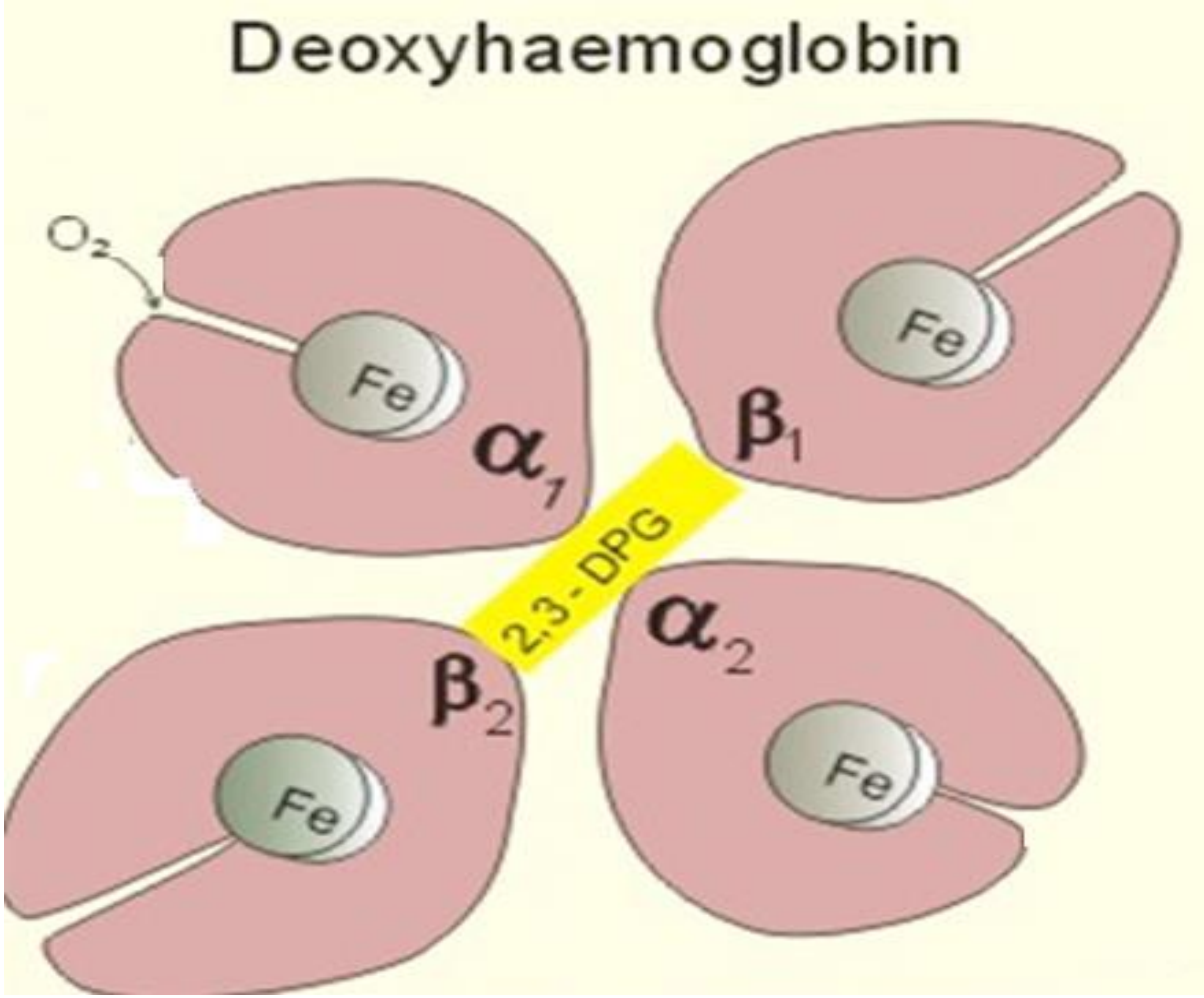
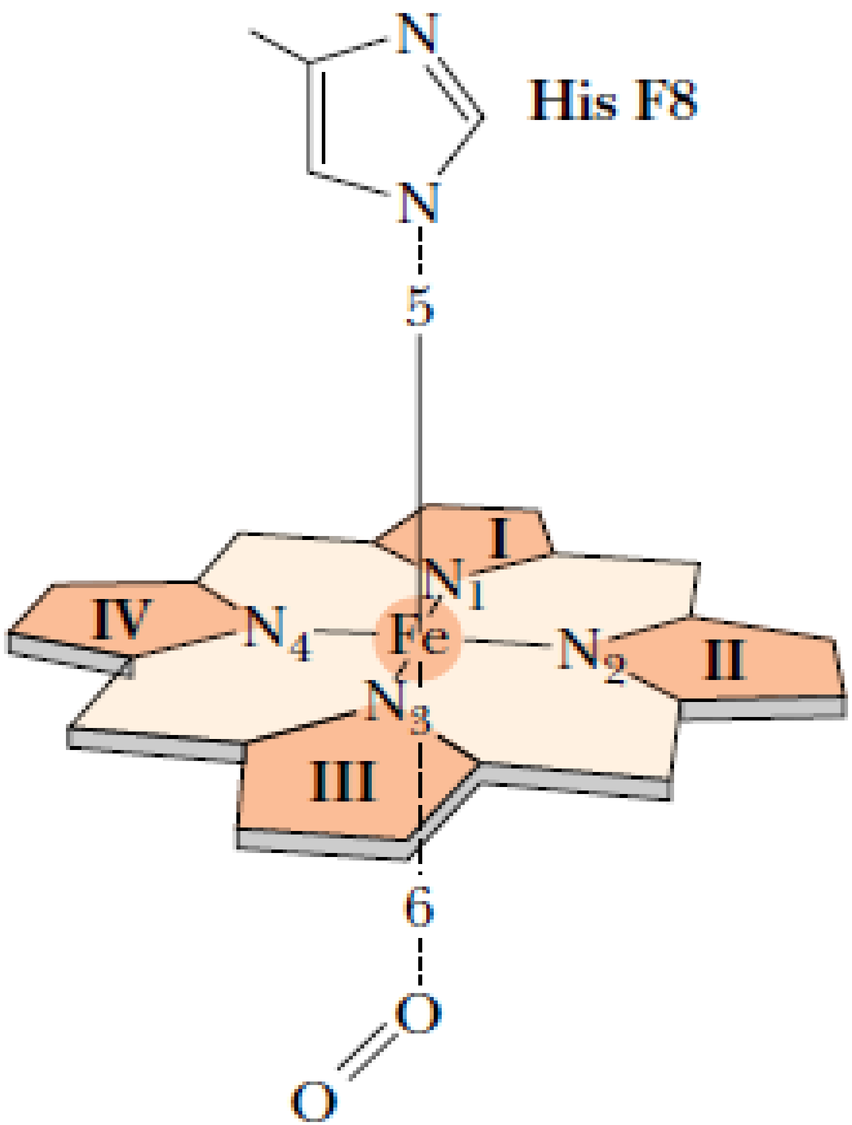
