



Biochemistry For First Year Medical Students

Lecture 3: Proteins I Proteins Structural levels

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Learning Objectives:

- **Understand Peptide bond, and Polypeptides formation.**
- **Explore the Structural levels of proteins.**
- **Outline protein primary, secondary, tertiary & quaternary structure with examples**

Proteins

The 20 amino acids commonly found in proteins are joined together by peptide bonds.

The linear sequence of the linked amino acids contains the information necessary to generate a protein molecule with a unique three-dimensional shape.

The complexity of protein structure is best analyzed by considering the molecule in terms of four organizational levels: primary, secondary, tertiary, and quaternary.

Peptide Bonds Formation:

- **Proteins are formed by joining the α - carboxyl group of one amino acid to the α - amino group of another amino acid. The bond formed between the two amino acids is called a peptide bond or CO-NH bridge. When two amino acids are joined a dipeptide is formed. (Figure1).**
- **Proteins are made by polymerization of amino acids through peptide bonds. Proteins contain Carbon, Hydrogen, Oxygen and Nitrogen as the major components while Sulphur and Phosphorus are minor constituents. Nitrogen is characteristic of proteins.**
- **Protein like substances that have molecular weights less than 10,000 amu about 100 amino acids) are called polypeptides or simply peptides. The name protein is given to compounds containing more than 100 amino acids.**
- **An amino acid unit in a polypeptide or protein is called a residue.**

- **Dipeptide= 2 amino acids linked together**
- **Tripeptide = 3 amino acids linked together**
- **Oligopeptide = 4 - 9 amino acids linked together**
- **Polypeptide = 10 – to less than 100 amino acids linked together**
- **polypeptide chains containing more than 100 amino acids are called proteins.**

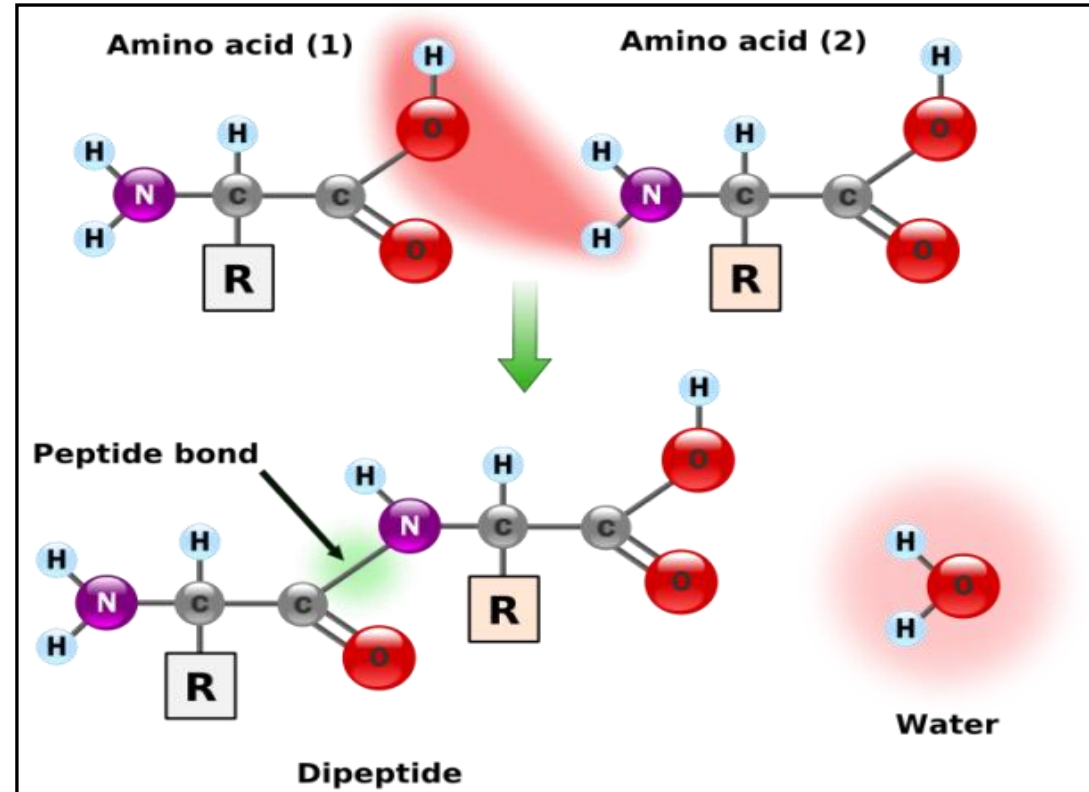


Figure 1: The condensation of two amino acids to form a dipeptide through a peptide bond.

- Peptides and proteins are written so that the free ammonium ion (NH_3^+) is on the left and the free carboxylate ion ($-\text{COO}^-$) is on the right.
- The amino acid at the left end of the chain is called the N-terminal amino acid and the amino acid at the other end is called the C-terminal amino acid (figure 2).
- Thus, glycine is the N-terminal amino acid and cysteine is the C-terminal amino acid in the tripeptide shown in Figure 2.

