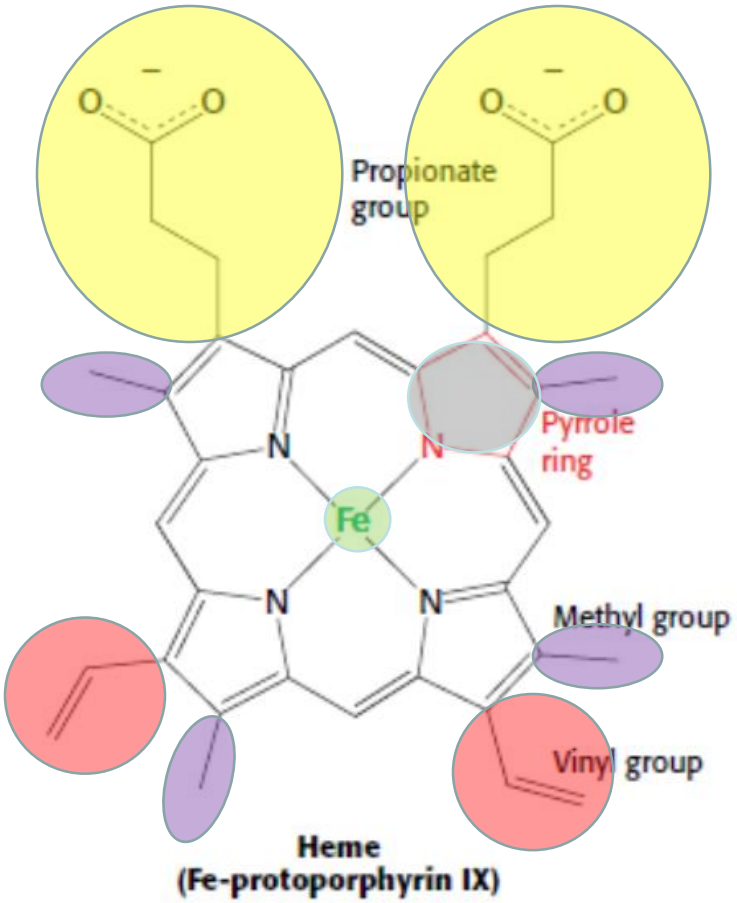
IRON

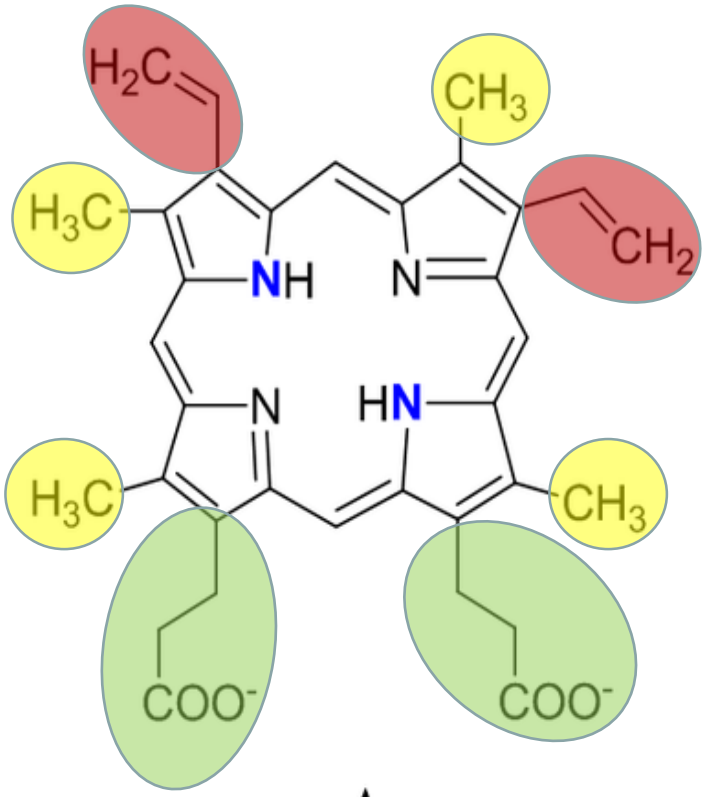
Distribution of the major iron-containing proteins in an adult human

protein	molecular mass of the protein (kDa)	amount of iron (g)	% of total body iron	type of iron: heme (*h*) or non-heme (*nh*)	number of iron atoms per molecule	function	mentioned in Section
hemoglobin	64.5	2.60	65	*h*	4	O_2 transport in blood	5.2
myoglobin	17.8	0.13	6	*h*	1	O_2 storage in muscle	5.2
transferrin	76	0.007	0.2	*nh*	2	iron transport	8.4.1
ferritin	444	0.52	13	*nh*	up to 4500	iron storage in cells	8.4.2
hemosiderin		0.48	12	*nh*		iron storage	8.4.3
catalase	260	0.004	0.1	*h*	4	metabolism of H_2O_2	6.3
peroxidases	variable	small	small	*h*	1	metabolism of H_2O_2	6.3
cytochrome *c*	12.5	0.004	0.1	*h*	1	electron transfer	6.1
cytochrome *c* oxidase	>100	<0.02	<0.5	*h*	2	terminal oxidation ($O_2 \rightarrow H_2O$)	10.4
flavoprotein oxygenases (e.g. P-450 system)	about 50	small	small	*h*	1	incorporation of molecular oxygen	6.2
iron–sulfur proteins	variable	about 0.04	about 1	*nh*	2-8	electron transfer	7.1-7.4
ribonucleotide reductase	260 (*E. coli*)	small	small	*nh*	4	transformation of ribonucleic acids to deoxyribonucleic acids	7.6

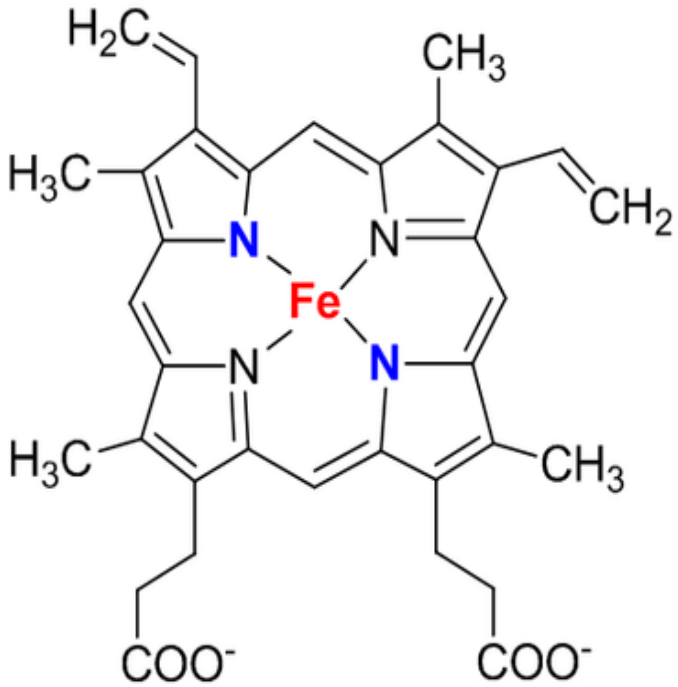


Heme
(Fe-protoporphyrin IX)

Heme
(Fe-protoporphyrin IX)



