

# Protein Structure II Highlights

1. Myoglobin is a protein that acts like a 'battery', storing oxygen in muscles until it is needed. It is related to the oxygen transport protein called hemoglobin, but does not have a significant function in transporting oxygen - only storing it.
2. Myoglobin contains a functional group called 'heme'. Heme is composed of a ring called Protoporphyrin IX plus an iron atom. Heme is closely related to chlorophyll.
3. The iron group in heme is held in place by 4 nitrogens of the heme and one N of a histidine above the ring. In addition to molecular oxygen, carbon monoxide can bind to the iron of the heme group.
4. Hemoglobin differs from myoglobin in containing four polypeptide subunits instead of one. Interactions between multiple polypeptide subunits of a protein are called quaternary structure.
5. Hemoglobin contains two alpha and two beta subunits, each carrying one heme molecule. Binding of an oxygen molecule by one subunit causes a slight conformational change in the subunit that causes a slight quaternary change that causes an adjacent subunit to bind oxygen with greater affinity. This is referred to as cooperativity. When hemoglobin is in the state of high affinity for oxygen (wants to bind oxygen), we say it is in the R state. When it is in the low affinity state for oxygen (wants to release oxygen), we say it is in the T state.
6. Cooperativity requires multiple subunits. Myoglobin, which has only one subunit, does not exhibit cooperativity. Thus, myoglobin's affinity for oxygen does not change as the oxygen concentration changes. This is not a good property for carrying oxygen, but is great for storing oxygen. It is for these reasons that myoglobin is used to store oxygen and hemoglobin is used to carry oxygen.
7. In the lungs, the oxygen concentration is high, so hemoglobin easily gets loaded up with oxygen. In tissues, where oxygen concentration is low, one of the oxygens comes off of hemoglobin and the reversal of what happened above occurs. Loss of one oxygen by hemoglobin favors loss of the others and oxygen is dumped where it is needed.
8. The Bohr effect relates to the fact that hemoglobin loses affinity for (lets go of) oxygen the more acidic the environment in which the hemoglobin is found. Any tissue, such as muscles, when actively using energy, produces acid. Active tissues require more oxygen than non-active tissues, as we will see later in the course. Thus active tissues get more oxygen dumped on them by hemoglobin, due to the Bohr effect.
9. Adult hemoglobin contains a tiny pocket in the middle of it that can bind a molecule called BPG (also called 2,3BPG). BPG is produced by actively respiring tissues. When it is bound, hemoglobin loses some affinity for its oxygen and lets it go. Hemoglobin drops BPG before it gets to the lungs and it is broken down readily, if you're not a smoker. I
10. In smokers, BPG is in greater abundance in the blood, so hemoglobin has reduced oxygen carrying capacity.
11. Hemoglobin can also carry carbon dioxide. CO<sub>2</sub> is a byproduct of active tissues. When hemoglobin picks up protons near active tissues, it dumps the oxygen and picks up CO<sub>2</sub>, which it transports it back to the lungs. In the lungs, the pH is low, the protons and CO<sub>2</sub> come off. They are actually forced off due to the high

oxygen concentration. When CO<sub>2</sub> comes off, it is exhaled.

12. Fetal hemoglobin differs from adult hemoglobin in that the two beta subunits are replaced by two gamma subunits. This changes hemoglobin's structure very slightly so that 2,3BPG can't bind. Consequently, fetal hemoglobin spends more time in the R state and can take oxygen away from adult hemoglobin.

13. Sickle cell anemia arises from a mutation in one of the hemoglobin subunits. This mutation causes hemoglobin to polymerize under low oxygen conditions and converts the blood cells into a sickle shape. They get stuck in capillaries when this happens. The mutation appears to convey a bit of protection against malaria when present heterozygously.