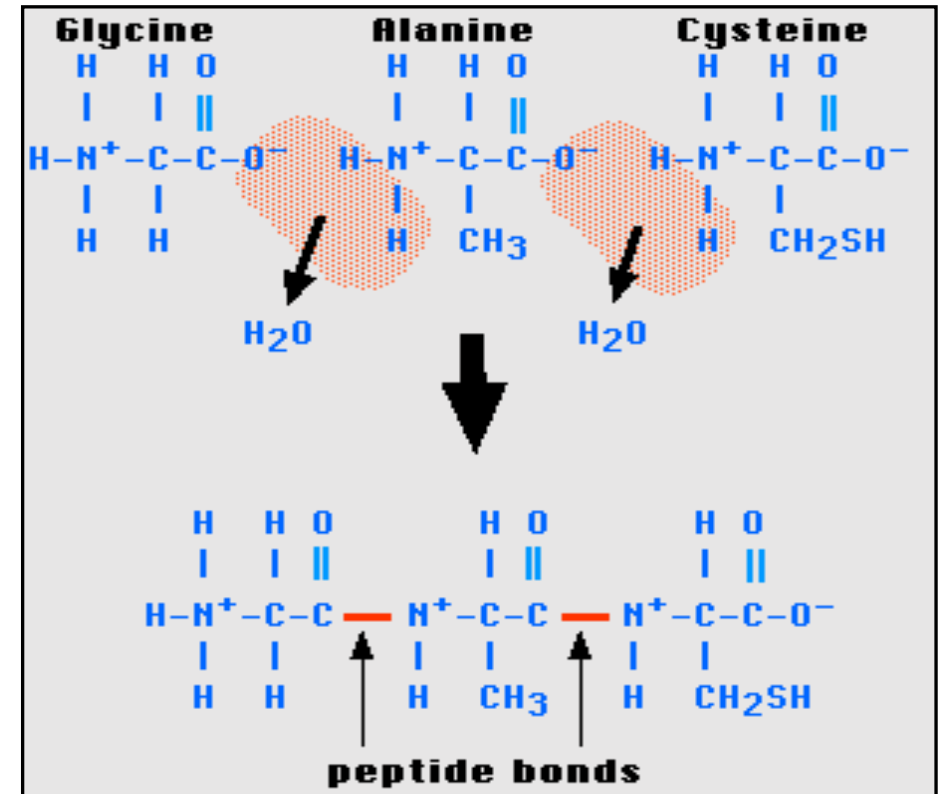
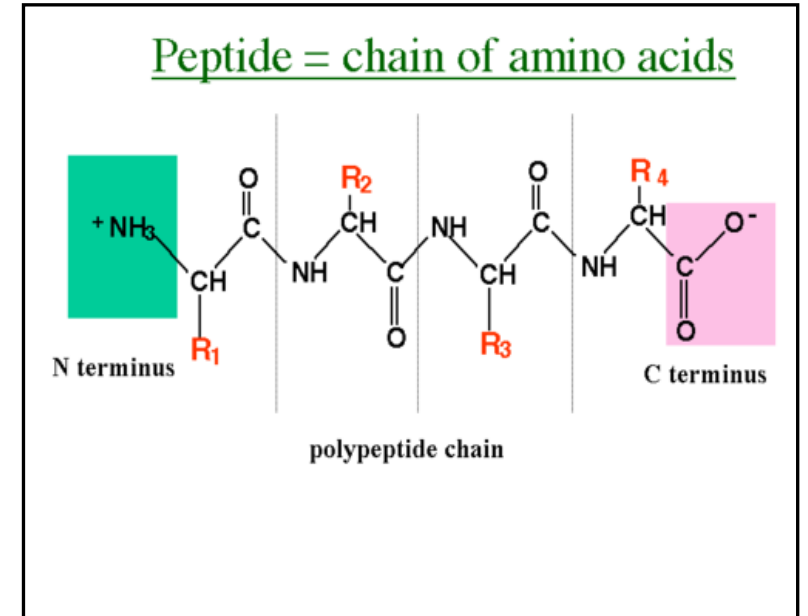


Figure 2

- **Polypeptides are linear sequences of amino acids joined together by peptide bonds. As a result, they are chain-like molecules.**
- **Many proteins contain a single chain of amino acids; others contain two or more chains.**
- **The sequence of amino acids is unique and precisely defined in each polypeptide or protein.**
- **It is this sequence that determines its biological function. If we are to understand how proteins function, we must learn their sequences of amino acids.**



Quickly
understand

Structure of Proteins

Primary



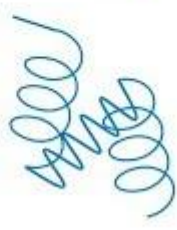
α Helix



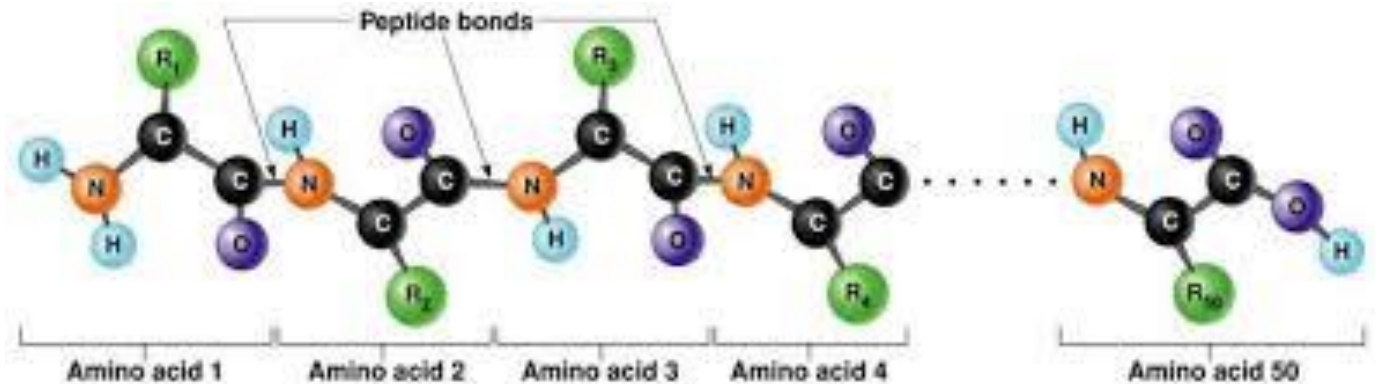
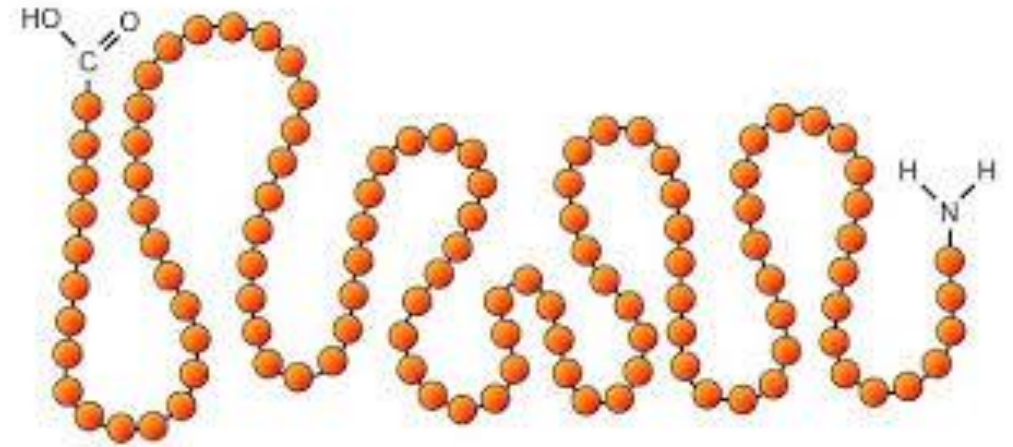
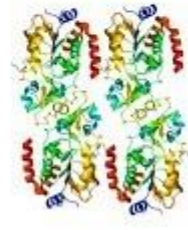
β sheet



