

Biochemistry

Peptide and proteins

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Peptides and Proteins

20 amino acids are commonly found in protein.

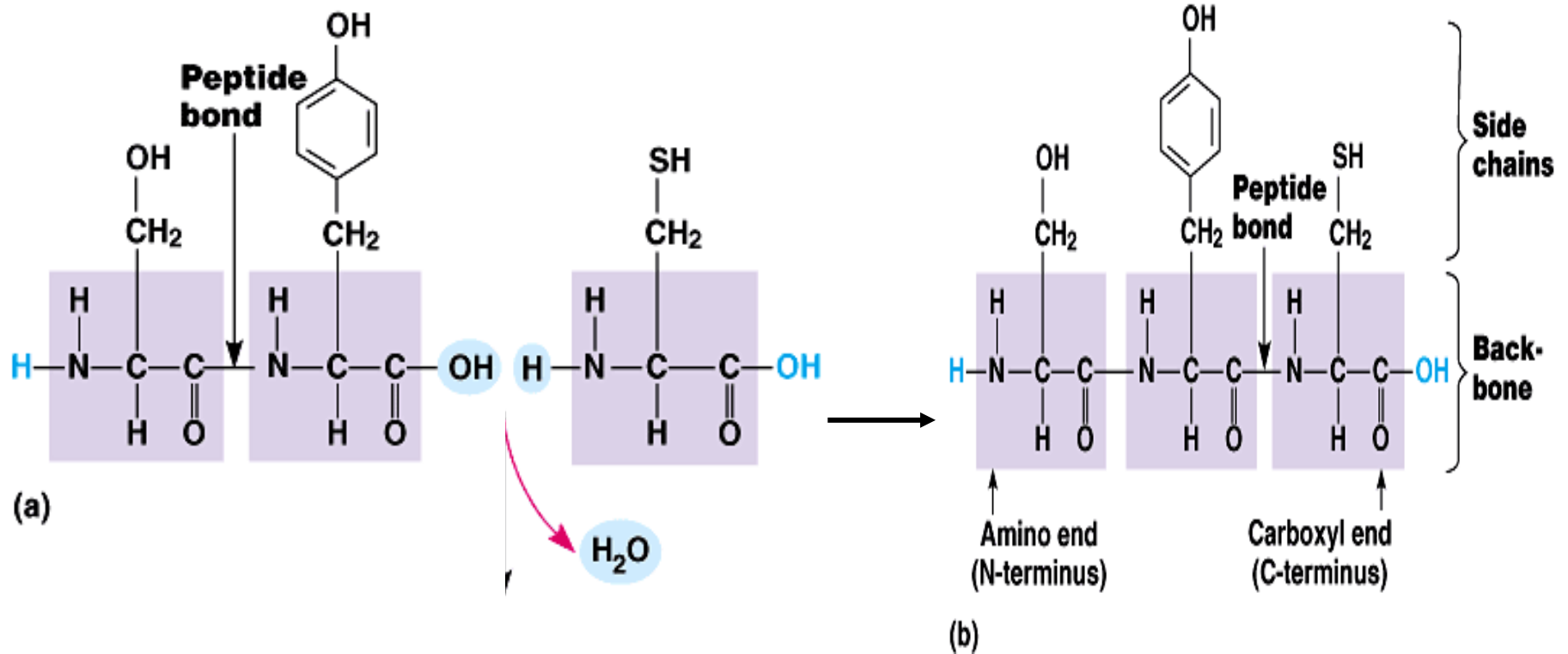
These 20 amino acids are linked together through “peptide bond forming peptides and proteins (what’s the difference?).

- The chains containing less than 50 amino acids are called “peptides”, while those containing greater than 50 amino acids are called “proteins”.

Peptide bond formation:

α -carboxyl group of one amino acid (with side chain R1) forms a covalent peptide bond with α -amino group of another amino acid (with the side chain R2) by removal of a molecule of water. The result is : **Dipeptide** (i.e. Two amino acids linked by one peptide bond). By the same way, the dipeptide can then forms a second peptide bond with a third amino acid (with side chain R3) to give **Tripeptide.** Repetition of this process generates a polypeptide or protein of specific amino acid sequence.

