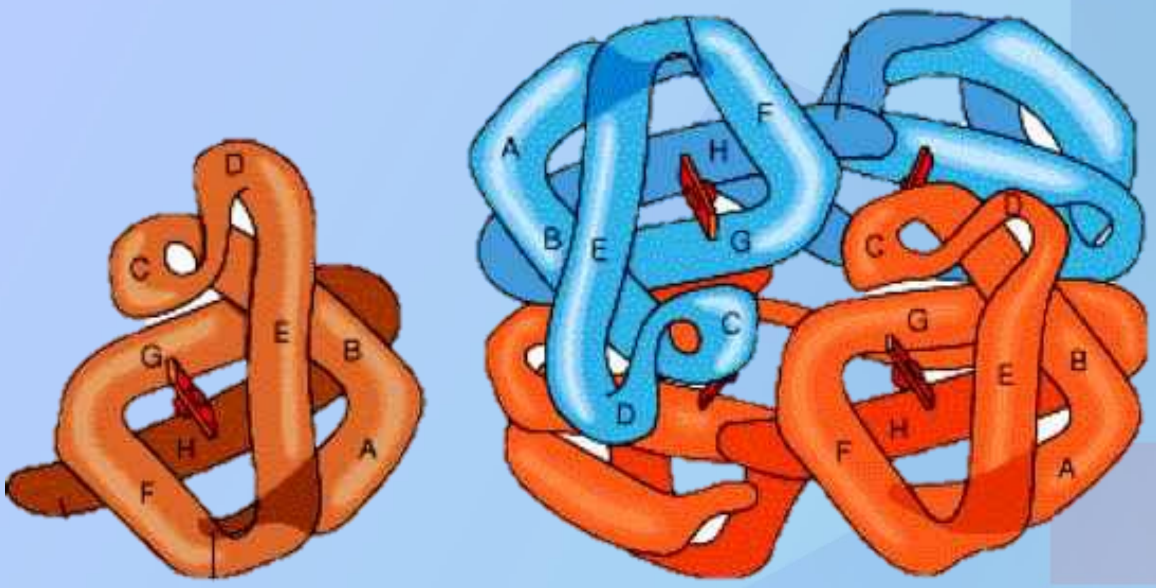
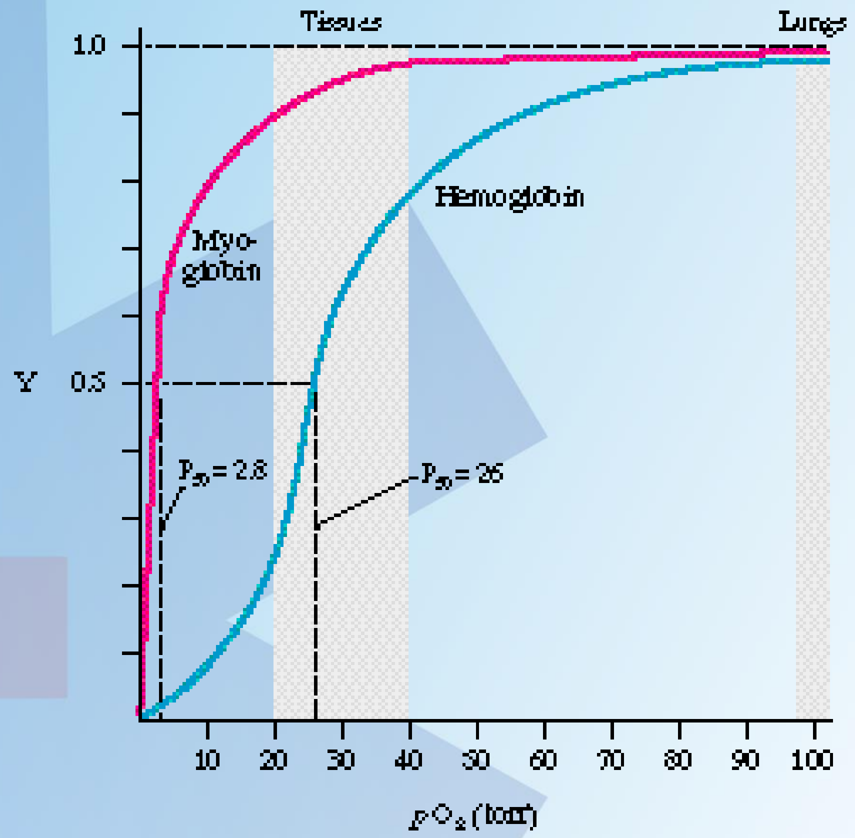




Myoglobin + Haemoglobin

Saturation Curve

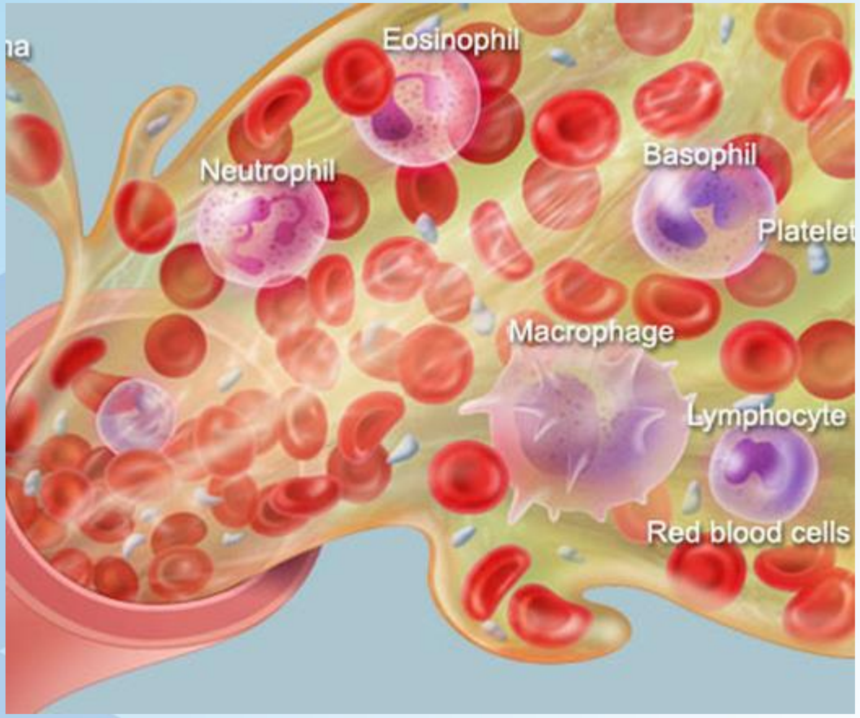
OXYGEN

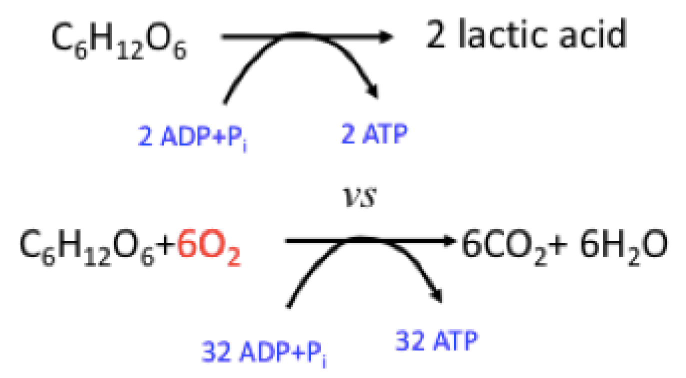
- At complete rest, a male requires:

  375L O_2/day (= 1900L air/day)

Why do we need oxygen?