A

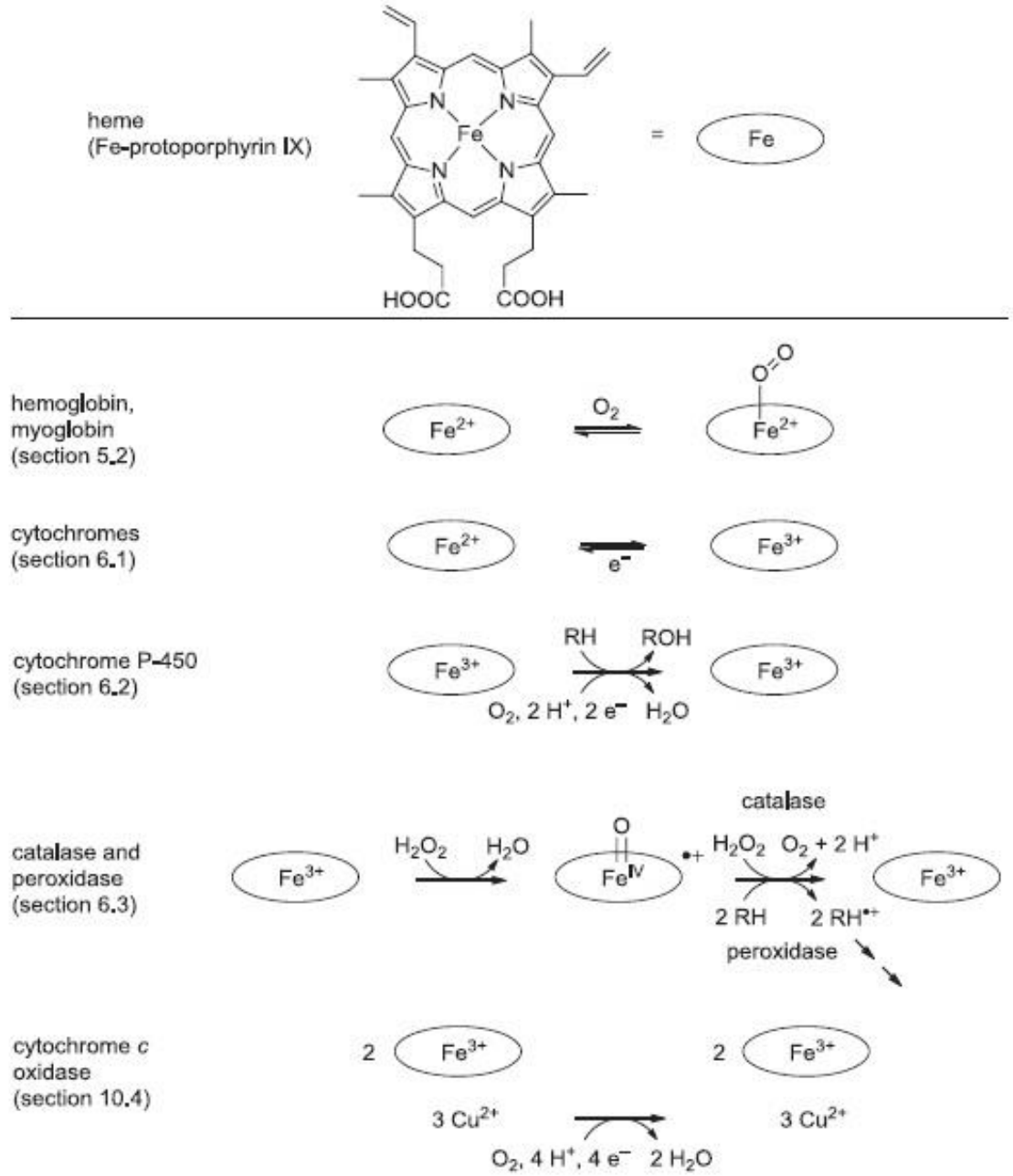


B

Protoporphyrin IX

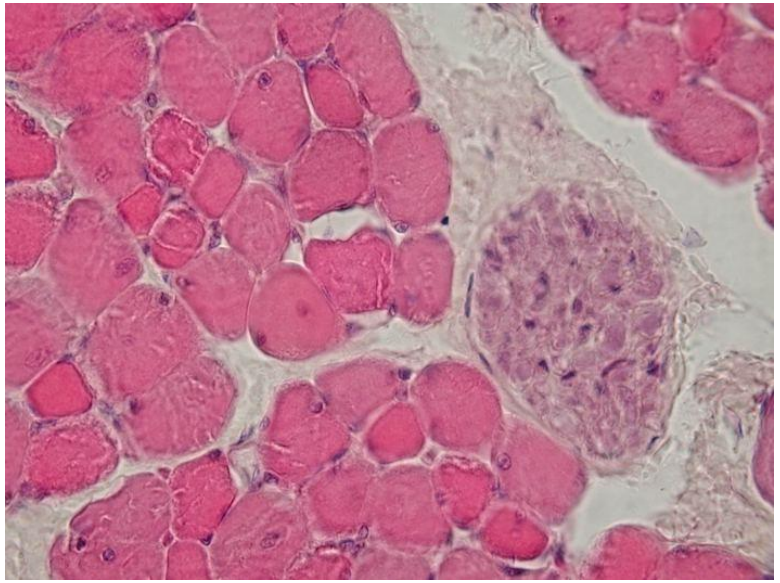
Heme

Type Heme Iron Proteins

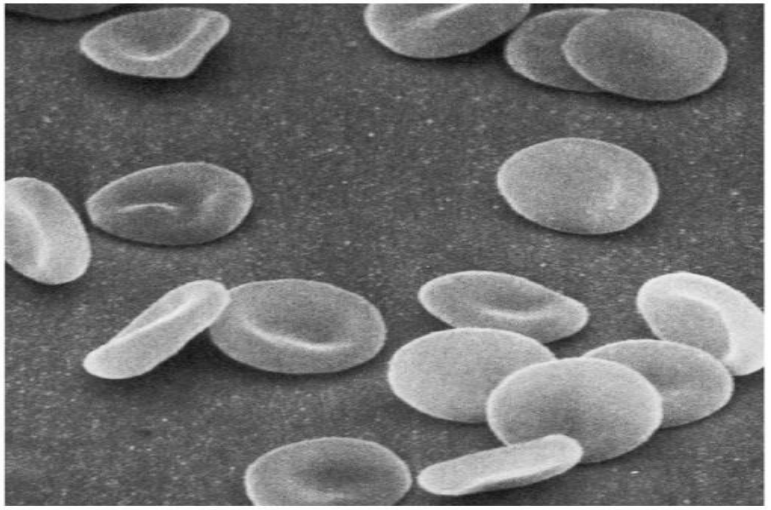


Myoglobin and Hemoglobin

- Reversibly bind oxygen
  - **Myoglobin** facilitates diffusion of oxygen in muscle
  - **Hemoglobin** transports oxygen in blood
- Both give tissues their red color

