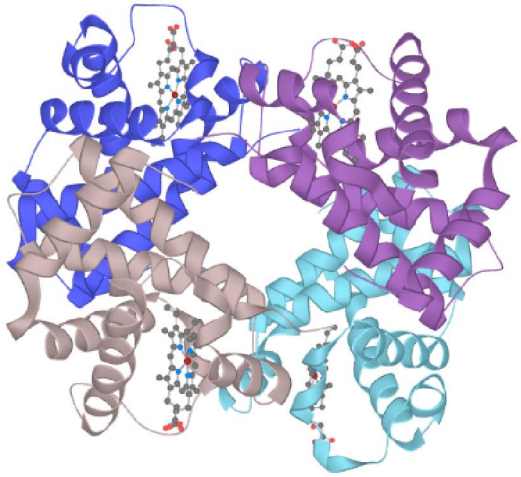
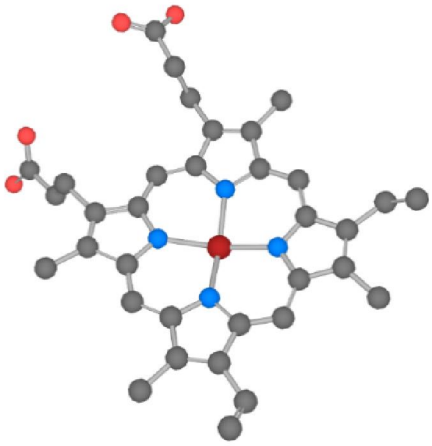
TB1 - Hemoglobin and Conjugated Proteins

HEMOGLOBIN AS A CONJUGATED PROTEIN

Conjugation means to connect two different things together. A **conjugated protein** is a protein which is connected to another species which isn't a protein. When proteins are broken down, they produce amino acids. But breaking down a conjugated protein will release amino acids as well as some molecules, or ions, which are not amino acids. These non-amino acid parts are called **prosthetic groups**, because they are different to the rest of the polypeptide. Prosthetic groups can be connected to the protein through either standard covalent interactions or non-covalent ones such as ionic bonds, depending on the nature of the system. Two classic examples of prosthetic groups are heme found in hemoglobins, and chlorophyll in plants.

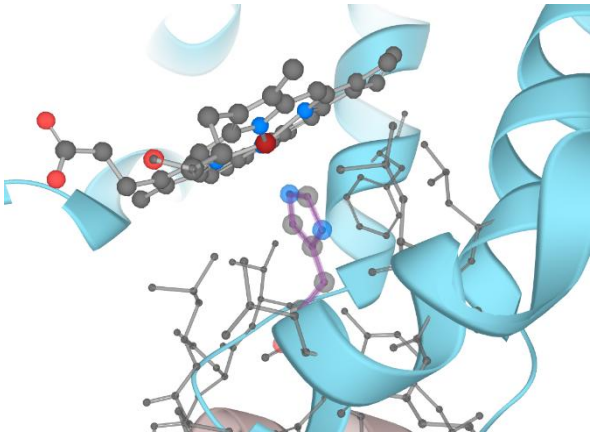


PDBe entry 1a3n. Deoxygenated human hemoglobin complex.



PDBe entry 1a3n. Deoxygenated heme group in human hemoglobin.

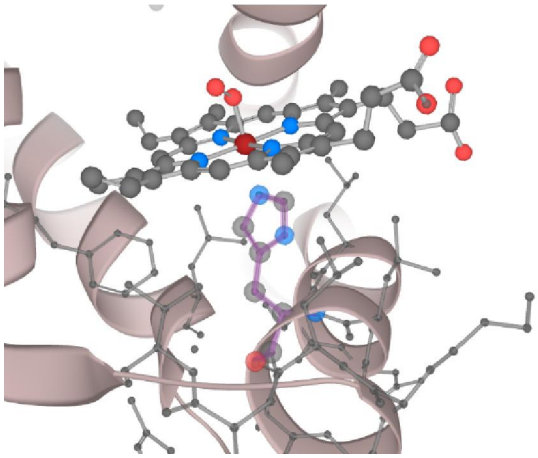
Hemoglobin contains four globular subunits, making it a tetramer. The heme unit contains a central iron atom, which can be in the Fe^{2+} oxidation state. This ion is coordinated to 4 nitrogen atoms in a porphyrin ring, and also to a fifth N atom, in the histidine residue of the alpha helix below. It's this interaction with the alpha helix that connects the prosthetic heme group to the polypeptide, and forms the conjugated protein. When an O atom coordinates to the Fe^{2+} in hemoglobin, it produces a six-coordinate, octahedral complex.



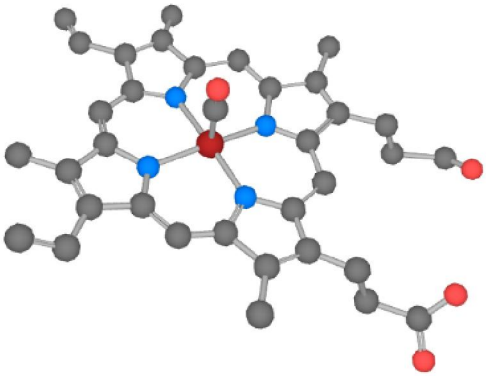
PDBe entry 1a3n. Deoxygenated heme group in human hemoglobin. The histidine residue below interacts with the iron ion and holds it in place.

PROSTHETIC GROUPS AS CARRIERS

In the blood, there are many different types of small molecules which are similar to O_2. Because of this, it is possible for molecules which are not O_2 to bind to the Fe^{2+}. One important example of this is CO. Carbon monoxide is an odourless, toxic gas which is produced by incomplete combustion, combustion which doesn't quite have enough oxygen to form CO_2. When CO binds to hemoglobin, it does so very strongly. Much stronger than O_2 does, and this blocks the hemoglobin sites. This means that hemoglobin cannot carry O_2 around the body, and the body experiences oxygen deprivation. This can occur even when there is plenty of O_2 nearby, as it struggles to displace the CO which has already blocked the sites.



PDBe entry 2dn1. Oxygenated form of human hemoglobin.



PDBe entry 2dn3. Human carboxyhemoglobin.