Chapter 3. Macromolecules: Their Chemistry and Biology

I Macromolecules: Giant Polymers

- What is a polymer? Poly means many; mer, units.
- They form with covalent linkages of smaller units called monomers.
- Molecules with molecular weights greater than 1000 daltons are usually classified as macromolecules.
- Examples of biological polymers are proteins, polysaccharides, nucleic acids and lipids.
- Macromolecules make up what we visually recognize as life.
- Some of the roles of macromolecules:
  1. Energy storage
  2. Structural support
  3. Catalysis
  4. Transport
  5. Regulation of metabolic activities
  6. Maintenance of homeostasis
  7. Provide means for movement, growth and development.
  8. Heredity
- Function of macromolecules is primarily related to shape, but also the chemical properties of their monomers.
- Proteins fold based on their base composition to generate a functional structure such as a catalyst or a strong flexible fiber like those found in spider webs.
- Carbohydrates (sugars) link to form cellulose, the wood fiber of trees, or starch.
- Some types of macromolecules contain many different monomers.
- Some contain the same simple units, repeatedly.

II Condensation Reactions

- Macromolecules are made from smaller monomers.
- Commonly, polymers are formed from monomers that are combined by removing an OH from one and an H from the other of the molecules that are being linked. *(See Figure 3.2)*
  - This is called a condensation or dehydration reaction.
  - It takes energy to make the polymer.
  - It also takes special proteins, called enzymes, to make polymers from monomers.
  - The reverse reaction, making monomers from polymers, is called hydrolysis.
  - A hydrolysis reaction (hydro - water, lysis - break) is one where water reacts with the bond that links the units together.
    - Whereas a strong acid or base solution can hydrolyze many types of polymers, in biological systems, enzymes, again, are mostly responsible

for hydrolysis.
  - In people, stomach acid hydrolyzes some of the linkages found in the polymers we eat.

III Proteins: Polymers of Amino Acids

- Proteins are molecules with diverse structure and function.
  - Proteins have important roles in:
    1. Structure support
    2. Protection
    3. Catalysis
    4. Transport
    5. Defense
    6. Regulation
    7. Movement
- Proteins are made of amino acids.
  - The amino is the nitrogen containing part $(NH_3)^+$.
  - The acid is a carboxyl group (-COOH).
  - Differences in amino acids come from the side chains, or the R-groups, found attached to the same carbon as the amino group. *(See Figure 3.2)*
- Proteins are made by a condensation reaction between an amino group and a carboxyl group in a condensation reaction. *(See Figure 3.4)*
  - Proteins are made by enzymes which are also proteins.
  - Enzymes are proteins that catalyze reactions.
  - Information for the amino acid sequence is provided by another macromolecule, DNA, via yet another macromolecule, RNA.
  - Proteins are synthesized with the first amino acid of the protein having its amino group free and the last amino acid added with its acid free (unbonded).
- Proteins range in size from a few amino acids to thousands.
  - A single chain of amino acids is called a polypeptide.
  - Some proteins are composed of a single polypeptide.
  - Some other proteins have more than one polypeptide chain.
- Folding is crucial to the function of a protein. Folding is largely influenced by the sequence of amino acids.
- Each different type of protein has a characteristic amino acid composition and order.
- Some proteins have additional, non-amino acid chemical structures called *prosthetic* groups. Types of these are carbohydrates, lipids, phosphate groups, ion-containing heme groups, metal ions and others.

A. **Proteins are composed of amino acids**

- The 20 common amino acids vary widely in properties. *(See Figure 3.2)*
- Common to all but one are that four different groups are attached to the α carbon.
  - A hydrogen atom, an amino group, and a carboxyl group are found bonded to the α carbon of all the different amino acids.
  - The fourth group, the R group, is what makes one type of amino acid different from another.
  - Glycine has H as its R group and is therefore the only one that has three different not four different groups attached to the α carbon.
  - Carbons with 4 different groups attached can exist in different stereoisomeric forms. All amino acids do except for glycine.
- Amino acids can be classified based on the characteristics of their R group.
  - Five of the 20 amino acids form ions in solution depending on the pH.
  - Four of the 20 have polar side chains.
  - Eight have non-polar R groups.
- Three amino acids: cysteine, glycine and proline, have some special properties.
  - Cysteine has a terminal disulfide (-S-S-) *(See Figure 3.3)*.
  - Glycine has hydrogen atom as the side-chain. This group is small enough to fit into small spaces and tight corners when the protein folds.
  - Proline has a modified amino group that forms a covalent bond with the R group.
    - Proline's ring limits rotation of the α carbon's bond.
    - Proline is often found at bends and loops of proteins.