Peptide bond formation:



- Each polypeptide chain starts on the left side by free amino group of the first amino acid enter in chain formation . It is termed (N- terminus).
- Each polypeptide chain ends on the right side by free COOH group of the last amino acid and termed (C-terminus).

Examples on Peptides:

1- Dipeptide (tow amino acids joined by one peptide bond):

Example: Aspartame which acts as sweetening agent being used in replacement of cane sugar. It is composed of aspartic acid and phenyl alanine.

2- Tripeptides (3 amino acids linked by two peptide bonds).

Example: GSH which is formed from 3 amino acids: glutamic acid, cysteine and glycine. It helps in absorption of amino acids, protects against hemolysis of RBC by breaking H_2O_2 which causes cell damage.

3- octapeptides: (8 amino acids)

Examples: Two hormones; oxytocine and vasopressin (ADH).

4- polypeptides: 10- 50 amino acids: e.g.
Insulin hormone

Protein structure:

There are four levels of protein structure (primary, secondary, tertiary and quaternary)

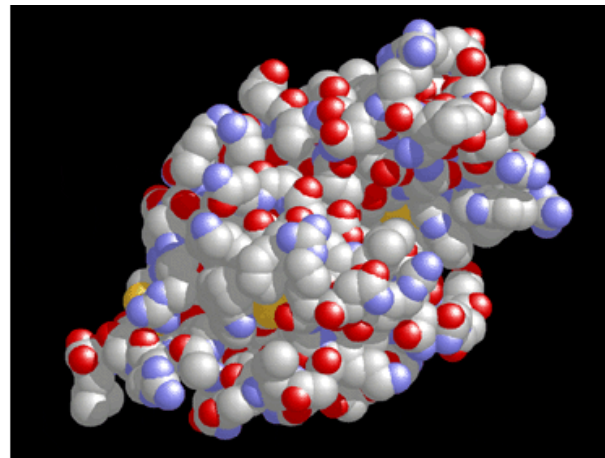
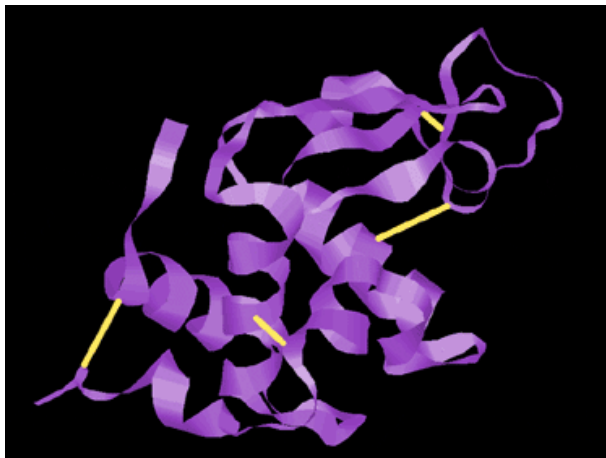
Primary structure:

- The **primary structure** of a protein is its unique sequence of amino acids.
 - Lysozyme, an enzyme that attacks bacteria, consists of a polypeptide chain of 129 amino acids.
 - The precise primary structure of a protein is determined by inherited genetic information.
 - At one end is an amino acid with a free amino group the (the N-terminus) and at the other is an amino acid with a free carboxyl group the (the C-terminus).



High orders of Protein structure

- A **functional protein** is **not just** a polypeptide chain, but **one or more** polypeptides precisely **twisted, folded and coiled** into a molecule of unique shape (**conformation**). This conformation is essential for some protein function e.g. Enables a protein to recognize and bind specifically to another molecule e.g. hormone/receptor; enzyme/substrate and antibody/antigen.

