Lecture Outline: Biological Macromolecules

I. **Introduction to Biological Macromolecules and Metabolism**
   A. **Four Biological Macromolecules**
      1. Proteins
      2. Lipids
      3. Nucleic Acids
      4. Polysaccharides
   B. **Polymers vs. Non-Polymers**
      1. **Polymers**: Built by stringing together monomers
         a. Polysaccharides
         b. Polynucleotides (Nucleic Acids)
         c. Polypeptides (Proteins)
      2. **Non-Polymers**: Lipids (big molecules, but built differently)
   C. **Chemical Reactions for Building and Breaking Down Molecules**
      1. Applies to all four categories of macromolecules
      2. **Building Bigger Molecules (Anabolism)**
         a. Process: **Dehydration Reaction** (also called dehydration synthesis)
         b. Mechanism: Smaller chunks (monomers) join by one losing an H and the other losing an O, forming water (H2O) as a byproduct
         c. Metabolism Subdivision: **Anabolism** (sum of reactions that build bigger things from smaller)
      3. **Breaking Down Bigger Molecules (Catabolism)**
         a. Process: **Hydrolysis** (means "using water to split")
         b. Mechanism: Water is required as an input, splits into H and O, which attach to the resulting smaller chunks

    c. Metabolism Subdivision: **Catabolism** (sum of reactions that break bigger things into smaller chunks)
4. **Metabolism**: The sum of all chemical reactions occurring in an organism (life itself)
5. Anabolism and Catabolism are opposite processes

II. **Polysaccharides (Carbohydrates)**

A. **General Characteristics of Carbohydrates**

1. Broad category of molecules
2. Macromolecules that are carbohydrates are **polysaccharides**
3. Monomers are **simple sugars** (monosaccharides)
4. General Formula for Monosaccharides: CN H2N O N (or CN (H2O)N), hence "carbo-hydrates" (carbon and water)
5. Composed of carbon, hydrogen, and oxygen
6. Sugars often end in "-ose" (e.g., monosaccharides, polysaccharides)

B. **Monosaccharides (Simple Sugars)**

1. Interchangeable terms: Monosaccharide and simple sugar
2. Can exist in either **linear form** or **ringed form**
3. In linear form, they feature a **carbonyl group** (carbon double-bonded to an oxygen)
    a. **Aldoses** (aldehyde sugars): Carbonyl group is at a "tip" or end of the carbon skeleton
    b. **Ketoses** (ketone sugars): Carbonyl group is somewhere other than a tip
4. **Classification by Number of Carbons** (value of 'N' in the formula)
    a. **Trioses**: 3-carbon sugars (e.g., glyceraldehyde, dihydroxyacetone)
    b. **Pentoses**: 5-carbon sugars (e.g., ribose, ribulose, deoxyribose)
    c. **Hexoses**: 6-carbon sugars (e.g., glucose, galactose)
5. **Isomers**: Substances with the same chemical formula but different structural arrangements (e.g., glyceraldehyde and dihydroxyacetone, glucose and galactose)
6. **Chirality**: Carbons connected to four different things can create left-

and right-handed versions of the sugar (e.g., glucose and galactose differ by the side of a hydroxyl group on a chiral carbon)

C. **Building Polysaccharides from Monosaccharides**

1. Requires monosaccharides to be in their **ringed form**
2. Built via **dehydration reactions**
3. The covalent bond formed between two adjacent monosaccharides is called a **glycosidic linkage**
4. **Branching**: Polysaccharides can be branched because ringed monosaccharides have multiple hydroxyl groups, allowing connections at various positions
5. **Oligosaccharides**: Intermediate length sugars (more than two, but not "many")

