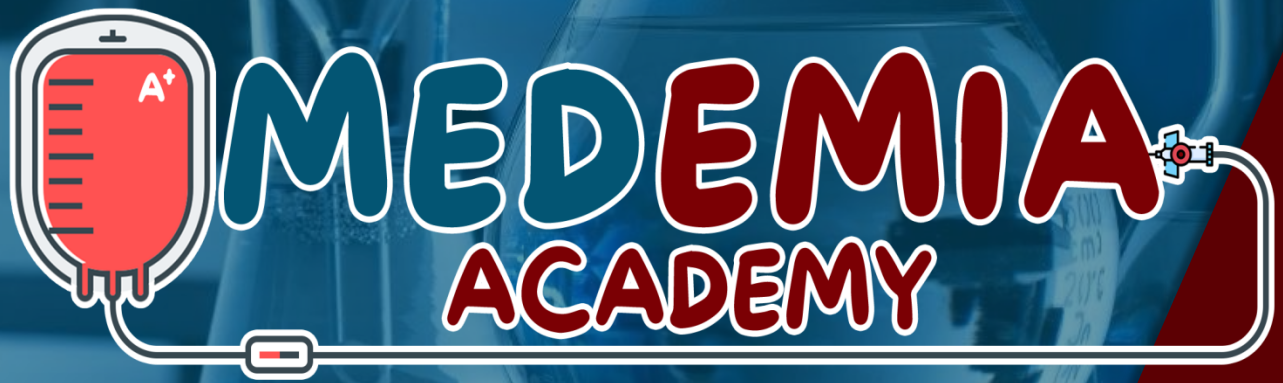
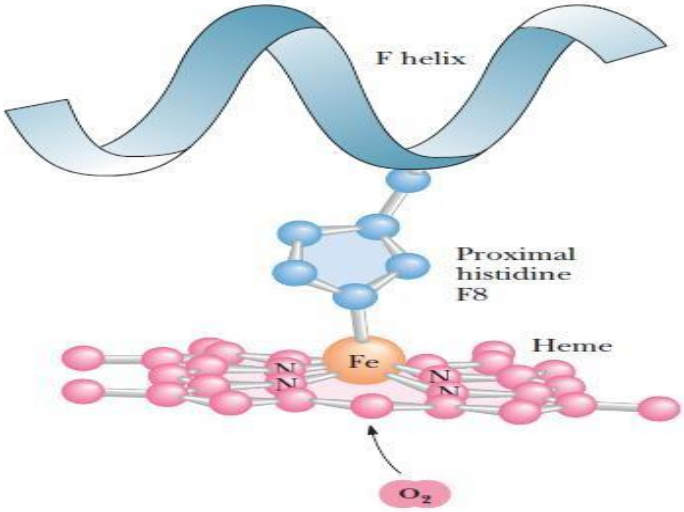
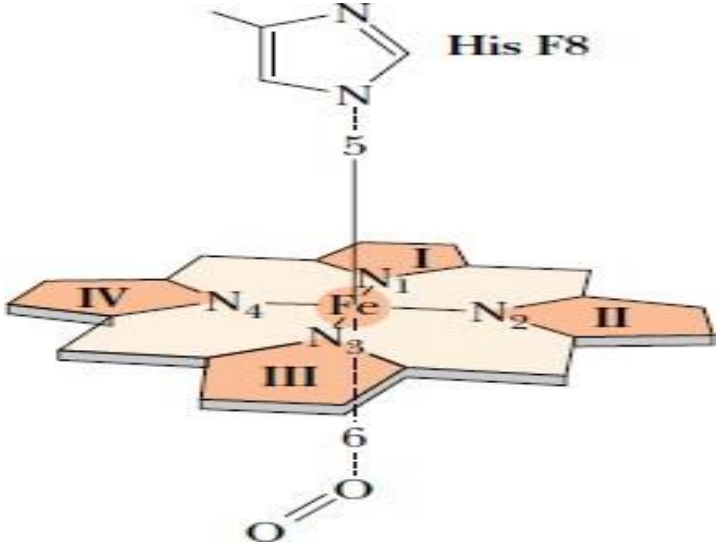
Oxygen Binding & O2 – Hgb dissociation Curve



