

Oxygen binding to Mb & Hb & Hb-O₂ dissociation curve



صورة تلخص المحاضرة :

Oxygen Binding to Hemoglobin & Myoglobin

Heme Structure

Iron-containing porphyrin ring enables oxygen binding in both hemoglobin and myoglobin.

T State Access

In hemoglobin's T state, oxygen is accessible only to α -chain heme groups.

Cooperative Binding

Salt bridges break progressively as oxygen binds, causing T to R transition with 15° subunit rotation.

Oxygen Dissociation Curves

The relationship between partial pressure of oxygen and saturation reveals key differences between hemoglobin and myoglobin.

pO ₂ (mmHg)	Location	Hb Saturation
100	Alveoli (lungs)	100%
40	Resting muscle	75% (delivers 25%)
20	Working muscle	20%
10	Vigorous exercise	10%

Main Point: Hemoglobin's sigmoidal curve reflects cooperative oxygen binding, delivering oxygen efficiently to tissues while maintaining reserves. Myoglobin's hyperbolic curve shows single-molecule binding with higher affinity at all pressures.

P50 Value

P50 is the pO₂ at which 50% of Hb is saturated. Normal range: **24-28 mmHg**. Changes signal diseases like anemia or respiratory disorders.

Factors Affecting Oxygen Binding

01

2,3-BPG (2,3-DPG)

Reduces Hb-O₂ affinity, shifting curve right. Levels increase in chronic hypoxia, high altitude, and anemia to enhance oxygen unloading in tissues.

02

CO₂ Binding

20% of CO₂ forms carbamino-hemoglobin at α -amino groups, stabilizing T state and decreasing oxygen affinity.

03

Bohr Effect (pH & CO₂)

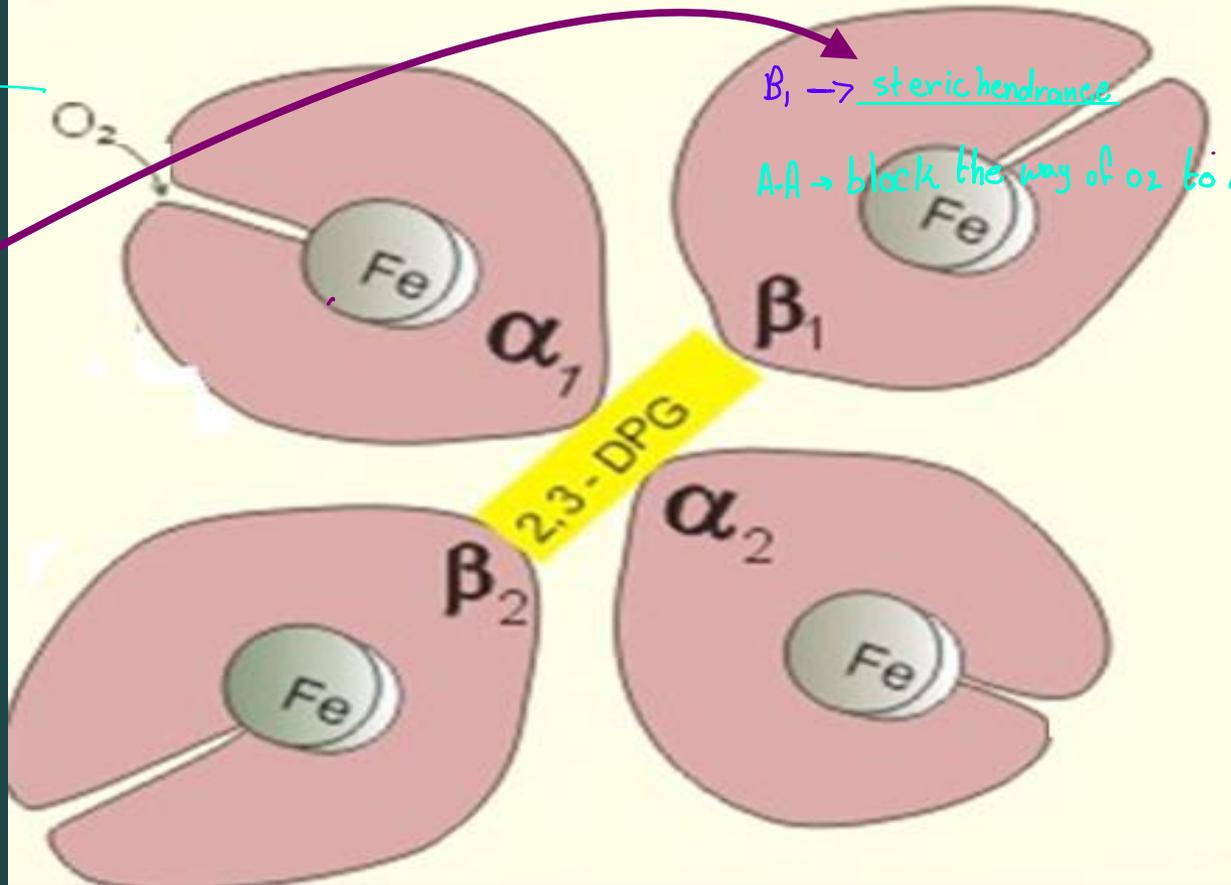
Lower pH or higher CO₂ shifts curve right (decreased affinity). Higher pH shifts left (increased affinity). Critical for oxygen release in metabolically active tissues.

04

Temperature

Increased temperature shifts curve right, facilitating oxygen unloading during exercise when muscle temperature exceeds 37°C.

