Tertiary and Quaternary Structure of Proteins

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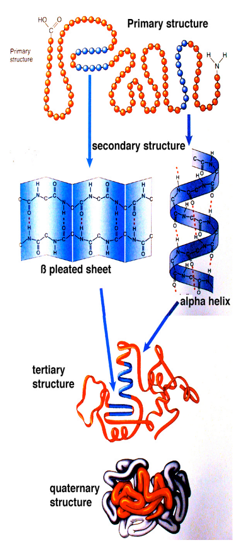
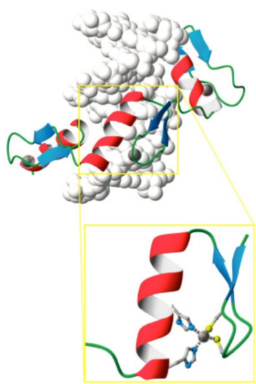
Protein structure



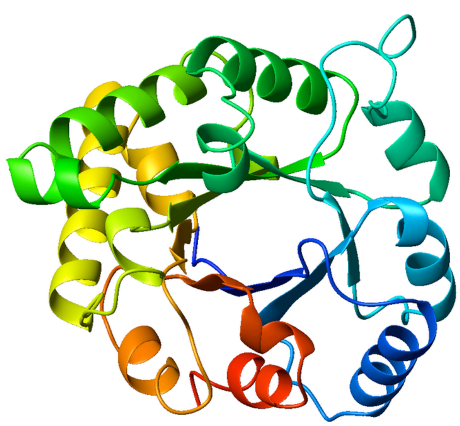
After secondary structure
we have super secondary structure or protein motifs.

From **Protein Structure and Function**
by Gregory A Petsko and Dagmar Ringe



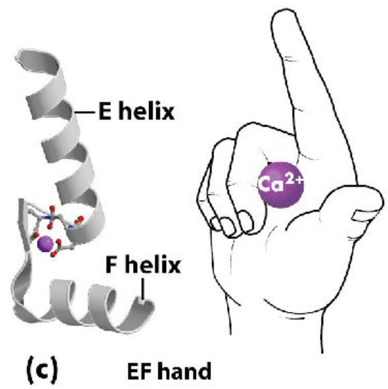
- Three Zinc finger proteins bound to DNA major grove.

Triose phosphate isomerase (TIM barrel) structure

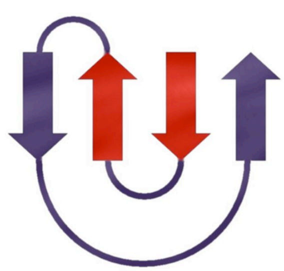


- Central 8 parallel β-barrel surrounded by a ring of 8 α - helical structures.

E-F hand
Calcium binding motif.

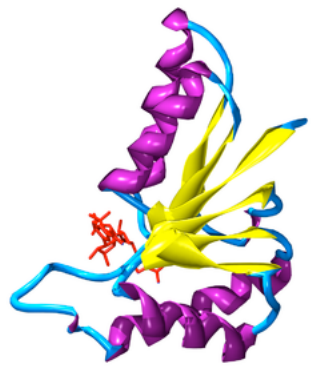


Greek Key Motif found in Cu, Zn superoxide dismutase



NAD binding fold in lactate dehydrogenase

- Red molecule is NAD that is bound to lactate dehydrogenase



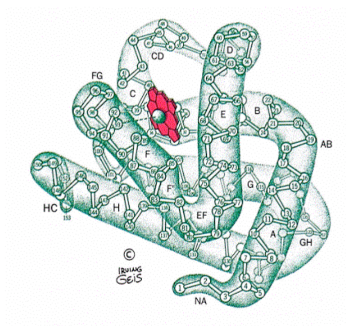
Tertiary structure

Tertiary structure deals with the spatial relationship of amino acids that are present far away from each other

- Gives a protein its biological activity.
- Proteins having entirely different amino acid sequence can still have the same tertiary structure. Example - myoglobin & hemoglobin.
- Proteins have very similar amino acid structure may have the same tertiary structure also.

