BIOCHEMISTY

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PROTEIN STRUCTURE

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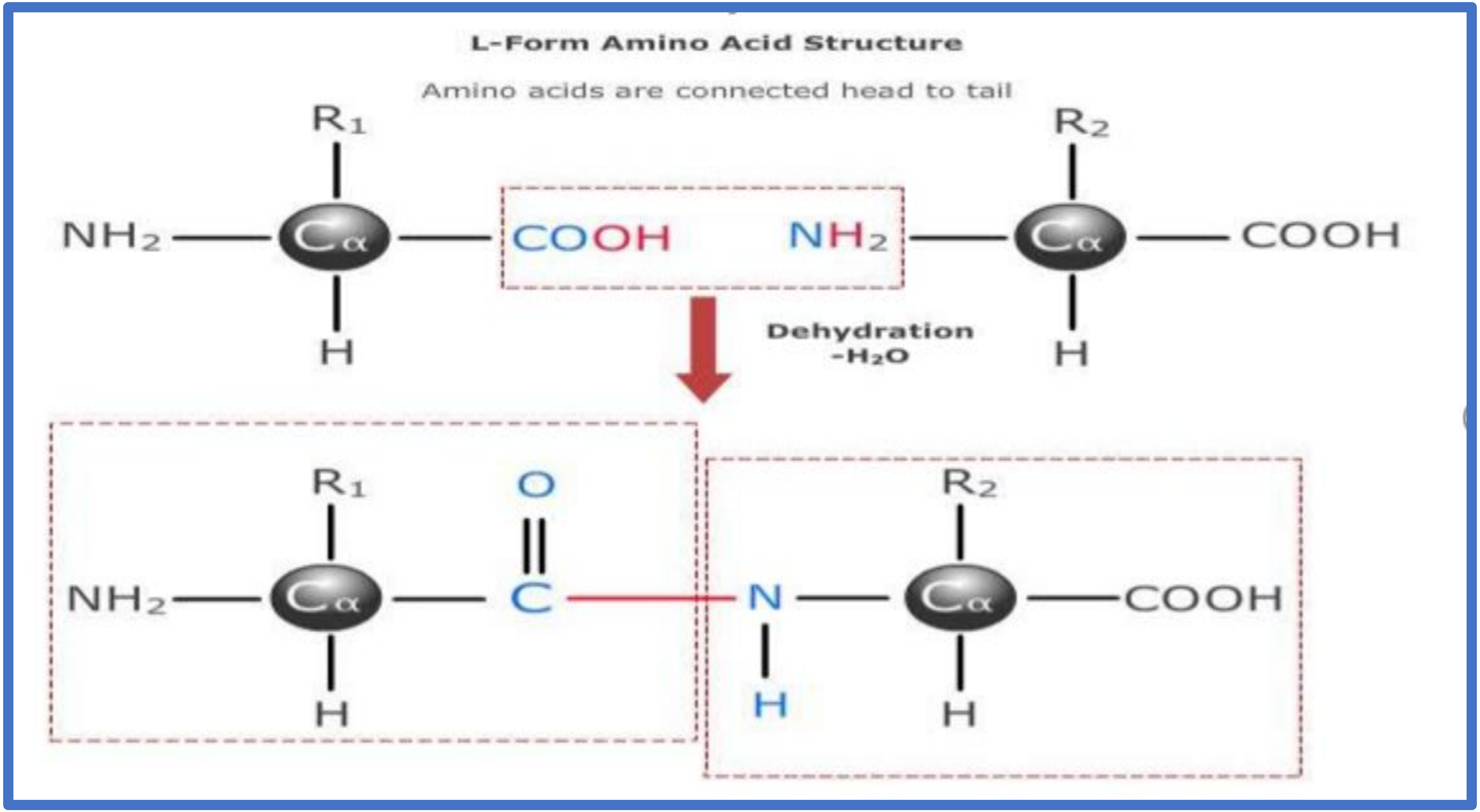
Proteins - linear sequences of amino acids linked by peptide bonds.

Amino acids => linked *head to tail*.

