The Structure and Function of Large Biological Molecules by Dr. Ty C.M. Hoffman

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All of the biological macromolecules are built from smaller subunits. Each subunit features -H and -OH substituents located somewhere on the subunit. This allows for assembly or disassembly of macromolecules via two classes of chemical reactions:

- In a dehydration reaction, two subunits are joined after one subunit is stripped of -OH and the other subunit is stripped of -H. The -OH and the -H that are removed form H_2O (water), which is why the reaction is so named.
- In a hydrolysis reaction, a molecule is split into smaller particles. One of the smaller particles is supplied with -H to satisfy the valence; the other is supplied with -OH. The -H and -OH come from water, which is required for a hydrolysis reaction.

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Monosaccharides are simple (one subunit) sugars. Monosaccharides can be classified on the basis of the number of carbon atoms making up the skeleton or on the basis of where the carbonyl group is located in the skeleton (i.e., on whether the monosaccharide is an aldehyde or a ketone).

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Any monosaccharide can exist in either a linear form or a ring form, and the monosaccharide can be converted back and forth between the two forms. Making the ring requires breaking the double bond, so a monosaccharide features a carbonyl group only when it is in the linear form.

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When two monosaccharides are in the ring form, they can be bound together by a dehydration reaction. The covalent bond that ties together the monosaccharides is called a glycosidic linkage. Two linked monosaccharides make up a disaccharide. When several or many monosaccharides are linked, a polysaccharide is formed.

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Starch (made by plants) and glycogen (made by animals) are both polysaccharides made up entirely of glucose subunits. Starch and glycogen function as storage polysaccharides, because excess fuel (glucose) is stored within the polysaccharide for later use as fuel.

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Monosaccharides (like glucose) can exist in multiple isomeric forms. If a plant links multiple α glucose monomers together, starch (a storage polysaccharide) is formed. A plant is also able to link many β glucose monomers together, which results in cellulose. Cellulose is a structural polysaccharide, because the glucose monomers have not been linked for the purpose of storing glucose for later use as fuel. Rather, in a structural polysaccharide, the structural strength of the molecule is put to use for making structural elements (like wood).

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Many organisms (including humans) are not able to produce the enzyme necessary for digesting cellulose, even though cellulose is made entirely of glucose monomers. Some mammals, like cows, house microorganisms in their digestive tracts. These microorganisms are able to digest cellulose. This living arrangement is an example of symbiosis, because both organisms benefit. Since one of the organisms lives within the other, the cow/microorganism example is specifically called endosymbiosis.

While plants can make structural polysaccharides (including cellulose), animals can make their own versions of structural polysaccharides, including chitin, which is made by insects to make the exoskeleton rigid.

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A fat is an example of a lipid. Fats are also called triglycerides, because a fat molecule is built by attaching three fatty acids onto a single glycerol molecule. Each connection of a fatty acid to the glycerol requires a dehydration reaction, and the resulting covalent bond is called an ester linkage. Because a fatty acid is made up almost entirely of a hydrocarbon chain, fats are excellent fuels.

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A fatty acid can be classified on the basis of absence or presence of double bonds.

- A saturated fatty acid is one that features no double bonds between carbons in its skeleton. This results in a linear (unbent) shape.
- An unsaturated fatty acid is one that features at least one double bond between carbon atoms. This results in a kink, or bend, which makes unsaturated fatty acids pack together more loosely than saturated fatty acids do.

An overall fat is saturated if all three of the fatty acids are saturated. If at least one of the fatty acids is unsaturated, the overall fat is unsaturated. Animals make mostly saturated fats, so animal fat products (like butter) are more solid than liquid at room temperature. Plants make mostly unsaturated fats, so fat products derived from plants are mostly liquid (oils).

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Phospholipids are lipids that are similar to fats but different in an important way. Whereas a fat has three fatty acids connected to a glycerol, a phospholipid has a glycerol that is connected to only two fatty acids. The third connection point on the glycerol joins to a phosphate head. This makes a phospholipid amphipathic, which means that it is partly polar and partly nonpolar. The fatty acids (just like hydrocarbons) are nonpolar, and the phosphate head is polar. Polar molecules are hydrophilic, because water is also polar. Nonpolar molecules are hydrophobic and therefore avoid water and other polar molecules. An amphipathic molecule like a phospholipid is partly hydrophobic and partly hydrophilic.

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When many phospholipids are in the presence of water, the phospholipids arrange themselves into a membranous bilayer with the fatty acid tails in one layer facing the tails in the other layer. The phosphate heads are facing the two surfaces of the bilayer. This arrangement allows the hydrophilic heads to be near water on either side of the membrane while allowing the hydrophobic tails to avoid water. This is how plasma membranes (and therefore the first cells) came into existence. The phospholipid bilayer makes up the framework of a plasma membrane, but a complete plasma membrane includes other particles embedded in that bilayer.

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Cholesterol is an important lipid made by animals. It is a component of plasma membranes (where it affects the fluidity of the membrane), and it serves as a precursor from which the steroid hormones can be produced.

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Any given protein is able to perform its specific function because of its specific shape. Proteins (compared to other macromolecules) have such a large variety of cellular functions, because proteins can be constructed with just about any shape imaginable.

Many of the proteins made by an organism function as enzymes, which are biological catalysts. A catalyst is a substance that greatly speeds up a chemical reaction. An enzyme is an excellent example of the relationship between a protein's shape and its function, because an enzyme must bind to a substrate (the particle on which it operates) before the reaction involving that substrate can readily occur. A substrate is able to bind to an enzyme, because that enzyme has just the right shape to fit the shape of the substrate.

