The module: Molecular, Gene and Diseases

Session 2: Lec3

Lecture Title: Protein structure and folding

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This Lecture was loaded in blackboard and you can find the material in:
(Lippincott's Illustrated Reviews: Cell and Molecular Biology Chapters 2,3)
For more detailed instructions, any question, or you have a case you need help in, please post to the group of session

The Learning Objectives (LO)

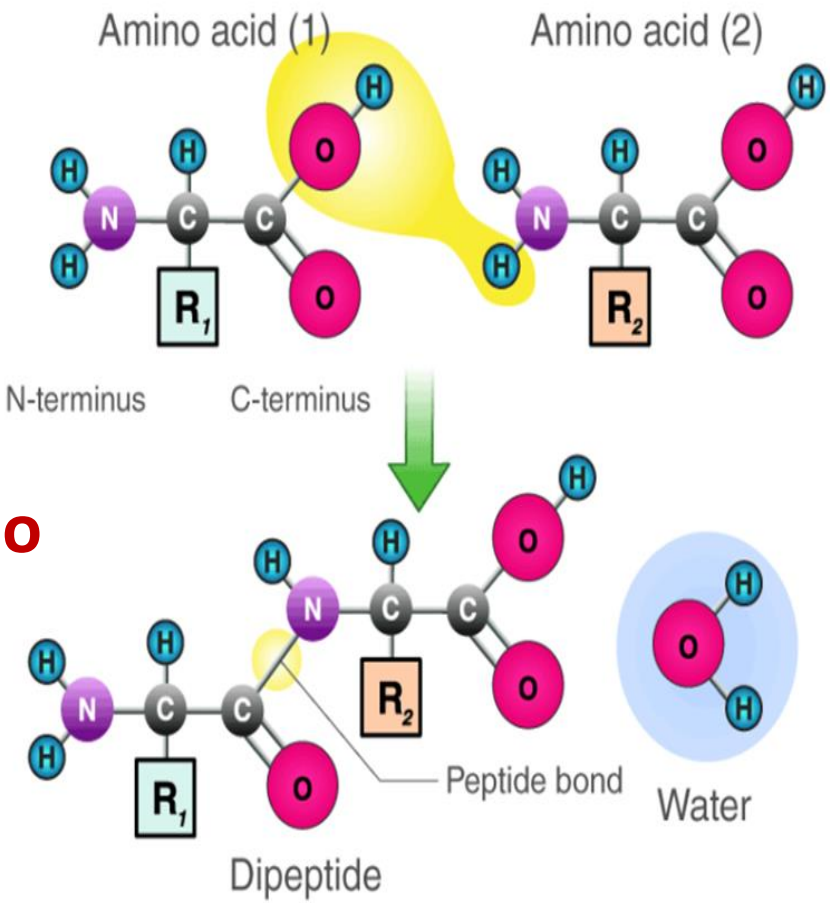
1. Describe what is meant by the **primary**, **secondary**, **tertiary** and **quaternary** structure of proteins.
2. Describe the types of **bonds** and **forces** involved in protein structure.
3. Explain the key features of the two major secondary structure elements of proteins (**α-helix** and **β -sheet**).

Peptides & Proteins

LO 2.1& 2.2

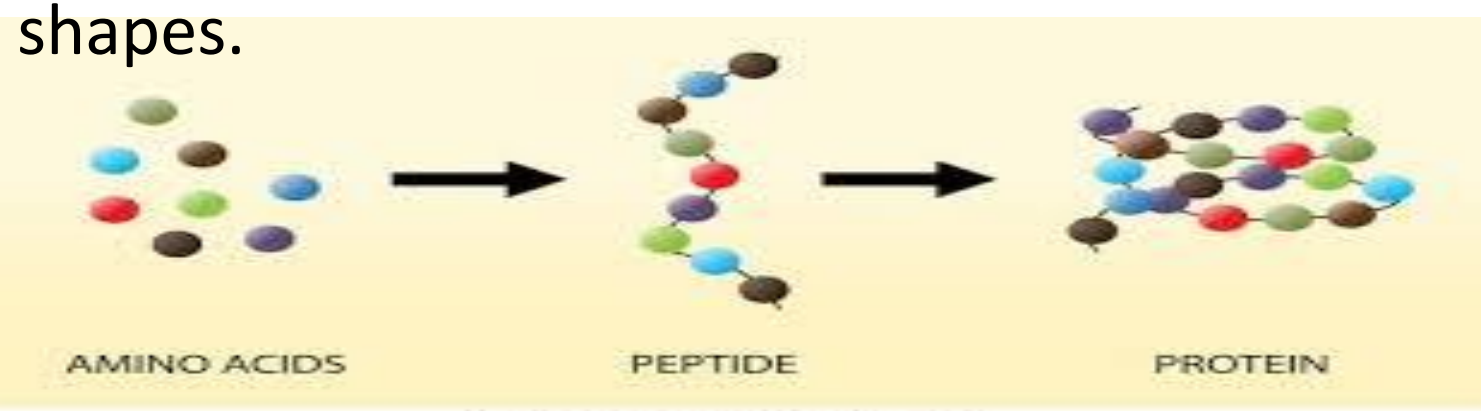
Peptide bond: Is a chemical bond formed between two molecules.

the **carboxyl group** of one molecule reacts with the **amino group** of the other molecule, releasing a molecule of **(H_2O).**



LO 2.1 & 2.2

- The amino acids in a peptide chain is named as amino acid residue.
- A peptide chain may consists of 2-50 amino acids.
- Amino acids are linked by peptide bonds to form a polypeptide chain. These chains can twist to form 3D protein shapes.



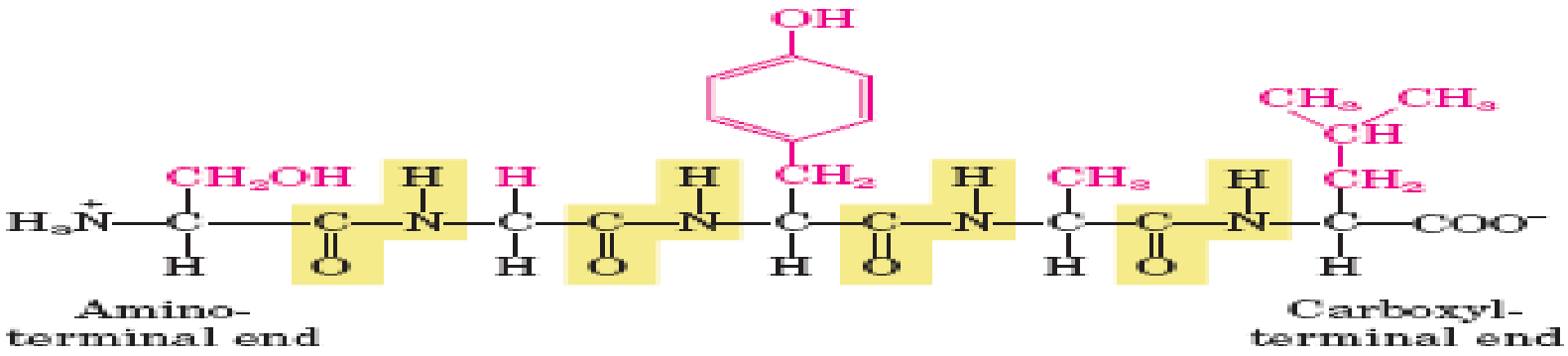
LO 2.1 & 2.2

- These chains have two terminal ends. One end is ended by an **amino group** and the other by a **carboxyl group.**
- the sequence of amino acids is written from **left** to **right.**

Serylglycyltyrosylalanylleucine

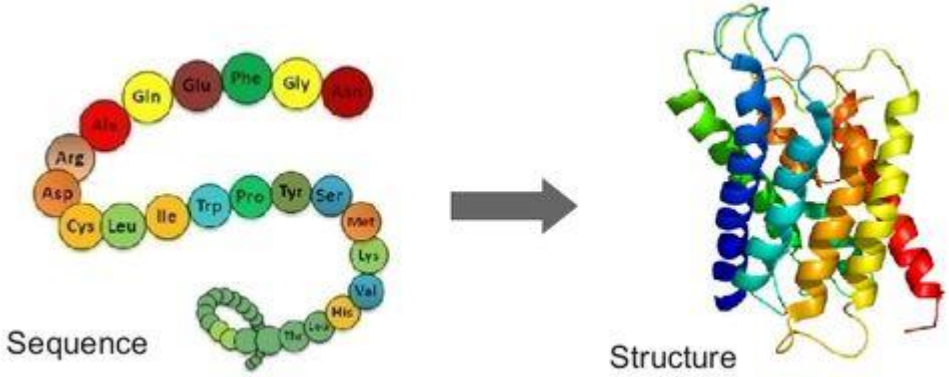
Or

$^{+}NH_3$-Ser-Gly-Tyr-Ala-Leu-COO^-



LO 2.1 & 2.2

- ✓ Proteins are organic polymers composed of amino acids between 50 and 2000 amino acid residues.
- ✓ The mean molecular mass of an amino acid residue is about 110 Dalton units (Da). Therefore the molecular mass of most proteins is between 5.5 and 220 kDa



- ✓ Proteins do not exist as linear polypeptides but fold into a unique 3-dimensional structure.

