
عليكم السلام

Structure of Proteins

Prepared by

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Structure of Proteins

Protein molecules are formed of **one or more** polypeptide chains.

Internal structure of proteins exists at:

3 or 4 levels;

1ry,

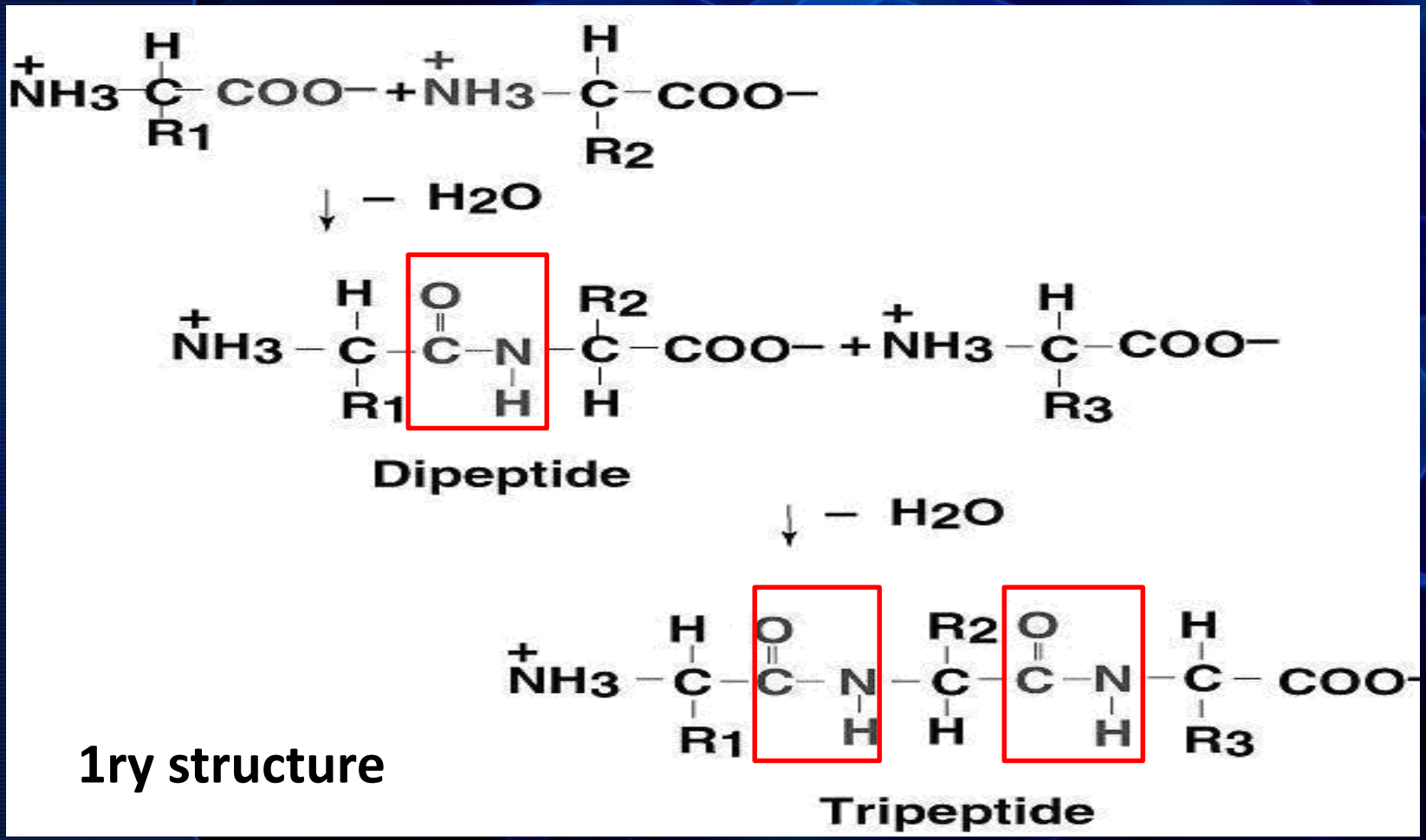
2ry,

Tertiary and/or

Quaternary

1. Primary Structure

- **Number, type and sequence of aa.** along the polypeptide chain.
- Each chain has a ***free amino*** group (N-terminus) on ***left*** side and its amino acid number **(1).**
- And a ***free COOH*** group and (carboxyl or C-terminus) on ***right*** side (**last** amino acid).
- Each chain has a ***unique aa.*** sequence decided by genes. 1ry structure is maintained by ***covalent*** peptide bonds. The C-N bond is ***'trans'*** in nature