Tertiary structure of myoglobin – α-helical protein

- 75% of the protein has α- helix.
- 8 α- helical segments.
- No apparent β- sheet structure
- Compact and globular
- Hydrophilic amino acids out side hydrophobic inside.



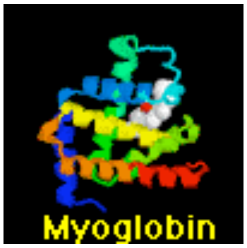
Tertiary Structure of RNAse – β-sheet protein

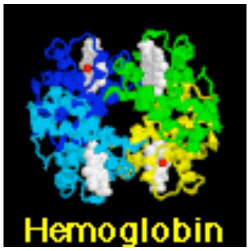
- RNAse is primarily made of β - sheet structure.
- Full of anti parallel β - sheet
- Very little α - helix (two small segments)
- Rest random coil structure.

Quaternary structure

- Few protein have more than one protein chains in them that are not usually connected.
- Example Hemoglobin. $\alpha_2\beta_2$− subunits can be easily dissociated.
- Quaternary structure usually ascribes regulatory properties to a protein.

Myoglobin and hemoglobin





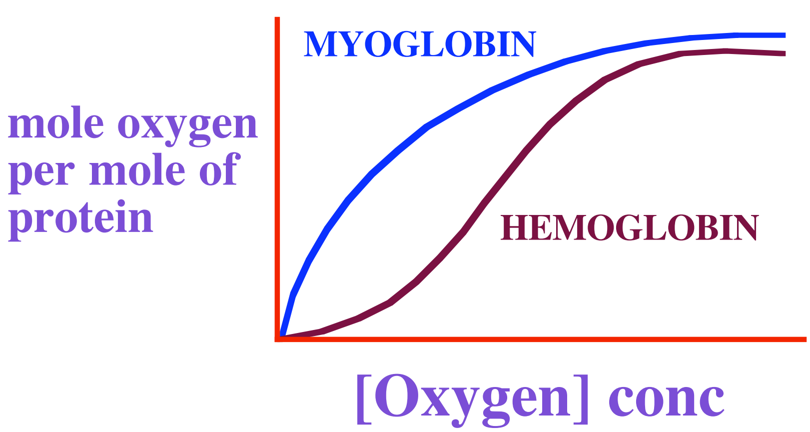
Monomer
M.wt 17,000 kDa
Single polypeptide
No subunit structure

Tetramer
M.Wt 64,000 kDa
Four polypeptide
Two kinds of subunit ($\alpha_2\beta_2$)

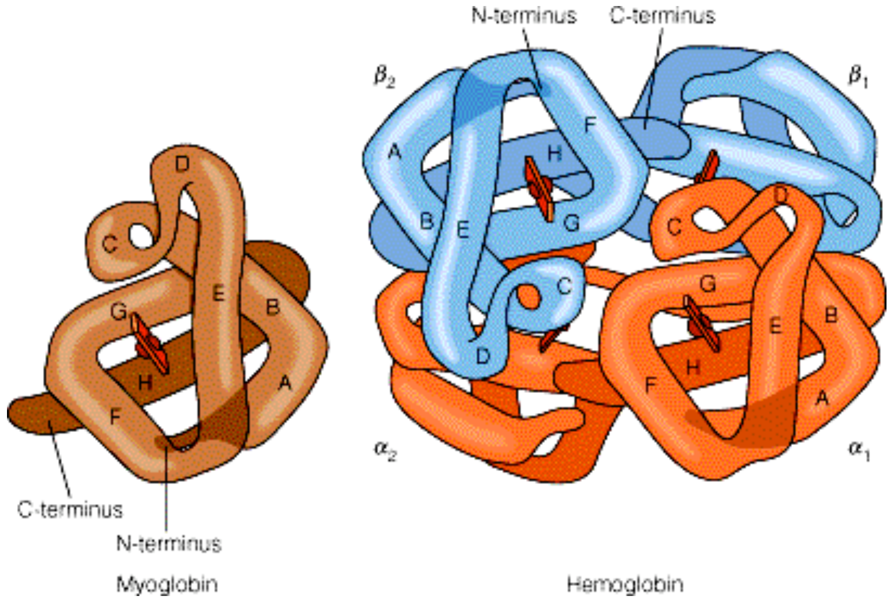
Quaternary Structure of Proteins

- Not all proteins have quaternary structure.
- Protein with quaternary structures have more than one subunit.
- Quaternary structure is usually associated with regulation of enzyme activity.