Deoxyhaemoglobin (No O₂)



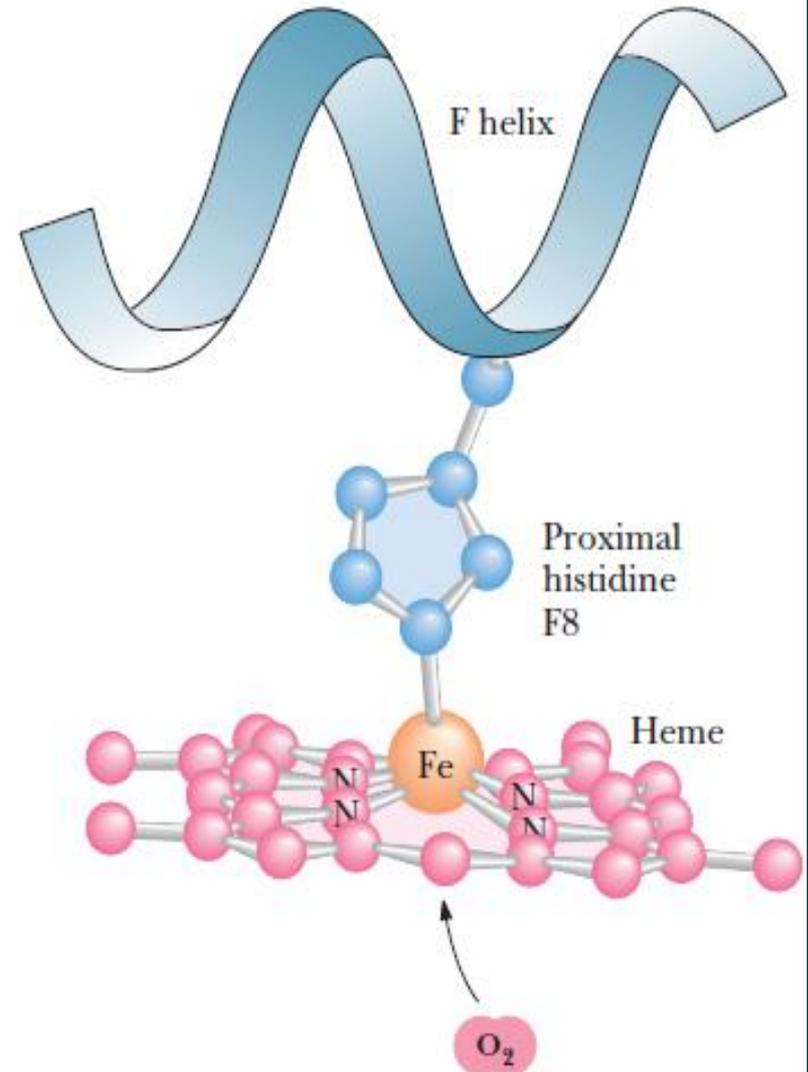
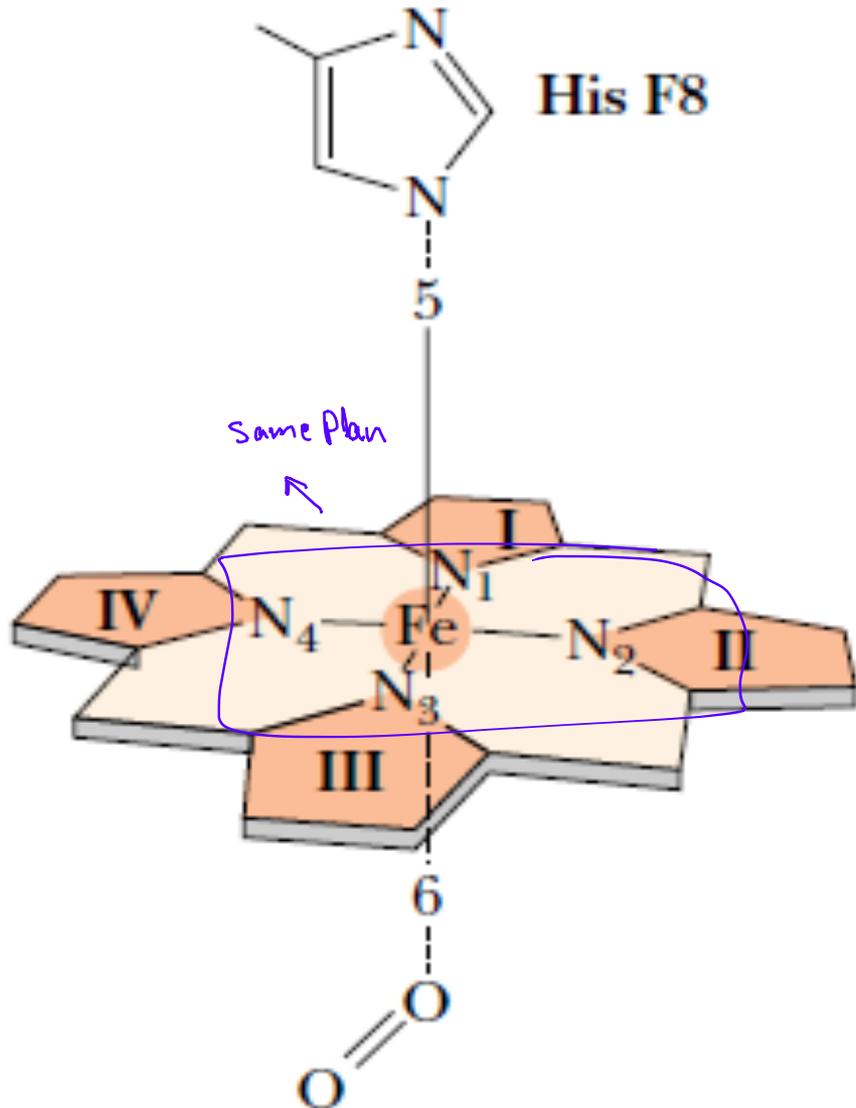
why
The first O₂ bind
very slow And
to α_1 subunit ? :
→ Because β_1
has

β_1 → steric hindrance
A.A → block the way of O₂ to bind

High Pressure
O₂ in lungs
forced Hb to
bind with it.

