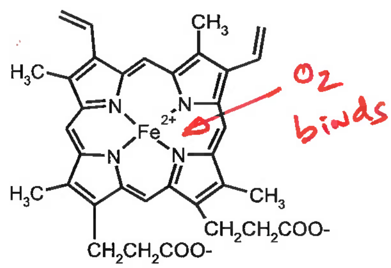
Lecture 12: O_2 Transport.

- Understand the molecular basis of oxygen binding by myoglobin and hemoglobin
- Understand the relationship between oxygen binding, oxygen transportation, and positive cooperativity.

Oxygen Transport: Oxygen is absolutely required for life in most organisms. All tissues need oxygen. Oxygen is usually taken up in the lungs by the protein **Hemoglobin (Hb)** and carried throughout the body in the circulatory system. **Myoglobin (myo)**, is used to store the oxygen and to facilitate its diffusion within cells.

Structural Features of Myoglobin and Hemoglobin

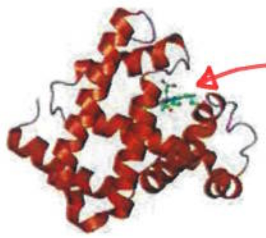


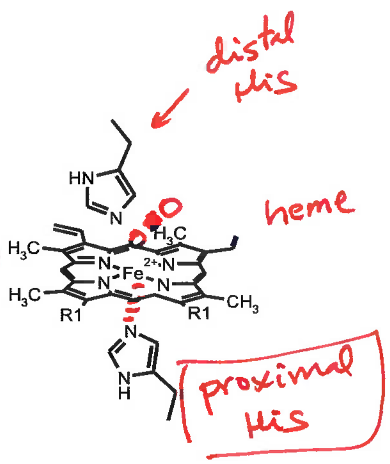
Properties of heme group

- Example of a **prosthetic group** in proteins. A prosthetic group is usually an organic compound or a metal ion what is tightly bound to the protein and plays an essential role in the function of that protein.
- Heterocyclic ring containing 4 pyrrole rings
- Central atom is Fe^{2+} (usual oxidation state) in Myo and Hb

Myoglobin (Mb)

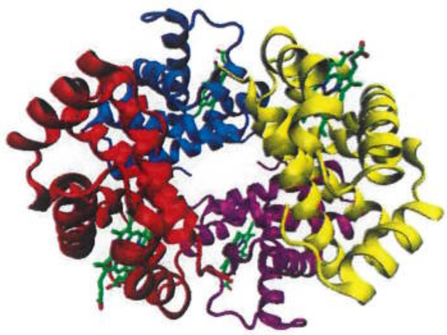
- Monomeric (tertiary structure)
- Contains a single heme group with a bound Fe^{2+}
- Binds 1 oxygen molecule per molecule of protein.





Hemoglogin (Hb)

- Tetrametric, two alpha chains and two beta chains - heterotetramer
- Each chain is structurally similar to myoglobin
- Each chain contains a bound heme-Fe^{2+}
- Binds a total of 4 oxygen molecules to its four heme groups.
- **Proximal histidine** is important in transducing the binding event to other protein subunits in hemoglobin, leading to cooperative binding.



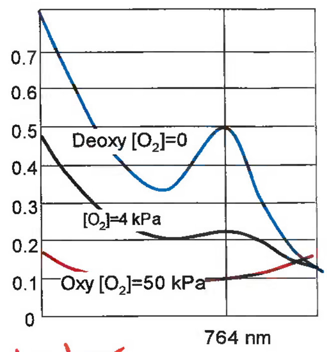
Oxygen Binding: The binding equilibrium, using myoglobin (Myo) as an example:

$$(Myo) + O_2 \leftrightarrow (Myo\text{-}O_2)$$

The ligand concentration is often given as pO_2, or the partial pressure of oxygen. The units are in kPa or in Torr. For oxygen binding proteins the K_D is also referred to as the "p_{50}", the amount of oxygen required to give a fractional saturation of Y=0.5. In the case of myoglobin, the K_D is about 0.25 kPa (see binding curve below).

$$Y = \frac{pO_2}{K_D + pO_2} = \frac{[L]}{K_D + [L]}$$

The degree of oxygen binding can be easily measured using absorption because the absorption spectra of the heme changes when oxygen bonds (see graph on right).