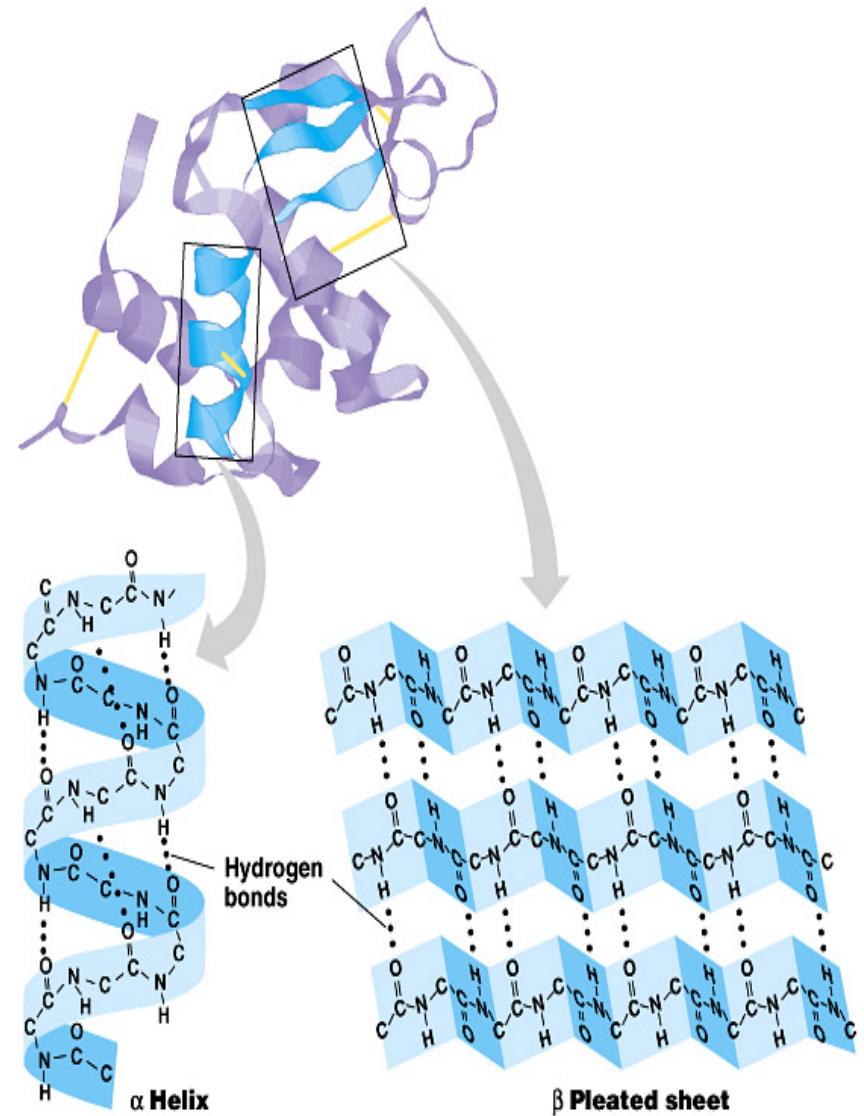


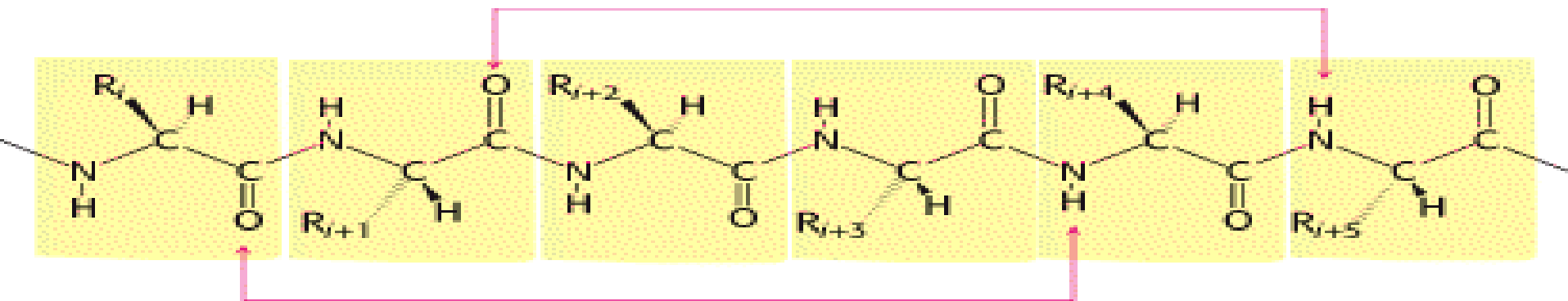
2- Secondary structure:

Results from hydrogen bond formation between hydrogen of -NH group of peptide bond and the carbonyl oxygen of another peptide bond. According to H-bonding there are two main forms of secondary structure:

α -helix: It is a spiral structure resulting from hydrogen bonding between one peptide bond and the fourth one

β -sheets: is another form of secondary structure in which two or more polypeptides (or segments of the same peptide chain) are linked together by hydrogen bond between H- of NH- of one chain and carbonyl oxygen of adjacent chain (or segment).





