Classification of proteins

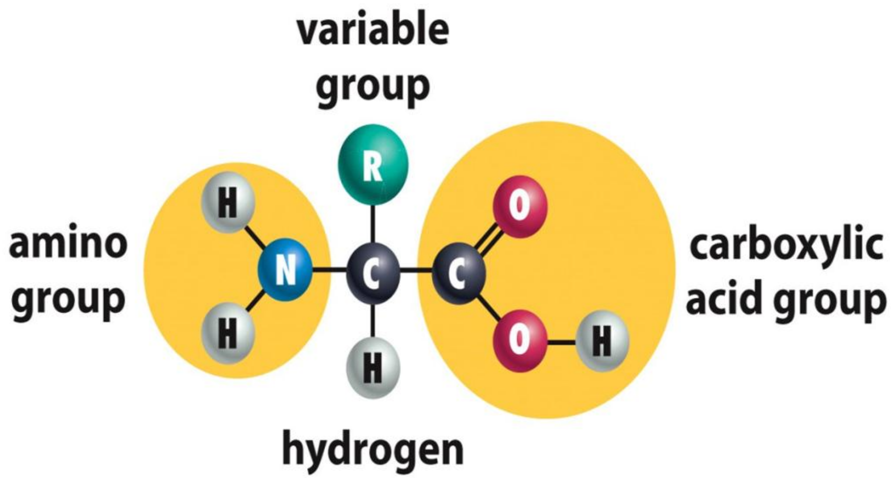
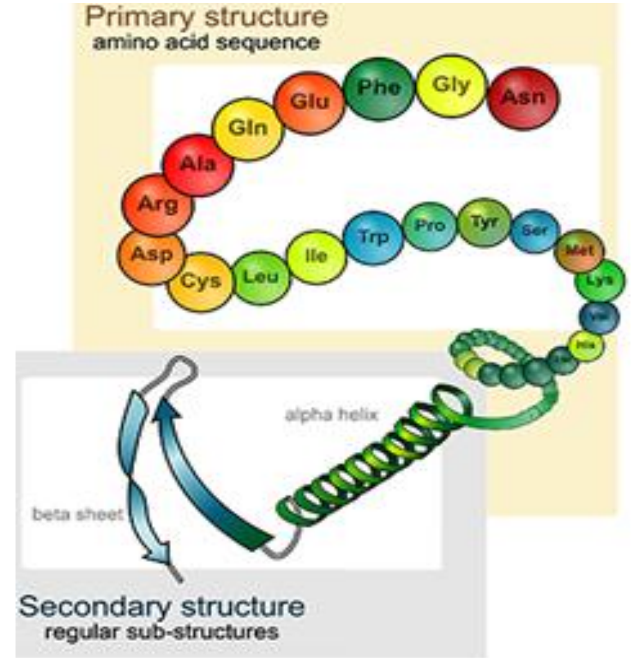
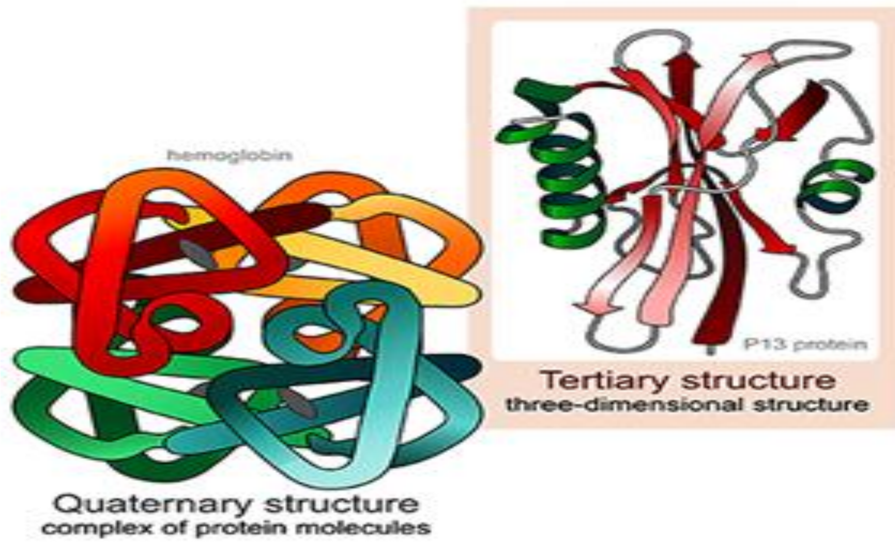


Figure 3-18 Biology: Life on Earth, 8/e





CLASSIFICATION OF PROTEINS

There is no single universally satisfactory system of protein classification so far.

