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# Module 1

**TEM**: transmission electron microscopy. Electrons are transmitted through the specimen

**SEM**: scanning electron microscopy. The surface of a specimen is scanned by a beam of electrons deflected from specimen ‘surface.

**Chromatography**: techniques used for sample preparation which let separate molecules by size, charge or binding affinity.

**Electrophoresis**: the cell is loaded into a gel and then an electric field is applied to the gel. This Electric field moves the molecules through the gel differentially

Since DNA molecules are negatively charged, when the electric field is applied to the gel, the DNA molecules moved towards the positive charges. But larger molecules move slowly and run through the argos matrix and run next to a sample of known molecular weight called the DNA ladder.

**Mass spectrometry or MassSpec**: measures mass to charge ratio of ions in a sample.

Cell membrane: a barrier which maintains physical integrity.

## Module 2- Macromolecules of the cell

## Proteins

### Cell processes

Transcription takes DNA and makes RNA out of it. Nature makes an RNA copy of DNA and by posttranscription makes mRNA out of it. Translation is the process where small molecules are added to the mRNA to build up first polypeptides, amino-acids in small repeat units. Then there is a process to convert polypeptides into a protein: post-translation. And when it takes a 3D shape it takes protein activity to effect particular functions like an effector molecule and then activate more functions.

### Small molecules

* **Amino acid**: monomeric components of proteins.
* **Aromatic bases** (purines and pyrimidines): components of nucleic acids: DNA and RNA.
* **Sugars** (monosaccharides):
  + Ribose: components of nucleic acids
  + Glucose: used in metabolism to make energy
* **Lipids**: components of phospholipids.

### Levels of organization in Protein structure

* **Primary**: Amino acid sequence based on covalent peptide bonds.
* **Secondary**: fold alpha-helix, beta-sheet or random coil based on hydrogen bonds.
* **Tertiary**: 3D folding of a single polypeptide chain based on hydrogen bonds, disulfide bonds, electrostatic interactions and hydrophobic effect.
* **Quaternary** (macromolecule): association of two or more polypeptides with same interactions seen in tertiary structure.

### 4 Protein major classes

* enzymes, (catalysts) that greatly increase rates of chemical reactions in cells.
* **Structural proteins**: provide support and shape to cells and organelles, giving cells their characteristic appearances.
* **Motility proteins**: play key roles in the contraction and movement of cells and intracellular structures.
* **Regulatory proteins**: are responsible for control and coordination of cellular functions, ensuring that cellular activities are regulated to meet cellular needs.
* **Mono-functional proteins**: have a single function: catalytic, structural, motility, or regulatory.
* **Bi-functional proteins** plays two different roles.

### The monomers are amino acids

* Proteins are linear polymers of amino acids.
* 60 different kinds of amino acids, but only 20 are used in protein synthesis.
* Every amino acid has the basic structure with a carbonyl group, an amino group, a hydrogen atom, and a R-group all attached to a single carbon atom.
* Except for glycine, for which the R group is a hydrogen atom, all amino acids have at least one asymmetric carbon atom. Therefore, most amino acids exist in two isomeric forms, L and D-amino acids.

### The structure of 20 amino acids

* **Group A**: hydrophobic and nonpolar R groups.
* **Group B**: hydrophilic and polar R group, uncharged.
* **Group C**: hydrophilic, polar R group, and protonated or ionized at cellular pH.

### The polymers are Polypeptides and Proteins

* Stepwise addition of new amino acid to a growing chain of amino acids by **a condensation) dehydration reaction**: formation of polymers and water molecule.
* The reaction could be reversed by adding back water molecules; used by cells to excrete water waste.
* -H and -OR groups are removed as water comes out and the covalent bond between the carboxyl group and an amino group is called **peptide bond**.

### Peptide bond formation

Always an N-terminus at one end and C-terminus at the other end.

### Polypeptide and Proteins

* Product of amino acid polymerization is a polypeptide (polymers of peptides).
* Monomeric protein consists in a single polypeptide vs. multimeric proteins, two polypeptides: a dimer, 3 polypeptides: a trimer.
* Ribonuclease is a monomeric protein.
* Hemoglobin is a multimeric protein. It contains 4 polypeptides, (2 alpha-subunit and 2 beta-subunits), a chain and II chain.
* Each subunit contains a heme group with an iron atom. Each heme iron can bind a single oxygen molecule.
* Homomeric and heteromeric.
* Protein synthesis.