- Peptide bond - covalent bond - α-amino group of one amino acid and the α-carboxyl group of another.
- Two amino acids join => form a dipeptide => further be linked to other amino acids in a similar manner => form chain linkages.
- oligopeptide - long, unbranched chain of amino acids (upto 25 amino acid residues)
- polypeptide - peptide chain >25 amino acids residues
- tetrapeptide +H3N-serine- tyrosine- phenylalanine-leucine-COO-

Way of writing: Peptide chains with free α-carboxyl group (C-terminal) on the right & free α-amino (N-terminal) on the left & a hyphen between amino acids => indicate peptide bonds

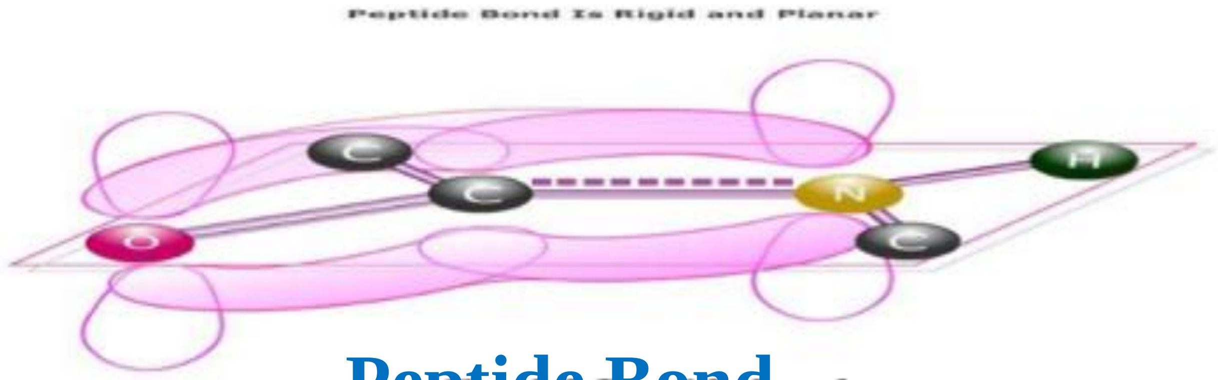
  - Ser-Tyr-Phe-Leu or S-Y-F-L.



Formation of peptide bond by dehydration

Peptide Bond

- Between N and carb, it exhibits => partial double bond character
  - This is due to closeness of carbonyl carbon – oxygen double bond and
  - Electron withdrawing property of N and O atoms => allowing the resonance structures.
- C-N bond length < normal C-N single bond and >C=O bond > normal >C=O bond.
  - The peptide bond is relatively rigid and planner
  - Free rotation takes place => about Cα-N and Cα-C bonds, permitting adjacent units to be at different angles.
- **H** of the amino group is nearly always **Trans** to **O** of carbonyl group, rather than **cis**



Peptide Bond

Protein Structure

- Peptide chain forms a specific **shape** (conformation).
- Conformation - **three dimensional** arrangement of atoms <= determined by the **amino acid sequence**.
- Structure : Four levels - **primary, secondary, tertiary** & **quaternary**.