1. Classifies proteins according to their composition or structure.
2. Classifies them according to solubility.
3. Classifies them according to their shape.
4. Classification of proteins based on their function.

Classification of proteins based on their composition

Proteins are divided into three major classes according to their structure.

1. Simple proteins: Simple proteins are made up of amino acids only.

On hydrolysis, they yield 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:

α1 globulin: e.g. antitrypsin: see later

α2 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 histamine 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 acids so it is water insoluble.

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

Collagen may be present as gel 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.
- ⅓ 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, loosing 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 hydroxylysine.

Emphysema: is a chronic obstructive lung disease (obstruction of air ways) resulting from deficiency of α1-antitrypsin particularly in cigarette smokers.

Role of α1-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.

α1-antitrypsin is an enzyme (secreted from liver) and inhibit elastase and prevent destruction of elastin. So deficiency of α1-antitrypsin especially in smokers leads to degradation of lung and destruction of lung (loss of elasticity of lung, a disease called emphysema).

2. **Conjugated proteins:** They are proteins containing non-protein part attached to the protein part. The non-protein part is linked to protein through covalent bond. The non-protein part is loosely called as prosthetic group. On hydrolysis, these proteins yield non-protein compounds and amino acids.

Conjugated protein → **Protein + Prosthetic group**

Example

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 H2O2)
- tryptophan pyrrolase (desrtroy 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.

3. **Derived proteins:** As the name implies this class of proteins are formed from simple and conjugated proteins. There are two classes of derived proteins.

(*i*) *Primary derived proteins:* They are formed from natural proteins by the action of heat or alcohol etc. The peptide bonds are not hydrolysed. They are synonymous with denatured proteins.

Example: Coagulated proteins like cooked-egg albumin.

(*ii*) *Secondary derived proteins:* They are formed from partial hydrolysis of proteins.

Examples: Proteoses, peptone, gelatin, and peptides.

Classification of proteins based on shape

Proteins are divided into two classes based on their shape.

1. **Globular proteins:** Polypeptide chain of these proteins are folded into compact globular (Spherical) shape.

Examples: Hemoglobin, myoglobin, albumin, lysozyme, chymotrypsin.

2. **Fibrous proteins:** Poly peptide chains are extended along one axis.

Examples: α-keratin, β-keratin, collagen and elastin.