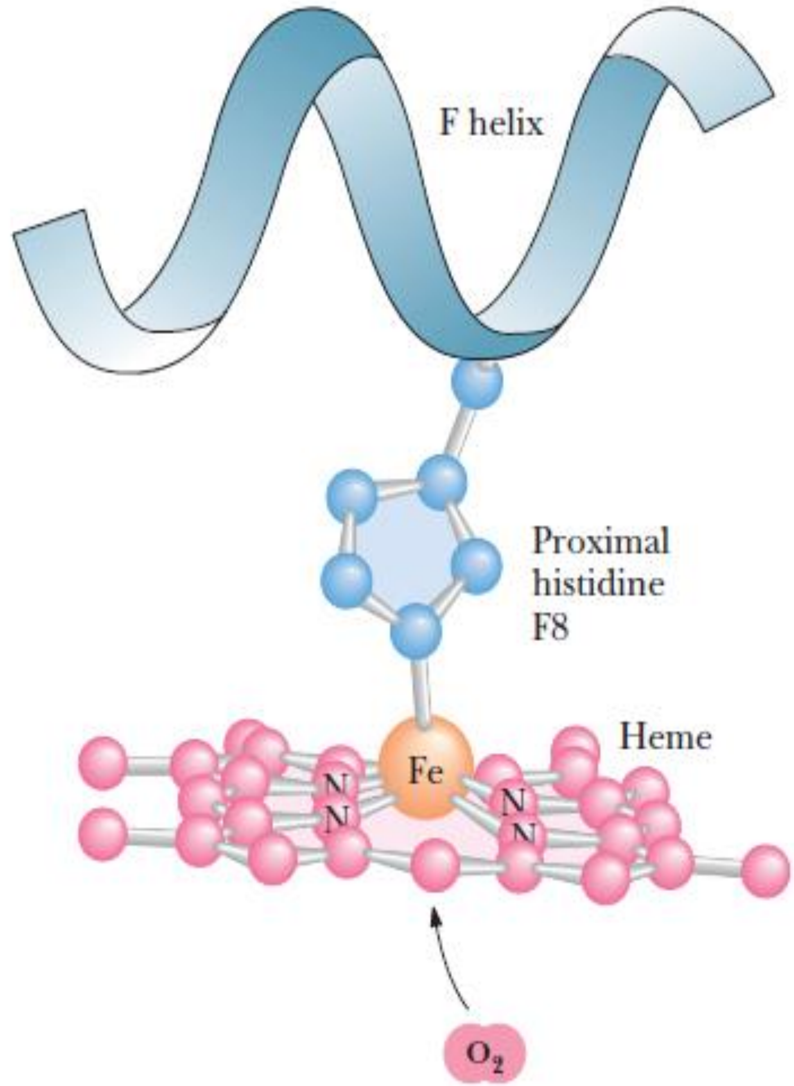
# Oxygen binding to Mb & Hb & Hb-$O_2$ dissociation curve



