BASUDEV GODABARI DEGREE COLLEGE
KESAIBAHAL, SAMBALPUR

BLENDED LEARNING STUDY MATERIALS

UNIT-II

DEPARTMENT: ZOOLOGY

SUBJECT : BOND STABILIZING PROTEIN STRUCTURE

SEMESTER : III

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Lect in zoology

BOND STABILIZING PROTEIN STRUCTURE

DEFINITION

Proteins are one of the most abundant organic molecules in living systems and have the most diverse range of functions of all macromolecules. Proteins may be structural, regulatory, contractile, or protective; they may serve in transport, storage, or membranes; or they may be toxins or enzymes. Each cell in a living system may contain thousands of proteins, each with a unique function. Their structures, like their functions, vary greatly. They are all, however, polymers of **amino acids**, arranged in a linear sequence.

Proteins have different "layers" of structure: primary, secondary, tertiary, quaternary.

Proteins have a variety of function in cells. Major functions include acting as enzymes, receptors, transport molecules, regulatory proteins for gene expression, and so on. Enzymes are biological catalysts that speed up a chemical reaction without being permanently altered. They have "active sites" where the substrate/reactant binds, and they can be either activated or inhibited (competitive and/or noncompetitive inhibitors).

The shape of a protein is critical to its function. For example, an enzyme can bind to a specific substrate at a site known as the active site. If this

active site is altered because of local changes or changes in overall protein structure, the enzyme may be unable to bind to the substrate. To understand how the protein gets its final shape or conformation,

there are four levels of protein structure:

