

Max Yan

Cluster 8

Modifying Heme Groups' Atoms to Increase Oxygen

Intake

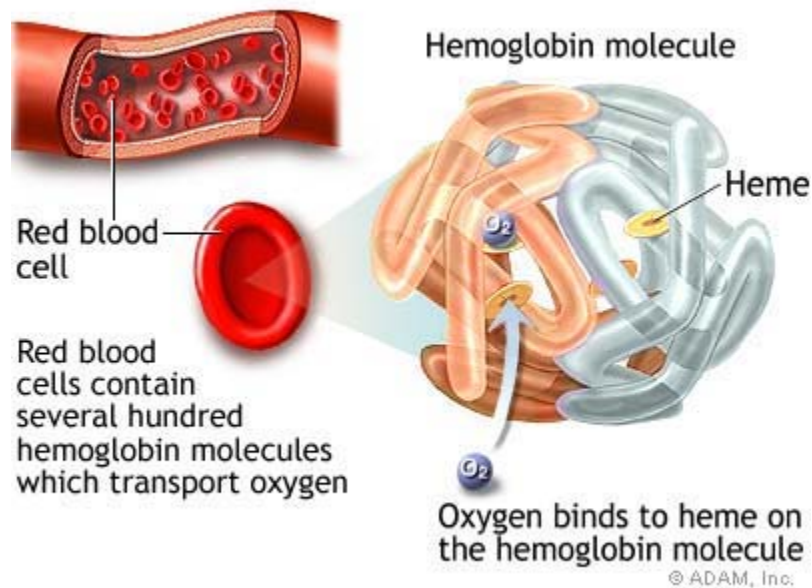


Figure 1: Red blood cells flow through the veins. Within each blood cell are hemoglobin proteins, which carry oxygen to other parts of the body. <http://graphics8.nytimes.com/images/2007/08/01/health/adam/19510.jpg>

Abstract:

Red blood cells consist of one essential protein: hemoglobin. People who live or climb in high altitudes or who are athletes breathe deeper and faster to increase the intake of oxygen because their bodies need more oxygen. This puts more stress on the heart to pump faster to move the oxygen rich blood around the body. By switching some carbon atoms with other atoms within the heme group's structure, I hope to increase the intake of oxygen. By replacing four carbon atoms with another element, the minimal energy level decreased and more oxygen molecules were attracted to the heme group more easily. While Polonium and Selenium had the best results, they are the most dangerous to the body.

