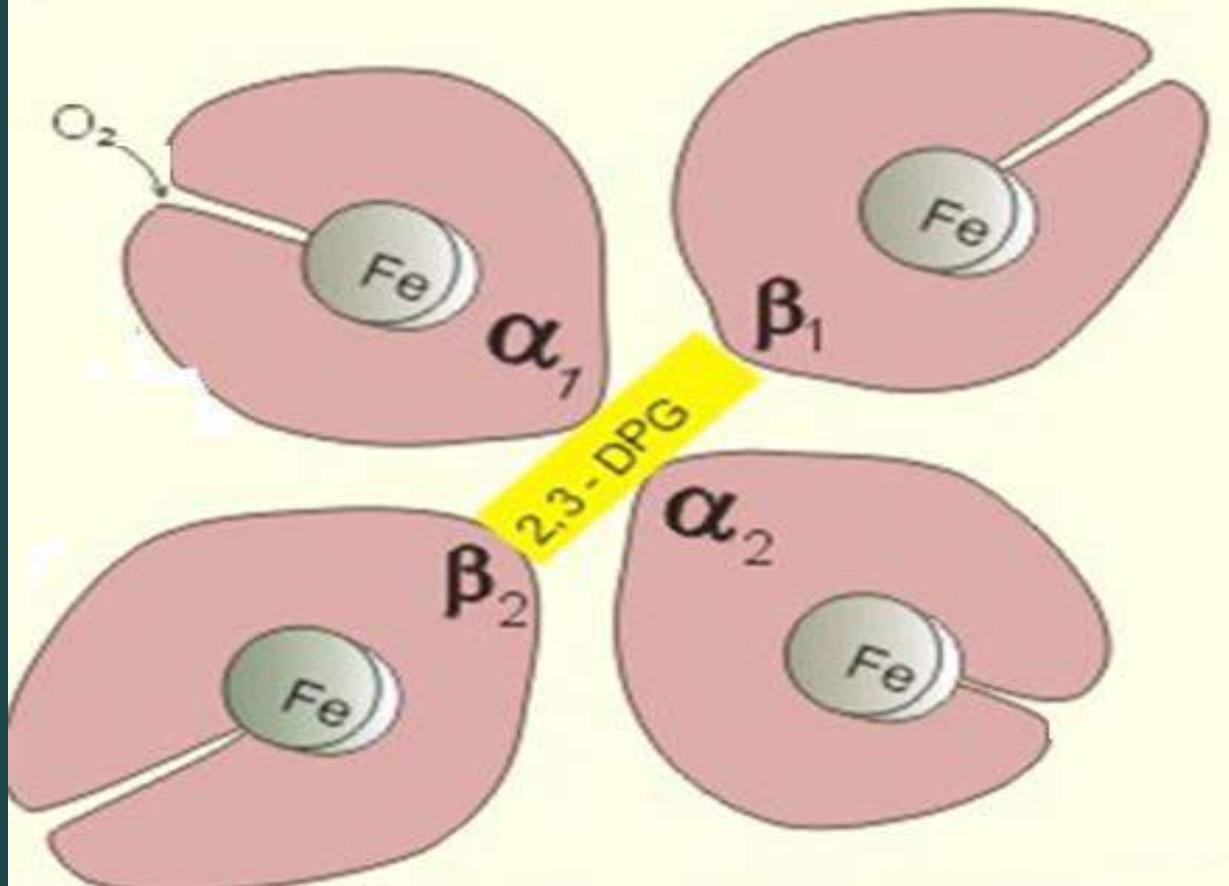


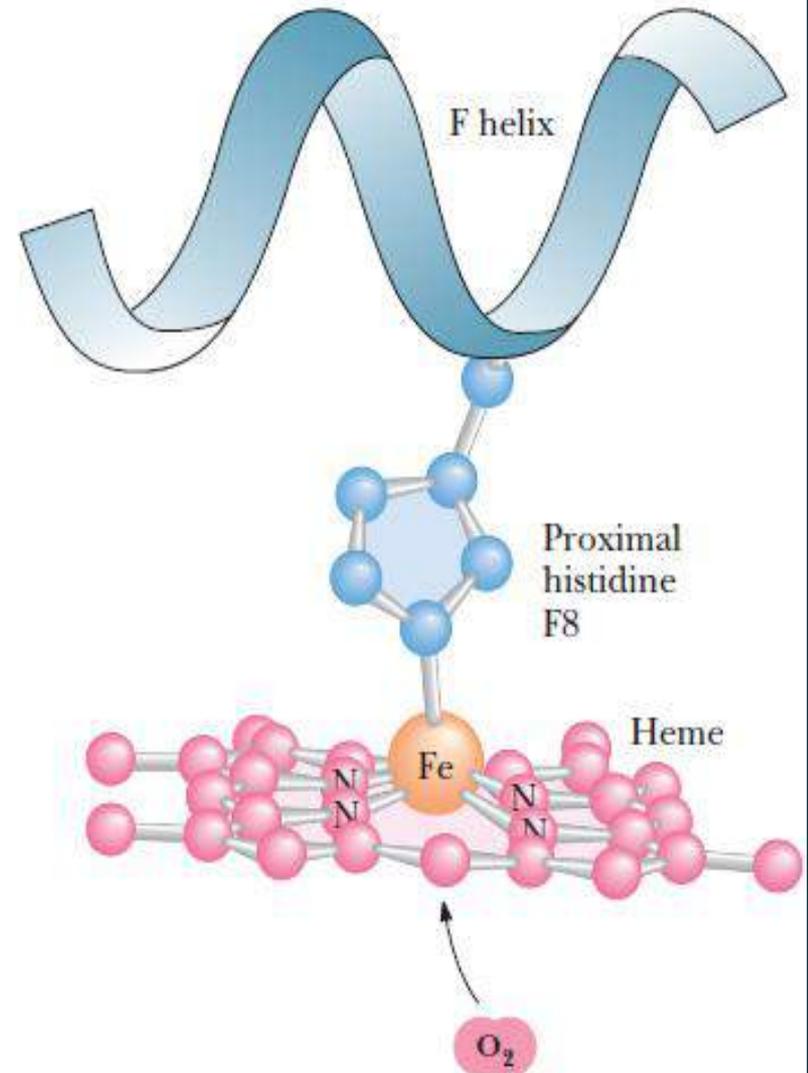
