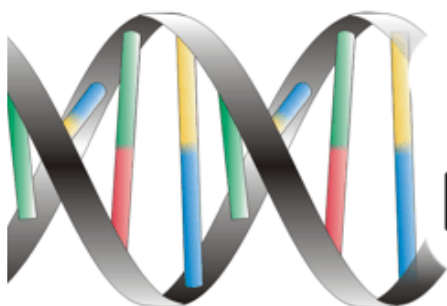



PROTEINS

(Foundation Block)



Color Index:

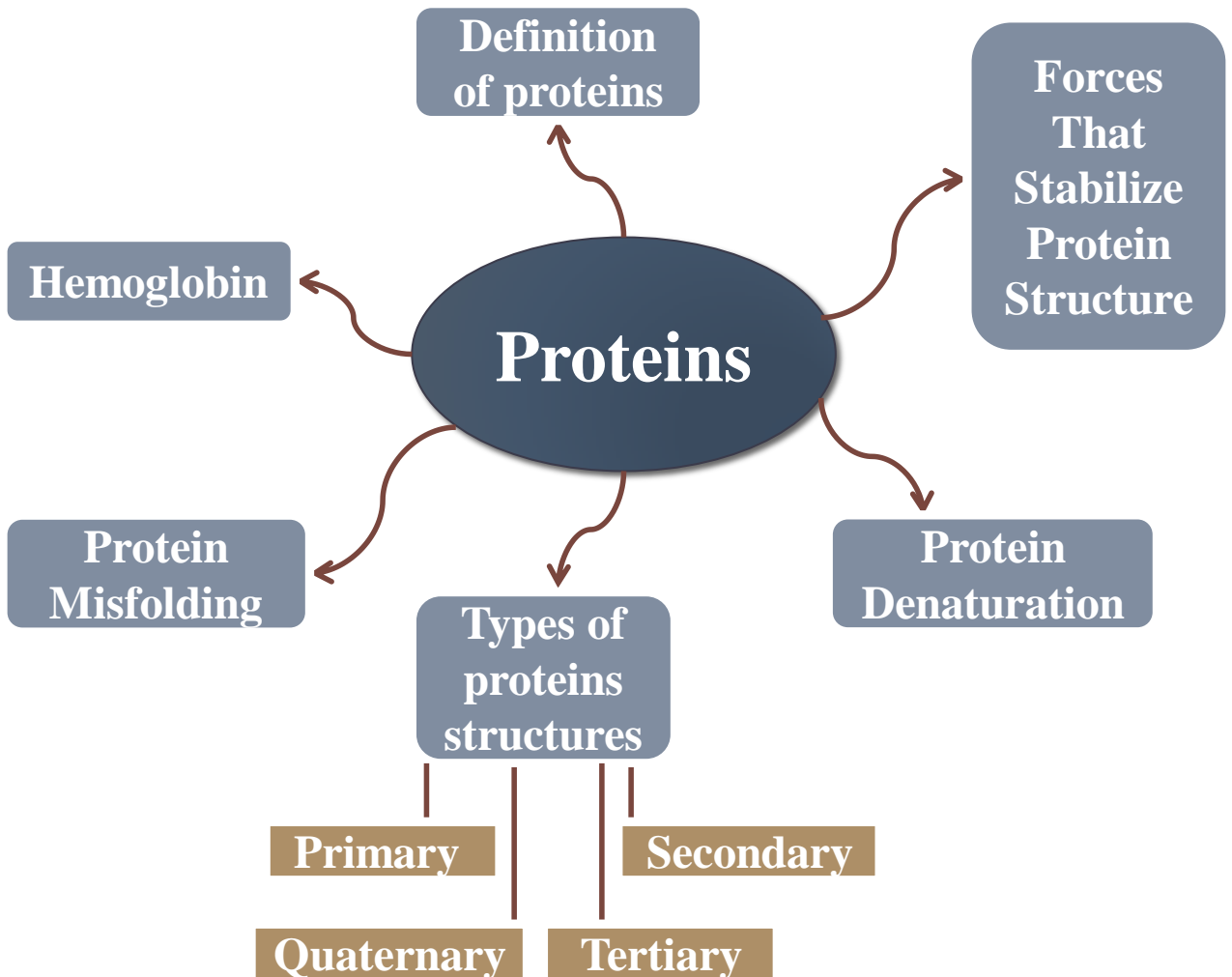
- Pink = Girls** ■
- Blue = Boys** ■
- Red = Important** ■



“Get going. Move forward. Aim High. Plan a takeoff. Don't just sit on the runway and hope someone will come along and push the airplane. It simply won't happen. Change your attitude and gain some altitude. Believe me, you'll love it up here.”

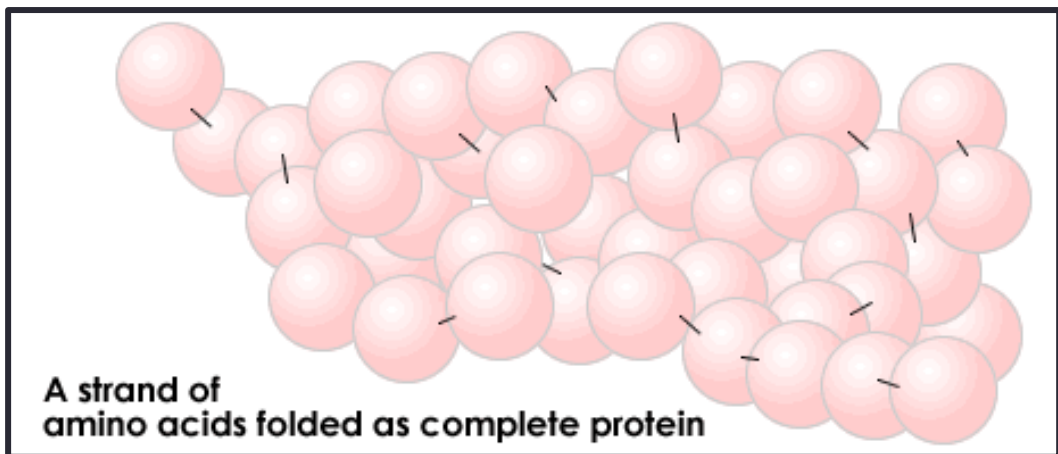
— Donald Trump





What are proteins?

