Function of Hemoglobin
“Oxygen Transport Mechanism”

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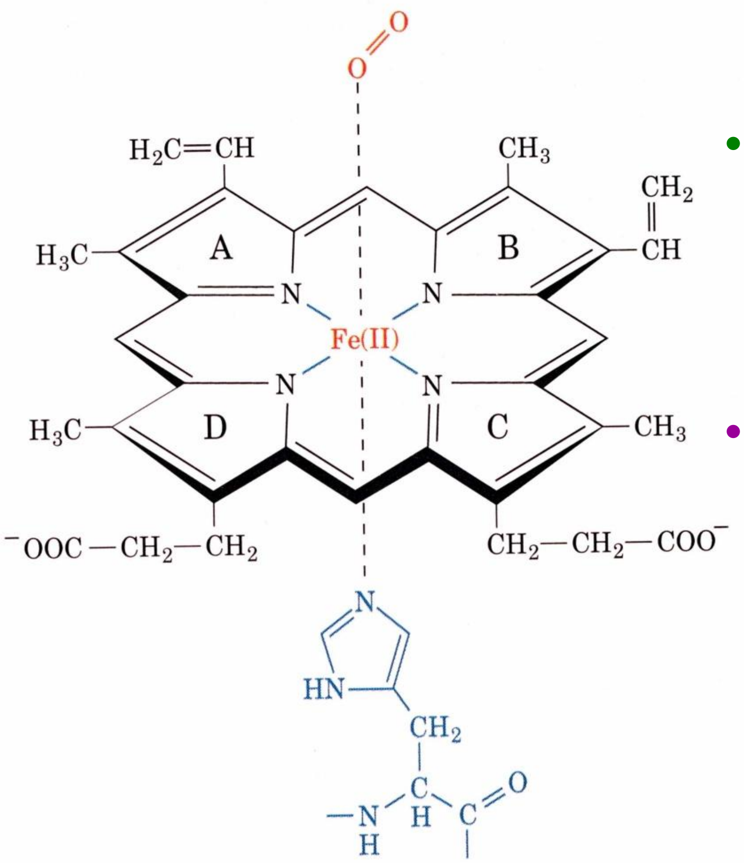
Bio-Inorganic Chemistry

The interface of Inorganic chemistry and Biology is called bioinorganic chemistry.
Metal ions are playing an important role in biology. E.g. Iron in Hb and Mg in Chlorophyll .

We discuss here,

The role of Iron metal ion in respiration which involve basic principal coordination chemistry & Hybridization of central Iron metal ion.

Structure and Function of Hemoglobin



- Hemoglobin may be considered as tetramer of myoglobin. contains four heme groups bound to four protein chains.
- Two of the chains have 146 amino acids (β) and are similar to myoglobin and other two α have 141 amino acids each sub-unit comprises of a porphyrin complex heme which contains Fe(II) in the center.
- The Fe(II) atom is bound to four pyrrole nitrogen atoms and fifth coordination is occupied by nitrogen atom of an imidazole of histidine and sixth coordination site is occupied by molecular oxygen O_2.

The hemoglobin and myoglobin exhibit different O_2 binding behavior. Myoglobin is a monomer while hemoglobin is a tetrameric molecule which accounts for higher binding affinity for O_2 molecule.