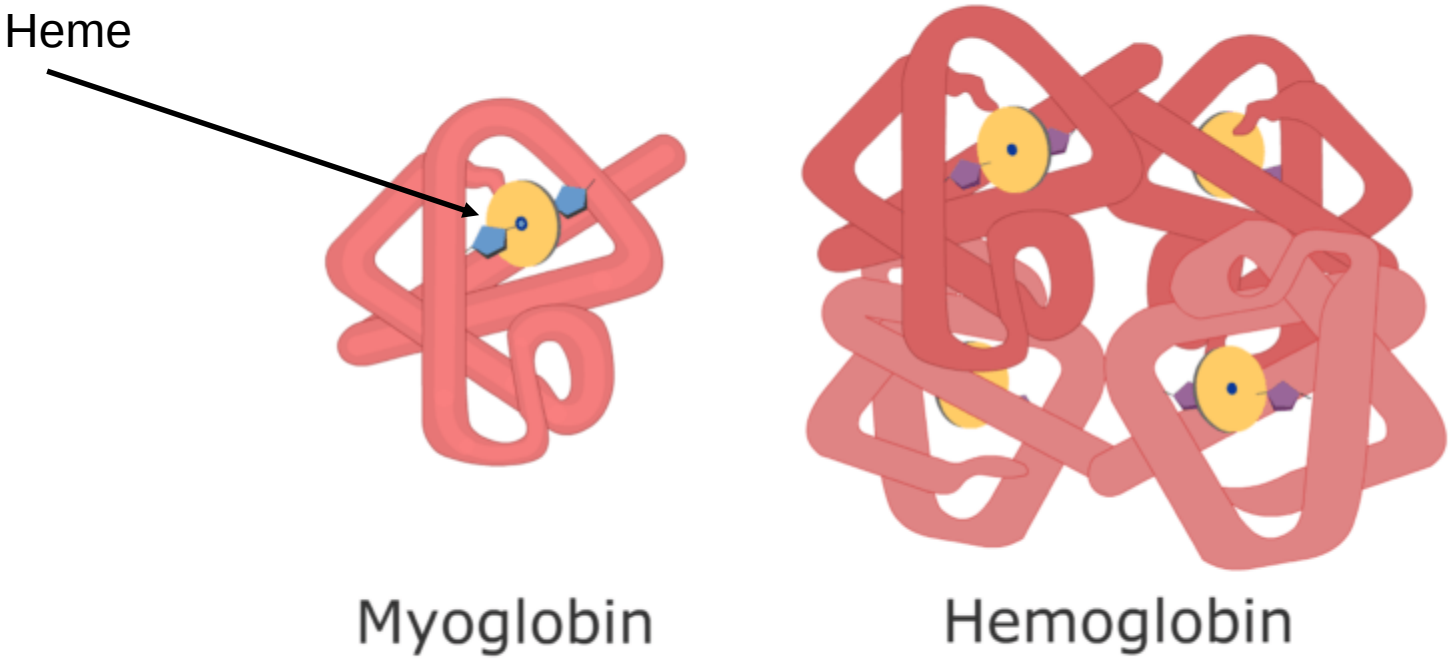


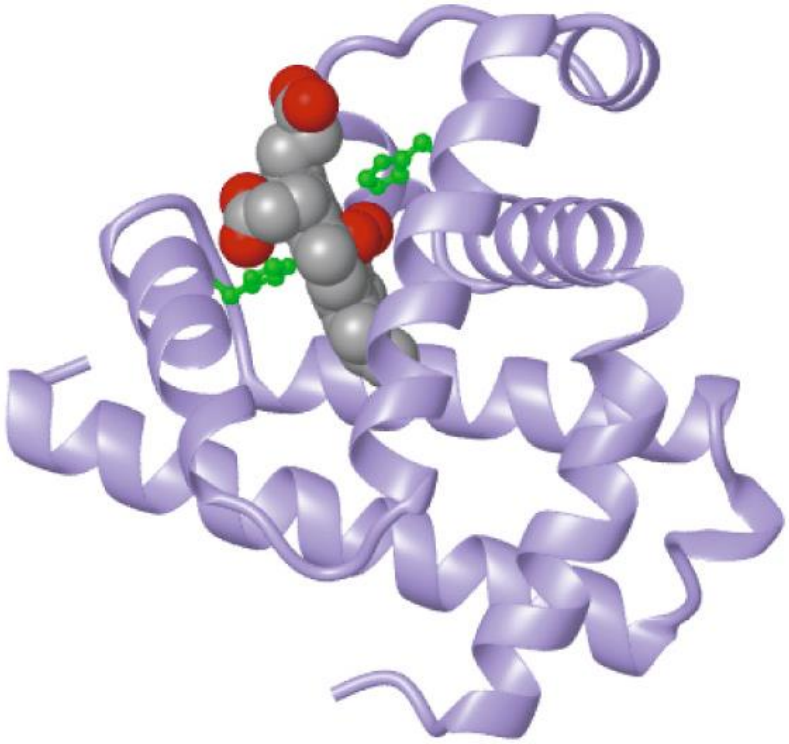
Muscle tissue



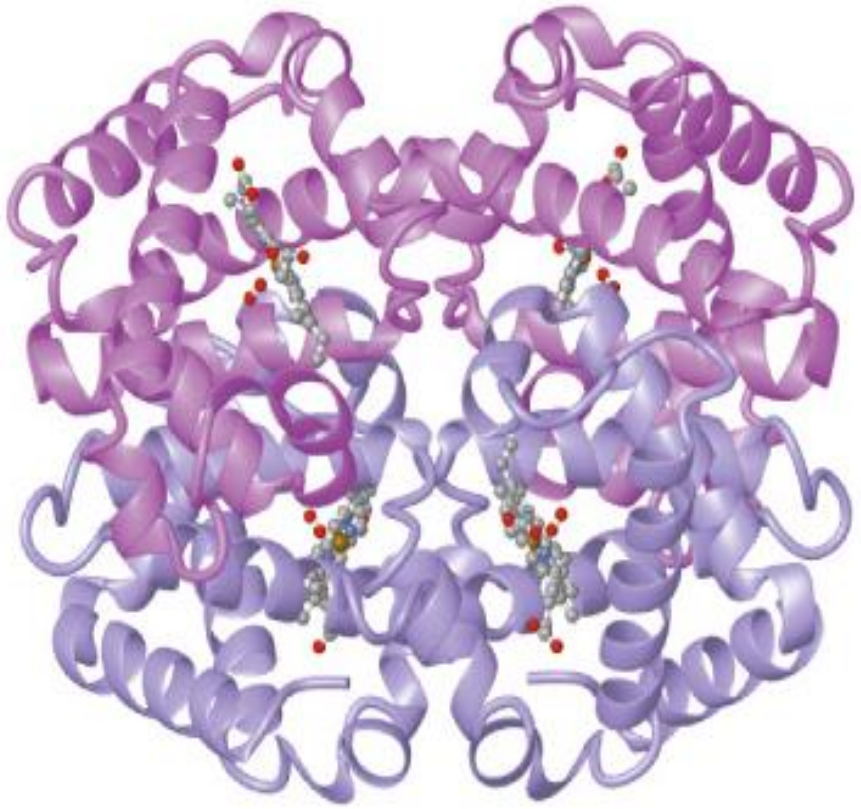
Red blood cells

Myoglobin is a monomer - Hemoglobin is a tetramer





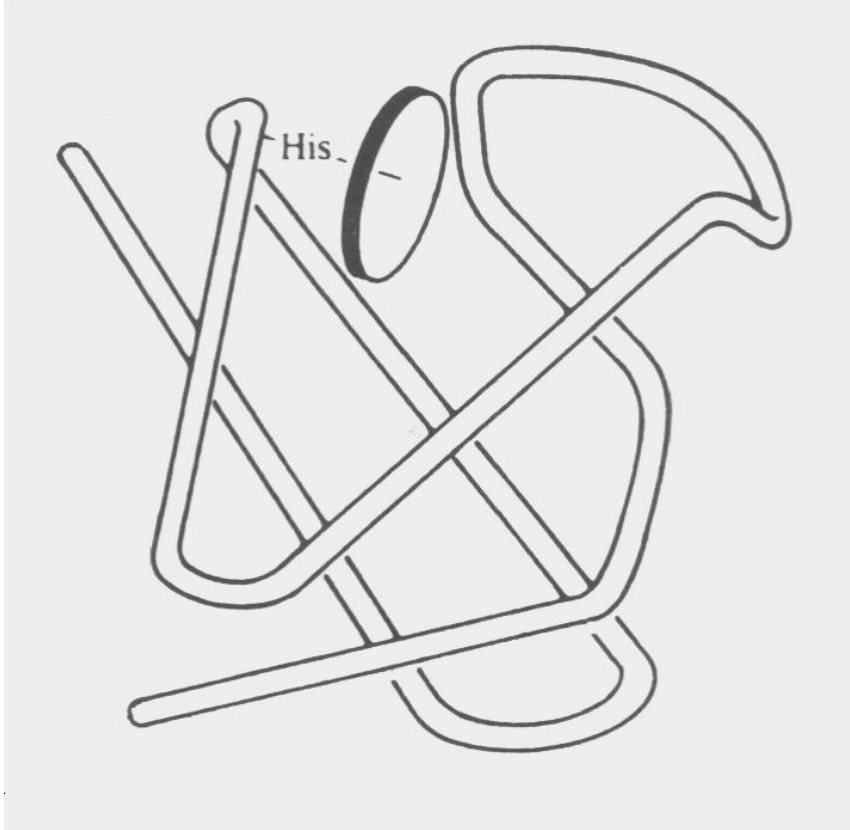
one heme group



four heme groups

La Mioglobina

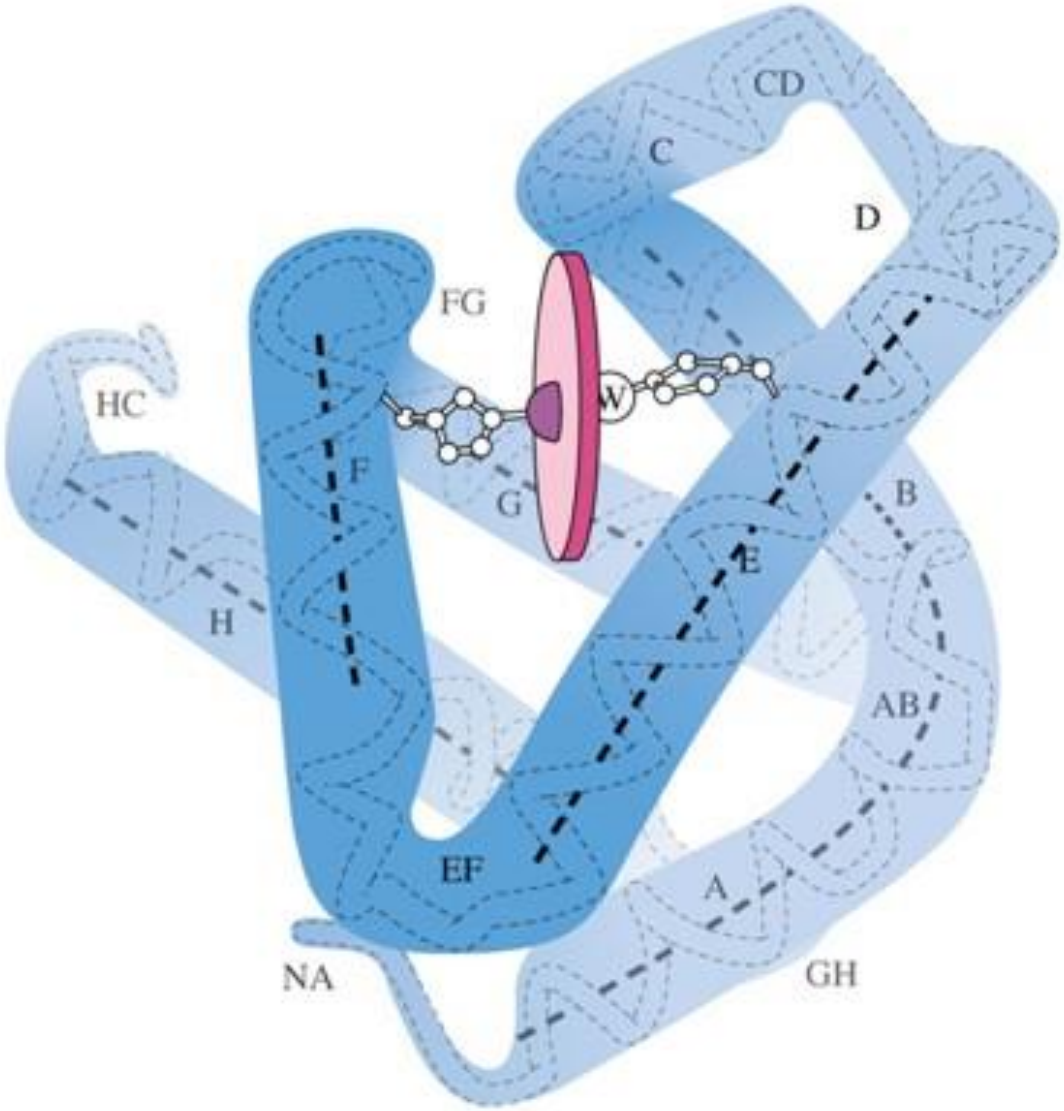
•La Mioglobina è una proteina presente nei muscoli, la cui funzione è proprio quella di “serbatoio” di ossigeno. La sua struttura secondaria comprende 8 porzioni di α-Elica.



•Al suo interno si trova un **gruppo Prostetico** (non costituito da amminoacidi) chiamato **Eme**, composto da una porfirina al cui centro si trova un atomo di Ferro ferroso (II) che è il vero e proprio sito di legame con l’ossigeno.

•Ogni Molecola di Mioglobina puo’ legare 1 molecola di Ossigeno.

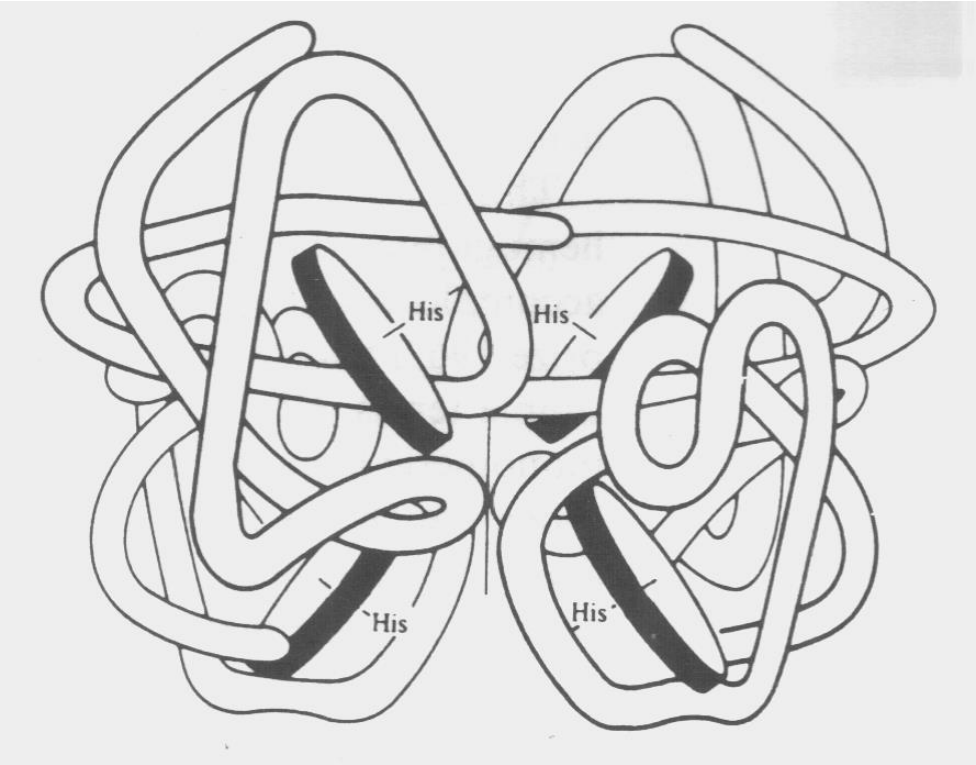
Deossimioglobina

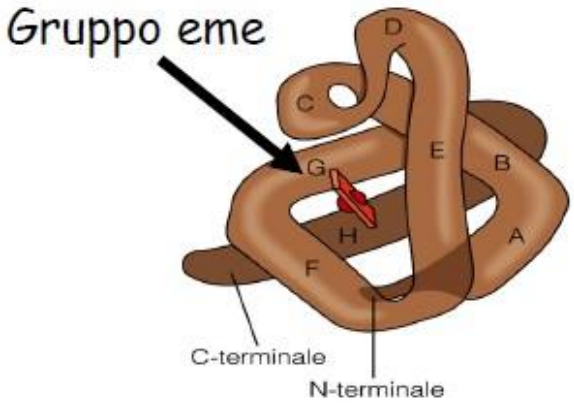


L’Emoglobina

L’Emoglobina è Formata da **4 subunità** molto simili, strutturalmente, alla Mioglobina. Ogni Molecola di Emoglobina può quindi legare 4 Molecole di Ossigeno.

Contrariamente alla mioglobina il lavoro dell’emoglobina è quello di prelevare ossigeno nei polmoni, rilasciarlo nelle cellule ove ce ne sia bisogno, prelevare anidride carbonica e rilasciarla nel polmoni dove il ciclo ricomincia.



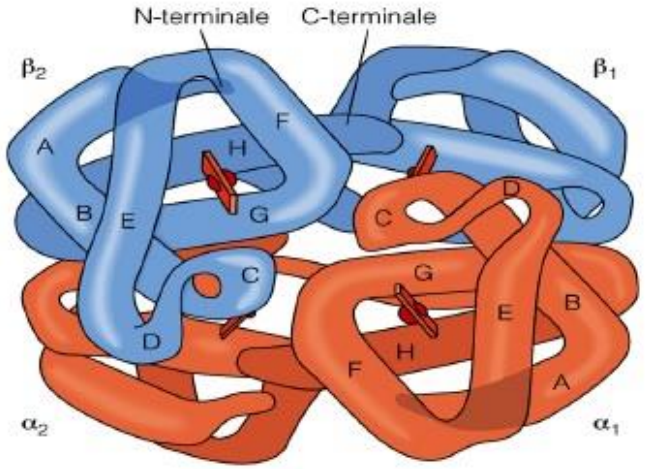


MIOGLOBINA (Mb)

↓

1 catena polipeptidica

(1 eme)