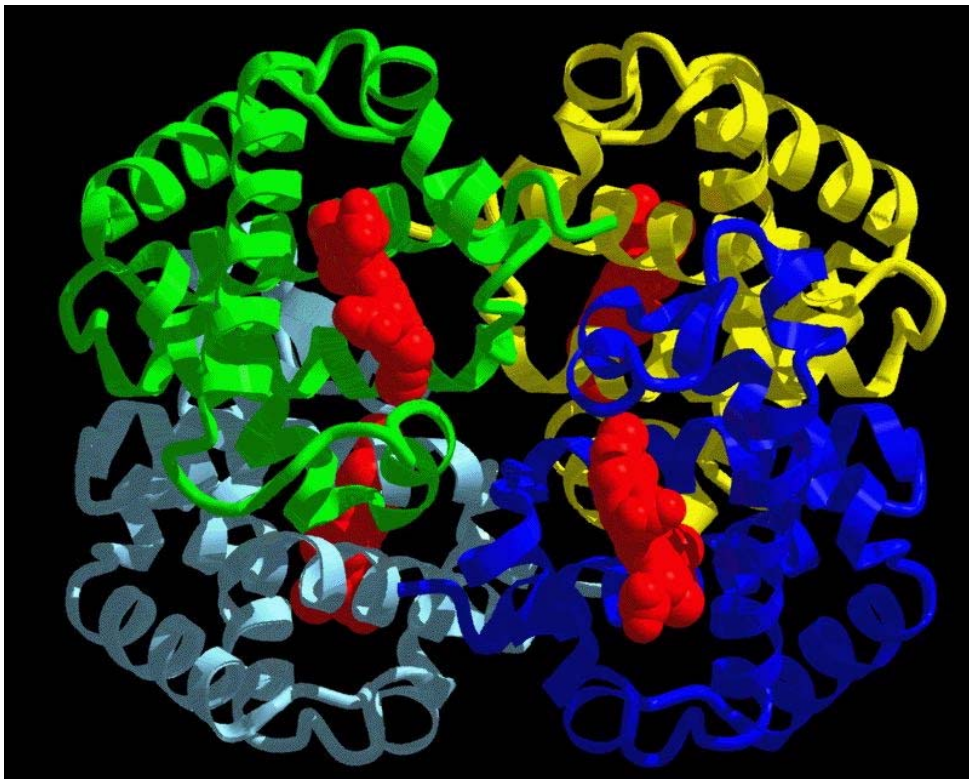


Figure 2: Here is an image of the hemoglobin protein. Each colored ribbons are subunits of the protein. The red molecule is called the heme group where the oxygen binds to the iron ion. <http://www.bio.davidson.edu/Courses/Molbio/MolStudents/spring2005/Heiner/hem>

People who lived in higher altitudes or did sports, and needed more oxygen to

keep their body functioning properly, they would have to breathe faster and heavier.

Rather than changing the structure of the whole hemoglobin protein, I modified a smaller part of the hemoglobin: the heme group. If we modify the structure of the heme group within the hemoglobin protein, oxygen would attract to the heme group more easily. With a lower energy level, more oxygen molecules will weakly bind to the hemoglobin protein and deliver the weak-bonded oxygen molecules to muscles and tissues near the heart, and the blood can deliver the oxygen molecule bonded to the iron ion. The main purpose of this paper is to show the effects of modifying the structure of the heme group.

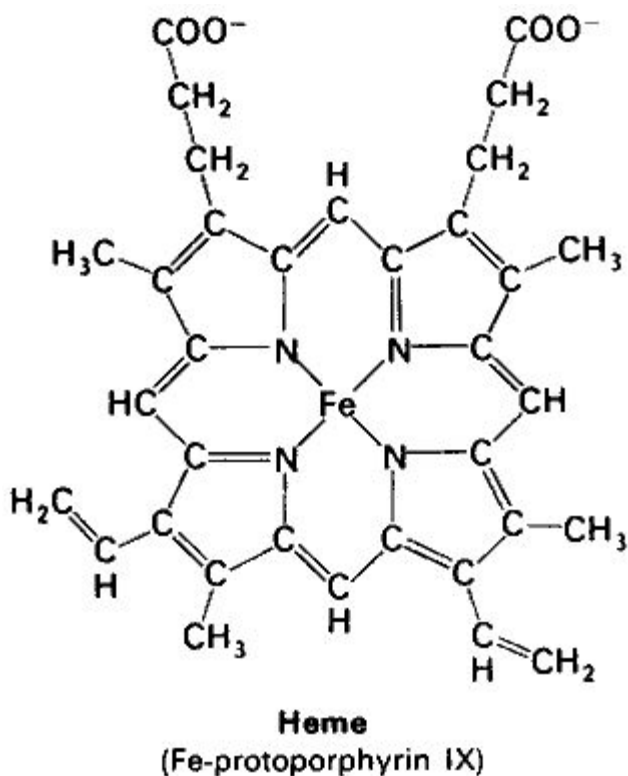


Figure 3: An image of the heme group showing all of the atoms and bonds.
<http://www.bio.davidson.edu/Courses/Molbio/MolStudents/spring2005/Heiner/hemoglobin.html>

Hemoglobin is essential for all animals' survival as it delivers oxygen around the whole body and it disposes the waste products. Red blood cells are mainly made up of

hemoglobin proteins, and each hemoglobin protein has four binding sites for the oxygen molecule: two alpha subunits and two beta subunits [6]. The only difference between the alpha and beta chains is that the beta chains are approximately five amino acids longer than the alpha chains [6]. Also, the hemoglobin molecules give the red blood cells their color. The hemoglobin binds to oxygen when surrounded by oxygen rich environments, and binds to carbon dioxide when the carbon dioxide concentration is bigger than the oxygen [5]. When the hemoglobin first binds to oxygen, the affinity is high, as the protein would like to have all four sites unoccupied, but once an oxygen molecule binds, the next three bind more easily as the affinity decreases. The same goes for once the protein has all four bonding sites filled with oxygen molecules; the hemoglobin wants to release all of the oxygen molecules [7]. This process of releasing and obtaining oxygen molecules is called cooperativity. When the alpha and beta subunits are filled with oxygen, the protein changes shape. The alpha beta dimer rotates approximately eighteen degrees. The changes in the structure help the protein deliver the oxygen molecules to the tissues more effectively. The hemoglobin delivers the oxygen when in the R-state, and when the hemoglobin releases its oxygen bonded molecules, the structure changes to the T-state where the hemoglobin will not accept any oxygen molecules to bond to it. Any slight changes to the structure of the protein may cause sickle cell disease, and the hemoglobin will not function properly. The function of the protein relies on the structure, so if I add an extra iron ion, there is a possibility that the hemoglobin protein will not survive and that could kill the person.