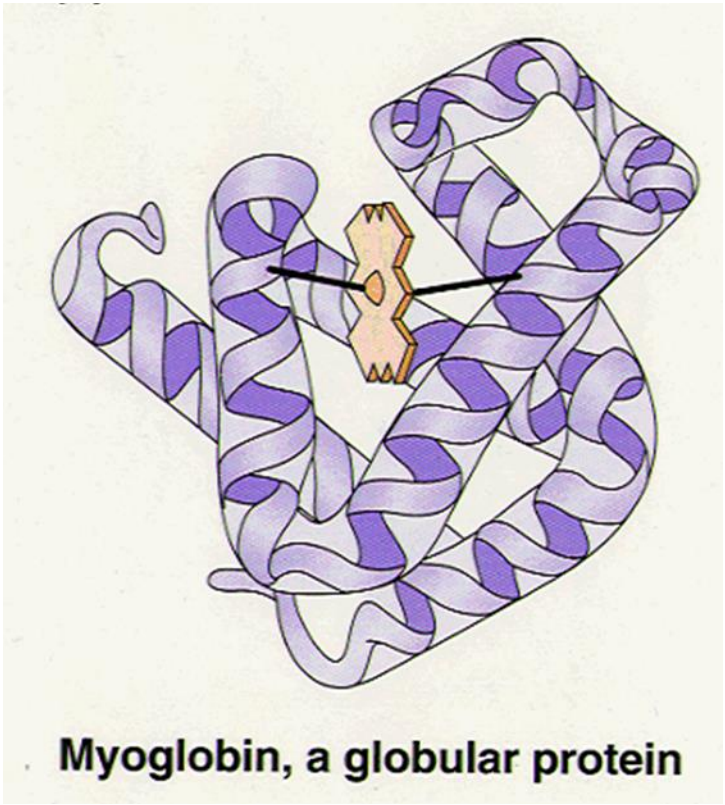
LO 2.1 & 2.2

✓ There are two general classes of protein molecules:

a) globular proteins

b) fibrous proteins.

- ❖ Globular proteins are generally:
  - Compact.
  - Soluble.
  - spherical in shape.

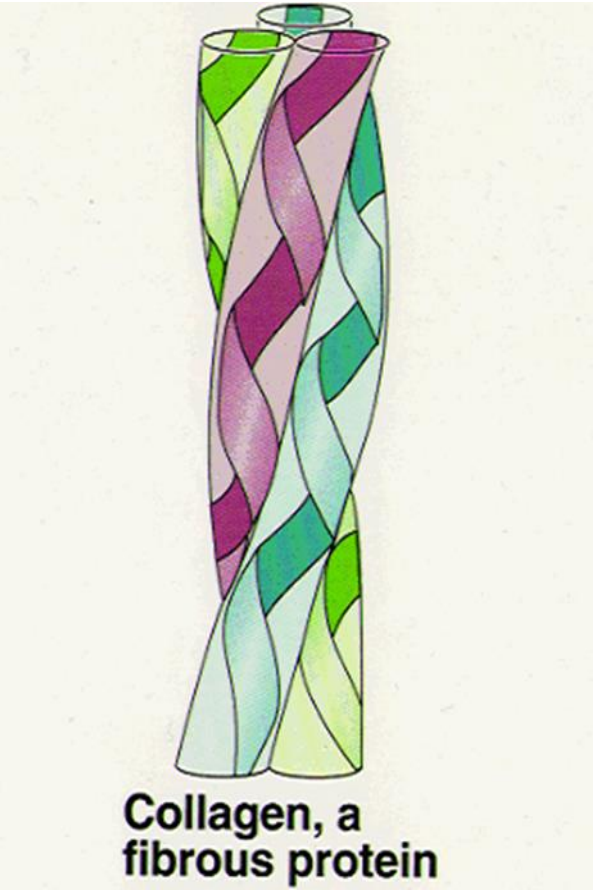


Myoglobin, a globular protein

LO 2.1 & 2.2

- Fibrous proteins are typically:
  - Elongated.
  - insoluble.

Globular and fibrous proteins may exhibit one or more of four types of protein structure



Globular vs Fibrous protein:

LO 2.1 & 2.2

	Fibrous	Globular
Shape	Long and narrow	Round / spherical
Purpose	Structural	Functional
Acid Sequence	Repetitive amino acid sequence	Irregular amino acid sequence
Durability	Less sensitive to changes in pH, temperature, etc.	More sensitive to changes in pH, temperature, etc.
Examples	Collagen, myosin, fibrin, actin, keratin, elastin	Enzymes, haemoglobin, insulin, immunoglobulin
Solubility	(Generally) insoluble in water	(Generally) soluble in water

LO 2.1 & 2.2

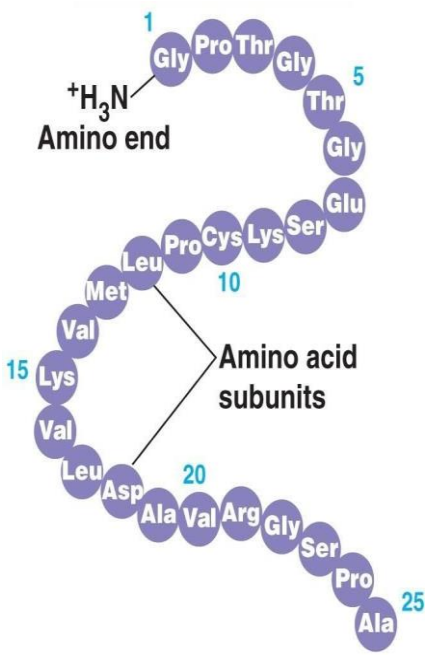
- ✓ The shape of the protein is important for defining the protein function.

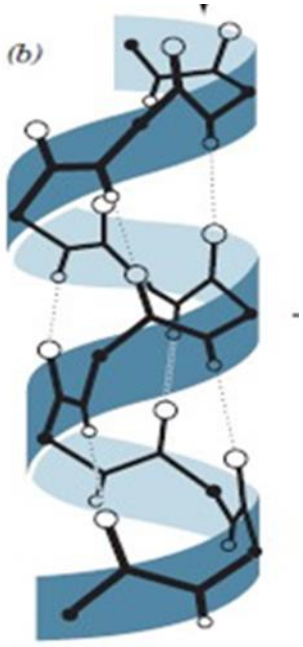
- ✓ The linear sequence of the linked amino acids contains the information necessary to generate a protein molecule with a unique three-dimensional shape.