MYOGLOBIN - MICHAELIS-MENTEN KINETICS.
HEMOGLOBIN - SIGMOIDAL KINETICS



Structure of myoglobin and hemoglobin

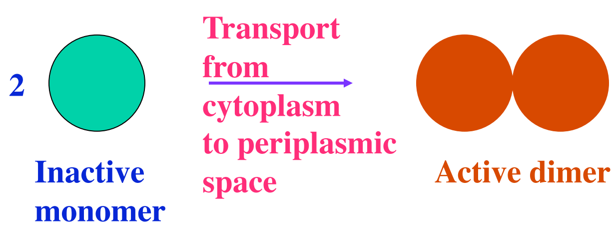


Differences between myoglobin and hemoglobin

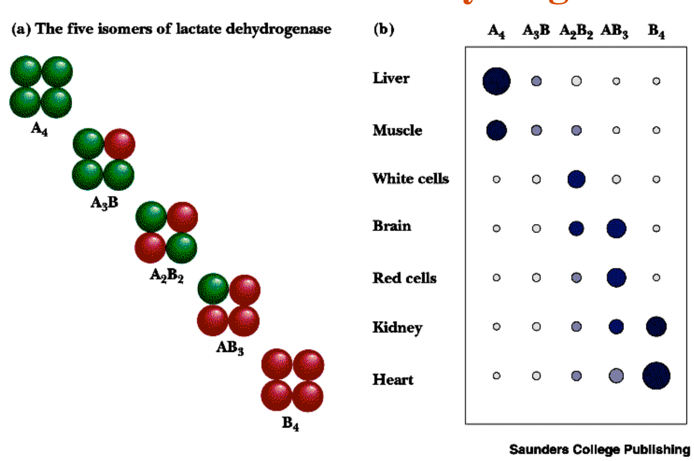
Myoglobin	Hemoglobin
• Storage protein	• Transport protein
• Monomeric in nature.	• Tetrameric in nature
• No subunit structure	• Two kind of subunits, $\alpha_2\beta_2$.
• M.M. Kinetics.	• Sigmoidal kinetics.
• pH has no drastic effect.	• pH inhibits O_2 binding.
• CO_2 - No effect.	• CO_2 inhibits O_2 binding.
• Diphosphoglycerate - No effect	• Diphosphoglycerate inhibits O_2 binding.
• Only one form.	• Exists in two forms
• NO has no effect	• Nitric oxide binding

Alkaline Phosphatase of *E.coli*

- Alkaline phosphatase of *E.coli* is synthesized as an inactive monomer in the cytoplasm.
- During phosphate starving conditions, the active form of the enzyme is assembled as a dimer in the periplasmic space.
- The active dimer cleaves any available organic phosphates in the medium providing the vital inorganic phosphate for the organism.



Isozymes - the case of lactate dehydrogenase



Enzymes can be regulated by the alteration in their quaternary structures. Arrangement of polypeptide subunits of an enzyme differently, each of which giving raise to different level of activity can lead to active enzyme with differential catalytic potential. The arrangement can be also be controlled by the level of expression of each subunit. These are called isozymes

References

- L. Jia, C. Bonaventura, J. Bonaventura and J. S. Stamler. S-nitroso hemoglobin: a dynamic activity of blood involved in vascular control. Nature. 380, 221-226 (1996).
- Jane. S. Richardson. Introduction: Protein motifs. The FASEB Journal 8, 1237- 1239 (1994).