### Primary structure

* Primary structure e is the amino acid sequence of the constituent polypeptides.
* Amino acids are always written from the N-terminal to the C-terminal, direction in which the polypeptide is synthesized.
* Once incorporated into a polypeptide chain, individual amino acids are called **amino acid residues**.
* **Disulfide bind**: very stable bond between two sulfur atoms of 2 cystine amino acid residues.

### Secondary structure

Because of the folding groups of amino acids are close to each other.

The group interactions result in two structural patterns: the alpha-helix and II sheet conformations.

### Categories of Proteins

* **Fibrous proteins**: have extensive secondary structure (either a helix or beta sheet) giving them a highly ordered and repetitive structure.
* **Globular proteins**: most of the proteins.
  + The polypeptide chain is folded in a compact structure. It is folded locally into alpha-helical or Beta-sheet structures. These regions are folded on one another to give the protein its compact, globular shape.
  + The folding is possible because the interspersed random coils allowing the polypeptide to loop and fold.
  + Have unique tertiary structures
  + They consist of a number of segments called domains. A domain is a discrete, locally folded unit of tertiary structure. A domain typically contains 50-350 amino acids, and usually has a specific function.

### Quaternary structure

* Level of organization concerned with subunit interactions and assembly.
* Applied only to multimeric proteins.
* The bonds and forces that maintain quaternary structure are the same as those responsible for tertiary structure: hydrogen bonds, electrostatic interactions, hydrophobic interactions, and covalent disulfide bonds.

### Disulfide Bond formation in Insulin

It could be reversed.

### The Primary structure of Insulin

Insulin consists of two polypeptides, A and B chains. The two chains are covalently linked by two inter-chain disulfide bonds.

### Structure of Hair

Alpha keratin protein: 3 helices of a-keratin wrap into protofibrils which then bond together to form microfibrils. Microfibrils, 9 + 2 structure. Microfibrils aggregate to form macrofibrils.

### The roles of DNA and RNA in Protein synthesis

mRNA: directs amino acids sequence of polypeptides.

tRNA: binds to amino acids and directs them to proper locations within the growing polypeptide chain.

rRNA: components of the ribosomes that serve as the site of protein synthesis.

## Nucleic Acids

### Transcription and Translation

* **Transcription**: DNA molecule is transcribed into an RNA molecule.
* **Translation**: takes RNA and converts into protein.

### Nucleic Acids

* Nucleic acids are macromolecules critical in the storage, transmission and expression of genetic information.
* Are linear polymers of nucleotides, strung together in a genetically determined order.
* Two major types are DNA and RNA.
* DNA contains the sugar deoxyribose, RNA contains 5-carbon sugar ribose in each of its nucleotides.
* DNA plays as the repository of genetic information, whereas RNA molecules play several different roles in the expression of that information during protein synthesis.
* **mRNA**: directs amino acids sequence of polypeptides that is during polypeptide synthesis.
* **tRNA**: binds to amino acids and directs them to proper locations within the growing polypeptide chain.
* **rRNA**: components of the ribosomes that serve as the site of protein synthesis.

### The Monomers are Nucleotides

* Nucleic acids are informational macromolecules that contain non-identical monomeric units in a specified sequence.
* The monomeric units of nucleic acids are called nucleotides.
* DNA and RNA each contain only four different kinds of nucleotides.
* Each nucleotide consists of a five-carbon sugar, a phosphate group, and a nitrogen-containing aromatic base. The sugar is either D-ribose (for IRNA) or D-deoxyribose (for DNA).
* The phosphate is joined by a phosophoester bond to the 5' carbon of the sugar, and the base is attached at the 1' carbon. The base maybe either a purine or a pyrimidine.
* DNA contains the **purines**: **adenine** (A) and **guanine** (G) and the **pyrimidines**: **cytosine** (C) and **thymine** (T). RNA also has **adenine**, **guanine**, and **cytosine** but contains the pyrimidine **uracil** (U) in place of thymine.
* ATP is the energy-rich compound used to drive a variety of reactions in the cell, including the activation of monomers for polymer formation.
* Nucleotides plays two roles in the cell:
  + Monomeric units of nucleic acids
  + Serve as intermediates in various energy transferring reactions.

