again, this difference gives fructose different chemical and structural properties from those of the aldoses, glucose, and galactose, even though fructose, glucose, and galactose all have the same chemical composition: $C_6H_{12}O_6$.
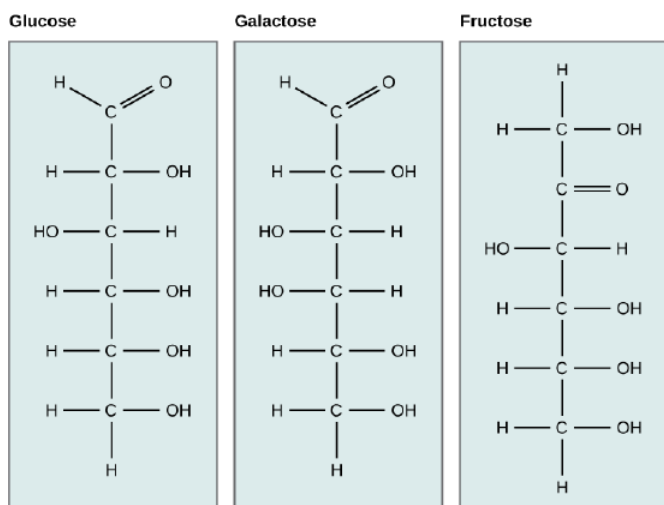

Figure 2. *Glucose, galactose, and fructose are all hexoses. They are structural isomers, meaning they have the same chemical formula ($C_6H_{12}O_6$) but a different arrangement of atoms.*

Linear versus ring form of the monosaccharides

Monosaccharides can exist as a linear chain or as ring-shaped molecules. In aqueous solutions, monosaccharides are usually found in ring form (Figure 3). Glucose in a ring form can have two different arrangements of the hydroxyl group (OH) around the anomeric carbon (C_1 that becomes asymmetric in the process of ring formation). If the hydroxyl group is below C_1 in the sugar, it is said to be in the alpha (α) position, and if it is above C_1 in the sugar, it is said to be in the beta (β) position.
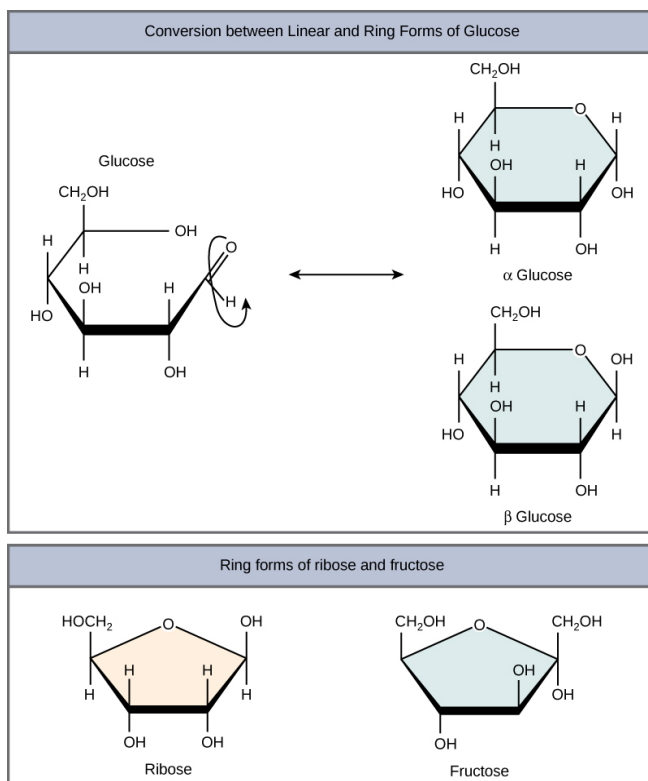
Figure 3. *Five- and six-carbon monosaccharides exist in equilibrium between linear and ring form. When the ring forms, the side chain it closes on is locked into an α or β position. Fructose and ribose also form rings, although they form five-membered rings as opposed to the six-membered ring of glucose.*