Primary structure

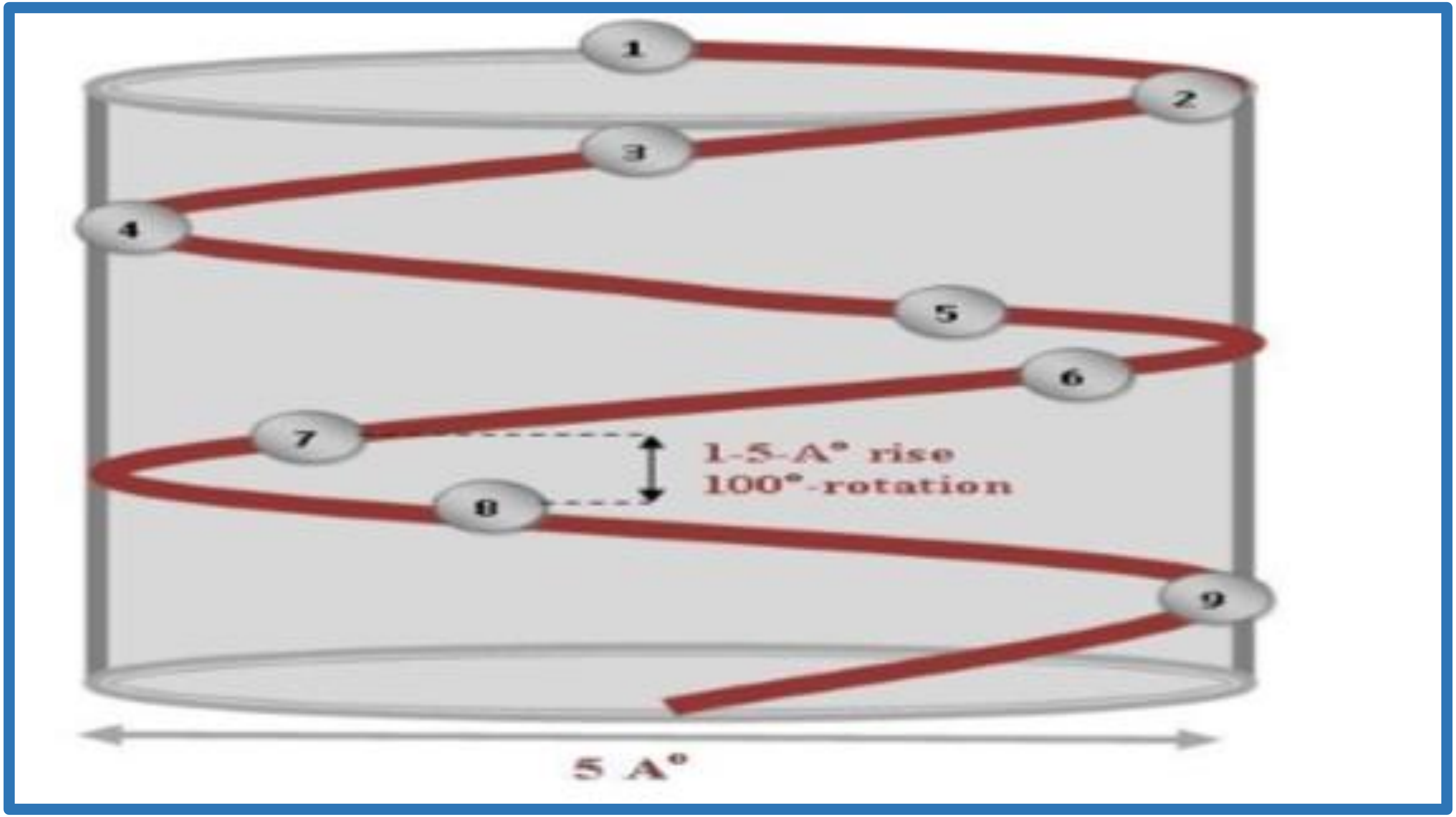
- **linear sequence** of a a joined by **peptide** bonds.
- Include **disulfide bonds** b/w cysteine residues => Formed by the oxidation of SH groups on cysteine residues => results in **cystine residues**
- Disulfide bonds are => present in **extracellular proteins**

Secondary structure

Regular folding of regions of the polypeptide chain. Types => **α-helix** & **β- Pleated sheet**

α-helix - **regular helical conformation -** in a rod shape.

- carbonyl oxygen is **hydrogen bonded -** to H on the amino group of **fourth amino acid**
- **3.6 amino acids** per turn of the helix
- cover a distance of 0.54 nm and
- each a a residue represents => 0.15 nm advance along helix axis.
- **side chain** => positioned => outside of the cylindrical helix.
- **Pro** is rarely found in α-helical regions - it can’t form the correct pattern of H-bonds - due to lack of a H atom on its N atom => **Pro** found at **end of an α-helix -** alters the direction of polypeptide chain & terminates helix .



