Consider the differences between the  $O_2$  binding properties of Hb and Mb.

The O<sub>2</sub> binding curve for Mb is shown in Fig 7.5. The curve describes the fraction,  $\theta$ , of molecules that have bound O<sub>2</sub> at various partial pressures of O<sub>2</sub>, P<sub>O2</sub>.

The relationship between  $\theta$  and  $P_{O_2}$  is determined from the equilibrium expression as shown in the handout.

The fraction of Mb molecules which have bound  $O_2$  can be determined from differences in the absorption spectra of Mb in the presence and absence of  $O_2$  as shown in Fig 9-2.

The shape of the  $O_2$  binding curve is hyperbolic.

 $\mathsf{P}_{50}$  is the  $\mathsf{P}_{O_2}$  at which 50% of the Mb has bound  $\mathsf{O}_2.$ 

Fig 7.8(a) shows that the  $O_2$  binding properties of Mb would not provide efficient transport of  $O_2$  from the lungs to tissues.

The partial pressure of  $O_2$  in the lungs is about 3 times that in the tissues (~ 100mm Hg compared to 30mm Hg) as shown in Fig 7.8(a).

Mb would not provide efficient  $O_2$  transport because at both these pressures most of the protein would be in the bound form, i.e., Mb would not release a significant fraction of its bound  $O_2$ .

The binding curve for Hb is sigmoidal as shown in Fig 7.8(d).

The binding curve is sigmoidal because  $O_2$  binding is cooperative.

By cooperative, we mean that the binding of  $O_2$  to the heme Fe in one subunit affects the binding affinity (K) of the other subunits.

In Hb, there is a progressive increase in the affinity of unbound subunits as the number of  $O_2$  bound subunits increase.

Because of cooperative binding, Hb will be almost fully saturated ( $\theta \approx 1$ ) with O<sub>2</sub> at 100mm Hg but only partially saturated ( $\theta \sim .4$ ) with O<sub>2</sub> at 30mm Hg.

Therefore most of the  $O_2$  bound by Hb in the lungs will be released by Hb at the tissues.

Fig 7.10 is a Hill plot of  $O_2$  binding to Hb and Mb. In the Hill plot the log of the ratio of  $O_2$  bound sites/unbound sites is plotted versus the log  $P_{O_2}$ .

For Mb, the plot is a straight line with a slope of 1.

For Hb, the plot is not linear, but the maximum slope is a measure of the cooperativety of binding, i.e., the greater the slope the more cooperative the binding. Consider how the binding of  $O_2$  to the heme Fe in one subunit affects the affinity of  $O_2$ binding to the other subunits.

X-ray crystal studies indicate that there are differences in the structures of oxyHb and deoxyHb.

Fig 7.13 is an attempt to show the change in structure as  $O_2$  is bound to Hb.

Figs 7.17 and 7.16 show the basis for the change.

The structure of deoxyHb is referred to as the T (tensed) state while the structure of oxyHb is referred to as the R (relaxed) state.

In the T state, the structure at the heme is not as conducive to  $O_2$  binding because of the orientation of the proximal His and the neighboring Val FG5 as shown in Fig 7.17.