D. **Functional Classifications of Polysaccharides**

1. **Storage Polysaccharides**
   a. Purpose: Efficiently store monosaccharides (fuel for later use)
   b. **Starch**: Plant storage polysaccharide; made entirely of glucose
   c. **Glycogen**: Animal storage polysaccharide; highly branched version of glucose polymer, more compact and faster to dismantle than starch
   d. **Glucose**: The "master fuel" in all cells; most common biological monosaccharide
   e. Liver's role in glucose regulation: Builds glycogen when blood glucose is high, dismantles it when low
2. **Structural Polysaccharides**
   a. Purpose: Provide structural support, act like strong fibers or "ropes"
   b. **Cellulose**: Major plant structural polysaccharide; made entirely of beta glucose monomers, resulting in staggered chains
   c. Forms long fibers, major component of plant cell walls
   d. **Indigestible for Humans**: Humans lack the enzyme to break the specific glycosidic linkages in cellulose, making it "roughage" with no nutritive value

e. **Animal Digestion of Cellulose**: Animals like cows house symbiotic microorganisms (bacteria) in their stomachs that produce the enzyme needed to break down cellulose (mutualistic endosymbiosis)

f. **Chitin**: Animal structural polysaccharide; tough material making up insect exoskeletons (also used for surgical thread)

III. **Lipids**

A. **General Characteristics**

1. Macromolecules, but not official polymers
2. Major subcategories include fats, phospholipids, and steroids

B. **Fats (Triglycerides / Triacylglycerols)**

1. **Structure**: Composed of a glycerol molecule (a triple alcohol) linked to three fatty acids
2. **Bond Name**: **Ester linkages** (three per fat molecule) formed via dehydration reactions
3. **Fatty Acids**

a. Structure: Contain a carboxyl group at one end (making them carboxylic acids) and a long hydrocarbon chain

b. Function: Hydrocarbon tails are excellent sources of energy due to numerous carbon-hydrogen bonds

c. Energy Density: Fats have more than twice the energy density of proteins or carbohydrates

d. Ways Fatty Acids Differ:

(1) **Chain Length**: Number of carbons in the hydrocarbon chain (typically 10 to high teens in organisms)

(2) **Degree of Saturation**:

1. **Saturated Fatty Acids**: (1) "Saturated with hydrogens," meaning all carbons in the hydrocarbon chain are connected by single bonds (2) Result in straight chains (3) Saturated fats (composed of only saturated fatty acids) tend to be solid at room temperature (e.g., animal fats like butter, lard)

2. **Unsaturated Fatty Acids**: (1) Contain one or more double bonds in the hydrocarbon chain, meaning they are not "saturated" with hydrogens (2) Double bonds cause "bends" or "kinks" in the chain (3) Unsaturated fats (containing at least one unsaturated fatty acid) tend to be liquid at room temperature (e.g., plant oils) (4) Can be **monounsaturated** (one double bond) or **polyunsaturated** (many double bonds)

C. **Phospholipids**

1. **Monumental Importance**: Essential for all life; form the plasma membrane of every cell
2. **Structure**: Similar to fats, but glycerol is linked to two fatty acids and one **phosphate group** (which is charged/polar)
3. **Amphipathic Nature**: Possess "dual feelings" or preferences
   a. Have a **polar head** (the phosphate group and anything attached to it)
   b. Have two **nonpolar tails** (the fatty acid hydrocarbon chains)
4. **Hydrophilic vs. Hydrophobic**
   a. **Hydrophilic**: "Water-loving"; polar molecules that like to be around water (e.g., phospholipid heads)
   b. **Hydrophobic**: "Water-fearing"; nonpolar molecules that avoid water (e.g., phospholipid tails)
5. **Self-Assembly in Water**: Due to their amphipathic nature, phospholipids spontaneously form a **bilayer** (two layers) in water, with hydrophobic tails facing each other and hydrophilic heads facing the water on both sides
6. Cell membranes can adjust their fluidity by using saturated or unsaturated phospholipids
7. This self-assembly mechanism was crucial for the initial formation of cells (vesicles)

D. **Steroids (e.g., Cholesterol)**

1. Characterized by a unique structure of **four fused carbon rings**

2. **Cholesterol**
   a. A type of sterol (solid alcohol)
   b. Produced by animals (plants produce similar phytosterols)
   c. Functions: (1) Major component of animal plasma membranes, influencing membrane permeability (2) Precursor for all **steroid hormones** (e.g., testosterone, estrogen, progesterone, cortisol), which are lipid-based chemical signals

IV. **Proteins**

A. **General Characteristics**

1. Perform almost every biological process and directly determine an organism's traits
2. **Polymers**: Called **polypeptides** when in polymeric form
3. **Monomers**: **Amino acids**
4. Tremendous functional diversity due to their varied shapes (conformations)
5. Organisms are limited to building proteins for which they have genetic instructions (e.g., humans roughly 20,000 genes/proteins)

