Oxygen Transport and uptake protein

a) Thermodynamic aspects of dioxygen as an oxidant

i) The four e^- transfer at a single step is rarest possibility
ii) one e^- red^n to produce superoxide O_2^{2-} is the most common pathway, but this is thermodynamically unfavourable and it needs a moderately strong reducing agent.
If O_2^- is formed, it undergoes disproportionation fast in aq. sol^n to give H_2O_2 and O_2. & overall red^n is a two e^- reduction.

$$2O_2 + 2e^- \longrightarrow 2O_2^-$$
$$2O_2^- + 2H^+ \longrightarrow H_2O_2 + O_2$$
$$O_2 + 2H^+ + 2e^- \longrightarrow H_2O_2.$$

from stoichiometry, it is difficult to discriminate between the one electron and two e^- reduction pathways.

b) Kinetic inertness of dioxygen as an oxidant

$$O_2 + 4H^+ + 4e^- \longrightarrow 2H_2O \qquad E_0 = +1.23\ V \quad (pH = 0)$$

At biological pH, the above half reaction ($E_0' = 0.81V$) has $\Delta G = -305$ KJ/mole. Now this indicates the spontaneous oxidation of organic molecules (of $E_{red} < 0.81$ V at biological pH) by O_2 to give

~~Oxe~~ CO_2, H_2O and oxides of N. But surpisingly the O_2 molecules donot get burnt away with O_2 inspite of this rxn being thermo-dynamically favorable, and it is due to the kinetic stability of the biological system

The kinetic inertness of O_2 is due to the fact that Ground state of dioxygen molecule is triplet ($^3\Sigma g$, $S = 1$) i.e. it contains two unpaired parallel electrons.

The typical organic molecules are singlets (i.e. $S=0$, no unpaired)
Now the rxn b/w triplet O_2 ($S=1$) and singlet Organic substance ($S=0$) is forbidden by rule of spin

The singlet O_2 is highly toxic to us. (The ligating property of singlet O_2 is different from that of triplet O_2. singlet O_2 with

$(\pi^*)^2(\pi^*)^0$ can use the π^* pair for σ-donation and the vacant π^*-MO is used for π-acceptance. So singlet O_2 can act as a better π-acid ligand and consequently its crystal field splitting power is more.

Storage and Transport / transfer of Oxygen

The transport and storage of molecular Oxygen is an essential physiological function. It is carried out by number of well known iron and copper containing species occur in the blood.

Hemoglobin (Hb)	Fe (II)	Carrier	porphyrin	Humans blood
Myoglobin (Mb)	Fe (II)	Storage	"	
Hemerythrin	Fe (II)	storage	Protein	Marine worms
Hemocyanin	Cu (I)	carrier	Protein	Crab blood

⇒ Hemoglobin(Hb) contains two parts :- heme groups and globin proteins

⇒ A porphyrin ring containing an Fe atom is called Heme group

⇒ It has a molar mass of about 64500 daltons. It is found in RBC that are called erythrocytes. Each hemoglobin molecule is made up of four subunits (tetrahedrally arranged) each of which consists of a globin protein in the form of folded helix or spiral and each heme unit of Hb, the four square planar coordination positions of Fe(II) are being occupied by the four nitrogen of the protopor-physrin ring, the fifth position of Fe(II) is occupied by the

imidazole nitrogen of histidine residue of the globin chain.
The globin proteins are of two types: 2 are α and two are β.
α has 141 A.Acids sequence.
β has 146 A " " .
Each protein has one polar and one non polar group.
The protein attached to Fe(II) in such a way that the polar grps of each protein are on the outside of the structure, leaving a hydrophobic interior. ∴ the Heme group is held in a water resistant protein pocket.

In free heme molecule there are two coordination positions above and below the plane of porphyrin molecule. These two positions are occupied by H_2O molecule.

