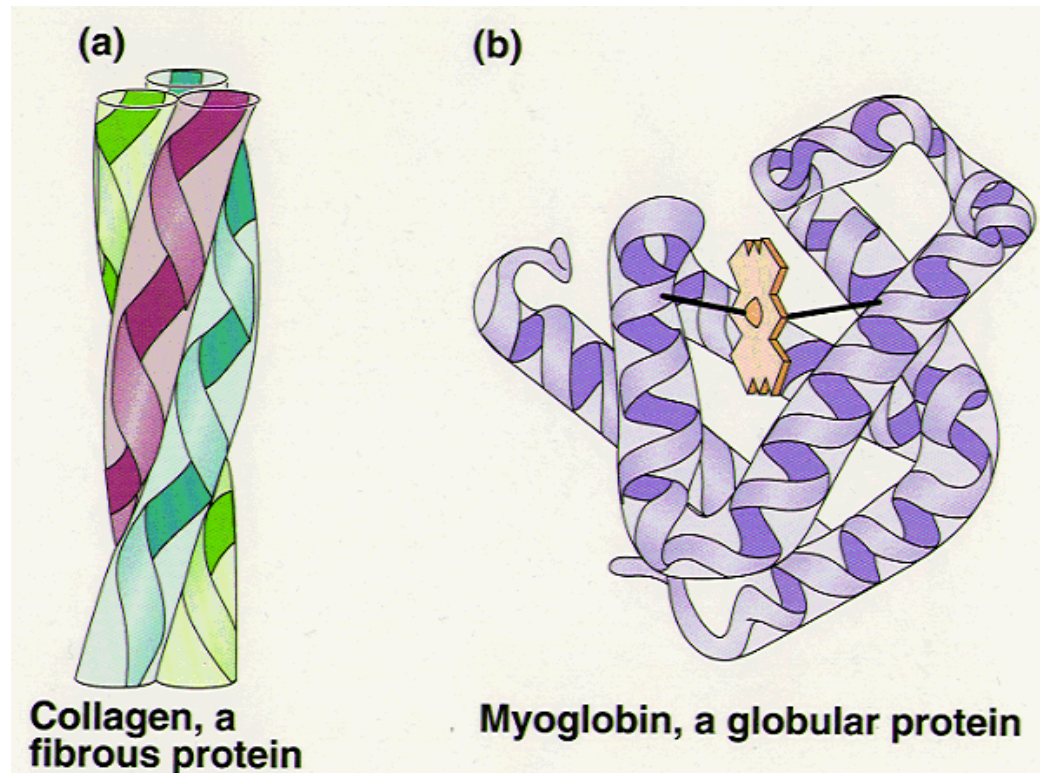


Types of proteins

- Proteins can be divided into two groups according to structure:
 - Fibrous (fiber-like with a uniform secondary-structure only)
 - Globular (globe-like with three-dimensional compact structures)