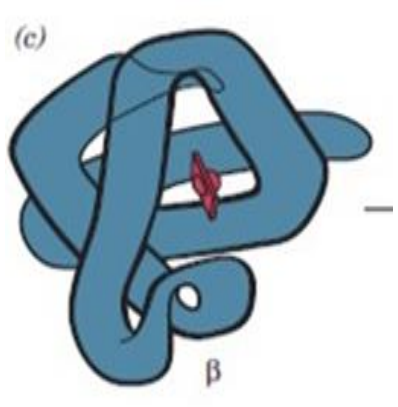
LO 2.1 & 2.2

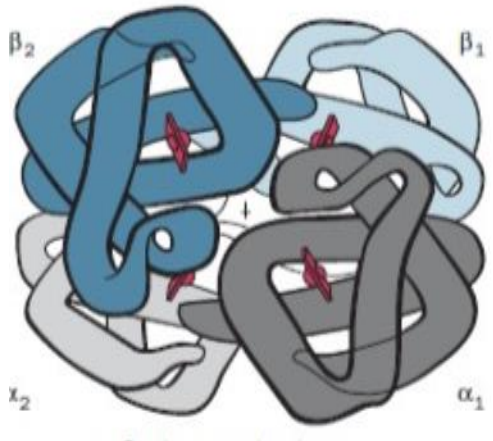
There are **four organizational levels** of protein structure:

A. Primary **B. Secondary** **C. Tertiary** **D. Quaternary**







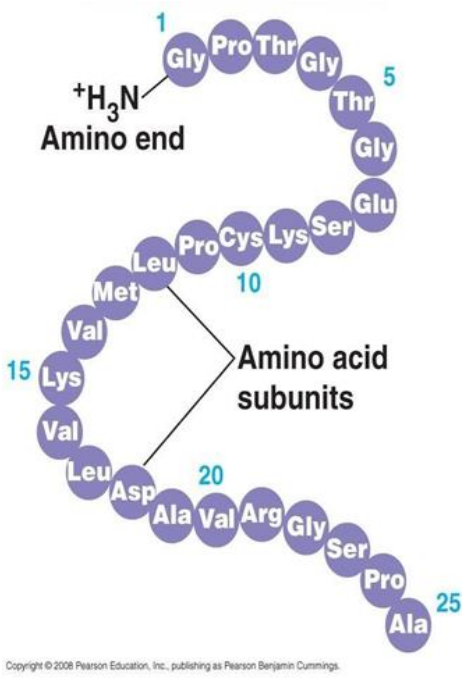


Primary Structure Of Proteins

LO 2.1, 2.2& 2.3

A. It's a linear sequence of amino acids. This linear sequence is referred to as a **polypeptide chain**.

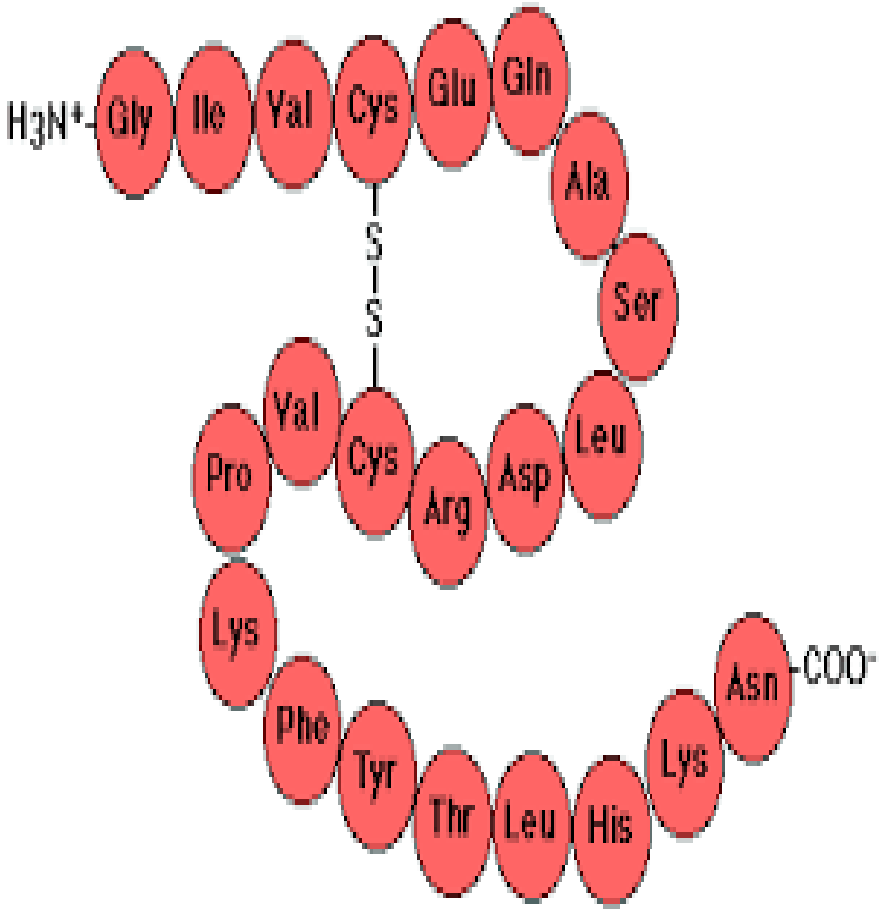
B. The amino acids in the primary structure are held together by **covalent bonds**.



Primary Structure Of Proteins

LO 2.1, 2.2& 2.3

The primary structure of the protein starts from the **amino terminal (N) end** and ends in the **carboxyl terminal (C) end**.



Primary Structure Of Proteins:

LO 2.1, 2.2& 2.3

- The sequence of an amino acids is unique, and defines the structure and function of the protein.
- The importance of the primary structure of proteins:

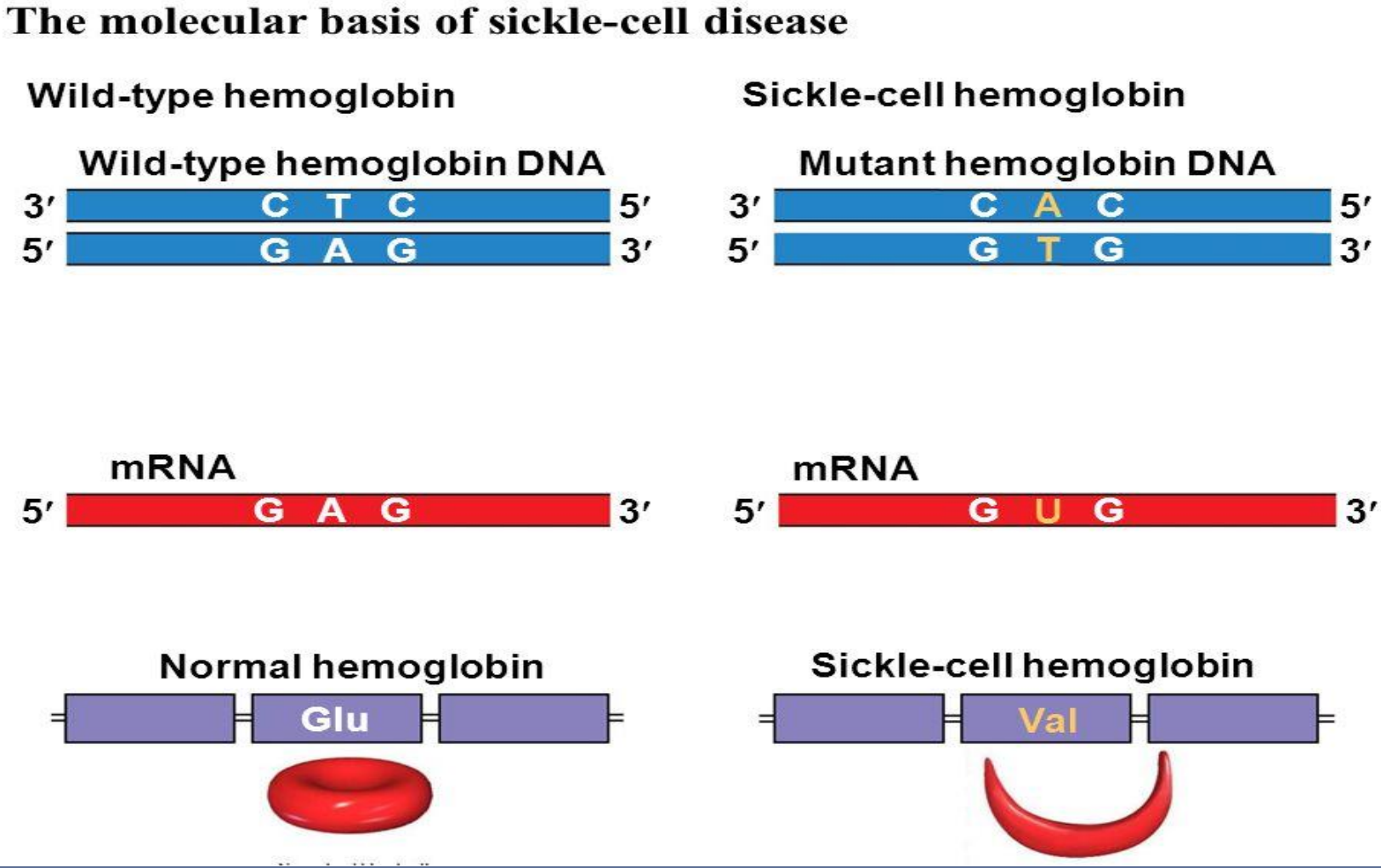
Is to understanding the genetic diseases that results due to proteins with abnormal amino acid sequences.