Tertiary



Quaternary



(a) Primary structure

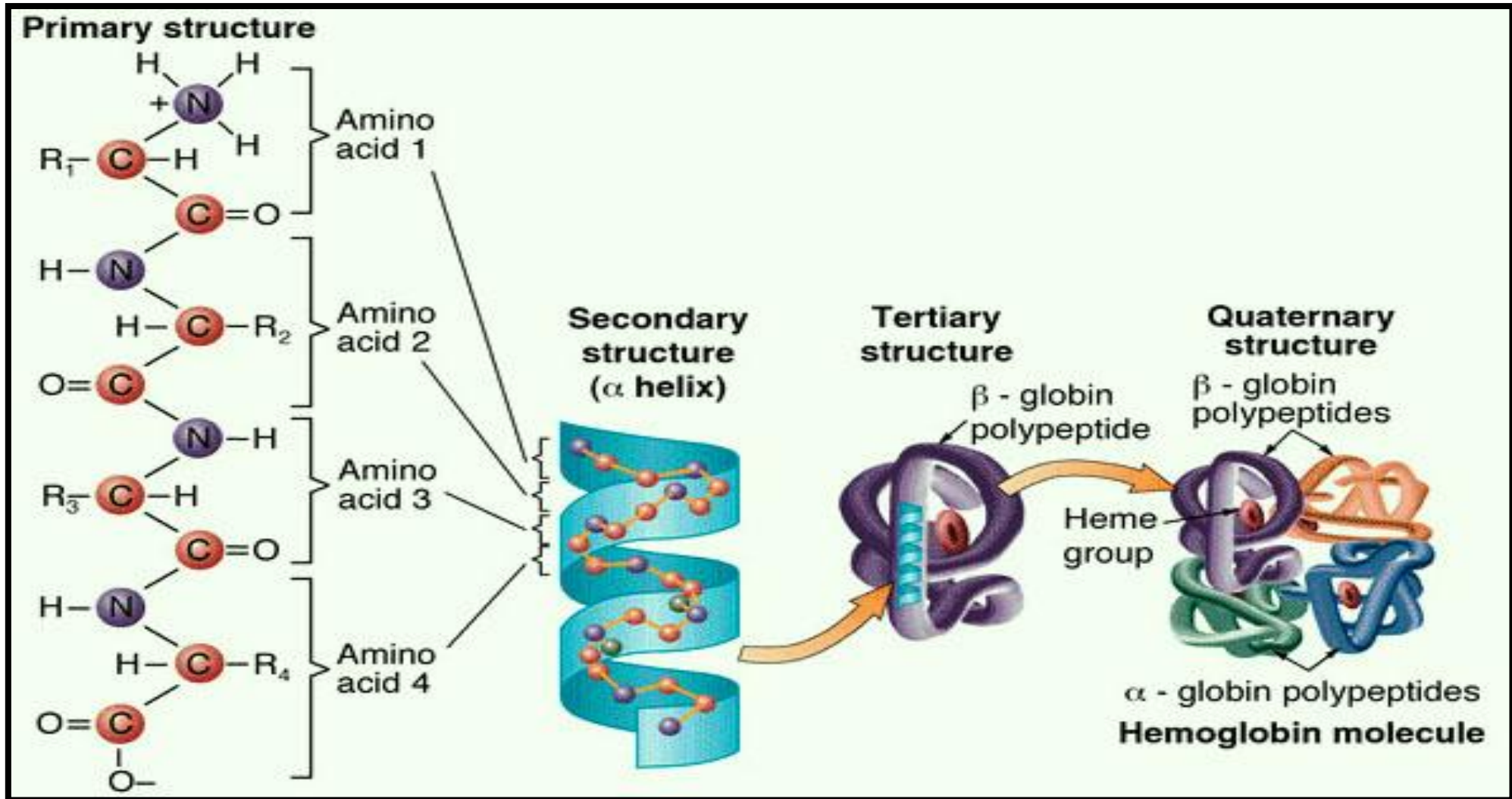


Figure 4: the four structural levels of proteins

Protein Structure : Organization of Proteins

1-The Primary structure of proteins:

The primary structure of the protein is the linear sequence of amino acids.

The remarkable thing about living systems is that they produce a particular protein with the same amino acid sequence from generation to generation.

The sequence of amino acids in a protein can be compared to the words in a sentence. The sequence of words gives a particular meaning to the sentence.

This sequence of amino acids is called the primary structure. It is responsible for the specific biological function of the protein. Even one amino acid incorrectly placed in a protein can alter its biological activity (figure-5).



An example is the disease sickle-cell anemia. It is caused by the fact that a glutamic acid molecule in normal hemoglobin is substituted by a valine molecule in the sickle cell hemoglobin (the amino acid substitution affects the functional properties of the protein. HbS or sickle cell hemoglobin is produced by a mutation of the beta chain in which the 6th position is changed to valine, instead of the normal glutamate. This minor change in the sequence of 146 amino acids in the protein alters its biological function and eventually results in the death of the person. The fragile sickle cells have a shorter life span than normal RBCs, causing severe anemia.