Examples

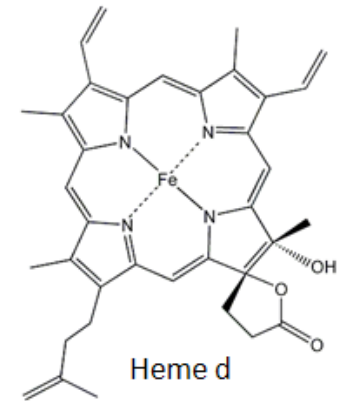
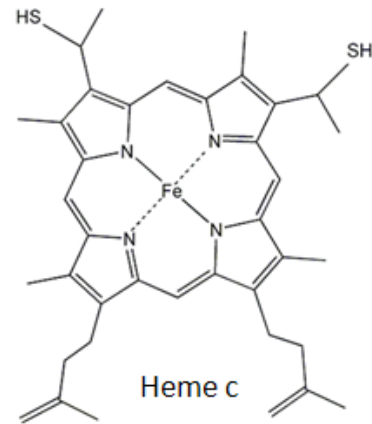
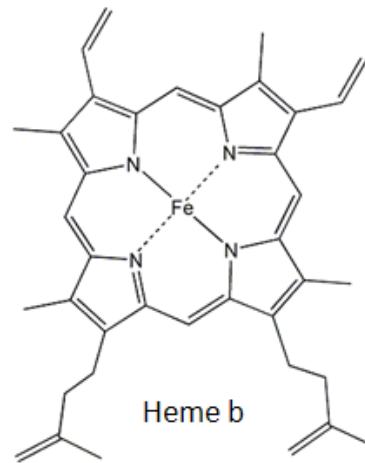
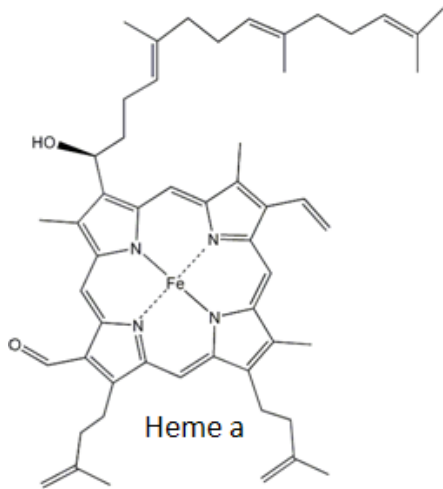
- Fibrous proteins: collagens, elastins, & keratins
- Globular proteins: myoglobin, hemoglobin, & immunoglobulin



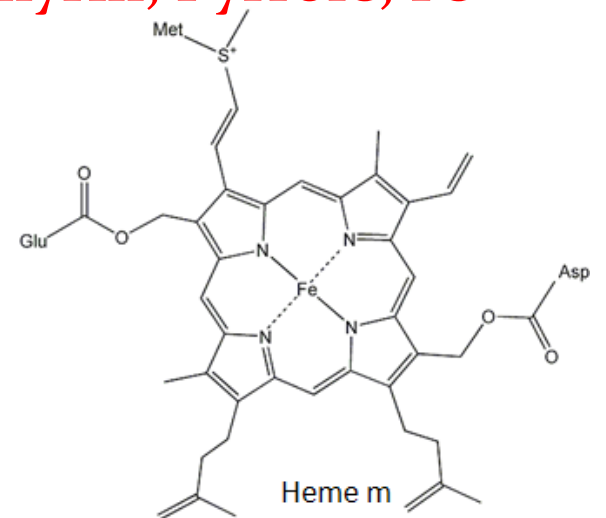
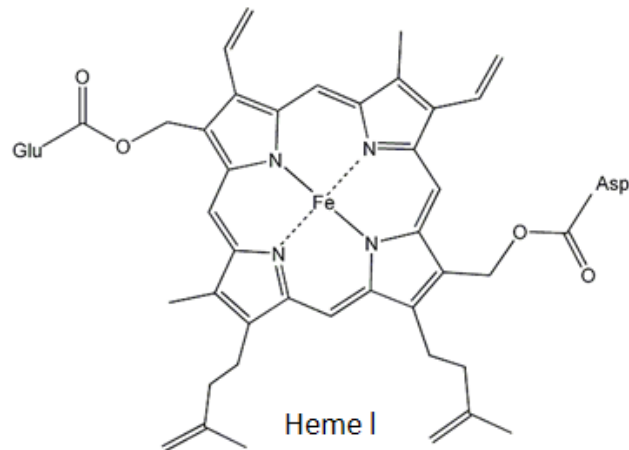
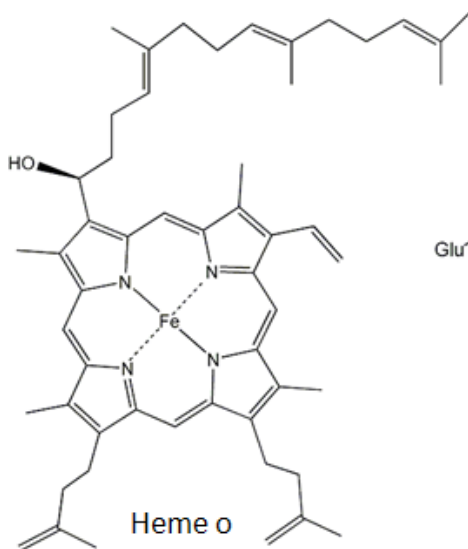
Myoglobin
Hemoglobin