1.primary structure

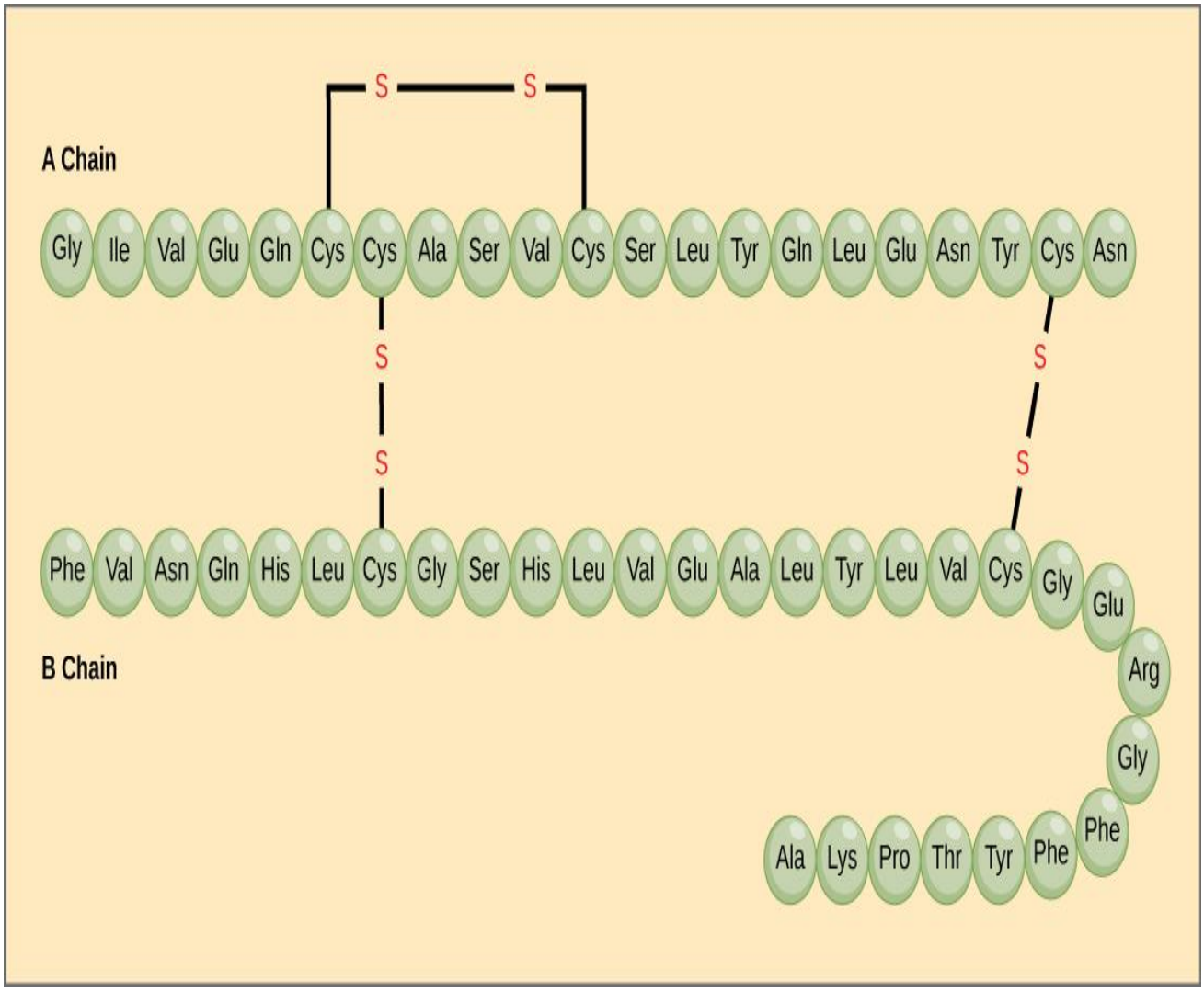
2.secondary structure

3. tertiary structure

4.quaternary structure

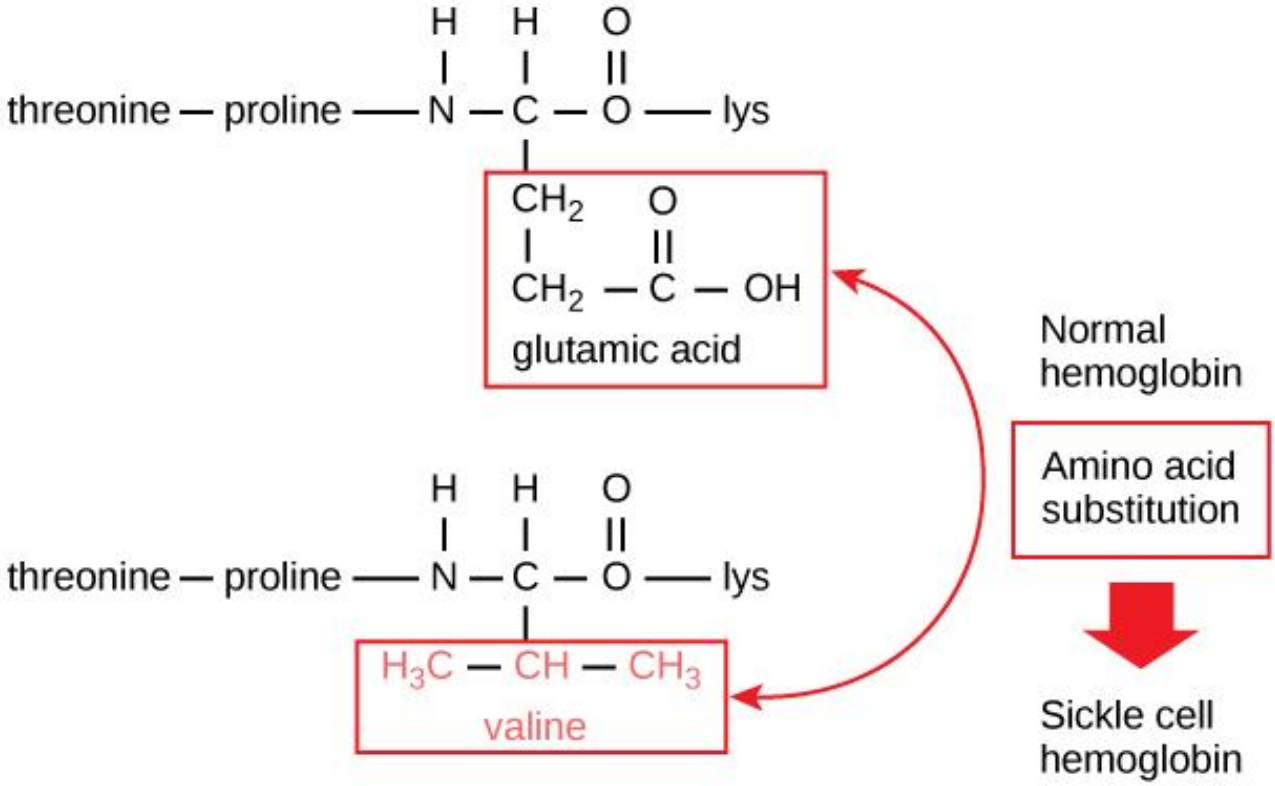
Primary Structure

- The unique sequence of amino acids in a polypeptide chain is its primary structure.
- For example, the pancreatic hormone insulin has two polypeptide chains, A and B, and they are linked together by disulfide bonds.
- The N terminal amino acid of the A chain is glycine, whereas the C terminal amino acid is asparagine.
- The sequences of amino acids in the A and B chains are unique to insulin.
- The unique sequence for every protein is ultimately determined by the gene encoding the protein.