The Fe(II) ion in Heme is very sensitive to ~~H_2~~ O_2 and it undergoes combination with it readily to form a labile Fe(II)-O_2 complex (Oxyheme) which changes into the Fe(III) protoporphyrin called Hematin or Hemin. the mech. for the formatn is as follows:-

1) $PFe^{II} + O_2 \rightleftharpoons PFe^{II}-O=O$

2) $PFe^{II}-O=O + PFe^{II} \longrightarrow PFe^{III}-O-O-Fe^{III}P$

μ-peroxocomplex

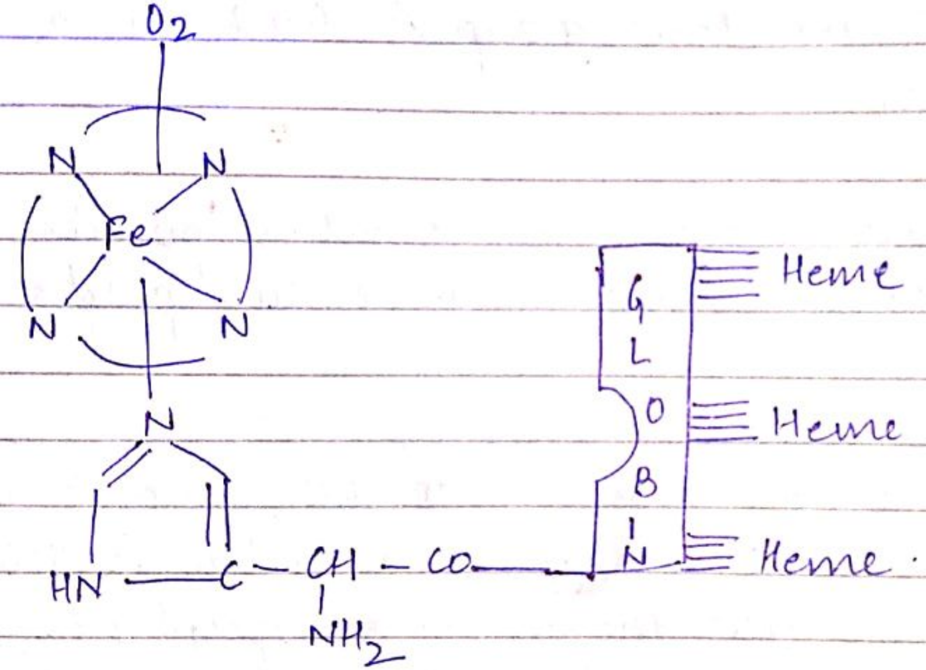
3) $PFe^{III}-O-O-Fe^{III}P \longrightarrow 2\,PFe^{IV}=O$

peroxo complex — ferryl complex

4) $PFe^{IV}=O + PFe^{II} \longrightarrow PFe^{III}-O-Fe^{III}P$

ferryl complex (Heme) another — Hematin

In hematin iron is Fe(III) H.S and it is unable to transport O_2.



An oxygenated Hb.

∴ The globin (protein) part serves three purpose:-

1. It furnishes a ligand to the iron
2. It restricts the motion of heme which prevents the formatn

of μ - oxo dimeric oxidation product.

3) It provide the heme with "a medium of low dielectric strength". (The H/C envt. of heme has a low dielectric constant and so it act as non polar solvent that cannot support extensive charge transfer from iron and reduction of Oxygen to superoxide.

The oxidised forms containing Fe(III) of Hb is called methemoglobin (Met-Hb)

Myoglobin (Mb):-

It is a protein which has only one heme group per molecule and serves as an oxygen storage molecule in the muscles. Molar mass (17,800). It binds O_2 more strongly than Hb. There are 7 helical segments in the α-chains and 8 in β forms in Mb.