Oxygen Binding

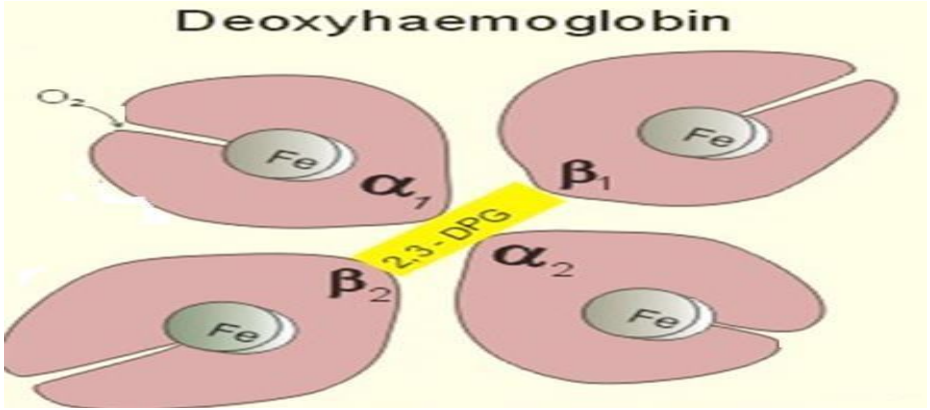
❖Oxygen is accessible only to the heme groups of the α-chains when hemoglobin is in T state.





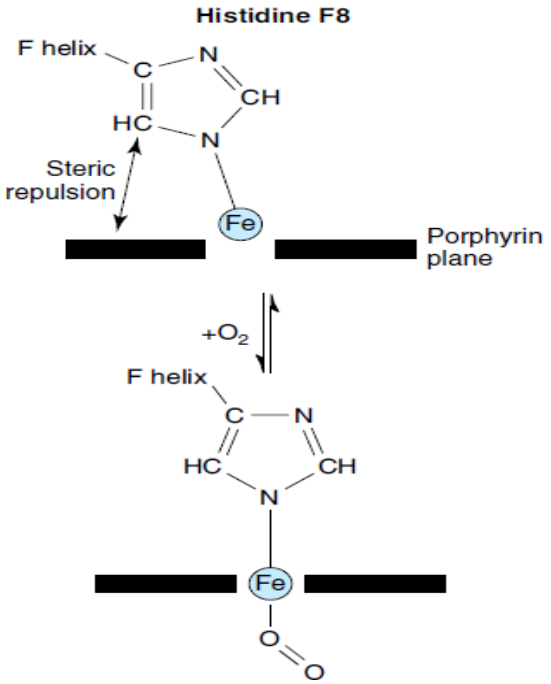
Cooperativity of O_2 Binding in Hemoglobin

- In the T state, the heme groups of the α-chains are accessible to O_2, while those of the β-chains are not due to steric hindrance from nearby amino acid residues
  - The binding of the first O_2 molecule is slow and depends on the conformational shift from T to R, which is initiated when O_2 binds to the α-chain heme groups



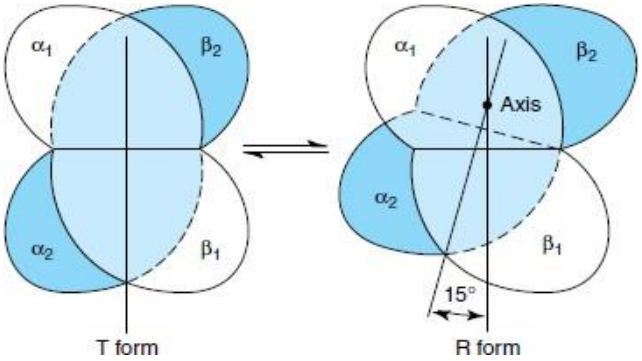
Cooperativity of O_2 Binding in Hemoglobin