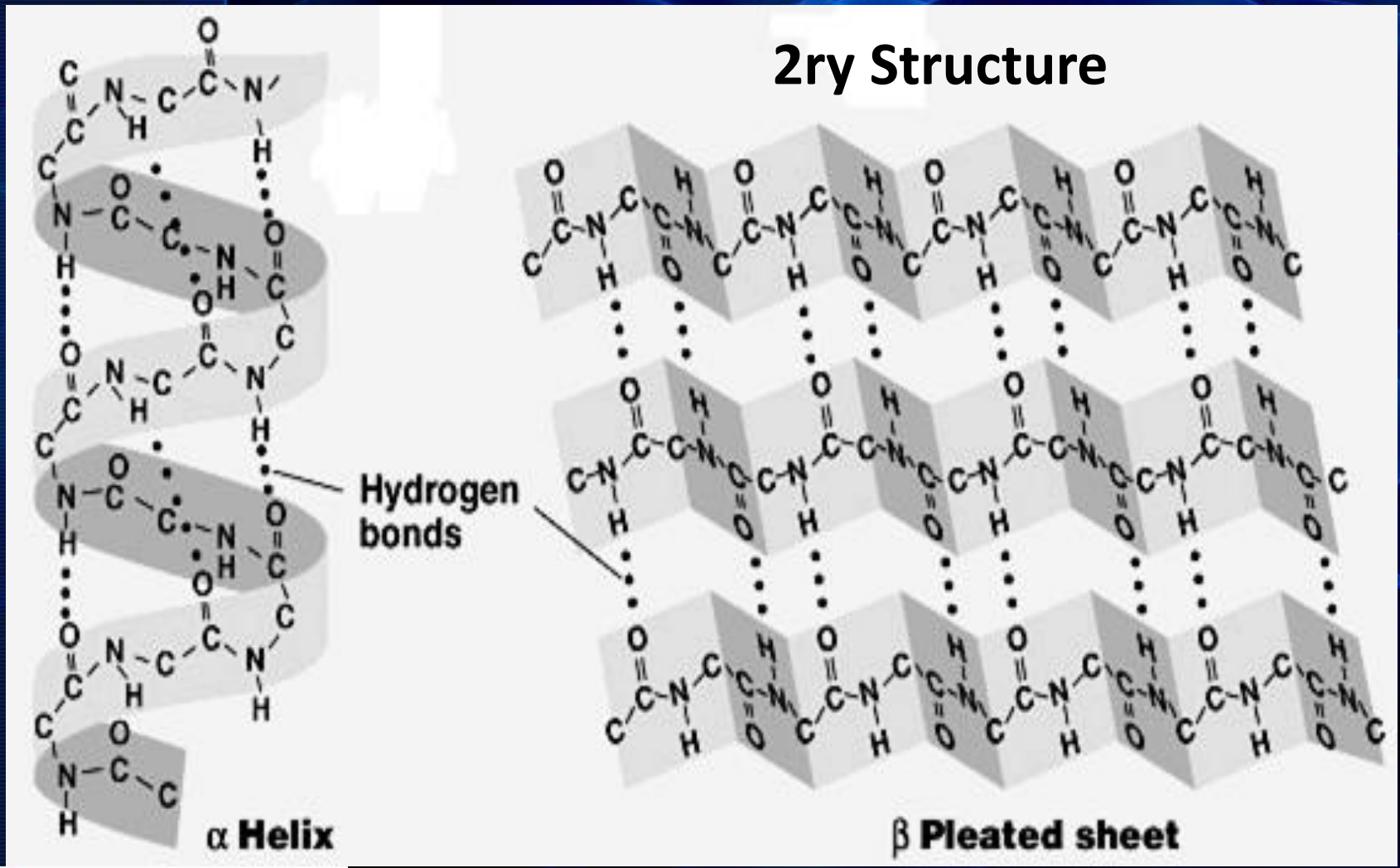
1ry structure

2ry Structure

- Folding of peptide chain held by **-S–S-** & **-O…H-**

1. ***α-helix:*** It is a coiled structure of fibrous protein. The **–O…H–** formed intrachain [right handed helix (clockwise)]. e.g. myosin and keratin in unstretched hair.
2. ***β-pleated sheets*** (extended structure of fibrous proteins): The **–O…H–** formed interchain [same direction (parallel) or opposing directions (anti parallel)]. e.g. silk & β-Keratin in stretched hair.

2ry Structure



3.Tertiary Structure

- It is the arrangement and inter-relationship of the twisted polypeptide chains.

4. Quaternary Structure:

- It is the aggregation of several chains to form a protein molecule. It describes the **spatial** relationships between the subunits, e.g. Insulin, 2 chains (A and B) connected by disulfide bond. Globin of Hb formed by 4 chains (2 α and 2 β).