Oxygenation behaviour of Hb and Mb / The physiology of Hemoglobin / M[illegible]

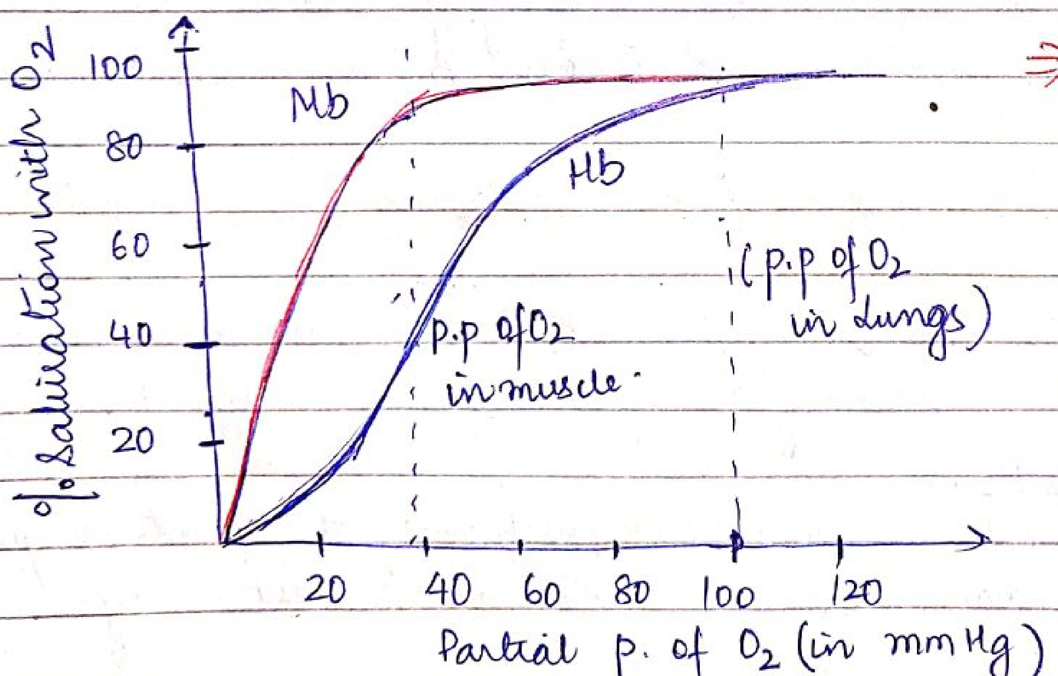
Hb has relatively high affinity for dioxygen at high partial pressures of dioxygen whereas Mb has relatively high affinity for dioxygen at lower partial pressures of O_2.

In vertibrates O_2 enters blood in the lungs where the partial pressure of dioxygen is relatively high and hemoglobin is virtually saturated with dioxygen in lungs. When hemoglobin carries dioxygen to muscle tissues, it experiences the low partial pressures of O_2 and its affinity for O_2 falls off rapidly & in this situation affinity of ~~for~~ Mb for O_2 is relatively high.

∴ In muscles tissues dioxygen is thermodynamically favourable transferred from hemoglobin to myoglobin. The reactions that are:-

$Hb + 4O_2 \longrightarrow Hb(O_2)_4$ (in lungs)

$Hb(O_2)_4 + 4\,Mb \longrightarrow 4\,Mb(O_2) + Hb$ (in muscle tissue)



⇒ O_2 dissociation curves for Hb & Mb showing how Hb is able to absorb O_2 efficiently in lungs yet transfer it to Mb in tissues

The oxygenation eqlbm for Mb is represented as:

$$Mb + O_2 \rightleftharpoons MbO_2$$

$$K_{Mb} = \frac{[MbO_2]}{[Mb][O_2]}$$

If 'f' is the fraction of myoglobin bearing O_2
pO_2 is the eqlbm partial pressure of dioxygen then,

$$K = \frac{f}{(1-f)\,pO_2}$$ 'K' is called the binding constant of Mb for O_2.

or $$f = \frac{K \cdot pO_2}{1 + K \cdot pO_2}$$

The Hb curve $\boxed{\text{doesnot}}$ follow such eqn
It follows an empirically modified form with pO_2 replaced by $p^n O_2$

$$\therefore K = \frac{f}{(1-f)\,p^n O_2} \quad \text{or} \quad f = \frac{K p^n O_2}{1 + K p^n O_2}$$

f=