Proteins are polymers of amino acids joined together by peptide bonds.



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Protein Structures

Primary Structure

Secondary Structure

Tertiary Structure

Quaternary Structure

α helix

β sheets

Collagen,
triple helix

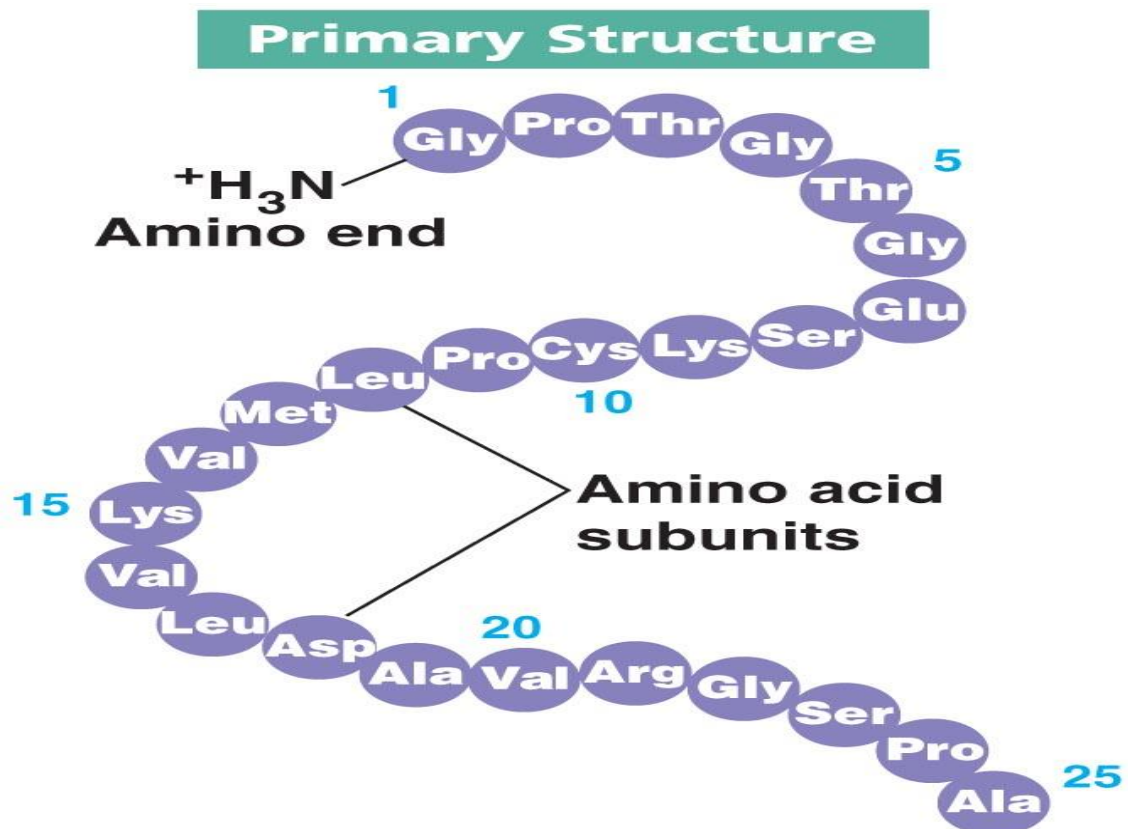
Antiparallel β sheets

Parallel β sheets

Primary Structure:

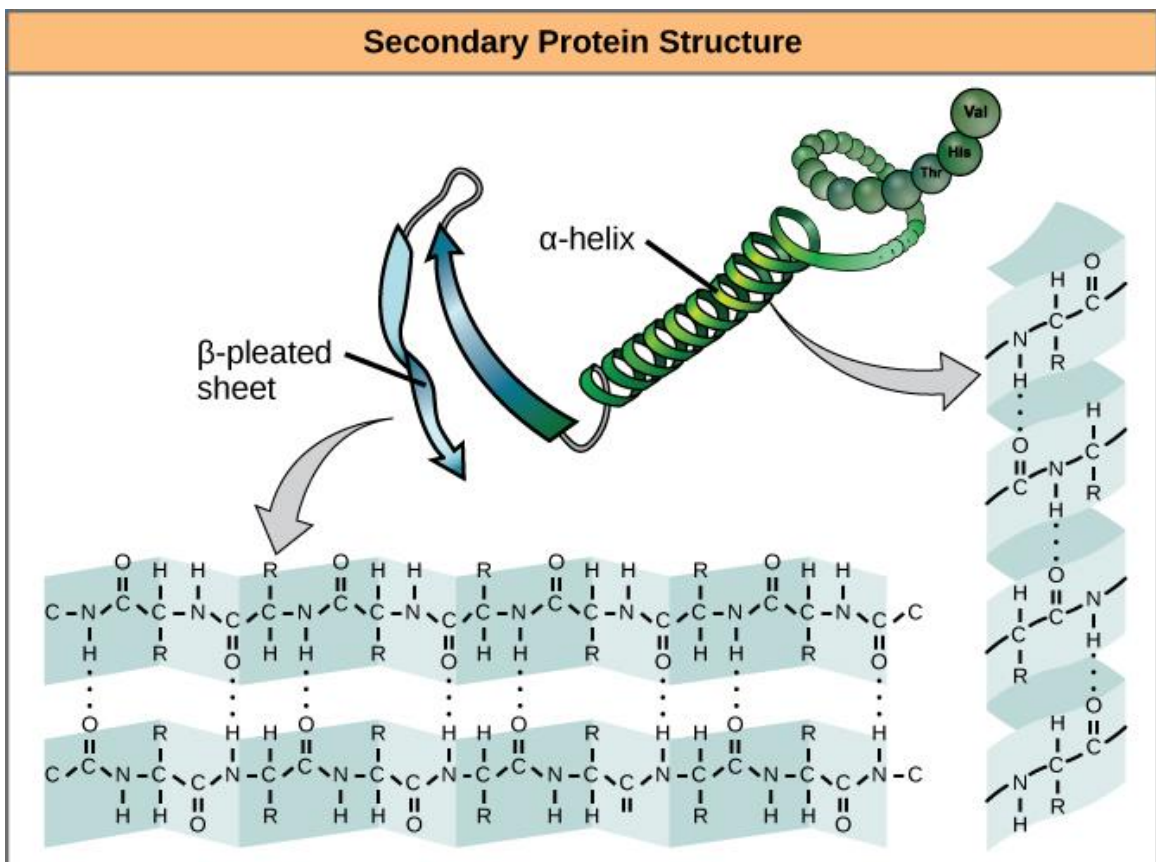
- The linear sequence of amino acids.
- Covalent bond: peptide bond and if SH (Sulfhydryl) is there, they make some disulfide bond.