Forces stabilizing the 2ry, 3ry, 4ry structures:

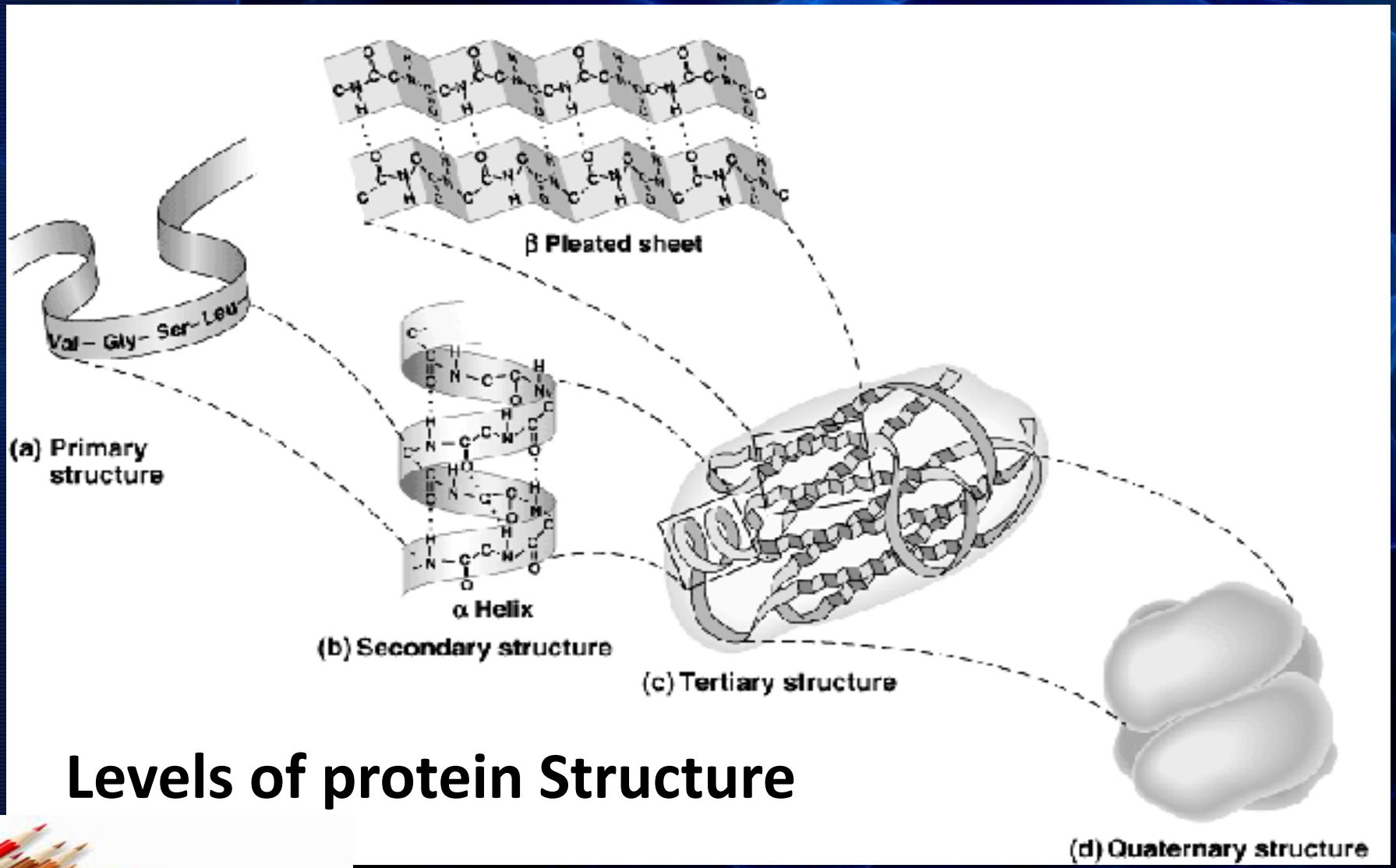
-NH----O=C-: between imino H and carbonyl O of the adjacent extended regions of peptide chain.