Disaccharides

Disaccharides ("di-" = two) form when two monosaccharides undergo a dehydration reaction (also known as a condensation reaction or dehydration synthesis). During this process, the hydroxyl group of one monosaccharide combines with the hydrogen of another monosaccharide, releasing a molecule of water and forming a covalent bond. A covalent bond formed between a carbohydrate molecule and another molecule (in this case, between two monosaccharides) is known as a **glycosidic** bond. Glycosidic bonds (also called glycosidic linkages) can be of the alpha or the beta type.
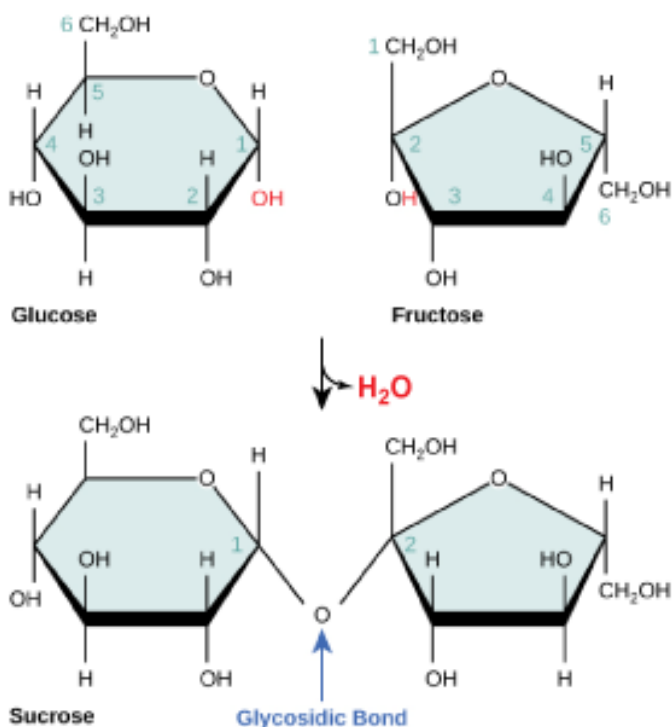
Figure 4. *Sucrose is formed when a monomer of glucose and a monomer of fructose are joined in a dehydration reaction to form a glycosidic bond. In the process, a water molecule is lost. By convention, the carbon atoms in a monosaccharide are numbered from the terminal carbon closest to the carbonyl group. In sucrose, a glycosidic linkage is formed between the C_1 carbon in glucose and the C_2 carbon in fructose.*
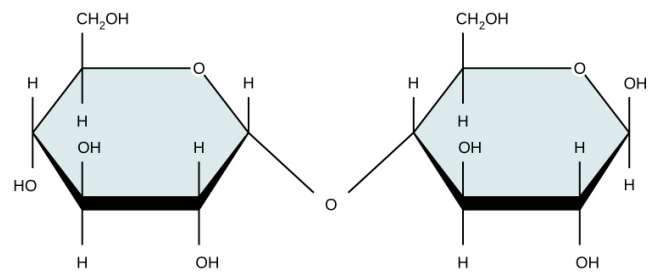
Common disaccharides include lactose, maltose, and sucrose (Figure 5). Lactose is a disaccharide consisting of the monomers glucose and galactose. It is found naturally in milk. Maltose, or malt/grain sugar, is a disaccharide formed by a dehydration reaction between two glucose molecules. The most common disaccharide is sucrose, or table sugar, which is composed of the monomers glucose and fructose.
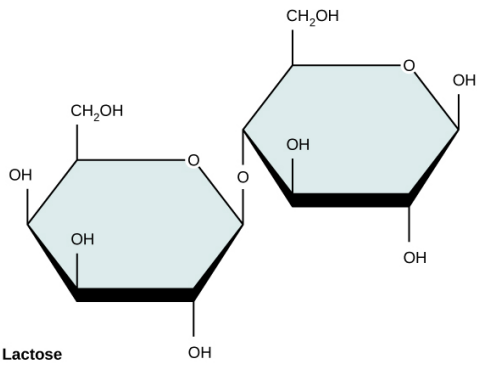
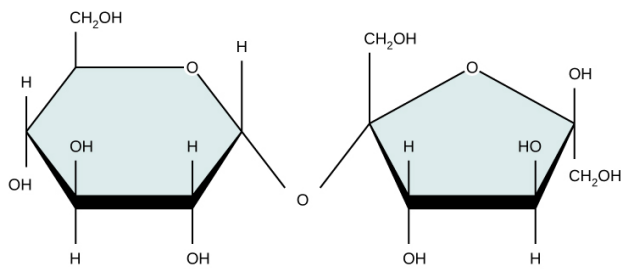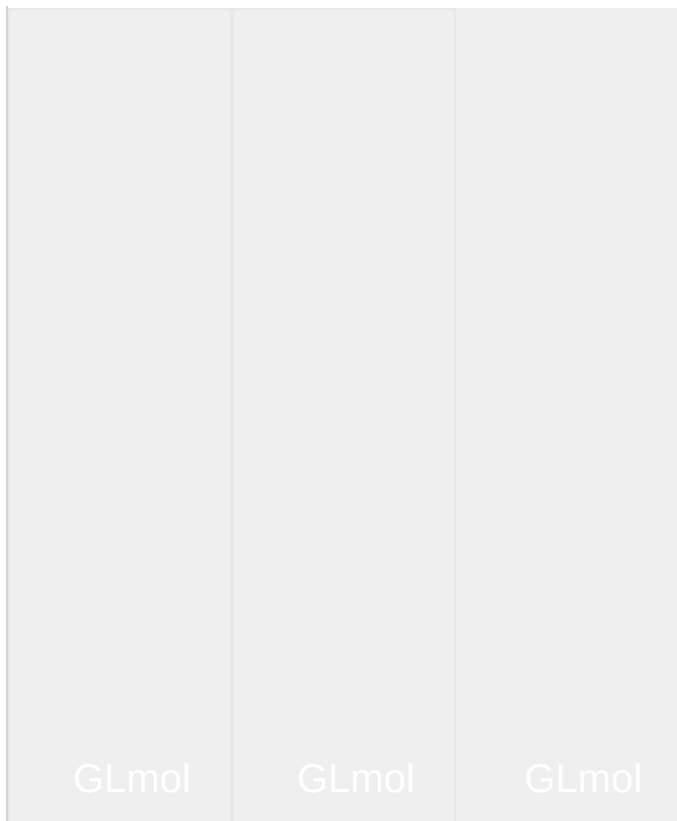**Figure 5.** *Common disaccharides include maltose (grain sugar), lactose (milk sugar), and sucrose (table sugar).*

