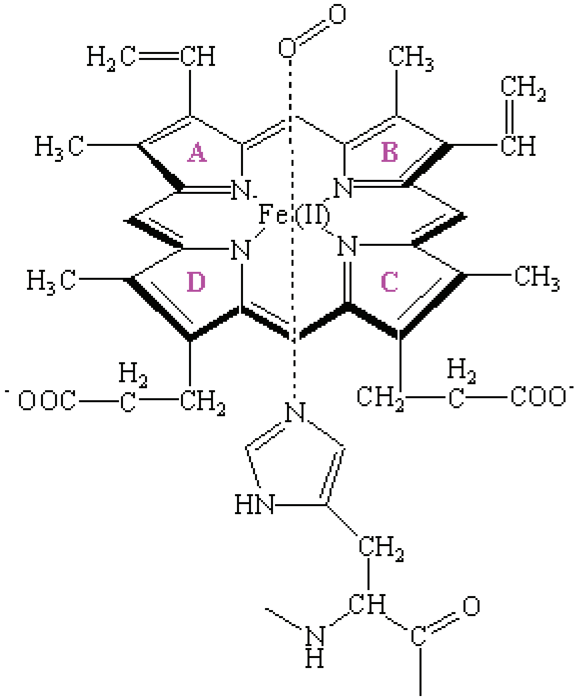
BLOOD OF ALL ANIMALS

The Chemistry of Hemoglobin and Myoglobin

At one time or another, everyone has experienced the momentary sensation of having to stop, to "catch one's breath," until enough O_2 can be absorbed by the lungs and transported through the blood stream. Imagine what life would be like if we had to rely only on our lungs and the water in our blood to transport oxygen through our bodies.

O_2 is only marginally soluble ($< 0.0001\ M$) in blood plasma at physiological pH. If we had to rely on the oxygen that dissolved in blood as our source of oxygen, we would get roughly 1% of the oxygen to which we are accustomed. (Consider what life would be like if the amount of oxygen you received was equivalent to only one breath every 5 min, instead of one breath every 3 s.) **The evolution of forms of life even as complex as an earthworm** required the development of a mechanism to actively transport oxygen through the system. Our blood stream contains about 150 g/L of the protein known as **hemoglobin** (Hb), which is so effective as an oxygen-carrier that the concentration of O_2 in the blood stream reaches 0.01 M the same concentration as air. Once the Hb-O_2 complex reaches the tissue that consumes oxygen, the O_2 molecules are transferred to another protein **myoglobin** (Mb) which transports oxygen through the muscle tissue.

The site at which oxygen binds to both hemoglobin and myoglobin is the **heme** shown in the figure below.



At the center of the heme is an Fe(II) atom. Four of the six coordination sites around this atom are occupied by nitrogen atoms from a planar **porphyrin** ring. The fifth coordination site is occupied by a nitrogen atom from a histidine side chain on one of the amino acids in the protein. The last coordination site is available to bind an O_2 molecule. The heme is therefore the oxygen-carrying portion of the hemoglobin and myoglobin molecules. This raises the question: What is the function of the globular protein or "globin" portion of these molecules?

The structure of myoglobin suggests that the oxygen-carrying heme group is buried inside the protein portion of this molecule, which keeps pairs of hemes group from coming too close together. This is important, because these proteins need to bind O_2 reversibly and the Fe(II) heme, by itself, cannot do this. When there is no globin to protect the heme, it reacts with oxygen to form an oxidized Fe(III) atom instead of an Fe(II)-O_2 complex.

Hemoglobin consists of four protein chains, each about the size of a myoglobin molecule, which fold to give a structure that looks very similar to myoglobin. Thus, hemoglobin has four separate heme groups that can bind a molecule of O_2. Even though the distance between the iron atoms of adjacent hemes in hemoglobin is very large—between 250 and 370 nm—the act of binding an O_2 molecule at one of the four hemes in hemoglobin leads to a significant increase in the affinity for O_2 binding at the other hemes.

This **cooperative interaction** between different binding sites makes hemoglobin an unusually good oxygen-transport protein because it enables the molecule to pick up as much oxygen as possible once the partial pressure of this gas reaches a particular threshold level, and then give off as much oxygen as possible when the partial pressure of O_2 drops significantly below this threshold level. The hemes are much too far apart to interact directly. But, changes that occur in the structure of the globin that surrounds a heme when it picks up an O_2 molecule are mechanically transmitted to the other globins in this protein. These changes carry the signal that facilitates the gain or loss of an O_2 molecule by the other hemes.

Drawings of the structures of proteins often convey the impression of a fixed, rigid structure, in which the side-chains of individual amino acid residues are locked into position. Nothing could be further from the truth. The changes that occur in the structure of hemoglobin when oxygen binds to the hemes are so large that crystals of deoxygenated hemoglobin shatter when exposed to oxygen. Further evidence for the flexibility of proteins can be obtained by noting that there is no path in the crystal structures of myoglobin and hemoglobin along which an O_2 molecule can travel to reach the heme group. The fact that these proteins reversibly bind oxygen suggests that they must undergo simple changes in their conformation—changes that have been called **breathing motions**—that open up and then close down the pathway along which an O_2 molecule travels as it enters the protein. Computer simulations of the motion within proteins suggests that the interior of a protein has a significant "fluidity," with groups moving within the protein by as much as 20 nm.

Source: http://chemed.chem.purdue.edu/genchem/topicreview/bp/1biochem/blood3.html

Absolutely fascinating that ALL CREATURES share blood characteristics!

Even the blood of worms has HEME.