- But! O_2 is not very soluble in blood





Need O_2, but it doesn't dissolve in blood?!

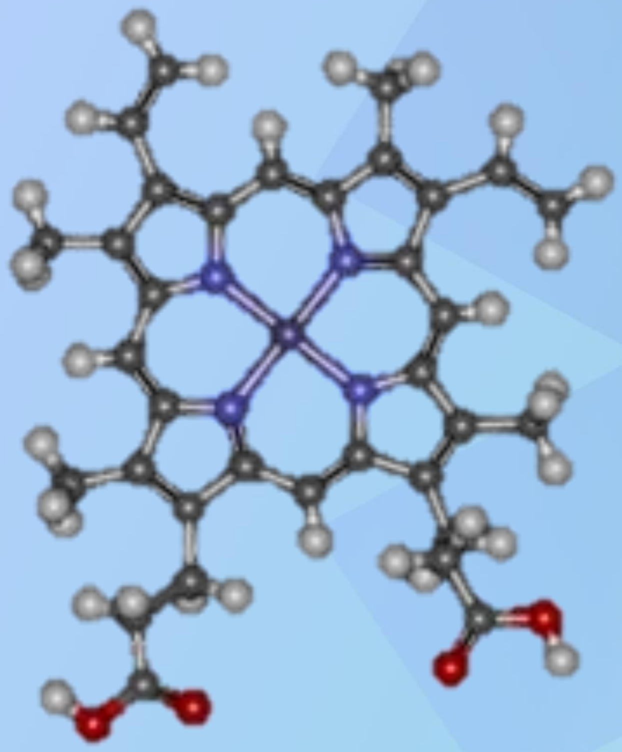
NEED

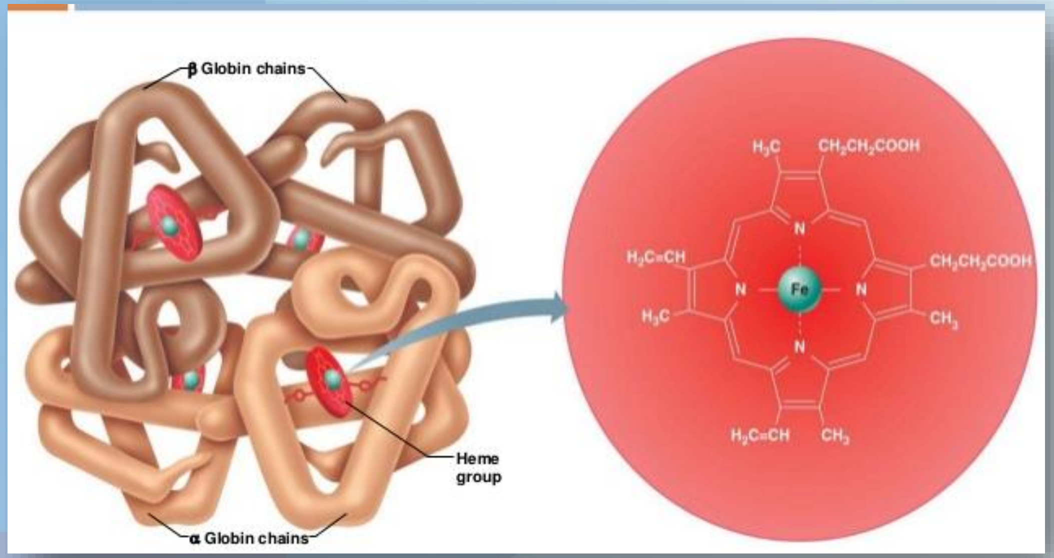
- Oxygen carrier

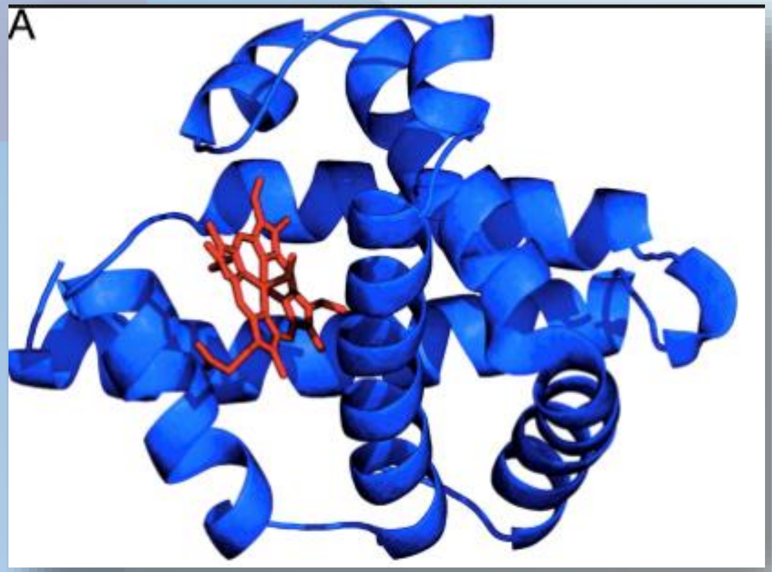
SOLUTION

- Use metal complex to bind O_2
- Must be reversible process

SOLUTION: Heme







Concept review

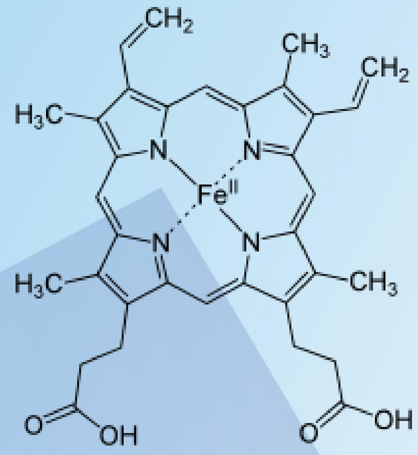
- **Protein-ligand interaction**
  - Reversible
  - Specific
  - Confirmational change upon binding = induced fit
  - If multisubunit protein → confirmational change → allosteric effect

