What are proteins

- **Proteins** are polymers of amino acids in which the adjacent **amino acids** are connected by **peptide bonds**.

- This polypeptide is short but has several features that are common to all proteins.
  - All proteins have an **N-terminal end**.
  - All proteins have a **C-terminal end**.
Peptide bonds

What is a peptide bond?

A C-N covalent bond between the Nitrogen of one amino acid and the carboxyl carbon of an adjacent **amino acid**.
Amino acids

What are amino acids?

- The term amino acids refers to a group of molecules which comprise the primary structure of a protein.

In general, amino acids have several features in common.

- The figure shows that amino acids have a central carbon, referred to as the alpha carbon.

  The alpha carbon is covalently bounded to:

  - A hydrogen (H)
  - A carboxyl functional group \((\text{COO}^-)\).
  - An amine functional group \((\text{NH}_3^+)\).
  - A side chain that distinguishes one kind of amino acid from another kind.

[Image of amino acid structure]
It is an acidic functional group frequently found in biological molecules.

- It is found in amino acids, proteins, fatty acids, acetic acids and other organic acids.

Because the carboxyl functional group is a weak acid it will dissociate.

- At a pH of 7 the carboxyl group is in the dissociated form (COO-).
- The carboxyl group of an amino acid will contribute a negative charge at neutral pH.
The amino functional group is basic and found in proteins, amino acids and the nitrogenous bases of DNA and RNA.

Under certain pH conditions the amino group can accept a proton and gain a positive charge of +1.

At a pH of 7 the amino group of an amino acid has a positive charge. The amino group then contributes a positive charge to the amino acid at pH 7.
N-terminal end of polypeptide

- The N-terminal end of the polypeptide has a free amine group.

C-terminal end of polypeptide

- The C-terminal end of the polypeptide has a free carboxyl group.
- Primary protein structure: It is a sequence of chain of amino acids.
- Secondary protein structure: It occurs when the sequence of amino acids are linked by hydrogen bonds.
- Tertiary protein structure: It occurs when certain attractions are present between α-helices and β-sheets.
- Quaternary protein structure: It is a protein consisting of more than one amino acid chain.
The sequence of the amino acids is: N-serine, valine, tyrosine, cysteine-C.
Another component of the primary structure is:

- The covalent bonds in the protein.

A single covalent bond between the sulfur atoms to two amino acids called cysteine.

What is the significance of disulfide bonds?

- Because it is a covalent bond, the disulfide bond can be considered as part of the primary structure of a protein.
- They are very important in determining the tertiary structure of proteins.
- They are very important in determining the quaternary structure of some proteins.

The structure of antibody molecules is a very prominent example showing the role of disulfide bonds.
II- The Secondary Structure of Protein

- **Secondary protein structure:** It occurs when the sequence of amino acids are linked by hydrogen bonds.
- The secondary structure of protein is formed of α-helical regions and β-pleated sheets.

**What is an alpha helix?**

- An alpha helix can be formed by making a rope coil in a left handed direction.
- The rope is represented by the N-C-C-N-C-C-N .... backbone of the polypeptide chain.
The alpha helix structure of protein depends on; bond angles, lengths and rotations.

The alpha helix could be a very stable structure because intra-chain hydrogen bonds could be formed that stabilized the helix.
Significance of alpha helix

- The alpha helix is one of the structures that together with the β-pleated sheets are called the secondary structures of proteins.
- Some proteins like keratin and collagen are almost entirely α-helical in structure.
- Most globular proteins have α-helical and β-pleated sheet regions in addition to regions that are neither alpha helical or beta pleated sheets.
- Charge amino acid side chains have a tendency to destabilize the α-helical or β-pleated sheet structures.
- Amino acids with hydrophobic side chains are compatible with the formation of α-helices and β-pleated sheets.
What is a beta pleated sheet?

A beta pleated sheet is a pleated structure that is composed of the C-C-N-C-C backbone of a polypeptide.