Bovine serum insulin is a protein hormone made of two peptide chains, A (21 amino acids long) and B (30 amino acids long). In each chain, primary structure is indicated by three-letter abbreviations that represent the names of the amino acids in the order they are present. The amino acid cysteine (cys) has a sulfhydryl (SH) group as a side chain. Two sulfhydryl groups can react in the presence of oxygen to form a disulfide (S-S) bond. Two disulfide bonds connect the A and B chains together, and a third helps the A chain fold into the correct shape. Note that all disulfide bonds are the same length, but are drawn different sizes for clarity.

- A change in nucleotide sequence of the gene's coding region may lead to a different amino acid being added to the growing polypeptide chain, causing a change in protein structure and function.
- In sickle cell anemia, the hemoglobin β chain has a single amino acid substitution, causing a change in protein structure and function.



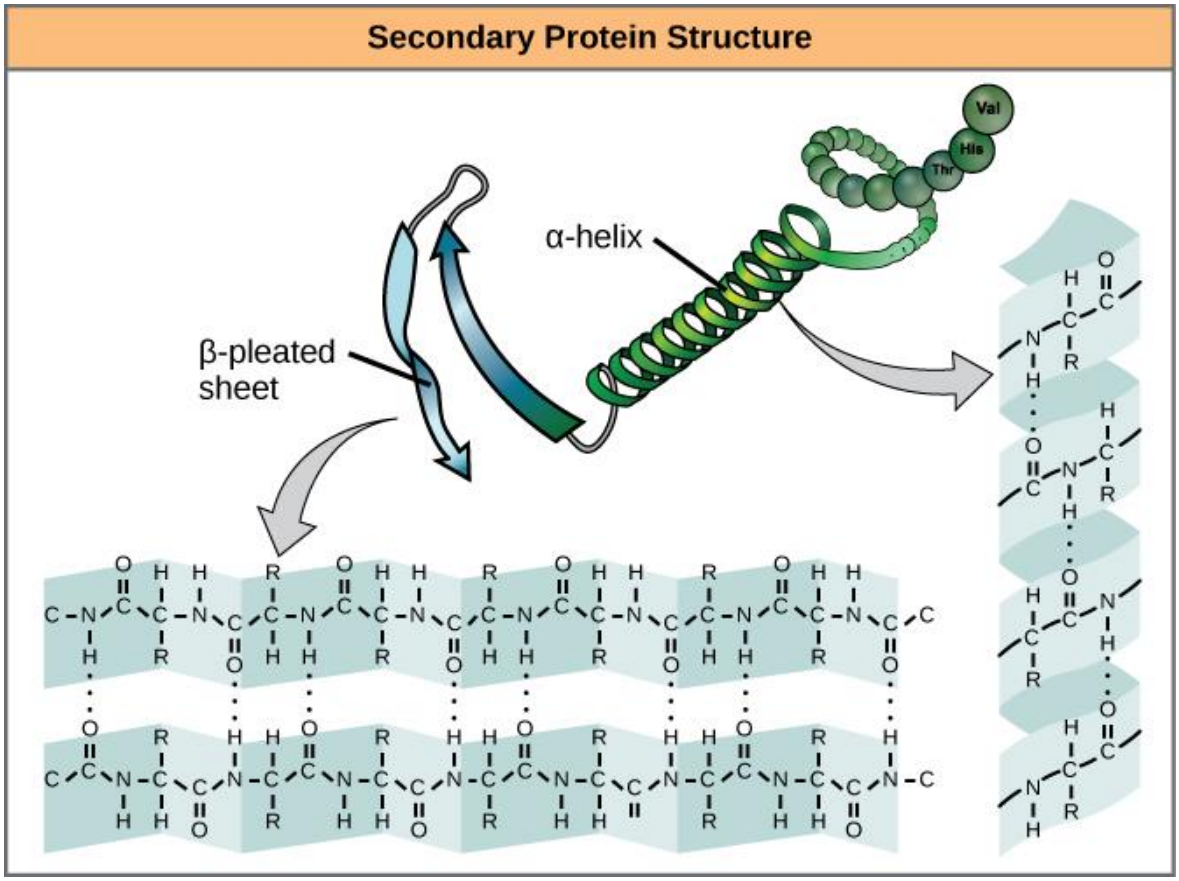
The beta chain of hemoglobin is 147 residues in length, yet a single amino acid substitution leads to sickle cell anemia. In normal hemoglobin, the amino acid at position seven is glutamate. In sickle cell hemoglobin, this glutamate is replaced by a valine.

