AMINO ACIDS, PEPTIDES AND PROTEINS

المرحلة الثالثة /قسم الكيمياء/الفصل الثاني

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Introduction to Peptide Structure Determination:

Protein Structure:

primary (1°) structure: the amino acid sequence

This sequence of amino acids is called the *primary structure*. It is responsible for the specific biological function of the protein. Even one amino acid incorrectly placed in a protein can alter its biological activity

secondary (2°): frequently occurring substructures or folds.

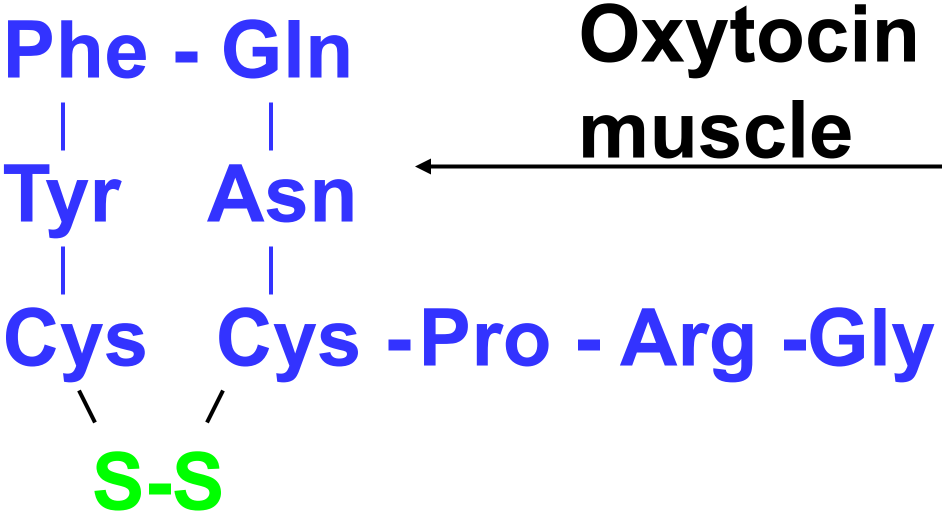
tertiary (3°): three-dimensional arrangement of all atoms in a single polypeptide chain.

quaternary (4°): overall organization of non-covalently linked subunits of a functional protein.

all the necessary information as to how a protein folds is encoded into the primary sequence!