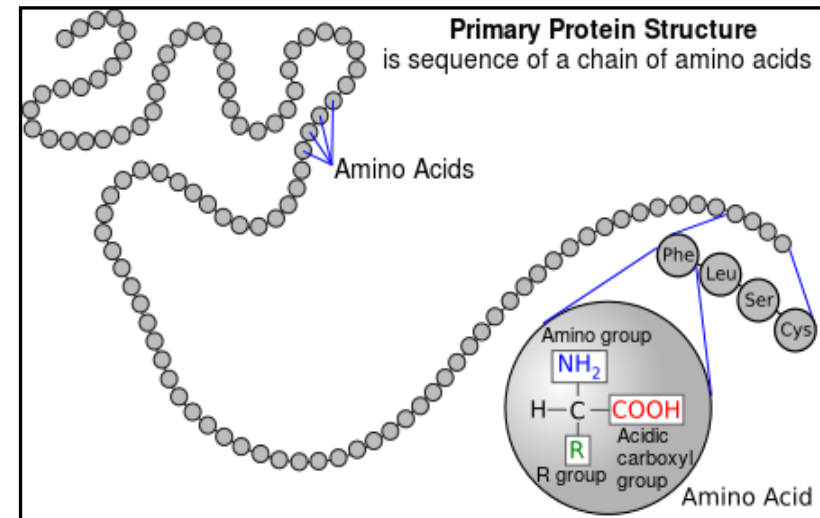
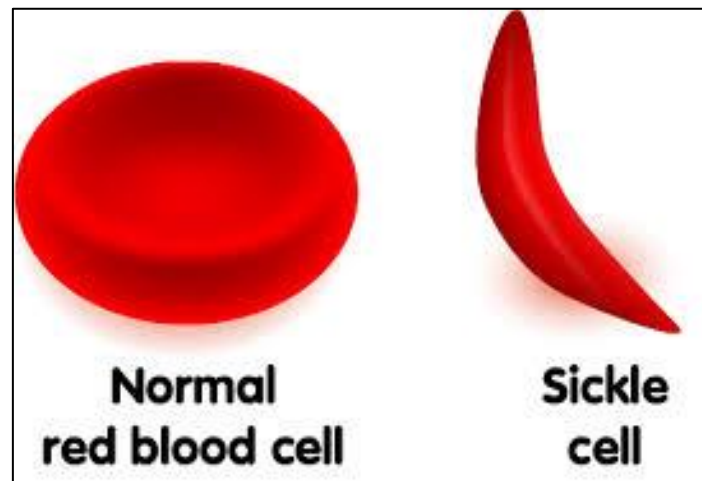


Figure-5: primary structure of proteins.

2-The Secondary structure of proteins:

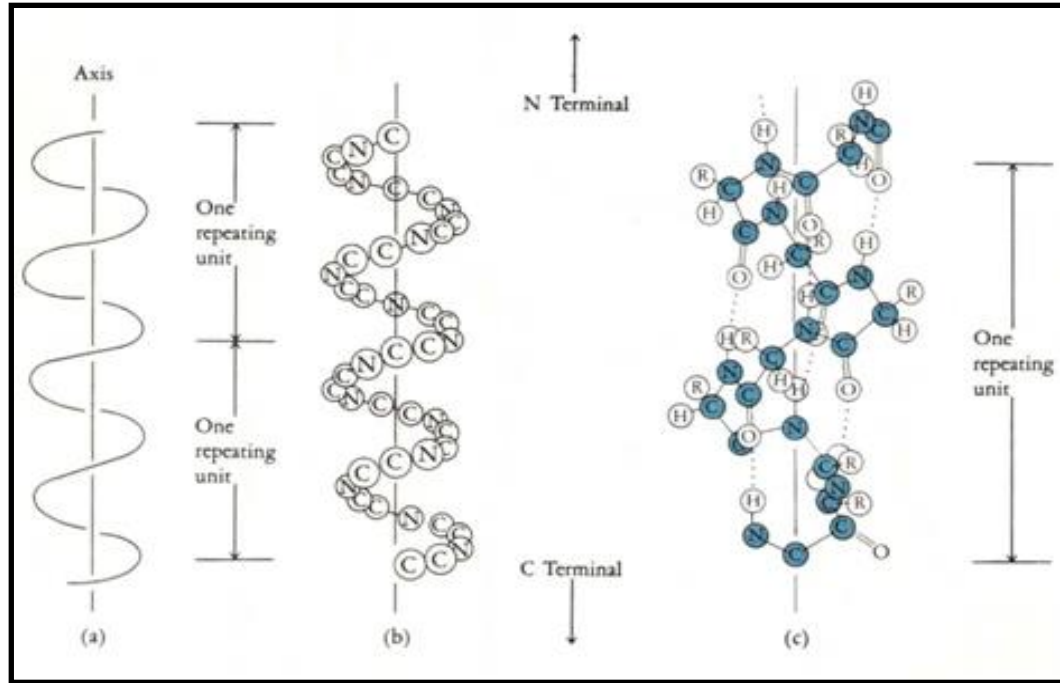
Three structures have been identified.

They are the α -helix, the β -pleated sheet, and the collagen triple helix.

The α -helical structure is shown in (Figure- 6 ,7).

In this structure, the chain of α -amino acids coils as a right-handed screw.

This helix is formed and retains its shape because hydrogen bonds are formed between the amide hydrogen of one peptide bond with the carbonyl oxygen that is located above it on the next turn of the helix, as shown in Figure- 6c.



**Figure-6: secondary structure of proteins.
Hemoglobin consists mainly of alpha helices.**

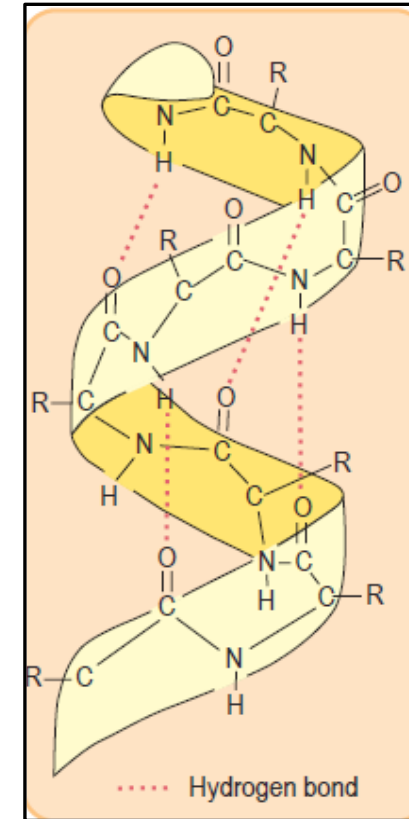


Figure -7: Protein secondary structural motifs. An α -helical secondary structure. Hydrogen bonds between backbone amide NH and C=O groups stabilize the α -helix.

- The β -pleated sheet structure is illustrated in Figure-8.
- In this structure, the polypeptide chains are arranged side by side and are held together by hydrogen bonds between the chains.
- Silk fiber is a protein that is known to exist predominantly as a β -pleated sheet.