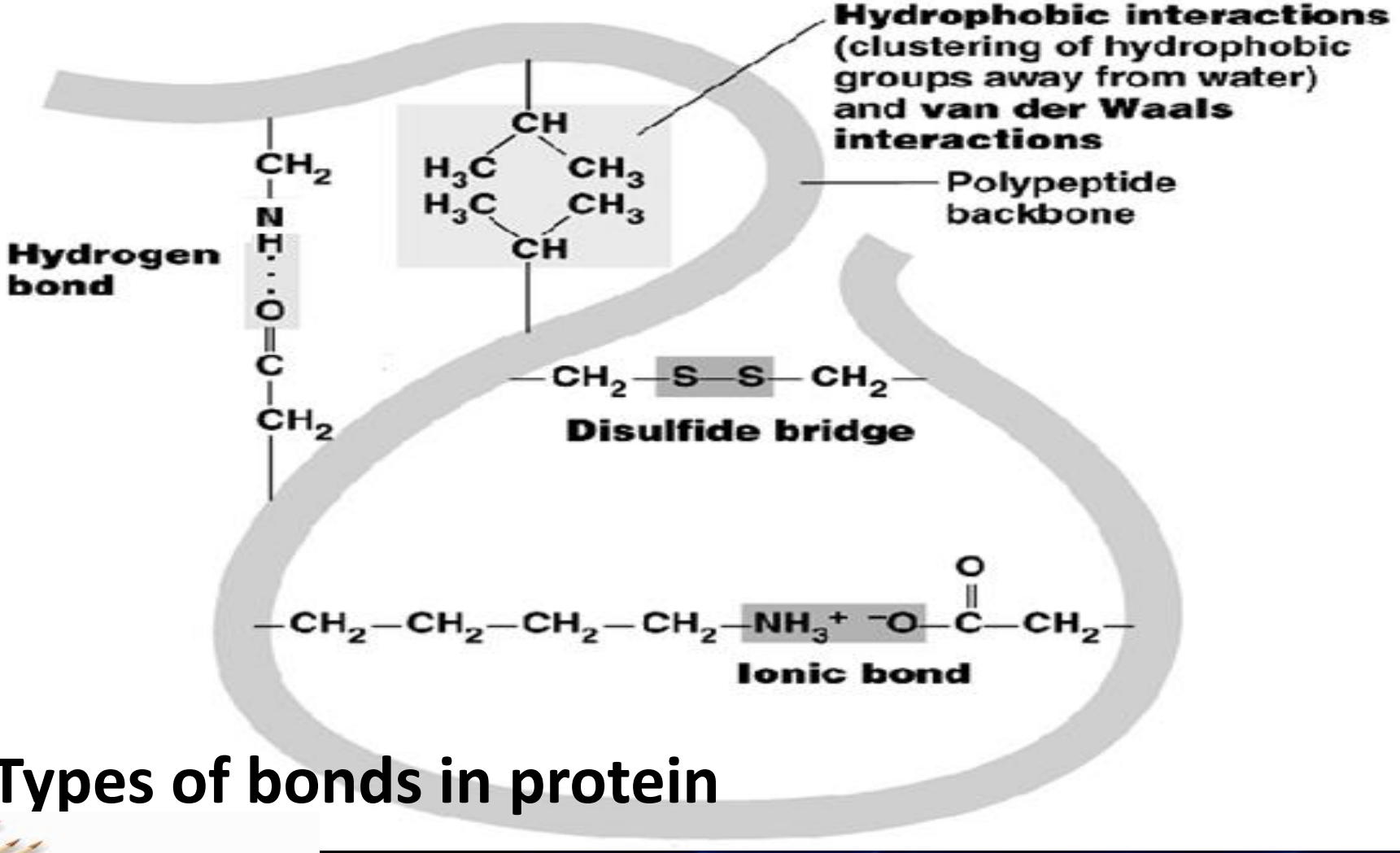
-S-S – : oxidative union of -SH groups of 2 cysteine residues, forming cystine.

ionic bond (-NH_3^+----OOC^-): between +ve and -ve side chain groups of basic and acidic aa. respectively. e.g. (NH_3^+ of lysine and COO^- of aspartic).

hydrophobic bond (-CH_3-----CH_3-): between non polar hydrophobic side chains of neutral aa. (alanine & valine)