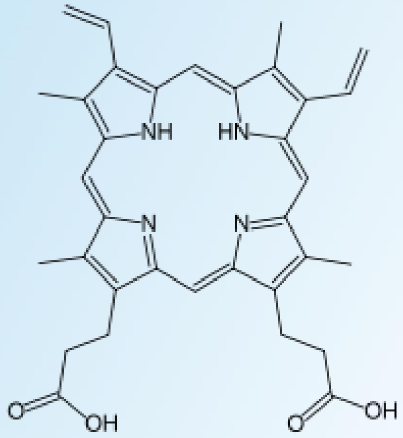
In the body: **O2** = *ligand*. **Myoglobin or hemoglobin** = *protein.*

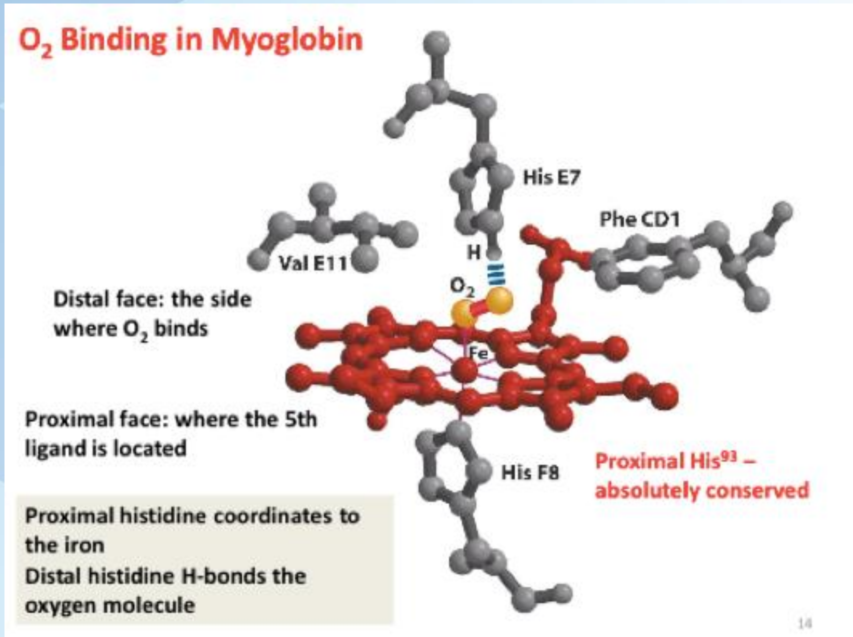
Heme

- Chelation of **Protoporphyrin IX** and **Fe^{2+}**

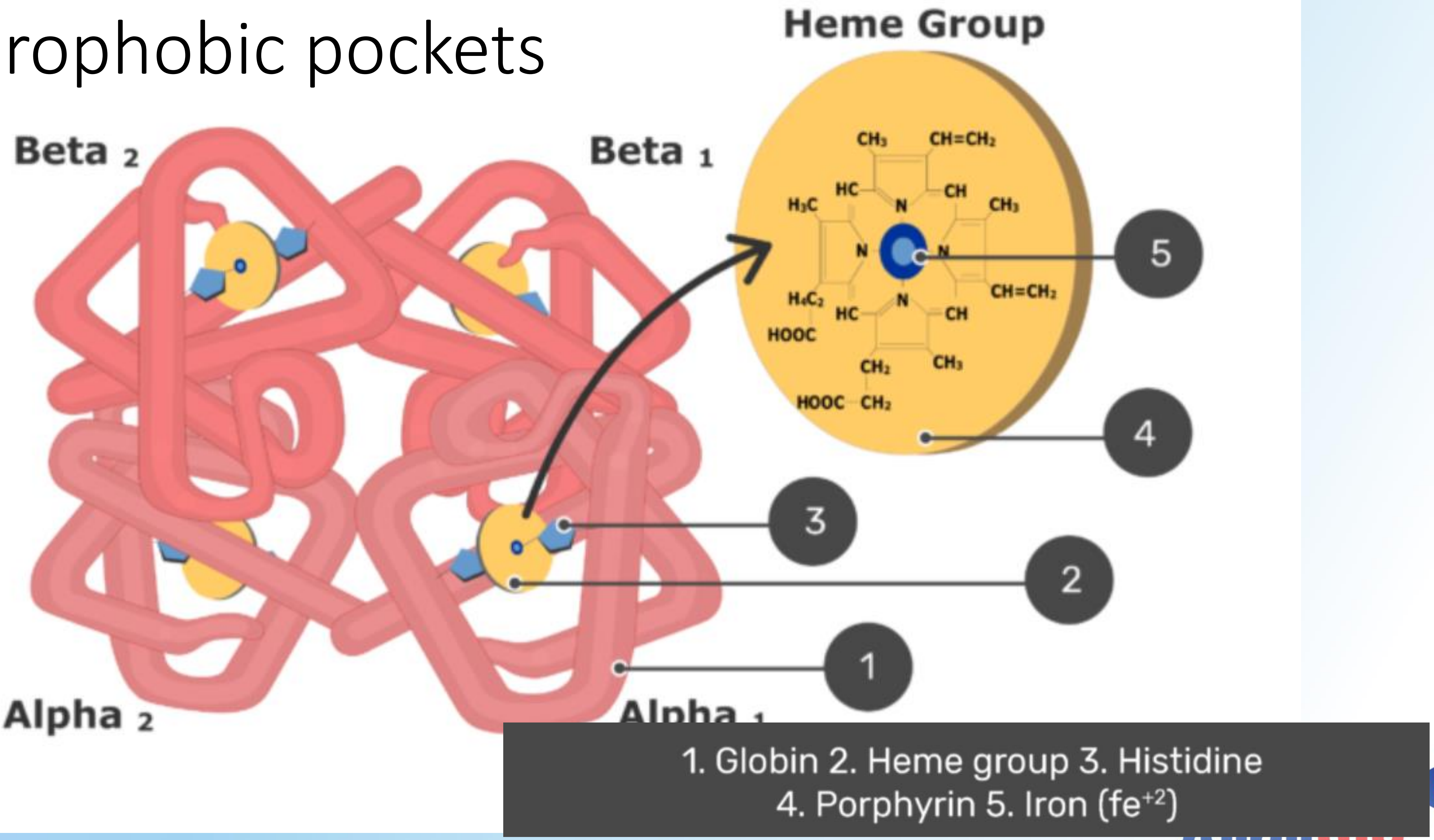
- *Fe* in center of heme by bonds of 4N of porphyrin ring
- Fe^{2+} can form 2 additional bonds
    - Histidine residue of globin molecule
    - O_2
- Prosthetic group
- In hemoglobin + myoglobin (+ cytochromes)