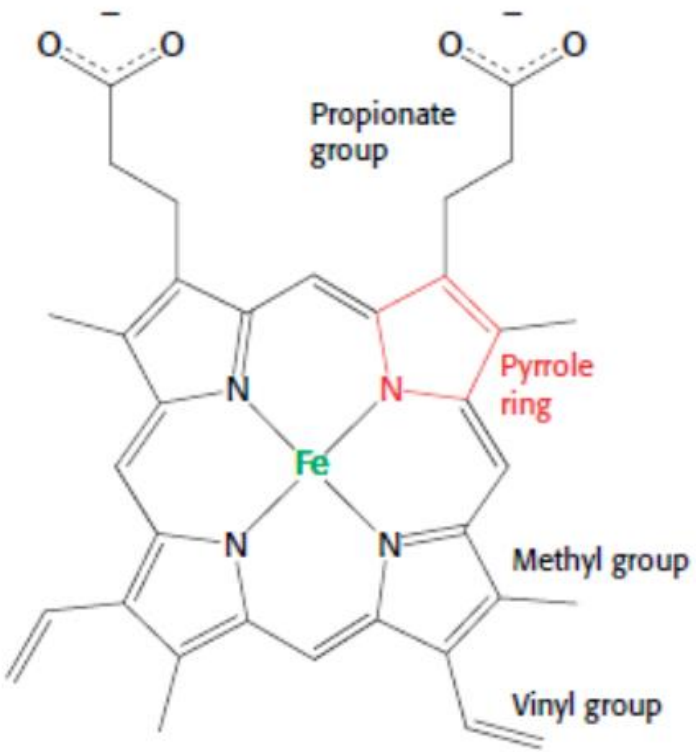


EMOGLOBINA (Hb)

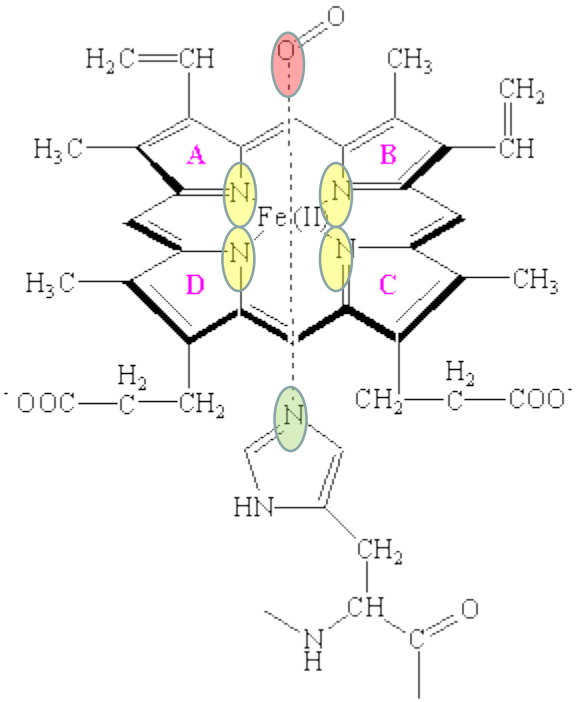
↓

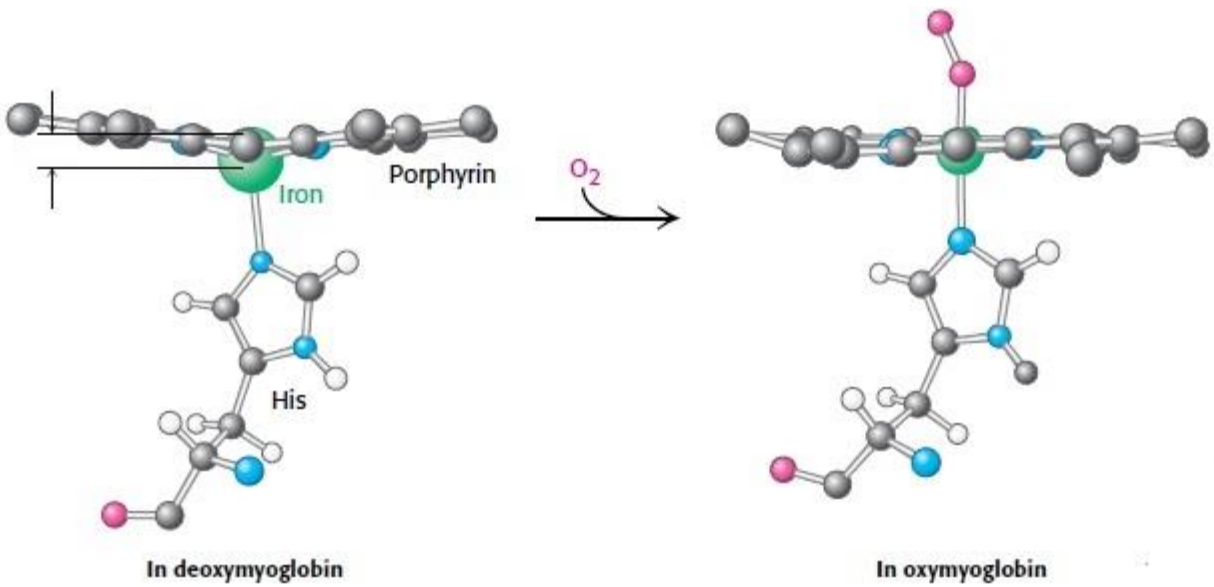
4 catene polipeptidiche

(4 eme)

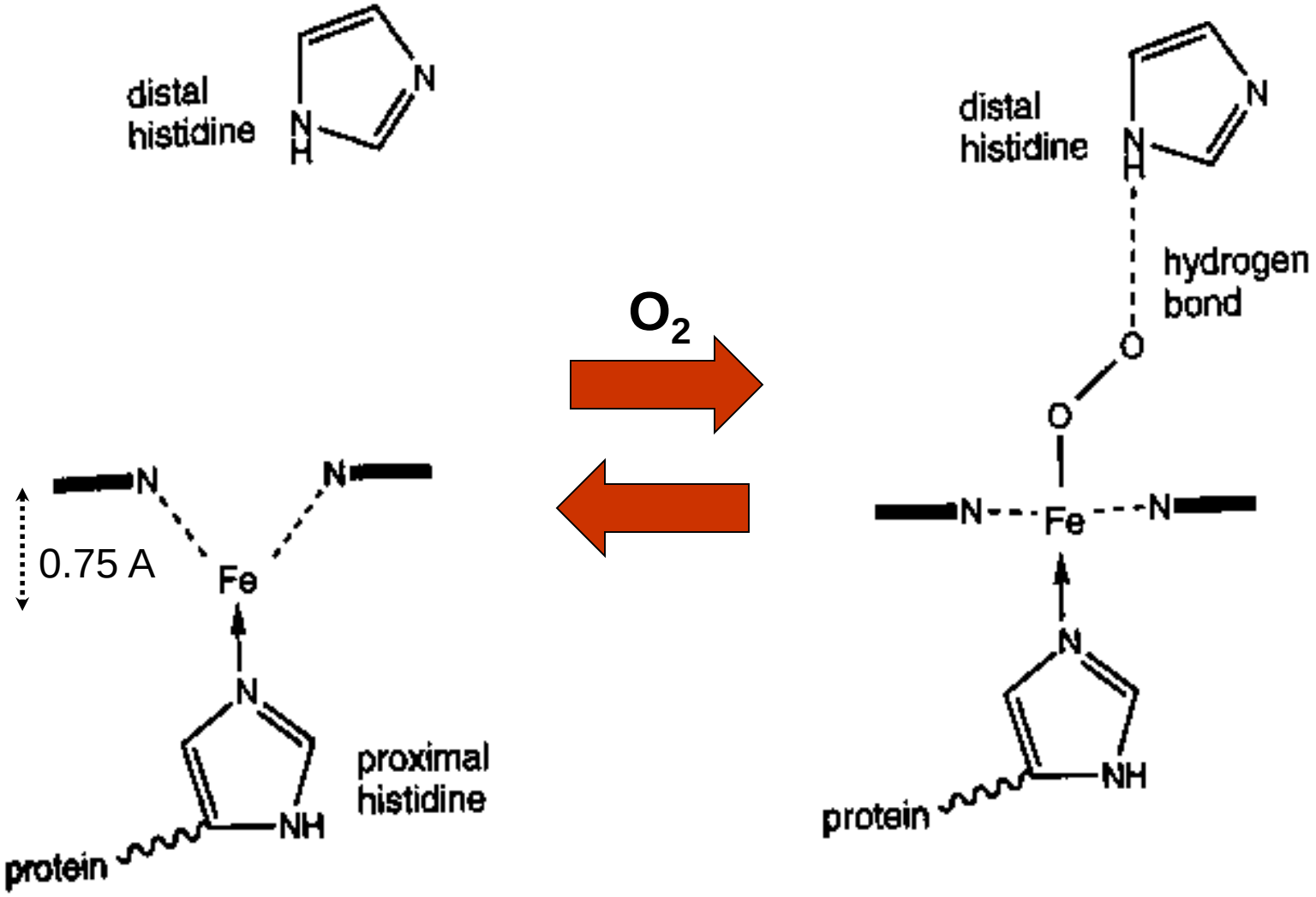


Heme
(Fe-protoporphyrin IX)

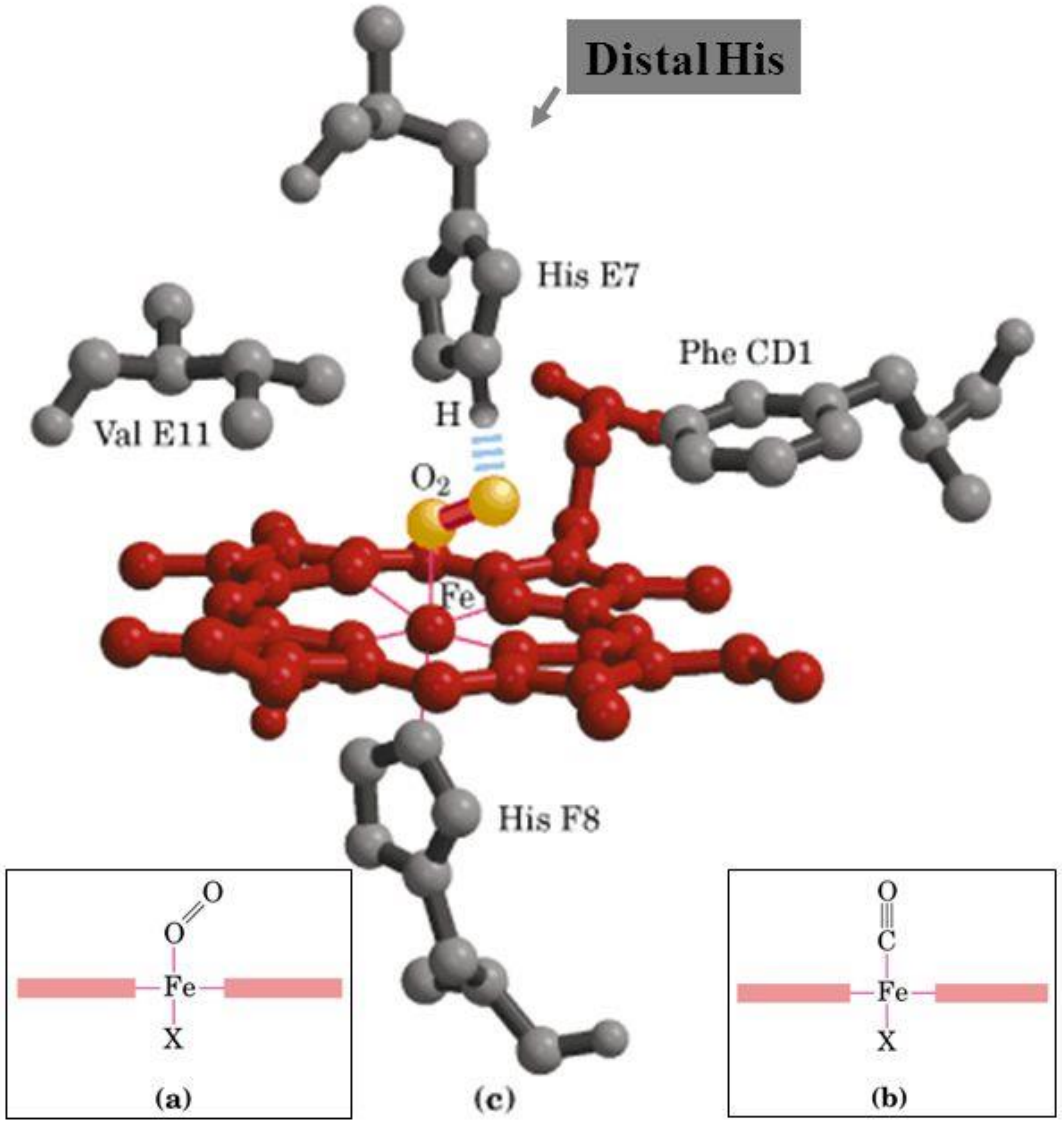

H2C=CH
CH3
CH2
CH
H3C
A
B
N
Fe(II)
N
N
N
H3C
D
C
CH3
OOC—C—CH2
H2
CH2—C—COO
H2
N
HN
CH2
CH
C
O
N
H


Iron
Porphyrin
O2
His
In deoxymyoglobin
In oxymyoglobin

Coordination of Heme Fe in deoxy- and oxy-hemoglobin (or Mb)