Sucrose	Lactose	Maltose

Polysaccharides

A long chain of monosaccharides linked by glycosidic bonds is known as a **polysaccharide** ("poly-" = many). The chain may be branched or unbranched, and it may contain different types of monosaccharides. The molecular weight may be 100,000 Daltons or more, depending on the number of monomers joined. Starch, glycogen, cellulose, and chitin are primary examples of polysaccharides.

Starch is the stored form of sugars in plants and is made up of a mixture of amylose and amylopectin; both are polymers of glucose. Plants are able to synthesize glucose. Excess glucose, the amount synthesized that is beyond the plant's immediate energy needs, is stored as starch in different plant parts, including roots and seeds. The starch in the seeds provides food for the embryo as it germinates and can also act as a source of food for humans and animals who may eat the seed. Starch that is consumed by humans is broken down by enzymes, such as salivary amylases, into smaller molecules, such as maltose and glucose.

Starch is made up of glucose monomers that are joined by 1-4 or 1-6 glycosidic bonds; the numbers 1-4 and 1-6 refer to the carbon number of the two residues that have joined to form the bond. As illustrated in Figure 6, amylose is starch formed by unbranched chains of glucose monomers (only 1-4 linkages), whereas amylopectin is a branched polysaccharide (1-6 linkages at the branch points).
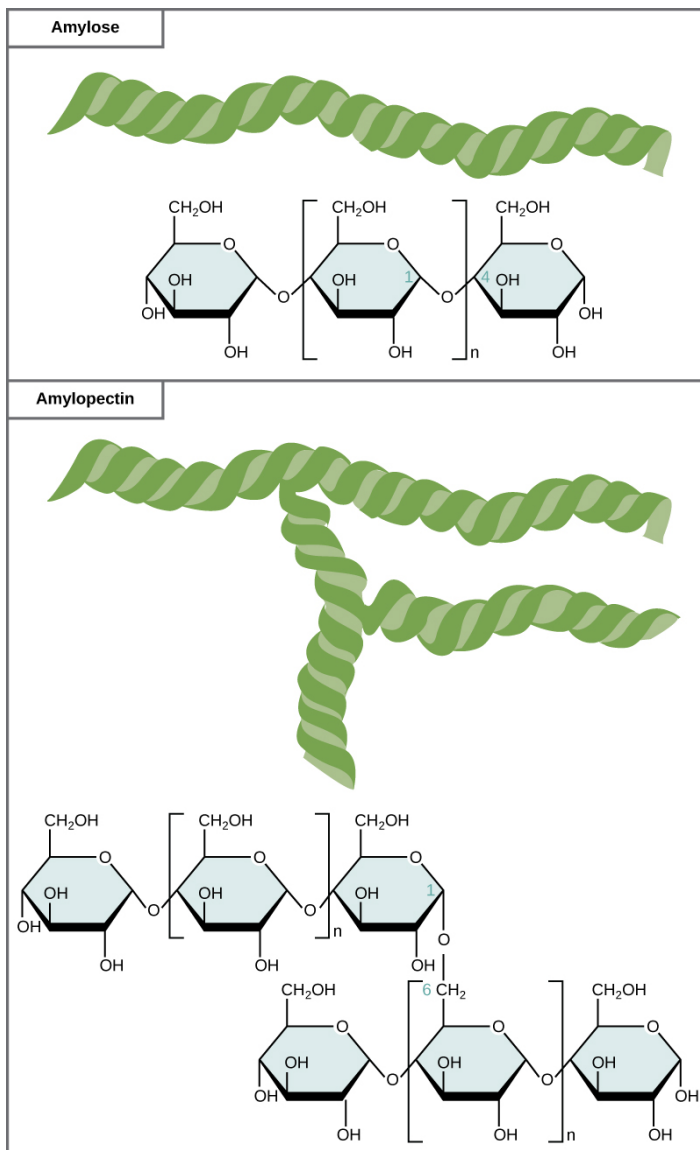
Figure 6. *Amylose and amylopectin are two different forms of starch. Amylose is composed of unbranched chains of glucose monomers connected by 1-4 glycosidic linkages. Amylopectin is composed of branched chains of glucose monomers connected by 1-4 and 1-6 glycosidic linkages. Because of the way the subunits are joined, the glucose chains have a helical structure. Glycogen (not shown) is similar in structure to amylopectin but more highly branched.*