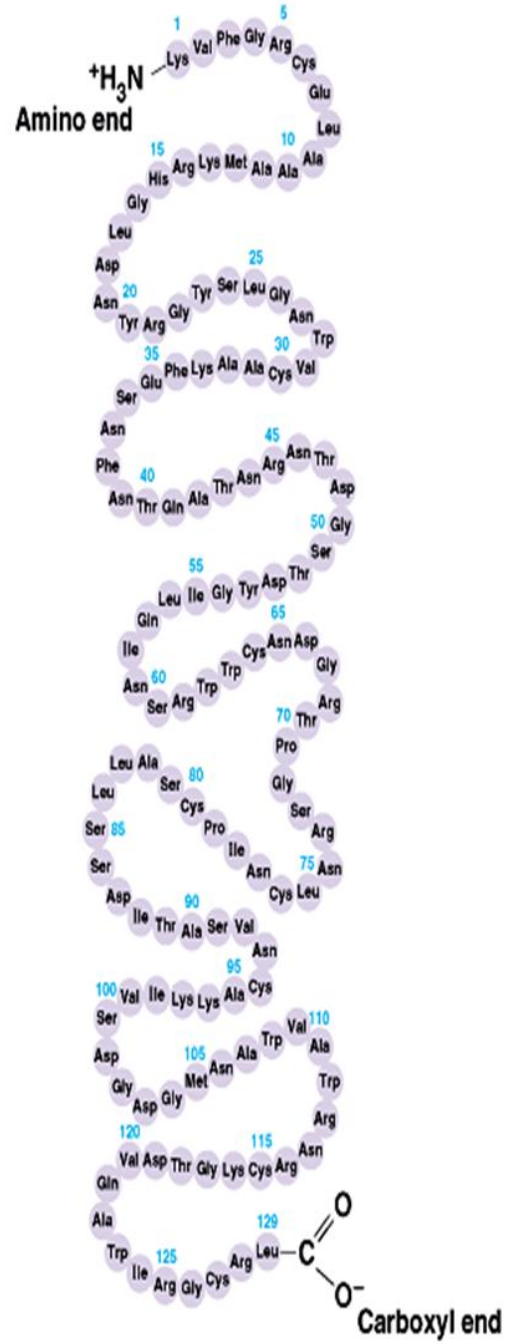
Protein Structure

Since proteins are built from amino acids by linking them in linear fashion, it may be viewed as proteins having long chain like structures. However, such arrangement is unstable and polypeptide or protein folds to specific shape known as *conformation,* which is more stable. Various stages involved in the formation of final conformation from linear chain are divided into four levels or orders of protein structure. They are

- Primary: Linear order of amino acids
- Secondary: Alpha helix and beta sheets
- Tertiary: Three dimensional folded shape of the protein
- Quaternary: More than one polypeptide chain interacting to form a single structure.

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.
- Arranging amino acids in a different order creates a polypeptide or protein that no longer has the same function as the initial sequence of amino acids.

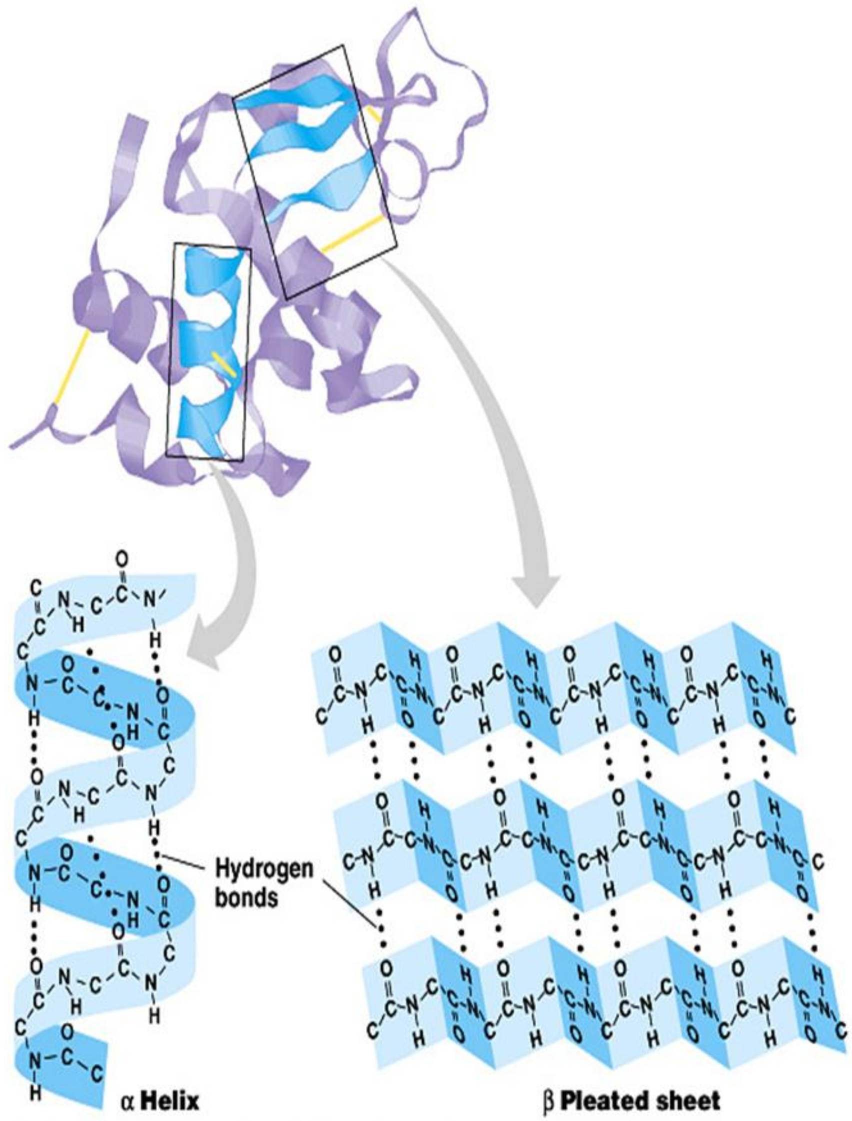


2- Secondary structure:

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:

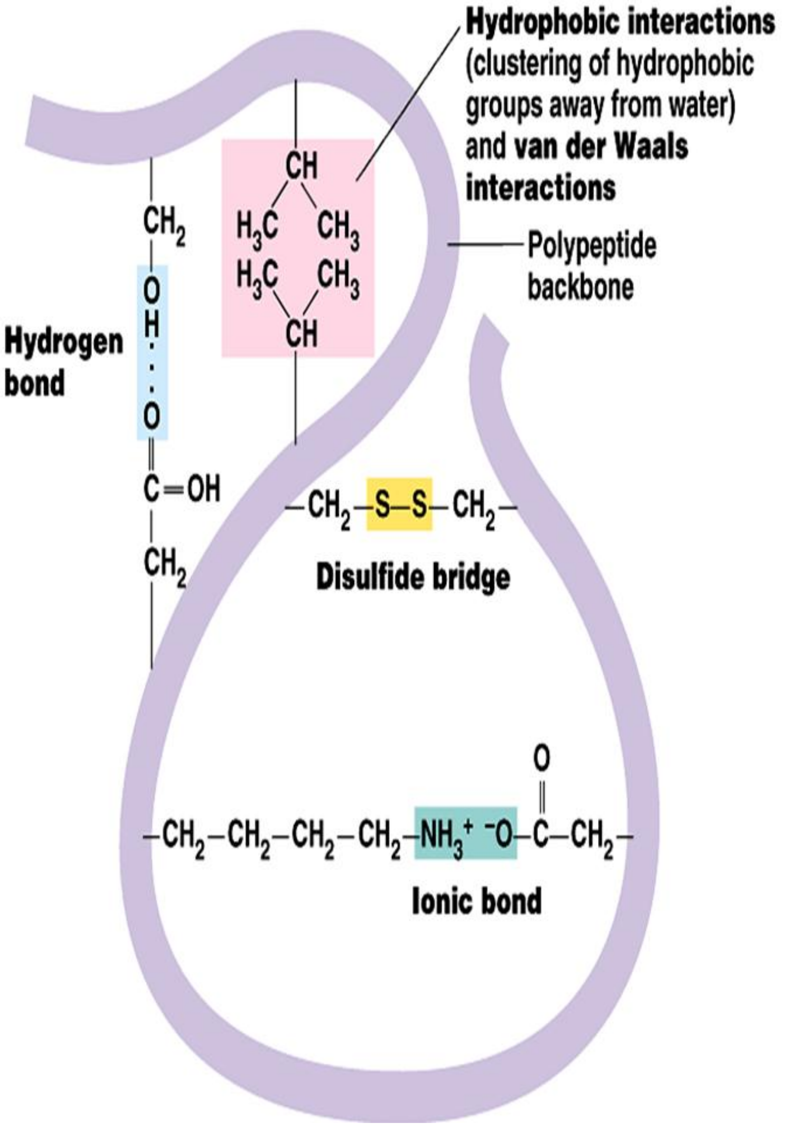
α-helix: It is a spiral structure resulting from hydrogen bonding between one peptide bond and the fourth one

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).



Tertiary Structure

- The complex interactions between the secondary structures that drive protein folding are typically mediated by hydrophobic interactions.
- 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.