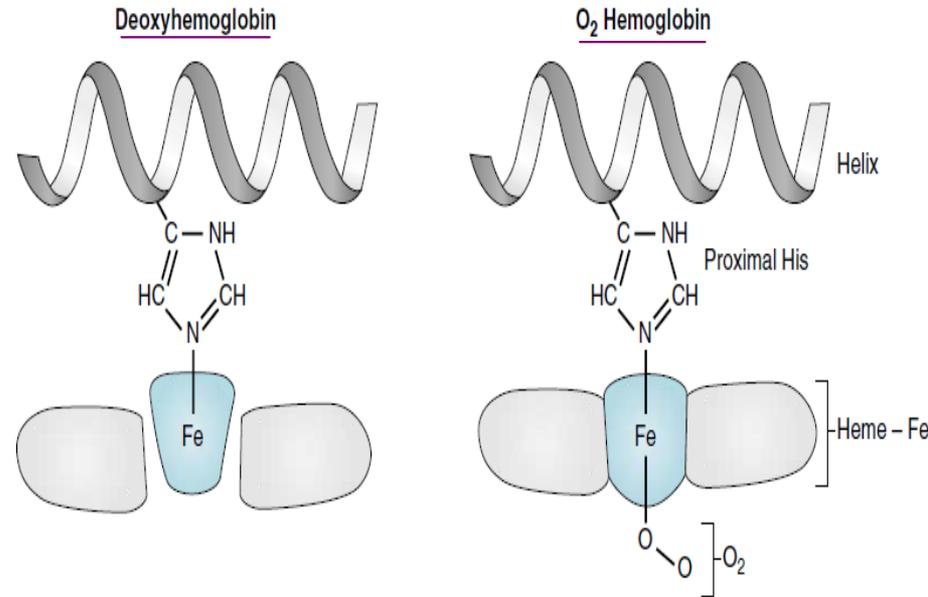
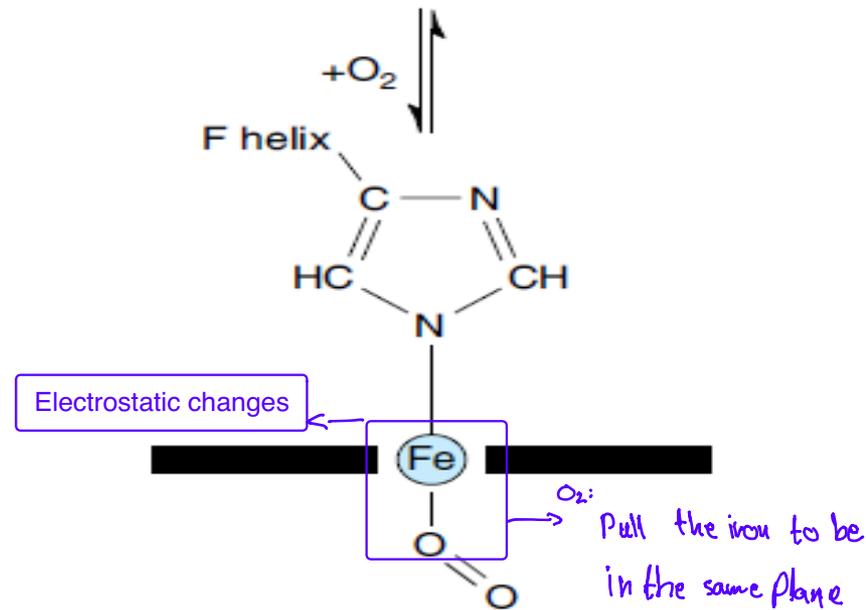
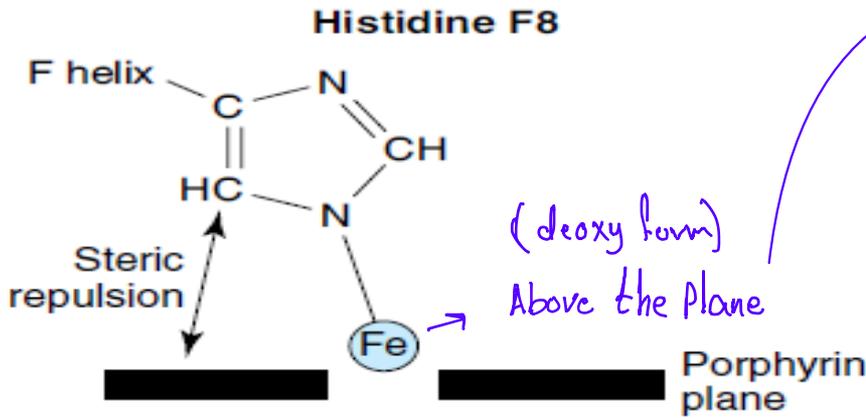
Oxygen is accessible only to the heme groups of the α -chains when hemoglobin is in T state.

Heme structure



Cooperativity of O₂ 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



→ the movement of iron will cause movement of His 93 will move α₁ subunit → will change T → R state.