Levels of protein Structure





Types of bonds in protein

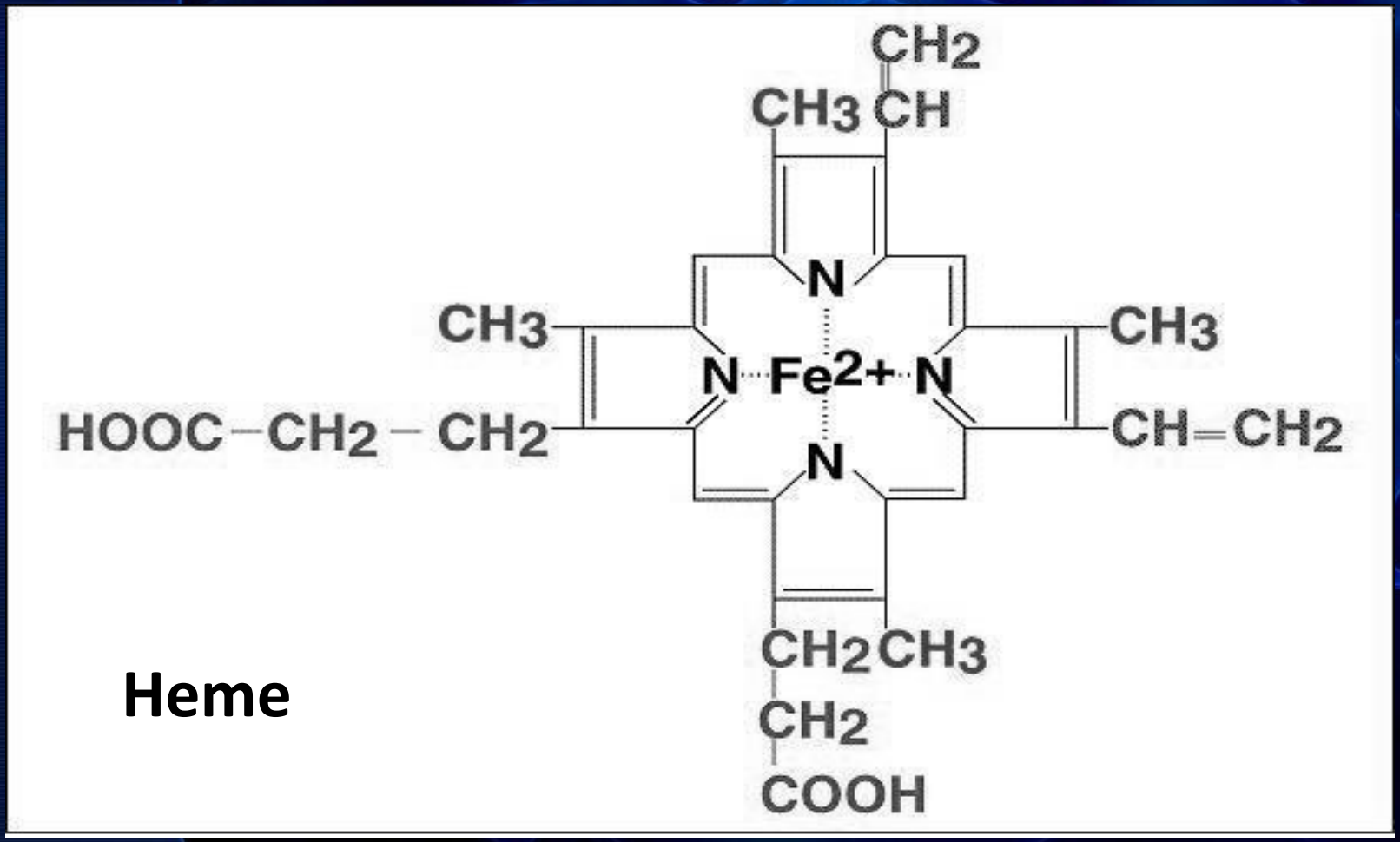
Hemoproteins

- Proteins containing **heme prosthetic** group.
- Heme is present in the body in:

1. **Hemoglobin & Myoglobin**
2. **Cytochrome & Cytochrome oxidase**
3. **Catalase & Peroxidase**
4. **Tryptophan dioxygenase**

Hemoglobin

- Hemoglobin is a **metallo-chromo-protein** (red color) present in RBCs.
- It is **conjugated** protein containing heme.
- Heme is a **ferrous protoporphyrin III**. The porphyrin part of heme is cyclic compound [four pyrrole units linked by methylene bridges **(-CH=)].**



Heme

➢ **Hemoglobin level**

Normally: **males: 14-18 g/dl** & **females 12-16 g/dl**.