(We only discuss the backbone, not the side chain).



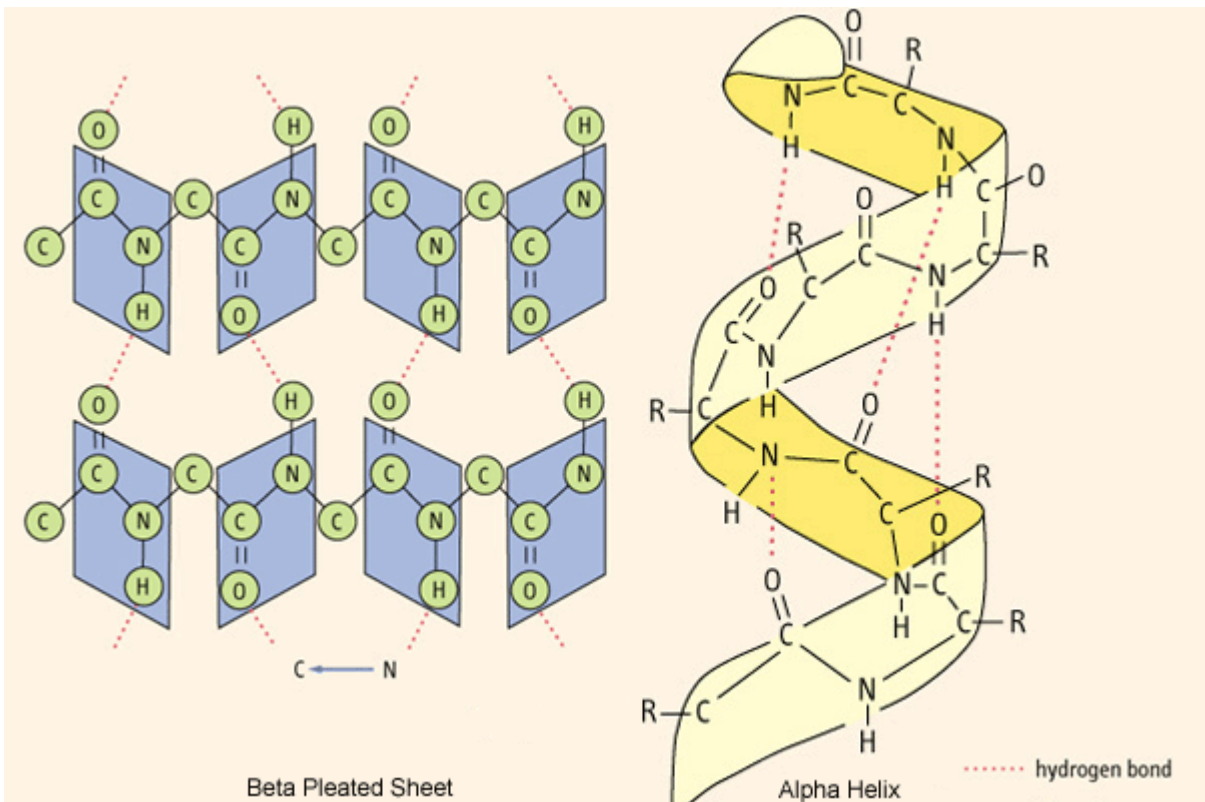
Secondary Structure:

- It is the local three-dimensional arrangement of a polypeptide backbone. (not the side chain.)
- Excluding the conformations (3D arrangements) of its side chains.



❖ α helix:

- Right handed.
- 3.6 amino acid residues per turn, stabilized by hydrogen bonding. (Between 1st carboxylic group and 4th amino group).
- Side chain points outward and downward.
- The core is tightly packed and its atoms are Van Der Waals contact.



❖ β sheets:

- Two or more polypeptide chains (**one if too long**) make hydrogen bonding.
- Also called pleated sheets because of their appearance.

Antiparallel β sheets	Parallel β sheets
Opposite direction.	Same direction.
Hydrogen bonding is more stable.	Less stable (distorted).