Hydrogen bonding in α -helix: In the α -helix CO of the one amino acid residue forms H-bond with NH of the forth one.

Supersecondary structure or Motifs :

occurs by combining secondary structure.

The combination may be: α -helix- turn- α -helix- turn.....etc

Or: β -sheet -turn- β -sheet-turn.....etc

Or: α -helix- turn- β -sheet-turn- α -helix

Turn (or bend): is short segment of polypeptides (3-4 amino acids) that connects successive secondary structures.

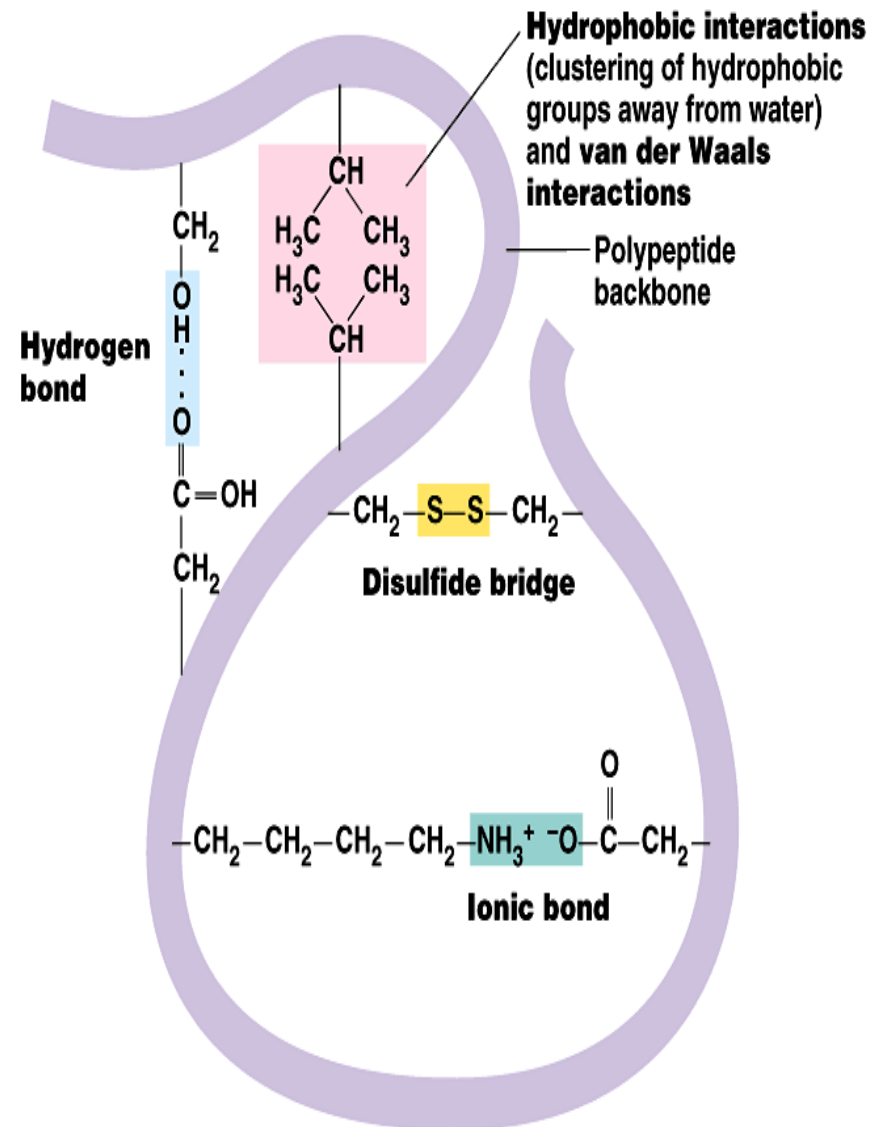
e.g. β -turn: is small polypeptide that connects successive strands of β -sheets.