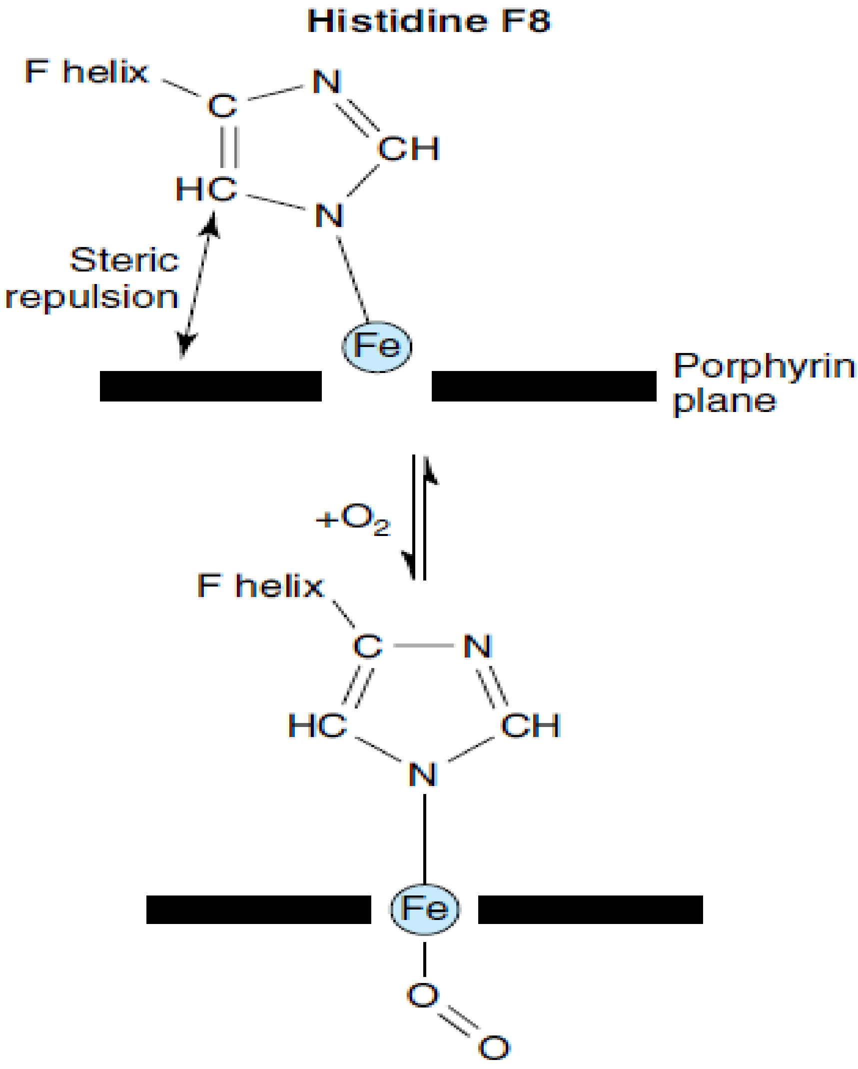

**Oxygen is accessible only to the heme groups of the α-chains when hemoglobin is in T state.**

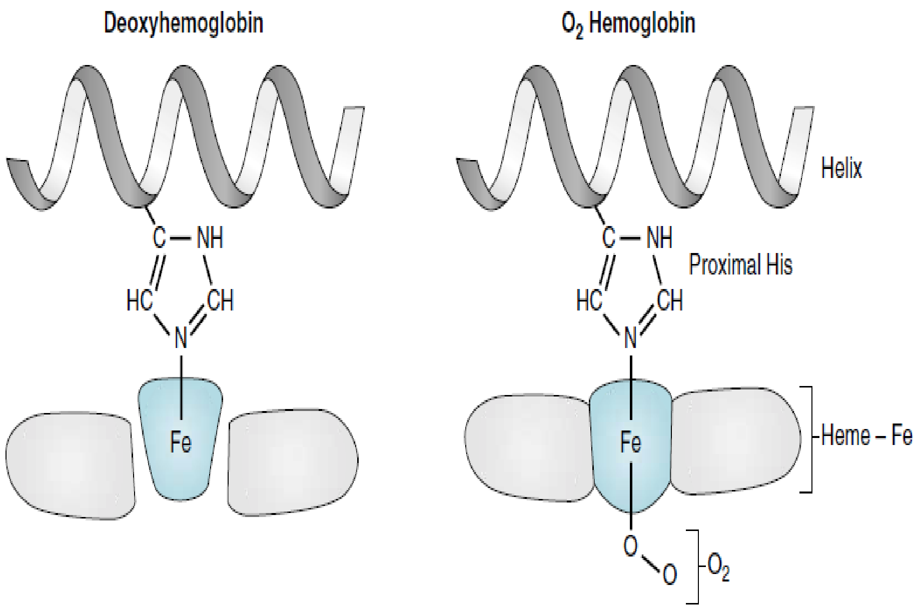
# Heme structure



# Cooperativity of $O_2$ Binding in Hemoglobin

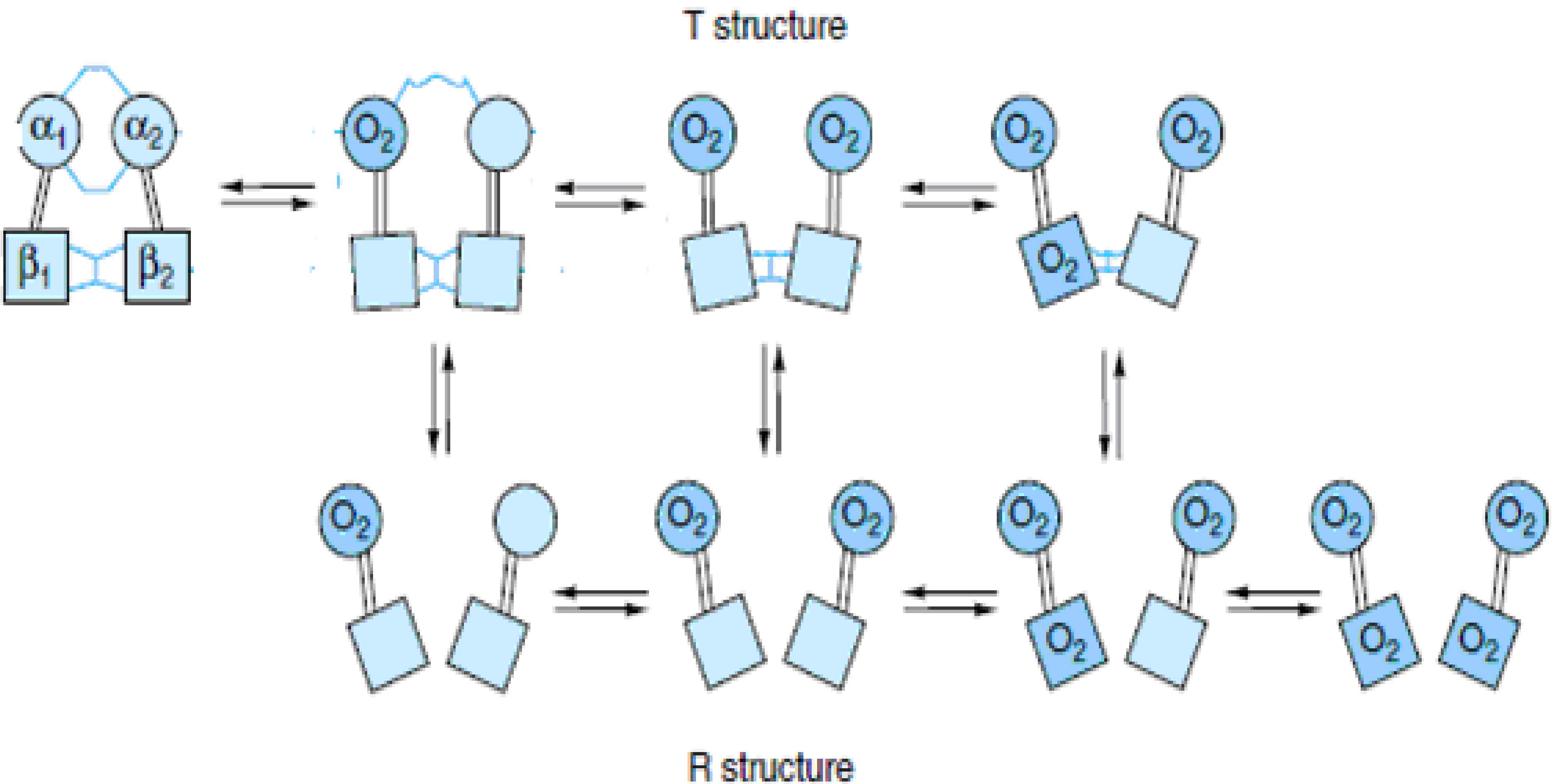


