

# Proteins



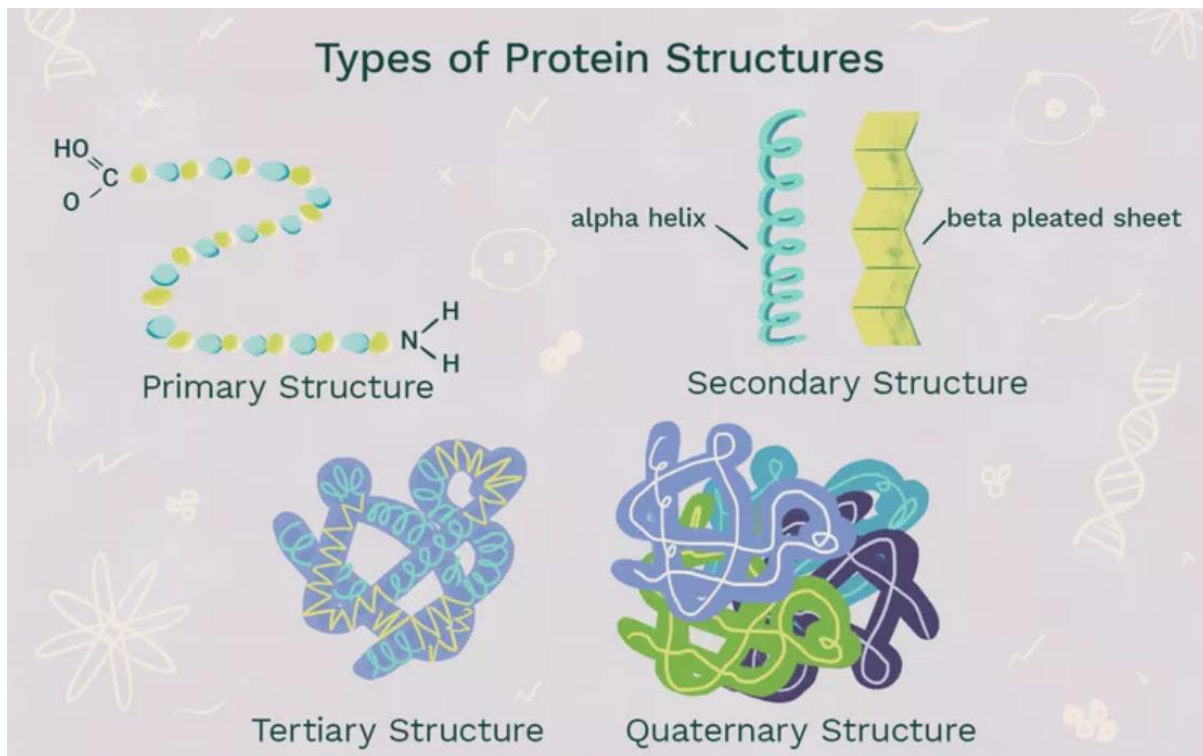
## Proteins

The word protein (Gk. **proteios** - first or foremost) was first coined by **Berzelius** (1838) and first used by Mulder (1838). It constitutes about 15% of our body by mass and involved in various functions like structural, storage, transport, signalling, movement, etc.

These are natural heteropolymer of substances like amino acids.

To understand the detailed structure of protein, we first take a close view of amino acids.