The reactions are as follows

Lungs (gills): $Hb + 4O_2 \rightarrow Hb(O_2)_4$

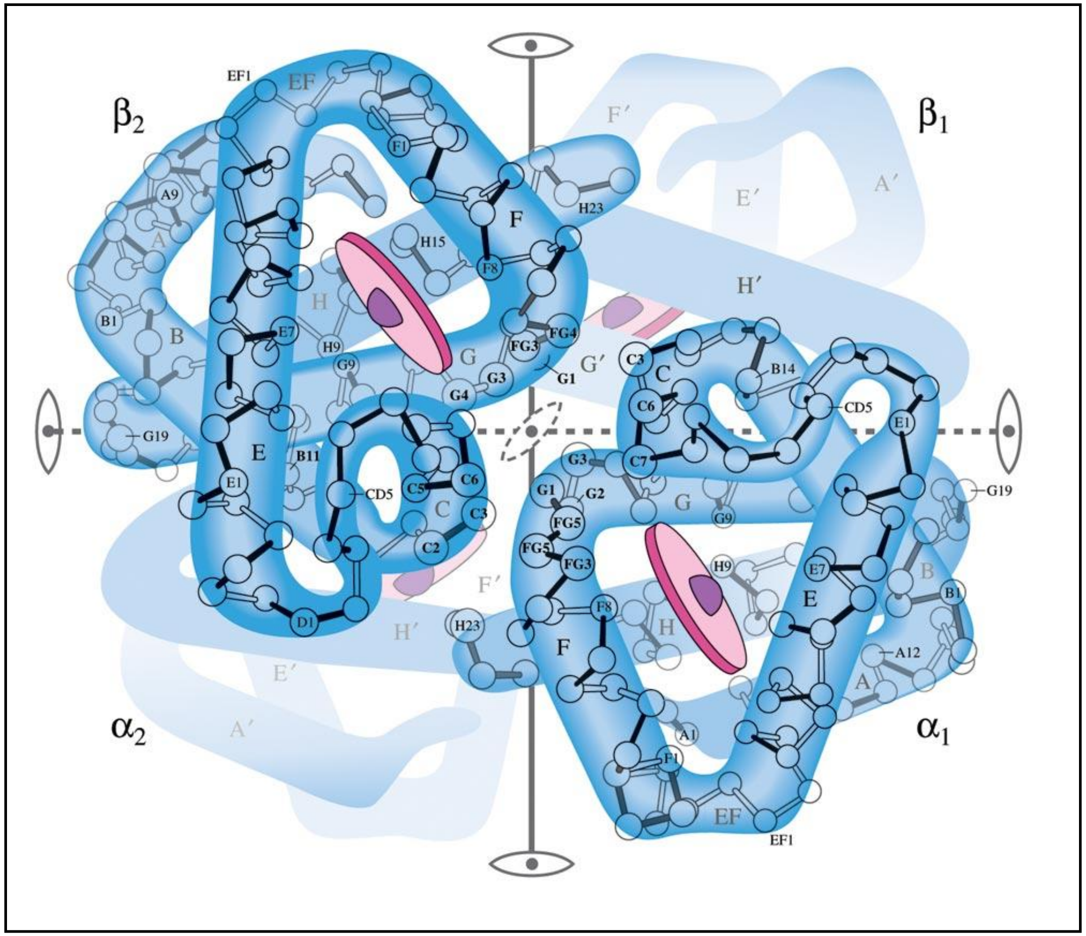
Tissues: $Hb(O_2)_4 + 4\ Mb \rightarrow 4Mb(O_2) + Hb$

$$K_{Mb} = [Mb(O_2)]/[Mb][O_2]$$

$$K_{Hb} = [Hb(O_2)_4]/[Hb][O_2]^{2.8}$$

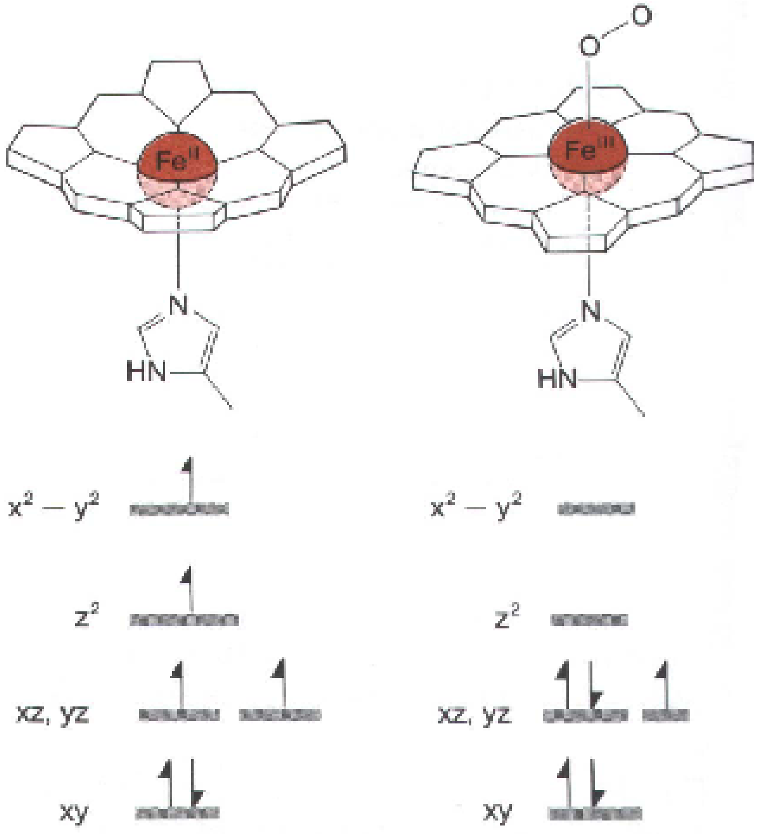
Each hemoglobin has two α chains and two β chains, each with a heme complex near the center.