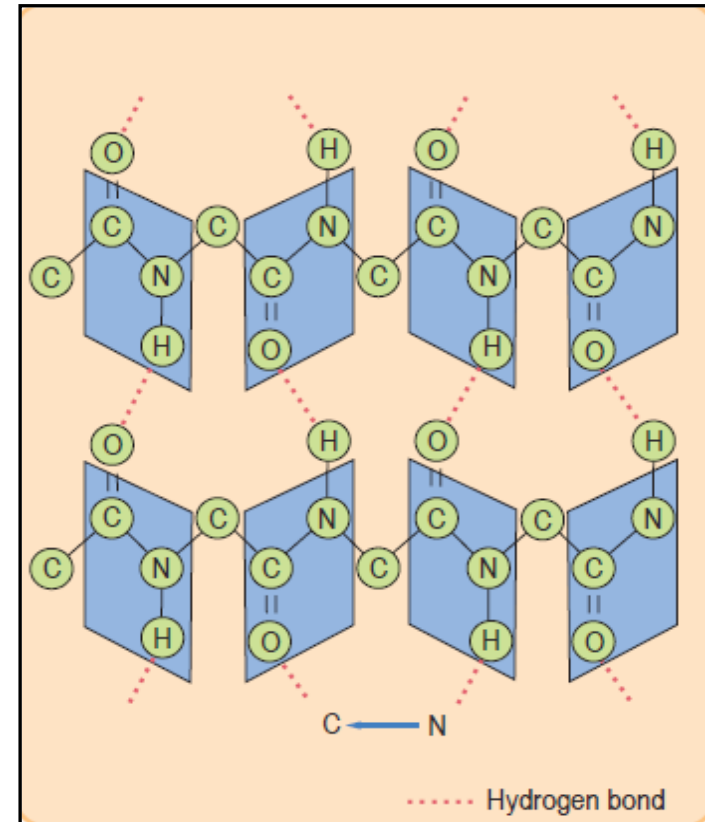


Figure-8: The parallel β -sheet secondary structure. In the β -conformation, the backbone of the polypeptide chain is extended into a zigzag structure. When the zigzag polypeptide chains are arranged side by side, they form a structure resembling a series of pleats.

The triple helix is the unique structural feature of collagen, the protein that gives strength to bones, tendons, and skin. The molecules of collagen are made up of a polypeptide called tropocollagen.

Each molecule of collagen is made up of three tropocollagen polypeptide chains wound around each other to form a triple helix. Such an arrangement looks like a three-strand rope, as shown in Figure-9.

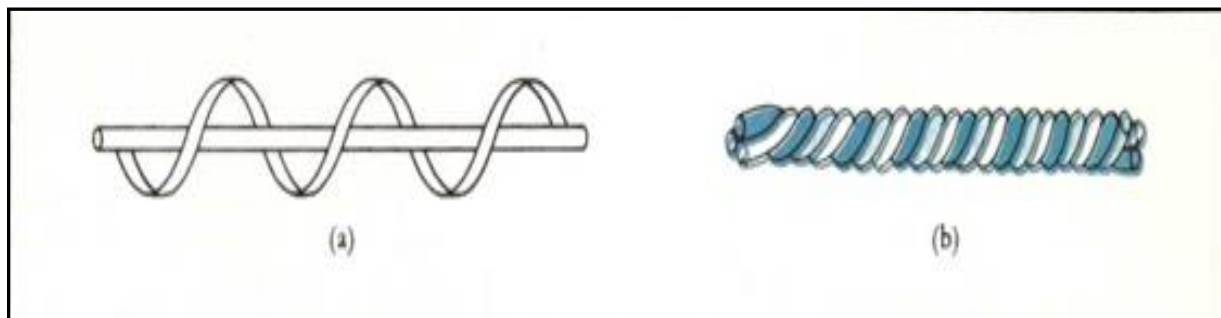
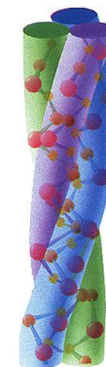


Figure-9

Collagen Protein Structure

- Secondary Structure
- Triple Helix of Collagen
 - Structural protein of connective tissues
 - bone, cartilage, tendon
 - aorta, skin
 - About 30% of human body's protein
 - Triple helix units = tropocollagen



3- Tertiary Structure of Proteins:

The structures of proteins can undergo further folding and bending, resulting in what is called the *tertiary structure* of proteins.

Attractive forces between the amino acid side chains making up the protein are responsible for the tertiary structure. These interactions and their effects on the structure are shown in Figure-10.

Among these attractive forces are:

- disulfide bonds
- hydrophobic interactions,
- hydrogen bonds
- salt bridges.

A salt bridge results from the attraction between two charged groups, one positive and negative, each located some distance apart on the same chain. In the tertiary structure of a protein, the hydrophobic groups are usually placed inside the folds and the hydrophilic side chains remain on the outside, where they are exposed to the aqueous environment of the cell.

This is an important factor in the biological role of proteins.