### Structural Level of Proteins



#### There are four structural levels in proteins

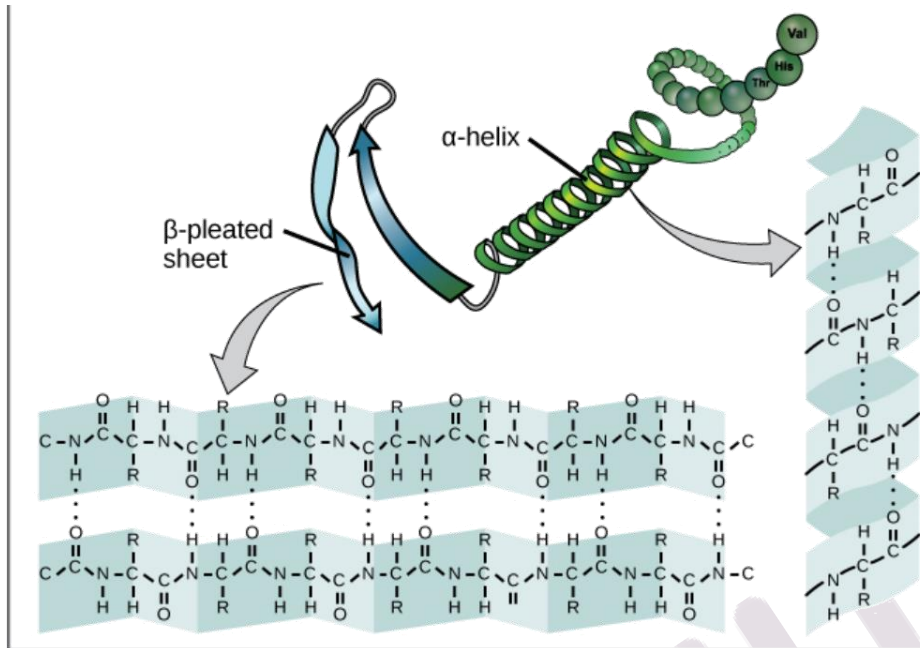
(i) **Primary structure** This includes number of polypeptides, number and sequence of amino acids in each polypeptide.

(ii) **Secondary structure** There are three types of secondary structures  $\alpha$ -helix,  $\beta$ -pleated sheet and collagen helix. The turns of helices and sheets are attached by hydrogen bonds.

(iii) **Tertiary structure** Tertiary structure is stabilised by several types of bonds-hydrogen bonds, ionic bonds, van der Waals interaction, covalent bonds and hydrophobic bonds. It gives 3-D conformation to protein.

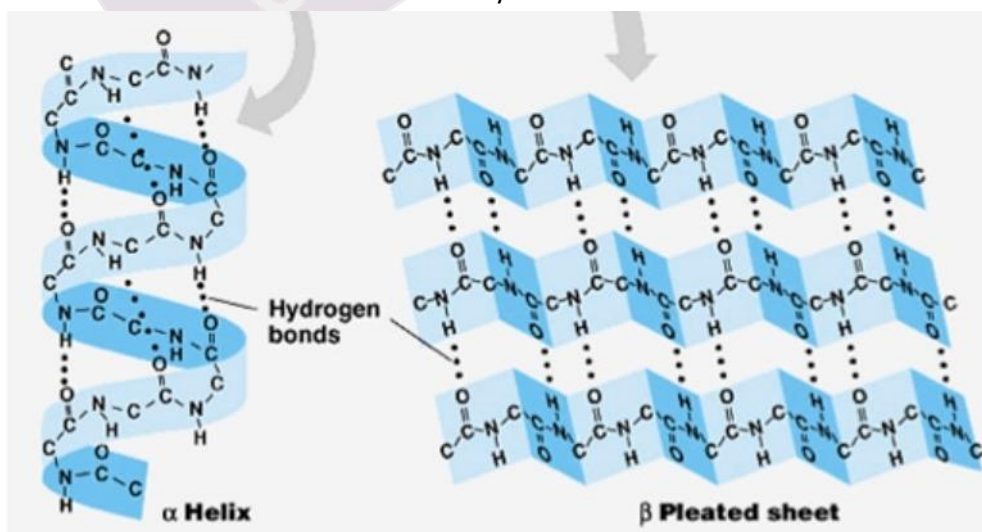
(iv) **Quaternary structure** Found only in multimeric protein, where two tertiary structures join as a subunit.

## SECONDARY STRUCTURE



### $\alpha$ -helix

- The  $\alpha$ -helix is a rigid, rod like structure that forms when a polypeptide chain twists into a helical conformation.
- The screw sense of  $\alpha$  helix can be right-handed (clockwise) or left-handed (counter clockwise).
- Right-handed helices are energetically more favourable.
- There are **3.6 amino acid residues per turn of the helix**
- The **pitch** (the distance between corresponding points per turn) is **0.54 nm**.
- Each residue is related to the next one by a **rise of 1.5 Å (0.15 nm)** along the helix axis.
- **A single turn of  $\alpha$ -helix involves 13 atoms** from O to the H of the H bond.  
**For this reason, the  $\alpha$ -helix is referred to as the 3.6<sub>13</sub> helix.**
- Length of  $\alpha$ -helix is usually 10-15 amino acid residues.
- Hydrogen bonds form between the N-H group of each amino acids and the carbonyl group of the amino acid four residues away.