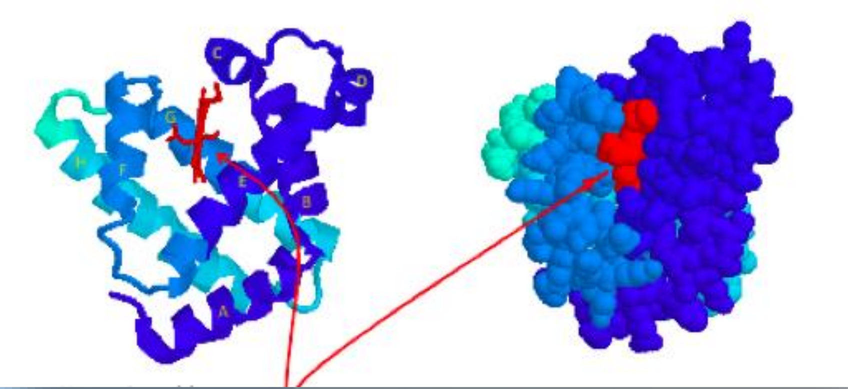
Hydrophobic pockets

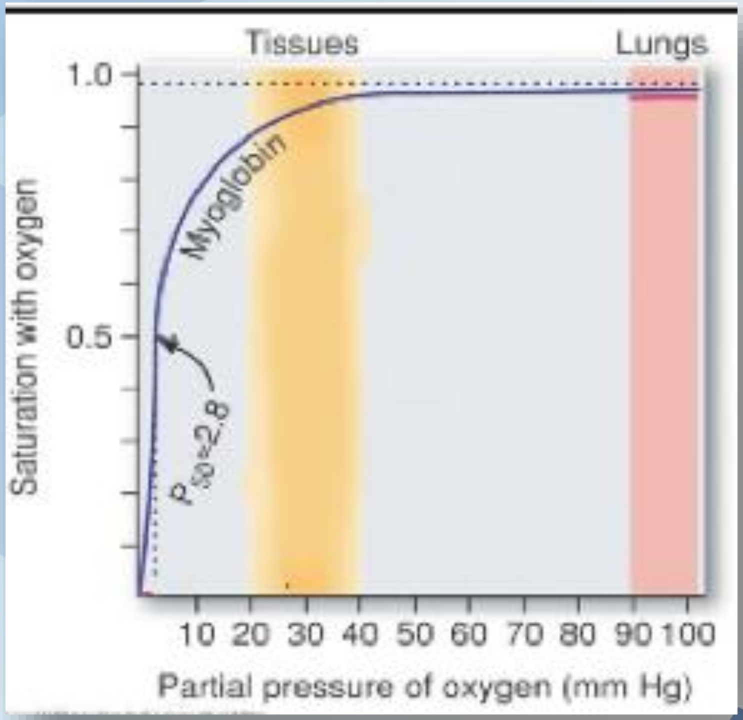


Myoglobin

- Heme protein in heart + skeletal muscle
- Function: Acts as reservoir for O_2
- 1 heme group = 1 O_2 binding site
- = 1 polypeptide chain

- Oxygen dissociation curve for myoglobin
  - **High affinity** for oxygen
  - **Hyperbolic**





- AFFINITY = 

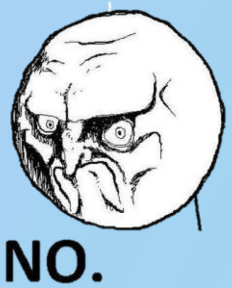
The higher the O_2 affinity the more tightly O_2 binds

QUESTION

1. Does Mb bind O_2 well?

Even at low PPO_2 – Mb is completely saturated

2. Is Mb a good candidate for O_2 transport through circulatory system?



Even at low PPO_2 – Mb is almost completely saturated

WANTED!

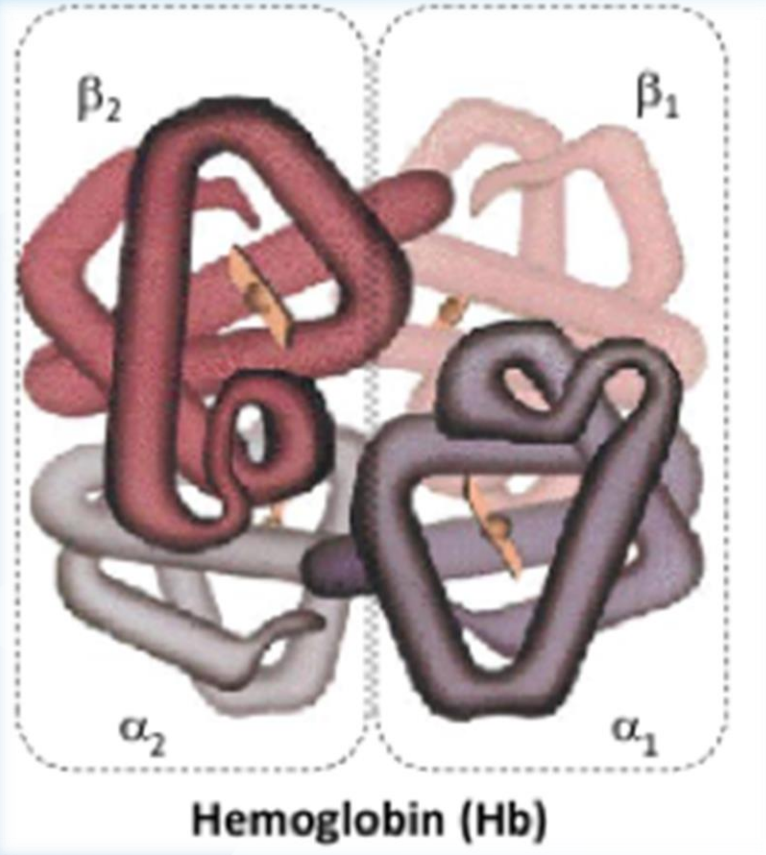
O_2-binding protein that

- Has HIGH affinity for O_2 when PPO_2 is HIGH (lungs)
- Has LOW affinity for O_2 when PPO_2 is LOW (tissues)
  - Release O_2 where it is needed

- A transporter that can alter its O_2-affinity depending on PPO_2

Hemoglobin

- 4 subunits = 4 polypeptides
  - 2 alpha chains
  - 2 beta chains
- 4 heme groups = 4 O_2 binding sites



100 ml of plasma dissolves **0,28mL of oxygen**

1g of Hgb binds **1,35mL of oxygen**

- 100 ml of blood = 12,5 – 17 g of Hgb
- THEREFORE 100ml of blood can transport approx **20mL of oxygen**

Why does **each heme** require **one polypeptide**?