Abnormal amino acid sequence → incorrect folding → loss of normal function ↓

GENETIC DISEASE

E.g. Sickle cell anemia

LO 2.1, 2.2& 2.3



LO 2.1, 2.2& 2.3

- ✓ The bonds responsible for the stabilization of primary structure is only the **peptide bonds**.
- ✓ Peptide bonds are not broken by conditions that denature proteins, such as:

Heating or high concentrations of urea.

LO 2.1, 2.2& 2.3

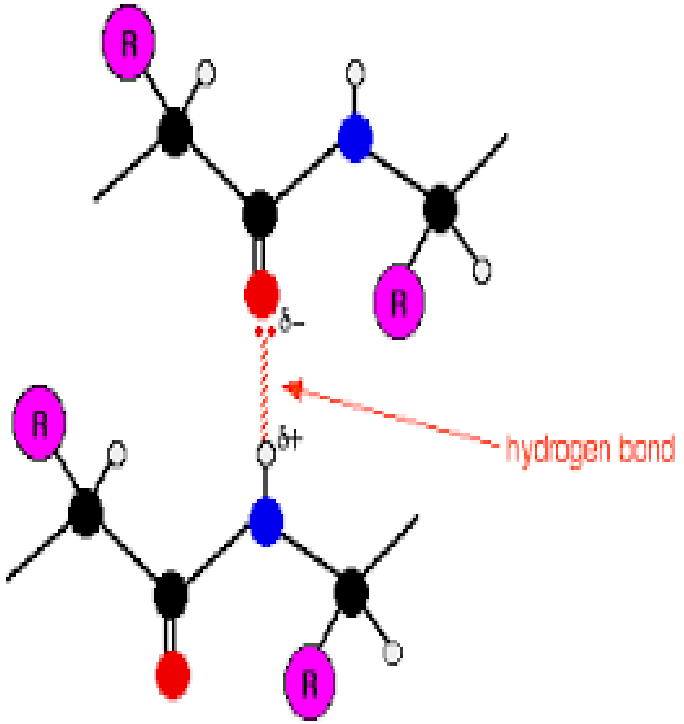
- ✓Prolonged exposure to **strong acid or base at elevated temperatures** is required to **hydrolyze these bonds non enzymatically.**

- ✓**Proteases or proteolytic enzymes** will enzymatically hydrolyse peptides.

B. Secondary Structure of Proteins

LO 2.1, 2.2& 2.3

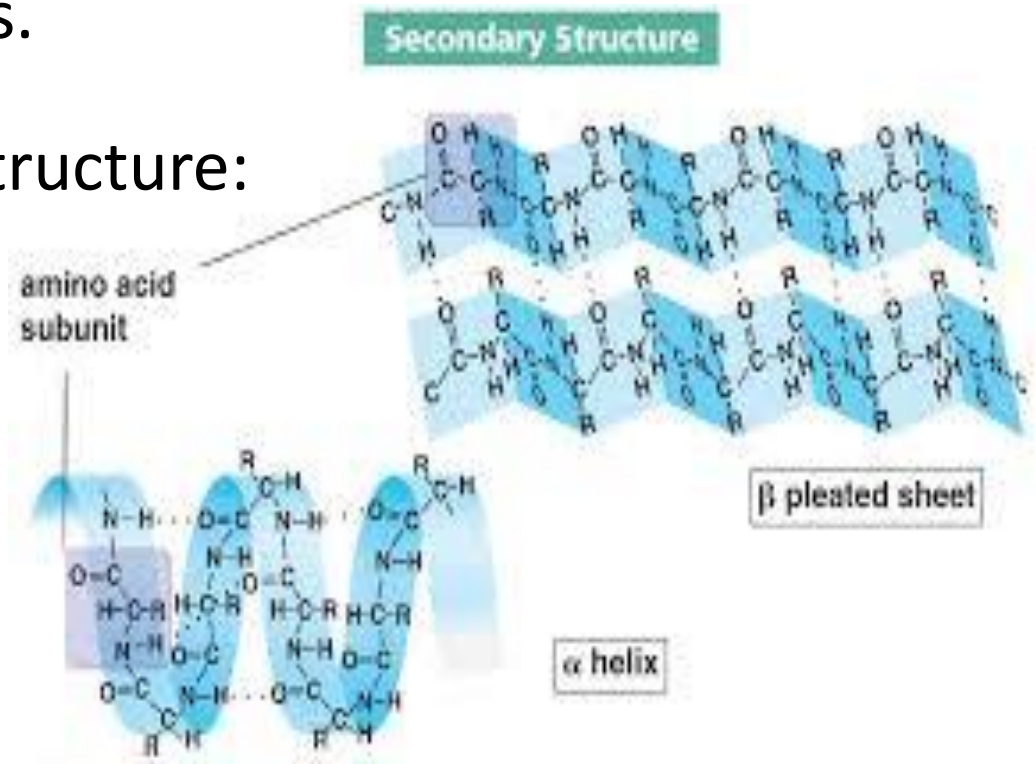
- ✓ The polypeptide forms regular arrangements of amino acids that are located near to each other in the linear sequence.
- ✓ They are 2-dimensional structures formed due to **hydrogen binding** between **hydrogen of amine groups** and **oxygen of the carbonyl groups**



B. Secondary Structure of Proteins

LO 2.1, 2.2& 2.3

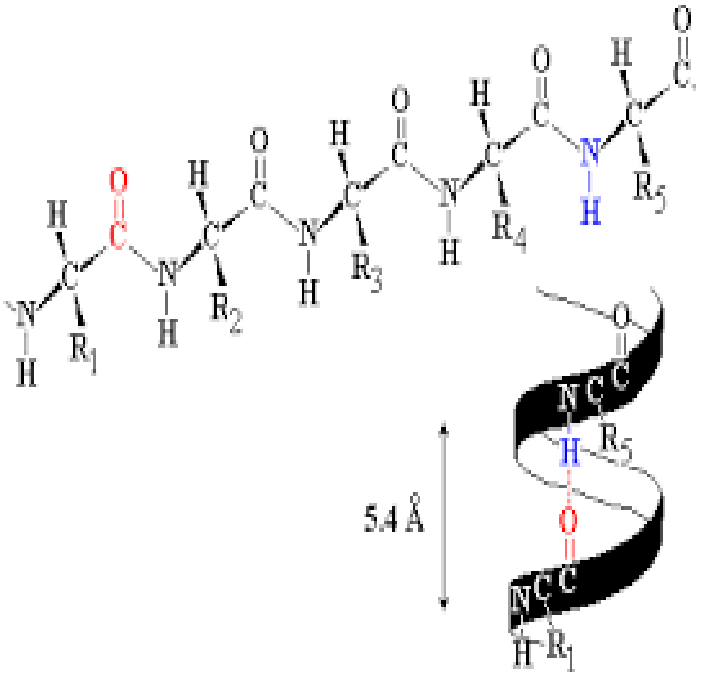
- Secondary structure was a result of hydrogen bonds between peptide groups.
- 2 types of secondary structure:
  - ✓ **α-helix**
  - ✓ **β-sheet**



A. The Alpha Helix

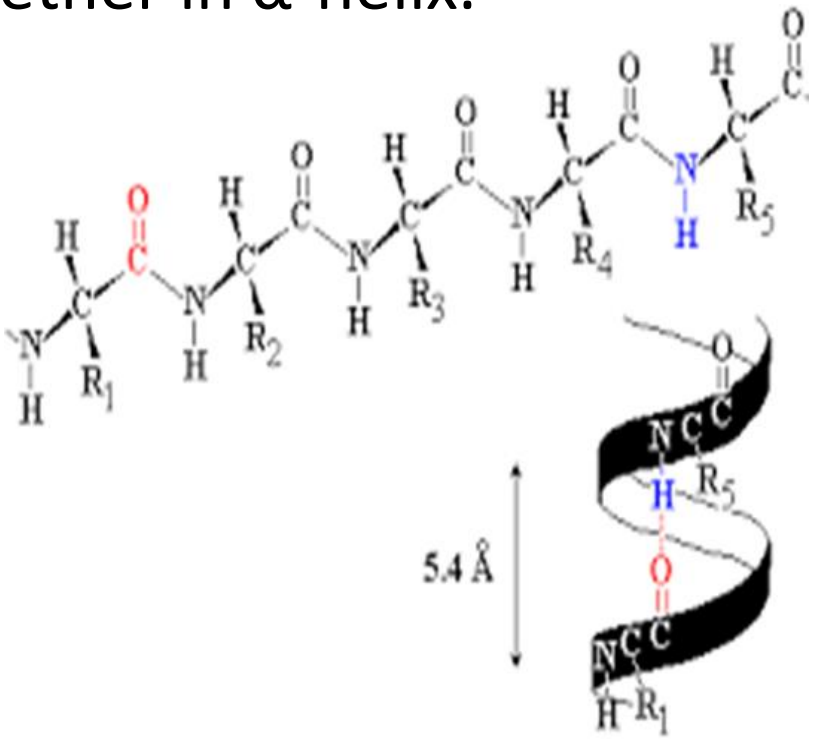
LO 2.1, 2.2& 2.3

- It's a Coiled Structure Stabilized by **Intra-chain Hydrogen Bonds.**
- The hydrogen bonds extend up the spiral from the carbonyl oxygen of one peptide bond to the -NH – group of a peptide linkage