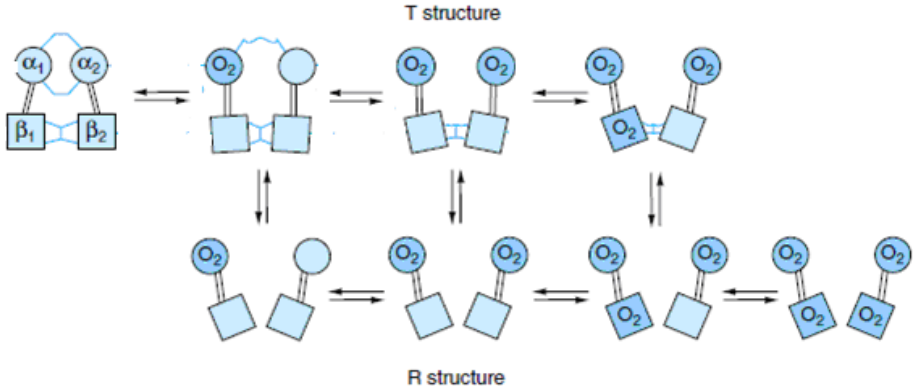
- **Binding** alters the electronic state of the heme, causing the iron (Fe^{2+}) to move into the plane of the porphyrin ring.
  - This movement pulls the proximal histidine closer to the ring, which then induces a shift in the adjacent α/β subunits.



Cooperativity of O2 Binding in Hemoglobin

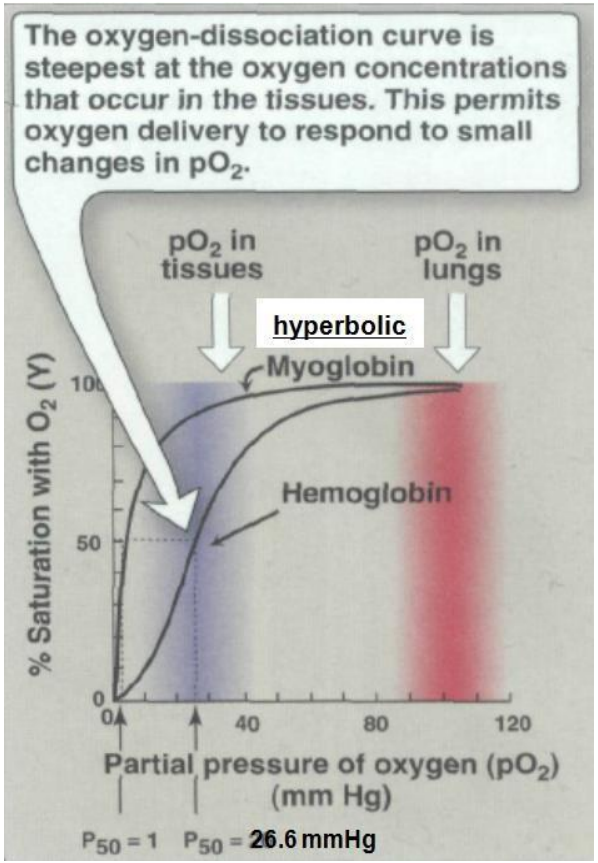
- Specifically, one pair of subunits rotates by about 15 degrees, **breaking salt bridges and promoting the T to R transition across all subunits**
- This conformational change significantly increases the affinity of the remaining unoxygenated hemes for O_2 . This binding of O2 to hemoglobin is known as **Cooperativity of O2 Binding** in Hemoglobin and is responsible for the sigmoidal oxygen saturation curve of hemoglobin





Oxygen dissociation curve

- **Definition**: Describes the relation between the partial pressure of oxygen (x axis) and the oxygen saturation (y axis)
  - The oxygen saturation is the ratio of the amount of oxygen bound to the hemoglobin
  - Hemoglobin's affinity for oxygen increases as more molecules of oxygen bind
  - The curve has a sigmoidal or S-shape
  - The curve for myoglobin has a hyperbolic shape



Oxygen dissociation curve

pO2 (mmHg)	% saturation of Hb	pO2 (mmHg)	% saturation of Hb
100 in alveoli	**98%**	**20** in working muscle	**20%**
40 in resting muscle	**75%** thus it deliver **23%** of its O_2 to resting muscle and leaving the rest of the oxygen in the blood as a reserve and to maintain life for four to five minutes if breathing is interrupted.	**10** in vigorous exercising muscle	**10%**

Agents that affect oxygen binding

- The 2,3-bisphosphoglycerate (**2,3-BPG** or 2,3-DPG)
  - High levels of 2,3-DPG **shift the curve to the right**
  - The binding of 2,3-BPG to Hb promotes the release of O2
    - The presence of 2,3-BPG significantly reduces the affinity of hemoglobin for oxygen
    - The concentration of 2,3-BPG in the red blood cell increases in response to chronic hypoxia seen in :