B. **Peptide linkages covalently bond amino acids together**

- Proteins are also called polypeptides. A dipeptide would be two amino acids long; a tripeptide, three. A polypeptide is many amino acids long.
- The second amino added during synthesis of a protein is added to the carboxyl group of the first amino acid in an enzyme catalyzed condensation reaction.
- The first amino acid of a peptide is called the N-terminus amino acid because the amino group is free, unbound.
- The last is called the C-terminus amino acid and has a free carboxyl group.
- The C to N peptide linkage forms a partial double bond, which is a single covalent and a polar attraction. This limits folding and restricts the ability to rotate.
- Within the central axis of the protein, there is a tendency to hydrogen bond. (Oxygen is partially negative and nitrogen slightly positive.)

C. **Primary structure of the protein is its amino acid sequence**.

- The sequence or order is directed by genetic information. *(See Figure 3.5)*
- The sequence is called its primary structure.

- The peptide backbone is repeating units N-C-C-N-C-C-N-C-C-N-C-C...
  - The portion on the left is the N-terminus, on the right is the C-terminus.
  - The protein is synthesized from the N-terminus to the C-terminus.
- Many proteins have now been sequenced.
  - The two conventions for representing the sequence are a three letter and a one letter system.
  - The three letters Met represent methione, the letter M also represents methionine.
- Amazing numbers of different proteins are possible.
  - With 20 amino acids, there are 400 different dipeptides possible (20 X 20 = 400) One would be glycine - glycine, another would be glycine - methione.
  - There are 20^{100} different possible proteins that are the relatively small size of 100 amino acids. That is 20 with 100 zeros, a huge number. Proteins can also be larger or smaller than 100, which make the number of different polymers mind-boggling.

D. The secondary structure of a protein requires hydrogen bonding.

- Secondary structure is the shape regions of the peptide take on as a folded polymer.
- This shape is primarily influenced by the amino acid sequence.
- There are two common secondary structures.
  - One is the α helix, a right-handed coiled *(See Figure 3.5b)*.
    - The peptide backbone takes on the helical shape due to polar attractions.
    - The R-groups point out away from the peptide backbone.
    - Large R groups tend to perturb the creation of this structure.
  - Insoluble fibrous structural proteins have α helix secondary structures. Examples are the proteins found in hair, feathers, and hooves. These proteins are called keratins.
  - Hair stretches because the hydrogen bonds and not covalent bonds are being broken when it is pulled.
- Another common secondary structure is β pleated sheets.
  - These form from peptide regions that lay parallel to each other. *(See Figure 3.5c)*
  - Sometimes the parallel regions are in the same peptide.
  - Sometimes the parallel regions are from different peptide strands.
  - This sheet-like structure is stabilized by hydrogen bonds between amino groups of one stretch with the C-O group of the parallel stretch.
  - Spider silk is made of β pleated sheets of separate peptides. Despite the weakness of hydrogen bonds, together they tend to be additive, so substances like spider silk can be remarkably strong.

E. The tertiary structure of a protein is formed by bending and folding

- Tertiary structure is the 3-dimensional shape of the completed polypeptide. *(See Figure 3.5d)*
- The primary determinant of the tertiary structure is the primary structure.
- Other factors are:
  1. the nature and location of secondary structures;
  2. the location of disulfide bridges, which form between cysteine residues;
  3. hydrophobic side chain aggregation and van der Waal forces which help stabilize them; and
  4. the ionic interactions, plus charge with minus, which can exist deep in the protein away from water.
- All these are mostly the result of the primary sequence of amino acids of the peptide.

F. The quaternary structure of a protein consists of protein subunits.

- Some proteins are composed of subunits, which are separate peptide chains that associate together to create the functional protein. Different regions of the DNA molecule code for these subunits. *(See Figure 3.5e)*
- This added dimension is called the quaternary structure and it adds to the 3-D shape of the finished protein.
  Hemoglobin is an example of such a protein; it has 4 subunits. *(See Figure 3.7)*

G. The surfaces of proteins have specific shapes.

- The shape is crucial to the functioning of some proteins.
  - The enzyme must bind substrates correctly, and the correct shape is how.
  - Cells in tissues snap together and are held by the complementary shapes.
  - Multi-component proteins are held together by their shape, charges, hydrophobic and sometimes disulfide bonds.
  - Hormones bind to receptor proteins because of the protein's shape. The shape of the bound protein must change precisely in response to the hormone binding.
  - It is the combination of attractions, repulsion, and interactions that determine the right fit. *(See Figure 3.8)*

H. Protein shapes are sensitive to the environment

- Changes in temperature, pH, salt concentrations, and oxidation or reduction conditions can change the shape of proteins.
- This is called denaturation.
- Often the denaturation is irreversible, like boiling egg white. *(See Figure 3.9)*
- Some chemically induced changes are reversed by removal of the chemical condition that caused them.