Each hemoglobin molecule can complex with four O_2 molecules.



- The equilibrium constant for Hb (oxy form) is complicated and 2.8 exponent (Hills constant) for dioxygen results from the fact that a single hemoglobin molecule can accept four dioxygen molecules and binding of the four is not independent.
- It is the **cooperativity** of the four heme groups that produces the sigmoidal curves . **This effect is called ‘Cooperativity Effect’.**
- The presence of several bound dioxygen molecules favors the addition of more dioxygen molecule and the net result is that at low dioxygen concentrations hemoglobin is less oxygenated and tends to release O_2 in muscle.
- At high dioxygen concentrations, hemoglobin is oxygenated to the same extent as if the exponent were 1. This results in a sigmoid curve for oxygenation of hemoglobin. This effect favors oxygen transport since it helps the hemoglobin becomes saturated in lungs and deoxygenated in the capillaries.

- $Fe^{2+} \rightarrow Fe^{3+}$
- hs → ls
- Porphyrin ring becomes more planar
- Lengthening of Fe-N(his) bond anchoring heme

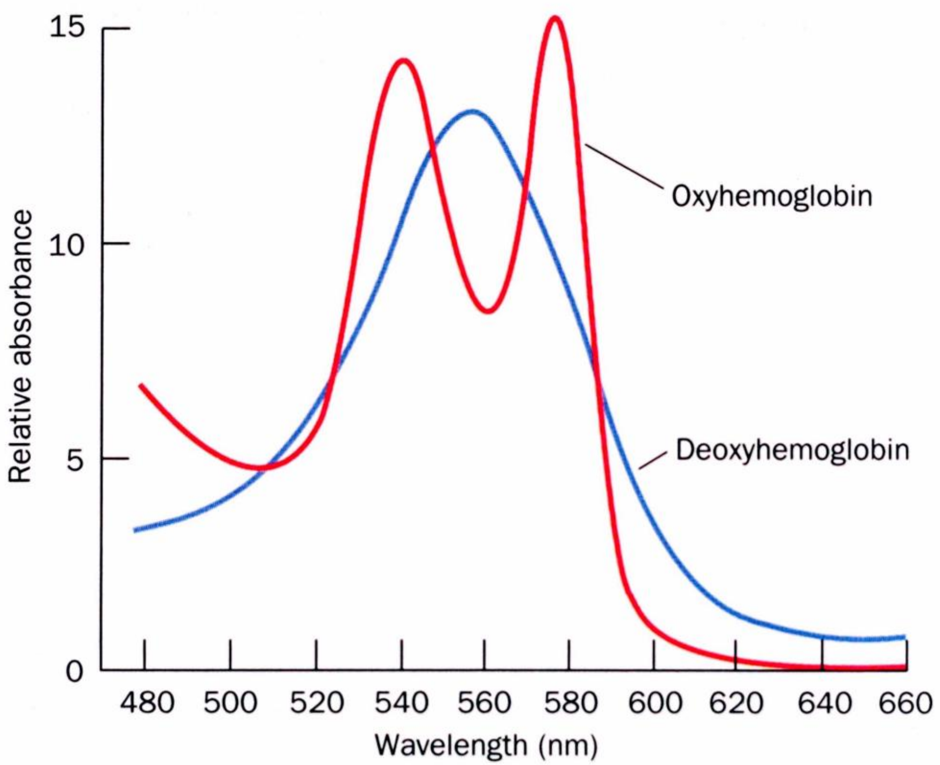


Binding of oxygen rearranges the electronic distribution and alters the d orbital energy.