    1. COPD 2. High altitudes 3. Chronic Anemia

Reduced Hb-O2 affinity: shift the curve to right

Increase Hb-O2 affinity: shift the curve to the left

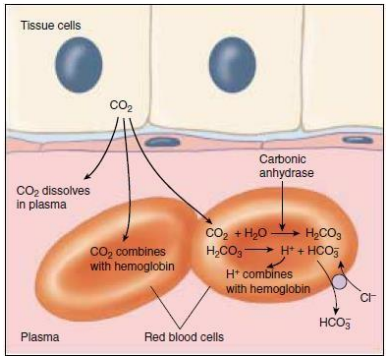
Agents that affect oxygen binding

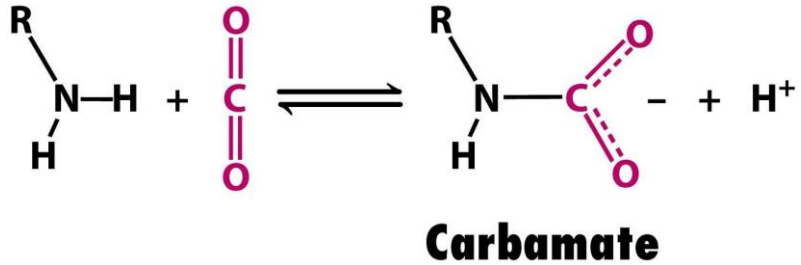
❖**Binding of CO2**, in two ways :

1. Formation of carbamino- hemoglobin
   - 20% of CO2 is carried as carbamino- hemoglobin bound to the uncharged α-amino groups of hemoglobin

Hb-NH2 + CO2 ↔ Hb-NH-COO- + H+

   - The binding of CO2 stabilizes the T (taut) or deoxyhemoglobin, resulting in a decrease in its affinity for oxygen

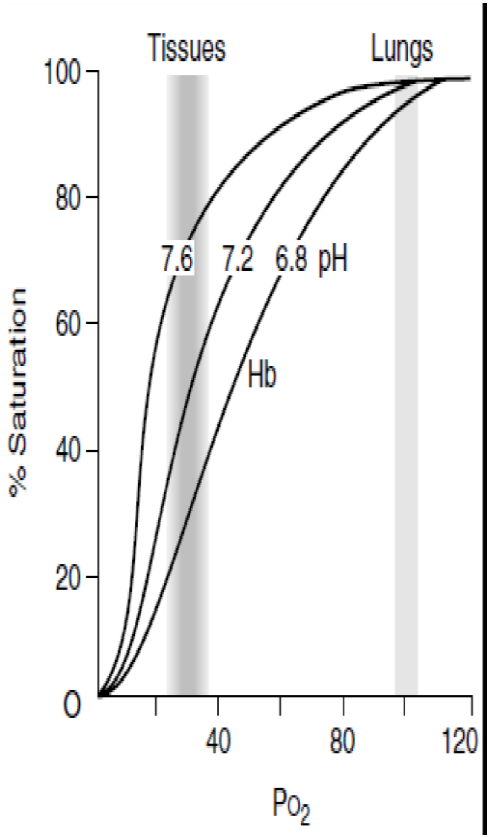




Unnumbered figure pg 194
Biochemistry, Sixth Edition

Agents that affect oxygen binding

- Binding of CO_2 , in two ways :
  2. B- Bohr effect
     - The binding of protons by hemoglobin lowers its affinity for oxygen therefore, a shift to the right in the oxygen dissociation curve.
     - The pH of the blood decreases as it enters the tissues because of CO_2 produced by metabolism
     - in tissues in which the pH of the blood is low because of the CO_2 produced by metabolism, oxygen is released from hemoglobin.



Agents that affect oxygen binding

❖Temperature

- An increase in temperature shifts the curve to the right
  - Increasing the temperature denatures the bond between oxygen and haemoglobin
  - This has physiological importance during exercise since the temperature of muscle tissue is higher than 37°C, and oxygen can be unloaded from Hb more easily at the higher temperature

The relationship of hydrogen ions is inversely proportionate with levels of 2,3 BPG