Secondary structure of Protein with α-helix

β-pleated sheet

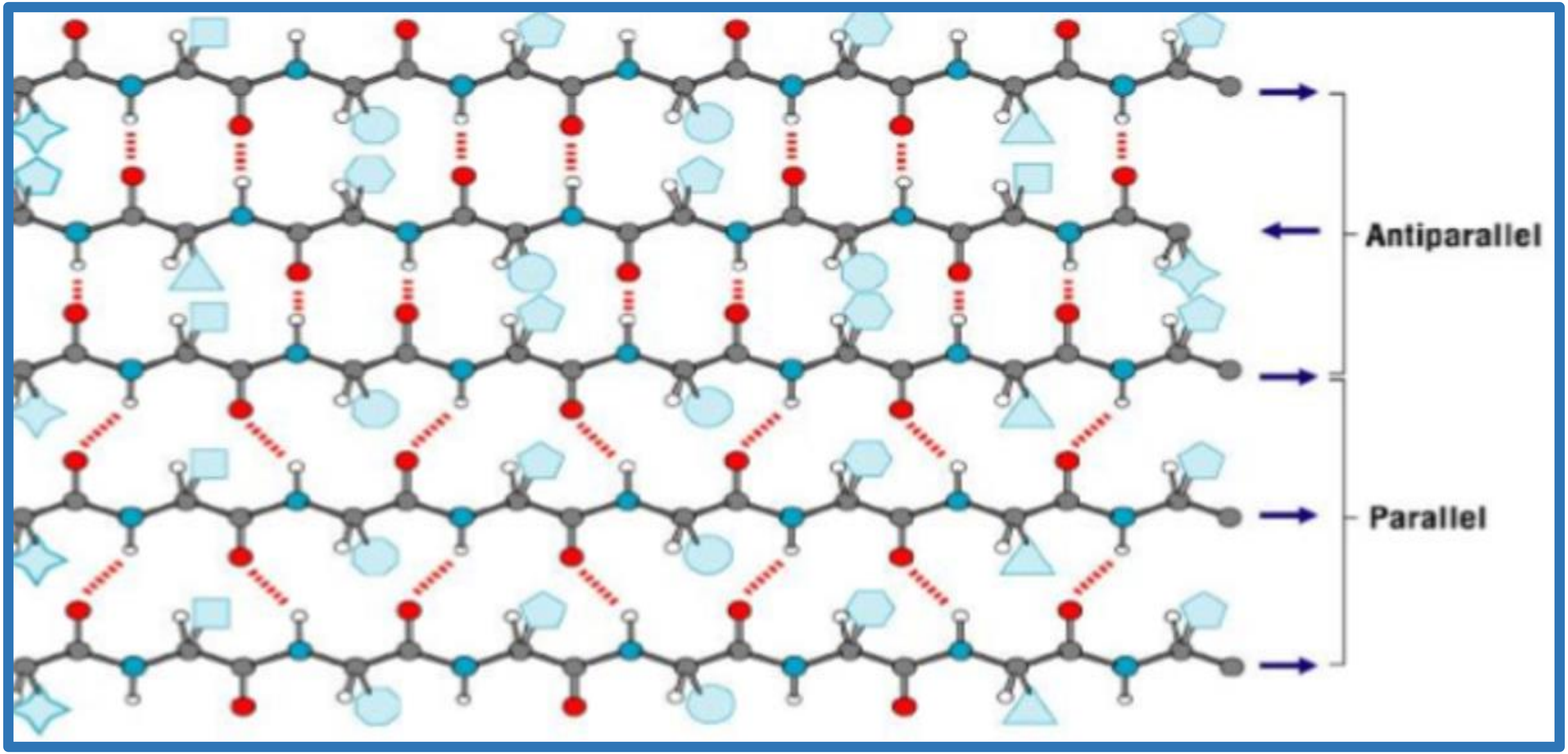
H-bonds form between the peptide bonds either

- in different polypeptide chains or
- in different sections of the same polypeptide chain.

- Planarity of the peptide bond => directs polypeptide => pleated with **the side chains(aa)** protruding **above and below** the sheet.

- **Adjacent polypeptide chains** in β-pleated sheet can be either
  - **parallel** or
  - **antiparallel** depending on directions
  - **fully extended**, with a distance of 0.35nm from Cα atom to next.
  - **Sheets => slightly curved** and,
  - if several polypeptides are involved, the sheet can form a **β-barrel**.