- **1° sequence dictates 2° and 3° structure**

Some Protein Sequences

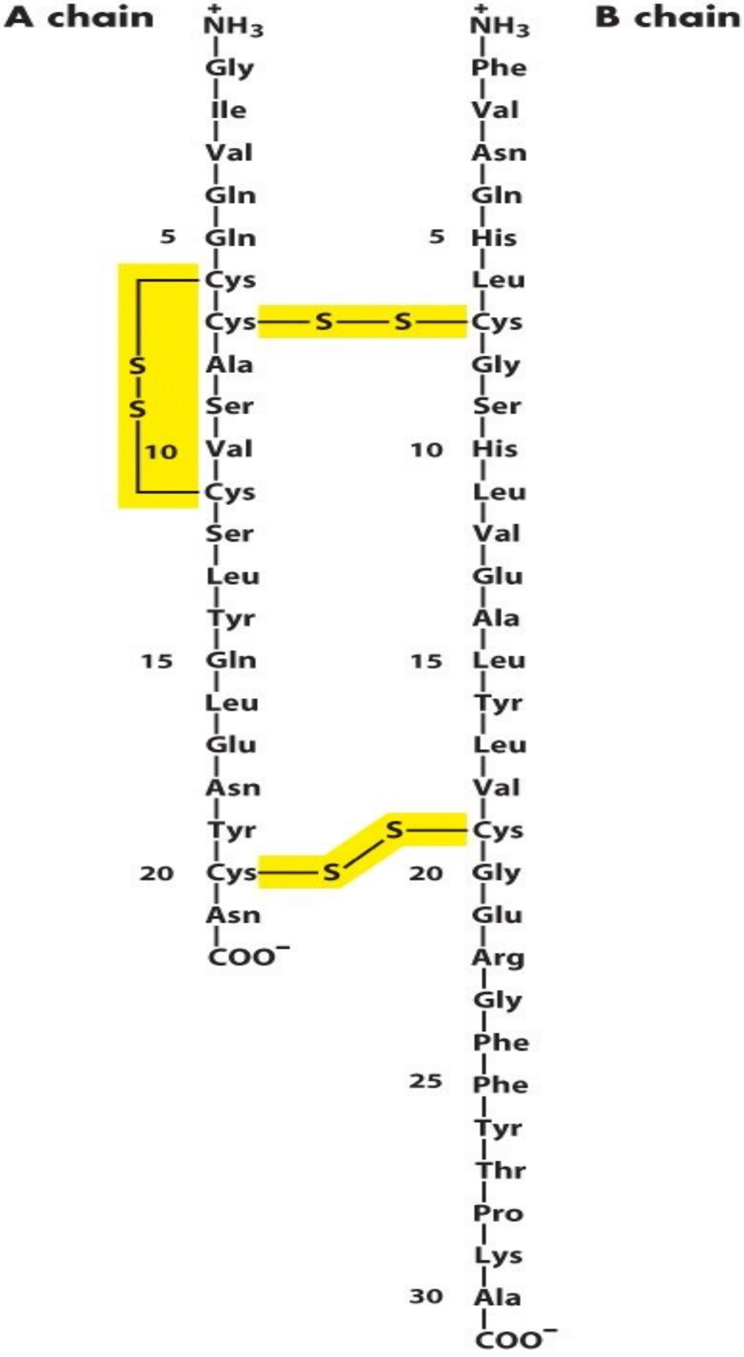


Oxytocin – contracts smooth muscle

(induces ‘labour’)

Vasopressin - diuretic

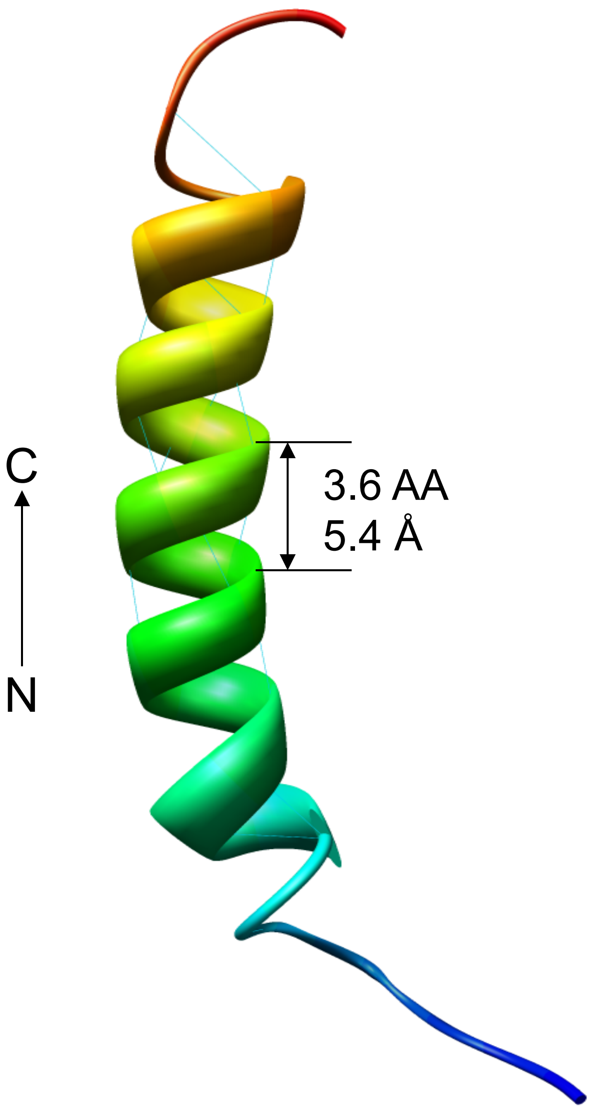
Insulin. Insulin has two peptide chains (the A chain has 21 amino acids and the B chain has 30 amino acids) held together by two disulfide linkages.