Globular Proteins

The heme

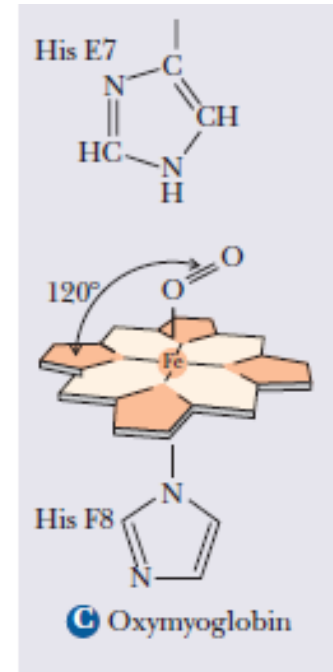
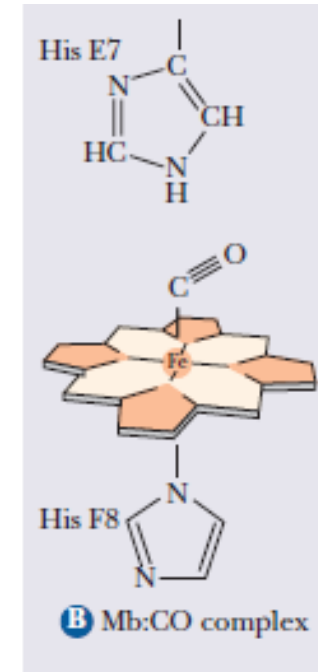
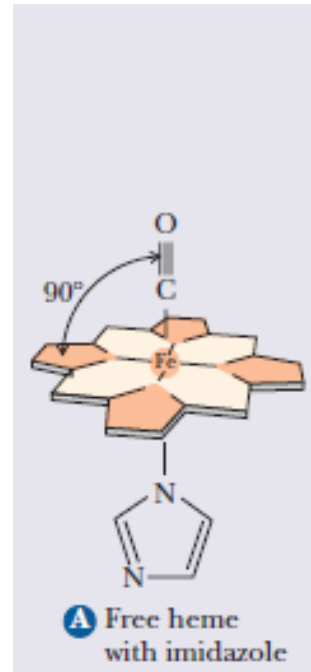
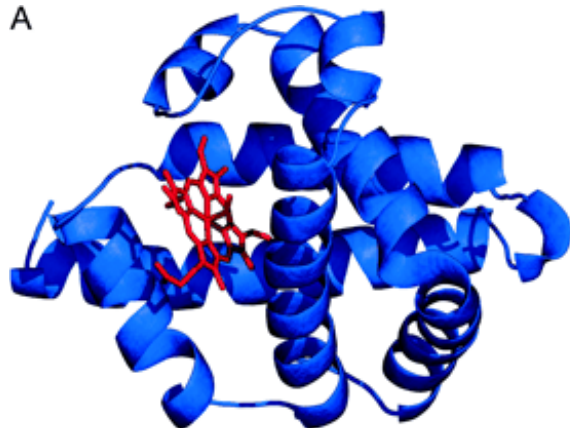
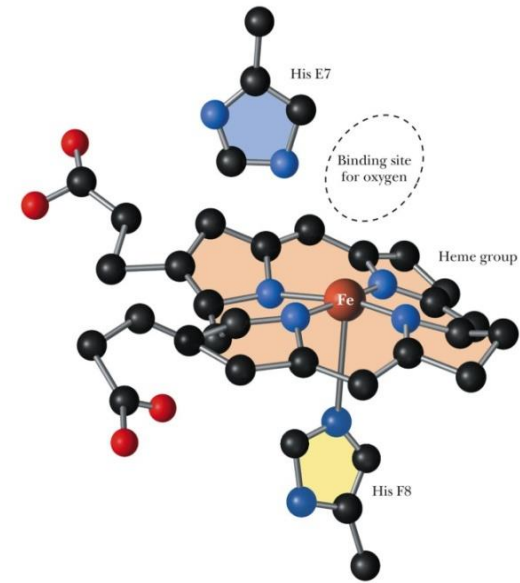