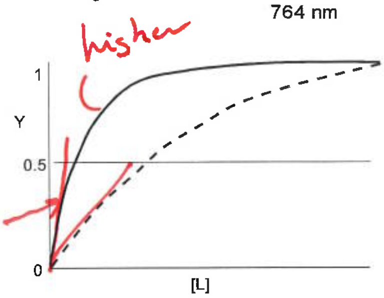
Example: A sample was made with an oxygen concentration of 4 kPa. What is the fractional saturation of hemoglobin at this oxygen concentration (use the absorption values at 764 nm)?

$A_M = 0.5$
$A_{ML} = 0.1$
$A = 0.25$

$$Y = \frac{A - A_M}{A_{ML} - A_M} = \frac{0.25 - 0.5}{0.1 - 0.5} = \frac{-0.25}{-0.4} = 0.65$$

Binding Curves:

1. High affinity corresponds to larger or smaller K_D?
2. Which of the following two curves represents higher affinity binding?
3. Which as the greater slope at low [L]?

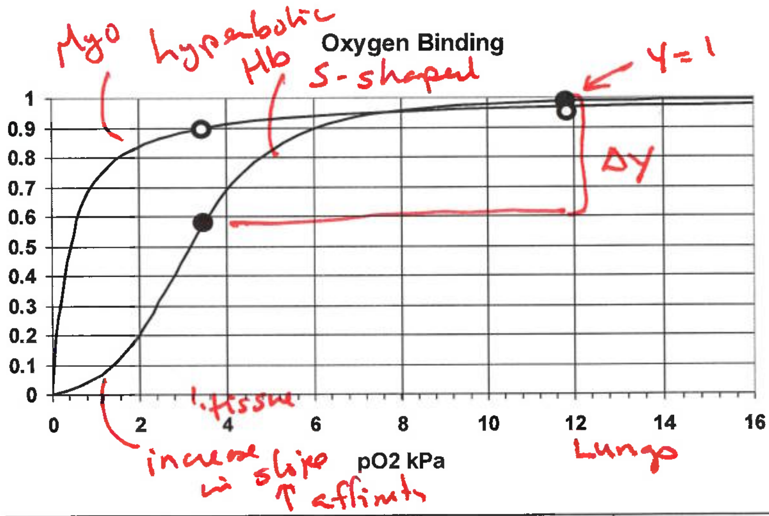


4. What is the "shape" of the curve? hyperbolic

Oxygen Delivery – The cooperative binding of O_2 to Hb:

The efficient delivery of oxygen to the tissues presents a difficult problem. How do you design a protein that will bind oxygen well in the lungs and then *efficiently* release that oxygen in the tissues where it can be bound by myoglobin.

A comparison of the oxygen binding curves of myoglobin (myo) and hemoglobin (hb) shows that Hb is effective at oxygen delivery due to its non-hyperbolic binding curve.

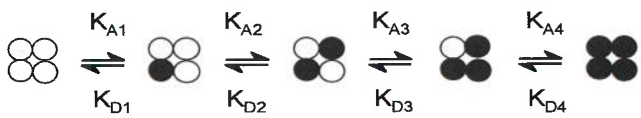


Calculating Oxygen Delivery.	Hemoglobin●	Myoglobin o
In the lungs $[O_2]$ ~12 kPa	**Y = 0.98**	**Y =0.96**
At the tissues $[O_2]$ ~ 3.5 kPa	**Y = 0.60**	**Y =0.90**
Amount delivered = ΔY	0.38	0.06

Reflection:

i) How does the binding curve differ between myoglobin (binds one O_2) and hemoglobin (binds 4)?

ii) Based on the initial slope (pO_2 ranging from 0 to 2), what is happening to the affinity as oxygen binds to Hb?



lower K_D →

$K_{D2} < K_{D1}$