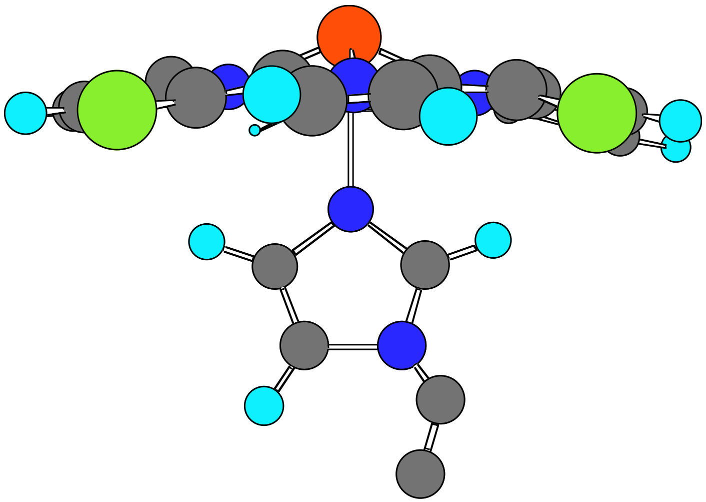
This causes a difference in the absorption spectra.

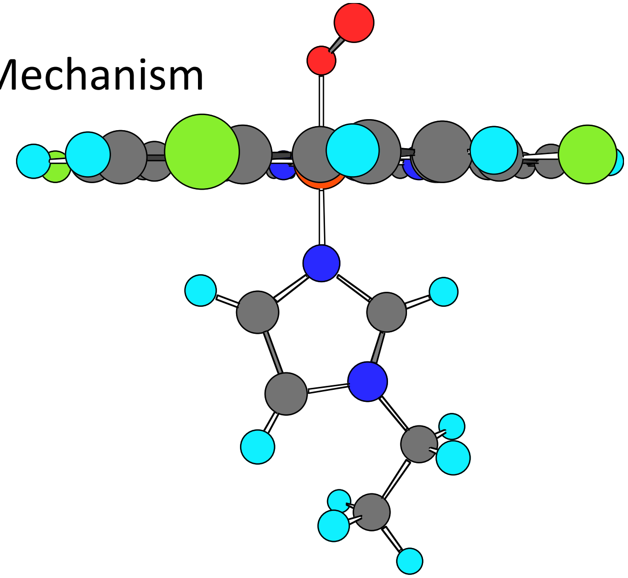
Bluish for deoxy Hb Reddish for Oxy Hb

Measuring the absorption at 578 nM allows an easy method to determine the percent of Oxygen bound to hemoglobin.

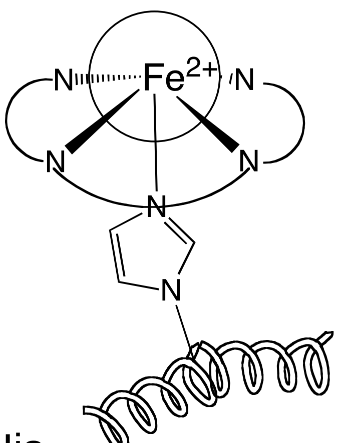


Perutz Mechanism



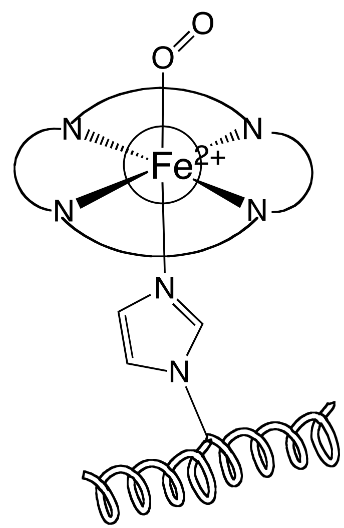


Large, high spin Fe(2+):