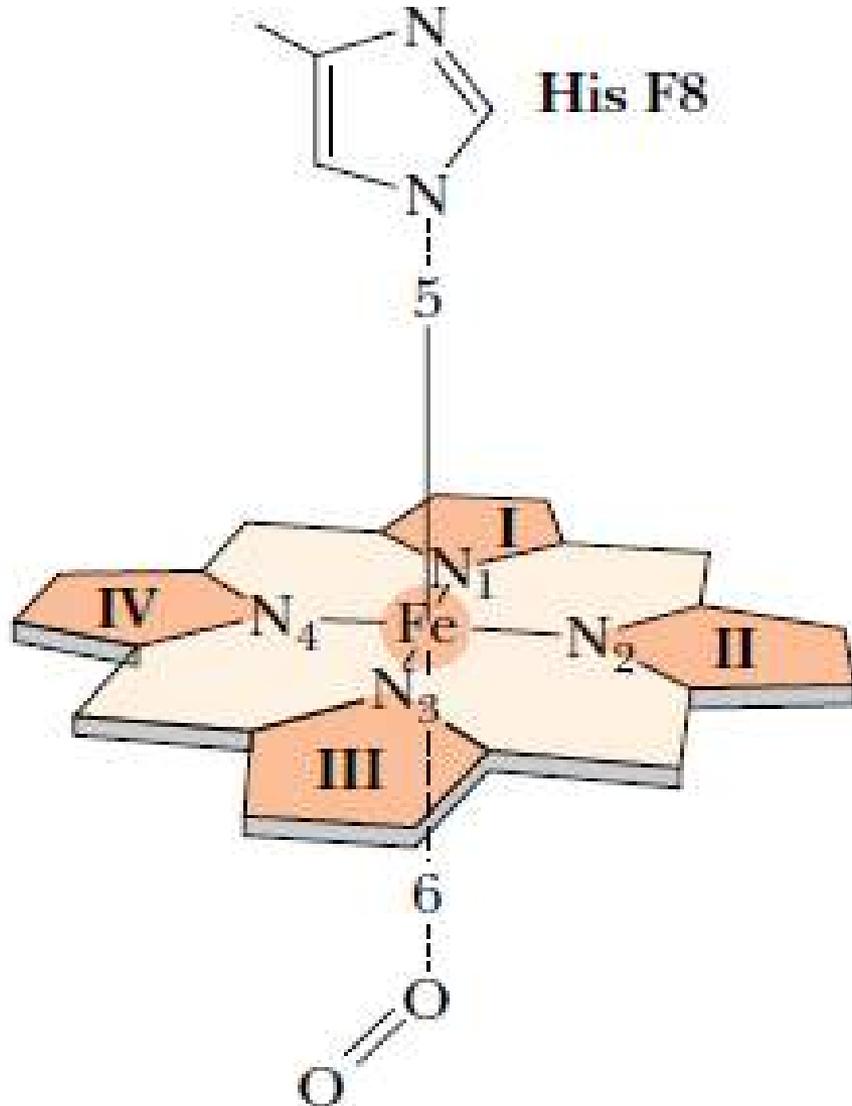
# Oxygen binding to Mb & Hb & Hb-O<sub>2</sub> dissociation curve