Glycogen

Glycogen is a common stored form of glucose in humans and other vertebrates. Glycogen is the animal equivalent of starch and is a highly branched molecule usually stored in liver and muscle cells. Whenever blood glucose levels decrease, glycogen is broken down to release glucose in a process known as glycogenolysis.
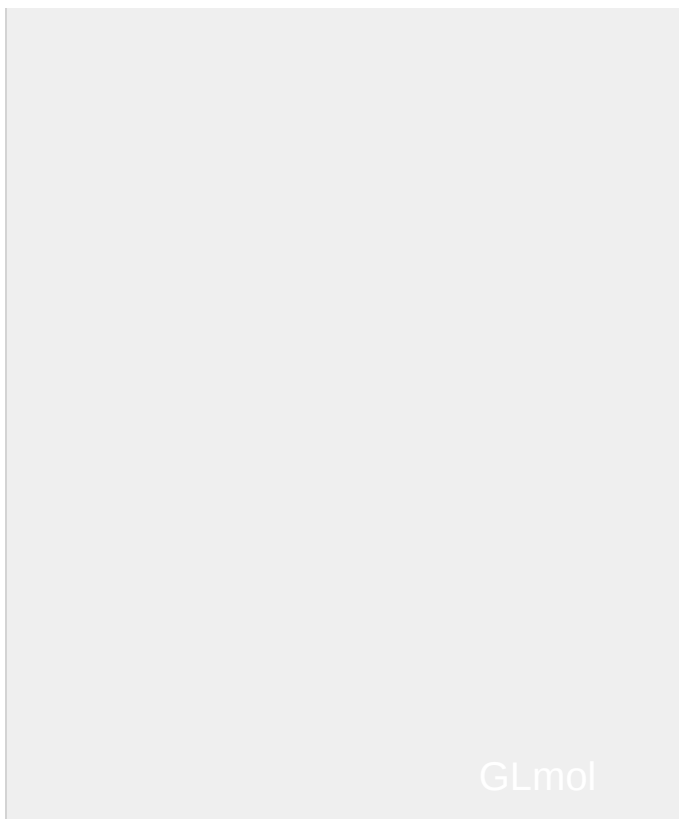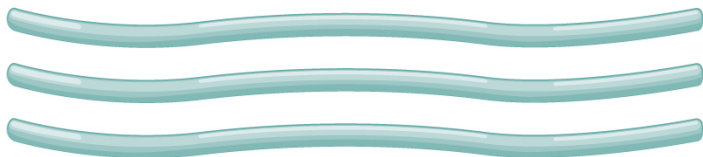
Glycogen

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Cellulose

Cellulose is the most abundant natural biopolymer. The cell wall of plants is mostly made of cellulose, which provides structural support to the cell. Wood and paper are mostly cellulosic in nature. Cellulose is made up of glucose monomers that are linked by β 1-4 glycosidic bonds.

Cellulose fibers

Cellulose structure
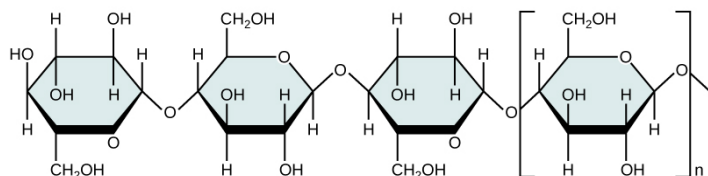

Figure 7. *In cellulose, glucose monomers are linked in unbranched chains by β 1-4 glycosidic linkages. Because of the way the glucose subunits are joined, every glucose monomer is flipped relative to the next one, resulting in a linear, fibrous structure.*

As shown in the figure above, every other glucose monomer in cellulose is flipped over, and the monomers are packed tightly as

extended, long chains. This gives cellulose its rigidity and high tensile strength—which is so important to plant cells. While the β 1-4 linkage cannot be broken down by human digestive enzymes, herbivores such as cows, koalas, buffalos, and horses are able, with the help of the specialized flora in their stomach, to digest plant material that is rich in cellulose and use it as a food source. In these animals, certain species of bacteria and protists reside in the rumen (part of the digestive system of herbivores) and secrete the enzyme cellulase. The appendix of grazing animals also contains bacteria that digest cellulose, giving it an important role in the digestive systems of ruminants. Cellulases can break down cellulose into glucose monomers that can be used as an energy source by the animal. Termites are also able to break down cellulose because of the presence of other organisms in their bodies that secrete cellulases.

Interactions with carbohydrates

We have just discussed the various types and structures of carbohydrates found in biology. The next thing to address is how these compounds interact with other compounds. The answer to that is that it depends on the final structure of the carbohydrate. Because carbohydrates have many hydroxyl groups associated with the molecule, they are therefore excellent **H-bond donors** and **acceptors**. Monosaccharides can quickly and easily form H-bonds with water and are readily soluble. All of those H-bonds also make them quite "sticky". This is also true for many disaccharides and many short-chain polymers. Longer polymers may not be readily soluble.

Finally, the ability to form a variety of H-bonds allows polymers of carbohydrates or **polysaccharides** to form strong intramolecular and intermolocular bonds. In a polymer, because there are so many H-bonds, this can provide a lot of strength to the molecule or molecular complex, especially if the polymers interact. Just think of cellulose, a polymer of glucose, if you have any doubts.