● Tertiary structure is

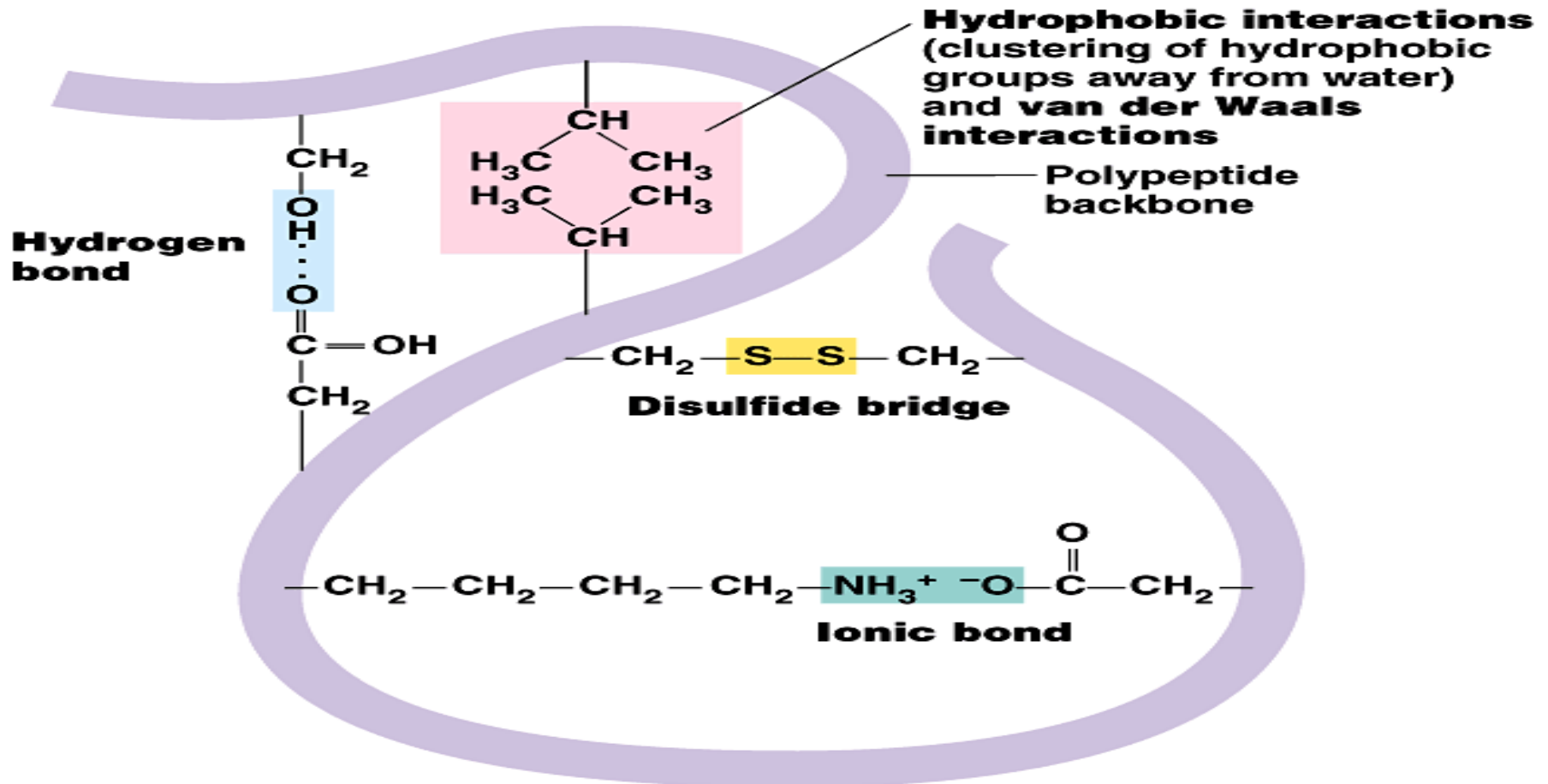
determined by a variety of interactions (bond formation) among R groups and between R groups and the polypeptide backbone.

a. The weak interactions include:

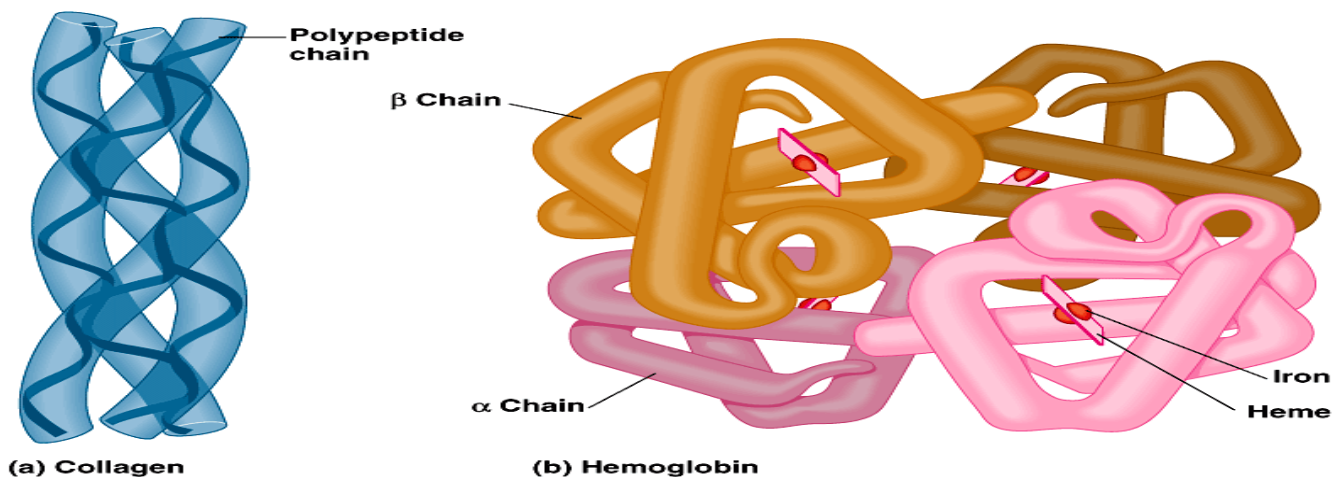
- **Hydrogen bonds** among polar side chains
- **Ionic bonds** between charged R groups (basic and acidic amino acids)
- **Hydrophobic interactions** among hydrophobic (non polar) R groups.