## Deoxyhaemoglobin



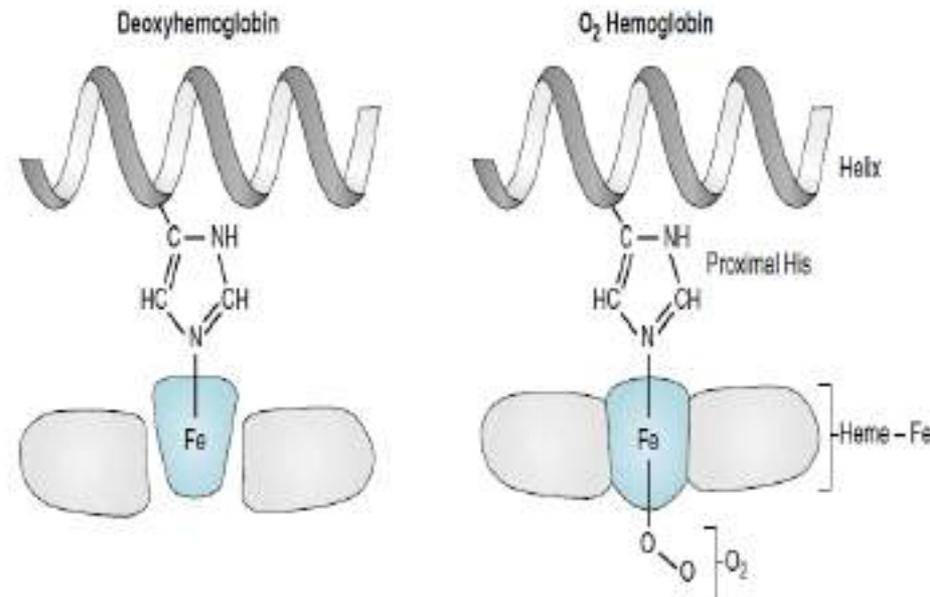
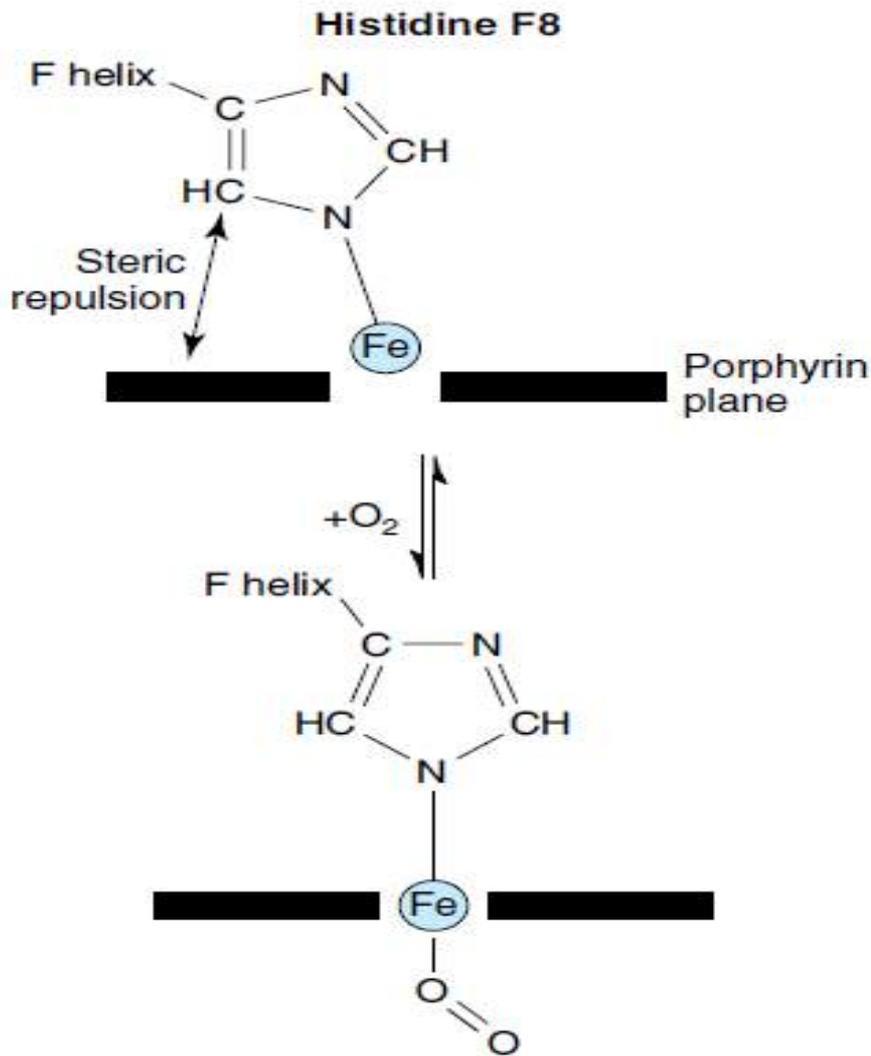
Oxygen is accessible only to the heme groups of the  $\alpha$ -chains when hemoglobin is in T state.

# Heme structure



# Cooperativity of O<sub>2</sub> Binding in Hemoglobin

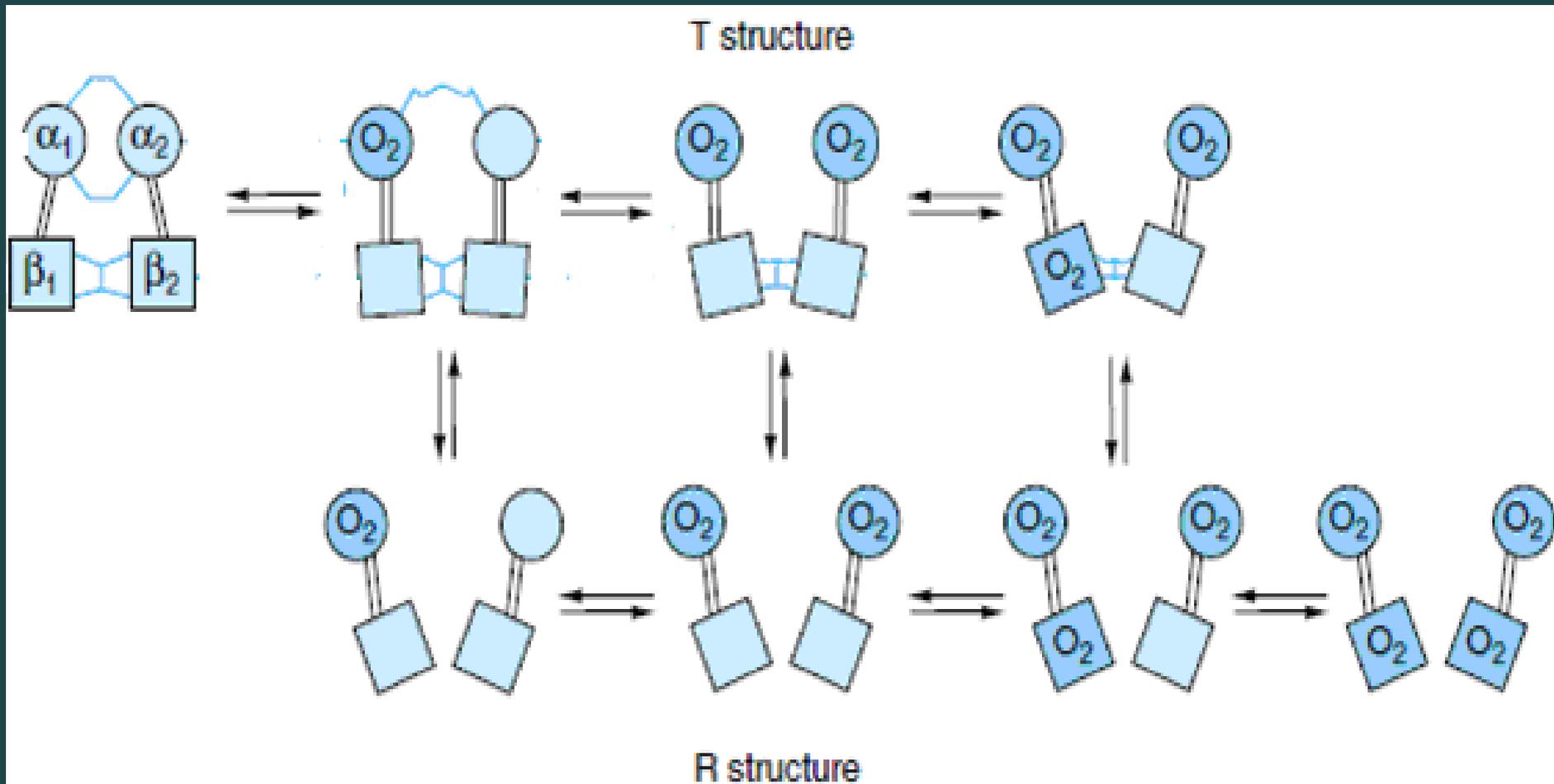
**Steric repulsion:** When atoms get very close to each other this leads to overlap of their electron clouds which create a repulsion force