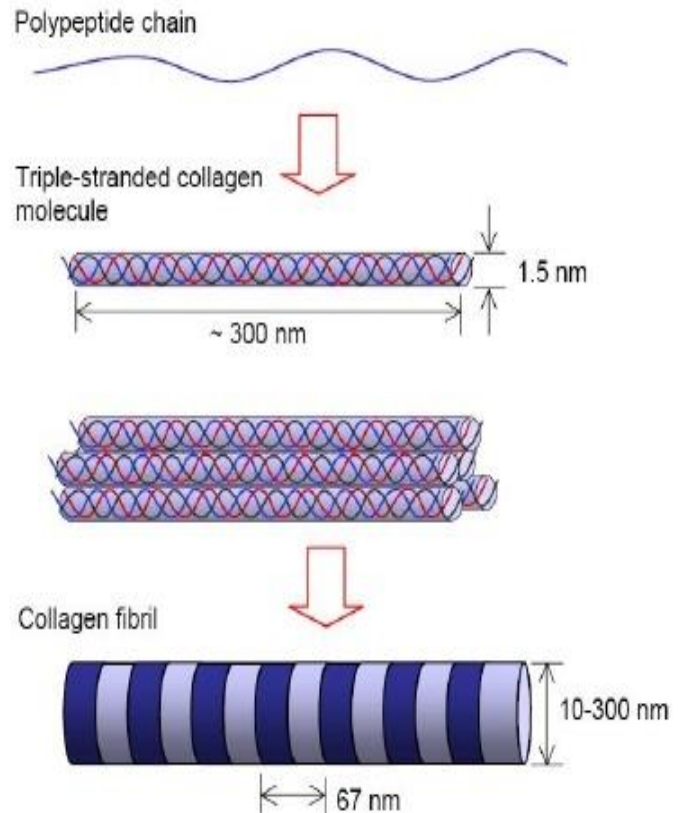
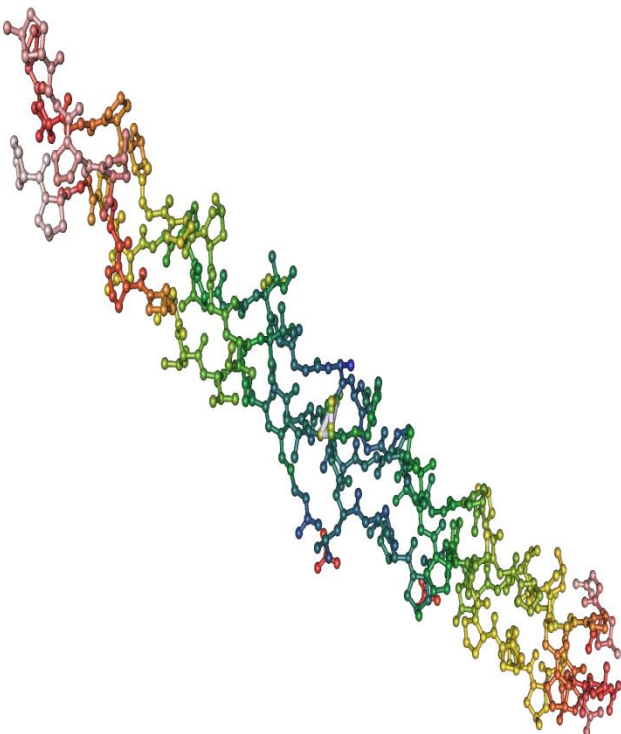


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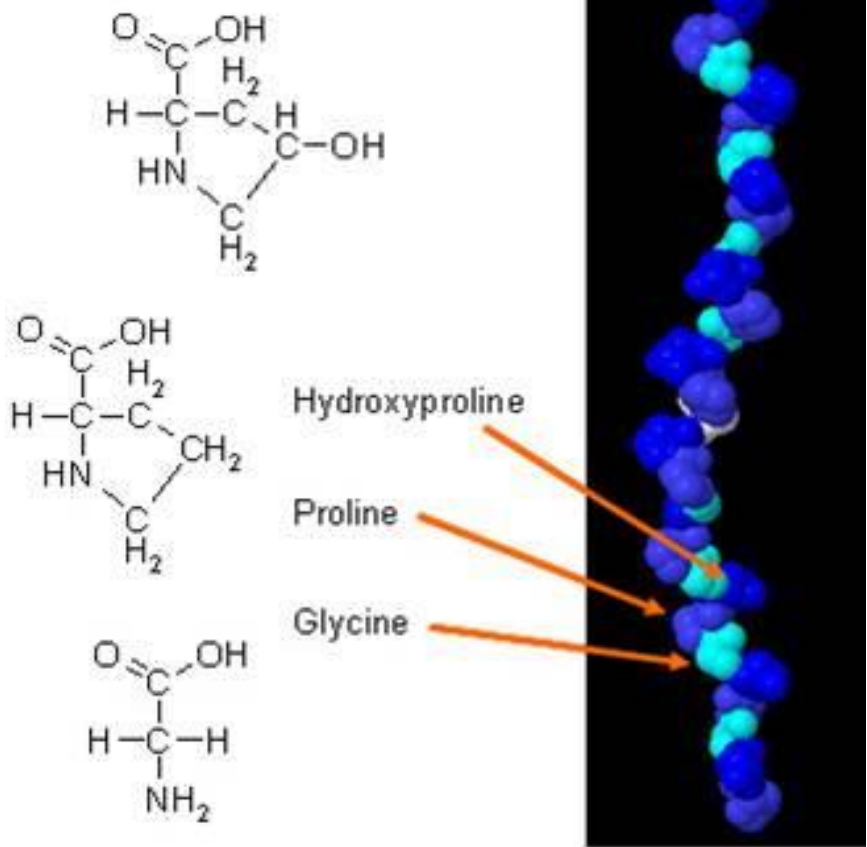
❖ Collagen, triple helix:

- 3 left handed coiled chains (not α helix)
- Fibrous protein.
- Rich in Proline.
- (Proline prevents forming α helix: 1. no backbone amino group. 2. Hydrogen bonding is possible).