Prosthetic, Flat, Porphyrin, Pyrrole, Fe



Myoglobin

- The first to be determined structurally
- A single polypeptide chain (153 a.a)
- A single heme in a hydrophobic pocket
- 8 α -helices (A-H); no β -sheets
- Most polar (exterior), Nonpolar (interior). Two His residues: E7 (distal), F8 (proximal)
- Oxy vs. deoxymyoglobin
- Fe(II) coordination (redox)

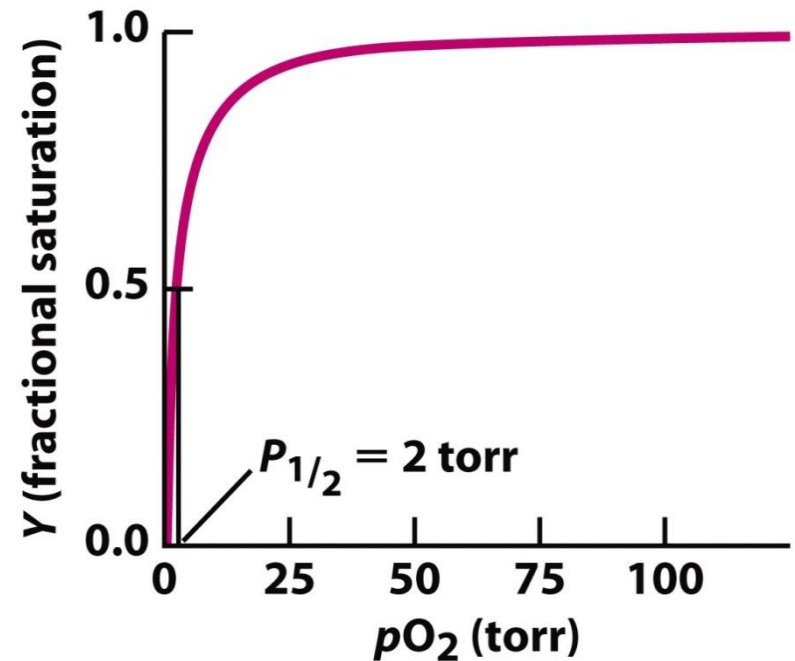


Structure-function relationship

- The heme fits into a hydrophobic pocket & myoglobin-heme interaction is stabilized by hydrophobic interactions
- The heme group stabilizes its' tertiary structure
- The distal histidine acts as a gate that opens and closes as O₂ enters the hydrophobic pocket
- The hydrophobic interior of myoglobin (or hemoglobin) prevents the oxidation of iron

Oxygen binding to myoglobin

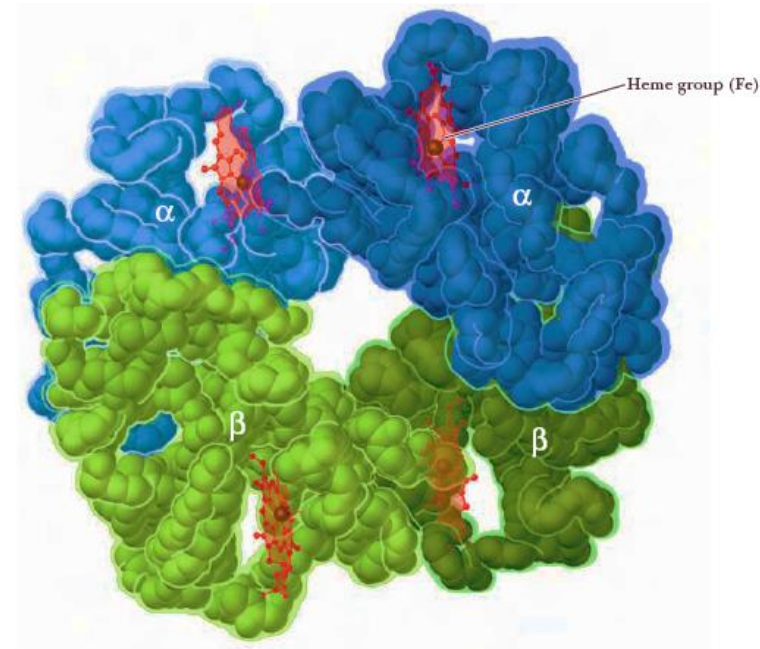
- High affinity
- The P_{50} : ~2 torrs or mm Hg
- Tissues O_2 pressure: ~20 mm Hg (saturation)