➢ **Functions of hemoglobin:**

A. Ideal respiratory function: 1 - Has a great solubility.

2- Transport large amounts of **O_2** at appropriate partial pressures

B. It is a powerful buffer.

➢ **Structure of hemoglobin (heme and globin):**

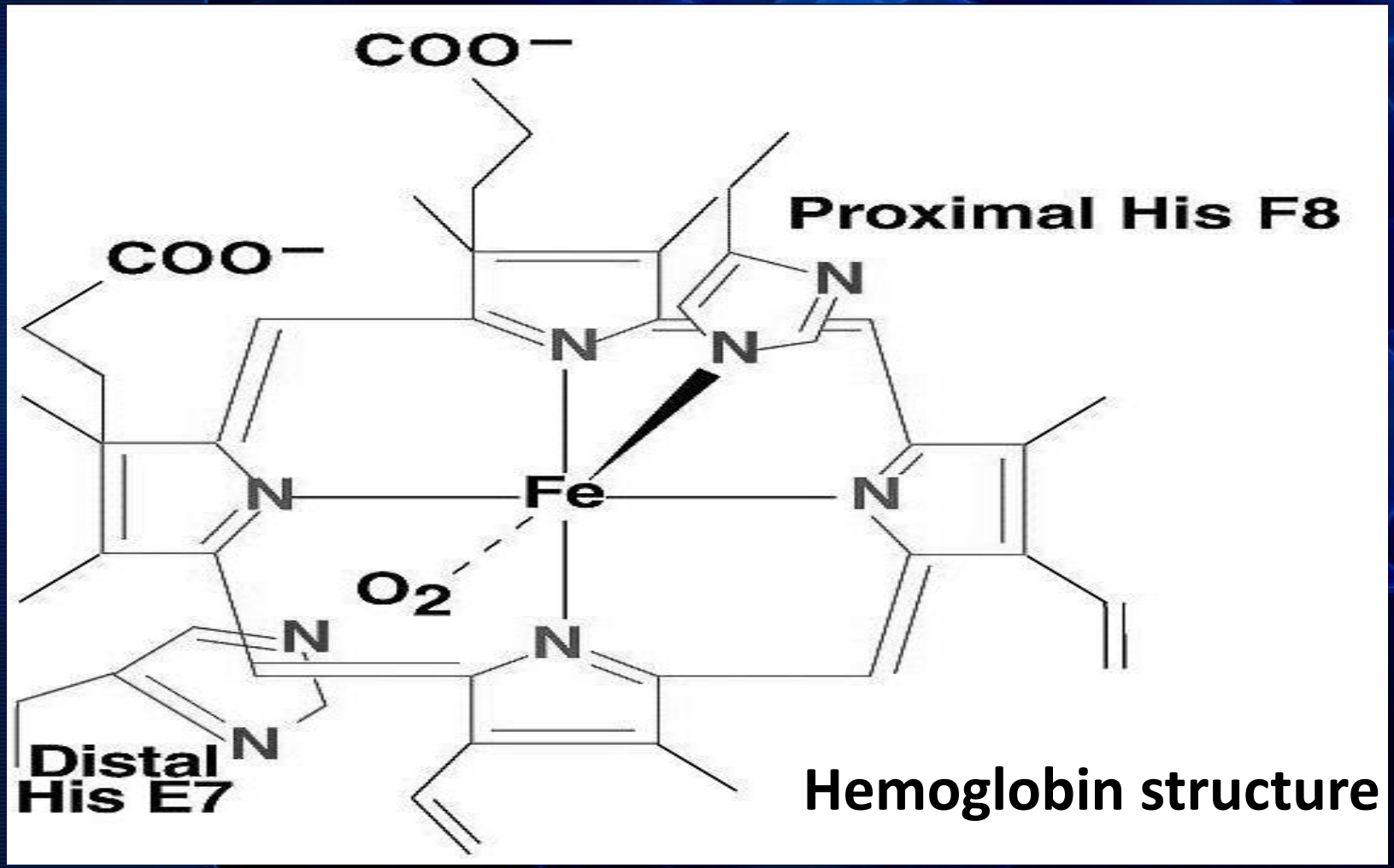
- The globin part is 4 chain and is globular in shape.
- Hb is different in structure from fetal life to adult life.

I. Adult hemoglobin:

Hb $A_{1.}$ **97% of adult Hb.**

- The globin is 2 α and 2 β chains **($\alpha_2\beta_2$).**
- α: 141 aa. and β, γ and δ : 146 aa.
- α chain gene (chr **16**) but β, γ and δ genes (chr **11**).
- There are 36 histidine in Hb molecule (buffering action)
- **58th** residue in α chain is **distal histidine (**away from iron).
- **87th** residue in α chain is **proximal histidine** (near iron).
- α and β chains are linked by relatively weak non-covalent bonds

Hb A_2: 2% of adult Hb. 2 α and 2 δ chains (α2δ2).