Possible NB Discussion Point

Lipids and carbohydrates are not just classes of macromolecules that we discuss in BIS 2A but are also two of the essential macronutrients that we can obtain from eating various foods. Some popularized diet programs (e.g., Atkins, ketogenic) suggest limiting carbohydrates and/or fats. As you learn more about biomolecules and their roles in living systems, are you refining your perspective on foods and diets? What have you learned so far? Do you think there is anything missing in your understanding? Are you able to better understand and evaluate certain diets, such as the aforementioned?

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Nucleic acids

There are two types of nucleic acids in biology: DNA and RNA. DNA carries the heritable genetic information of the cell and is composed of two antiparallel strands of nucleotides arranged in a helical structure. Each nucleotide subunit is composed of a pentose sugar (deoxyribose), a nitrogenous base, and a phosphate group. The two strands associate via hydrogen bonds between chemically complementary nitrogenous bases. Interactions known as "base stacking" interactions also help stabilize the double helix. By contrast to DNA, RNA can be either be single stranded, or double stranded. It too is composed of a pentose sugar (ribose), a nitrogenous base, and a phosphate group. RNA is a molecule of many tricks. It is involved in protein synthesis as a messenger, regulator, and catalyst of the process. RNA is also involved in various other cellular regulatory processes and helps to catalyze some key reactions (more on this later). With respect to RNA, in this course we are primarily interested in (a) knowing the basic molecular structure of RNA and what distinguishes it from DNA, (b) understanding the basic chemistry of RNA synthesis that occurs during a process called transcription, (c) appreciating the various roles that RNA can have in the cell, and (d) learning the major types of RNA that you will encounter most frequently (i.e. mRNA, rRNA, tRNA, miRNA etc.) and associating them with the processes they are involved with. In this module we focus primarily on the chemical structures of DNA and RNA and how they can be distinguished from one another.

Nucleotide structure

The two main types of nucleic acids are **deoxyribonucleic acid (DNA)** and **ribonucleic acid (RNA)**. DNA and RNA are made up of monomers known as **nucleotides**. Individual nucleotides condense with one another to form a **nucleic acid** polymer. Each nucleotide is made up of three components: a nitrogenous base (for which there are five different types), a pentose sugar, and a phosphate group. These are depicted below. The main difference between these two types of nucleic acids is the presence or absence of a hydroxyl group at the C_2 position, also called the 2' position (*read "two prime"*), of the pentose (see Figure 1 legend and the section on the pentose sugar for more on carbon numbering). RNA has a hydroxyl functional group at that 2' position of the pentose sugar; the sugar is called ribose, hence the name ribonucleic acid. By contrast, DNA lacks the hydroxyl group at that position, hence the name, "deoxy" ribonucleic acid. DNA has a hydrogen atom at the 2' position.
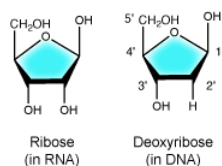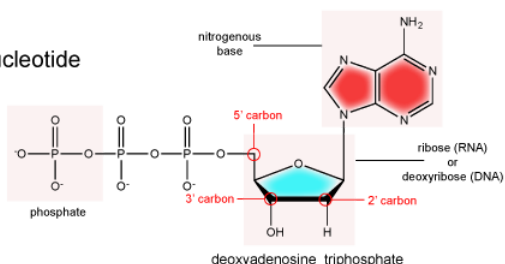
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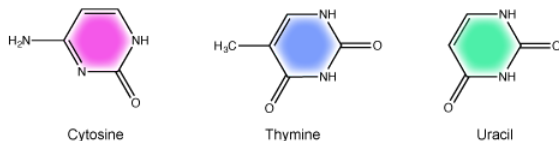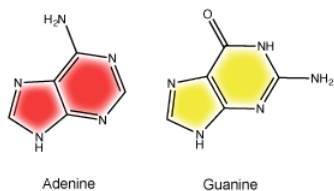
Figure 1. *A nucleotide is made up of three components: a nitrogenous base, a pentose sugar, and one or more phosphate groups. Carbons in the pentose are numbered 1' through 5' (the prime distinguishes these residues from those in the base, which are numbered without using a prime notation). The base is attached to the 1' position of the ribose, and the phosphate is attached to the 5' position. When a polynucleotide is formed, the 5' phosphate of the incoming nucleotide attaches to the 3' hydroxyl group at the end of the growing chain. Two types of pentose are found in nucleotides, deoxyribose (found in DNA) and ribose (found in RNA). Deoxyribose is similar in structure to ribose, but it has an -H instead of an -OH at the 2' position. Bases can be divided into two categories: purines and pyrimidines. Purines have a double ring structure, and pyrimidines have a single ring.*
Attribution: Marc T. Facciotti (original work)

The nitrogenous base

The nitrogenous bases of nucleotides are organic molecules and are so named because they contain carbon and nitrogen. They are bases because they contain an amino group that has the potential of binding an extra hydrogen, and thus acting as a base by decreasing the hydrogen ion concentration in the local environment. Each nucleotide in DNA contains one of four possible nitrogenous bases: adenine (A), guanine (G), cytosine (C), and thymine (T). By contrast, RNA contains adenine (A), guanine (G) cytosine (C), and uracil (U) instead of thymine (T).