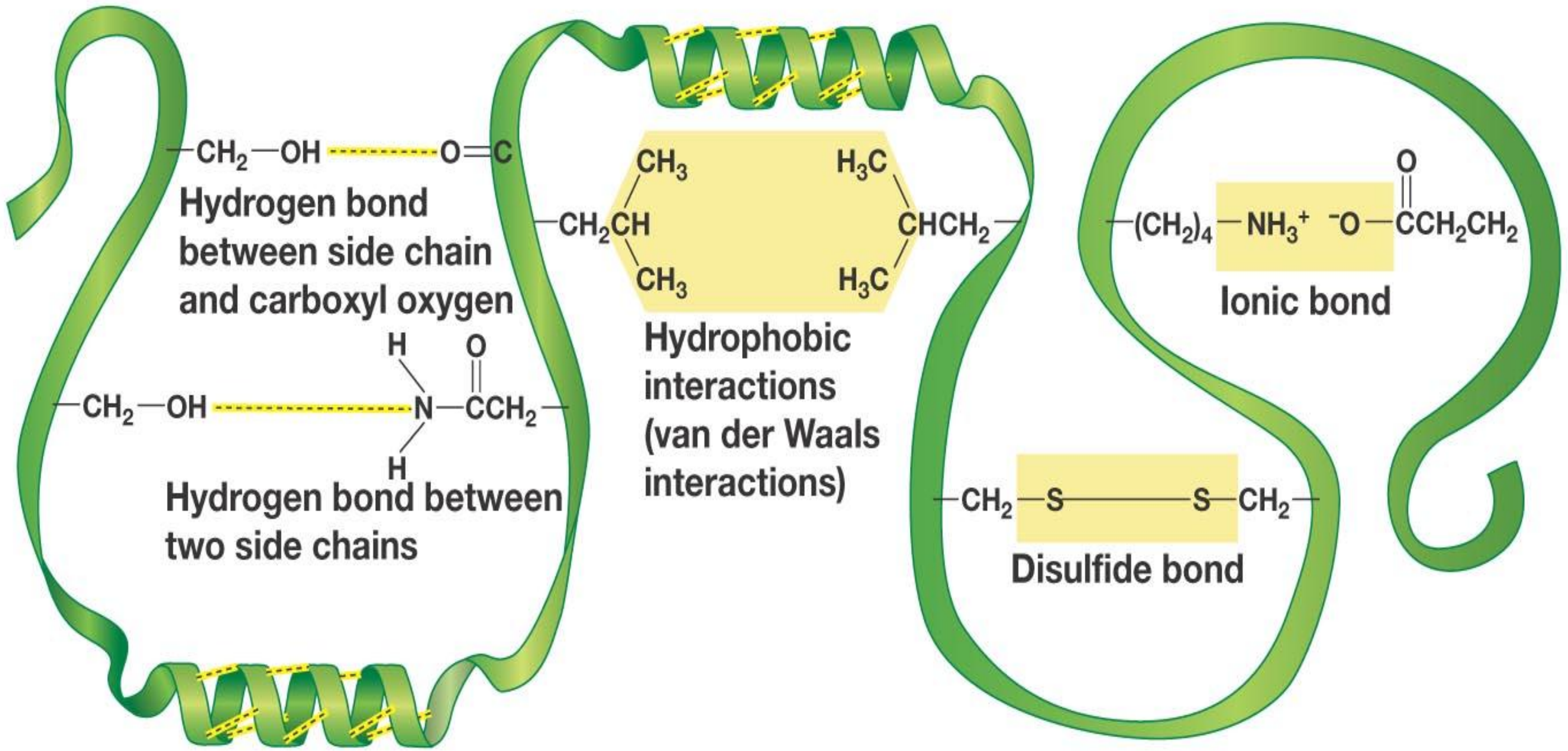


Tertiary Structure

- The tertiary structure is the three-dimensional structure of the protein.
- It involves twisting and folding of the polypeptide chain caused by hydrophobic and hydrophilic interactions between the side chains of the amino acids.
- The nonpolar amino side chains end up in the interior of the protein away from the aqueous environment.
- The polar side chains appear on the surface of the protein since they are attracted to the aqueous surroundings.
- Stabilization of the tertiary structure is by:
- Attractive forces between the side chains and aqueous environment
- Attractive forces between side chains themselves
- These attractive forces cause the protein to fold into a specific three-dimensional shape.

<u>B-Strong covalent bonds</u> include disulfide bridges, that form between the sulfhydryl groups (SH) of cysteine monomers, stabilize the structure.

(a) Interactions that determine the tertiary structure of proteins



Quaternary Structure

- The quaternary structure is two or more polypeptide chains interacting to form a biologically active protein.
  - **Collagen** is a fibrous protein of three polypeptides (trimeric) that are supercoiled like a rope.
  - Insulin : two polypeptide chains (dimeric)
  - This provides the structural strength for their role in connective tissue.