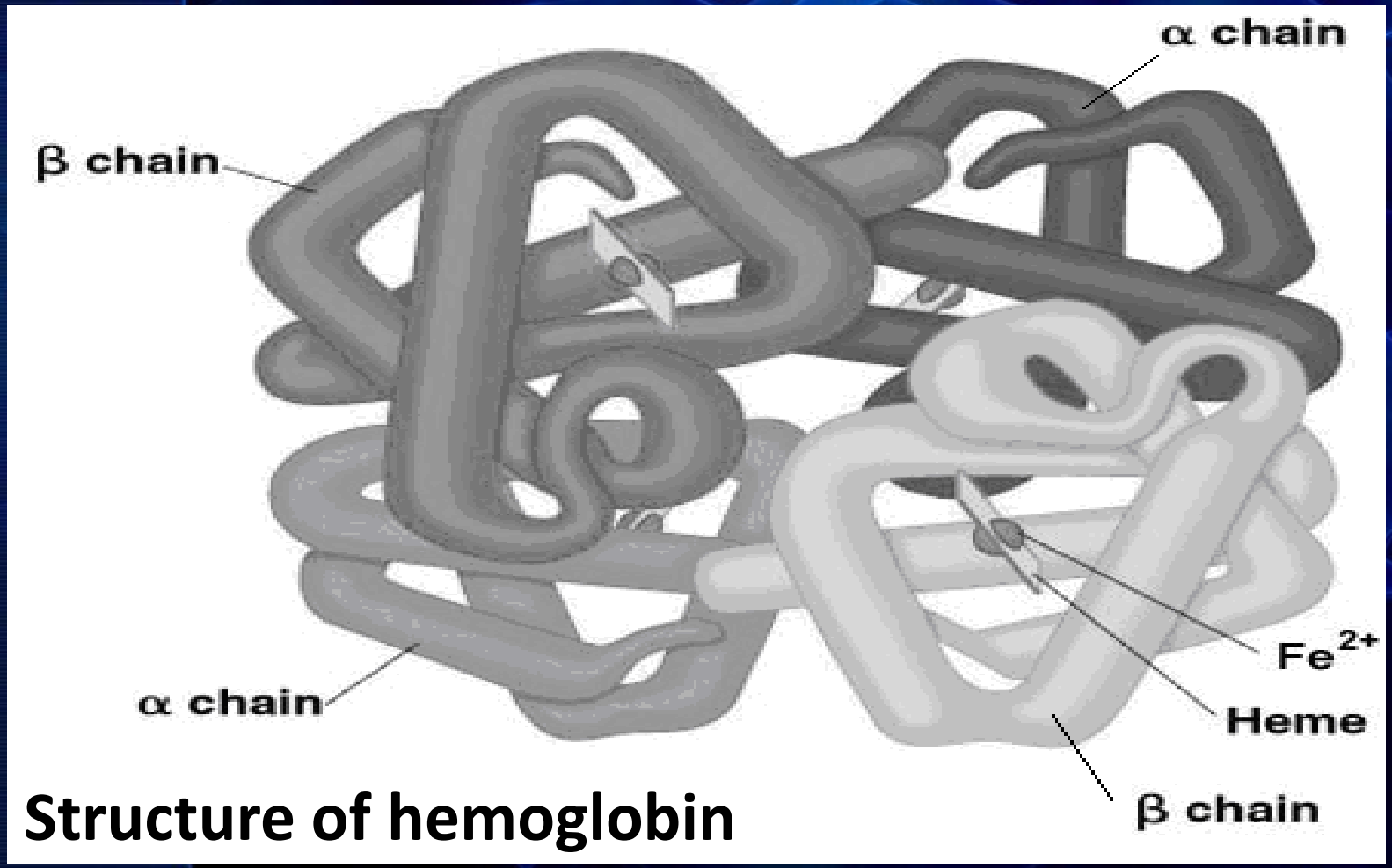
Hemoglobin structure

II. Fetal hemoglobin:

- Hb F: 1% of adult Hb. **($\alpha_2\gamma_2$).**
- Has higher affinity for O_2 than maternal Hb, this allows HbF to take O_2 from maternal blood.
- Present normally during fetal life and disappears gradually after birth.

Attachment of heme with globin chain:

- 4 heme/Hb molecule, one for each subunit.
- The 4 heme (**4%** of whole Hb mass).
- Heme is located in hydrophobic cleft of globin chain.
- **Iron** occupies **central** position of porphyrin ring.
- Reduced iron is Fe^{2+} and the oxidized is Fe^{3+}
- Fe^{2+} has **6** valencies and Fe^{3+} has 5 valencies. Hb has Fe^{2+}
- The iron is linked to pyrrole nitrogen by **4 bonds** and a **5th** bond to **imidazole nitrogen** of proximal histidine. In oxy-Hb, the **6th** valency binds **O_2.**



Structure of hemoglobin

Functions of Globin:

– Keeps iron of Hb in ferrous state.

– Renders heme soluble facilitating its function.

– Buffering action.

– Enlarges heme, preventing its escape outside RBCs.

– Responsible for sigmoid oxygen dissociation curve.