- Globin protein keeps the iron in the reduced state
- Prevents O2 from reacting with the heme
- Minimizes the chance of other ligands binding = specificity

Hemoglobin Cooperation

- Between Hgb O_2 binding sites
- As O_2 is bound to one subunit, adjacent subunits' affinity for O_2 INCREASES
  - Binding the 1st O_2 makes binding of the 2nd O_2 easier…
  - …But also makes it harder to lose

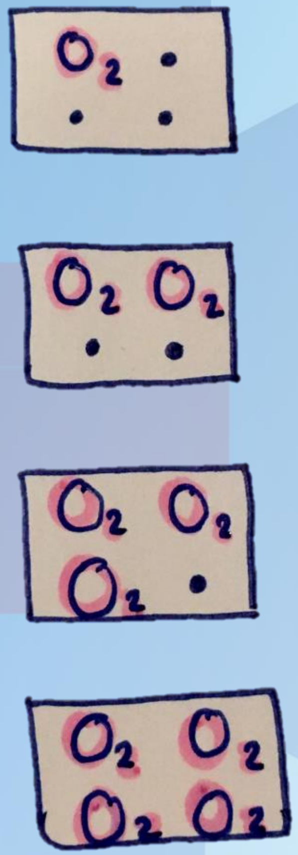
Saturation of Hgb with O_2

$K_1 : Hb_4(O_2) \Leftrightarrow Hb_4 + O_2$

$K_2 : Hb_4(O_2)_2 \Leftrightarrow Hb_4(O_2) + O_2$

$K_3 : Hb_4(O_2)_3 \Leftrightarrow Hb_4(O_2)_2 + O_2$

$K_4 : Hb_4(O_2)_4 \Leftrightarrow Hb_4(O_2)_3 + O_2$



Affinity for K_4 Hgb is ≈ 300 times greater than K_1

TISSUES

Less tightly bound

INCREASE affinity for O_2
(increase strength of O_2 binding)

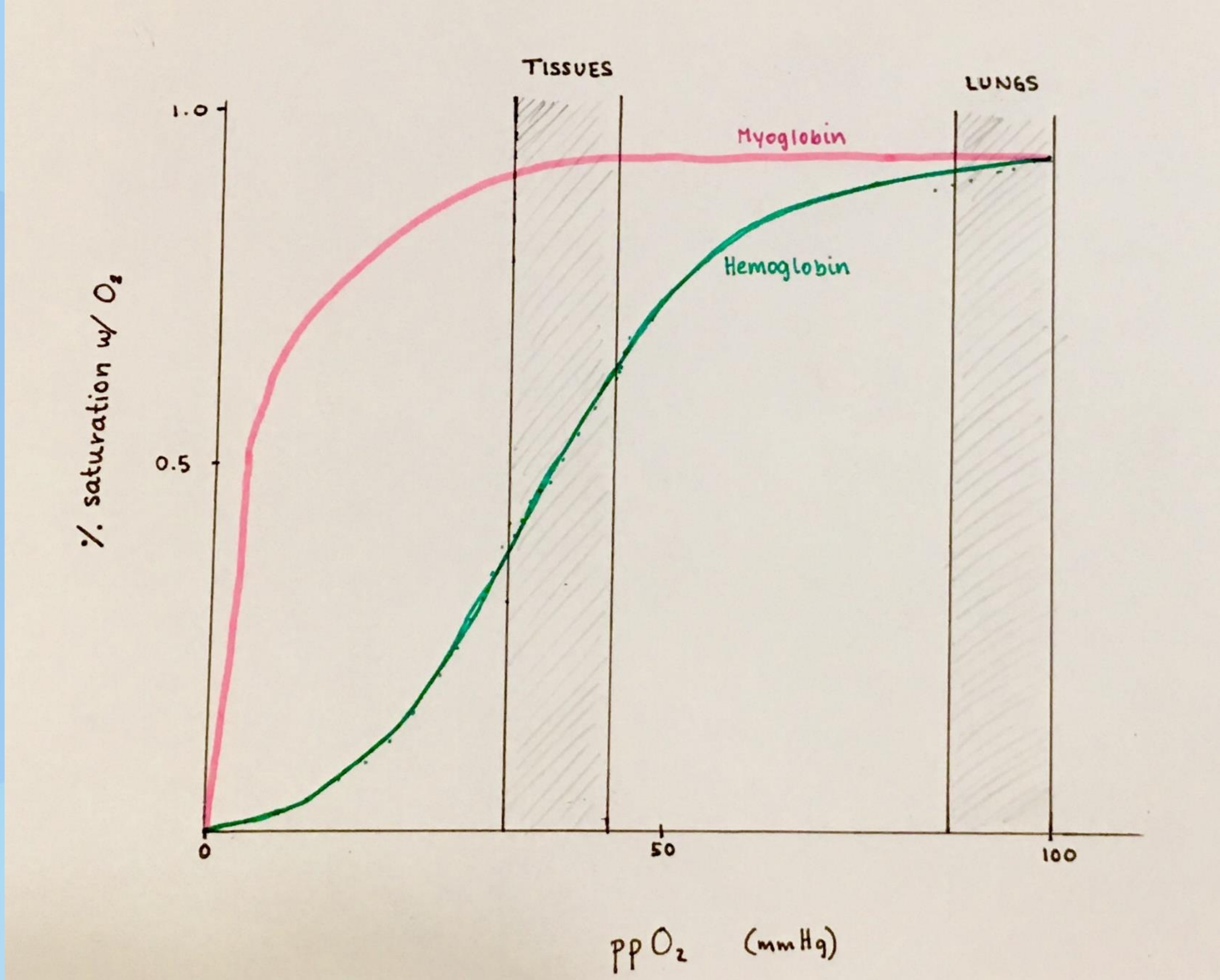
More tightly bound

LUNGS

OXYGEN DISSOCIATION CURVE FOR MYOGLOBIN + HEMOGLOBIN

- **Oxygen dissociation curve for hemoglobin**
  - Lower affinity for oxygen
  - Sigmoid

Molecular level?