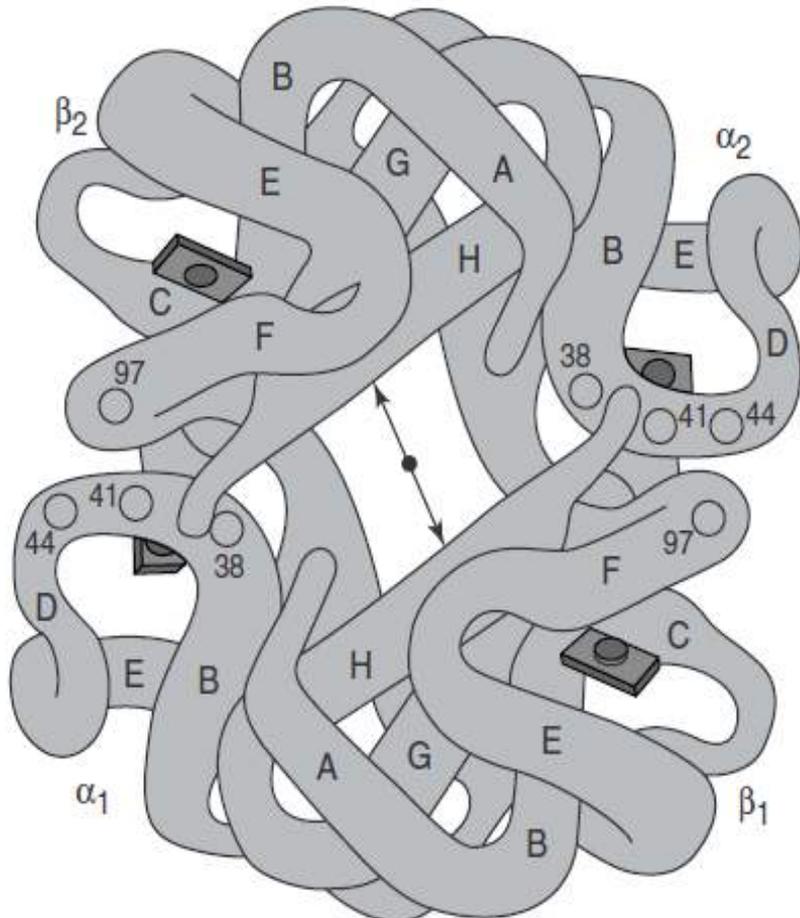
# Cooperativity of O<sub>2</sub> Binding in Hemoglobin