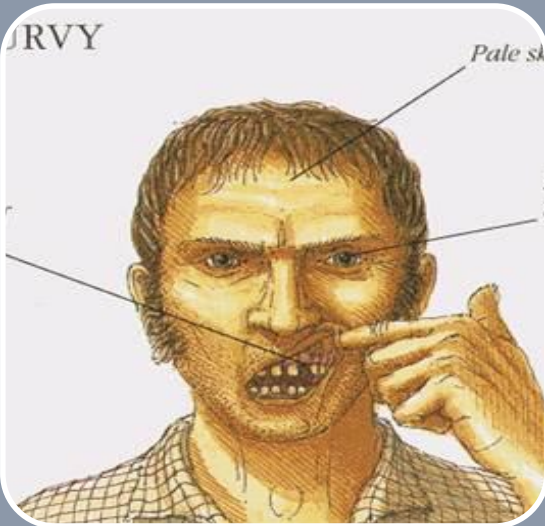


None-standard amino acids in collagen

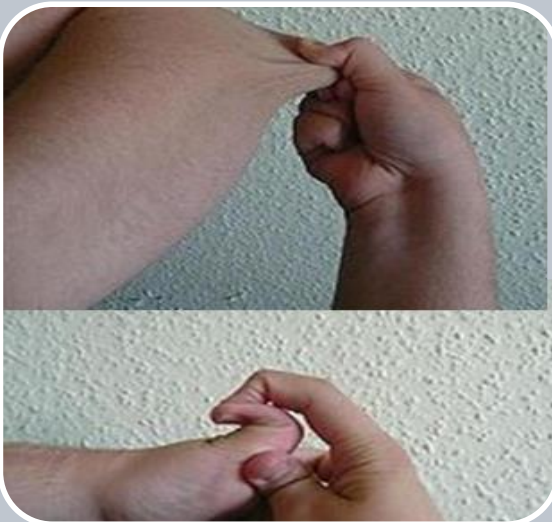
- Proline is converted to 4-hydroxyprolyl residues by prolyl hydroxylase enzyme.
- The enzyme requires vitamin C for its function.



Collagen Diseases:



Scurvy:
due to vitamin C deficiency.



Ehlers-Danlos
Syndromes:
hyperextensibility of
joints and skin.

Other Secondary Structures:

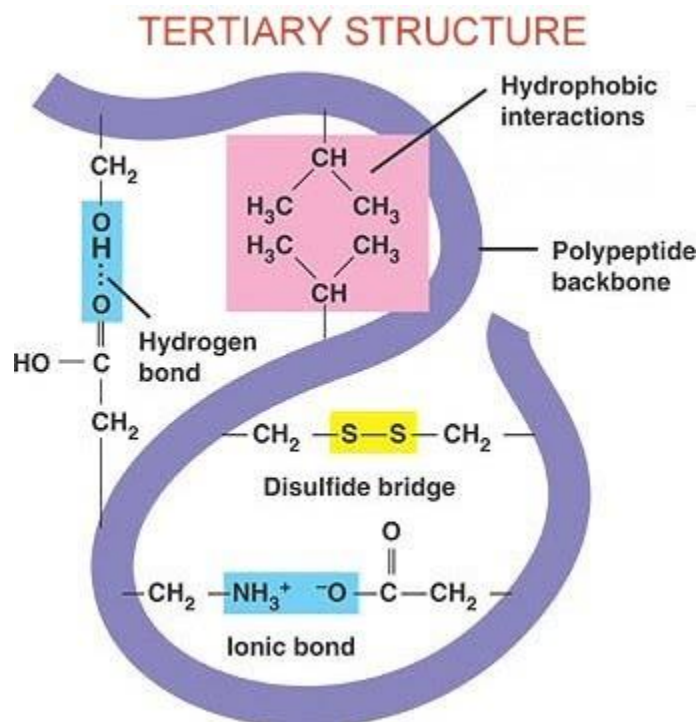
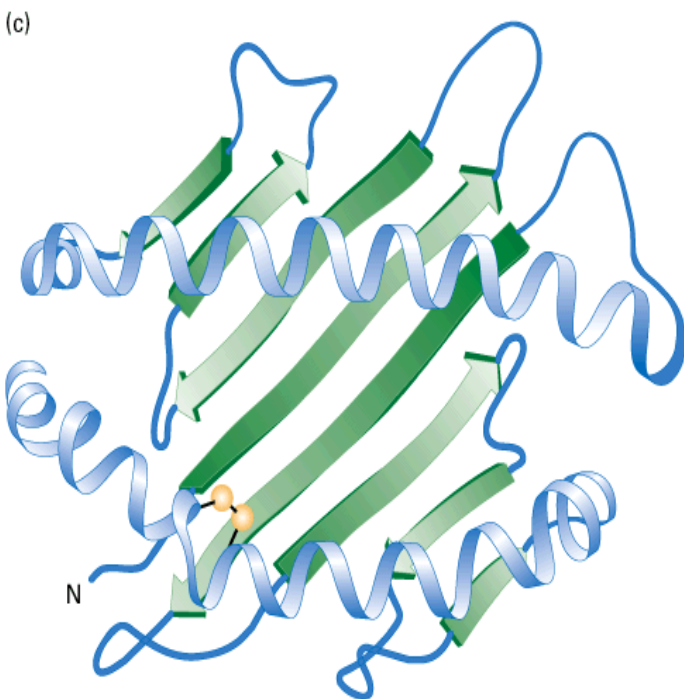
Turns (reverse turns), Loops, β bends and Random coils.

Super-secondary Structures or Motifs:

- β α β motif: a helix connects two β sheets
- β hairpin: reverse turns connect antiparallel β sheets (The turns have poline).
- α α motif: two α helices together (loops).
- β barrels: rolls of β sheets
- Random coil: some area might have random structures, not repeated a lot.