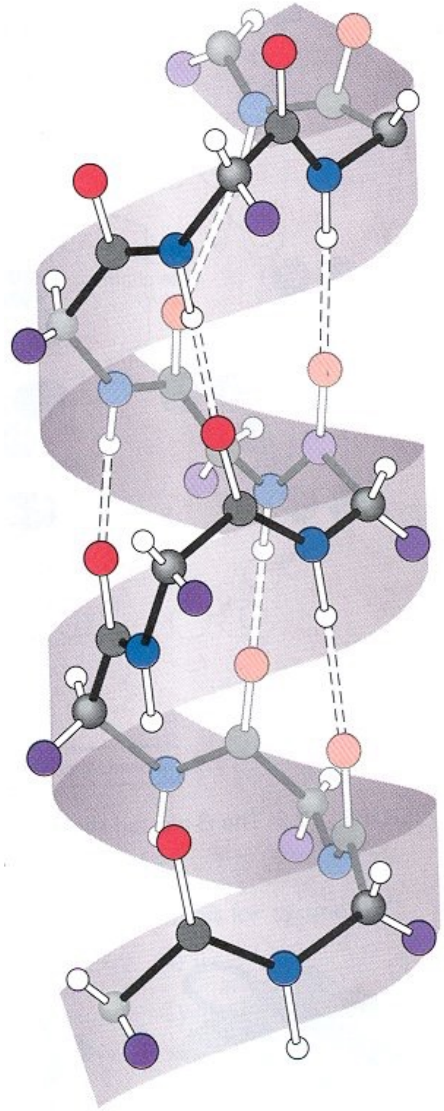
Secondary structure of Proteins

- Is the fixed arrangement of amino acids resulting from interactions between amide linkages that are close to each other in the protein chain
- Interactions can be hydrogen bonds (~ 5 kcal/mol each)
- Many H bonds are sufficient to define the shape

α-helix: 3.6 amino acids per coil, 5.4 Å



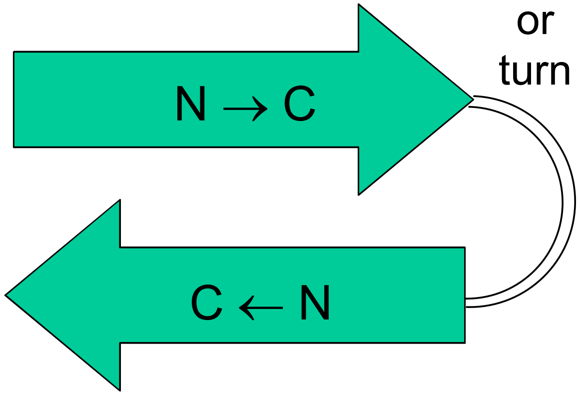
H-bonding - intramolecular



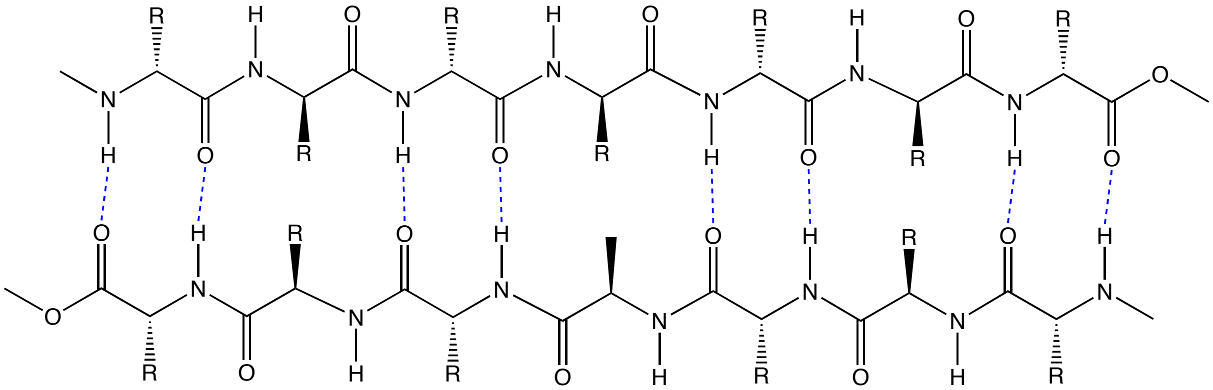
β-sheet:

Two or more extended peptide chain, in which the amide backbones are associated by hydrogen bonded

anti-parallel

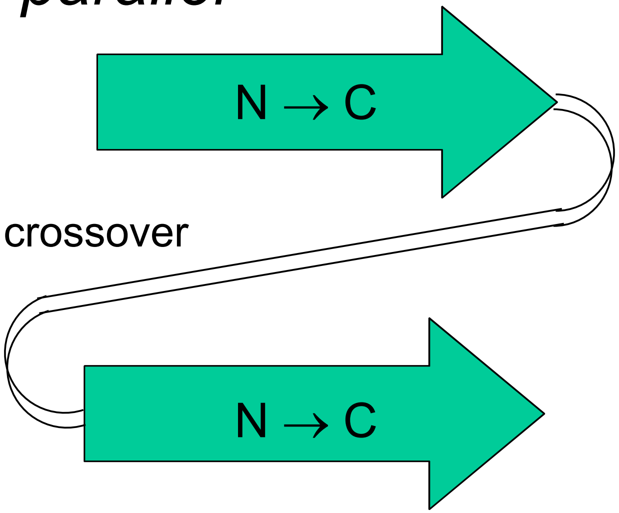


N → C

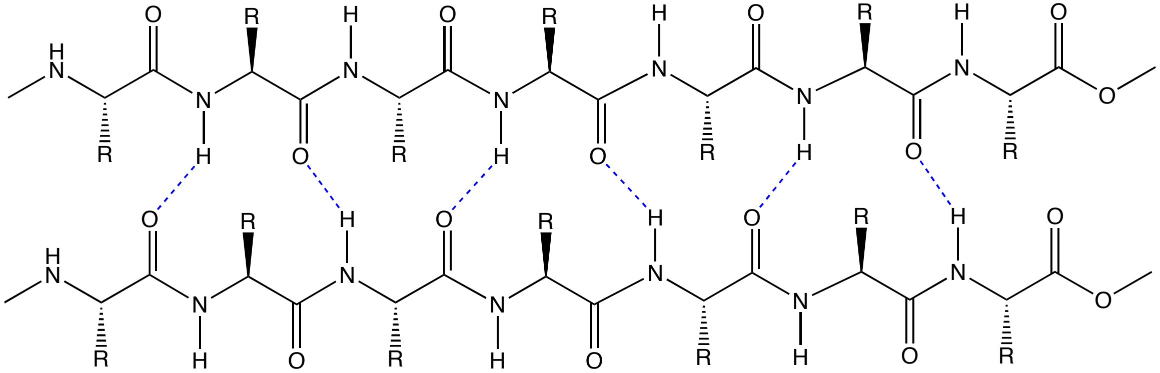


C ← N

parallel



N → C



N → C

TERTIARY STRUCTURE (3°)

- **Global 3-dimensional arrangement of ALL atoms in a protein**

Includes:

2° structural elements (alpha helices and beta sheets) Amino acid side chains

Prosthetic groups

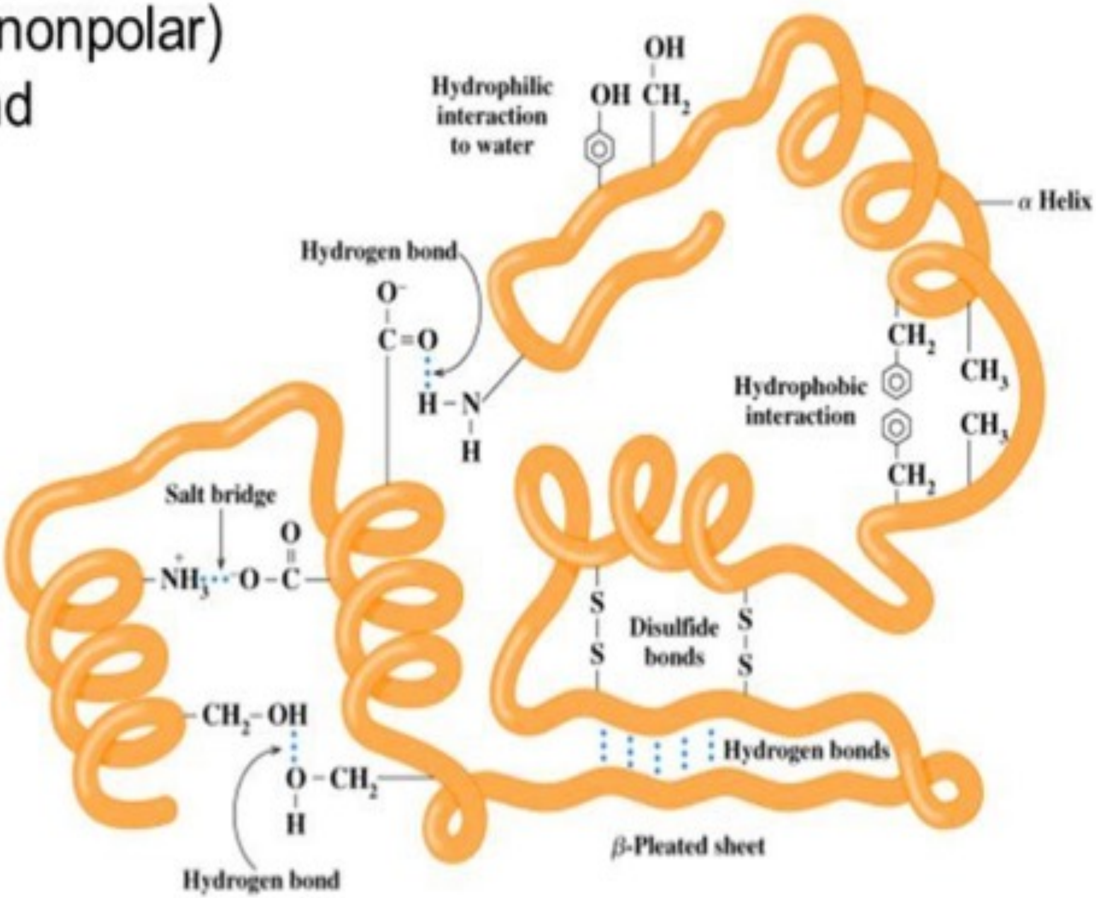
- **Small organic molecule or metal ion associated with a protein**

