

BERG/STRYER V STUDY GUIDE

CHAPTER 10

1. Homework 7, 8, 19. Omitting Chapter 9 and most of Chapter 10 is difficult, but there just isn't the time in one semester to cover everything. If you read all of these chapters you will be smarter and you will understand enzymes better. But I am covering only from pages 269 to 274, including 10.1.6 and all of 10.2, the Hemoglobin material.

2. MYO means "muscle" and **Myoglobin** is found in muscle (p. 61-62 and 179). HEMO is Greek for "blood" and that is where **Hemoglobin** is found, in the red cells (RBC) or **Erythrocytes**. You should be able to at least sketch a **heme group** (p. 270) and understand that it is the prosthetic group for various proteins including the globins and the cytochromes. The 3D structures of myoglobin (Mb) and the subunits of hemoglobin (Hb) are extremely similar (Fig. 7.13). On pages 61-62 Mb is described as folded into 8 alpha-helices, with an interior composed almost entirely of non-polar residues. The complete sequence of human Mb is given several times in Chapter 7 including the very beginning (p. 171). Certain features are worth noting. The **histidine** which attaches to the heme iron (Fig. 10.18 p. 270) can be located in the sequence QSHATK. Prolines cannot be within an alpha helix except at positions 1, 2, or 3, so it is easy to see some of the boundaries between helices (look for P). For more information, see handout on whale myoglobin.

3. Structurally the main difference between Mb and Hb is that Mb has only a single subunit, whereas Hb has **four** subunits, each of which resembles Mb. Hb has less affinity for oxygen than Mb. Study the loading curves on p. 273. The curve for Mb, or for Hb without **2,3-BPG**, would run up the Y axis to about 0.9 and then across the top. The **negative allosteric modulator** 2,3-Bis-phosphoglycerate (2,3 BPG p. 272) fits into the center of the tetrahedral structure of deoxy-Hb. It "props" Hb into the "Tense" or "T" form. Adding oxygens to the 4 heme groups of Hb converts the shape to "R" or "Relaxed" and squeezes the 2,3 BPG out. This helps to explain the co-operative nature of Hb and the sigmoidal loading curve with oxygen. Binding to oxygen increases the affinity for oxygen.

4. The **Bohr effect** describes the fact that CO₂ and H⁺ also act as negative allosteric modulators. Thus more oxygen is unloaded into tissues or muscles which are metabolizing glucose, because the final products of glucose metabolism include lactic acid (H⁺) or CO₂. Normal adult human Hb is known as **HbA**, has the structure $\alpha_2\beta_2$. Fetal hemoglobin has a higher affinity for oxygen, and is **HbF** or $\alpha_2\gamma_2$.

5. **Sickle-cell anemia** is mentioned only in the homework in this edition. The sequence of the β chain is shown in Fig 7.4. The α chain of human Hb is similar. The normal β chain starts with the sequence VHLTPEEK. **HbS**, sickle Hb, has a single mutation on the β chain and begins with VHLTPEEK. This new valine can't be hydrated, so it makes for a "sticky spot" and thus deoxy-HbS molecules stick together in long needle-shaped crystals, which can grow longer than the normal diameter of the RBC they are in. The distorted RBC's break open leading to painful anoxia and anemia. Sickle cell **disease** is only found in **homozygotes**, people with two copies of the HbS gene. Many African-Americans have the sickle cell **trait**, meaning that they are **heterozygotes** with one HbS and one HbA gene. Sickle trait protects against Plasmodium falciparum or **malaria**, which develops inside RBC.