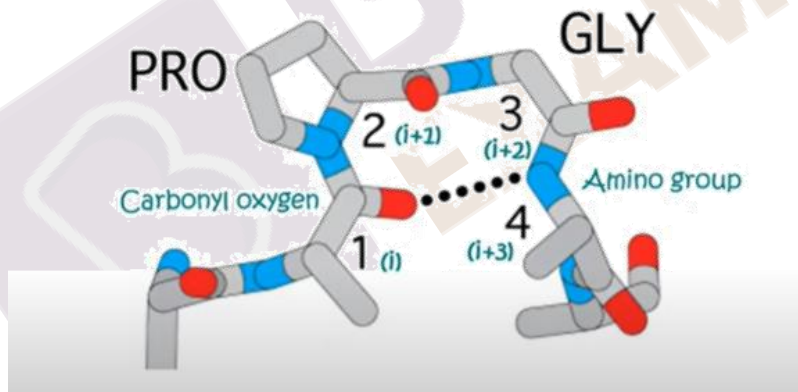


### $\beta$ -pleated sheets

- $\beta$  -pleated sheets form when two or more polypeptide chain segment line up side by side.
- Each individual segment is referred to as a  $\beta$  -strand.
- Each  $\beta$  -strand is fully extended.
- The distance between adjacent amino acids along a  $\beta$  strand is approximately  $3.5 \text{ \AA}$ .
- $\beta$  -pleated sheets are stabilized by hydrogen bonds that form between the polypeptide backbone N-H and carbonyl groups of adjacent strand.
- Adjacent strand can be either parallel or antiparallel.

### Turns

- Most proteins have compact, globular shapes, requiring reversals in the direction of their polypeptide chains. Many of these reversals are accomplished by a common structural element called the turn.
- Turns, composed of **three or four residues**.
- Turns are classified as a **third type of secondary structure**.
- They are **U-shaped** secondary structures are stabilized by a hydrogen bond between their end residues.
- **Glycine and proline** are commonly present in turns.
- The lack of a large side chain in glycine and the presence of a built-in bend in proline allow the polypeptide backbone to fold into a tight U shape. Turns allow large proteins to fold into highly compact structure.



### Conditions allowing denaturation of Proteins:

#### Strong acids or bases

- Changes in pH result in protonation or deprotonation of side group of amino acids of protein
- It alters hydrogen bonding and salt bridge patterns.

#### Organic solvents

- Water-soluble organic solvents such as ethanol interfere with hydrophobic interactions because they interact with nonpolar R groups and form hydrogen bonds with water and polar protein groups.
- Nonpolar solvents also disrupt hydrophobic interactions.

#### Detergents

- These amphipathic molecules disrupt hydrophobic interactions, causing proteins to unfold into extended polypeptide chains

### Reducing agents

- In the presence of reagents such as urea, reducing agents such as  $\beta$ -mercaptoethanol convert disulphide bridges to sulfhydryl groups.

### Heavy metal ions

- They disrupt salt bridges by forming ionic bonds with negatively charged groups. Heavy metals also bond with sulfhydryl groups.

### Temperature change

- As the temperature increases, the rate of molecular vibration increases. Eventually, weak interactions such as hydrogen bonds, van der Waal interaction are disrupted and the protein unfold.

## SOLUBILITIES OF PROTEINS

### Effect of pH:

- At pI, the protein molecules carry no net charge. At pI, protein has minimum solubility. Hence when the pH of a protein mixture is adjusted to the pI of the protein to be isolated, its precipitation occurs due to decrease in solubility.

### Effect of ionic strength:

- The solubility of a protein at low ionic strength generally increases with salt concentration. This process is known as **salting in**.
- The binding of salt ions to the protein's ionizable groups decreases interaction between oppositely charged groups on the protein molecules. Water molecules then can form solvation spheres around these groups. However, when large amounts of salt are added to a protein in solution, a precipitate forms. This process is referred to as **salting out**.

### Effect of solvent:

- Organic solvents such as acetone, ethanol, due to their low dielectric constants lower the solvating power of their aqueous solutions for proteins.

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