LO 2.1, 2.2& 2.3

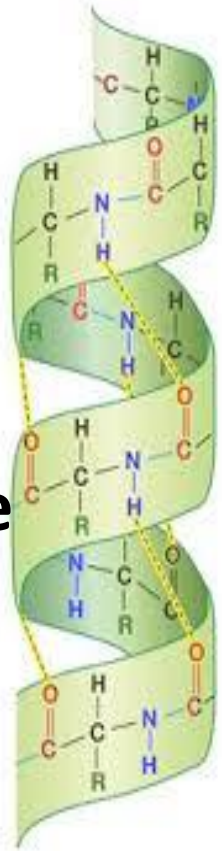
- Thus, amino acids spaced three or four apart in the primary sequence are close together in α-helix.
- Most common polypeptide helices.
- Stable rigid conformation.



Amino acids that disrupt an α-Helix: LO 2.1, 2.2& 2.3

- **Proline:** it cannot donate an amide hydrogen bond.
- **Tryptophan:** Because of steric interference.

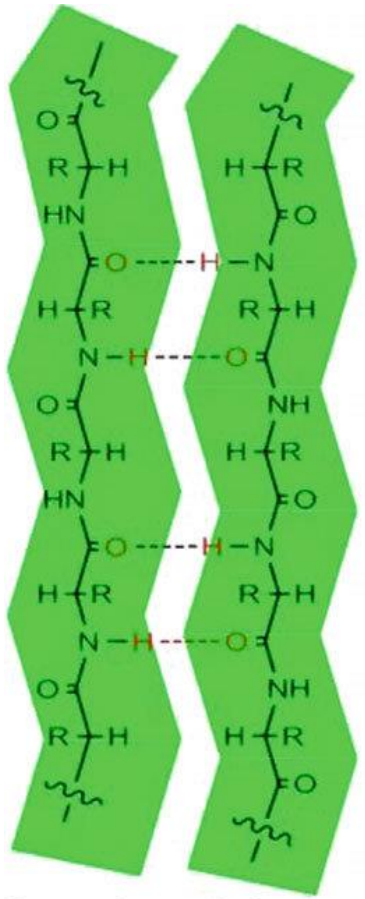
  Steric effects are nonbonding interactions that influence the shape
- **branched amino acids** e.g. **valine** and **isoleucine** because of steric interference.
- **acidic and basic amino acids** because they form ionic bonds or electrically repel each other.



B. β-Sheet:

LO 2.1, 2.2& 2.3

- all of the peptide bond components are involved in hydrogen bonding.
- The amino acid residues of a β sheet form a zigzag in which the R groups of adjacent residues is in opposite directions.

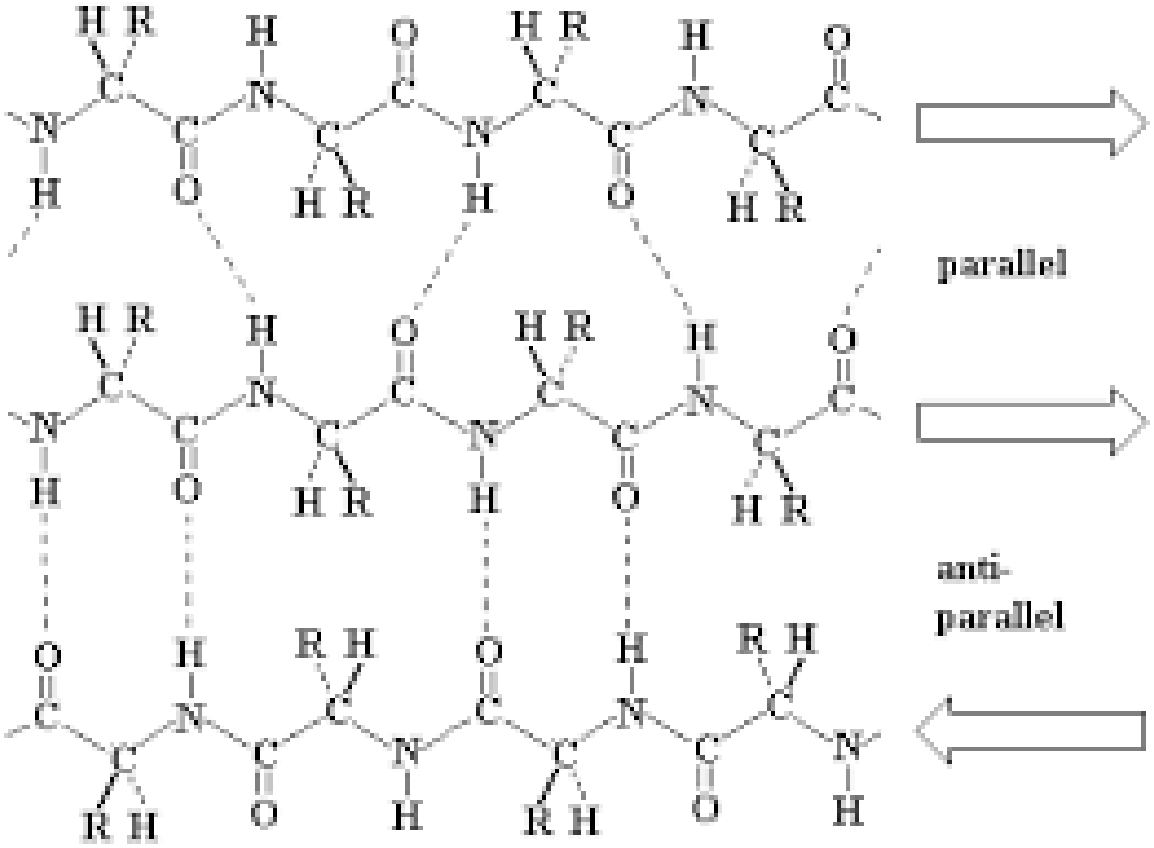


Beta pleated sheets

β-Sheet may be:

LO 2.1, 2.2& 2.3

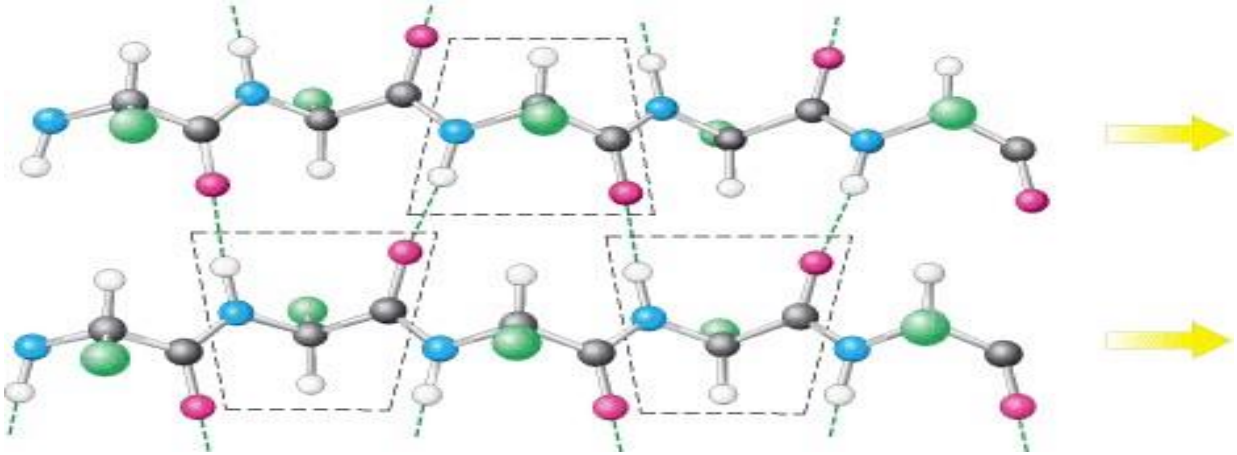
- Parallel
- Antiparallel



Parallel β-Sheet:

LO 2.1, 2.2& 2.3

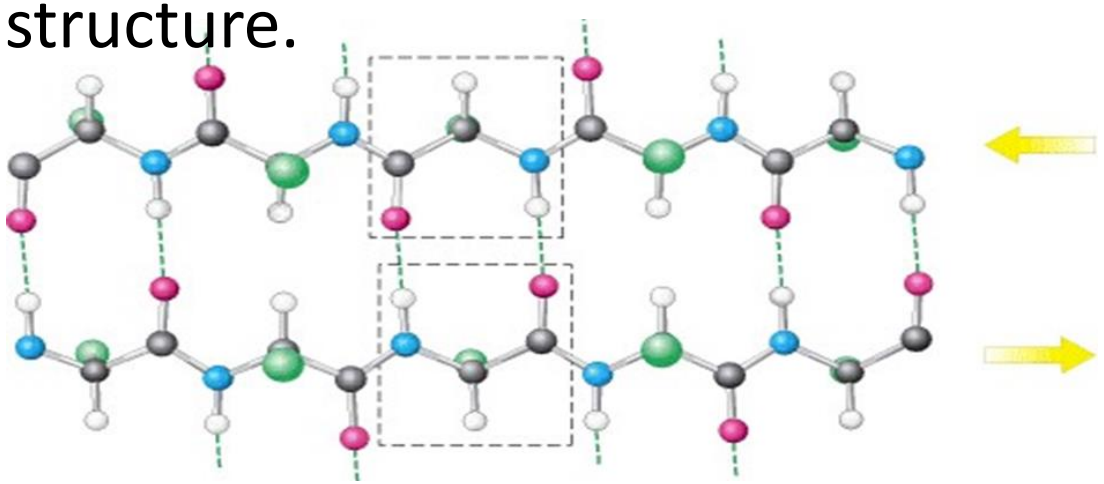
- ✓ Adjacent β-strands run in the same direction.
- ✓ Hydrogen bonds connect each amino acid on one strand with two different amino acids on the adjacent strand.



Antiparallel β Sheet:

LO 2.1, 2.2& 2.3

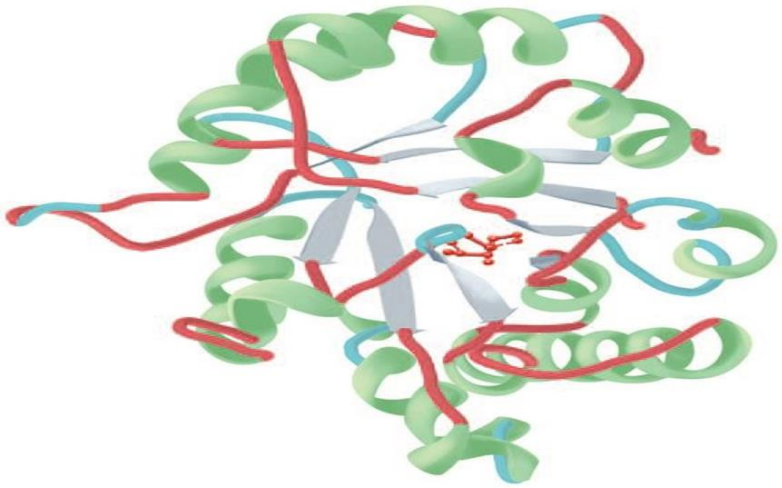
- ✓ Adjacent β strands run in opposite directions.
- ✓ Hydrogen bonds between NH and CO groups connect each amino acid to a single amino acid on an adjacent strand, stabilizing the structure.



β Sheet in Globular Proteins:

LO 2.1, 2.2& 2.3

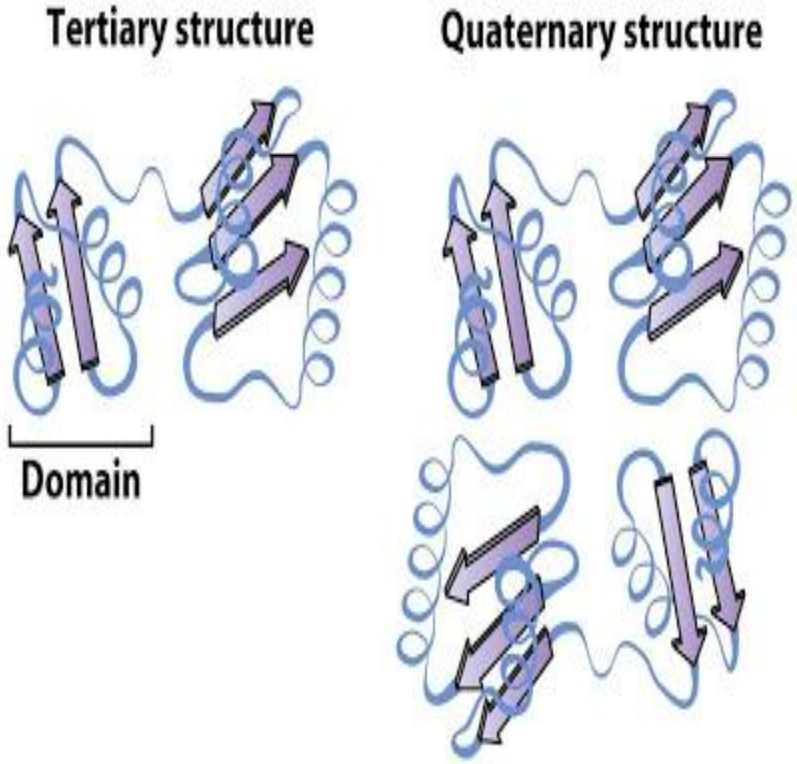
- ✓ Most β sheets are not flat but have a right- handed twist.
- ✓ Clusters of twisted strands of β sheet form the core of many globular proteins.



C. Tertiary Structure of proteins:

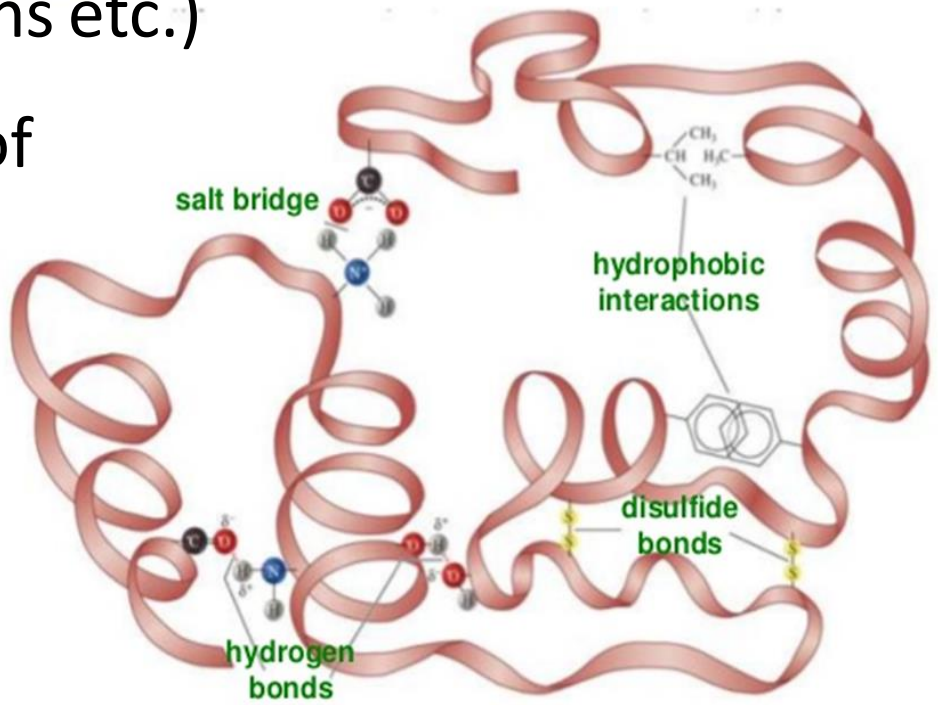
LO 2.1, 2.2& 2.3

- Folding up of the secondary structures, so that amino acids far apart in the primary sequence may interact, and a **3-dimensional structure** is formed.
- Polypeptide chains that are greater than **~200** amino acids in length generally consist of two or more **domains**.