→ 20% → slow, 2, faster - 3... 4 ⇒ 800 faster Hb₁

Cooperativity of O₂ Binding in Hemoglobin

Transition from the T to R structure

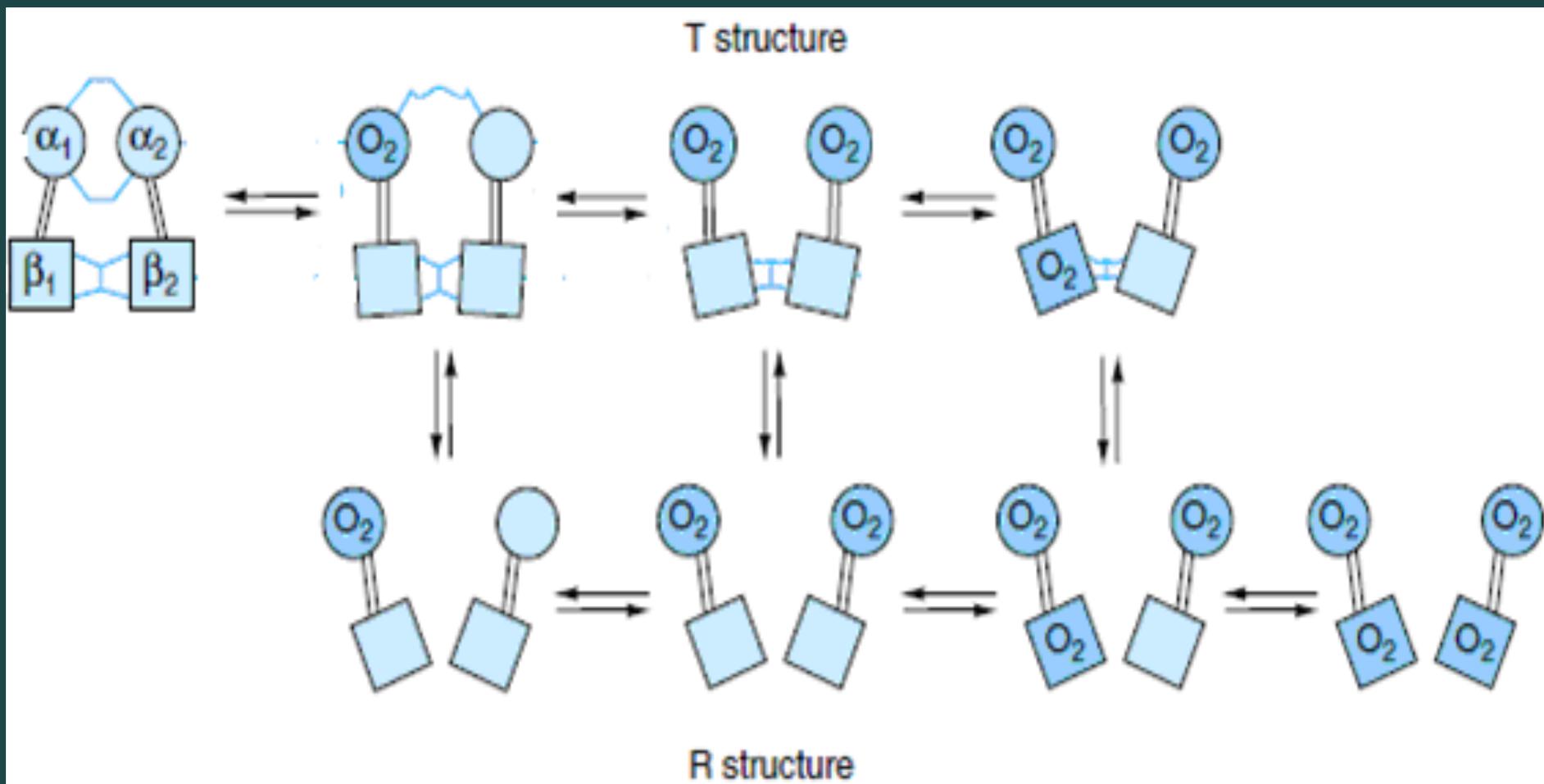
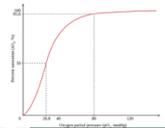
(weak ionic, hydrogen bond.)

صورة للتوضيح →

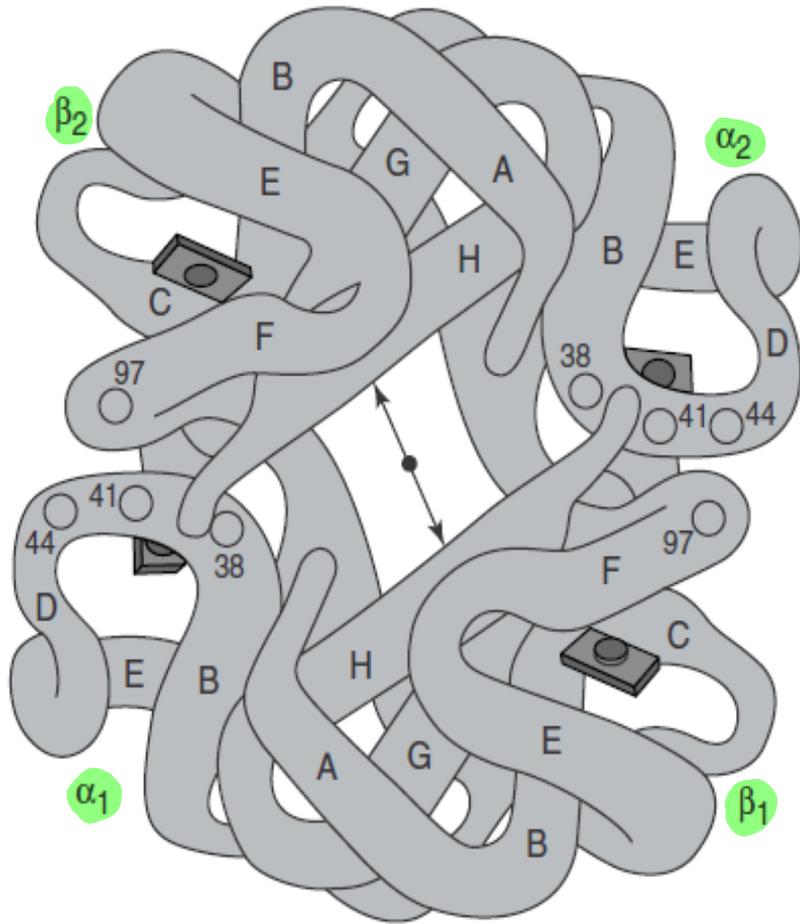
Salt bridges (thin lines) linking the subunits in the T structure break progressively as oxygen is added