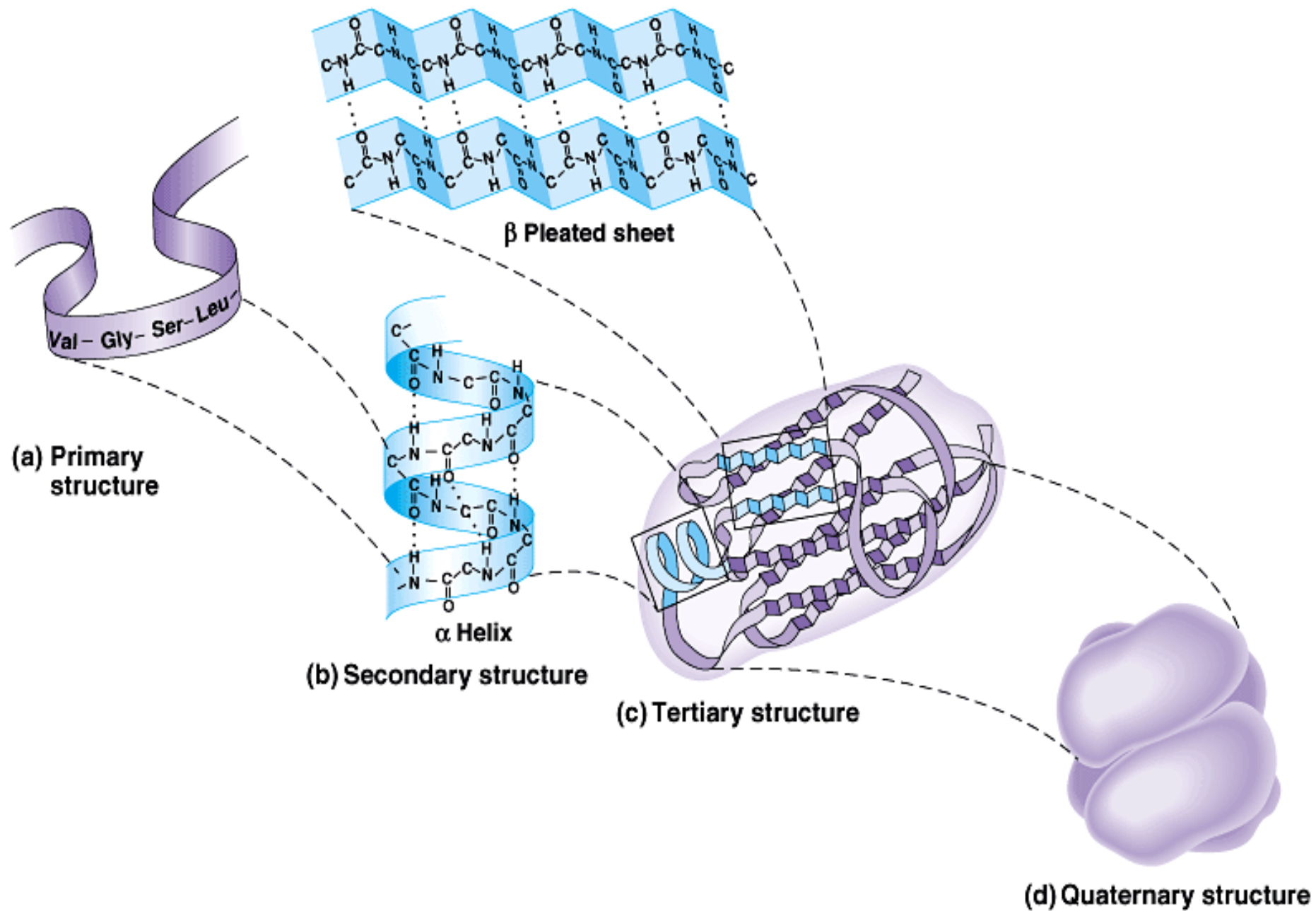


- b. Strong covalent bonds** include **disulfide bridges**, that form between the sulfhydryl groups (SH) of cysteine monomers, stabilize the structure.



- **Quaternary structure:** results from the aggregation (combination) of two or more polypeptide subunits held together by non-covalent interaction like H-bonds, ionic or hydrophobic interactions.
- Examples on protein having quaternary structure:
 - **Collagen** is a fibrous protein of three polypeptides (trimeric) that are supercoiled like a rope.
 - This provides the structural strength for their role in connective tissue.
 - **Hemoglobin** is a globular protein with four polypeptide chains (tetrameric)
 - **Insulin**: two polypeptide chains (dimeric)





Classification of proteins

I- Simple proteins:

i.e. on hydrolysis gives only amino acids

Examples:

1- Albumin and globulins: present in egg, milk and blood

They are proteins of high biological value i.e. contain all essential amino acids and easily digested.

Types of globulins:

α 1 globulin: e.g. antitrypsin: see later

α 2 globulin: e.g. hepatoglobin: protein that binds hemoglobin to prevent its excretion by the kidney

β -globulin: e.g. transferrin: protein that transport iron

γ -globulins = **Immunoglobulins** (antibodies) : responsible for immunity.

2- Globins (Histones): They are basic proteins rich in histidine amino acid.

They are present in :

- a - combined with DNA
- b - combined with heme to form hemoglobin of RBCs.

3- Gliadines are the proteins present in cereals.

4- Scleroproteins: They are structural proteins, not digested.
include: keratin, collagen and elastin.

a- α -keratin: protein found in hair, nails, enamel of teeth and outer layer of skin.

- It is α -helical polypeptide chain, rich in cysteine and hydrophobic (non polar) amino



b- collagens: protein of connective tissues found in bone, teeth, cartilage, tendons, skin and blood vessels.

- Collagen may be present as gel e.g. in extracellular matrix or in vitreous humor of the eye.
- Collagens are the most important protein in mammals. They form about 30% of total body proteins.
- There are more than 20 types of collagens, the most common type is **collagen I** which constitutes about 90% of cell collagens.
- **Structure of collagen:** three helical polypeptide chains (trimeric) twisted around each other forming triplet-helix molecule.
- $\frac{1}{3}$ of structure is glycine, 10% proline, 10% hydroxyproline and 1% hydroxylysine. Glycine is found in every third position of the chain. The repeating sequence –Gly-X-Y-, where X is frequently proline and Y is often hydroxyproline and can be hydroxylysine.