Tertiary Structure:

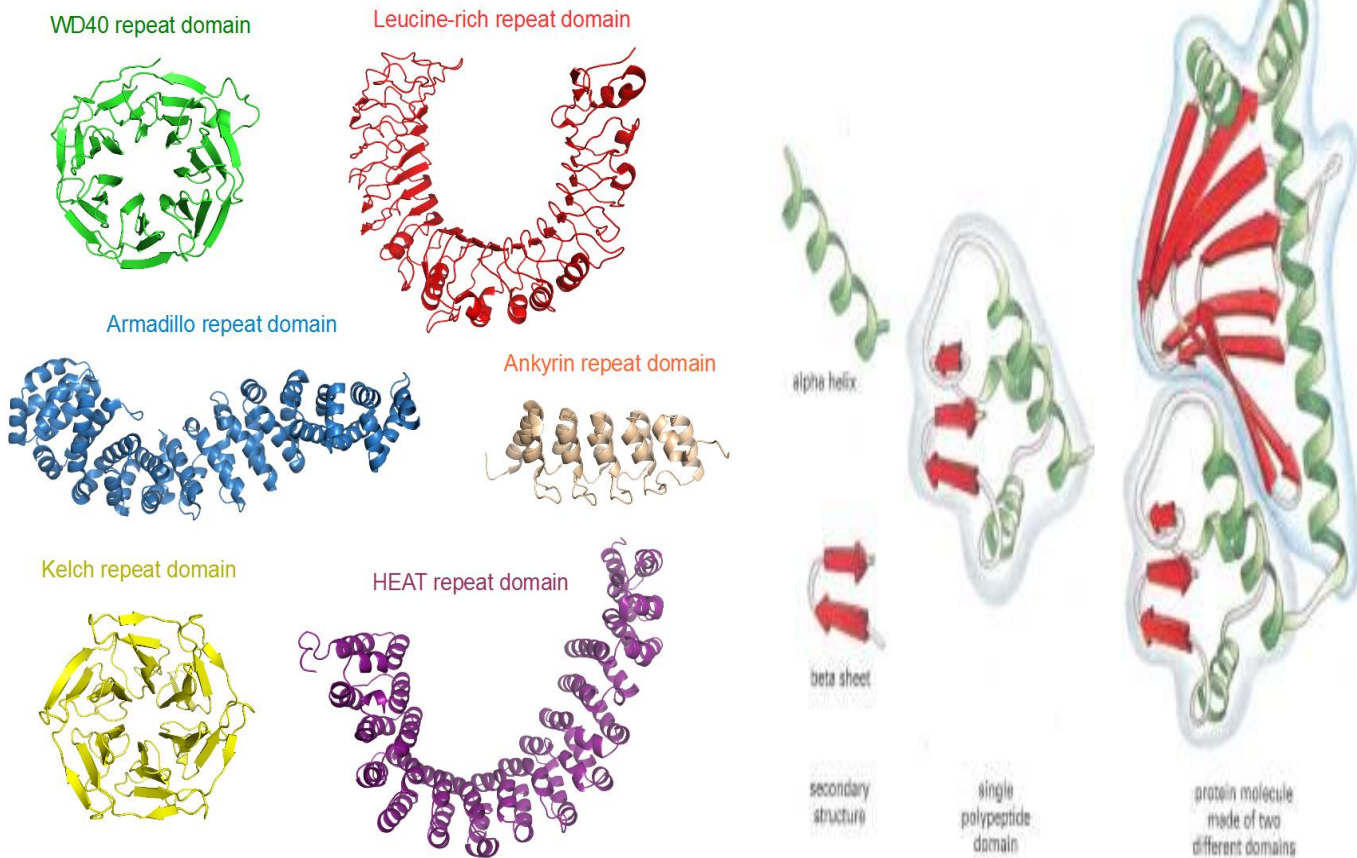
- It is the 3-d structure of an entire polypeptide chain including side chains.
- It includes the folding of secondary structure (α helix and β sheets) and side chains.
- Helices and sheets can be combined to form tertiary structure.
 - Domains interact and form tertiary structure.
 - Final level is quaternary structure but if the protein is monomer then tertiary is the final.



Domains:

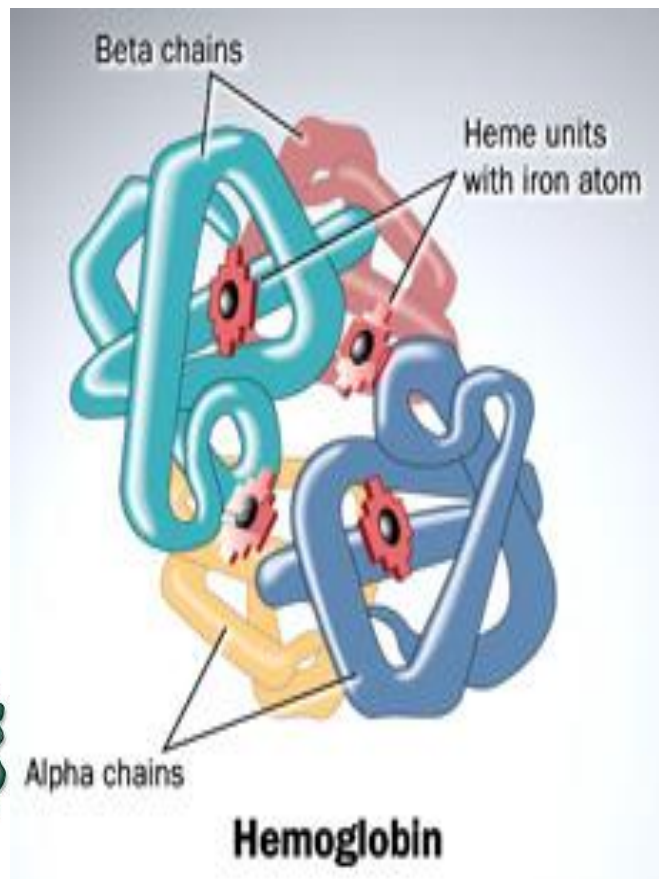
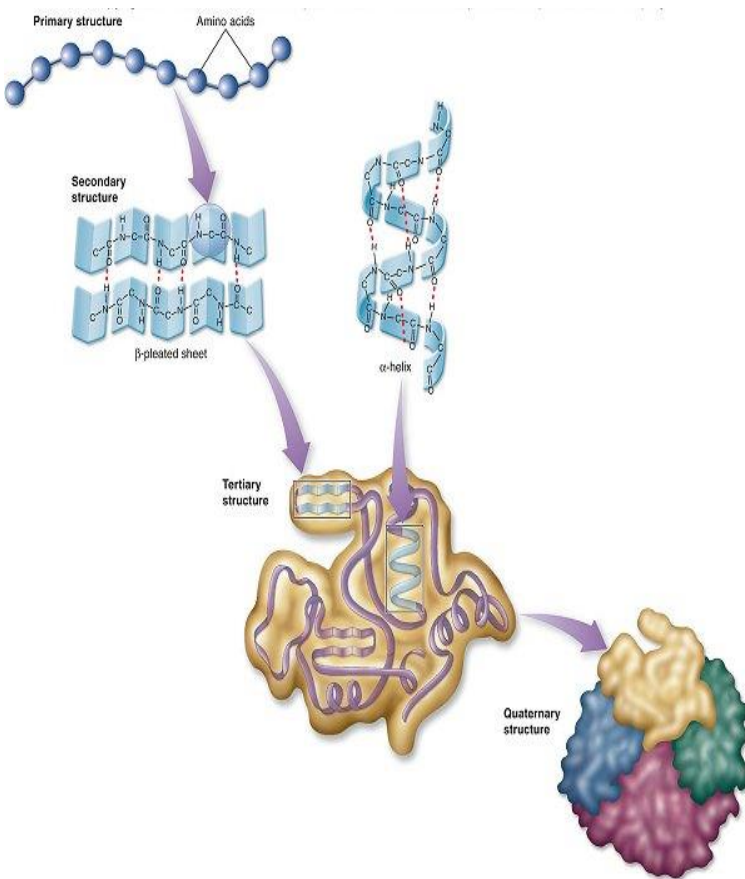
- Polypeptide chains (>200 amino acids) fold into two or more clusters known as domains.
- Domains are functional units that look like globular proteins.
- Domains are parts of protein subunits.