Specifically, the amino acid glutamic acid is substituted by valine in the β chain.

- The most remarkable to consider is that a hemoglobin molecule is made up of two alpha chains and two beta chains that each consist of about 150 amino acids.
- The molecule, therefore, has about 600 amino acids.
- The structural difference between a normal hemoglobin molecule and a sickle cell molecule—which dramatically decreases life expectancy—is a single amino acid of the 600.
- What is even more remarkable is that those 600 amino acids are encoded by three nucleotides each, and the mutation is caused by a single base change (point mutation), 1 in 1800 baseIn this blood smear, visualized at 535x magnification using bright field microscopy, sickle cells are crescent shaped, while normal cells are disc-shaped. (Credit: modification of work by Ed Uthman; scale-bar data from Matt Russell)
- Because of this change of one amino acid in the chain, hemoglobin molecules form long fibers that distort the biconcave, or disc-shaped, red blood cells and assume a crescent or “sickle” shape, which clogs arteries .
- This can lead to myriad serious health problems such as breathlessness, dizziness, headaches, and abdominal pain for those affected by this disease.

Secondary Structure

- The local folding of the polypeptide in some regions gives rise to the secondary structure of the protein.
- The most common are the α-helix and β-pleated sheet structures
- Both structures are the α-helix structure—the helix held in shape by hydrogen bonds.
- The hydrogen bonds form between the oxygen atom in the carbonyl group in one amino acid and another amino acid that is four amino acids farther along the chain.
- Every helical turn in an alpha helix has 3.6 amino acid residues. The R groups (the variant groups) of the polypeptide protrude out from the α-helix chain.
- In the β-pleated sheet, the "pleats" are formed by hydrogen bonding between atoms on the backbone of the polypeptide chain.
- The R groups are attached to the carbons and extend above and below the folds of the pleat.
- The pleated segments align parallel or antiparallel to each other, and hydrogen bonds form between the partially positive nitrogen atom in the amino group and the partially negative oxygen atom in the carbonyl group of the peptide backbone.
- The α-helix and β-pleated sheet structures are found in most globular and fibrous proteins and they play an important structural role.

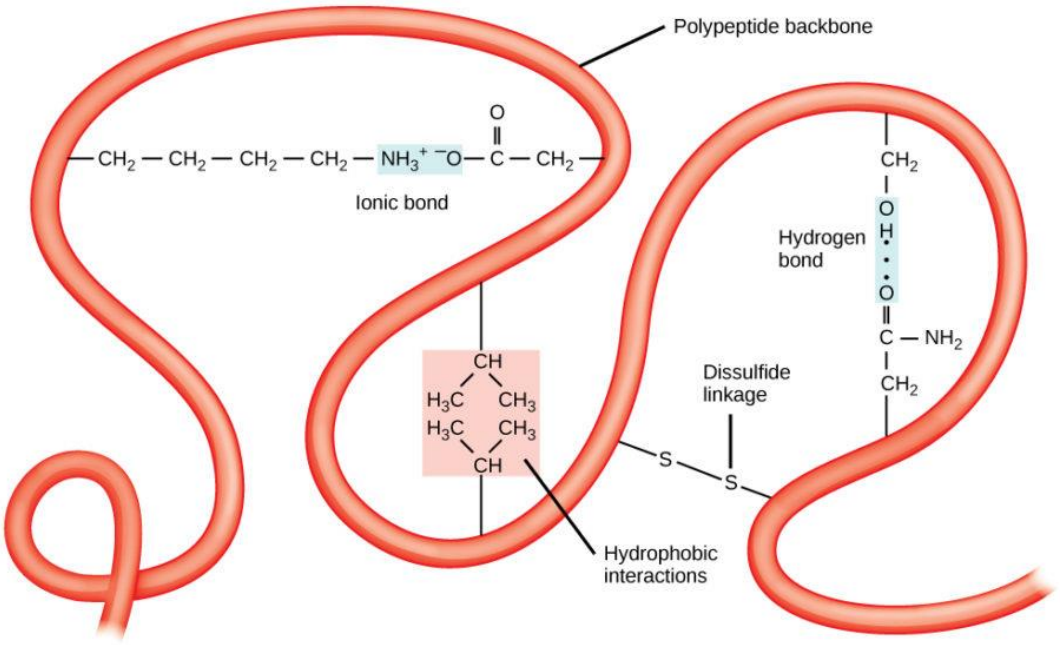


The α-helix and β-pleated sheet are secondary structures of proteins that form because of hydrogen bonding between carbonyl and amino groups in the peptide backbone. Certain amino acids have a propensity to form an α-helix, while others have a propensity to form a β-pleated sheet.