Transition from the T to R structure

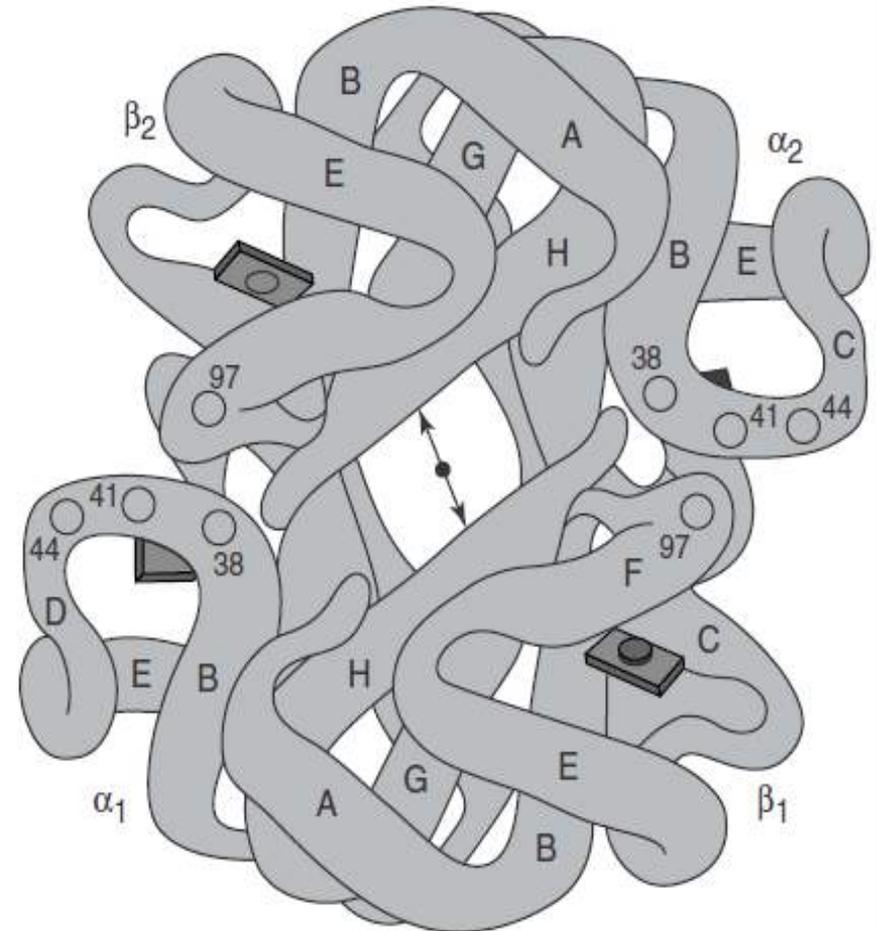
Salt bridges (thin lines) linking the subunits in the T structure break progressively as oxygen is added