Adenine and guanine are classified as **purines**. The primary distinguishing structural feature of a purine is double carbon-nitrogen ring. Cytosine, thymine, and uracil are classified as **pyrimidines**. These are structurally distinguished by a single carbon-nitrogen ring. You will be expected to recognize that each of these ring structures is decorated by functional groups that may be involved in a variety of chemistries and interactions.

Possible NB Discussion Point

Take a moment to review the five nitrogenous bases in Figure 1 above. Identify functional groups as described in class. For each functional group identified, describe what type(s) of chemistry you expect it to be involved in. Will the functional group act as a hydrogen bond donor, acceptor, or both?

The pentose sugar

The pentose sugar contains five carbon atoms. Each carbon atom of the sugar molecule are numbered as 1′, 2′, 3′, 4′, and 5′ (1′ is read as "one prime"). The two main functional groups that are attached to the sugar are often named in reference to the carbon to which they are bound. For example, the phosphate residue is attached to the 5′ carbon of the sugar and the hydroxyl group is attached to the 3′ carbon of the sugar. We will often use the carbon number to refer to functional groups on nucleotides so be very familiar with the structure of the pentose sugar.

The pentose sugar in DNA is called deoxyribose, and in RNA, the sugar is ribose. The difference between the sugars is the presence of the hydroxyl group on the 2' carbon of the ribose and its absence on the 2' carbon of the deoxyribose. You can, therefore, determine if you are looking at a DNA or RNA nucleotide by the presence or absence of the hydroxyl group on the 2' carbon atom—you will probably be asked to do so on numerous occasions, including exams.

The phosphate group

There can be anywhere between one and three phosphate groups bound to the 5' carbon of the sugar. When one phosphate is bound, the nucleotide is referred to as a Nucleotide MonoPhosphate (NMP). If two phosphates are bound the nucleotide is referred to as Nucleotide DiPhosphate (NDP). When three phosphates are bound to the nucleotide it is referred to as a Nucleotide TriPhosphate (NTP). The phosphoanhydride bonds between that link the phosphate groups to each other have specific chemical properties that make them good for various biological functions. The hydrolysis of the bonds between the phosphate groups is thermodynamically exergonic in biological conditions; Nature has evolved many mechanisms to couple this negative change in free energy to help drive many reactions in the cell. Figure 2 shows the structure of the nucleotide triphosphate Adenosine Triphosphate, ATP, which we will discuss in greater detail in other chapters.

> ### Note: "high-energy" bonds
>
> The term "high-energy bond" is used A LOT in biology. This term is, however, a verbal shortcut that can cause some confusion. The term refers to the amount of negative free energy associated with the hydrolysis of the bond in question. The water

(or other equivalent reaction partner) is an important contributor to the energy calculus. In ATP, for instance, simply "breaking" a phosphoanhydride bond - say with imaginary molecular tweezers - by pulling off a phosphate would not be energetically favorable. We must therefore be careful not to say that breaking bonds in ATP is energetically favorable or that it "releases energy". Rather, we should be more specific, noting that the hydrolysis of the bond is energetically favorable. Some of this common misconception is tied to, in our opinion, the use of the term "high-energy bonds". While in Bis2a we have tried to minimize the use of the vernacular "high energy" when referring to bonds, trying instead to describe biochemical reactions by using more specific terms, as students of biology you will no doubt encounter the potentially misleading - though admittedly useful - shortcut "high-energy bond" as you continue in your studies. So, keep the above in mind when you are reading or listening to various discussions in biology. Heck, use the term yourself. Just make sure that you really understand what it refers to.
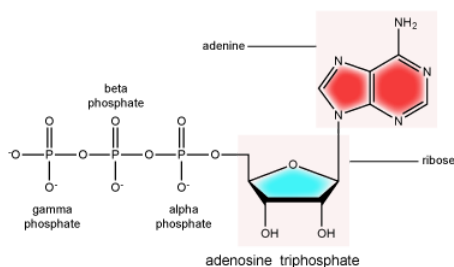