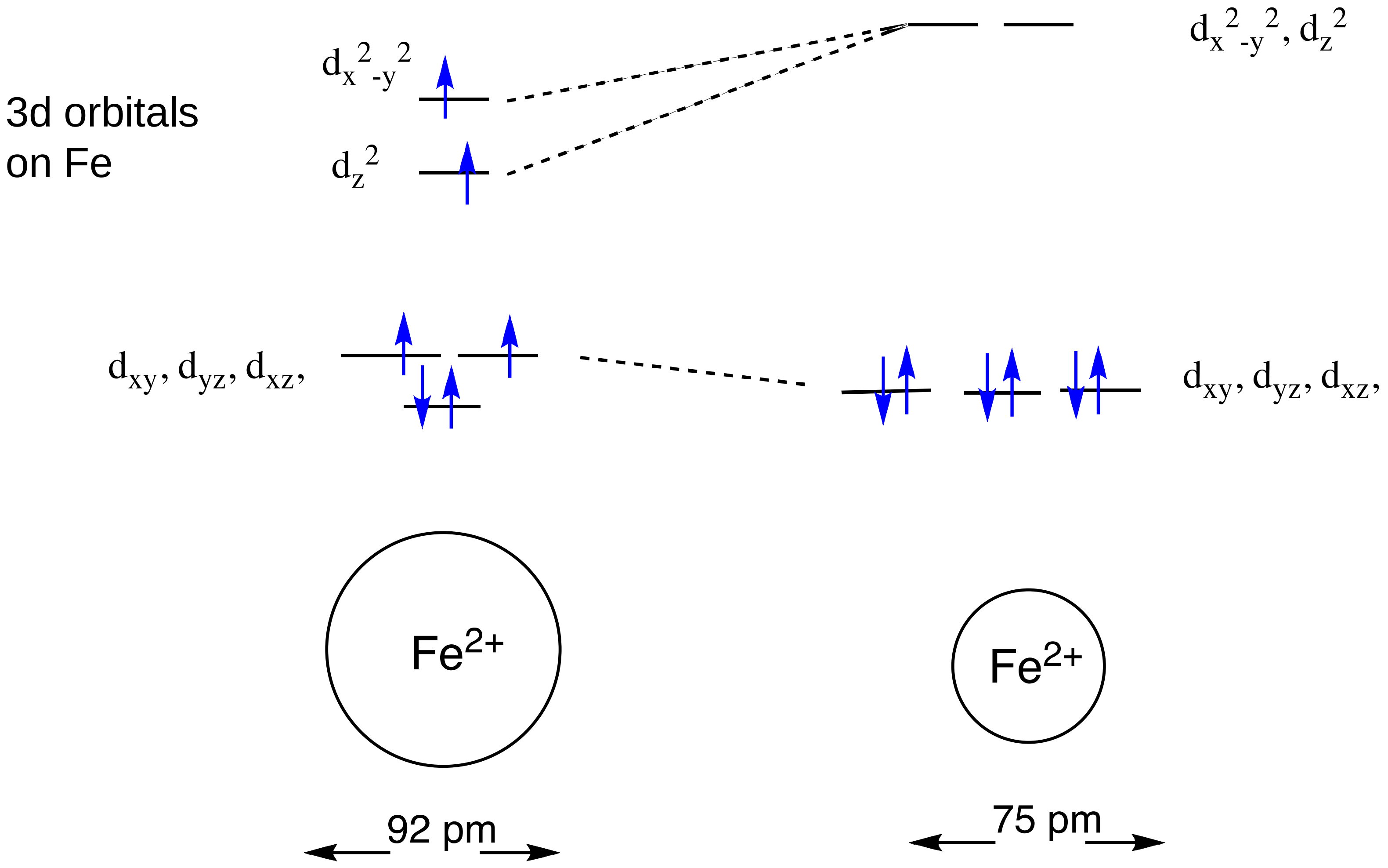


In T state, transmitted by His on protein helix

Small, low spin Fe(2+):