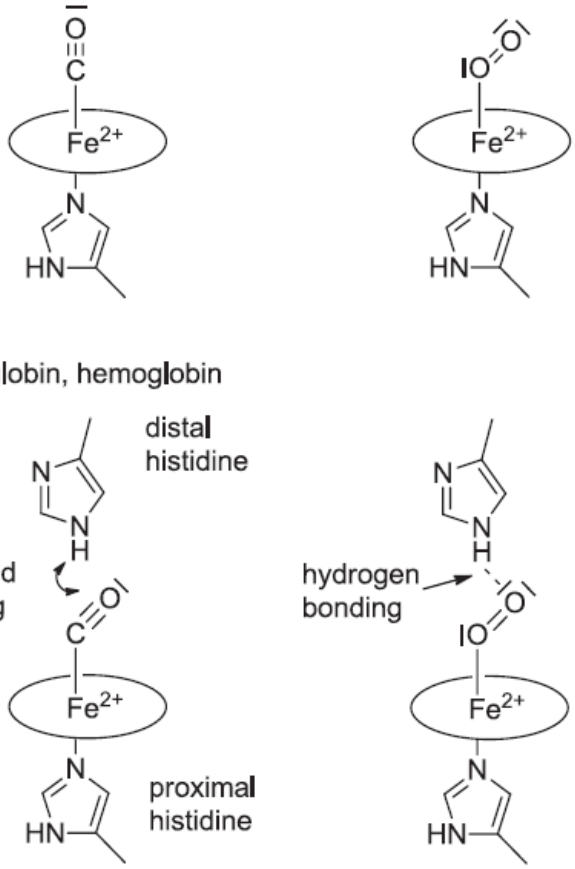


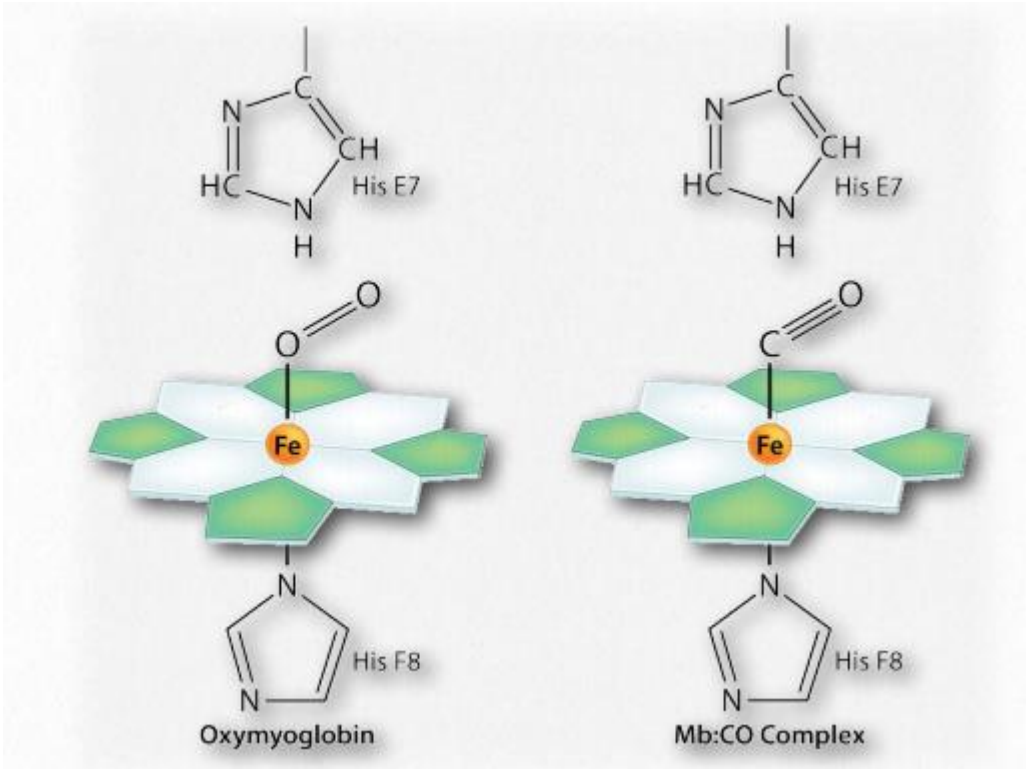
CO poisoning



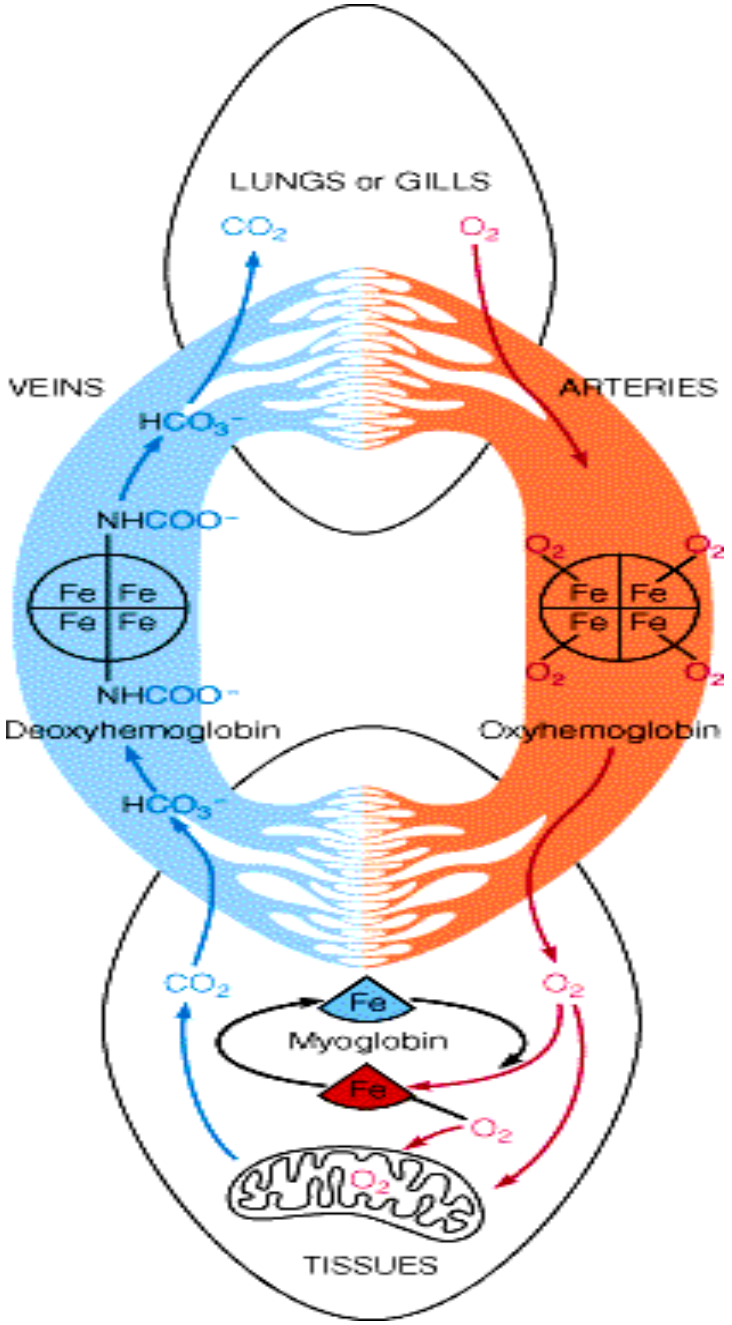
CO (carbon monoxide) binds to free heme molecules over 20,000 times **better than** does O_2 ,

but binds only about 200 times better when the heme is bound in myoglobin.


myoglobin, hemoglobin
distal
histidine
enforced
bending
proximal
histidine
hydrogen
bonding


His E7
His F8
Oxymyoglobin
His E7
His F8
Mb:CO Complex

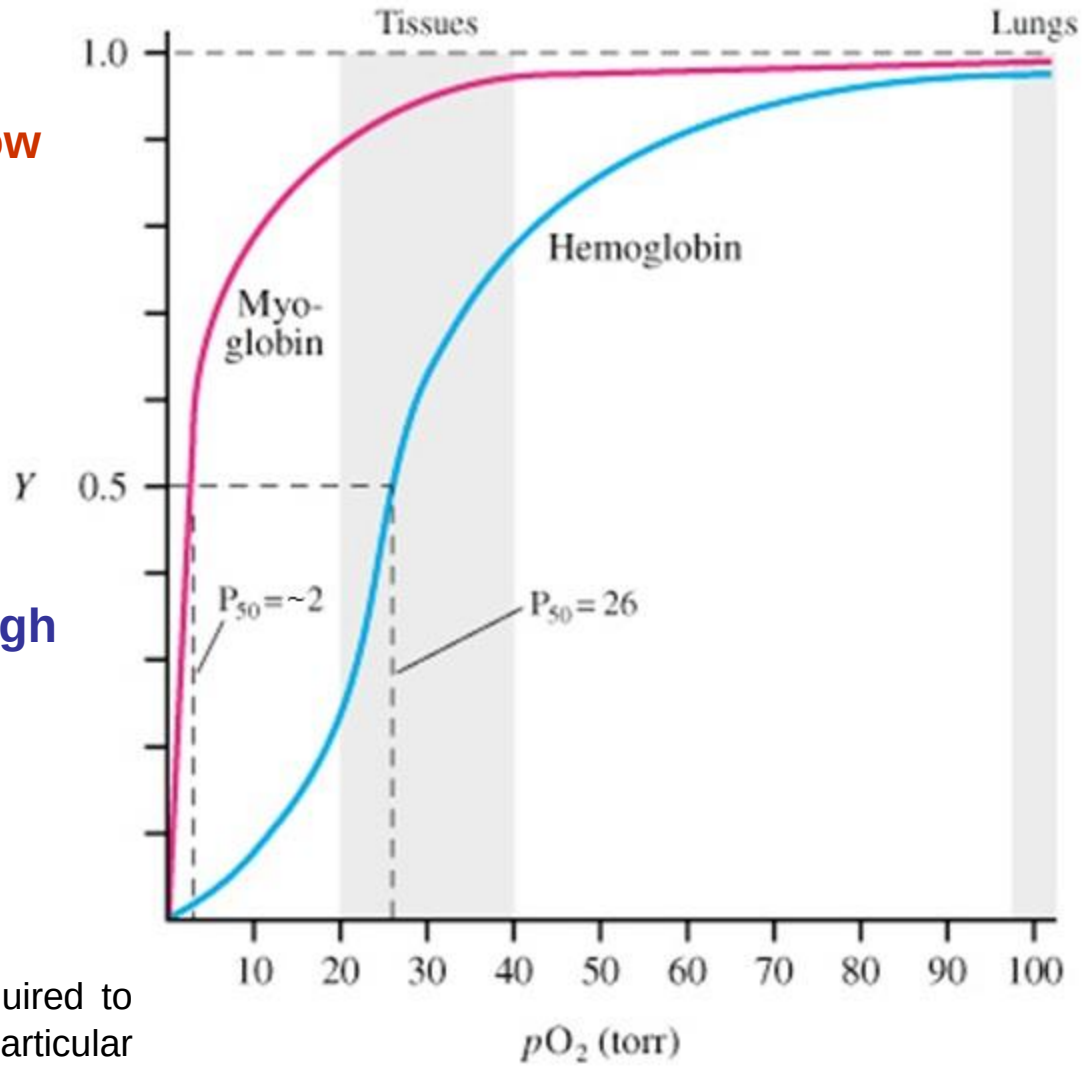
Role of the globins in oxygen transport and storage