### Polymers: DNA and RNA

* Nucleic acids are linear polymers formed by linking each nucleotide to the next through a phosphate group.
* The result of a condensation reaction with the -H and -OH groups come off from the sugar and the phosphate group respectively is **a 3’,5’ phosphodiester bond**.
* Incoming nucleotides must be added in a specific, genetically determined sequence. The template to specify nucleotide order is DNA for both DNA and RNA synthesis.
* **Purines: Adenine, Guanine**
* **Pyrimidines: Thymine, Uracil, Cytosine**
* Purine and pyrimidine bases have carbonyl groups and nitrogen atoms capable of hydrogen bonds formation under appropriate conditions.
* Paring of A with T (or U) and G with C

### A DNA molecule is double-stranded Helix

* The double helix consists in two complementary chains of DNA twisted together around a common axis to form a right-handed helical structure.
* The two chains are oriented in opposite directions along the helix, one in 5’3’ direction and the other in 3’-5’ direction.
* The sugar phosphate backbones of the two strands could be envisioned as the sides of a circular staircase where each step corresponds to a pair of bases held in place by hydrogen bonding.
* The right-handed helix is an idealized version of the B-DNA, the main form of DNA.
* Z-DNA is a left-handed double helix, with a longer, thinner sugar phosphate backbone.

### RNA Structure

* Secondary and tertiary structures are well understood only for tRNA molecules.
* A nucleotide is composed of three components, namely a nitrogenous base, phosphate group, and sugar. A nucleoside is composed of two components, namely a nitrogenous base and sugar. This is the basic difference between a nucleotide and a nucleoside.

### The Phosphorylated Forms of Adenosine

* Adenosine occurs as the free nucleoside, the monophosphate (AMP), the diphosphate (ADP), and the triphosphate (ATP).
* The bond that links the first phosphate to the ribose of adenosine is a low-energy phosphoester bond, whereas the bonds that link the second and third phosphate groups to the molecule are higher-energy phosphoanhydride bonds.

### Hydrogen Bonding in Nucleic Acid Structure

AT pair held together by two hydrogen bonds, whereas the CG pair has three hydrogen bonds.

## Polysaccharides

### Polysaccharides

* No known informational role in the cell.
* They are the storage polysaccharides starch and glycogen and the structural polysaccharide cellulose.
* Each of these polymers contains the 6-carbon sugar glucose and its single repeat unit.

### The Monomers are Monosaccharides

* The repeats are single sugar called monosaccharides.
* A sugar can be an aldehyde or ketone that has two or more hydroxyl groups.
* 2 categories of sugars: aldosugars, with a terminal carbonyl group and the ketosugars, with an internal carbonyl group.
* Sugars are classified as triose (3 carbons), a tetrose (4), a pentose (5), a hexose (6), or a heptose (7).
* Most common: aldhohexose D-glucose, C6H12O6.

### Polysaccharides

Glucose also occurs in disaccharides consisting of 2 monosaccharide units linked covalently.

* Maltose: 2 glucose units linked together.
* Lactose: glucose linked to a galactose.
* Sucrose: glucose linked to a fructose.

### Polysaccharide Polymers are Storage and Structural

* Polysaccharides perform either storage or structural functions in cells. The most familiar storage polysaccharides are the starch of plant cells and the glycogen of animal cells. Both of these polymers consist of alpha-d-glucose units linked together by a glycosidic bond.

### Glycogen (storage)

* Glycogen is highly branched, with linkages occurring every 8 to 10 glucose units along the backbone and giving rise to short side chains of about 8 to 12 glucose units.
* Glycogen is stored mainly in the liver and in muscle tissue.  
  In the liver it is used as a source of glucose to maintain blood sugar levels, whereas in muscle it serves as a fuel source to generate the ATP needed for muscle contraction.

### Starch (storage)

* Starch occurs both as un-branched amylose and as branched amylopectin.
* Like glycogen, amylopectin has a (1 -> 6) branches along the backbone and give rise to longer chains.
* Starch deposits are about 10-30% amylose and 70-90% amylopectin.

### Cellulose (structural polysaccharide)

* Cellulose is an important polymer quantitatively; more than half of the carbon in higher plants is present in cellulose.
* Like starch and glycogen, cellulose is also a polymer of glucose, but the repeating monomer is beta-d-glucose and the linkage is therefore beta (1 -> 4).
* Cellulose forms rigid, linear rods. These aggregate into microfibrils.
* Plant and fungal cell walls consist of these rigid microfibrils of cellulose embedded in a **noncellulosic matrix**.
* Mammals do not possess an enzyme that utilize cellulose as food (cannot cleave glycosidic bonds).