Oxygen-Hgb Binding

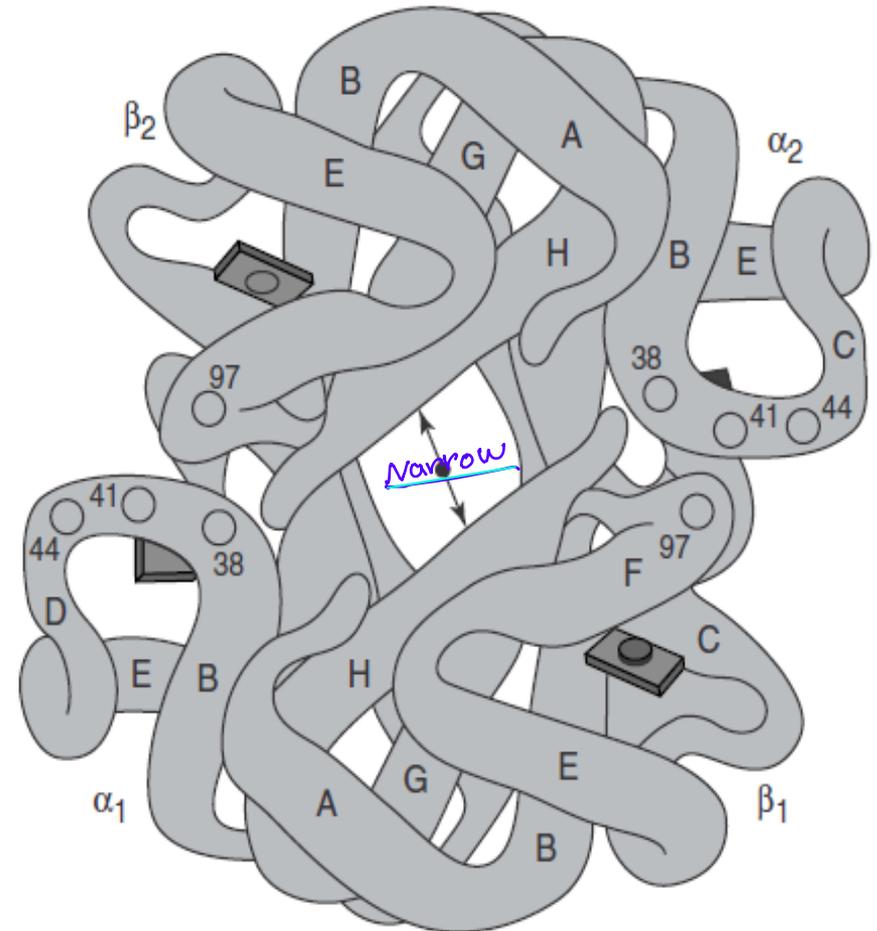
- Four heme groups do not simultaneous oxygenate
- First O₂ molecule INCREASES affinity for 2nd molecule
- Second O₂ molecule INCREASES affinity for 3rd molecule
- Third O₂ molecule INCREASES affinity for 4th molecule
- Affinity last O₂ = 300 times affinity for first O₂
- **Positive cooperativity**
- Makes curve S shaped