Myoglobin and hemoglobin have different O_2-binding characteristics

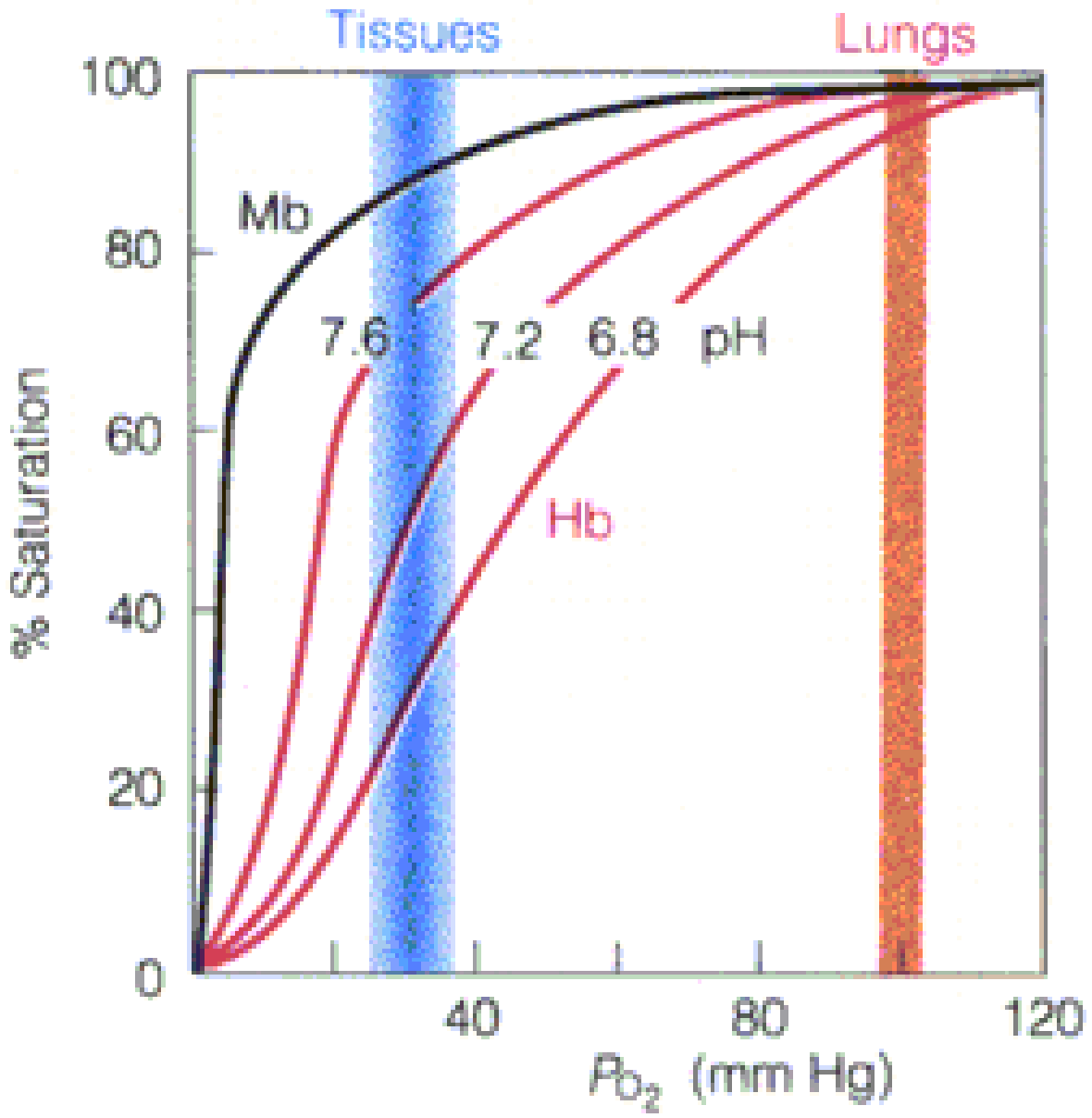
- **Myoglobin**
  - **Higher affinity for O_2 (low P50)**
  - **Hyperbolic binding**
  - **O_2 :Mb 1:1**
  - **Binds/releases O_2 in tissues**

- **Hemoglobin**
  - **Lower affinity for O_2 (High P50)**
  - **sigmoidal binding**
  - **O_2 :Hb 4:1**
  - **Binds O_2 in lungs, releases in tissues**



P_{50}= the partial pressure of a gas required to achieve 50% saturation of a particular protein's binding sites

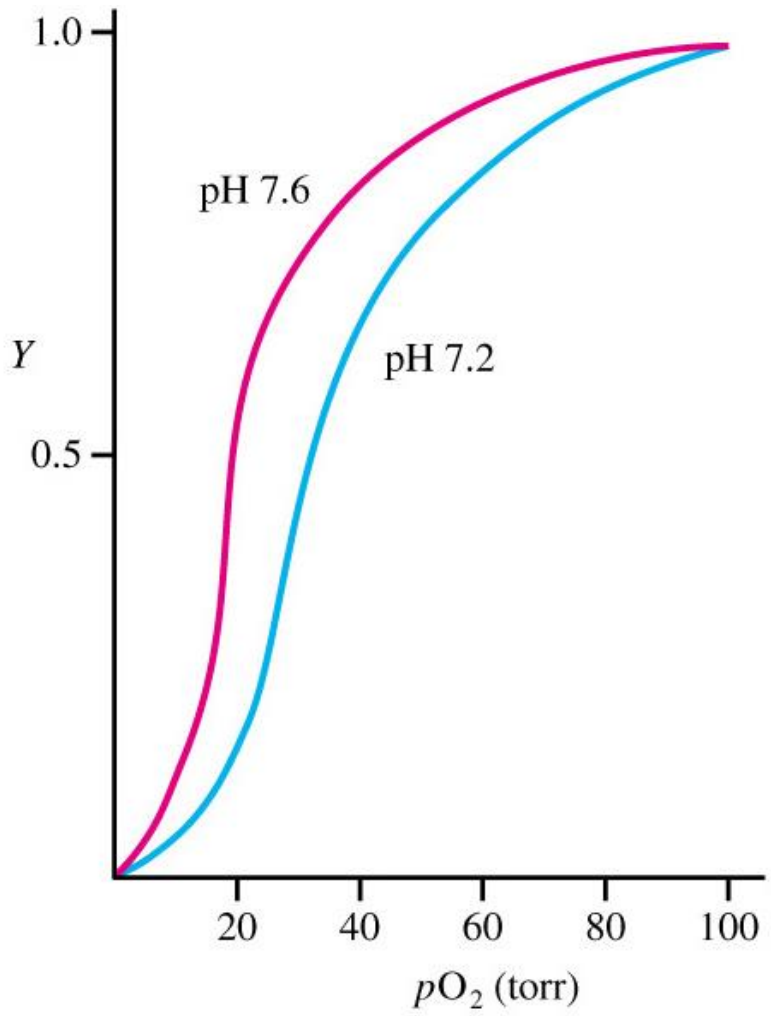
Effetto Bohr



La presenza di alti livelli di H^+ e CO_2 favorisce il rilascio di O_2

Regulation of Hemoglobin by CO_2

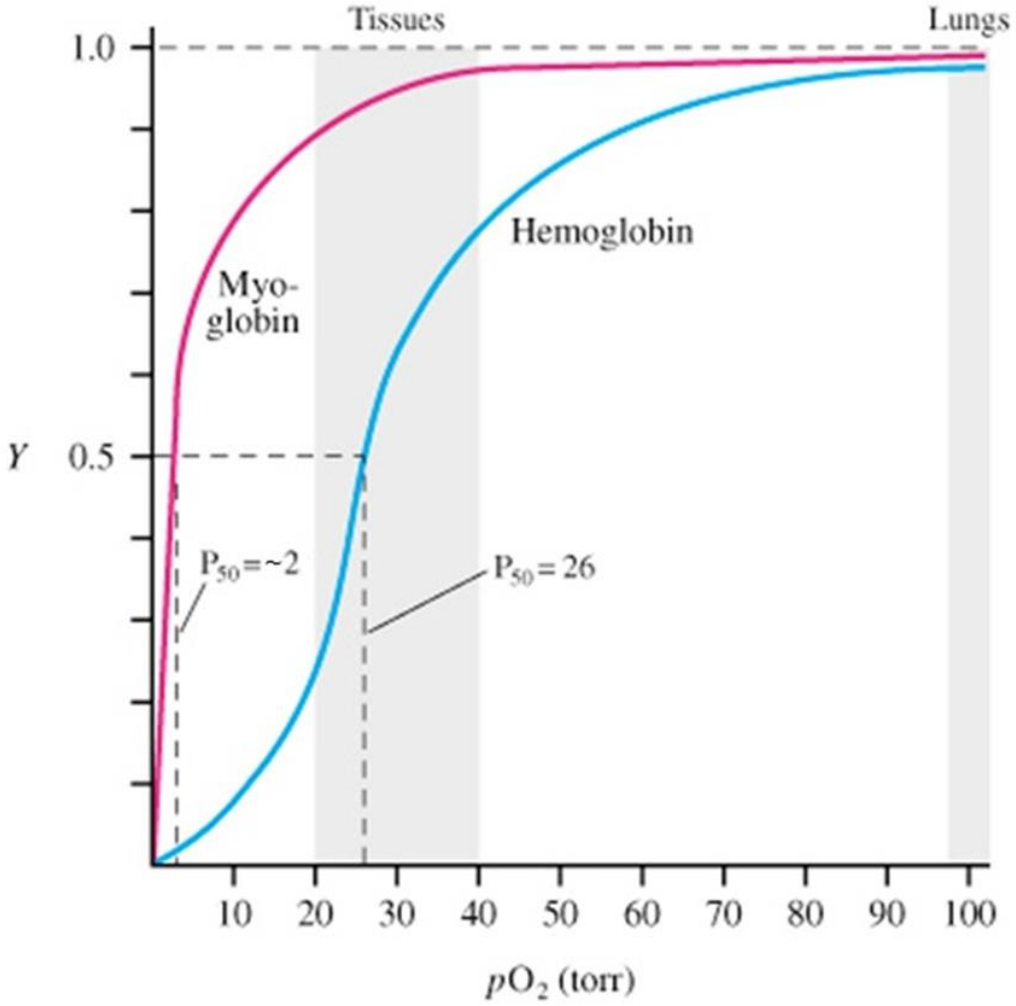
- CO_2 level is low in lung and high in tissues
- Bohr effect:
  - Increase in CO_2 decreases pH
  - Decrease in pH increases P50 of Hb
  - CO_2 vs O_2
- N-termini of Hb reversibly react with CO_2 to form carbamate adducts in tissues – released in lungs