- **Multiple β-pleated** sheets => give **strength and rigidity** in **structural** proteins, eg. **silk** fibroin => consists of **antiparallel** β-pleated sheet stacks



Secondary structure of Protein with β- sheet

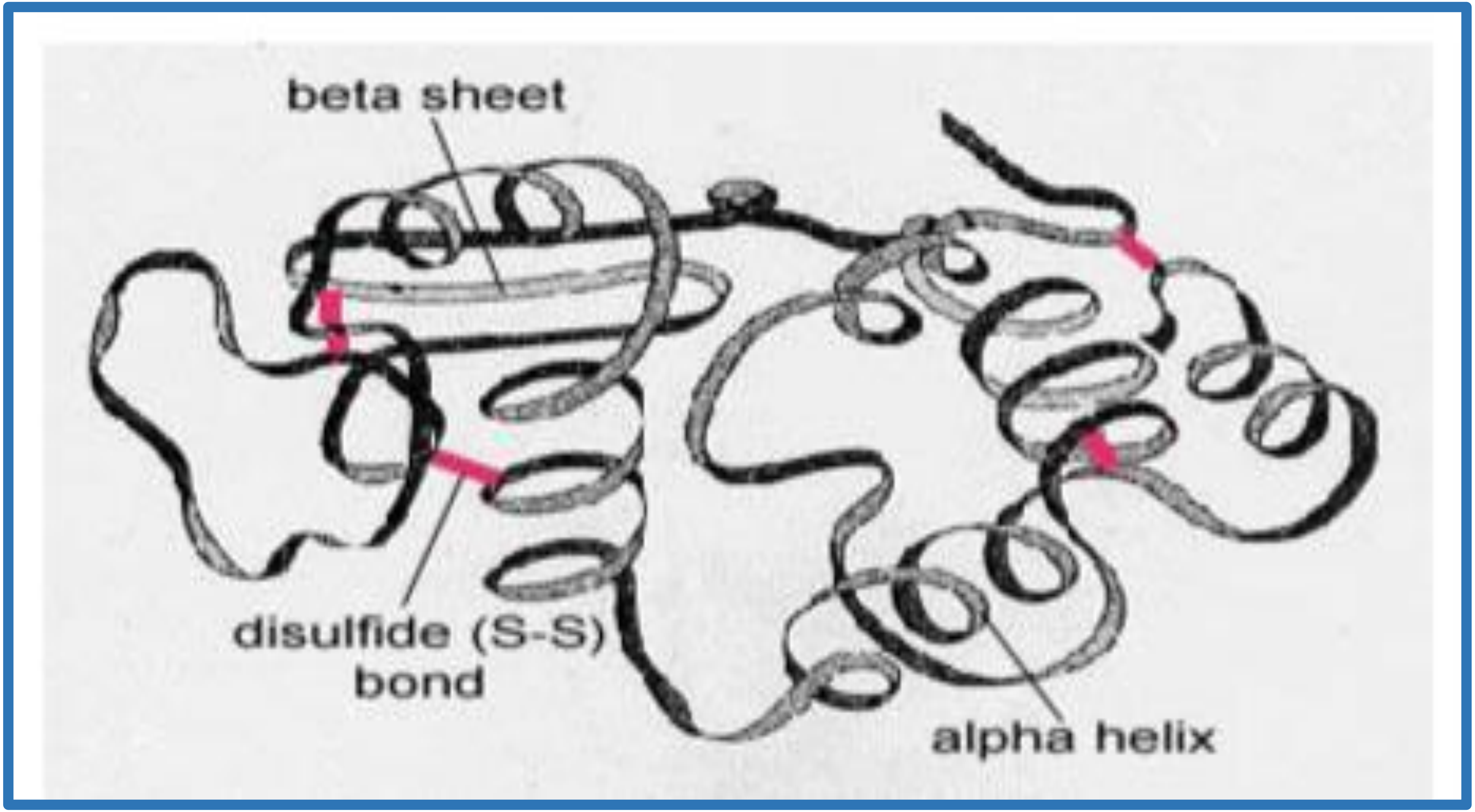
Tertiary structure

Spatial arrangement of amino acids - far apart in linear sequence; residues - adjacent.