- A few proteins, like ribonuclease, resist denaturation, can be boiled for days and retain activity upon cooling.

I. Chaperonins help shape proteins

- Chaperonins are specialized proteins that help keep other proteins from interacting inappropriately with other proteins prior to positioning.
- Some chaperonins help folding. Some prevent folding until the appropriate time. *(See Figure 3.10)*

IV Carbohydrates: Sugars and Sugar Polymers

- Carbohydrates are carbon molecules with hydrogen and hydroxyl groups.
  - They act as energy storage and transport molecules.
  - They also serve as structural components.
- Carbohydrate monomers have a molecular weight of approximately 100 daltons.
- Polymers from monomers have molecular weights up to hundreds of thousands.
- There are four major categories:
  1. monosaccharides;
  2. disaccharides which consist of two monosaccharides;
  3. oligosaccharides have several monosaccharides; and
  4. polysaccharides are large and composed of hundreds to hundreds of thousands.
- The general formula for a carbohydrate monomer is $(CH_2O)_x$.
  - During the polymerization, which is a condensation reaction, water is removed.
  - Therefore the carbohydrate polymer has a slightly different chemical formula.

A. Monosaccharides are simple, single sugars.

- All living cells have glucose ($C_6H_{12}O_6$).
- Green plants produce monosaccharides - other organisms acquire glucose, or the energy to make it from plants.
- Cells break down glucose to release energy with the final product being carbon dioxide and water.
- Glucose exists as straight chain and a ring. *(See Figure 3.11)*
  - Ring form is most predominant (>99%).
  - The two forms exist in equilibrium when dissolved in water.
- Different monosaccharides have either different numbers or arrangements of carbons. *(See Figure 3.12)*
  - Hexoses (six-carbon sugar) include the following structural isomers: glucose, fructose, mannose and galactose.
  - Two examples of pentoses (5 carbon sugars) are ribose and deoxyribose.
  - Deoxyribose is minus an oxygen atom at the carbon 2.
  - These two sugars are part of RNA and DNA.

B. Glycosidic linkages bond monosaccharides together

- These bonds are created by enzymes and are condensation reactions.
- Disaccharides have just one.
  - Sucrose (table sugar), is glucose bonded to a fructose.
  - Lactose (milk sugar) is glucose bonded to a galactose.
  - Maltose has two glucose molecules.
  - Cellobiose has two glucose molecules also, but they are bonded differently.
- See *Figure 3.11* to understand the different types of glycosidic linkages possible.
- Maltose and cellobiose have the same chemical formula but are structural isomers.
- The shape difference changes the biological nature of the molecules.
  - Enzymes that breakdown maltose fail to breakdown cellobiose.
  - Humans can breakdown maltose, but not cellobiose.
- Oligosaccharides contain more than two monosaccharides.
  - Many proteins found on the outer surface of cells have oligosaccharides attached to the R-group of certain amino acids, or to lipids.
  - The human ABO blood types get their specificity from oligosaccharide chains.

C. Polysaccharides serve as energy storage molecules or as structural materials.

- Starch is a polysaccharide of glucose with glycosidic linkages in the α-1,4 orientation. *(See Figure 3.13)*
- Cellulose is a giant polymer of just glucose. The linkages are β–1,4.
- Starch can be readily degraded by action of chemicals or enzymes.
- Cellulose, is much more stable chemically and more difficult to hydrolyze chemically and enzymatically.
- Starches vary by the amount of branching. *(See Figure 3.14)*
  - Plant starches, called amylases, are slightly branched.
  - The animal starch called glycogen is highly branched.
  - Starches are molecules that store glucose.
  - Each polymer molecule exerts essentially the same effect as a monomer on the osmotic pressure of a solution.
  - Combining many glucose molecules into just one molecule reduces the osmotic effect, allowing storage of lots of energy, without disturbing the water content of a cell too much.