Regions of SECONDARY structure INTERACT to give a protein it TERTIARY structure

Major forces stabilizing tertiary structure are hydrophobic interactions among nonpolar side chains in the compact core of the proteins.

Tertiary Structure

(1) Disulfide (-S-S-)
(2) salt bridge (acid-base)
(3) Hydrophilic (polar)
(4) hydrophobic (nonpolar)
(5) Hydrogen bond

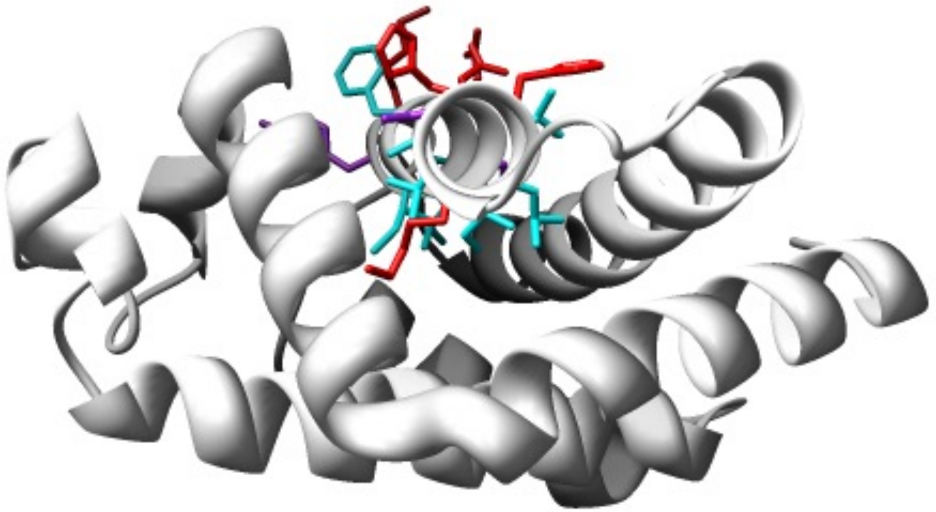


Tertiary Structure of polypeptides and Proteins.

Fibrous. Polypeptides strands that "bundle" to form elongated fibrous assemblies; insoluble.