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Proteins are polymers, which are formed by connecting many subunit molecules to make a larger molecule. In the case of proteins, those subunits are amino acids. Any amino acid features a central carbon atom that is connected to an amino group, a hydrogen atom, and a carboxyl group. The fourth bond of the central carbon can be made with anything else, represented as R. Since the R group can be anything, there are many different amino acids. However, organisms use the same set of twenty different amino acids from which to assemble their proteins.

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The twenty biological amino acids can be grouped according to their chemical properties. These chemical properties result from the specific arrangement of atoms making up the R group, which is the only thing that varies from one kind of amino acid to the next.

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A polypeptide is an end-to-end arrangement of amino acid subunits. Each polypeptide therefore is constructed as a strand, although that strand might fold up into a globular shape. Any protein consists of one or more polypeptides. To link two amino acids, a dehydration reaction is required. The resulting covalent bond between adjacent amino acids is called a peptide bond.

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A single polypeptide can be represented by a ribbon, which serves as a reminder that a polypeptide is constructed as a linear (non-branching) arrangement of amino acids.

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The shape of a protein determines its function, as in this example. The shape of the antibody is just right for recognizing the shape of a specific antigen (in this case a flu virus).

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There are four levels of protein structure:

- Primary structure is the specific sequence of amino acids making up a polypeptide.
- Secondary structure includes two frequently occurring substructures within a polypeptide. These are α helices and β pleated sheets. A given polypeptide can contain any number (including none) of either of these substructures.
- Tertiary structure is the overall three-dimensional shape of a single polypeptide.
- Quaternary structure is the way in which multiple polypeptide subunits are brought together to form a complex protein. Quaternary structure applies only to proteins consisting of multiple polypeptides.

A protein consisting of just one polypeptide exhibits only primary, secondary, and tertiary structure (not quaternary structure). In this case, "polypeptide" and "protein" refer to the same thing. In the case of a complex protein (with quaternary structure), a polypeptide is only part of the overall protein.

The three-dimensional (tertiary) structure of a polypeptide can be stabilized by any of four classes of interactions between R groups of non-adjacent amino acids.

- Hydrogen bonding can occur between polar R groups.
- Hydrophobic interactions can occur between non-polar R groups.
- Disulfide bridges can occur between two sulfur-containing cysteine residues.
- Ionic bonds can occur between charged residues of opposite polarity.

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There are two main categories of proteins, based on shape:

- Fibrous proteins have an elongated shape.
- Globular proteins fold up into a compact form.

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The shape of a polypeptide depends on its particular sequence of amino acids (i.e., its primary structure), because this determines how amino acids within that polypeptide interact. The primary sequence is determined by the sequence of nucleotides in the gene that codes for that polypeptide. If a change is made to even one of the many amino acids in a polypeptide, the shape can be profoundly affected. This is exemplified by sickle cell disease, in which a mutation (a change in the DNA sequence) causes the wrong amino acid to be placed in one of the positions within a polypeptide subunit of hemoglobin. Though all of the other amino acids are correct, the polypeptide is severely deformed.

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The shape of a protein is its conformation, and conformation changes slightly under different normal conditions. Under more extreme conditions, the conformation can change so drastically as to disable to protein. This is called denaturation.

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Some newly made proteins assume their proper (functional) shape on their own. Others require the help of special proteins called chaperone proteins. A chaperone protein serves as a small container for a newly made protein. This isolates the protein from the rest of the cytoplasm and provides the proper environment for the folding of the protein to occur.

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Gene expression refers to the process of decoding a gene ad making a polypeptide using the information in that code. Gene expression is therefore the link between DNA and protein. This occurs in two major steps:

- Transcription is the process in which the DNA sequence in a gene is read, and an RNA molecule (called messenger RNA, or mRNA) is constructed according to the code in the DNA.
- Translation is the process of assembling the polypeptide one amino acid at a time. This occurs at a ribosome, using the instructions encoded in the mRNA that was produced during transcription.

Nucleic acids (including DNA and RNA) are linear (unbranched) polymers of subunits (monomers) called nucleotides. Any single nucleotide consists of three components:

- A pentose sugar is the central component. The pentose (by definition) contains five carbon atoms, but there are two possibilities. If the sugar is ribose, the nucleotide is a ribonucleotide, and it is part of RNA (ribonucleic acid). If the sugar is deoxyribose, the nucleotide is a deoxyribonucleotide, and it is part of DNA (deoxyribonucleic acid).
- Attached to one side of the pentose sugar is a phosphate group.
- Attached to the other side of the pentose sugar is a nitrogenous base. There are five commonly used nitrogenous bases (adenine, guanine, cytosine, thymine, and uracil). However, only four are used in DNA (A, G, C, and T), and only four are used in RNA (A, G, C, and U). Nitrogenous bases are the only components within a nucleic acid molecule that differ from nucleotide to nucleotide. They therefore are responsible for the genetic differences between different species and between different individuals of the same species.

A strand of nucleotides is called a polynucleotide. Most DNA occurs as two polynucleotides (strands) held together by hydrogen bonds. Most RNA occurs as a single polynucleotide. Regardless of type (DNA or RNA), a polynucleotide is held together by a series of covalent bonds, called phosphodiester bonds, occurring between adjacent nucleotides. Because a phosphodiester bond joins the sugar component of one nucleotide to the phosphate component of the next nucleotide, the entire strand is held together along its length by what is called the sugar-phosphate backbone.

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A DNA molecule is a double-helix made up of two complementary DNA polynucleotides held together by hydrogen bonds between nitrogenous bases at the same lengthwise position but on opposite strands. Though the hydrogen bonds hold the strands together, the hydrogen bonds are easily broken, which is important, because both of DNA's functions (transcription and self-replication) require the two strands to be at least temporarily separated.