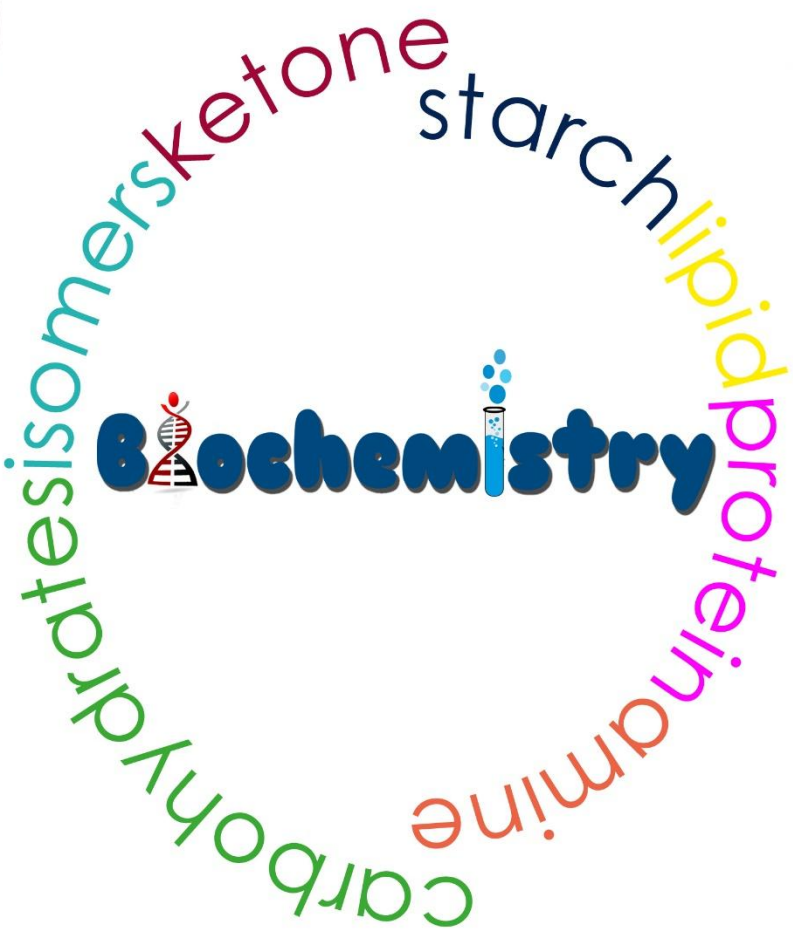


◉Sheet ○Slides

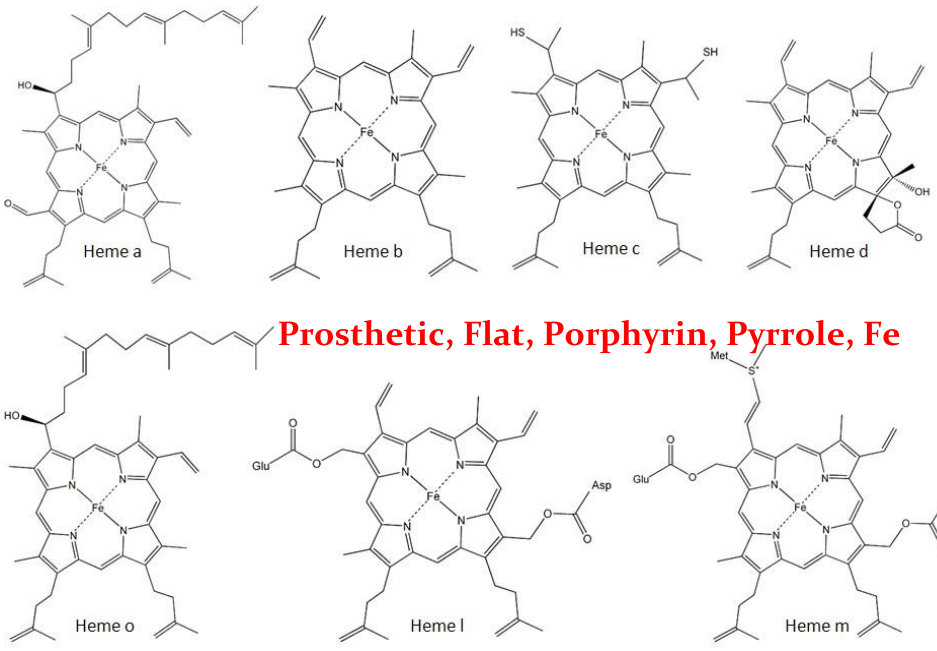
Subject :	Structure-function relationship 2
Done by :	Yaman Jarrar
Corrected by :	Motasem Abu_Mallouh
Number :	6

In this sheet we are going to talk about two **globular proteins**: Myoglobin and Hemoglobin, what is common between them? Both are oxygen carriers because the presence of a heme group.

Heme group: an organic structure synthesized within our bodies, in the center of each heme we have an Iron atom. Iron have to be obtained from outside of the body.