***Globular*.** Proteins that fold into a "spherical" conformation.

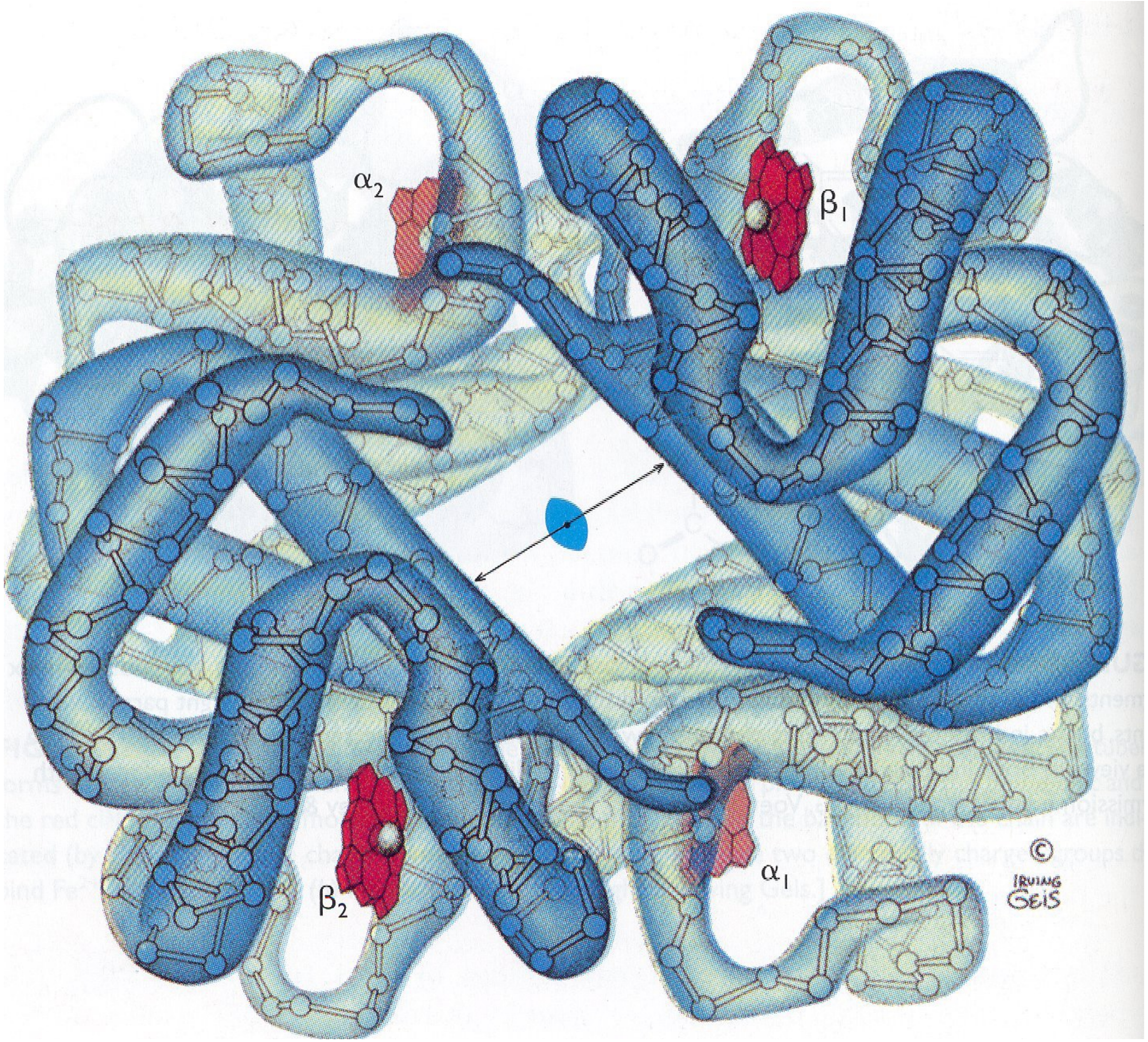
Hydrophobic effect. Proteins will fold so that *hydrophobic* amino acids are on the inside (shielded from water) and *hydrophilic* amino acids are on the outside (exposed to water)



Pro • Ile • Lys • Tyr • Leu • Glu • Phe • Ile • Ser • Asp • Ala • Ile • Ile • His •Val • His • Ser • Lys

Tertiary Structure (3^0) - braids & globs

collagen



hemoglobin

QUATERNARY STRUCTURE (4°)

Arrangement of multiple protein molecules into COMPLEXES

The three dimensional structure of a protein made of >1 polypeptide

Complexes of 2, 3, 4 etc... protein molecules are called dimers, trimers, tetramers...oligomers

- **Oligomers may be:**

Formed with identical protein monomers = HOMO OLIGOMER Formed with different protein monomers = HETERO OLIGOMERS Example: Hemoglobin:

2 alpha subunits

2 beta subunits

- **Protein subunits of oligomers interact through NON-COVALENT interactions**

Hemoglobin(H) and Myoglobin (M)

- H has 4 polypeptide chains : carries O_2, CO_2 and H^+ in the blood, and possesses quaternary structure
- M has a single chain of 153 amino acids: carries O_2 from the blood vessels to the muscles and stores it until needed.
- Both have Fe II containing heme unit in each chain that binds O_2.