Solubility: collagen is insoluble in all solvents and not digested.

•When collagen is heated with water or dil. HCl it will be converted into **gelatin** which is soluble , digestible and used as diet (as jelly).
Gelatin is classified as derived protein.

Some collagen diseases:

1- Scurvy: disease due to deficiency of vitamin C which is important coenzyme for conversion of proline into hydroxyproline and lysine into hydroxylysine. Thus, synthesis of collagen is decreased leading to abnormal bone development, bleeding, loosening of teeth and swollen gum.

2- Osteogenesis Imperfecta (OI): Inherited disease resulting from genetic deficiency or mutation in gene that synthesizes collagen type I leading to abnormal bone formation in babies and frequent bone fracture in children. It may be lethal.

C- Elastin: present in walls of large blood vessels (such as aorta). It is very important in lungs, elastic ligaments, skin, cartilage, .. It is elastic fiber that can be stretched to several times as its normal length.

Structure: composed of 4 polypeptide chains (tetramer), similar to collagen being having 33% glycine and rich in proline but in that it has low hydroxyproline and absence of hydroxy lysine.

Emphysema: is a chronic obstructive lung disease (obstruction of air ways) resulting from deficiency of α 1-antitrypsin particularly in cigarette smokers.

Role of α 1-antitrypsin: Elastin is a lung protein. Smoke stimulate enzyme called elastase to be secreted form neutrophils (in lung). Elastase cause destruction of elastin of lung.

α 1-antitrypsin is an enzyme (secreted from liver) and inhibit elastase and prevent destruction of elastin. So deficiency of α 1-antitrypsin especially in smokers leads to degradation of lung and destruction of lung (loss of elasticity of lung, a disease called emphysema.

Conjugated proteins

i.e. On hydrolysis, give protein part and non protein part and subclassified into:

1- Phosphoproteins: These are proteins conjugated with phosphate group. Phosphorus is attached to oH group of serine or threonine.
e.g. Casein of milk and vitellin of yolk.

2- Lipoproteins:

These are proteins conjugated with lipids.

Functions: a- help lipids to transport in blood
 b- Enter in cell membrane structure helping lipid soluble substances to pass through cell membranes.

3- Glycoproteins:

proteins conjugated with sugar (carbohydrate)

e.g. – Mucin

- Some hormones such as erythropoietin
- present in cell membrane structure
- blood groups.

4- Nucleoproteins: These are basic proteins (e.g. histones) conjugated with nucleic acid (DNA or RNA).

e.g. a- chromosomes: are proteins conjugated with DNA
 b- Ribosomes: are proteins conjugated with RNA

5- Metalloproteins: These are proteins conjugated with metal like iron, copper, zinc,

a- Iron-containing proteins: Iron may present in heme such as in

- hemoglobin (Hb)
- myoglobin (protein of skeletal muscles and cardiac muscle),
- cytochromes,
- catalase, peroxidases (destroy H_2O_2)
- tryptophan pyrrolase (destroy indole ring of tryptophan).

Iron may be present in free state (not in heme) as in:

- Ferritin: Main store of iron in the body. ferritin is present in liver, spleen and bone marrow.
- Hemosidrin: another iron store.
- Transferrin: is the iron carrier protein in plasma.

b- Copper containing proteins:

- e.g. - Ceruloplasmin which oxidizes ferrous ions into ferric ions.
- Oxidase enzymes such as cytochrome oxidase.

c- Zn containing proteins: e.g. Insulin and carbonic anhydrase

d- Mg containing proteins: e.g. Kinases and phosphatases.

6-Chromoproteins: These are proteins conjugated with pigment. e.g.

- All proteins containing heme (Hb, myoglobin,)
- Melanoprotein: e.g. proteins of hair or iris which contain melanin.

Derived proteins

Produced from hydrolysis of simple proteins.

- e.g. - Gelatin: from hydrolysis of collagen
- Peptone: from hydrolysis of albumin