The binding of O_2 to myoglobin follows a hyperbolic saturation curve

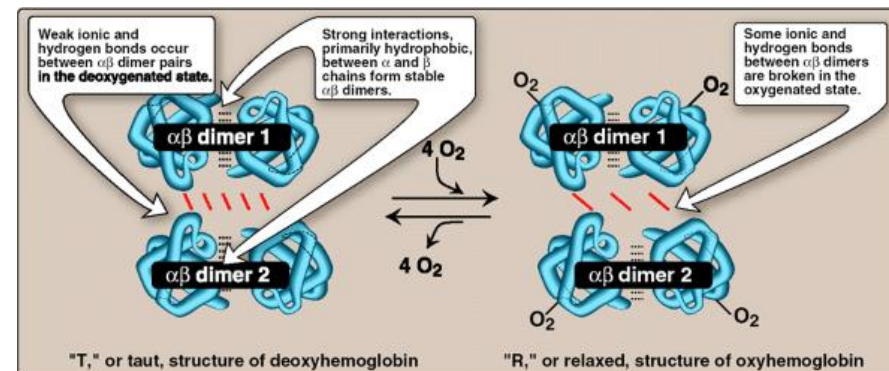
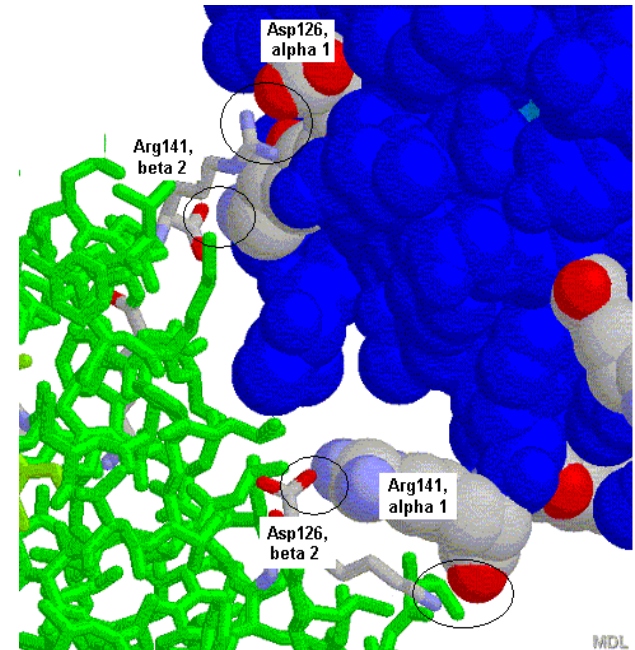
Hemoglobin

- A tetramer $\alpha_2\beta_2$:
 - α -chains (141 a.a) - 7 α -helices
 - β -chains (146 a.a) - 8 α -helices
- 1 heme group in each (4O_2)
- Myoglobin (storage) vs. hemoglobin (transport): positive cooperativity & saturation percentage
- lungs (100 torr), capillaries (20 torr)