Common examples of protein domains with a solenoid architecture



Quaternary Structure:

- Many proteins contain two or more polypeptide chains.
- Each chain forms a three-dimensional structure called subunit.
- It is the 3D arrangement of different subunits of a protein.

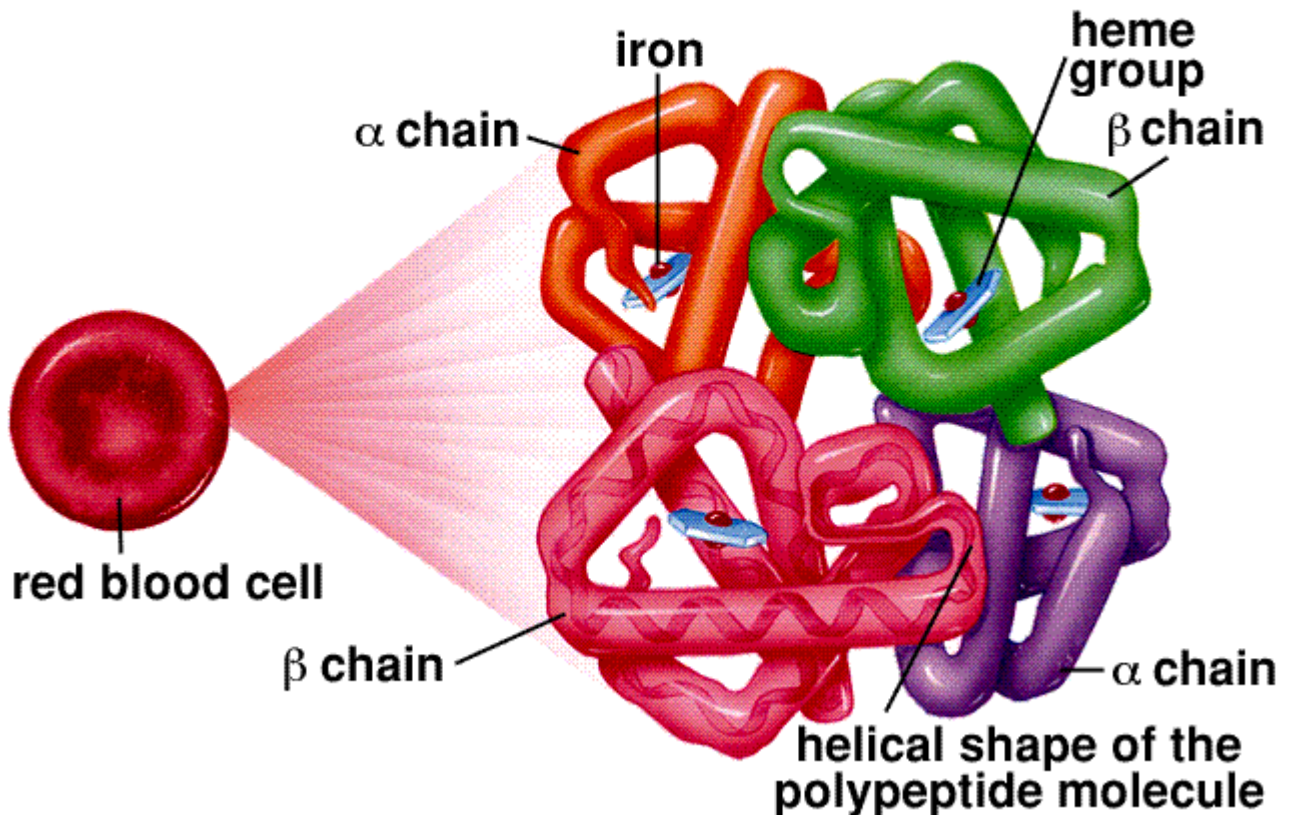


Hemoglobin:

- Hemoglobin is a globular protein.
- A multi-subunit protein is called oligomer.
- Composed of α 2 β 2 subunits (4 subunits).
- Two same subunits are called protomers.