Hemoglobin

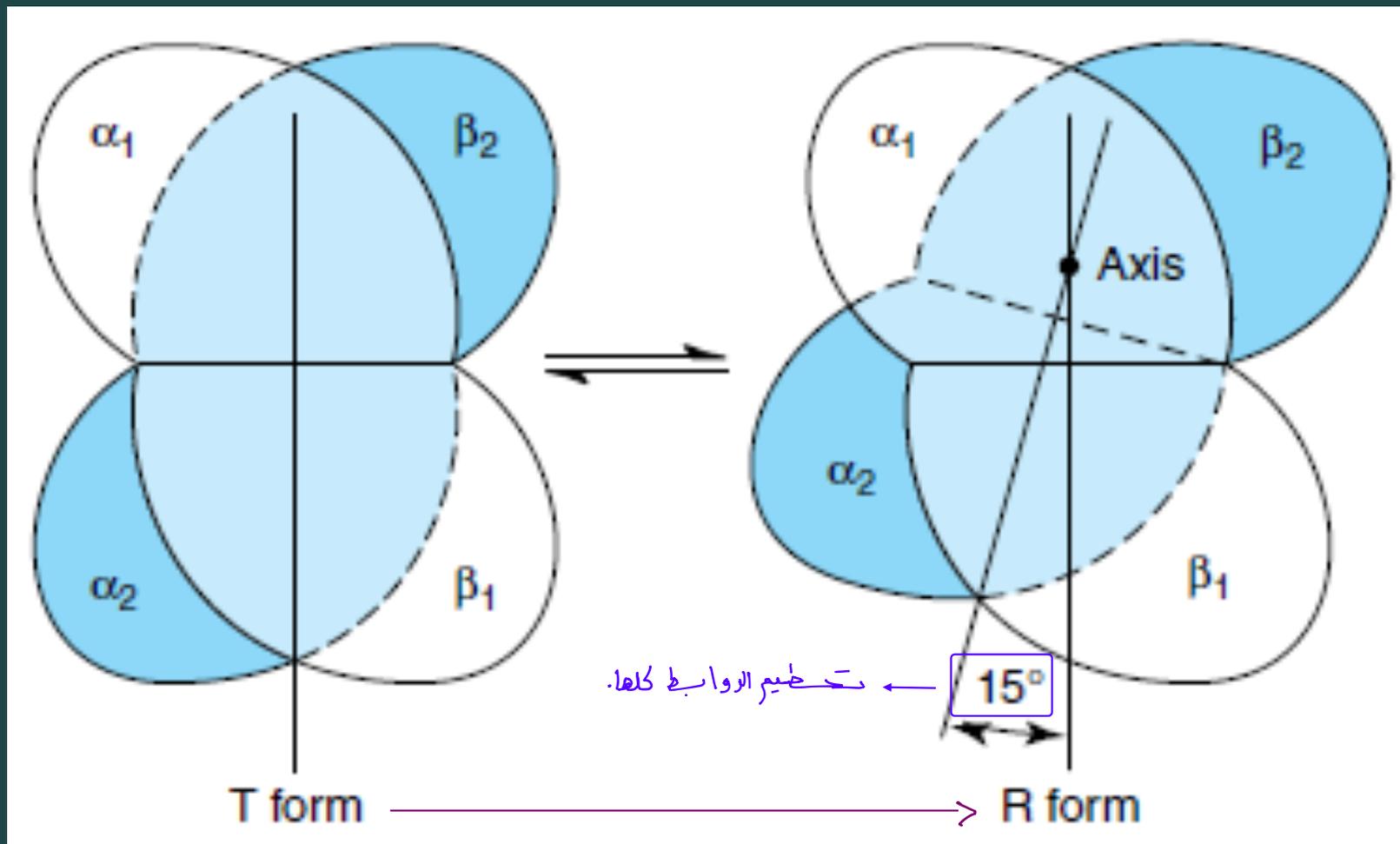


Deoxyhemoglobin



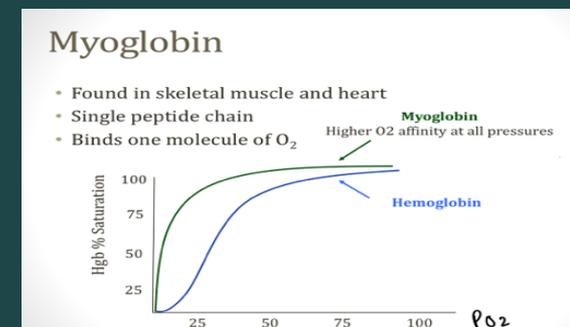
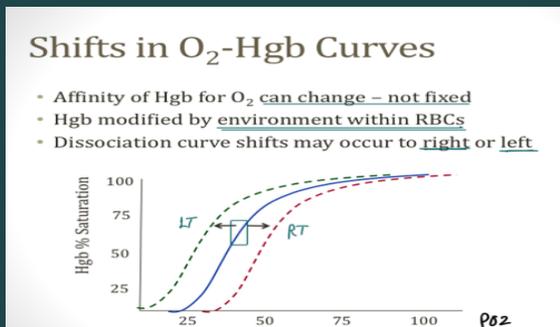
Oxyhemoglobin

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

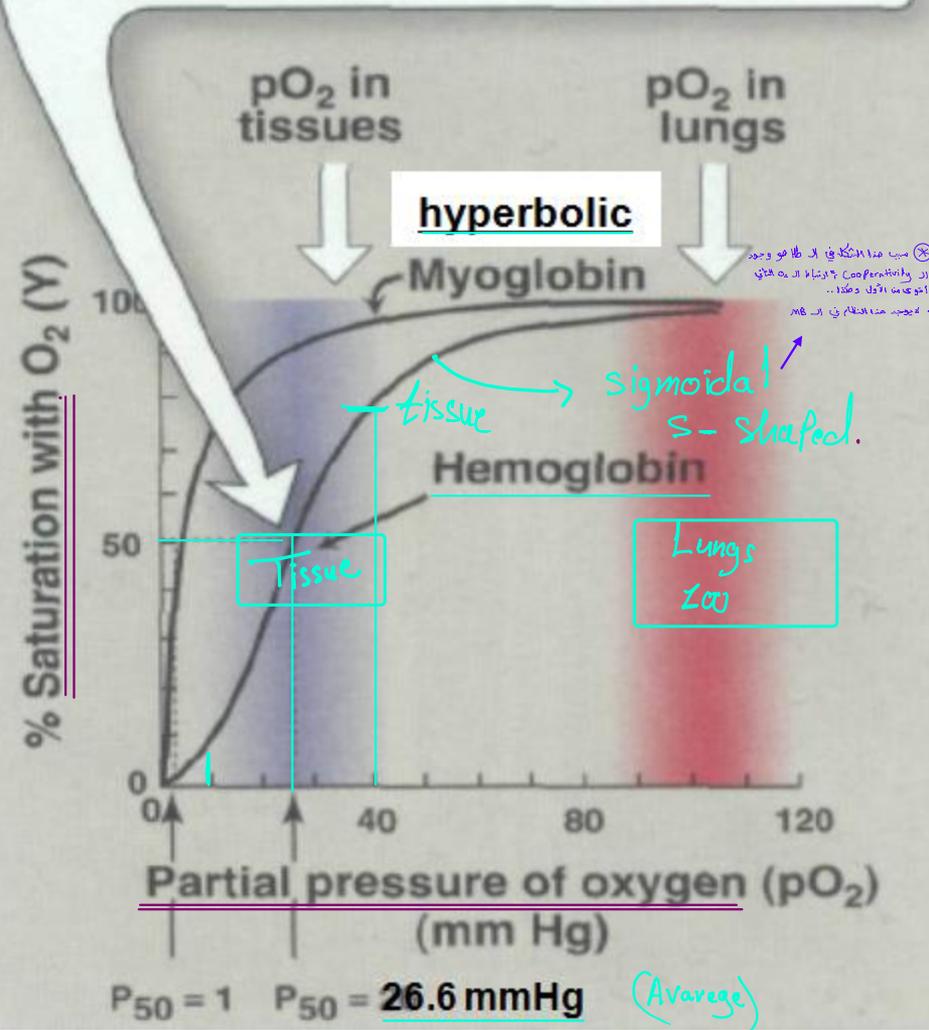


Oxygen dissociation curve

<u>pO₂ (mmHg)</u>	<u>% saturation of Hb</u>
100 in alveoli	<u>100%</u>
40 in resting muscle	<u>75%</u> (unloading) thus it deliver <u>25%</u> 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% (90% unloading)

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 pO₂.



P50

- P50 is the partial pressure of O₂ at which 50% of Hb is saturated with O₂.
- 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 pO₂ 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 MbO₂ and deoxygenated (Mb) myoglobin exist in a simple equilibrium:
- **Mb + O₂ ↔ MbO₂** *No - COOPeration*
- The equilibrium is shifted to the right or to the left as oxygen is added to or removed from the system.

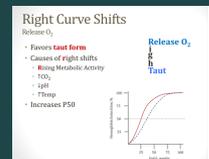
Agents that affect oxygen binding

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

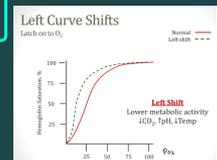
- The binding of 2,3-BPG to Hb promotes the release of O₂
- The presence of 2,3-BPG significantly reduces the affinity of hemoglobin for oxygen
- High levels of 2,3-DPG shift the curve to the right, while low levels of 2,3-DPG cause a leftward shift
- This reduced affinity enables hemoglobin to release oxygen efficiently at the partial pressures found in the tissues
- Hemoglobin stripped of BPG is saturated with O₂ at low pO₂ of only 20 mmHg , and it cannot release its oxygen within tissues, where the pO₂ is typically 40 mmHg.