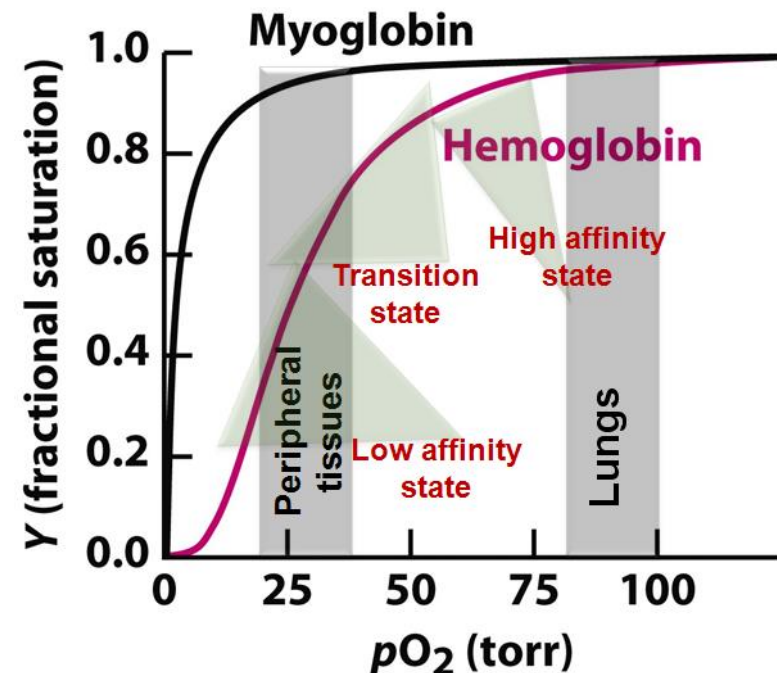
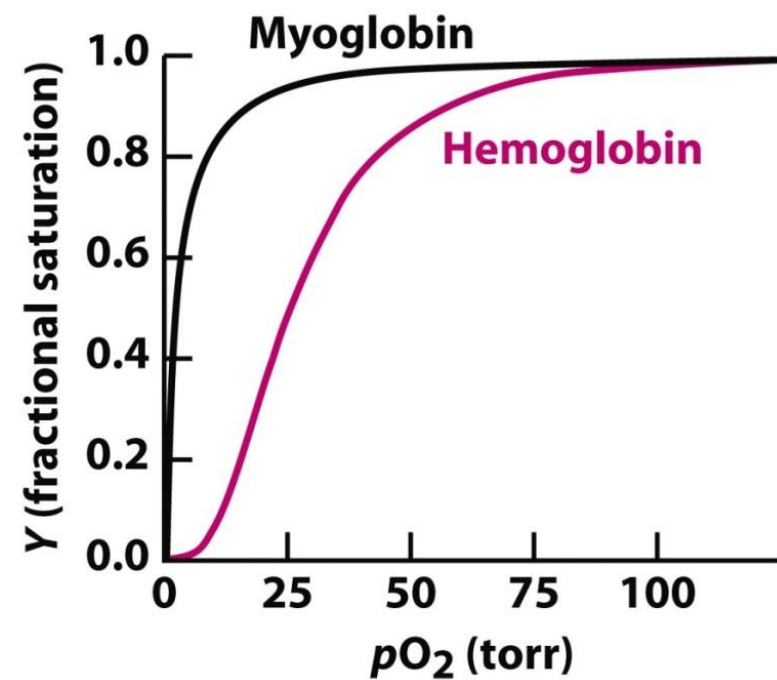
Chain interaction

- The chains interact with each other via hydrophobic interactions
 - Therefore, hydrophobic amino acids are not only present in the interior of the protein chains, but also on the surface
- Electrostatic interactions (salt bridges) and hydrogen bonds also exist between the two different chains



The saturation curve

- The saturation curve of hemoglobin binding to O_2 has a sigmoidal shape
- At 100 mm Hg, hemoglobin is 95-98% saturated (oxyhemoglobin)
- As the oxygen pressure falls, oxygen is released to the cells
- In contrast to a low p_{50} for myoglobin, the p_{50} of hemoglobin is approximately 26 mm