If someone has an anemia we give him iron supplement , so when we increase iron in the blood the body synthesis heme group as a result of that body synthesis globin protein then heme associated with globin protein

Heme is composed of a porphyrin ring + Iron atom, heme structure is formed by four small rings called pyrrole rings which contains Nitrogen bonded to an Iron atom. Types of heme differs in what is extra on the ring, most common heme is heme B which is found in Myoglobin and Hemoglobin.



Prosthetic, Flat, Porphyrin, Pyrrole, Fe

Iron have the ability to make 6 bonds, Iron atom in the free form of heme makes 4 bonds thus called 4 coordinated heme,

Free form heme has 2 vacant spaces, heme within protein will be binding to one of the amino acids in the chain in order to fix the heme in its place while the the other space should be vacant so the ligand (O2 or CO) can bind, heme in binding protein is called 5 coordinated heme (when it binds with oxygen becomes 6 coordinated so without oxygen it is 5 coordinated)

Why heme have the ability to transfer electrons?

Because Iron can go in different oxidation states Fe+2 (ferrous-reduced) and Fe+3 (ferric-oxidized), this is why heme protein can be used in electron transfer such as: cytochrome C oxidase in electron transport chain(this type have 6 coordinated heme).

***Myoglobin**

It is the first protein to be crystalized by crystallography technique.

the function: Myoglobin storage oxygen in whole cells in the body and it concentrated in muscle cells

Contains only Alpha helices (8 helices with one heme group) and 153 Amino Acids.

Heme group fits in the protein in a pocket (hydrophobic pocket) which helps to keep the iron in the reduced state.

Presence of heme stabilize the tertiary structure of the protein.

Iron has to be in the reduced state (ferrous) in order to bind oxygen, when Iron is oxidized, it has a very low affinity for oxygen. However, when it is reduced it has a high affinity for binding oxygen.

Hemoglobin when its iron is in oxidized state called Methemoglobin. Methemoglobinema is a disease caused by the mutation of the enzyme which reduce the Iron causing a very low oxygen carrying capacity.

Nitrates can inhibit enzymes which reduce the iron and can cause Blue Baby Syndrome.

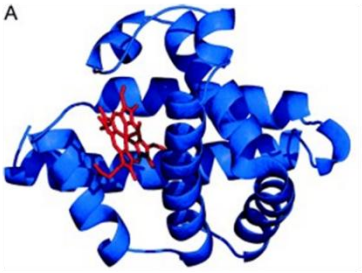
The fifth bond that is linked to the iron atom is from an amino acid which is histidine(iron bind with N in histidine) and it is proximal(F8).

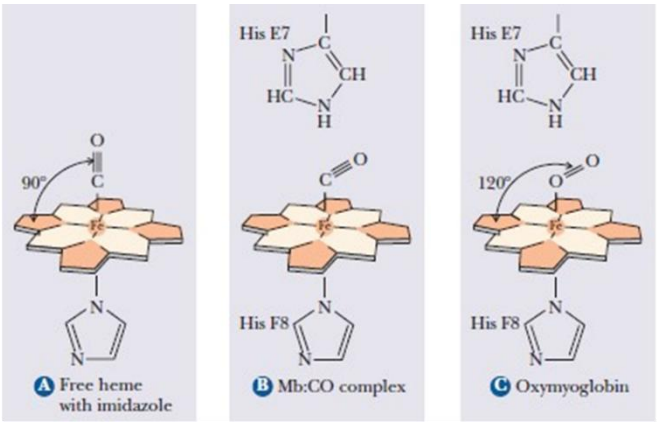
Histidine can be found in active sites of enzymes and binding areas of proteins, why? Because it Pka (6) which is near the physiological pH of the human.

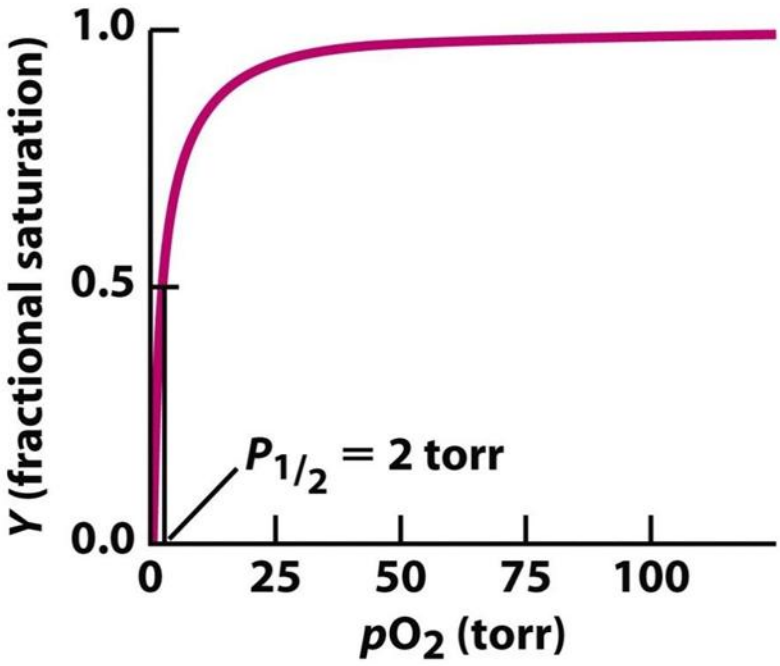
Distal binding area is for the ligand and proximal binding area is for the histidine.