Any Agent ↓

بوجود 2,3-BPG، يسهل الهيموغلوبين مرتفع الألفة جدا للأوكسجين،
فإنه ينجح بسرعة حتى عند PO₂ منخفضة، لكنه يفشل في تحرير الأوكسجين للأنسجة



- **Reduced** Hb-O₂ affinity----- shift the curve to **right**; while **Increase** Hb-O₂ 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 CO₂

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

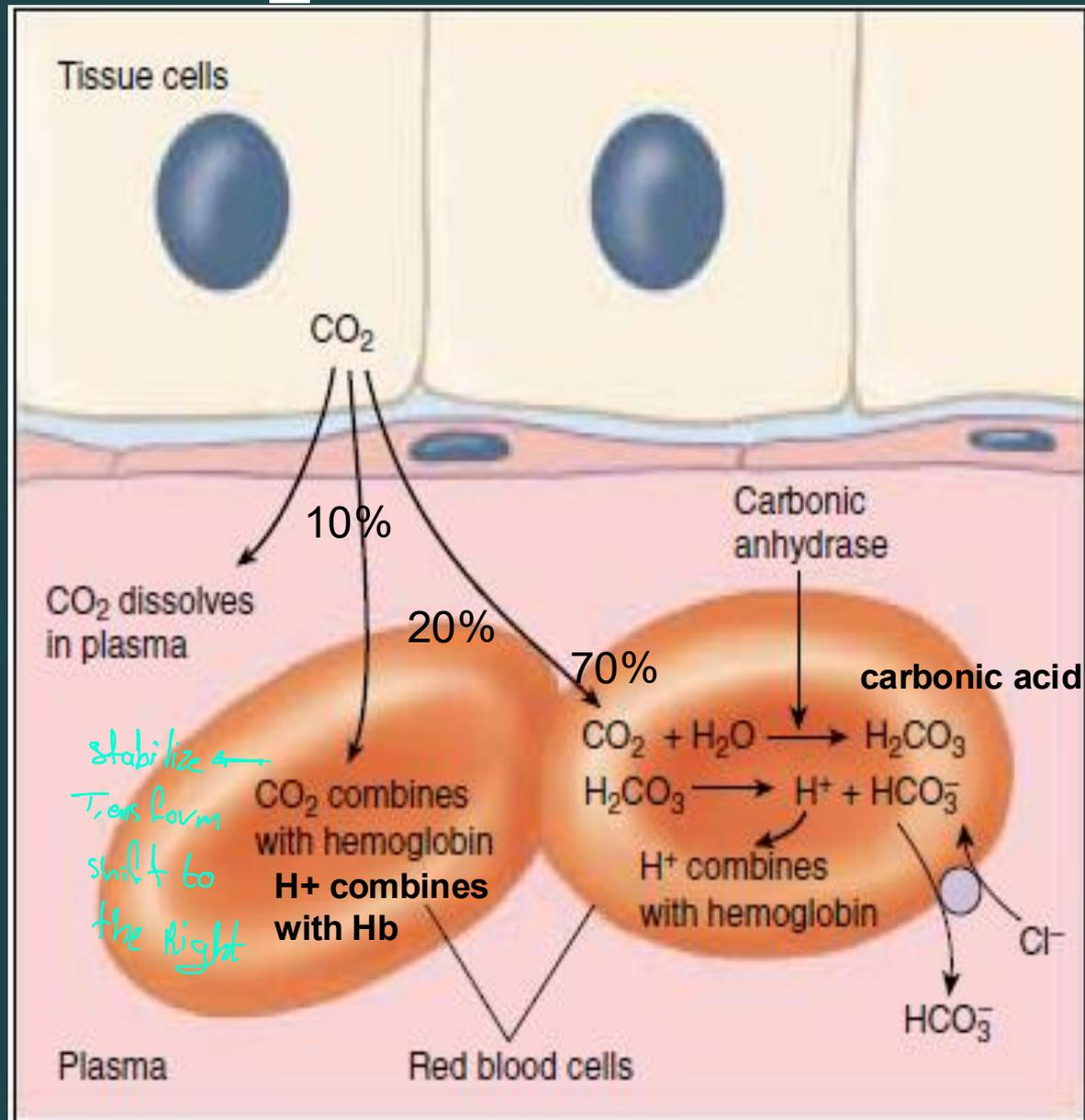
A. Formation of carbamino- hemoglobin

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



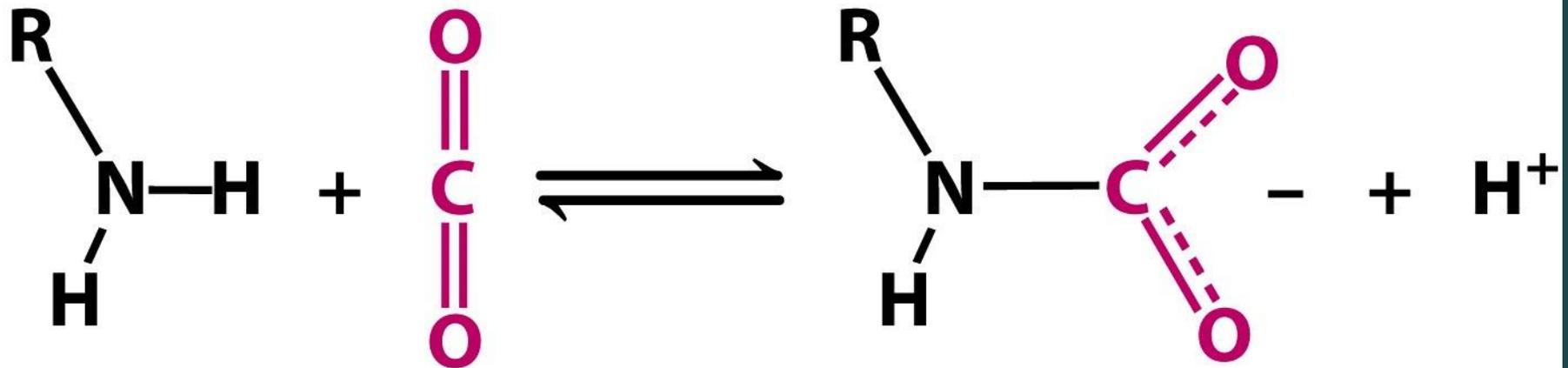
- The binding of CO₂ stabilizes the T (taut) or deoxyhemoglobin, resulting in a decrease in its affinity for oxygen.
- Hemoglobin resists oxygenation because the deoxy form is stabilized by specific hydrogen bonds and salt bridges (ion-pair bonds).