Figure 2. *ATP (adenosine triphosphate) has three phosphate groups that can be removed by hydrolysis to form ADP (adenosine diphosphate) or AMP (adenosine monophosphate). Attribution: Marc T. Facciotti (original work)*
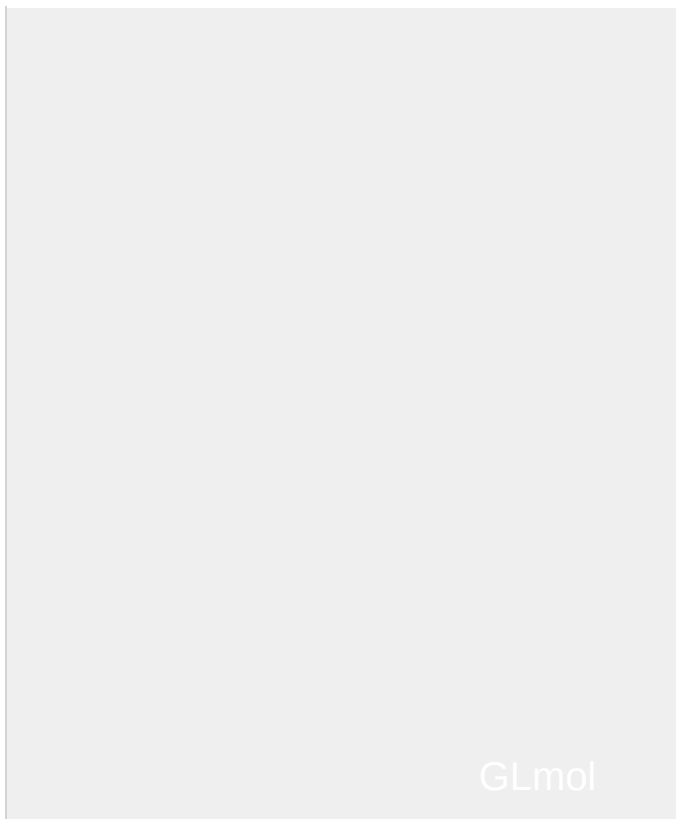
Adenosine triphosphate

GLmol

Double helix structure of DNA

DNA has a double helix structure (shown below) created by two strands of covalently linked nucleotide subunits. The sugar and phosphate groups of each strand of nucleotides are positioned on the outside of the helix, forming the backbone of the DNA (highlighted by the orange ribbons in Figure 3). The two strands of the helix run in opposite directions, meaning that the 5′ carbon end of one strand will face the 3′ carbon end of its matching strand (See Figures 4 and 5). We referred to this orientation of the two strands as **antiparallel**. Note too that phosphate groups are depicted in Figure 3 as orange and red "sticks" protruding from the ribbon. The phosphates are negatively charged at physiological pHs and therefore give the backbone of the DNA a strong local negatively charged character. By contrast, the nitrogenous bases are stacked in the interior of the helix (these are depicted as green, blue, red, and white sticks in Figure 3). Pairs of nucleotides interact with one another through specific hydrogen bonds (shown in Figure 5). Each pair of separated from the next base pair in the ladder by 0.34 nm and this close stacking and planar orientation gives rise to energetically favorable base-stacking interactions. The specific chemistry associated with these interactions is beyond the content of Bis2a but is described in more detail here for the curious or more advanced students. We do expect, however, that students are aware

that the stacking of the nitrogenous bases contributes to the stability of the double helix and defer to your upper-division genetics and organic chemistry instructors to fill in the chemical details.
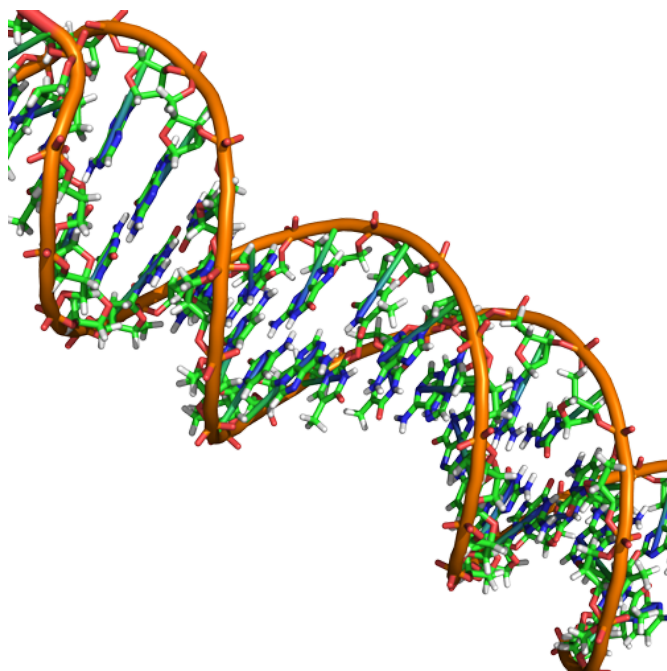

Figure 3. *Native DNA is an antiparallel double helix. The phosphate backbone (indicated by the curvy lines) is on the outside, and the bases are on the inside. Each base from one strand interacts via hydrogen bonding with a base from the opposing strand. Attribution: Marc T. Facciotti (original work)*

In a double helix, certain combinations of base pairing are chemically more favored than others based on the types and locations of functional groups on the nitrogenous bases of each nucleotide. In biology we find that:

Adenine (A) is chemically complementary with thymidine (T) (A pairs with T)

and

Guanine (G) is chemically complementary with cytosine (C) (G pairs with C).

We often refer to this pattern as "base complementarity" and say that the antiparallel strands are **complementary** to each other. For example, if the sequence of one strand is of DNA is 5'-AATTGGCC-3', the complementary strand would have the sequence 5'-GGCCAATT-3'.