Tertiary Structure

- The unique three-dimensional structure of a polypeptide is its tertiary structure.
- This structure is in part due to chemical interactions at work on the polypeptide chain.
- Primarily, the interactions among R groups creates the complex three-dimensional tertiary structure of a protein.

- The nature of the R groups found in the amino acids involved can counteract the formation of the hydrogen bonds described for standard secondary structures.
- For example, R groups with like charges are repelled by each other and those with unlike charges are attracted to each other (ionic bonds).
- When protein folding takes place, the hydrophobic R groups of nonpolar amino acids lay in the interior of the protein, whereas the hydrophilic R groups lay on the outside.
- The former types of interactions are also known as hydrophobic interactions.
- Interaction between cysteine side chains forms disulfide linkages in the presence of oxygen, the only covalent bond forming during protein folding.
- All of these interactions, weak and strong, determine the final three-dimensional shape of the protein.
- When a protein loses its three-dimensional shape, it may no longer be functional.

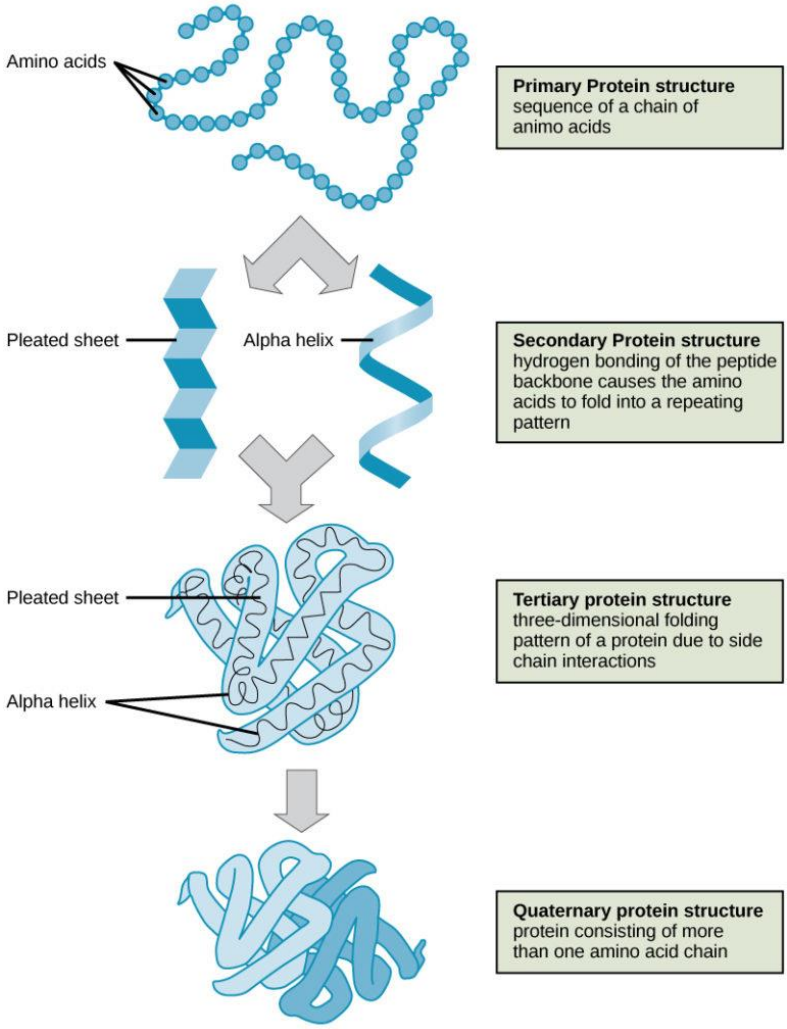


The tertiary structure of proteins is determined by a variety of chemical interactions. These include hydrophobic interactions, ionic bonding, hydrogen bonding and disulfide linkages.

Quaternary Structure

- In nature, some proteins are formed from several polypeptides, also known as subunits, and the interaction of these subunits forms the quaternary structure.
- Weak interactions between the subunits help to stabilize the overall structure.
- For example, insulin (a globular protein) has a combination of hydrogen bonds and disulfide bonds that cause it to be mostly clumped into a ball shape.
- Insulin starts out as a single polypeptide and loses some internal sequences in the presence of post-translational modification after

the formation of the disulfide linkages that hold the remaining chains together.



- The four levels of protein structure can be observed in these illustrations.

- Silk (a fibrous protein), however, has a β-pleated sheet structure that is the result of hydrogen bonding between different chains. The four levels of protein structure (primary, secondary, Tertiary and quaternary) are illustrated.