Distal histidine(E7) is close to the distal area, why? 1- histidine works as a gate 2-if histidine does not exist, the bond between ligan and heme is going to be vertical which means a very strong bond thus harder to release the ligand, so the presence histidine makes the binding with angle so the bond become weaker (decrease in the affinity).

(distal), F8 (proximal)
Oxy vs. deoxymyoglobin
Fe(II) coordination (redox)







The following plot express the relationship between partial pressure of oxygen and the fractional saturation for Myoglobin. As we can see, with a small change in partial pressure we can achieve a high saturation percentage.

50% saturation of myoglobin occurs at 2 torrs, that means that myoglobin has a high affinity for oxygen, and this binding follows a hyperbolic saturation curve.

Myoglobin needs 2 Torrs to be get 50% of myoglobin saturated, if the partial pressure of oxygen is more than 2 torrs, oxygen easily binds to myoglobin. If the partial pressure is less than 2 torrs, oxygen is released from myoglobin.

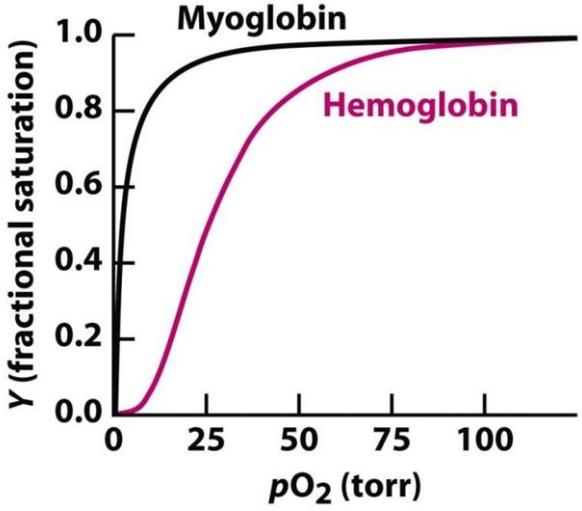
Tissues oxygen pressure is 20 torrs so myoglobin binds oxygen because the partial pressure of oxygen is higher than 2 torrs.

***Hemoglobin**

Hemoglobin is composed of four subunits: 2 alphas and 2 betas, each subunit have a heme group.

The function: 1)transport of O2 and CO2 2) blood buffering

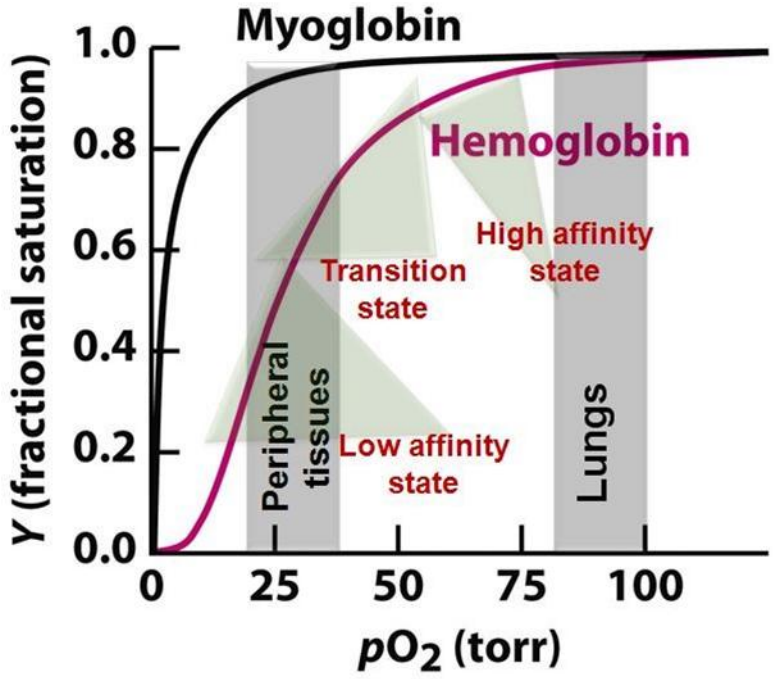
Hemoglobin binds oxygen cooperative binding: when the first oxygen binds to the first subunit, it becomes easier for the next subunits to bind oxygen.



This plot show the relationship between partial pressure of oxygen and the fractional saturation of hemoglobin and myoglobin:

At 100 torrs hemoglobin is 98% saturated(lungs), at 20 torrs hemoglobin is less the 50% saturated so it release the oxygen (tissues).

The saturation of hemoglobin binding to oxygen has a sigmoidal shape (S shape), because of the cooperative behavior.



Hemoglobin changes its function due to the partial pressure, binding oxygen in lungs and releasing oxygen in tissues.

The P50 of hemoglobin is 26 torrs, in lungs PO2=100 so oxygen binds to hemoglobin, in tissues PO2=20 so oxygen is released from hemoglobin.