Transport of CO₂ by the blood



Carbamino (Carbamate) formation

⊗ Covalent binding at the N-terminus of each subunit



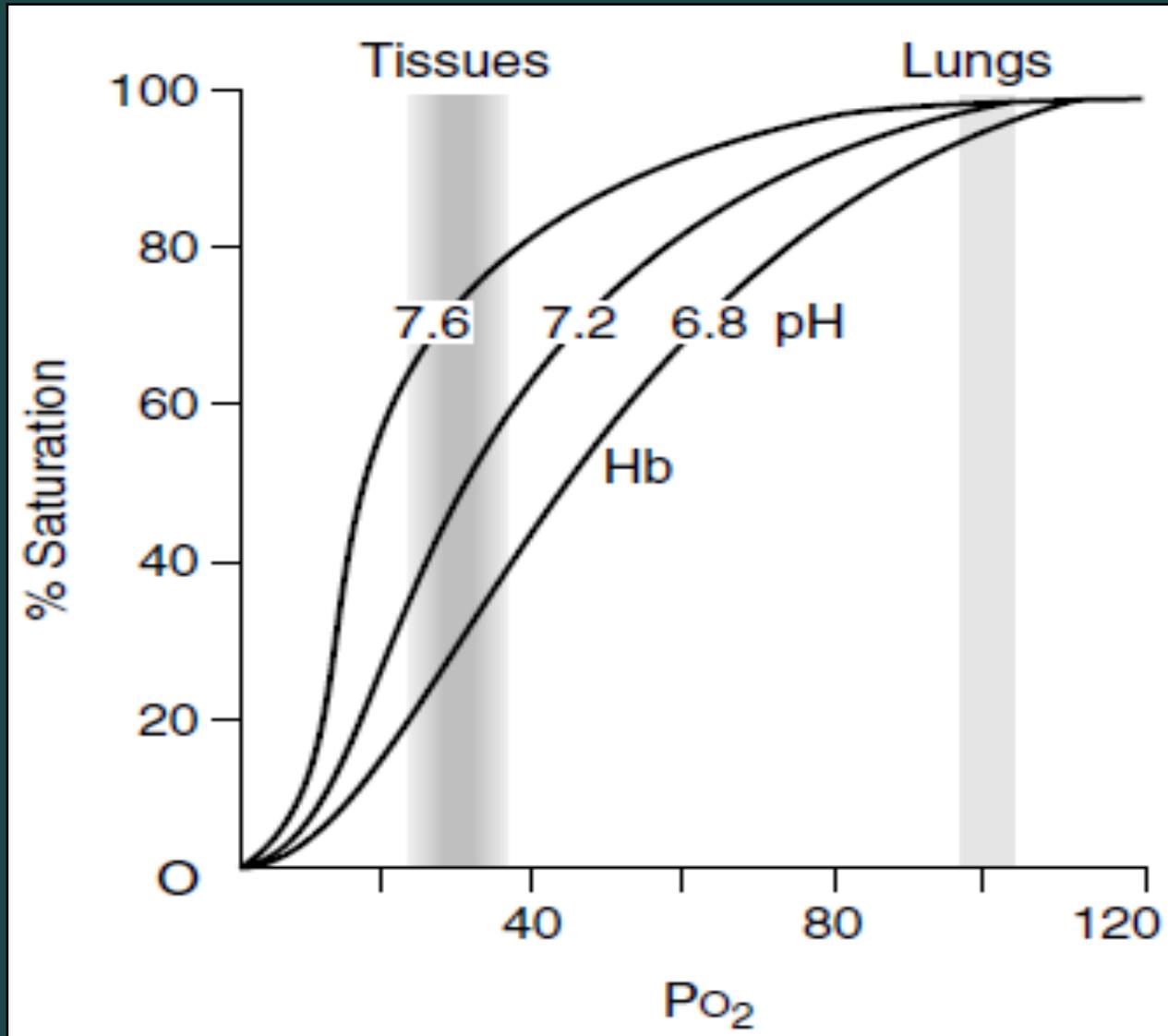
Carbamate

- **B- Bohr effect**

- The effect of CO₂ and pH on O₂ dissociation curve is known as Boher effect
- Raising the pH or lowering the concentration of CO₂ 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 CO₂ produced by metabolism stimulating oxygen release from hemoglobin.

[pH↑, CO₂↓, O₂↑]

Bohr effect



3. Temperature

[Temp ↑ , CO₂ ↑ , PH ↓]

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).

- Myoglobin
- as an oxygen storage protein, has a greater affinity for O₂ than hemoglobin at all oxygen pressures.
- Hemoglobin, as the oxygen carrier, becomes saturated with O₂ in the lungs, where the partial pressure of O₂ (pO_2) is about 100 torr. In the capillaries of tissues, pO_2 is typically 40 torr so oxygen is released from Hb.

في الرئتين... الهيموغلوبين يلتقط الأوكسجين (يتشبع).
في الشعيرات الدموية (الأنسجة)... الهيموغلوبين يحرر الأوكسجين (يتخفف تشبعه)

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 PO₂ of atmospheric air is $0.21 \times 760 \text{ mmHg} = \boxed{160 \text{ mmHg at sea level.}}$

Partial
Pressure of
O₂.