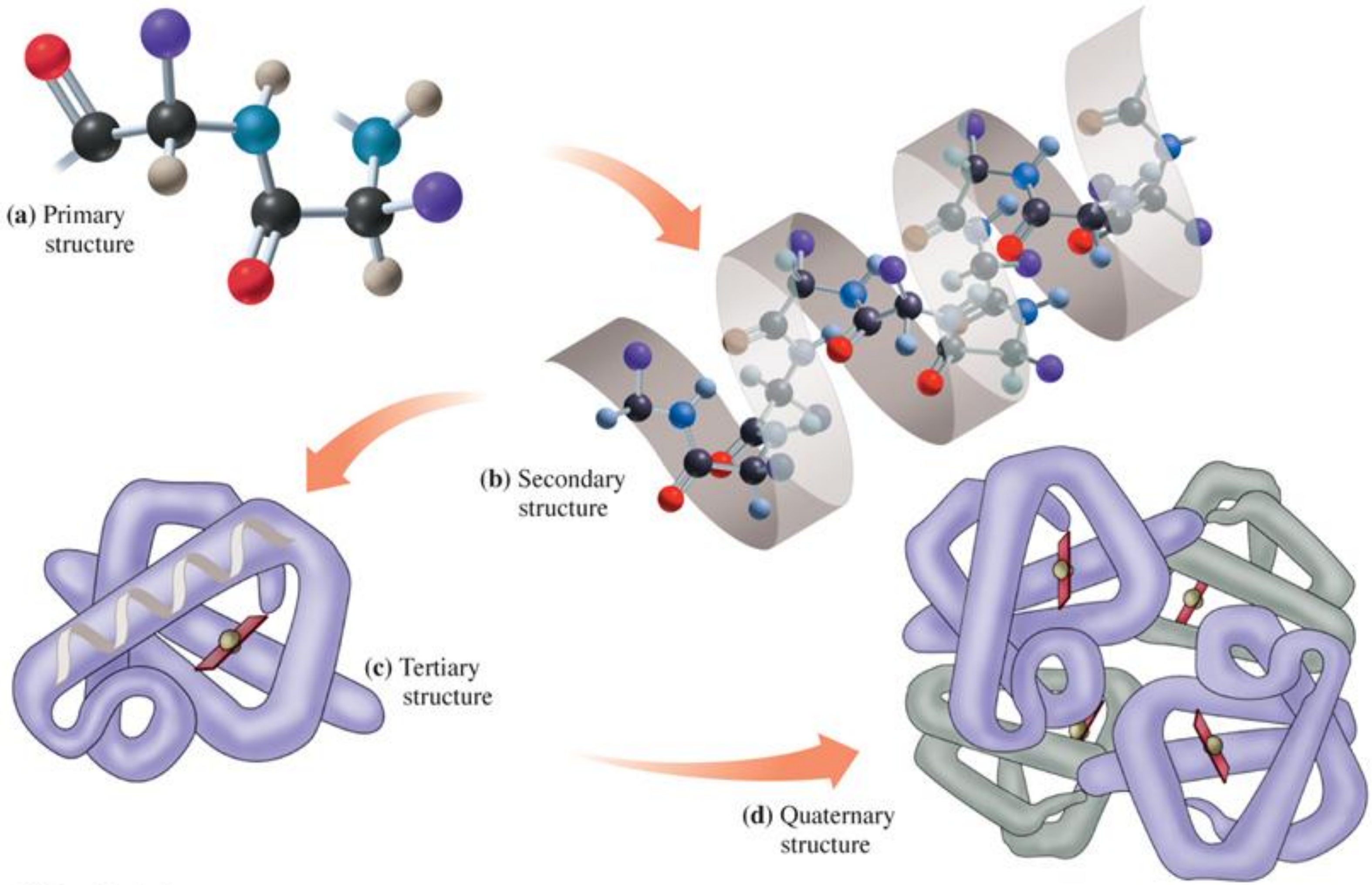
  - **Hemoglobin** is a globular protein with four polypeptide chains (tetrameric)

- Hemoglobin, an oxygen transport protein, is an example of a protein with a quaternary structure.
- It consists of four polypeptide chains or subunits.
- It has two identical alpha subunits and two identical beta subunits.
- All four subunits must be present for the protein to function as an oxygen transport.
- Not all proteins have a quaternary structure.

Denaturation of Proteins

- Denaturation is a process that disrupts secondary, tertiary, and quaternary structures.
- The primary structure is not destroyed during denaturation.
- Frying an egg is an example of denaturation by heat.
- Heat disrupts intermolecular forces such as hydrogen bonding and polar interactions.

- Changes in pH, which alters the ability of the acidic and basic side chains to form salt bridges
- Organic compounds, which will disrupt the disulfide bonds
- Heavy metals that disrupt salt bridges and disulfide bonds


(a) Primary
structure
(b) Secondary
structure
(c) Tertiary
structure
(d) Quaternary
structure