# Hemoglobin

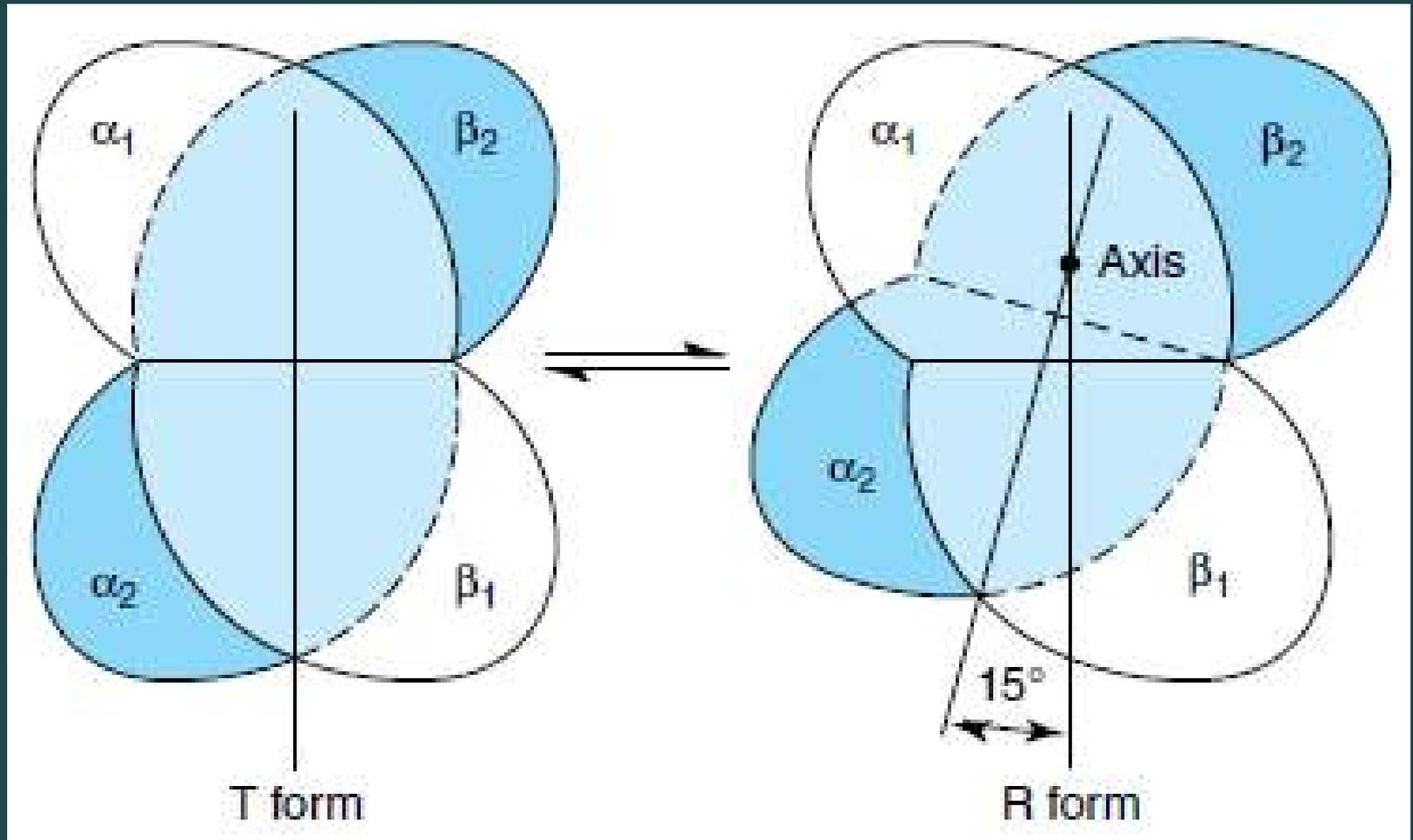


Deoxyhemoglobin



Oxyhemoglobin

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



# Oxygen dissociation curve

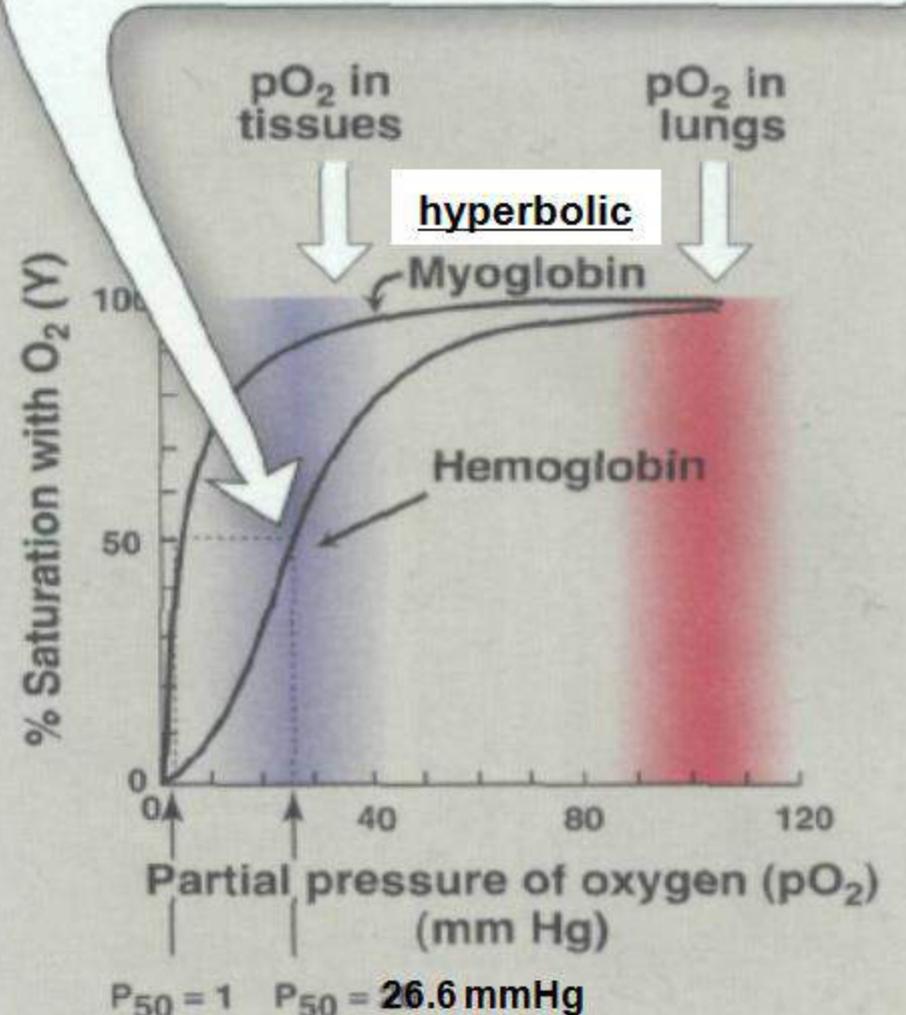
- Describes the relation between the partial pressure of oxygen (x axis) and the oxygen saturation (y axis)
- The oxygen saturation is the ratio of the amount of oxygen bound to the hemoglobin, to the oxygen carrying capacity of the hemoglobin
- The amount of oxygen bound to the hemoglobin is related 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

<u>pO<sub>2</sub> (mmHg)</u>	<u>% saturation of Hb</u>
100 in alveoli	100%
40 in resting muscle	75% thus it deliver 25% of its O <sub>2</sub> 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)

The oxygen-dissociation curve is steepest at the oxygen concentrations that occur in the tissues. This permits oxygen delivery to respond to small changes in pO<sub>2</sub>.



## P50

- P50 is the partial pressure of O<sub>2</sub> at which 50% of Hb is saturated with O<sub>2</sub>.
- Normal range of P50 for adults is 24-28 mmHg.
- P50 is very important to understand tissue oxygenations
- Changes in P50 is a signal of diseases such as: paediatric acute respiratory syndrome, anaemia, RBCs disorders.

- **Myoglobin**
- 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 **hyperbolic** shape. This reflects the fact that myoglobin reversibly binds a single molecule of oxygen. Thus, oxygenated MbO<sub>2</sub> and deoxygenated (Mb) myoglobin exist in a simple equilibrium:
- **$Mb + O_2 \leftrightarrow MbO_2$**
- 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<sub>2</sub>
- 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<sub>2</sub> at low pO<sub>2</sub> of only 20 mmHg , and it cannot release its oxygen within tissues, where the pO<sub>2</sub> is typically 40 mmHg.
- Reduced Hb-O<sub>2</sub> affinity----- shift the curve to right; while  
Increase Hb-O<sub>2</sub> 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<sub>2</sub>