D. Chemically modified carbohydrates contain other groups

- Cells modify carbohydrates. *(See Figure 3.15)*
- Glucose can oxidize to acquire a carboxyl group (-COOH), producing glucuronic acid.

- Phosphate is enzymatically added to one or more of the -OH sites, creating a sugar phosphate such as 1,6 - bisphosphate.
- Amino groups can be substituted for an -OH, making an amino sugar such as glucosamine and galactosamine.
  - Amino sugars are important to the extracellular matrix, the systems that hold tissues together.
  - Galactosamine is a major component of cartilage such as found in your kneecaps.
  - A glucosamine derivative is part of chitin, the polysaccharide in the skeletons of insects, prawns, and crabs. It is also found in the cell walls of fungi.

V Nucleic Acids: Informational Macromolecules

- Nucleic acid polymers are linearly arranged information molecules.
- Two types of nucleic acid polymers are DNA (deoxyribonucleic acid) and RNA (ribonucleic acid).
- The DNA molecules of humans are enormous. Greater than 130 million is the number of nucleotides found in just one of the human chromosomes of average length.
- Information stored in DNA is transferred to RNA molecules.
  - The average length of RNA, although occasionally thousands of bases in length, is much shorter than DNA molecules.
  - The DNA molecule contains information for the production of many different RNA molecules.

A. The nucleic acids have characteristic structures and properties

- DNA differs from RNA due to the absence of the oxygen in the 2-carbon position of the ribose.
- DNA typically is found double-stranded: two separate polymers are associated together.
- The association is not haphazard but complementary.
  - At each position where a purine is found on one strand, a pyrimidine is found on the other.
  - Purines have a fused double-ring structure.
  - Pyrimidines have just one ring.
  - Pairing of a purine with a pyrimidine maintains 3 rings in the center of the molecule, so that the backbones of the two strands maintain a constant distance along the length of the double-stranded molecule.
- The polymers are enzymatically made and, like all the other polymers mentioned so far, are created during a condensation reaction.
- The linkages that hold the monomeric residues in the polymer are called phosphodiester linkages. *(See Figure 3.17)*

- These linkages are formed between the 3rd carbon of the deoxyribose and a phosphate group that is associated with a 5th carbon of the deoxyribose.
- The backbone consists of alternating sugar-phosphate.
- The two strands are antiparallel, looking at one end, one of the strands will end with a free 5th carbon of the ribose, the other with a 3rd carbon of a ribose.
- The two strands are held together by the attractions formed by nitrogenous bases in the center of the double stranded molecule.
- The attractions are hydrogen bonds that form due to partial positive and negative charges as described in Chapter 2.

B. The uniqueness of a nucleic acid resides in its base sequence

- Hydrogen bonds form because of the complementary nature of the two strands.
  - Four different DNA bases are found in the DNA.
  - They are adenine (A), cytosine (C), guanine (G), and thymine (T).
  - Every position on one strand where an A is found, a T is found at the same point in the complementary strand.
  - Wherever a G is found, a C is found on the other.
  - It is between these bases that hydrogen bonds form.
  - DNA complementary strands form a double helix, a molecule with a right-hand twist.
- DNA is an information molecule and serves no other purpose. The information is stored in the *order* of the four different bases.
- The order is transferred to RNA molecules which are used to direct the order of the amino acids in proteins.
- DNA has a much more uniform shape than proteins. There is enough shape differences to allow a DNA binding protein to recognize specific sites from the millions found in a chromosome.
- DNA has no other purpose than information storage, but RNA does.
- RNA polymers with enzymatic activity like proteins have been discovered. These are called ribozymes.
- RNA molecules are similar to DNA molecules except:
  - RNA has ribose, which has oxygen at the 2nd carbon of the sugar.
  - Instead of having thymine, RNA molecules have uracil.
  - RNA is single-stranded, because just one strand is synthesized and no complementary molecule is available.

C. DNA is a guide to evolutionary relationships

- The sequence of bases in DNA molecules change slowly over time.
- The information has drifted and different organisms have appeared.
- Those organisms that had more recent common ancestors can be distinguished from more distant relations.

- One surprising discovery has been that starlings are closely related to mockingbirds.

D. Nucleotides have other important roles in the cell

- RNA monomers have important roles in energy transfer within cells.
- The ribonucleotide ATP acts as an energy transducer in many biochemical reactions. It is the cash form of cellular energy.
- The ribonucleotide GTP powers protein synthesis.
- Both cAMP and cGMP are cyclic ribonucelotides that transfer information.