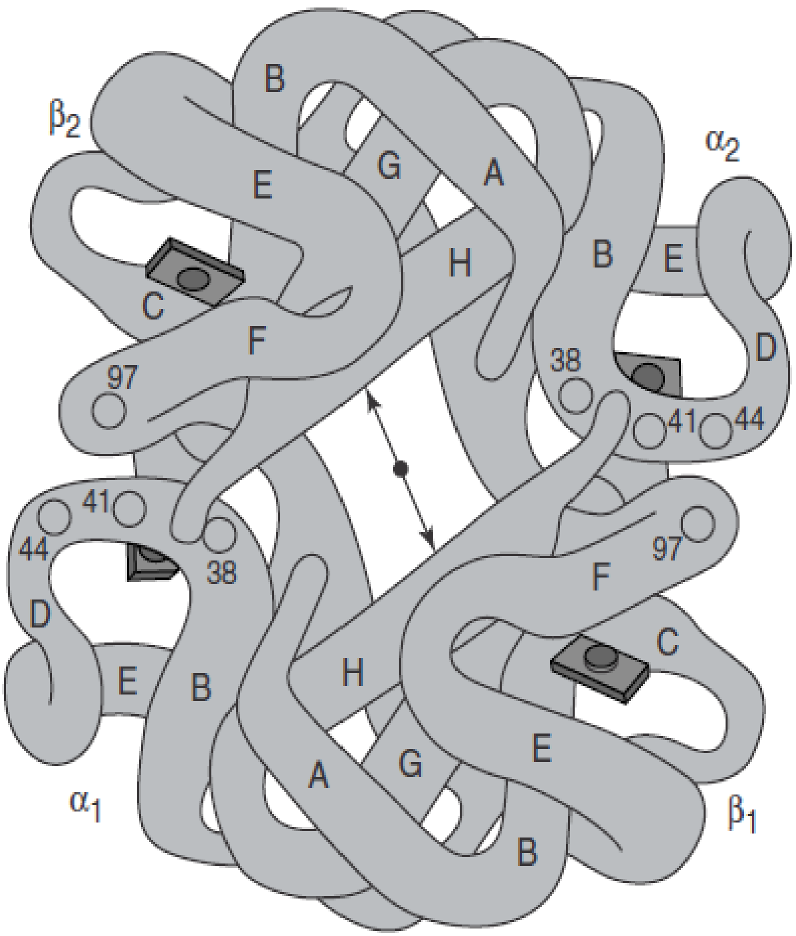
# Cooperativity of O2 Binding in Hemoglobin

## Transition from the T to R structure

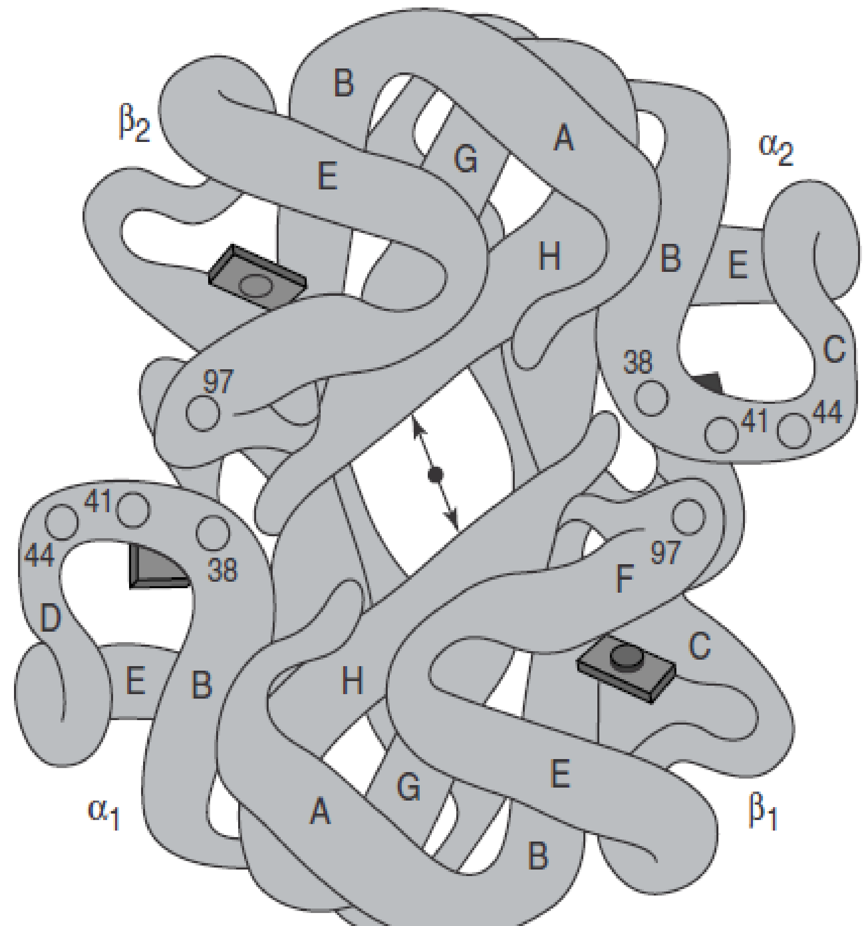
**Salt bridges (thin lines) linking the subunits in the T structure break progressively as oxygen is added**