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

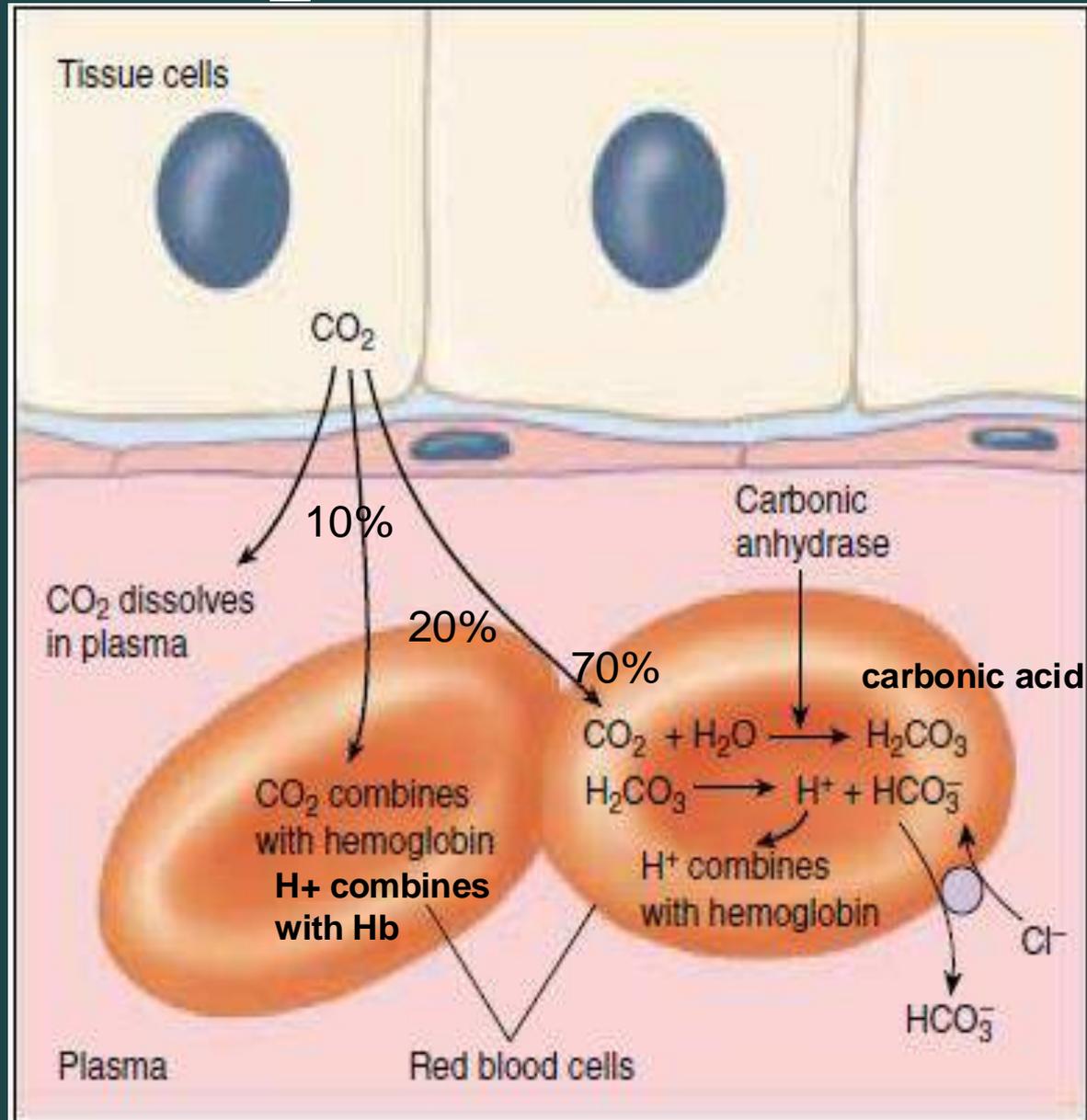
### A. Formation of carbamino- hemoglobin

- 20% of CO<sub>2</sub> is carried as **carbamino-** hemoglobin bound to the uncharged α-amino groups of hemoglobin, which can be represented schematically as follows:



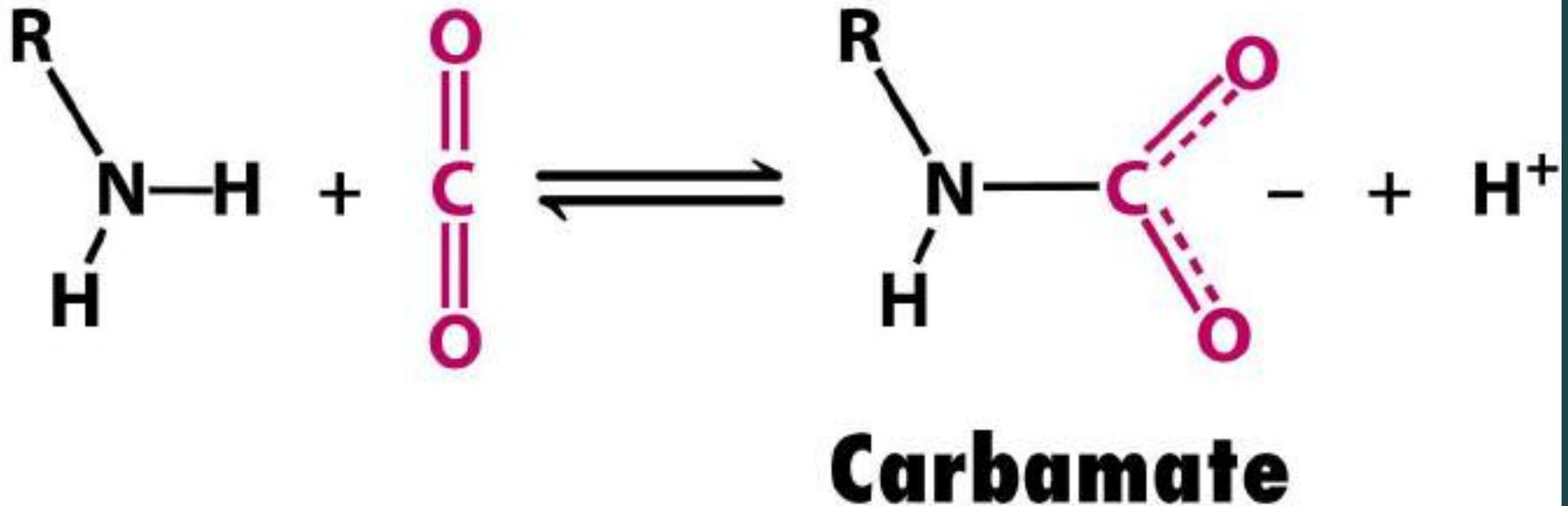
- The binding of CO<sub>2</sub> stabilizes the T (taut) or deoxyhemoglobin, resulting in a decrease in its affinity for oxygen.
- Hemoglobin resists oxygenation because the deoxy form is stabilized by specific hydrogen bonds and salt bridges (ion-pair bonds).

