CONCEPT: HEME PROSTHETIC GROUP

Why is the Heme Prosthetic Group on Mb/Hb Important?

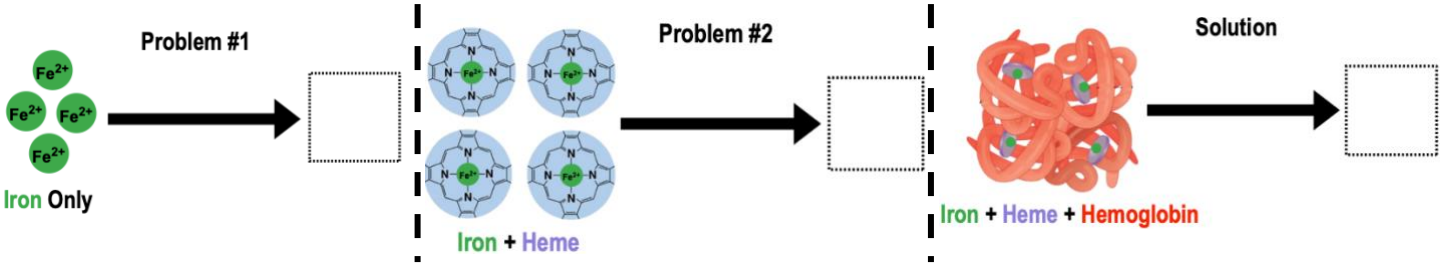
●Amino acids lack affinity to O_2, so Mb & Hb *binding* to O_2 depends on a *prosthetic group* called _____.

●Unlike amino acids, *iron* (Fe^{2+}) can reversibly bind O_2, but unbound _____ iron is reactive & turns O_2 into free radicals.

□ *Problem #1*: free iron generates free radicals, which can damage and/or _____ the cell.

□ *Problem #2*: Fe^{2+} in free-heme (heme not bound to protein) is oxidized to Fe^{3+}, which does *NOT* bind O_2.

□ Solution: Fe^{2+} in protein-bound heme is less reactive & reversibly binds O_2.

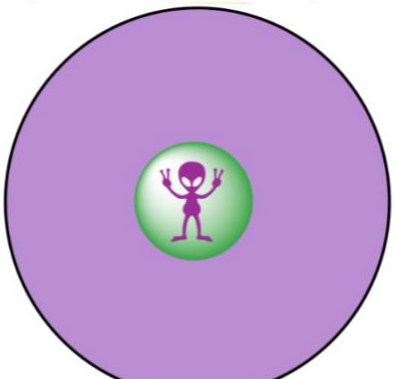


Structure of Heme

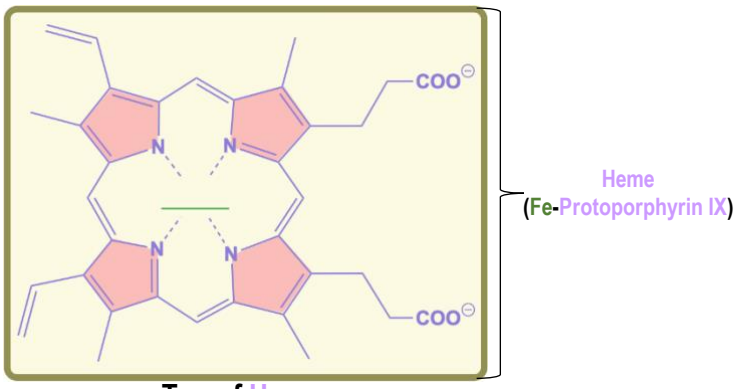
●Heme is mostly a nonpolar structure surrounded by _____ amino acids deep within the Hb & Mb proteins.

□ Heme attaches to the Hb & Mb proteins via _____ interactions.

●Ferrous _____ (Fe^{2+}) complexes with a *planar tetra*pyrrole ring system (protoporphyrin IX) to form the _____.



Top of "UFO"

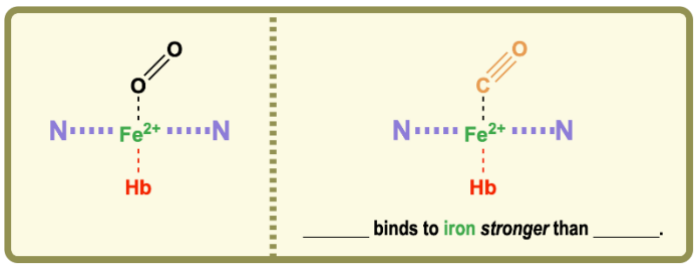


Top of Heme

●O_2 binds to Fe^{2+} _____ the *plane* of the heme prosthetic group *without* reacting to form free radicals.