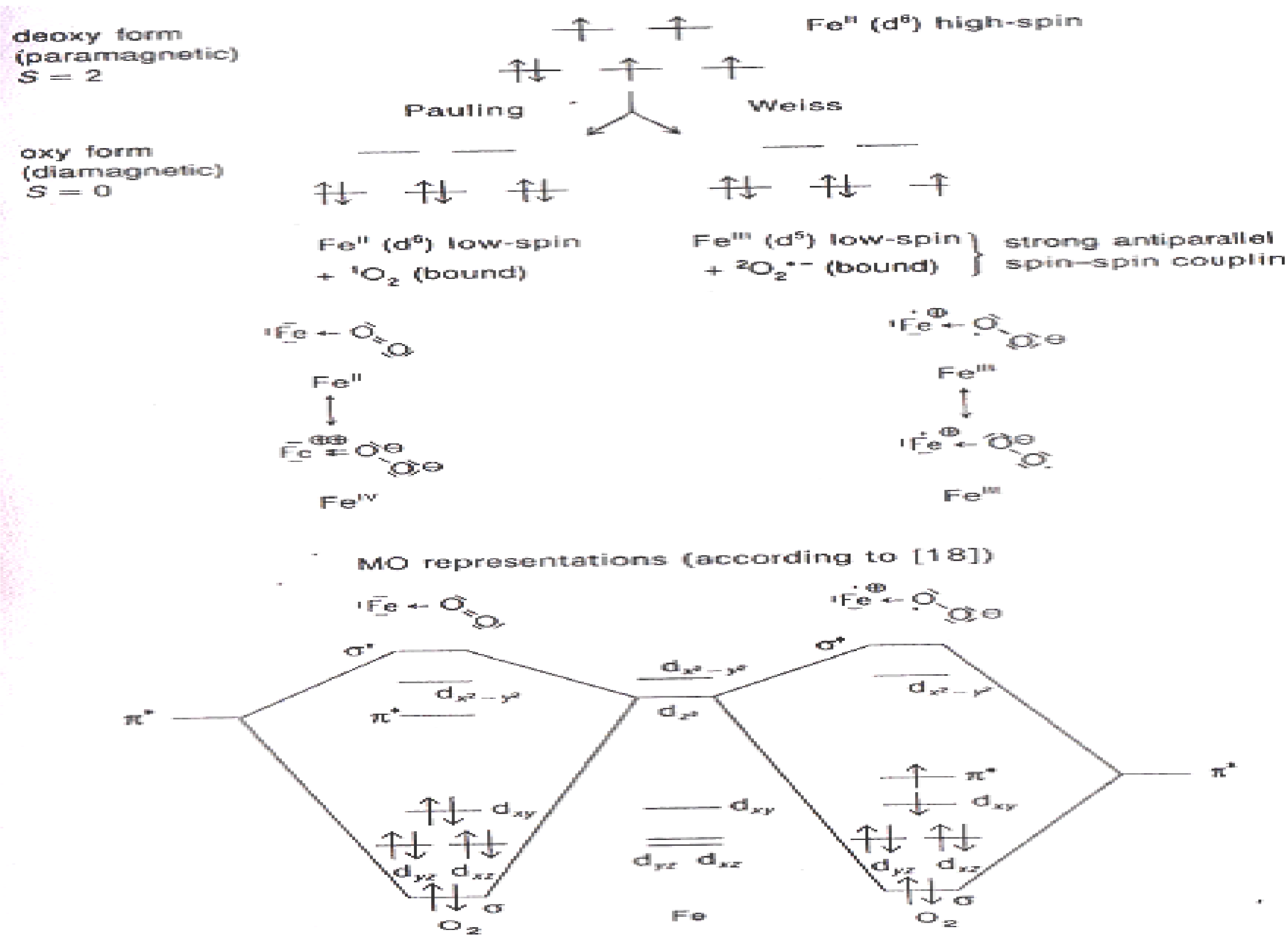


In R state, transmitted to His on protein helix



Spin State affects the size of ion

Oxidation and spin state in heme-O_2 system



Pauling Weiss

THANK YOU