LO 2.1, 2.2& 2.3

- **Domains:** are regions of the polypeptide that have distinct structures and serve particular roles (e.g. ligand binding, interaction with other proteins etc.)
- Tertiary structure is a result of side chains interactions



LO 2.1, 2.2& 2.3

- Tertiary structure of protein is stabilized by different types of bonds and interactions between amino acids R groups.

- These includes:

A) Hydrogen bonds.

B) Covalent (disulphide) bonds.

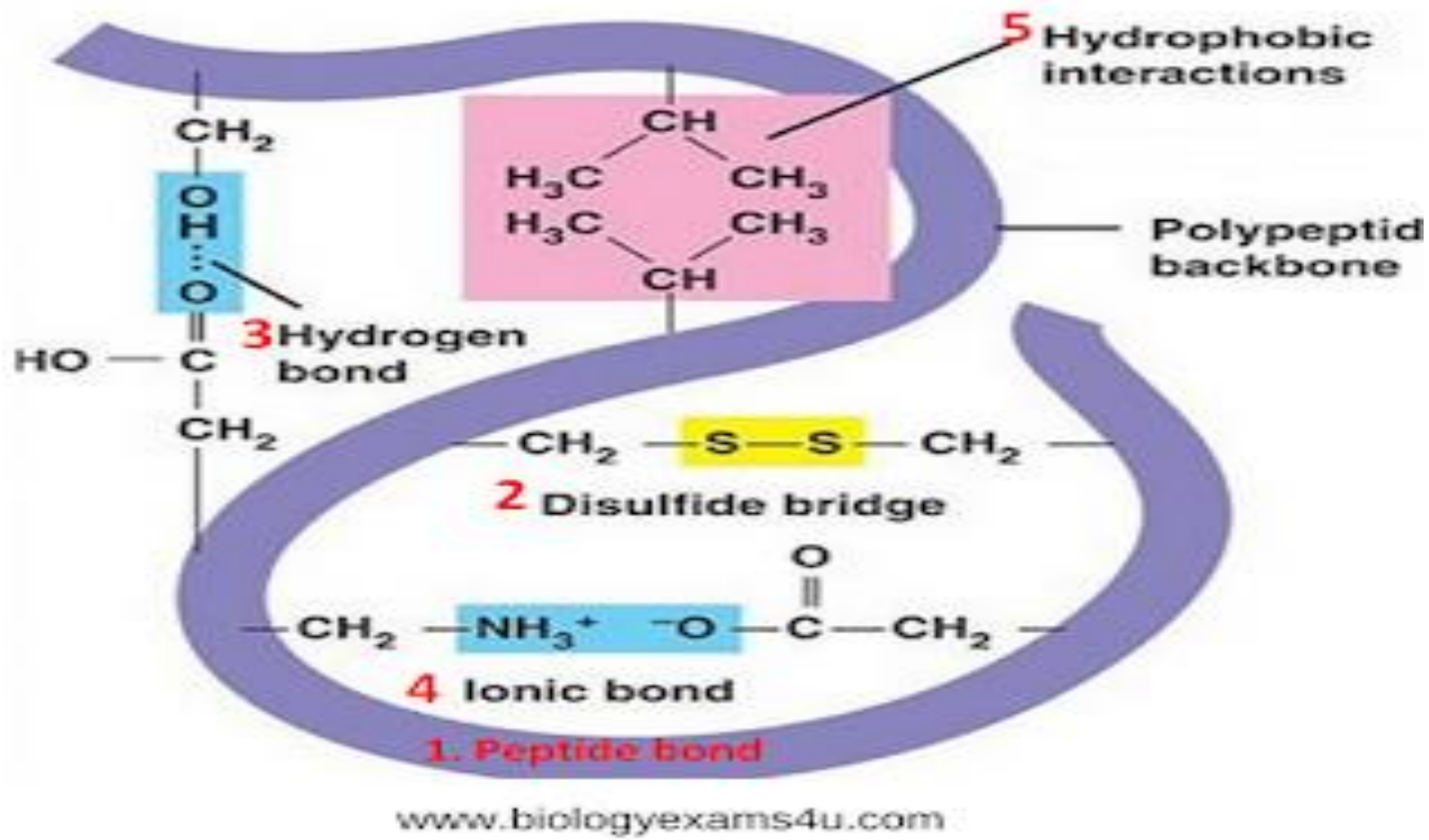
C) Hydrophobic interactions.

D) Ionic interactions &Van der Waals interaction.

- E. g: **myoglobin** (1 polypeptide chain **monomeric** proteins)

Tertiary Structure of proteins:

LO 2.1, 2.2& 2.3



Protein folding:

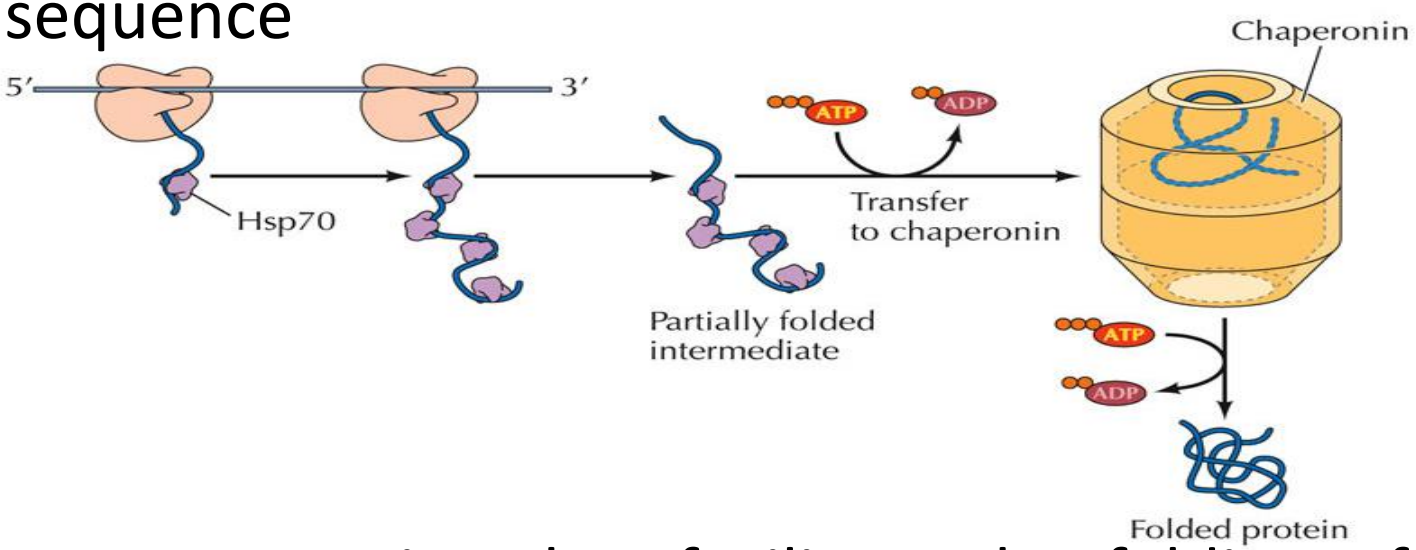
LO 2.1, 2.2& 2.3

- Protein folding is the process by which a protein structure assumes its functional shape or conformation.
- By coiling and folding into a specific three-dimensional shape they are able to perform their biological function.
- Unfolded or misfolded **proteins** contribute to the pathology of many diseases.
- Protein folding occurs in a cellular compartment called the **endoplasmic reticulum**.