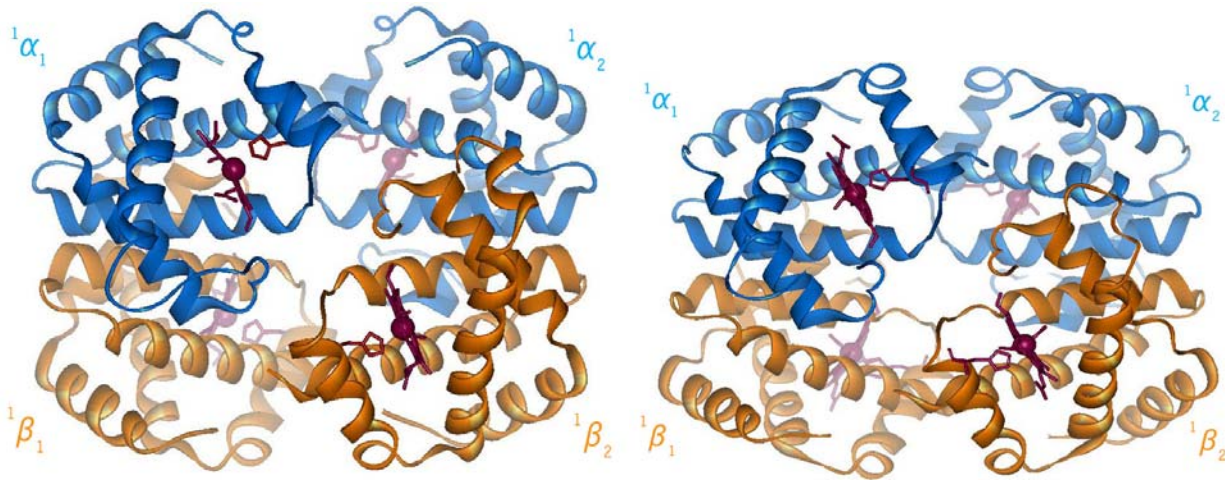


Figure 4 (right): Here is the hemoglobin in the R-state. When in the R-state, the hemoglobin will accept oxygen molecules.
<http://www.sicklecellinfo.net/hemoglobin.htm>

Figure 5(left): The hemoglobin protein in its T-state. When in the T-state, the hemoglobin will not accept any oxygen molecules.
<http://www.sicklecellinfo.net/hemoglobin.htm>

Max Perutz, a scientist, first developed a three-dimensional model of hemoglobin and its close cousin: myoglobin. With the 3-D model of hemoglobin, scientists were able to figure out how the hemoglobin protein functioned. The protein folds itself around the heme group, so when the iron binds to the oxygen molecule, it forms a weak bond rather than the strong bond that would oxidize the iron ion. If the iron ion were to securely bond to the oxygen, it would become an iron ion with a 3+ charge rather than the 2+ charge needed to bind with oxygen. Oxygen molecules cannot bind to 3+ charge iron ions as it would become useless to the red blood cell would not be able to carry oxygen throughout the body [1, 6].

External factors also affect oxygen's ability to bind to the hemoglobin. Carbon monoxide has a higher affinity than oxygen and when it binds to the heme group, oxygen cannot bind. The average pH level for oxygen to bind is 7.4. The Bohr Effect,

where the affinity decreases as the pH is lowered, helps prevent oxygen from binding onto the iron and delivering the oxygen molecules to the tissues that need the oxygen or have high levels of carbon dioxide. Also, the carbon dioxide binds to the hemoglobin when the hemoglobin is in its T-structure. When the carbon dioxide binds to the hemoglobin in place of the oxygen, the carbon dioxide binds to the N-terminus instead of the iron ion like the oxygen molecule does. Lastly, the DPG (2,3-diphosphoglycerate), which also decreases the oxygen affinity, binds to the heme group where the hemoglobin's T-shape is kept longer [4]. All of the external factors have higher affinities than oxygen and they bind to the hemoglobin proteins when it is in the T-shape.

