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

- **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
- **Group C**: hydrophilic 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 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.
- Ribonuclease is a monomeric protein.
- Hemoglobin is a multimeric protein. It contains 4 polypeptides, 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.

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.