Hill coefficient

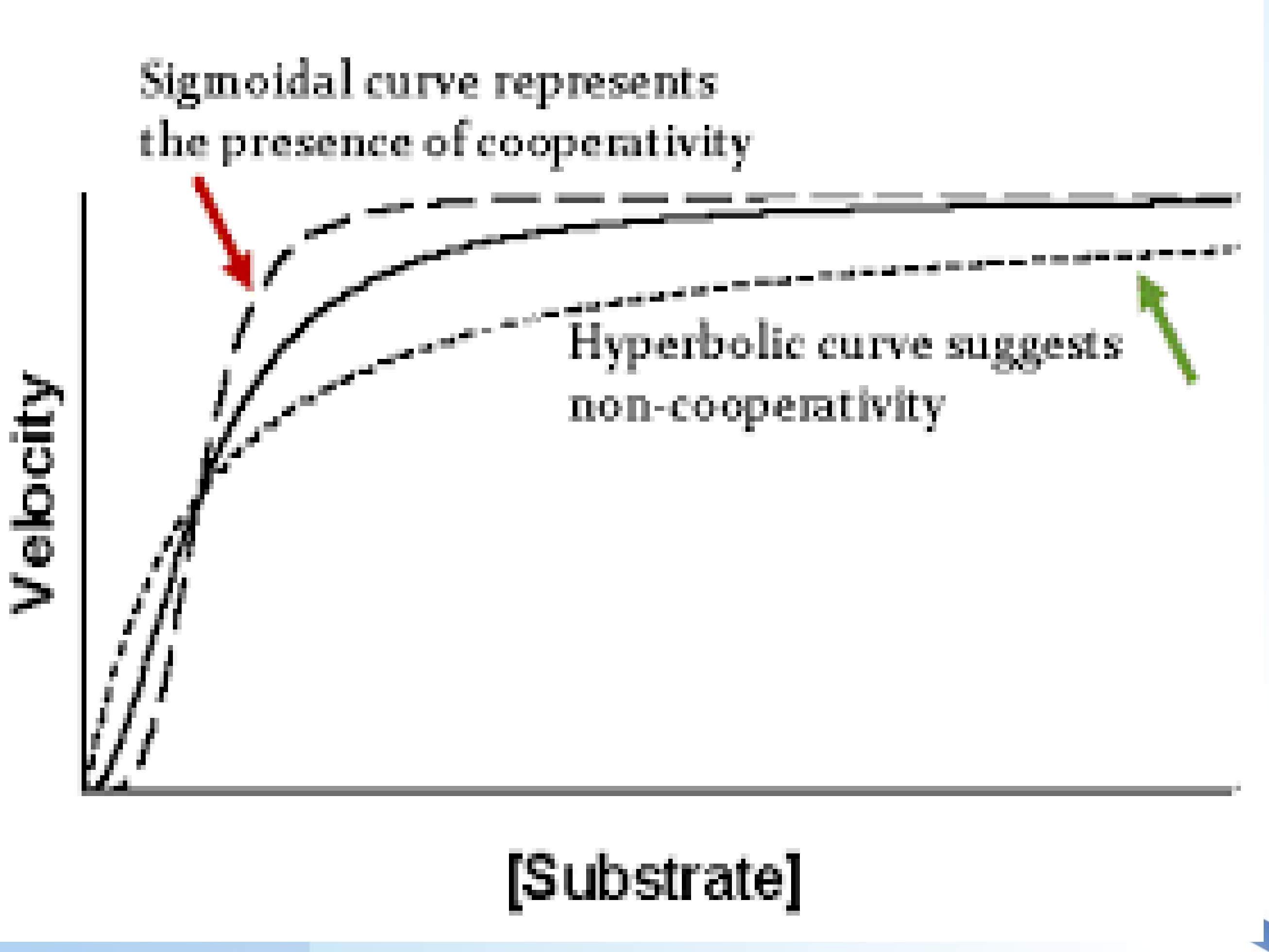
Equation used to determining the degree of cooperativeness of ligand-protein interaction

Myoglobin:

Hill coefficient = 1

Hemoglobin:

Hill coefficient = 2.8



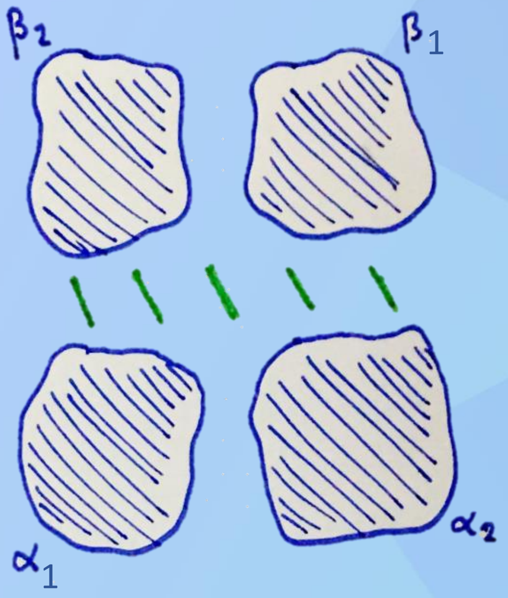
Questions?

Next part: saturation curves

R – Respiration.
T – Tissue.

T form

Deoxyhemoglobin

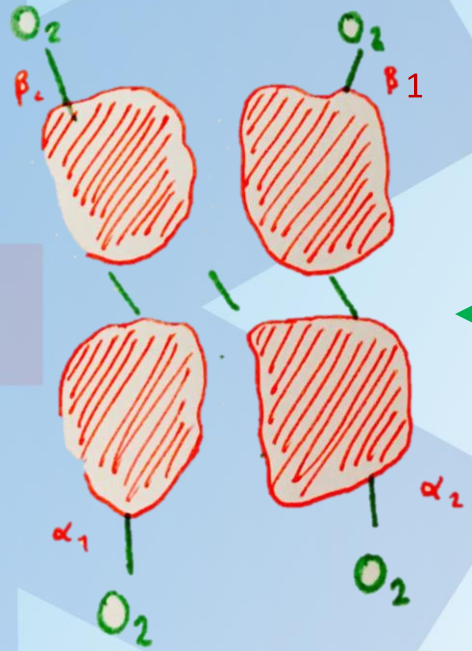


LOW affinity to O_2

(Easier **to unload O_2**)

R form

Oxyhemoglobin



Some ionic + H bonds between alpha-beta dimers are broken in oxygenated form

HIGH affinity to O_2

(Harder **to unload O_2**)