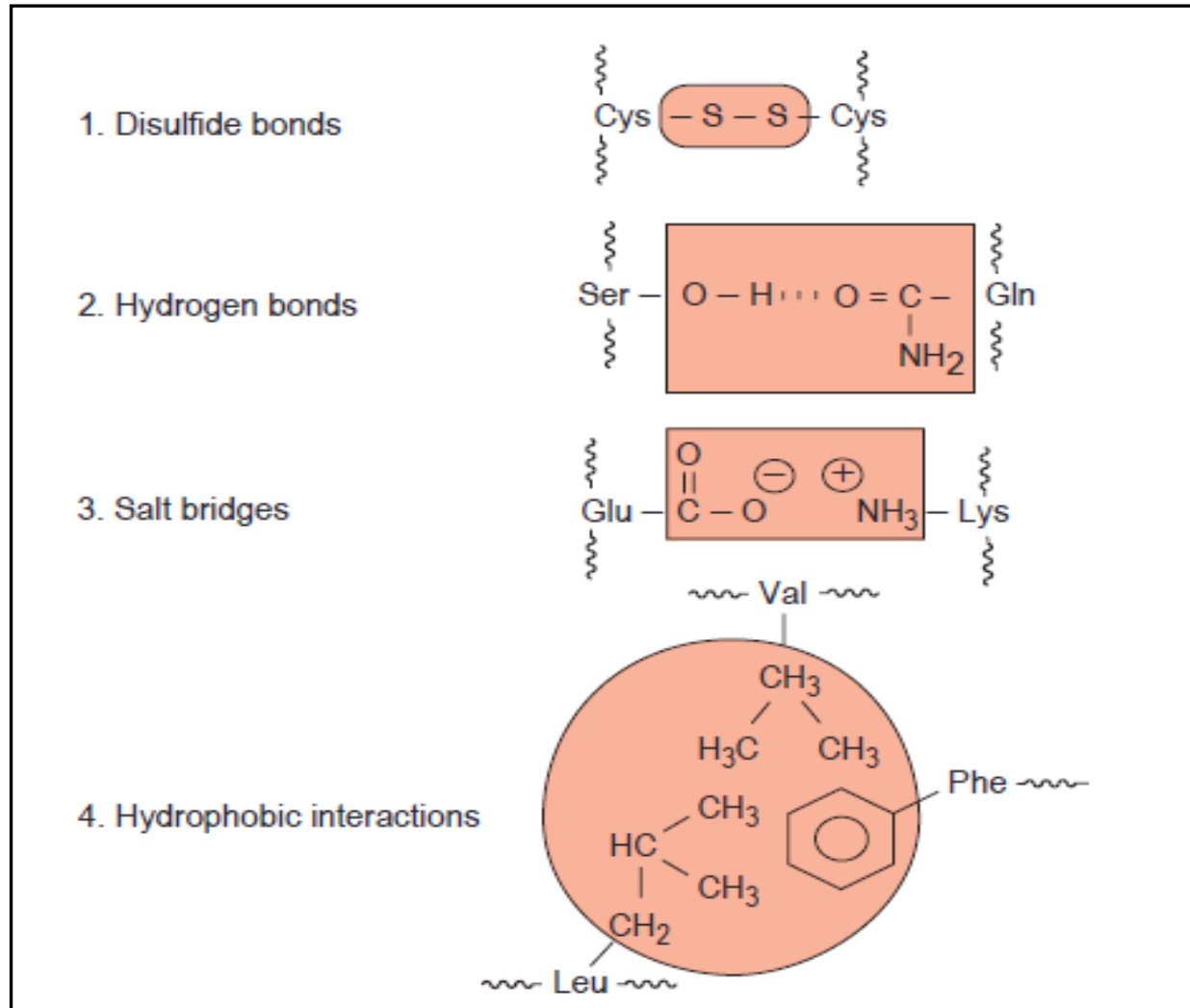
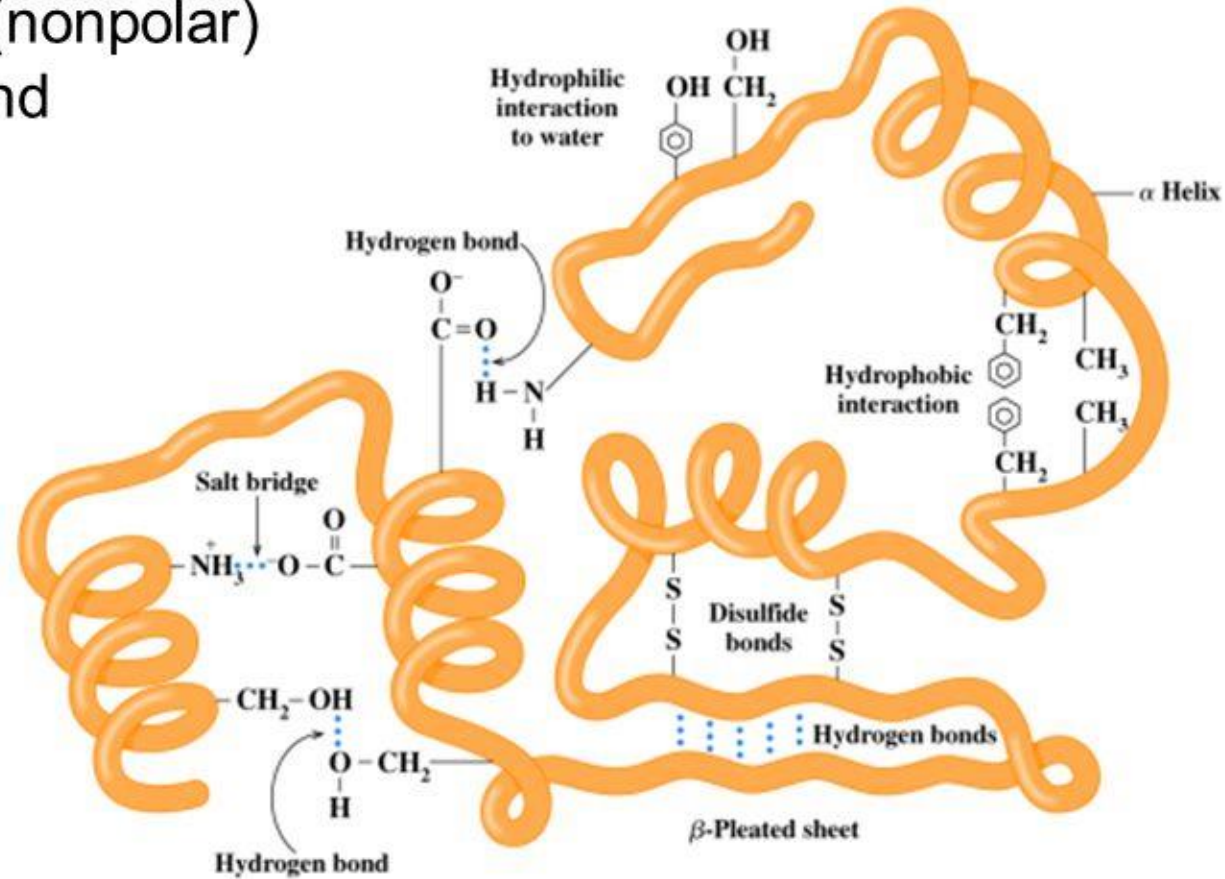


Figure 10: Elements of tertiary structure of proteins. Examples of amino acid side chain interactions contributing to tertiary structure.