B. **Diverse Functions of Proteins**

1. **Enzymes**: Biological catalysts that speed up specific chemical reactions; are reusable and not consumed in reactions
2. **Structural Proteins**: Provide support and strength (e.g., collagen and keratin in skin, hair, nails)
3. **Storage Proteins**: Store amino acids for later use (e.g., albumin in egg white); less common as primary energy storage than fats or carbohydrates
4. **Transport Proteins**: Move substances (e.g., hemoglobin transports oxygen and carbon dioxide in blood; transmembrane proteins move substances across cell membranes)
5. **Hormonal Proteins**: Act as chemical signals (e.g., protein-based hormones like insulin)
6. **Receptor Proteins**: Bind to specific signal molecules (ligands) to trigger a cellular response; typically on cell surface or inside cells

7. **Contractile and Motor Proteins**: Involved in movement (e.g., muscle contraction, intracellular transport)
8. **Defensive Proteins**: Involved in immunity (e.g., antibodies, which recognize and neutralize foreign substances called antigens)

C. **Polypeptides vs. Proteins**

1. **Polypeptide**: Always refers to a single linear chain of amino acids
2. **Protein**:
    a. Can consist of a **single polypeptide chain** (in which case "polypeptide" and "protein" are interchangeable)
    b. Can be a **multimer**: Composed of two or more individual polypeptide chains that associate together (e.g., hemoglobin consists of four polypeptides)

D. **Amino Acids (Monomers of Proteins)**

1. **General Structure**: A central carbon atom (alpha-carbon) bonded to four different groups:
    a. A **carboxyl group** (acidic)
    b. An **amino group** (basic)
    c. A hydrogen atom
    d. An **R group** (or side chain): This is the only variable part and determines the specific properties of each amino acid
2. Named "amino acids" due to the presence of both amino and carboxyl groups
3. All known organisms use the same set of **20 biological amino acids** (evidence of common ancestry)
4. **Classification of Biological Amino Acids by R Group Properties**:
    a. **Non-polar Amino Acids**: R groups are primarily hydrocarbons, which have evenly shared electrons due to similar electronegativities of carbon and hydrogen
    b. **Polar Amino Acids**: R groups contain electronegative atoms (like oxygen or sulfur) that create partial charges due to unequal electron sharing

c. **Charged Amino Acids**: R groups carry a full positive or negative charge
   (1) Acidic: Negatively charged R groups
   (2) Basic: Positively charged R groups

E. **Building Polypeptides from Amino Acids**

1. Occurs via **dehydration reactions**
2. The covalent bond linking two amino acids is called a **peptide bond**
3. Amino acids are linked in only one specific way: the carboxyl group of one amino acid connects to the amino group of the next
4. This forms a directional chain with an "amino end" and a "carboxyl end"
5. **No Branching**: Unlike polysaccharides, polypeptide chains are unbranched
6. Polypeptides differ from each other based on their **length** (number of amino acids) and their precise **sequence** of amino acids
7. The R groups hang off the side of the main chain and are not involved in forming the peptide bonds; they are crucial for determining the polypeptide's unique 3D shape

F. **Protein Structure (Confirmation)**

1. The 3D shape (confirmation) of a protein is essential for its function
2. Every protein has at least the first three levels of structure; multimer proteins also have quaternary structure
3. The primary structure dictates all higher levels of structure
4. **Levels of Protein Structure**:
   a. **Primary Structure**: (1) The unique linear sequence of amino acids in a single polypeptide chain (2) Includes both the number and specific order of amino acids (3) An immense number of possible sequences exist (e.g., 20^N for a chain of N amino acids)
   b. **Secondary Structure**: (1) Localized, repeating structural motifs within a polypeptide chain (2) Formed by hydrogen bonds between atoms of the polypeptide backbone (3) Two common motifs: (a) **Alpha helix**: A coiled or corkscrew shape (b) **Beta pleated sheet**:

A folded, accordion-like shape

c. **Tertiary Structure**: (1) The overall, intricate three-dimensional shape of a single polypeptide chain (2) Arises from interactions between the R groups (side chains) of the amino acids as the polypeptide folds (3) Types of R-group interactions that stabilize tertiary structure: (a) **Hydrophobic Interactions**: Very weak attractive forces between non-polar R groups that cluster together to avoid water (b) **Disulfide Bridges**: Strong covalent bonds formed between the sulfhydryl (-SH) groups of two cysteine amino acids, locking the protein into a stable shape (c) **Ionic Bonds**: Attractions between oppositely charged (acidic and basic) R groups (d) **Hydrogen Bonds**: Weak attractions between polar R groups
d. **Quaternary Structure**: (1) The overall three-dimensional arrangement formed when two or more individual polypeptide chains (subunits) associate together in a multimer protein (2) Example: Hemoglobin, which is composed of four distinct polypeptide chains

5. **Impact of Primary Structure on Function**: Even a single amino acid change in the primary sequence can drastically alter a protein's 3D shape (tertiary and quaternary structure) and thus its function (e.g., sickle cell disease caused by a single amino acid substitution in hemoglobin)
6. **Denaturation**:
    a. Definition: The loss of a protein's normal 3D shape (confirmation) due to changes in environmental conditions, leading to a loss of function
    b. Causes: Drastic changes in temperature (e.g., boiling) or pH (e.g., highly acidic or basic conditions)
    c. Reversibility: Mild denaturation can be reversed (**renaturation**) by restoring optimal conditions, which can restore function; drastic denaturation is permanent
7. **Chaperone Proteins**: Some proteins require assistance from specialized "chaperone proteins" to fold correctly, providing a protected

environment for proper folding

V. **Nucleic Acids**

A. **General Characteristics**

1. **Polymers**: Called **polynucleotides**
2. **Monomers**: **Nucleotides**

B. **Nucleotides (Monomers of Nucleic Acids)**

1. Each nucleotide has three necessary components:

a. A **Pentos (5-carbon sugar)**:

(1) **Ribose**: The sugar found in RNA nucleotides (RNA = ribonucleic acid)

(2) **Deoxyribose**: The sugar found in DNA nucleotides (DNA = deoxyribonucleic acid); it is similar to ribose but lacks an oxygen atom at one position

d. A **Phosphate group** (identical in all nucleotides)

e. A **Nitrogenous Base** (nitrogen-containing compound):

(1) There are five common nitrogenous bases: (1) **Adenine (A)** (2) **Guanine (G)** (3) **Cytosine (C)** (4) **Thymine (T)** (5) **Uracil (U)**

(2) DNA uses A, G, C, and T

(3) RNA uses A, G, C, and U (Uracil replaces Thymine)

C. **DNA (Deoxyribonucleic Acid)**

1. Usually **double-stranded**, meaning it consists of two individual polynucleotide chains
2. Forms a **double helix** in three dimensions (each strand is corkscrew-shaped)
3. The "backbone" of each strand is formed by covalent bonds between the sugar and phosphate parts of adjacent nucleotides
4. The nitrogenous bases "hang off" the backbone and form hydrogen bonds between the two strands
5. **Complementarity**: The nitrogenous bases pair specifically between the two strands:

    a. Adenine (A) always pairs with Thymine (T)
    b. Cytosine (C) always pairs with Guanine (G)
6. **Major Functions of DNA**:
    a. **Replication**: The process by which DNA copies itself exactly, enabled by complementarity, ensuring genetic information is passed to new cells
    b. **Transcription**: The process where the genetic code stored in DNA is "rewritten" into an RNA molecule (messenger RNA)

D. **RNA (Ribonucleic Acid)**
1. Most RNA molecules are **single-stranded** (one polynucleotide chain)
2. **Messenger RNA (mRNA)**: Carries the genetic code from DNA to the ribosomes for protein synthesis

E. **Gene Expression (The Central Dogma: DNA to Protein)**
1. The overall process by which DNA's instructions are used to build proteins
2. Involves two main steps:
    a. **Transcription**: (1) Occurs in the nucleus of eukaryotic cells (where DNA is located) (2) The DNA sequence (gene) is read and copied into a messenger RNA (mRNA) molecule (3) DNA acts as a stable "library" of instructions
    b. **Translation**: (1) Occurs in the cytoplasm at **ribosomes** (2) The messenger RNA (mRNA) sequence is read by the ribosome, which then assembles amino acids into a specific sequence to form a polypeptide chain