●Carbon monoxide (CO) binds heme *stronger* than O_2 & outcompetes O_2 for binding to Fe^{2+}, which is why CO is _____.

Side of "UFO"



Side of Heme

CONCEPT: HEME PROSTHETIC GROUP

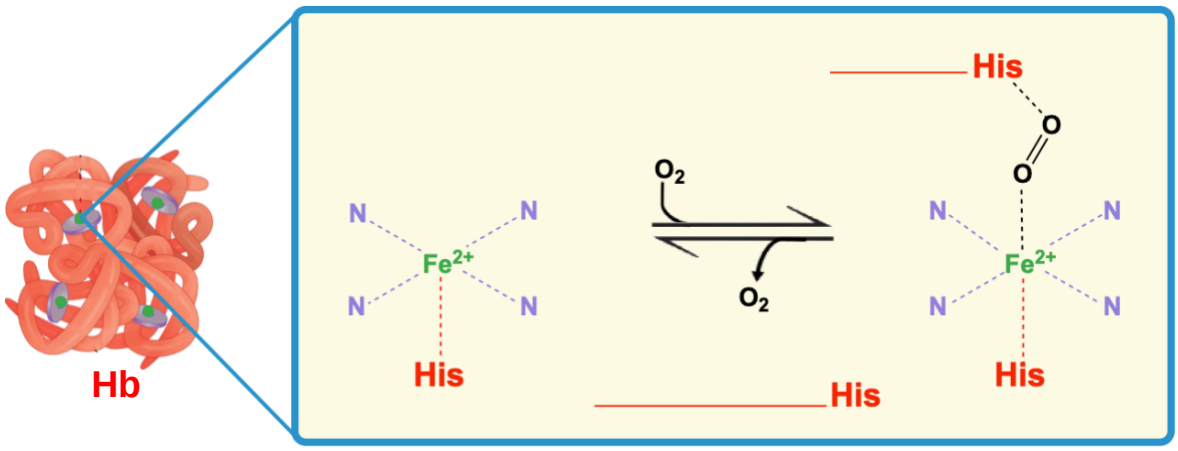
Interactions of Fe^{2+} in the Heme

●The Fe^{2+} atom of the protein-bound heme can form a total of _____ *noncovalent* bonds:

□ _____ bonds with N atoms of protoporphyrin IX (same plane). □ ____ bond with a *proximal* His residue (below).

□ ____ bond with O_2 (above).

EXAMPLE: Fe^{2+} Interactions.



●A _____ His residue stabilizes O_2 in the O_2-bound heme via hydrogen bonding & prevents conversion of Fe^{2+} to Fe^{3+}.

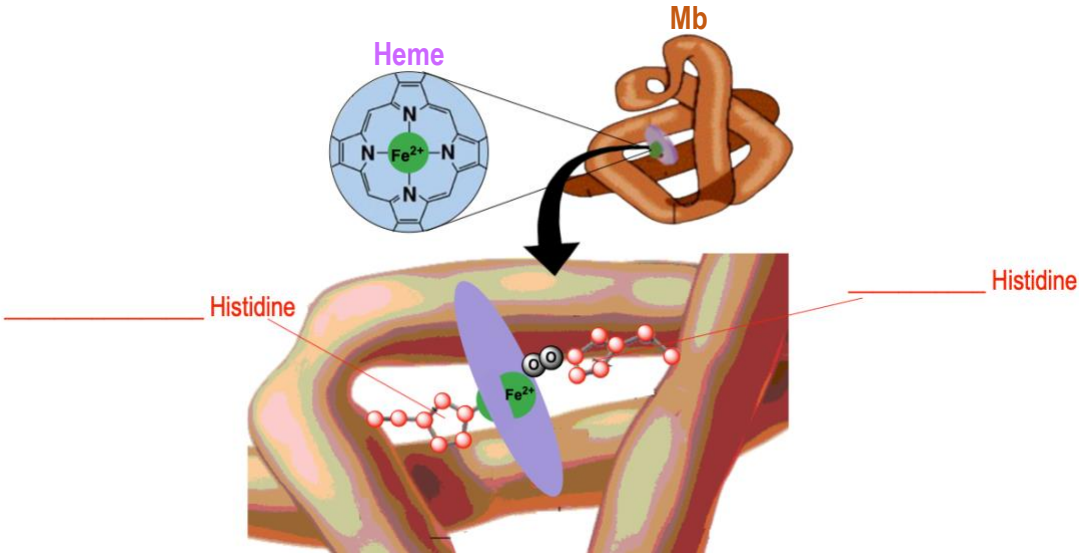
□ The *distal* His also _____ carbon monoxide's (CO) ability to bind to the heme group.