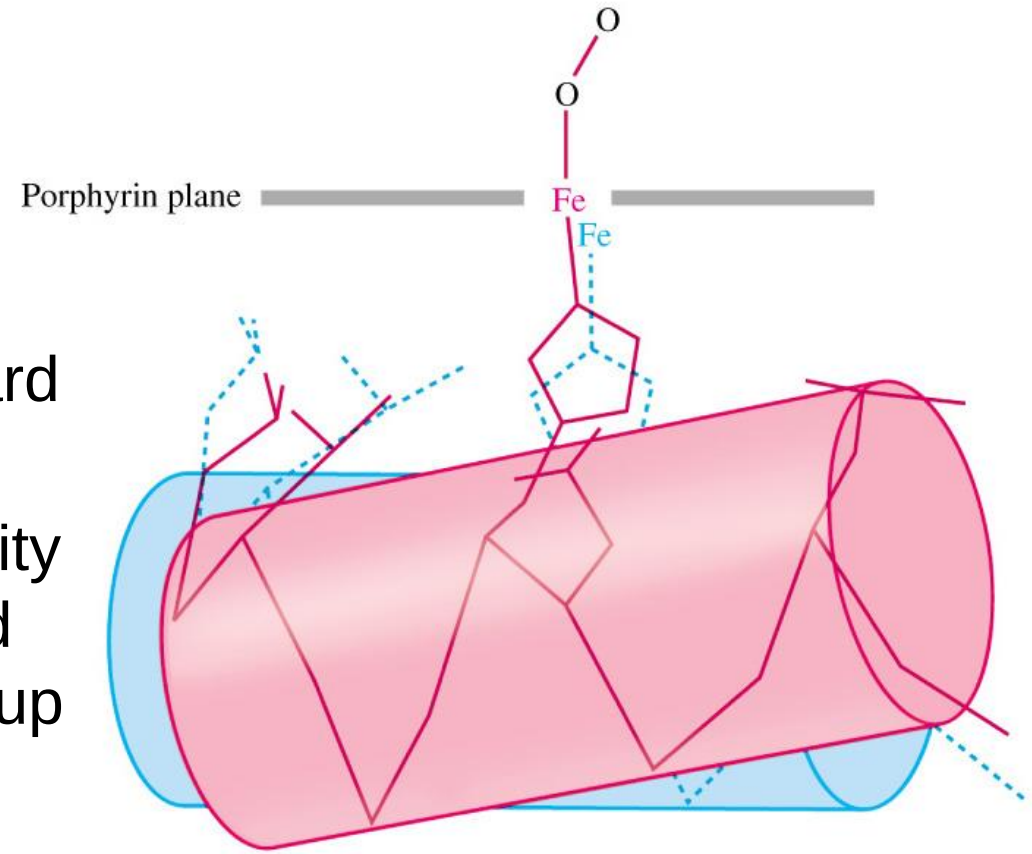
Molecular explanation for sigmoidal binding curve of hemoglobin

Hemoglobin has two conformations

- T state
  - *Taut*
  - Low affinity
  - Deoxy-
- R state
  - *Relaxed*
  - High affinity
  - Oxy-



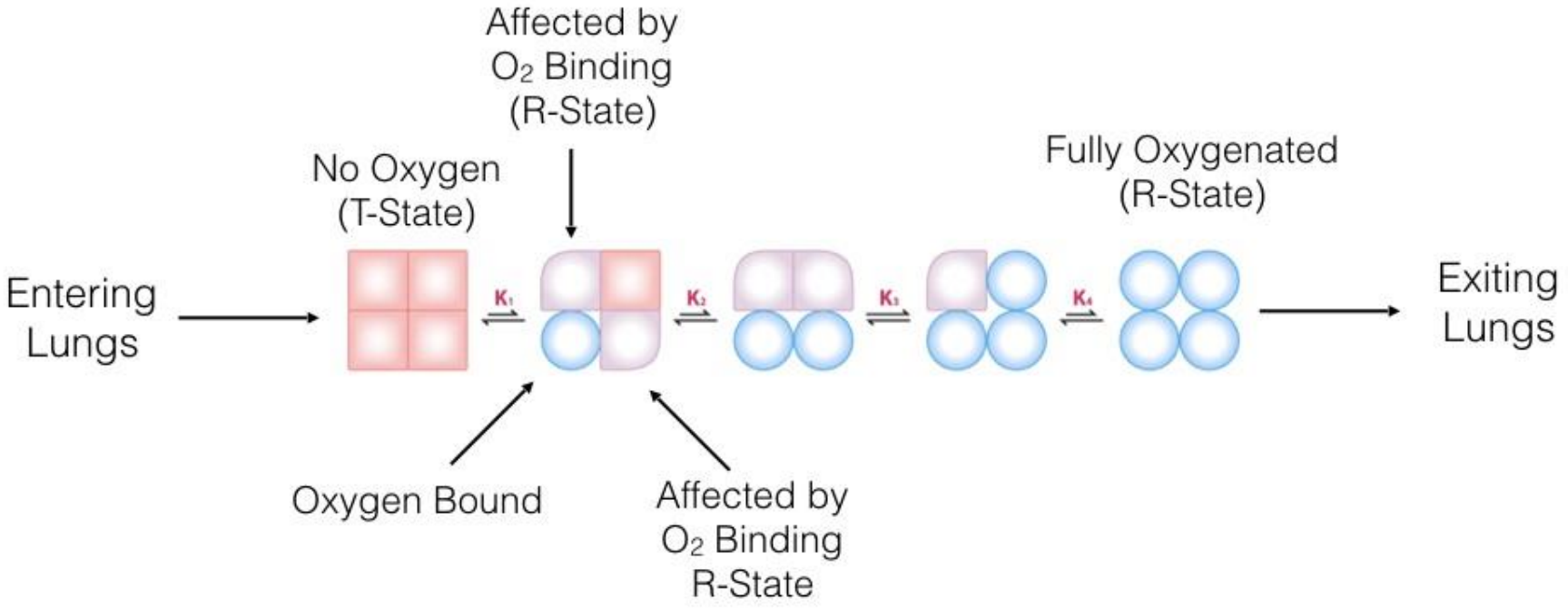
- Binding of O_2 to first subunit
  - Locks it in R state
  - induces neighboring subunits to shift toward R state
- Increase in binding affinity progresses as more and more subunits bind O_2 (up to 500 fold)



Oxyhemoglobin
Deoxyhemoglobin

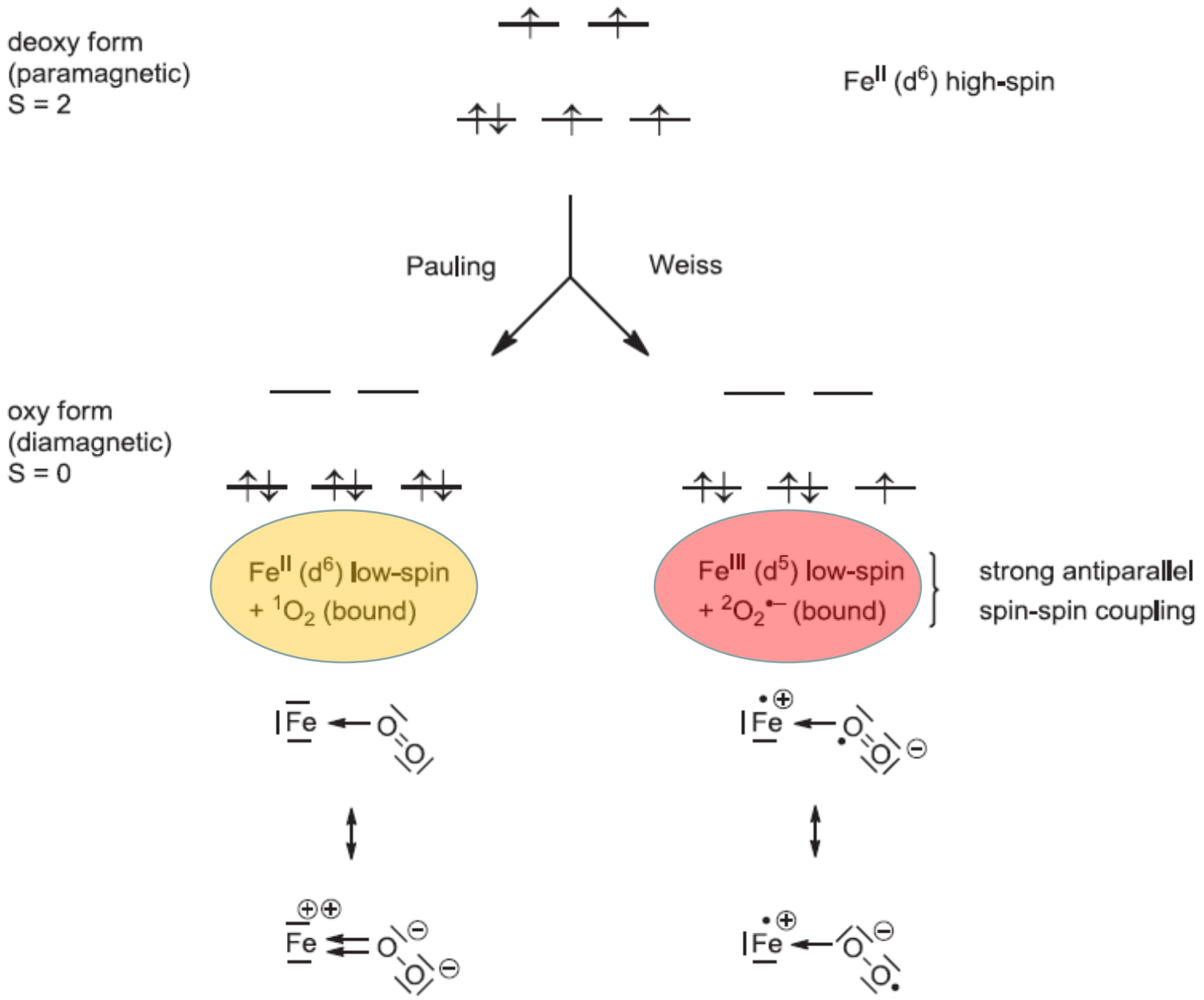
Hemoglobin and the Movement of Oxygen

- Cooperativity



Binding of the first O_2 favors binding of second, etc. - Cooperatively
Cooperatively Important as Hemoglobin Rapidly Passes Through Lungs