# Hemoglobin

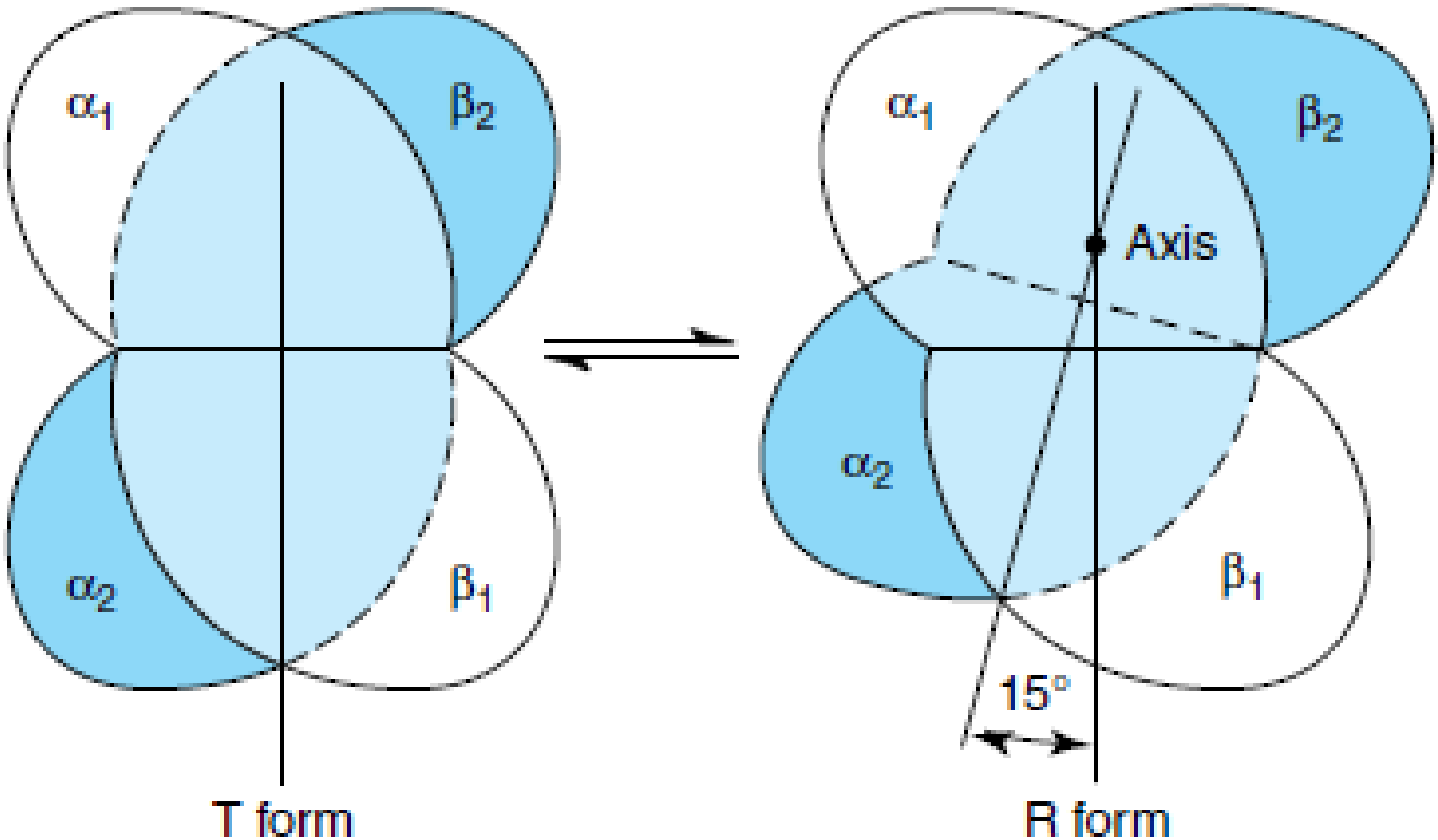



Deoxyhemoglobin




Oxyhemoglobin

## During transition of the T to R form of hemoglobin, one pair of subunits rotates through 15 degrees



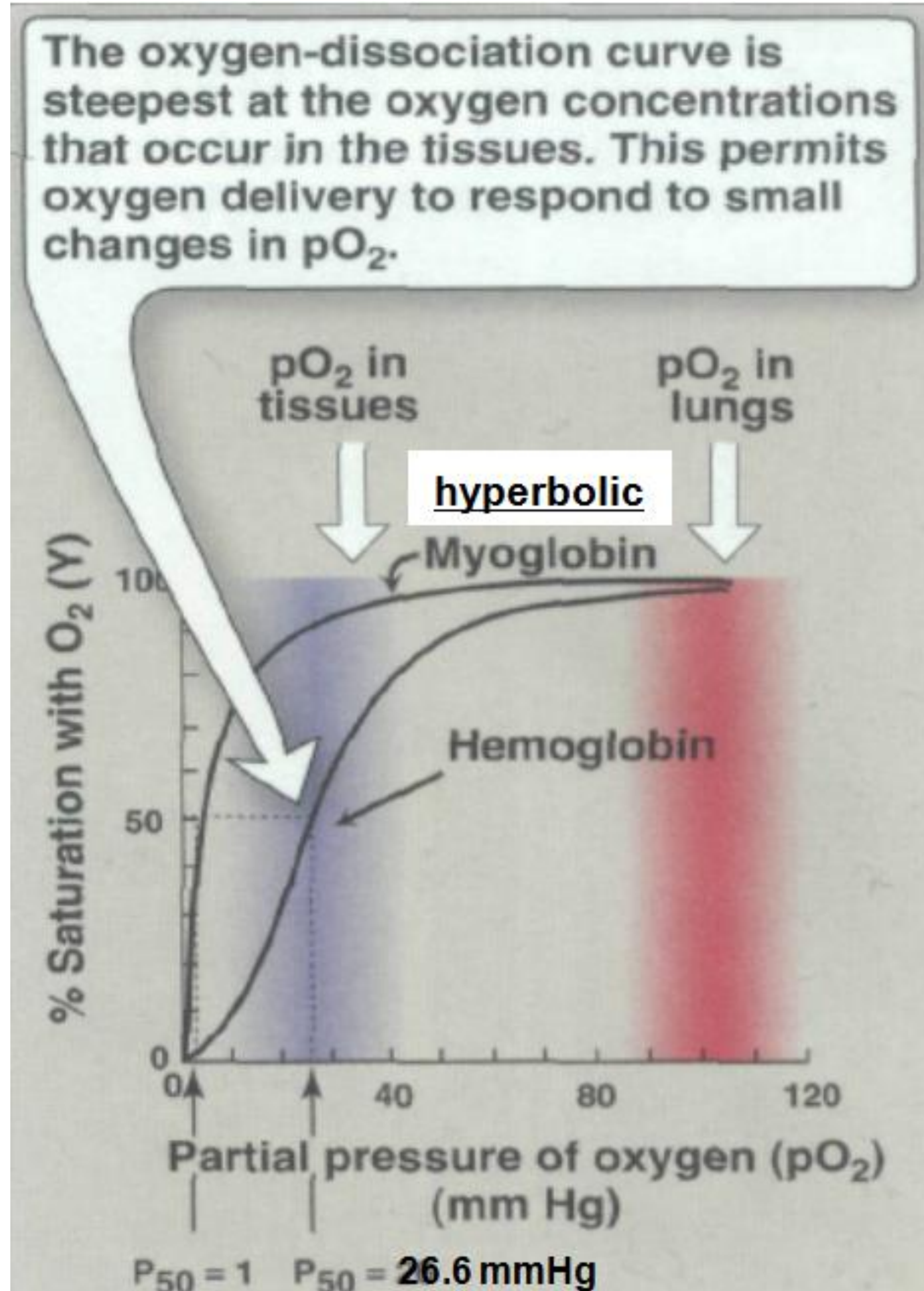
# Oxygen dissociation curve

- 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, to the oxygen carrying capacity of the hemoglobin
- The amount of oxygen bound to the hemoglobin is related to the $O_2$ pressure
- Hemoglobin's affinity for oxygen increases as more molecules of oxygen bind
- The curve has a sigmoidal or S-shape

# Oxygen dissociation curve

| pO2 (mmHg) | % saturation of Hb |
|---|---|
| **100** in alveoli | **98%** |
| **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. |
| **20** in working muscle | **20%** |
| **10** in vigorous exercising muscle | **10%** |

**1 Torr is approximately equal to 1 mmHg (millimeter of mercury)**



- **<u>Cooperativity Hb-$O_2$</u>**
- **<u>Sigmoidal Hb</u>**
- **<u>Hyperbolic Mb</u>**

- **<u>Myoglobin</u>**
- Myoglobin is designed to bind oxygen released by hemoglobin at the low $pO_2$ found in muscle. Myoglobin, in turn, releases oxygen within the muscle cell in response to oxygen demand.
- The oxygen dissociation curve for myoglobin has a **<u>hyperbolic</u>** shape. This reflects the fact that myoglobin reversibly binds a single molecule of oxygen. Thus, oxygenated MbO2 and deoxygenated (Mb) myoglobin exist in a simple equilibrium:

- **Mb + O2 ↔ MbO2**