PRACTICE: When O_2 binds to a heme group, the two bonds of Fe^{2+} that are not planar with the heme are occupied by:

a) One O_2 molecule and one Ser amino acid atom.
b) One O_2 molecule and one His amino acid atom.
c) One O_2 molecule and a nitrogen atom of the heme.
d) Two O_2 molecules.

Myoglobin's Heme Interactions

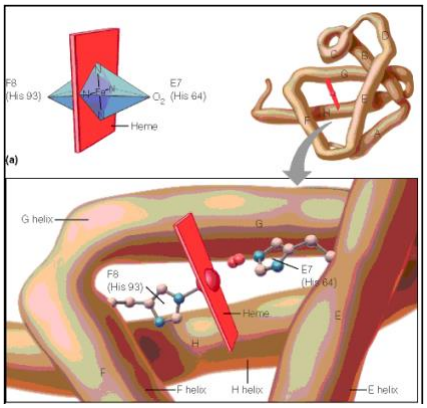
●Like hemoglobin, myoglobin's heme group forms very *similar* Fe^{2+} interactions:



CONCEPT: HEME PROSTHETIC GROUP

PRACTICE: The distal histidine residue in myoglobin acts to:

a) Prevent oxidation of the heme Fe^{2+}.
b) Lower the relative affinity for CO.
c) Assist in the binding of O_2.
d) Prevent release of N_2.
e) a & b.
f) a, b & c.
g) All the above are true.



Heme O_2-Binding Causes Hb's Conformational Changes

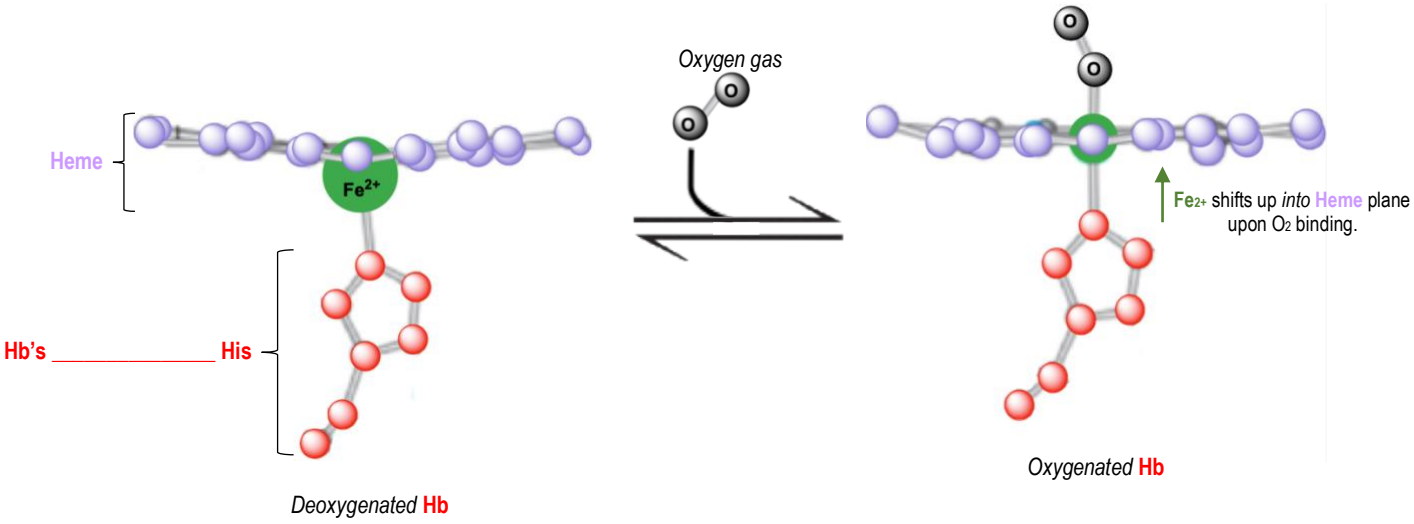
●Recall: Hb is an _____ protein with ____ state & ____ state conformations.

●Binding of O_2 to the heme prosthetic group causes a slight change in the heme's conformation.

□ Fe^{2+} atom becomes _____ upon binding to O_2, allowing it to shift up *into the plane* of the heme.

□ This ultimately causes the other Hb protein subunits to change conformations too from T state → ____ state.

□ Leads to _____ *cooperativity* between Hb subunits.



PRACTICE: In hemoglobin, the equilibrium transition from T state to R state is triggered by:

a) Fe^{2+} binding.
b) Heme binding.
c) Oxygen binding.
d) Protease cleavage.