## Lipids

* The distinguished feature of lipids is their **hydrophobic nature**.
* They resemble one another more in their soluble properties than in their chemical structures.
* Not the result of stepwise polymerization found for proteins, nucleic acids, and polysaccharides.
* Ruch in nonpolar hydrocarbon regions and have relatively few polar groups.
* Some lipids are amphipathic having both a polar and a nonpolar region.
* They play at least 3 main roles in the cell:
* Energy storage
* Membrane structure
* Transmission of chemical signals into and within cells.
* The six main classes of lipids are fatty acids, triacylglycerols, phospholipids, glycolipids, steroids, and terpenes.

### Fatty Acids Are the Building Blocks of several classes of Lipids

* A fatty acid is a long, unbranched hydrocarbon chain with a carboxyl group at one end.
* It is amphipathic; the carboxyl group renders one end (“head”) polar whereas the hydrocarbon, “tail” is nonpolar.
* Fatty acid yields a great deal of energy upon oxidation.
* Fatty acids without double bonds are saturated fatty acids: every carbon atom in the chain has the maximum number of hydrogen atoms attached to it.
* Unsaturated fatty acids contain one or a few double bonds.
* General formula: n carbon atoms Is **CnH2nO2**.

### Triacylglycerol Are Storage Lipids

* Triacylglycerols (triglycerides) consist of a glycerol molecule with 3 fatty acids linked to it.
* Glycerol is 3-carbon alcohol with a hydroxyl group on each carbon.
* Fatty acids are linked to glycerol by ester bonds, formed by the removal of water.
* Triglycerides are synthesized stepwise, with one fatty acid added at a time.
* Monoglycerides contain a single esterified fatty acid, diglycerides have 2, triglycerides have 3.
* Triglycerides are usually solid or semi-solid at room temperature and are called fats.
* In plants, mots triglycerides are liquid at room temperature – vegetable oils.

### Phospholipids Are Important in Membrane Structure

* Critical to the bilayer structure found in all membranes.
* Phospholipids are phosphoglycerides or sphingolipids.

### Steroids Are Lipids with a Variety of Functions

* Are derivatives of a 4-membered ring compound called phenanthrenes which makes them structurally distinct from other lipids.
* Only property that links to other classes of lipids: relatively nonpolar and therefore hydrophobic.
* Cholesterol is an amphipathic molecule, with a polar head group and a nonpolar hydrocarbon body and tail.
* Cholesterol found primarily in membranes.
* Cholesterol is the starting point for the synthesis of all the steroid hormones, which include the male and female sex hormones, the glucocorticoids and mineralocorticoids.

### Terpenes are Formed from Isoprene

Terpenes, synthesized from 5-carbon compound isoprene, also called isoprenoids.

Isoprene and its derivatives are joined together in various combinations to produce vitamin A1, carotenoid pigments.

## Module 3 – Introduction to Cells and Organelles

## Types of Cells and Their Properties

* The main distinction between two cell types (Prokaryotes vss. Eukaryotes) is the membrane bound nucleus of eukaryotic cells.
* Prokaryotic cells can be divided into bacteria and archaea.
* Phylogenetic Tree of Life: ancestral cell -> bacteria, Archaea, Eukarya.
* Gram’s stain: staining to distinguish bacteria:
  + Gram-positive microorganisms have higher peptidoglycan content, whereas gram-negative organisms have higher lipid content.

### There Are Three Limitations on cell size

* Need to maintain adequate surface are to volume ratio

Cells that are specialized for absorption have characteristics to maximize surface area/volume.

* Diffusion rates of Molecules

Eukaryotic cells avoid the problem of slow diffusion rates by using carrier proteins or vesicles.

* The Need for adequate local concentration of essential substances

The larger the cell is, the more difficult to maintain these higher concentrations required for different type of reactions to occur.

### Eukaryote Cells use Organelles to compartmentalize Cellular Function

* As cell size increases, the number of molecules increase proportionately with volume .

The challenges of diffusing macro-molecules across the cell or accumulating higher concentrations in certain regions of cells can be mitigated by eukaryote cell development of organelles.

### Chromosome

DNA is tightly packed into gene and into chromosome and contained in the nucleus.