VI Lipids: Water-Insoluble Molecules.

- Life is cellular; the differences between what is outside and inside a cell defines life.
- A class of biological molecules called lipids maintains the differences.
- Lipids are chemically diverse but share the common chemical property of being regionally water insoluble.
  - Insolubility is due to non-polar bonds.
  - Hydrogen and carbon form such non-polar molecules.
- Lipids aggregate away from water and attract to each other via van der Waal's forces.
- The roles for lipids in organisms include energy storage (fats and oils), cell membranes (phospholipids), capture of light energy (carotinoids), hormones and vitamins (steroids and modified fatty acids), thermal insulation, electrical insulation of nerves, and water repellent (waxes and oils).

A. Storage of Energy

- Fats and oils are triglycerides. *(See Figure 3.19)*
- Glycerol (or glycerin) is a three-carbon molecule with 3-OH groups, one for each carbon.
  - Each OH is the site where an enzyme adds a fatty acid.
  - Fatty acids are long linear chain hydrocarbons with a carboxyl at one end. *(See Figure 3.19)*

B. Fatty acids are hydrocarbon molecules with a carboxyl at one end.

- There are three fatty acids per molecule.
- In saturated fatty acids, the hydrocarbon tail has only single bonded carbon to carbon bonds. Hydrogen atoms complete the valence requirements.
  - Saturated fatty acids are solid or semi-solid at room temperature. *(See Figure 3.20a)*
  - Animal fats are saturated.

- Unsaturated fatty acids are those that have at least one double bonded carbon in one of the hydrocarbon tails. At these positions, there are two fewer hydrogen atoms.
    - They are called unsaturated *because* they have fewer hydrogen atoms.
    - Unsaturated fatty acids are liquid at room temperature.
    - They are liquid because double bonds are inflexible and cause kinks in the hydrocarbon tails, which prevents tight packing. See *(Figure 3.20b)*
    - The plants commonly have unsaturated fatty acids.
    - Short and/or unsaturated fatty acids are associated with greater fluidity, even at cold temperatures.
- Fats and oils are storehouses for energy.

C. Phospholipids form the core of biological membranes

- Because the hydrocarbons fail to dissolve in water or interact directly with ions, lipids play an important role in maintaining differences in ion and other chemicals' composition of living cells.
- Phospholipids have two fatty acid tails and one hydrophilic phosphate attached to the glycerol. *(See Figure 3.21)*
- This orients the molecules so that the phosphate group faces water and the tail faces away.
- In aqueous environments, these lipids form bilayers, heads facing outward, tails facing inward. *(See Figure 3.22)*
- Cell membranes are structured this way.

D. Carotenoids and Steroids

- Carotenoids trap light energy.
    - Carotenoids, light absorbing pigments, are found in plants and animals.
    - One, beta-carotene, is a plant pigment used to trap light. In animals, it is a pigment that when broken into two identical pieces is used in sight.
- Steroids are organic compounds with a series of fused rings. *(See Figure 3.24)*
    - Cholesterol is an example. It is a common part of animal cell membranes.
    - Cholesterol is synthesized in the liver and absorbed from food.
    - In addition to being a membrane constituent, it also is an initial substrate for synthesis of testosterone and estrogen.
    - Steroids also function as hormones. Hormones are signaling molecules.

E. Some lipids are vitamins *(some vitamins are lipids)*

- Vitamins are small organic molecules.
- They are essential to health and not synthesized by humans.
- Vitamin A is made from betacarotene. *(See Figure 3.23)*
    - It is important for normal development, maintenance of cells and night vision.

- Also, it is a signaling molecule that regulates the expression of DNA.

- Vitamin P is important to absorption of calcium in the intestines.
- Vitamin E is an anti-oxidant. It protects membranes.
- Vitamin K is a component for normal blood clotting.

F. Waxes repel water.

- Wax protects our hair, birds' feathers and insects' eggs either from the damaging effects of water or the damaging effects of water loss.
- Waxes are long fatty acids bonded to long fatty alcohols via an ester linkage.
- A fatty alcohol is like a fatty acid except the last carbon has an OH instead of a carboxyl.

VII Combination Macromolecules

- Some types of macromolecules are bonded to other types.
  - Glycoproteins have polysaccharides covalently bonded to a protein.
  - Glycolipids have polysaccharide-bonded lipid.
- Proteins construct biological macromolecules and break them down as well.
- Some proteins are capable of recognizing and affecting other macromolecules, like proteins, carbohydrates, lipids and DNA.