Hemoglobin derivatives:

1. **Oxy hemoglobin** carries **O_2** present in arterial blood.
2. **Reduced hemoglobin** present in venous blood.
3. **Carboxy hemoglobin** carries **CO** which is toxic
4. **Met-hemoglobin** **cannot** carry **O_2** (iron is ferric).

(N.B. NADPH + H^+ resulting from HMP shunt keeps Fe^{2+} of Hb)

Difference between oxygenation and oxidation:

When Hb carries O_2, Hb is oxygenated; iron is still Fe^{2+}. Oxidized Hb is called Met-Hb and then iron is Fe^{3+} with loss of O_2 carrying capacity.

Hemoglobinopathies

The abnormalities in primary sequence of globin chains

1. Hemoglobin S (HbS) sickle cell hemoglobin:

- Genetic; **glutamate at 6th** position of β chain is replaced by valine. Solubility of HbS in deoxygenated form is 50 times lesser than oxygenated form → crystallization & sickle. HbS is slower than HbA1 in electrophoresis.
- Heterozygous for HbS do not acquire sickle cell disease and resist malaria; infected cells require larger O_2 than uninfected, so cells sickle & ed from circulation.

2. Hemoglobin C:

- Genetic; replacement of glutamate at 6^{th} position of β chain of HbA by lysine. Homozygotes suffer from mild hemolytic anemia.

3. Hemoglobin E:

- Genetic; replacement of glutamate at 26^{th} position of β chain of HbA by lysine.

4. Hemoglobin D:

- Genetic; replacement of glutamate at 121^{st} position of β chain of HbA by glutamine.

5. Thalassemias

- **Reduced formation** of **α or β chain**, due to mutation in genes coding them producing abnormal Hb with impaired O2 binding.

Types: According to the chain affected:

I. α-Thalassemia: **α** -globin genes are duplicated (4) so one to four a-globin genes may be mutated:

a) one deficient **α**-globin gene (completely *normal* , **only carrier*).***

b) 2 deficient **α**-globin genes (***a-Thalassemia trait,*** only *mild anemia)*.

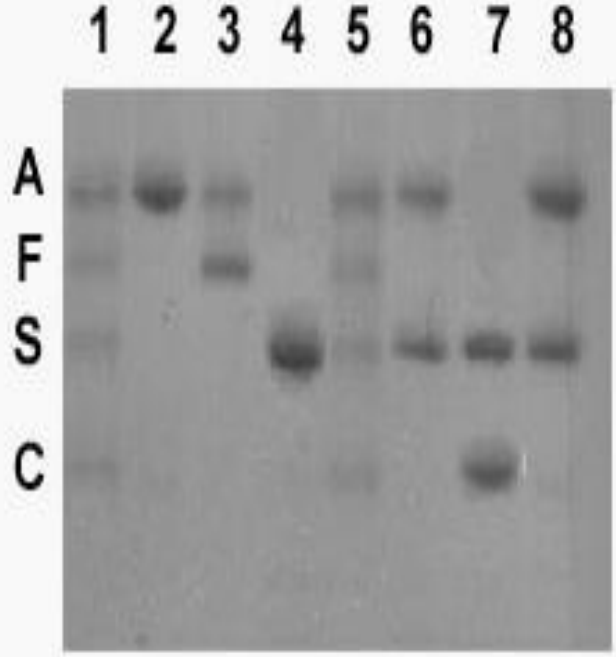
c) 3 deficient α-globin genes (**a-Thalassemia major,** a).

-globin genes (**Homozygous α-Thalassemia**, die soon after birth).

II. β-Thalassemia:

a) **Thalassemia minor or trait:** Heterozygotes carrying **one** mutated **β**-globin gene. These patients have *mild form of anemia* and will have a normal life span.

b) **Thalassemia major:** Homozygotes carrying **two** mutated **β**-globin gene, (*severe hemolytic anemia* with many complications). They rarely live to adulthood.



Pattern of hemoglobin electrophoresis from several different individuals. Lanes 1 and 5 are hemoglobin standards. Lane 2 is a normal adult. Lane 3 is a normal neonate. Lane 4 is a homozygous HbS individual. Lanes 6 and 8 are heterozygous sickle individuals. Lane 7 is a SC disease individual.

Myoglobin

- Formed of **one heme & one peptide** chain.
- Found in high concentrations in skeletal and cardiac muscles giving these tissues their characteristic red color
- The protein component of myoglobin (**apomyoglobin**) contains **153** aa residues.
- Myoglobin has much higher affinity for O_2 than Hb at low O_2 tension (30mm Hg pO_2). Its function is to store O_2 in muscles and releases it during muscular exercise when pO_2 is reduced to 5 mmHg.


Thank you