Sylvia S. Mader, Inquiry into Life, 8th edition. Copyright © 1997 The McGraw-Hill Companies, Inc. All rights reserved.

Hemoglobin Molecule



Forces That Stabilize Protein Structure:

- **Hydrophobic Effect:**

- Present in the core of the protein.
- Nonpolar groups to minimize their contacts with water.
- Nonpolar side chains are in the interior of a protein.

- **Hydrogen Bonding:**

- A weak electrostatic bond between one electronegative atom like O or N and a hydrogen atom.

- **Electrostatic Interactions (ion pairing):**

- Between positive and negative charges.

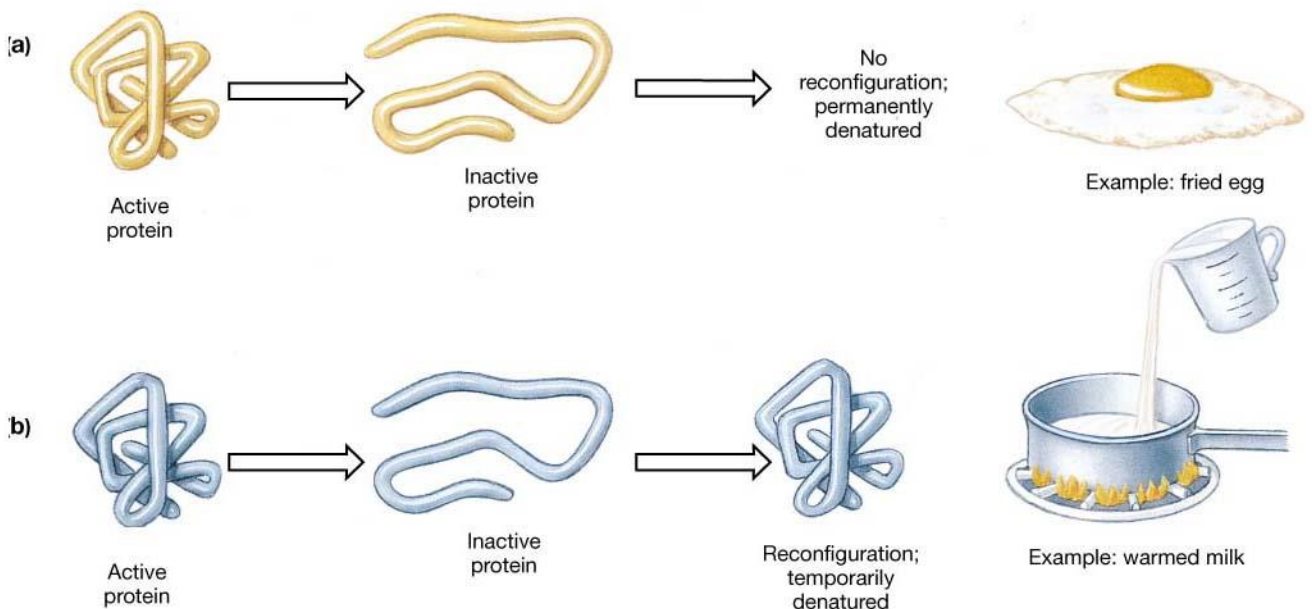
- **Van Der Waals Forces (weak polar forces):**

- Weak electrostatic interactions between neutral molecules.

Protein Denaturation:

❖ Denaturation:

- A process in which a protein loses its native structure.
 - Leads to opening and destruction to the structure.
 - When we say denaturation the protein usually loses its secondary and tertiary structure (loses function). Primary structure is not lost easily due to very strong forces.
 - Example: denaturation in eggs.



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▶ From 1:48

Factors that cause denaturation:

- **Heat**: disrupts hydrogen bonding.
- **Change in pH**: alters ionization states of amino acids.
- **Detergents**:
 - They have hydrophobic and hydrophilic ends like in soap.
 - Interfere with hydrophobic interactions.
- **Chaotropic Agents**:
 - Ions or small organic molecules that disrupt hydrophobic interactions.

Protein Misfolding:

- Every protein must fold to achieve its normal conformation and function.
- Abnormal folding of proteins leads to a number of diseases in humans.

Alzheimer's disease

β amyloid protein is a misfolded protein.

It forms fibrous deposits or plaques in the brains of Alzheimer's patients.

Creutzfeldt-Jacob or Prion Disease

Prion protein is present in normal brain tissue.

In diseased brains, the same protein is misfolded.

Therefore it forms insoluble fibrous aggregates that damage brain cells.

Summary

- **Proteins:** Proteins are polymers of amino acids joined together by peptide bonds.
- **Protein Structures:**
 - Primary structure.
 - Secondary structure:
 - α helix
 - β sheets
 - Collagen, triple helix
 - Other Secondary Structures
(Turns (reverse turns), Loops, B bends and Random coils).
 - Super-secondary Structures or Motifs
($\beta \alpha \beta$ motif, β hairpin, $\alpha \alpha$ motif, β barrels).
 - Tertiary structure.
 - Quaternary structure.
- **Hemoglobin:**
 - Hemoglobin is a globular protein.
 - Composed of α 2 β 2 subunits (4 subunits).

Summary

- **Forces That Stabilize Protein Structure:**
 - Hydrophobic Effect.
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 - Electrostatic Interactions (ion pairing).
 - Van Der Waals Forces (weak polar forces).
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 - **Denaturation:** a process in which a protein loses its native structure.
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 - Heat.
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- **Protein Misfolding:**
 - **Alzheimer's disease**
(β amyloid protein is a misfolded protein).
 - **Creutzfeldt-Jacob or Prion Disease**
(In diseased brains, Prion protein is misfolded).