Oxy hemoglobin d-orbital splitting



Stato	S	Molteplicità di spin	Valori possibili di $m_S = S_Z / \hbar$
Singoletto	0	1	0
Doppietto	1/2	2	±½
Tripletto	1	3	0, ±1
Quadrupletto	3/2	4	±1/2, ±3/2
...	...	...	...
(2S + 1)-pletto	S	$2S + 1$	S, S-1, ..., -S+1, -S

Numero atomico

26

Fe

Ferro

55,847

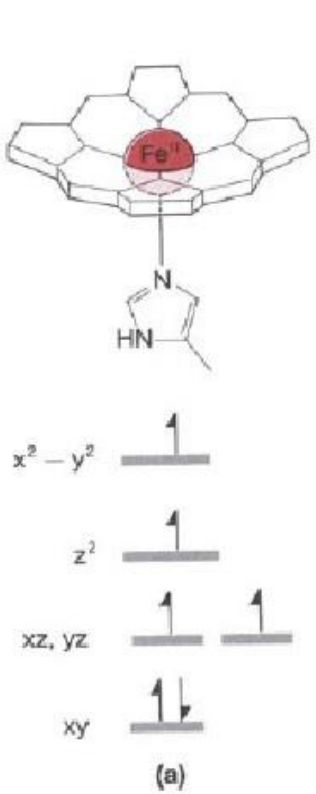
[Ar] $3d^6$ $4s^2$

Simbolo atomico

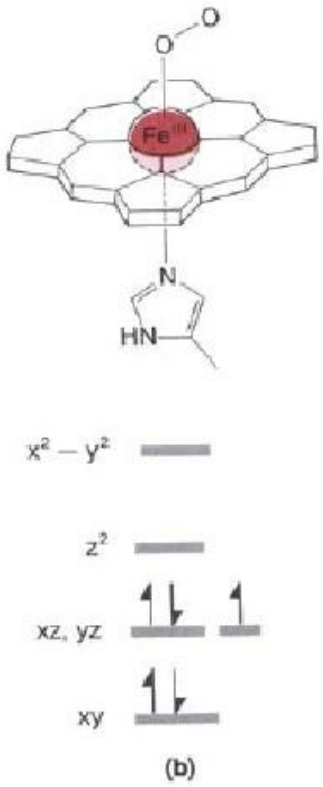
Nome dell'elemento

Peso atomico

Configurazione elettronica

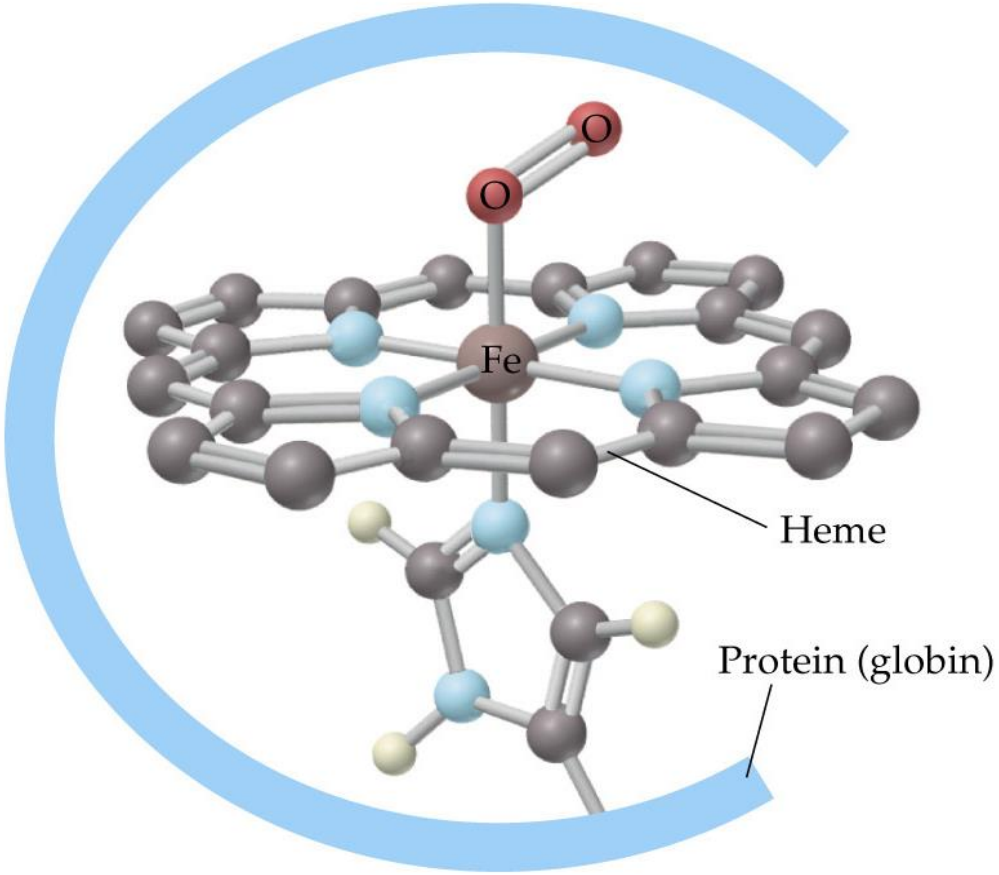


High spin

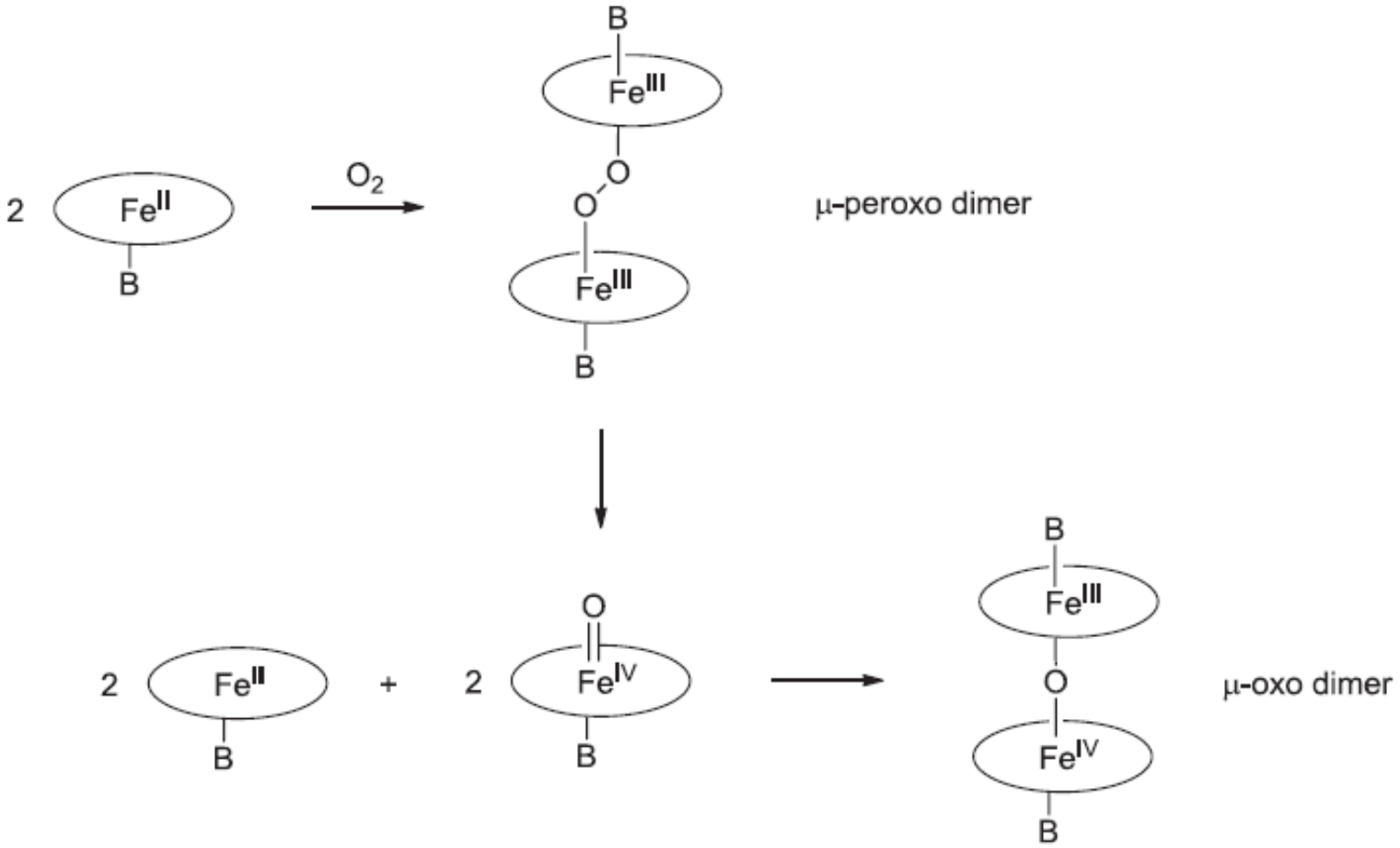


Low spin

Does the heme group bind reversibly O_2 in the absence of the protein ?



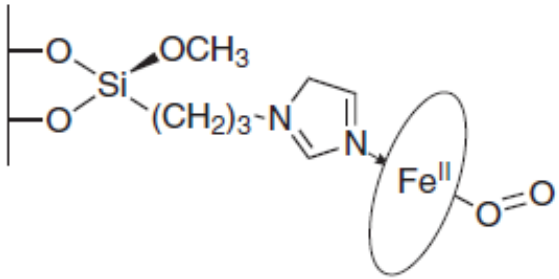
The answer is NO!



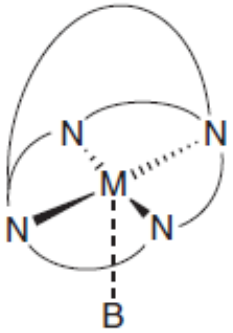
B: nitrogen base

Use of model compounds to mimic the protein

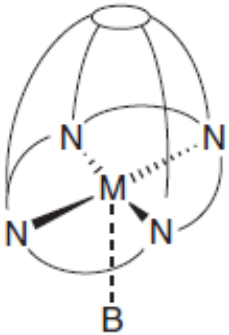
immobilization at a (polymeric) support:



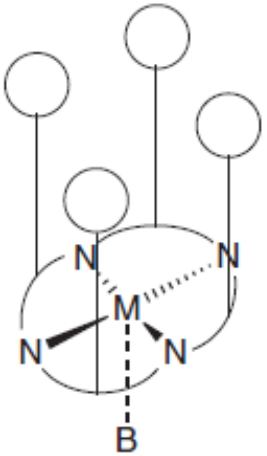
shielding in cavities:



strapped



capped



picket fence