We sometimes choose to represent complementary double-helical structures in text by stacking the complementary strands on top of on another as follows:

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5' - GGCCAATTCCATACTAGGT - 3'
3' - CCGGTTAAGGTATGATCCA - 5'
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Note that each strand has its 5' and 3' ends labeled and that if one were to walk along each strand starting from the 5' end to the 3' end that the direction of travel would be opposite the other for each strand; the strands are antiparallel. We commonly say things like "running 5-prime to 3-prime" or "synthesized 5-prime to 3-prime" to refer to the direction we are reading a sequence or the direction of synthesis. Start getting yourself accustomed to this nomenclature.
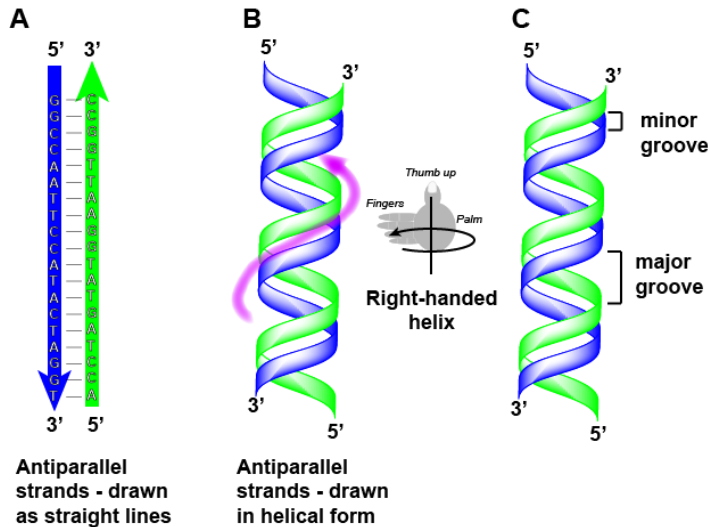
A

Antiparallel strands - drawn as straight lines

B

Thumb up

Fingers

Palm

Right-handed helix

Antiparallel strands - drawn in helical form

C

minor groove

major groove

Figure 4. *Panel A. In a double-stranded DNA molecule, the two strands run antiparallel to one another so that one strand runs 5' to 3' and the other 3' to 5'. Here the strands are depicted as blue and green lines pointing in the 5' to 3' orientation. Complementary base pairing is depicted with a horizontal line between complementary bases. Panel B. The two antiparallel strands are depicted in double-helical form. Note that the orientation of the strands is still represented. Note that the helix is right-handed - the "curl" of the helix, depicted in purple, winds in the direction of the fingers of the hand if the right hand is used and the direction of the helix points towards the thumb. Panel C. This representation shows two structural features that arise from the assembly of the two strands called the major and minor grooves. These grooves can also be seen in Figure 3.*
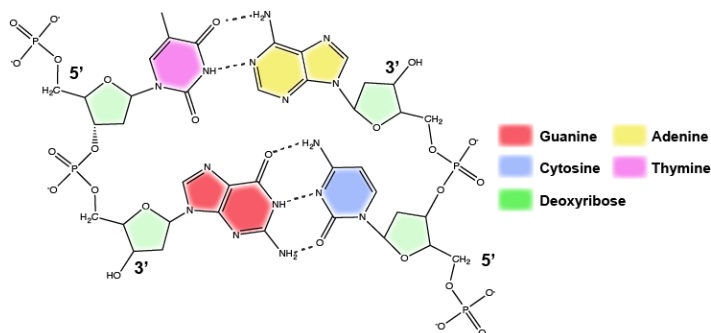*Attribution: Marc T. Facciotti (original work)*

Guanine   Adenine
Cytosine   Thymine
Deoxyribose

Figure 5. A zoomed-in molecular-level view of the antiparallel strands in DNA. *In a double-stranded DNA molecule, the two strands run antiparallel to one another so that one strand runs 5' to 3' and the other 3' to 5'. The phosphate backbone is located on the outside, and the bases are in the middle. Adenine forms hydrogen bonds (or base pairs) with thymine, and guanine base pairs with cytosine.*
Attribution: Marc T. Facciotti (original work)

Functions and roles of nucleotides and nucleic acids to look out for in General Biology

Besides their structural roles in DNA and RNA, nucleotides such as ATP and GTP also serve as mobile energy carriers for the cell. It surprises some students when they learn to appreciate that the ATP and GTP molecules we discuss in bioenergetics are the same as those involved in the formation of nucleic acids. We will cover this in more detail when we discuss DNA and RNA synthesis reactions. Nucleotides also play important roles as co-factors in many enzymatically catalyzed reactions.

Nucleic acids, RNA in particular, play a variety of roles in in cellular process besides being information storage molecules. Some roles that you should keep an eye out for as we progress through the course include: (a) **Riboprotein** complexes - RNA-Protein complexes in which the RNA serves both catalytic and structural roles. Examples of such complexes include, ribosomes (rRNA), RNases, splicesosome complexes, and telomerase. (b) Information storage and transfer roles. These roles include molecules like DNA, messenger RNA (mRNA), transfer RNA (tRNA). (c) Regulatory roles. Examples of these include various non-coding (ncRNA). Wikipedia has a comprehensive summary of the different known RNA molecules that we recommend browsing to get a better sense of the great functional diversity of these molecules.