- **“Tertiary structure”** - **three dimensional conformation of a polypeptide**.
  - indicates, in 3D space, how **secondary structural features assemble** => form **domains** and
    how these domains **relate spatially to one another**.
- **domain** - a section of protein structure sufficient to **perform a particular chemical or physical task**

  eg.,binding of a substrate or other ligand.

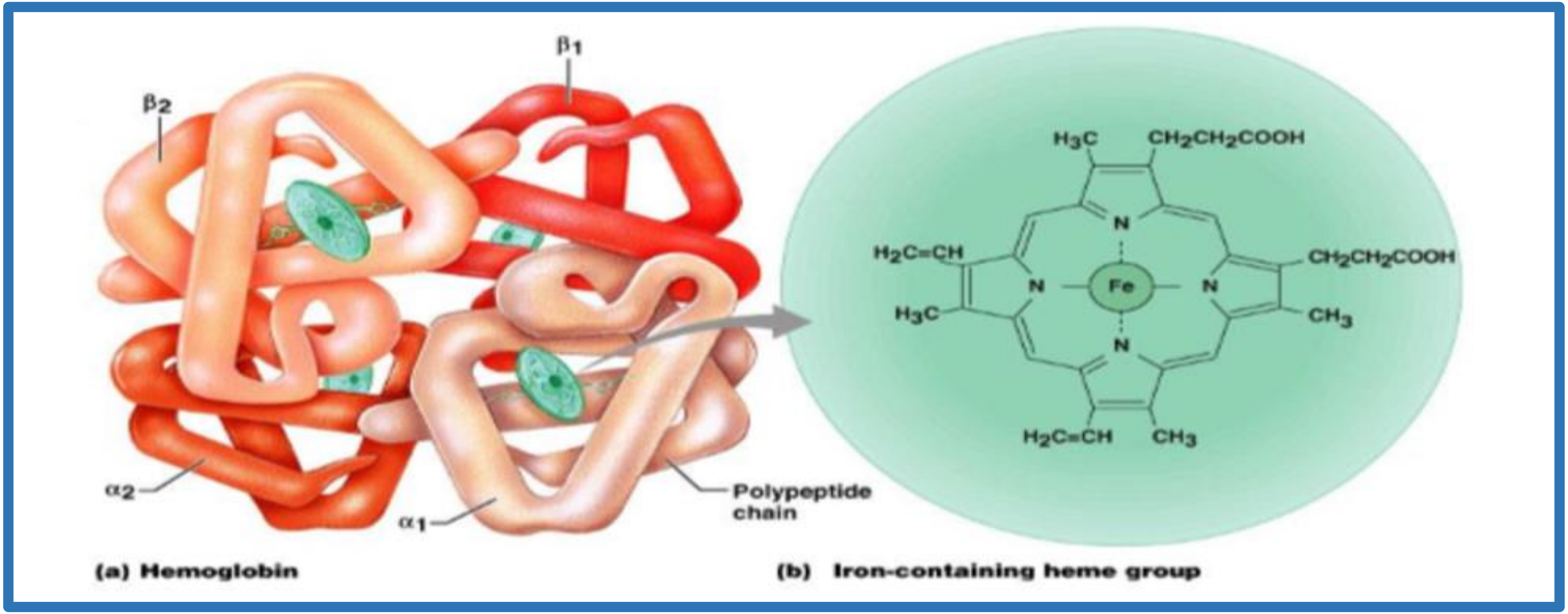
  eg., **myoglobin**, a globular protein, polypeptide chain folds spontaneously so that
  majority of its polar , charged side chains are on the surface, and
  majority of its hydrophobic side chains are buried in the interior
- **Once folded** , the 3D, biologically active(native) **conformation is maintained** by
  - hydrophobic interactions,
  - hydrogen bonding,
  - electrostatic forces (including salt bridges, Vander Waals interactions), and
  - covalent disulfide bonds.



Tertiary structure of Protein

Quaternary structure

- \> one polypeptide chains
  - such as haemoglobin => quaternary / tetrahedral structure.
- spatial arrangement of the polypeptide subunits and the nature of the interactions between them.
- These interactions may be covalent links or noncovalent interactions



(a) Hemoglobin

(b) Iron-containing heme group

Quaternary structure of Protein