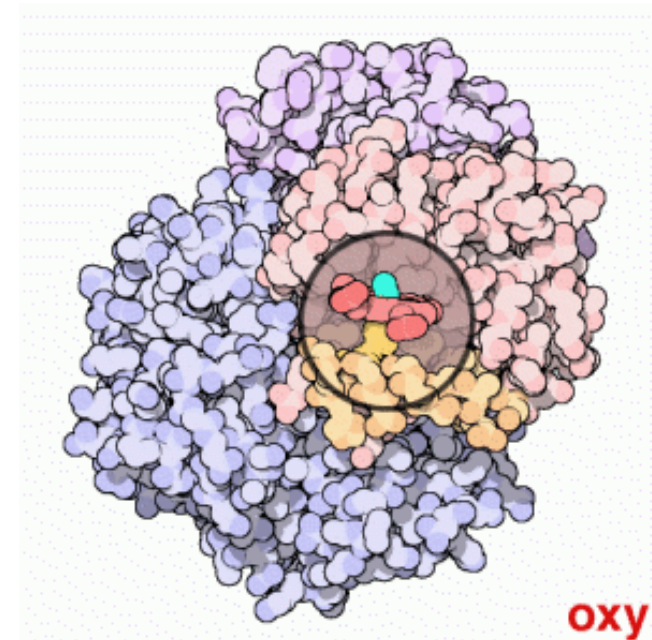
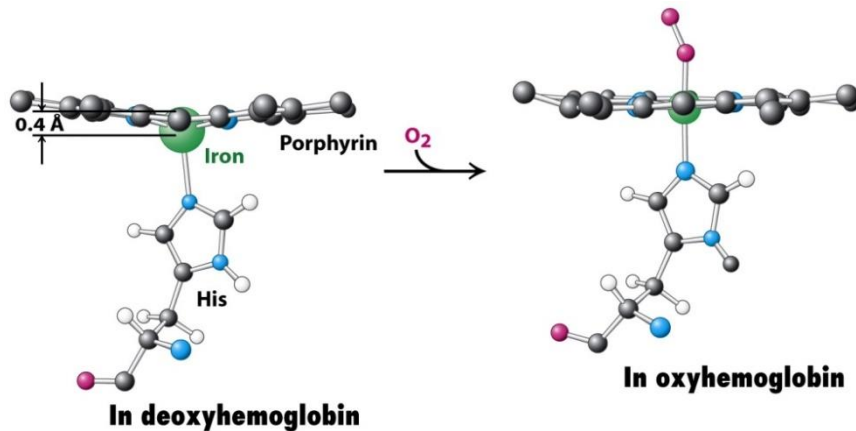


Hemoglobin is allosteric – Myoglobin not

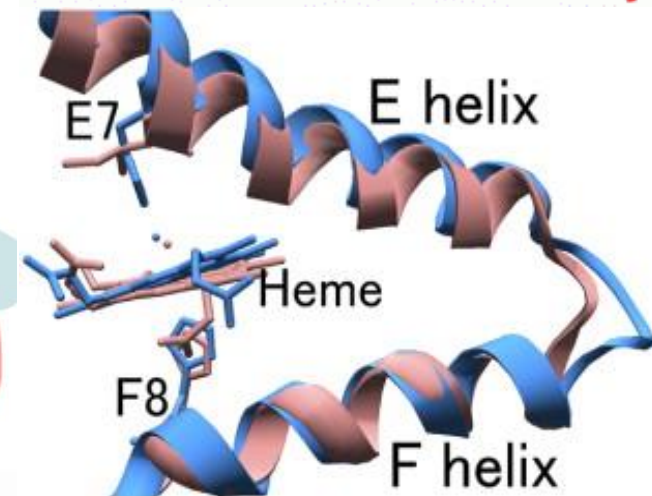
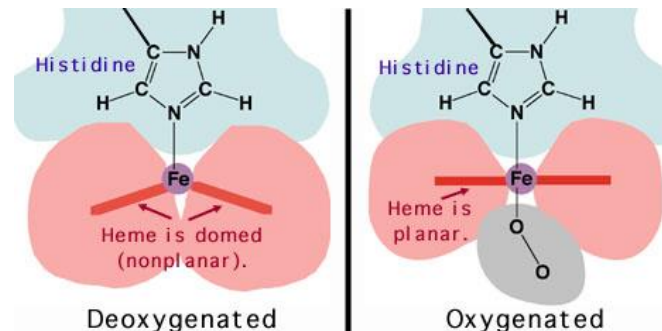
- Hemoglobin is an allosteric protein (from Greek "allos" = "other", and "stereos" = "shape").
 - An allosteric protein: a protein where binding of a molecule (ligand) to one part of the protein affects binding of a similar or a different ligand to another part of the protein
- Hemoglobin exists in two forms (myoglobin only 1 state):
 - T-state: "taut" or "tense"; low-binding affinity to oxygen
 - R-state: "relaxed"; 500 times higher affinity to oxygen
- Binding of O₂ causes conformational changes in hemoglobin, converting it from the low affinity T-state to the high affinity R-state