# Transport of CO<sub>2</sub> by the blood



# Carbamino (Carbamate) formation

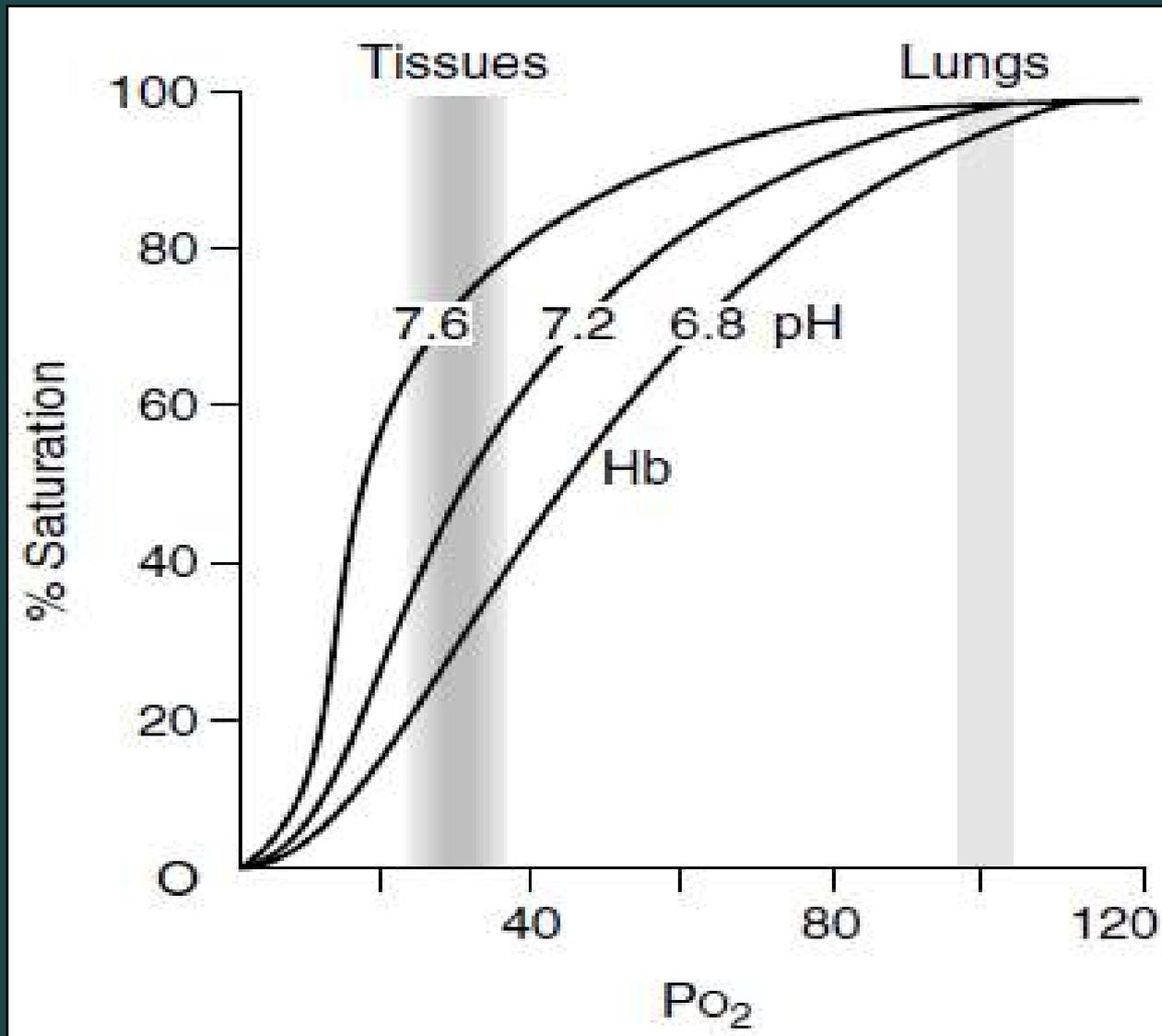
Covalent binding at the N-terminus of each subunit



- **B- Bohr effect**

- The effect of CO<sub>2</sub> and pH on O<sub>2</sub> dissociation curve is known as Boher effect
- Raising the pH or lowering the concentration of CO<sub>2</sub> results in a greater affinity for oxygen, and a shift to the left in the oxygen dissociation curve.
- 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<sub>2</sub> produced by metabolism stimulating oxygen release from hemoglobin.

# Bohr effect



### 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  $37^{\circ}\text{C}$ , and oxygen can be unloaded from Hb more easily at the higher temperature (lowered oxygen affinity).

- Myoglobin

- 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  $PO_2$  of atmospheric air is  $0.21 \times 760 \text{ mmHg} = 160 \text{ mmHg}$  at sea level.