- The equilibrium is shifted to the right or to the left as oxygen is added to or removed from the system.

# Agents that affect oxygen binding

1- The 2,3-bisphosphoglycerate (2,3-BPG or 2,3-DPG)

- The binding of 2,3-BPG to Hb promotes the release of $O_2$
- The presence of 2,3-BPG significantly reduces the affinity of hemoglobin for oxygen
- High levels of 2,3-DPG shift the curve to the right, while low levels of 2,3-DPG cause a leftward shift
- This reduced affinity enables hemoglobin to release oxygen efficiently at the partial pressures found in the tissues
- Hemoglobin stripped of BPG is saturated with $O_2$ at low $pO_2$ of only 20 mmHg , and it cannot release its oxygen within tissues, where the $pO_2$ is typically 40 mmHg.

- Reduced Hb-$O_2$ affinity------- shift the curve to right; while Increase Hb-$O_2$ affinity -------shift the curve to the left

- The concentration of 2,3-BPG in the red blood cell increases in response to chronic hypoxia, such as that observed in obstructive pulmonary emphysema, or at high altitudes, where circulating hemoglobin may have difficulty receiving sufficient oxygen.
- Intracellular levels of 2,3-BPG are also elevated in chronic anaemia, in which fewer than normal red blood cells are available to supply the body's oxygen needs.
- Elevated 2,3-BPG levels lower the oxygen affinity of hemoglobin, permitting greater unloading of oxygen in the capillaries of the tissues

## 2- Binding of $CO_2$

- Carbon dioxide affect the curve in two ways:
- A. Formation of carbamino- hemoglobin
- B. Bohr effect