Protein folding:

LO 2.1, 2.2& 2.3

The classic principle of protein folding is that all the information required for a protein to adopt the correct three-dimensional conformation is provided by its amino acid sequence



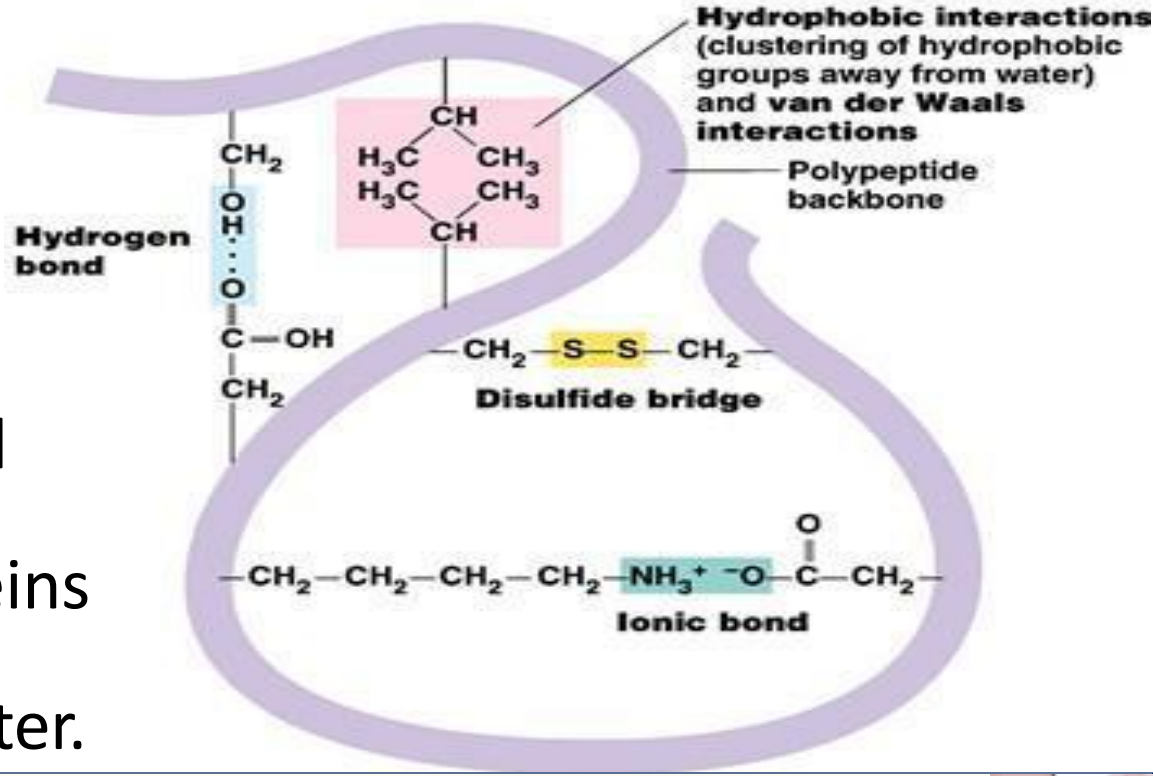
- chaperones are proteins that facilitate the folding of other proteins.

Protein folding:

LO 2.1, 2.2& 2.3

- The side chains of highly **polar** amino acids tend to reside on the **exterior** of proteins, where they can form hydrogen bonds with water.

- The side chains of **nonpolar** amino acids are normally clustered in the **interior** of proteins to shield them from water.

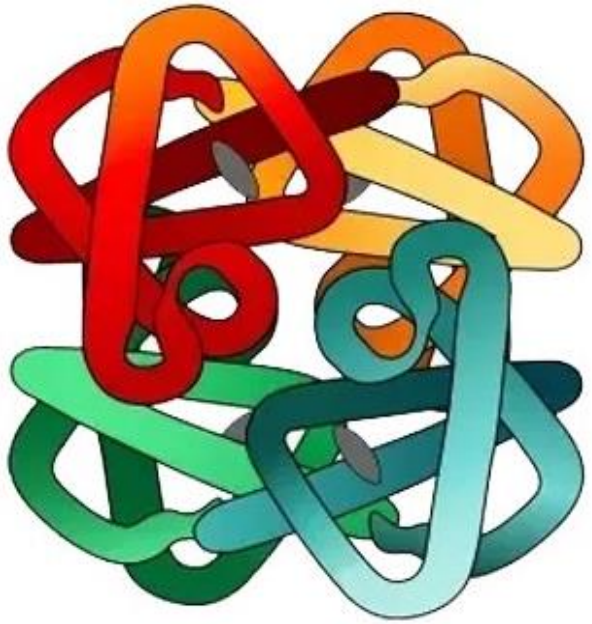


D.Quaternary Structure:

LO 2.1, 2.2& 2.3

- Quaternary structure involves the association of two or more polypeptides into functional proteins.

These separate polypeptides are held together by the same intermolecular forces found in secondary and tertiary structures.



- **Haemoglobin** is an example of heteromeric protein

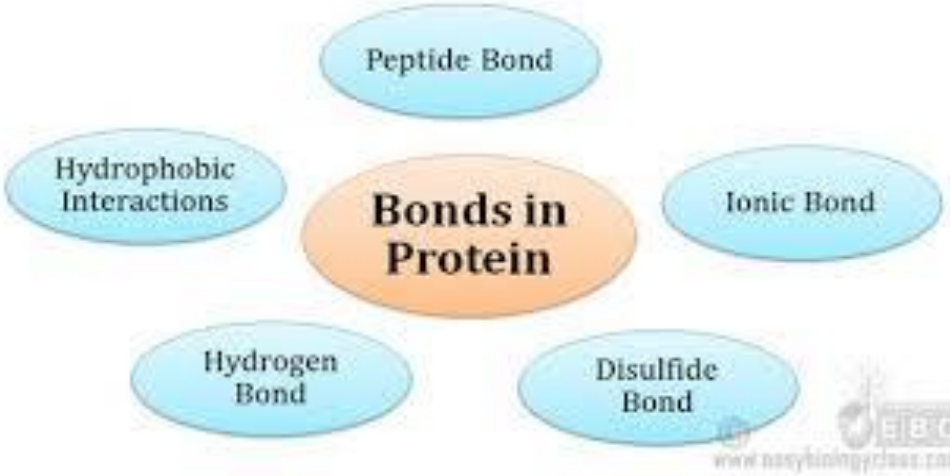
LO 2.1, 2.2& 2.3

- The polypeptide chains may be identical (**homomeric**) or different (**heteromeric**).
- Some proteins contain covalent disulfide (**S—S**) bonds that link the sulfhydryl groups of cystein residues.
- Intra-polypeptide disulfide bonds stabilize 3-D structure of peptide.
- inter-polypeptide disulfide bonds (between subunits) stabilize the quaternary structure of proteins.

LO 2.1, 2.2& 2.3

Protein Denaturation:

- The loss of protein structure sufficient to cause the loss of function is known as **denaturation**.
- Denaturation is brought about by breaking the bonds that hold and maintain the protein's tertiary and secondary structure.



LO 2.1, 2.2& 2.3

- Denaturing agents include heat, organic solvents, mechanical mixing, strong acids or bases , detergents, and ions of heavy metals such as lead and mercury.
- As the disulfides are reduced by **B- mercaptoethanol,** the latter is oxidized and forms dimers.

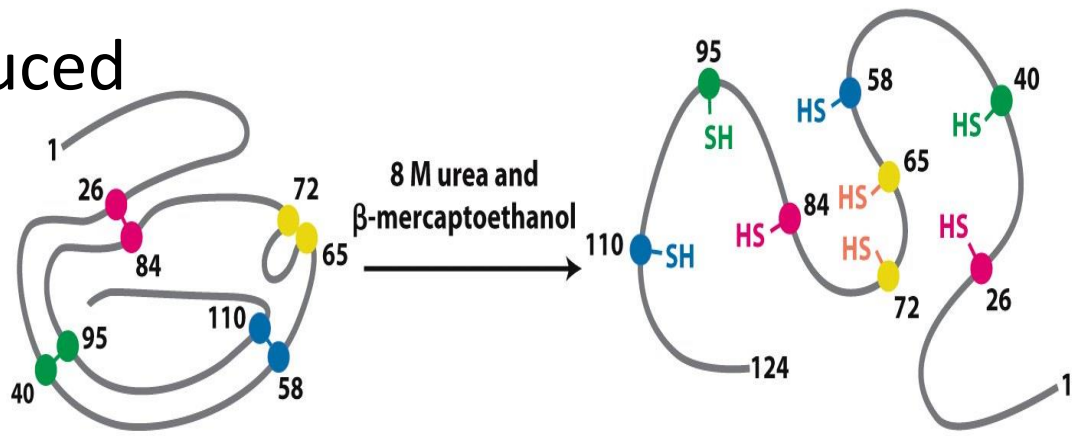


Figure 2.53
Biochemistry, Seventh Edition


Thank
You