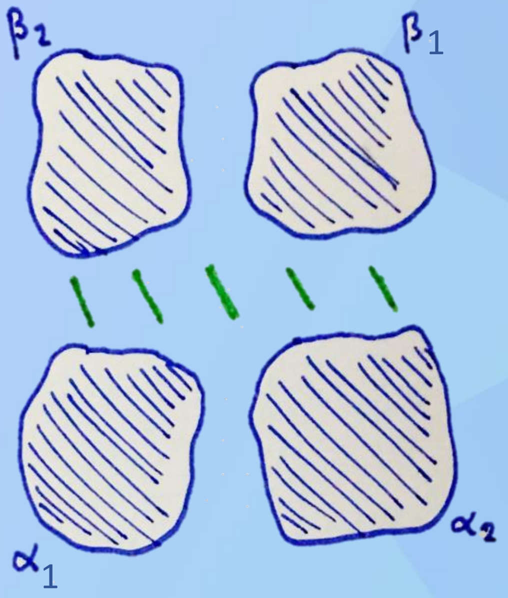
Allosteric Effectors

*Affect **Hemoglobin** O_2 binding; NOT **Myoglobin** O_2 binding*

- pO_2
- pH or $[H^+]$
- pCO_2
- Temperature
- 2,3-BPG
  - Enables Hgb to release O_2 efficiently at lower pO_2
  - DECREASES O_2 affinity of Hgb
  - Binds only to T state (deoxyHgb)
  - Conc. increases in high altitudes
  - Always associate it with babies = HgF → **need higher affinity for mom's venous blood → binds LESS 2,3-BPG**

T form

Deoxyhemoglobin

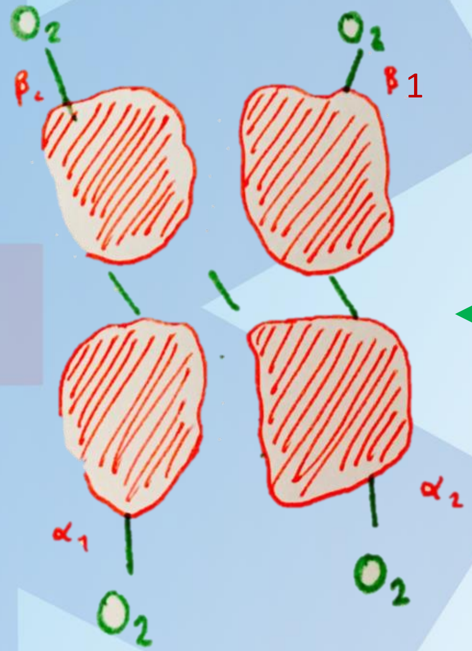


O_2 *CO*

H^+, CO_2, 2,3-BPG

R form

Oxyhemoglobin



Some ionic + H bonds between alpha-beta dimers are broken in oxygenated form

LOW affinity to O_2

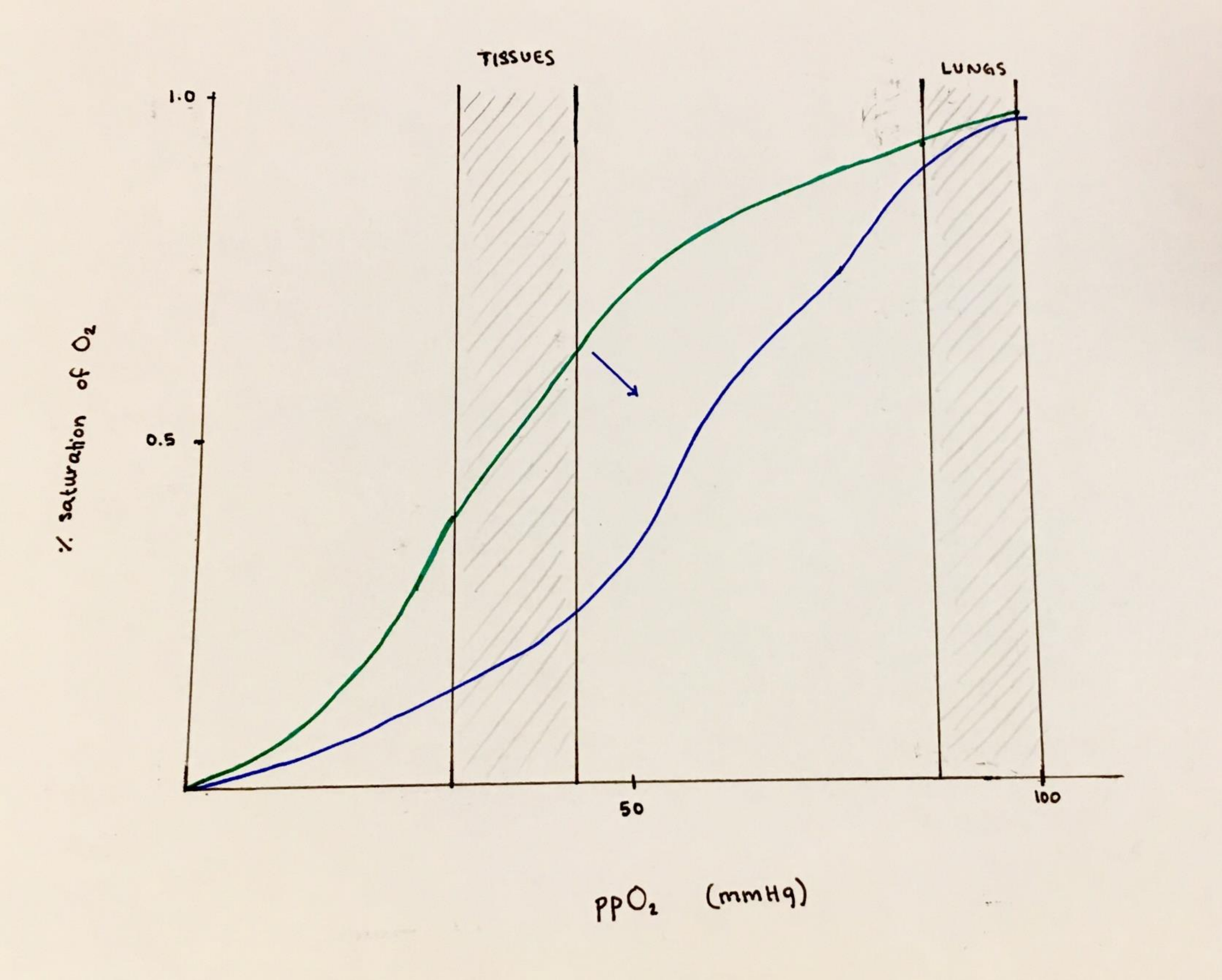
(Easier **to unload O_2**)