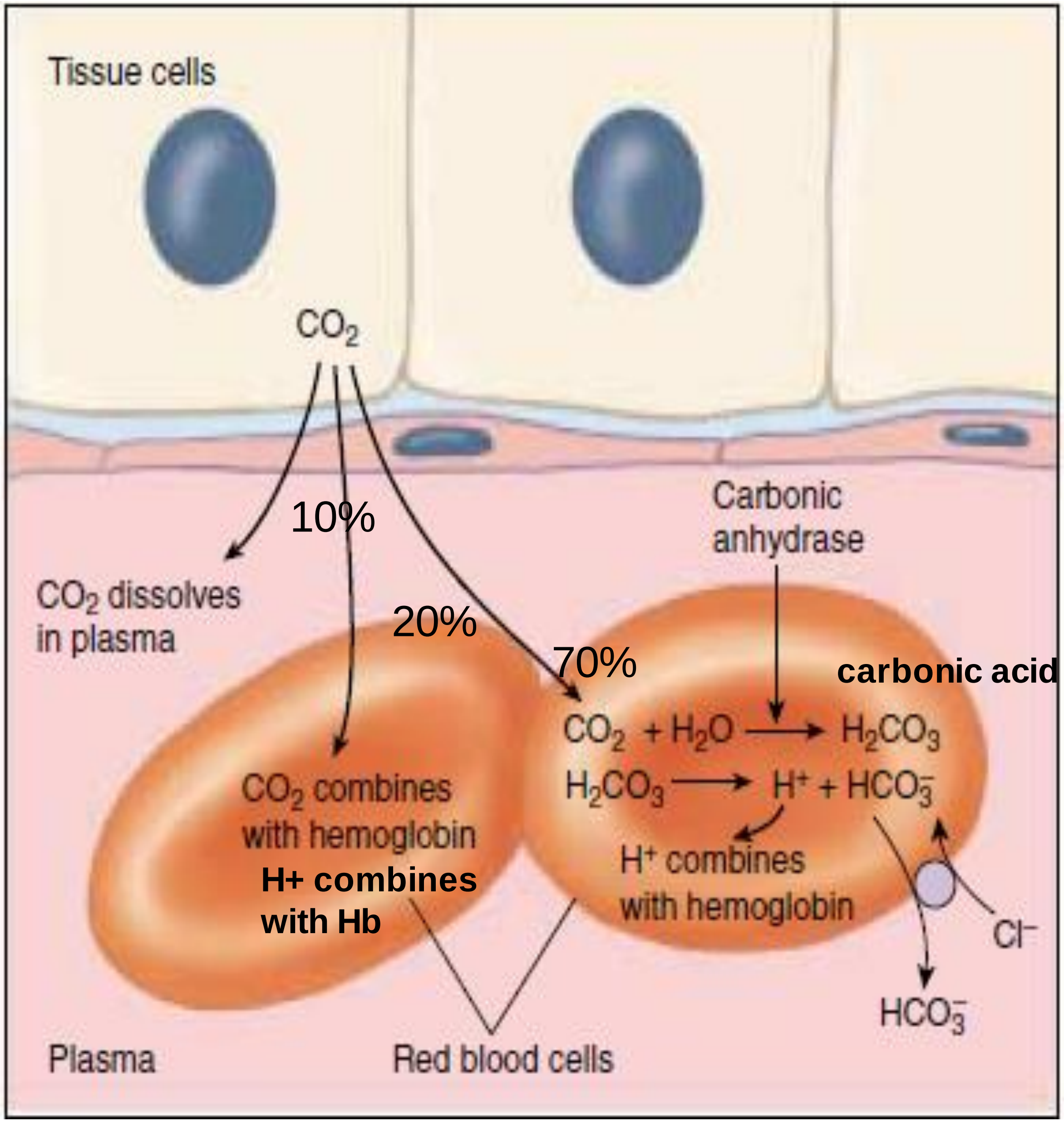
## A. Formation of carbamino- hemoglobin

- 20% of CO2 is carried as **carbamino-** hemoglobin bound to the uncharged α-amino groups of hemoglobin, which can be represented schematically as follows:

$$\mathbf{Hb\text{-}NH_2 + CO_2 \leftrightarrow Hb\text{-}NH\text{-}COO^- + H^+}$$

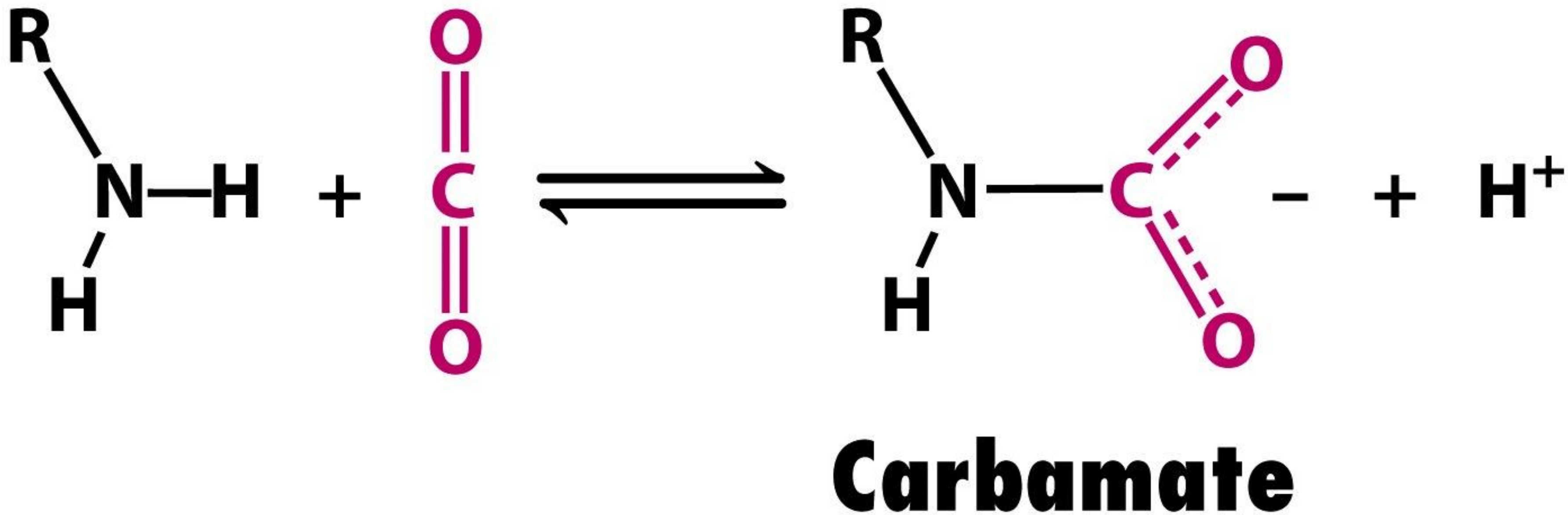
- The binding of $CO_2$ stabilizes the T (taut) or deoxyhemoglobin, resulting in a decrease in its affinity for oxygen.
- Hemoglobin resists oxygenation because the deoxy form is stabilized by specific hydrogen bonds and salt bridges (ion-pair bonds). All of these interactions are broken in oxyhemoglobin, as the molecule stabilizes into a new conformation.