How does the structure change? (1)

- Dome (deoxy) – Fe out of the plane
- Planar (Oxy) – Fe into the plane → pulling proximal His (F8)

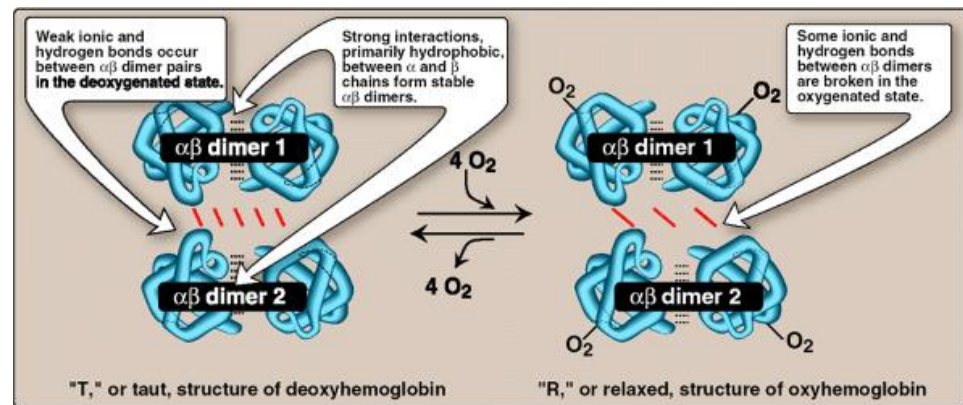
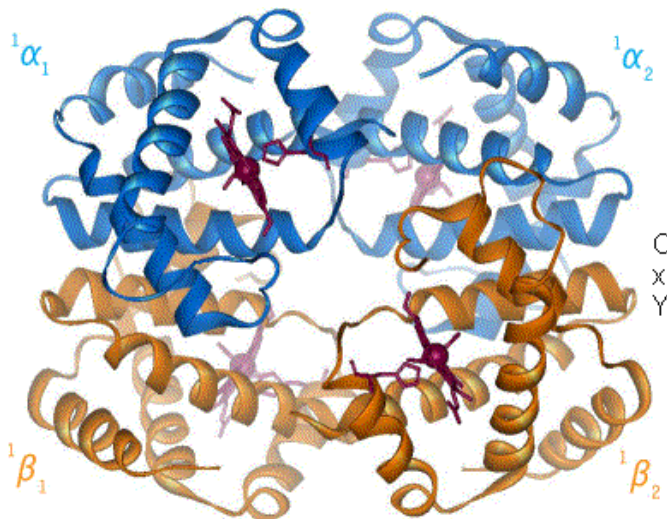


Myoglobin:
movement of the
helix doesn't affect
the function



How does the structure change? (2)

- This movement triggers
 - Changes in tertiary structure of individual hemoglobin subunits and
 - Breakage of the electrostatic bonds at the other oxygen-free hemoglobin chains



The saturation curve is sigmoidal because...

- Conformational changes lead to cooperativity among binding sites
- Binding of the first O_2 breaks some salt bridges with the other chains increasing the affinity of the binding of a second molecule
- & so on