- Each chain of CCNCC… has a N to C polarity in the direction opposite to that of its neighbor.
- The line on the left and far right have the N-to-C polarity from top to bottom.
- The line in the middle has the N-to-C polarity from bottom to top.
- These chains are said to be antiparallel because they run in the opposite directions.
- If the chains run in the same N-C direction they are said to be parallel.
The beta pleated sheet structure is stabilized by hydrogen bonds between the different chains.
III- Tertiary Structure of Proteins

- recognize the β-pleated sheets (ribbons with arrows) and the α-helical regions (barrel shaped structures).
- In addition to these secondary structures, the protein has additional twists and turns which give the protein its unique shape.
Forces that give rise to tertiary structure

- Ionic bonding.
- Hydrogen bonding.
- Hydrophobic interaction.
- Disulfide bonds.
1- Ionic bonding.

They are forces of attraction between ions of opposite charge (+ and -)

What kinds of biological molecules form ionic bonds?
Any kind of biological molecule that can form ions

- An example of a functional group that can enter into ionic bonds is shown. The carboxyl group is shown.
- Under the right conditions of pH the carboxyl group will ionize and form the negatively charged COO⁻ ion and a positively charged H⁺ ion (or proton)
Here is another representation of the carboxyl group. In this case the covalent bonds are shown by the lines and the shared electrons are shown by the black dots.

When ionization of the carboxyl group occurs a proton dissociates from the OH group, leaving the shared electrons behind with the oxygen. Thus the COO$^-$ ion has an excess of electrons over protons and is an anion. The proton that is released has no associated electron and is therefore a cation.
Functions of ionic bonds in biology?

- They are important in all biological processes. A few examples are:
  - They play an important role in determining the shapes (tertiary and quaternary structures) of proteins
  - They are involved in the process of enzymatic catalysis
  - They are important in determining the shapes of chromosomes.
  - They play a role in muscle contraction and cell shape
  - They are important in establishing polarized membranes for neuron function and muscle contraction
2- Hydrogen Bonds

Properties of hydrogen bonds.

- Is formed when a charged part of a molecule having polar covalent bonds forms an electrostatic interaction with a substance of opposite charge.

- Strength.
Hydrogen bonds are classified as weak bonds because they are easily and rapidly formed and broken under normal biological conditions.

- What classes of compounds can form hydrogen bonds?
Under the right environmental conditions, any compound that has polar covalent bonds can form hydrogen bonds.

- Importance in biological systems.
  * Stabilizing and determining the structure of large macromolecules like proteins and nucleic acids.
  * They are involved in the mechanism of enzyme catalysis.
The Covalent Bond

Non-polar Covalent Bond

Hydrocarbons
In Biological systems:
The molecule that predominance in non-polar covalent bonds is called **hydrophobic**

Polar Covalent Bond

Water
In Biological systems:
It allow the formation of the weak Hydrogen bond.
Hydrophobic Interactions

Hydrophobic interactions are more correctly called hydrophobic exclusions.

There are two regions containing hydrophobic substances. Each of the substances is excluded from the water matrix. Over period of time, the two areas of hydrophobic substances will encounter one another, combine and form one larger hydrophobic region that is excluded from the water matrix. This combined state is more energetically favorable than the one in which the hydrophobic substances were separate. Thus this combined state will persist.

http://academic.brooklyn.cuny.edu/biology/bio4fv/page/hydropho.htm
VI- Quaternary Structure of Proteins

The quaternary structure of proteins is the shape that results from the orderly interaction of the polypeptides of a multisubunit protein.

**Multisubunit protein**

- Some proteins are composed of more than one polypeptide.
- Each polypeptide is called a subunit. For example, if a protein is composed of two polypeptides, then it has two subunits.
- The polypeptides may or may not be different in primary structure. This is dependent upon the nature of the protein.
Forces that give rise to the quaternary structure

Ionic bonding
hydrogen bonding
hydrophobic interaction
disulfide bonds
covalent bonds
(a) Primary structure

Amino end

Carboxyl end

(b) Secondary structure

Hydrogen bonds between amino acids at different locations in polypeptide chain

α helix

Pleated sheet
(a) Primary structure

(b) Secondary structure

(c) Tertiary structure
Primary protein structure is a sequence of a chain of amino acids.

Secondary protein structure occurs when the sequence of amino acids are linked by hydrogen bonds.

Tertiary protein structure occurs when certain attractions are present between alpha helices and pleated sheets.

Quaternary protein structure is a protein consisting of more than one amino acid chain.

Image adapted from: National Human Genome Research Institute.
Examples of amino acid subunits

β pleated sheet

α helix