# Transport of $CO_2$ by the blood



# Carbamino (Carbamate) formation

## Covalent binding at the N-terminus of each subunit

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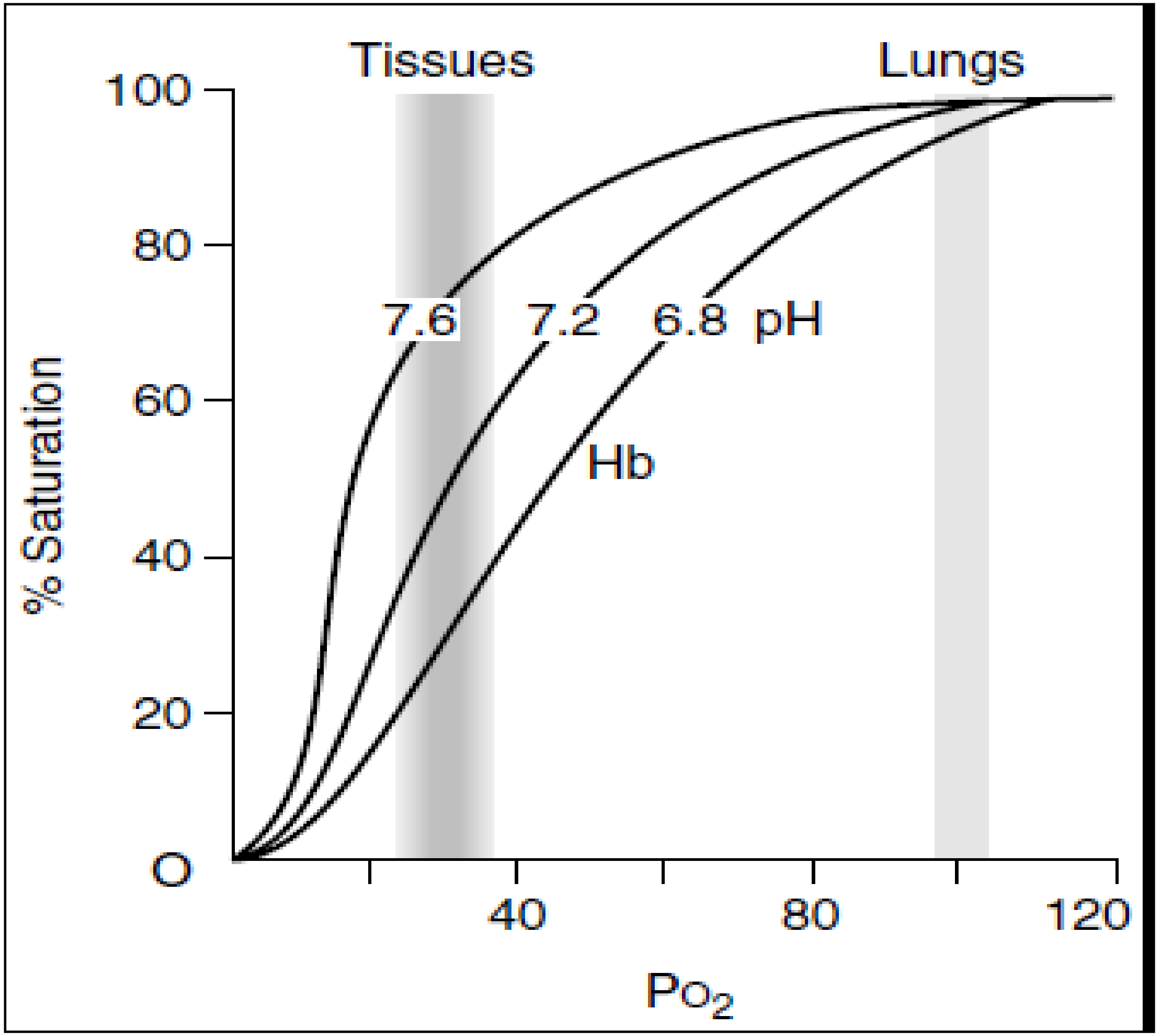
- **B- Bohr effect**
- The binding of protons by hemoglobin lowers its affinity for oxygen therefore, a shift to the right in the oxygen dissociation curve.
- Raising the pH or lowering the concentration of $CO_2$ results in a greater affinity for oxygen, and a shift to the left in the oxygen dissociation curve.
- This phenomenon is known as the Bohr effect.
- The pH of the blood decreases as it enters the tissues because of $CO_2$ produced by metabolism.
- Protons that react with several amino acid residues in hemoglobin (such as histidine side chains), causing conformational changes that promote the release of oxygen.
- Thus, in tissues in which the pH of the blood is low because of the $CO_2$ produced by metabolism, oxygen is released from hemoglobin.

# Bohr effect


Tissues
Lungs
100
80
60
40
20
O
% Saturation
7.6
7.2
6.8
pH
Hb
40
80
120
$Po_2$

## 2,3 BPG and $H^+$ relationship and effect on curve

- The relationship of hydrogen ions is inversely proportionate with levels of 2,3 BPG which stating that an elevation of the hydrogen ion concentration in red blood cells will result in decreases in 2,3 BPG and vice versa.
- This is evident at high altitudes where lower oxygen levels induce hyperventilation, causing pCO2 and hydrogen ions to decrease which leads to leftward shifting of the dissociation curve. This left shift leads to an increase in red blood cell production of 2,3-BPG, which leads to shifting the curve back to the right and establishes an essential mechanism of respiratory compensation

## 3. Temperature

An increase in temperature shifts the curve to the right whilst a decrease in temperature shifts the curve to the left. 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 (lowered oxygen affinity).

- **<u>Myoglobin</u>**
- as an oxygen storage protein, has a greater affinity for $O_2$ than hemoglobin at all oxygen pressures.

- Hemoglobin, as the oxygen carrier, becomes saturated with $O_2$ in the lungs, where the partial pressure of $O_2$ ($pO_2$) is about 100 torr. In the capillaries of tissues, $pO_2$ is typically 40 torr so oxygen is released from Hb.

Atmospheric air consists primarily of nitrogen (approximately 79 percent) and oxygen (approximately 21 percent), with very small quantities of water vapour, carbon dioxide, and inert gases. The sum of the partial pressures of all these gases is termed atmospheric pressure, or barometric pressure. It varies in different parts of the world as a result of differences in altitude (it also varies with local weather conditions), but at sea level it is 760 mmHg. Since the partial pressure of any gas in a mixture is the fractional concentration of that gas times the total pressure of all the gases, the *P*O2 of atmospheric air is

0.21 X 760 mmHg = 160 mmHg at sea level.