Tertiary Structure

- (1) Disulfide (-S-S-)
- (2) salt bridge (acid-base)
- (3) Hydrophilic (polar)
- (4) hydrophobic (nonpolar)
- (5) Hydrogen bond



- **So far, we have learned about the structure of proteins made up of only one polypeptide chain. But many proteins contain more than one chain. This introduces another structural feature.**

4- Quaternary Structure of Proteins:

Many proteins are made up of several identical or closely related polypeptide chains. The way that these polypeptide chains, called subunits, are joined together to form the protein is called its quaternary structure. Most proteins of molecular weight greater than 50,000 atomic mass unit (amu) consist of a number of noncovalently joined subunits.

In general, most proteins consist of more than one chain and are referred to as dimeric, trimeric or multimeric proteins. Many multisubunit proteins are composed of different kinds of functional subunits, such as the regulatory and catalytic subunits.

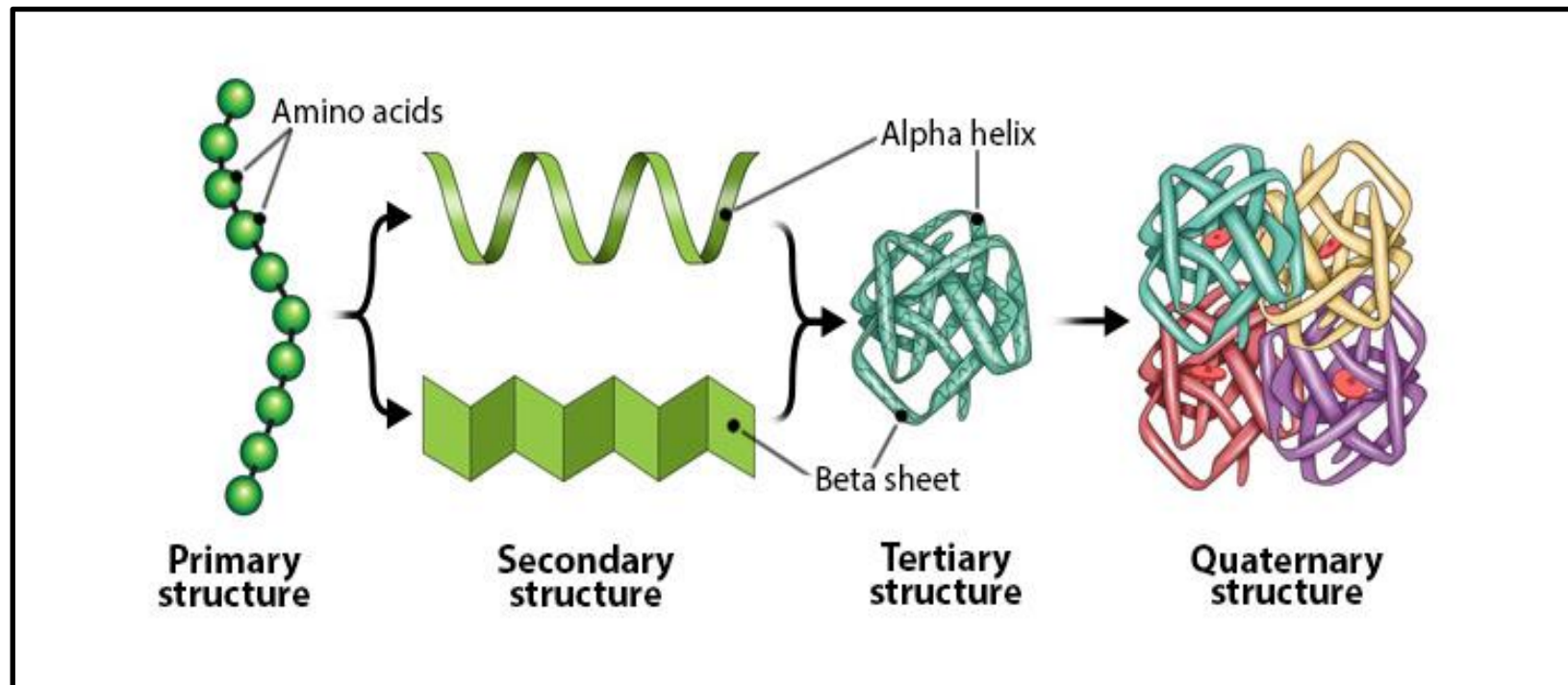


Figure 12: the structural levels

Hemoglobin is an example of such a protein (tetrameric proteins), as shown in Figure-13.

It is made up of four separate subunits. Two called α chains contain 141 amino acids each.

The other two, called the β chains, contain 146 amino acids each.

These subunits are held together by the attractive interactions. Each subunit also contains one molecule of heme.