HIGH affinity to O_2

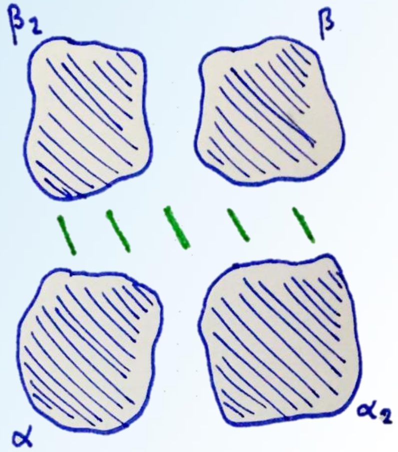
(Harder **to unload O_2**)

studyaid

DECREASE O_2 affinity



T form



OXYGEN DISSOCIATION CURVE FOR HEMOGLOBIN

- Shift to **RIGHT**
- **↓O_2 affinity**
  - ↑ temp
  - ↑CO_2
  - ↑ $[H^+]$ **(↓pH)**
  - ↑2,3-BPG
- Favors T form

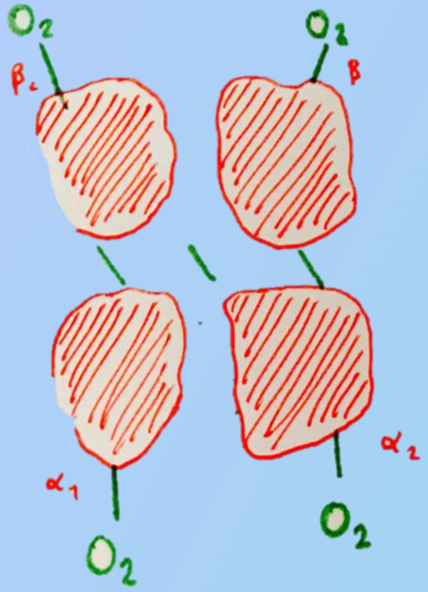
OXYGEN DISSOCIATION CURVE FOR HEMOGLOBIN

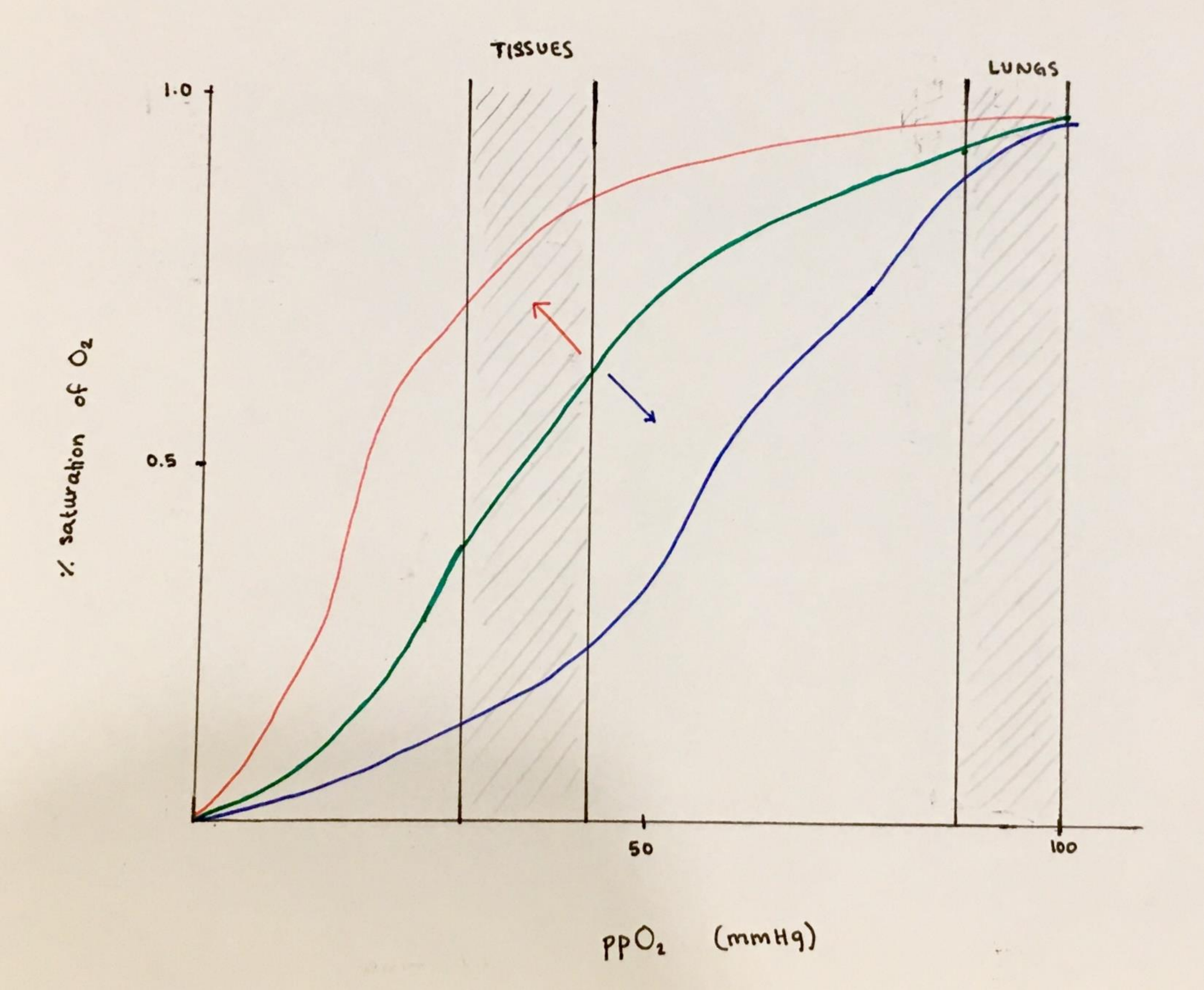
- Shift to **LEFT**
- **↑O_2 affinity**
  - ↓ temp
  - ↓ CO_2
  - ↓ $[H^+]$ (↑ pH)
  - ↓ 2,3-BPG
- Favors **R Form**

studyaid

INCREASE O_2 affinity

R form





Bohr Effect

- NOT in myoglobin
- Lungs: HIGHER pH
- Tissues: LOWER pH
  - Higher CO_2 + H^+ conc. in metabolically active tissues
- Favors unloading of O_2 in peripheral tissues and loading of O_2 in lungs

- FACILITATE unloading of O_2 by oxyhemoglobin (R) → stabilize doexyhemoglobin (T)

UWAGA

	Hemoglobin	Myoglobin
Heme groups (O_2 binding sites)	4	1
Location	Only in Red Blood Cells	Skeletal + cardiac muscle
Affinity	Lower affinity for O_2	Higher affinity at ALL partial pressures of O_2 values
O2 Saturation curve	Sigmoidal shape	Hyperbolic shape
Cooperation	YES	NO