### Genetic Information

Eukaryotic cells replicate DNA and then distribute their chromosomes into daughter cells by mitosis and meiosis, followed by cytokinesis, division of the cytoplasm.

## The Eukaryotic Cell – Plasma Membrane, Organelles, And The Endosymbiont Theory

* A typical eukaryotic cell has: a plasma membrane, a nucleus, a membrane bounded organelles, and the cytosol supported by a cytoskeleton.
* The Plasma Membrane Defines Cell Boundaries and Retains Content
* Membrane proteins are also amphipathic, with polysaccharides attached to them: **glycoproteins**.
* Plasma membrane is selectively permeable membrane: only certain compounds can move across this membrane, tight control of transport across in either direction for the cell.

### The nucleus is the information center of the Eukaryotic cell

* The nuclear envelope has numerous pores controlled by various proteins constituting a **nuclear pore complex**.
* The **endosymbiont theory**: mitochondria and chloroplasts and bacteria are similar, it suggests that mitochondria and chloroplasts originated from prokaryotes.

### The Endoplasmic Reticulum

* Cisternae, internal space of ER is the lumen.
* Rough and Smooth ER.
* Sarcoplasmic reticulum has critical functions in contraction.

### The Golgi Complex

* Role of sending off proteins to distant locations within the cells through vesiclesss.
* Packaging station or the post office.
* The contents of vesicles from the ER are modified and processed in the Golgi complex.
* secretory and membrane proteins are mainly glycosylated the addition of short-chain carbohydrates).

## Cell Vesicles, Structural Components, and Examples of Cellular Invaders

The cytoplasm contains the cytosol and cytoskeleton

### Ribosome

Ribosomes read or translate mRNA to link amino acids together and form proteins.

### Cytoskeleton



The cytoskeleton is a 3-D array oof interconnected **microfilaments**, **microtubules**, and **intermediate filaments**.

### Microtubules

* Are critical to mitosis
* They form the mitotic spindle fibers that separate chromosomes prior to cell division.
* Play a role in the organization of the cytoplasm: overall shape, organelle organization, movement of macromolecules, distribution of microfilaments.
* Cylinders of longitudinal arrays of protofilaments with a hollow center called a lumen.
* Each protofilament is a linear polymer of tubulin with polarity.
* Tubulin is a dimeric protein (alpha-tubulin and beta-tubulin).

### Microfilaments

* Form connections with plasma membrane to give structure and affect movement.
* But also help to move cell in specific way during cell division.
* Are polymers of the protein actin.
* Actin is synthesized as a monomer called **G-actin**.
* Subunits are polymerized into **F-actin**.
* Have a polarity.

### Vacuoles

* Membrane containers for temporary storage and movement oof compound.
* Plant vacuole large to keep the plant upright.

### Secretory Vesicles

* After being processed by the Golgi complex, materials are exported from the cell into secretory vesicles.
* They move to the plasma membrane and fuse with it, releasing their content outside the cell.
* Endomembrane system of the cell: ER, Golgi, secretory vesicles and lysosomes.

### Lysosome

* Single membrane organelles that store hydrolases, enzymes that can digest any biological molecules.
* A special carbohydrate coating on the inner lysosome membrane protects it from digestion.
* All of the lysosomal enzymes are acid hydrolases, are active at low pH, but not at higher pH (7.2), pH of the inner cell.

### The Phagolysosome

* **Phagocytosis**: ingestion of bacteria by phagocytes.
* **Phagolysosome**: merge of phagosomes with lysosomes to destroy bacterial pathogens.

### Peroxisome

* Similar to lysosome but contains peroxide.
* Helps to break down fatty acids.

### Hydrogen Peroxide

* H2O2 highly toxic to cells but can be formed into water and oxygen by the enzyme catalase.
* These reactions are confined to peroxisomes that contain **catalase**, so that
* cells are protected from the harmful effects of peroxide
* Peroxide production is increased during cellular stress (infection, disease, UV exposure) and can serve as a useful biomarker for early infections.

### Viruses

* Invade and infect cells, using synthetic machinery to produce more viruses’ particles.
* No cytoplasm, organelles, or ribosomes and consist of only a few different molecules of nucleic acid and protein.
* Consist of a coat (capsid) or protein surrounding a core, containing DNA or RNA.
* Viruses that infect bacteria are **bacteriophages** or **phages**.

### Bacteriophage

In theory, bacteriophage exist for every type of bacterium.