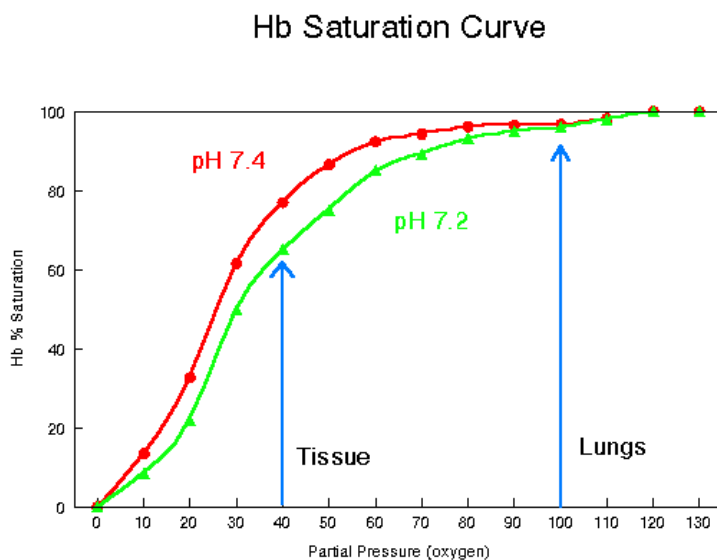


Table 1: The graph above shows the ability of the protein to bind to oxygen when in certain pH levels. As the pH levels decrease, the affinity to bind to an oxygen molecule decreases. <http://www.bio.davidson.edu/Courses/Molbio/MolStudents/spring2003/Stone>

One form of mutation in the red blood cell is the sickle cell. Rather than forming the circular shape a red blood cell normally forms, the sickle cell forms a crescent shape due to abnormal shapes of the hemoglobin proteins [2, 5]. The sickle cells are inflexible

and sticky; unlike its normal counterpart. The sickle cells have a shorter life than normal red blood cells where the sickle cells live approximately ten to twenty days, so people with sickle cell anemia disease will have a deficit of red blood cells as the bone marrow is unable to produce more blood cells at a rate equivalent to the dying sickle cells [2]. There are treatments for the symptoms, but there is hardly a chance of curing the disease [2]. A small number of bone marrow transplants have been reported successful in curing the disease [2].

High altitude birds have developed a mutation in their hemoglobin protein's structure. These birds have mutations in the hemoglobin where the oxygen affinity is increased even though the oxygen pressure in the higher altitudes is lower. The main mutation in the birds' hemoglobin is that they replaced a proline group with an alanine group, freeing up two carbons [6]. The extra space relaxes the T-structure of the hemoglobin, so the oxygen affinity in the deoxyhemoglobin state increases and the birds are able to breathe normally even when the oxygen pressure is low. Using the blood from birds and possibly making human blood to look like that of a bird may solve the problem for people who like to climb or live in high altitudes [6].

With the results of switching the four carbons in separate benzene rings, the minimal energy level decreased. I tested out seven other atoms when switching the carbons for: nitrogen, oxygen, sulfur, phosphorus, selenium, tellurium, and polonium. Also, for each element I used, I ran three separate tests for minimizing the energy levels: the first test I only switched one atom, the second I switched two atoms, and the third I

switched four atoms. The general trend was that as I switched more atoms, the lower the energy level was for the heme group. The only exception was that oxygen increased the energy level of the heme group because the electro negativity matched that of the oxygen molecules trying to bond to the iron ion. The most dramatic change between the regular heme group structure and the modified one was when I used selenium and polonium, with energy levels of 85.8067 and 78.5465 compared to the regular heme group's energy level of 123.4660. However, if we use these atoms to modify the structure of the heme group, they will have fatal consequences. Selenium is poisonous, and polonium is radioactive and hardly found in the nature [10]. Oxygen had the lowest minimal energy level when I only switched one oxygen molecule, with an energy level of 108.8815. Nitrogen had an energy level of 99.9674 when four carbons were replaced. Sulfur had 93.4157 with 4 of them, and tellurium had 114.1792 when four carbons atoms were replaced. The best bet for modifying the heme group safely is by switching the carbons with phosphorus as the element is stable, abundant, and essential for life [10]. Phosphorus had a minimal energy level of 86.7299. If the protein is not too sensitive to change and still functions after the modifications, hemoglobin could attract more oxygen molecules around it and deliver the weakly bonded oxygen molecules to tissues and muscles near the heart and deliver the oxygen bonded to the iron ion to other parts of the body.

In the far future, mutating hemoglobin synthetically maybe become possible and could help athletes and people who live or climb to high altitudes. Eventually, though,

hemoglobin will evolve by itself and change into a better structure, where the oxygen intake will increase.

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