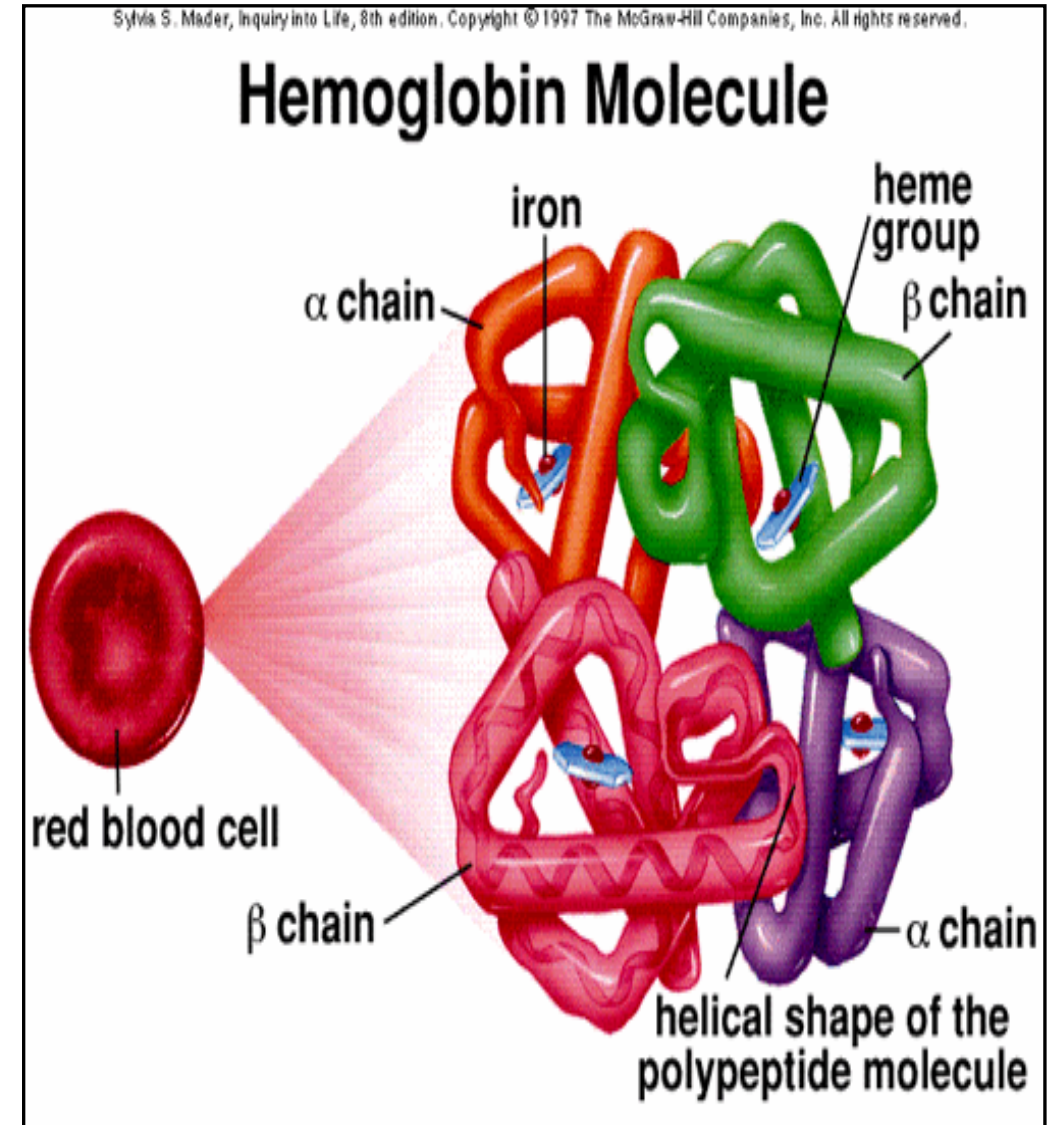
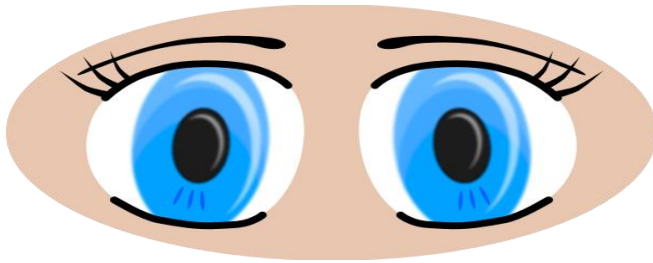


Figure-13: Hemoglobin quaternary structure.

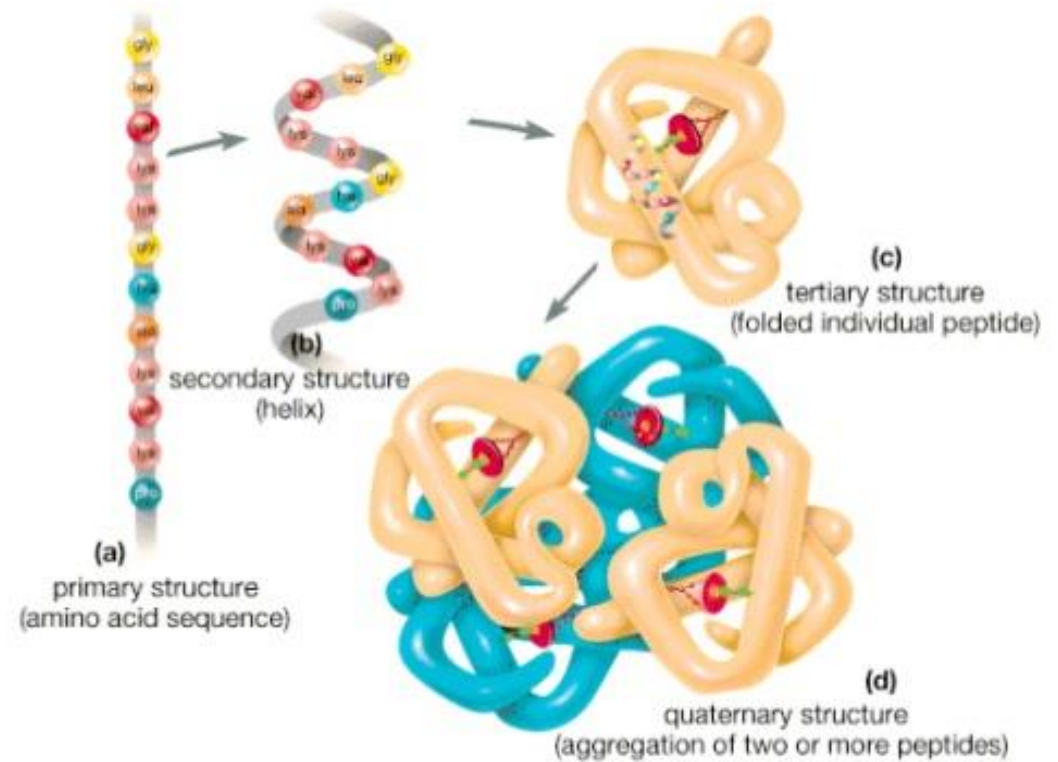
- **Thalassemia is a hereditary hemolytic in which an imbalance occurs in the synthesis of hemoglobin chains:**
- The name is derived from the Greek word, “thalassa”, which means “sea”. Greeks identified this disease present around Mediterranean sea.
- Thalassemia may be defined as the normal globin chains in abnormal proportions. The gene function is abnormal, but there is no abnormality in the polypeptide chains.
- Reduction in alpha chain synthesis is called alpha thalassemia, while deficient beta chain synthesis is the beta thalassemia. **(A superscript indicates whether a subunit is completely absent (α^0 or β^0) or whether its synthesis is reduced (α^+ or β^+)).**
- Beta thalassemia is more common than alpha variety. Beta type is characterized by a decrease or absence of synthesis of beta chains.
- Alpha thalassemia is rarer because alpha chain deficiency is incompatible with life.

Summary:

Just look at the figures only



Four Levels of Protein Structure



Assessment and Evaluation:

Q: Write brief notes about the structural levels of proteins?

Q: What is the biochemical defect in sickle cell anemia?

Q: What is the biochemical defect in thalassemia?

Good Luck