Chemistry 5.07
Problem Set 1 (Sizes and Equilibria)

Problem 1.

For cells to thrive they must control their own physical and chemical properties. The dilute solutions traditionally favored by experimenters do NOT simulate the cytoplasm where macromolecular crowding occurs and may dominate critical processes. Figure 1 is the drawing of an *E. coli* cell by David Goodsell. Over the course of the semester, you will see that it is important to think about and have some intuition about sizes and time scales in biology. It is estimated that there is typically 350 mg of protein/mL in cells. This problem is designed to help you start to think about these issues. Shown below in Figure 2 is a eukaryotic red blood cell (left) and a prokaryotic *Staphylococcus (Staph) aureus.*

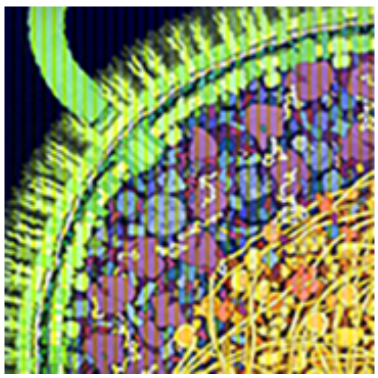

Figure 1. Illustration of the interior of an Escherichia coli cell, which is densely packed.

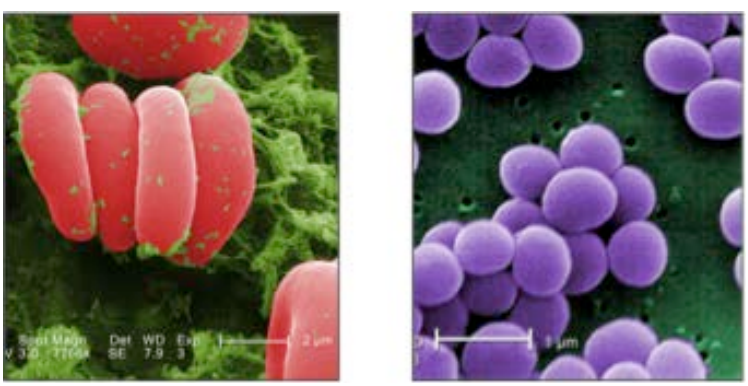

Figure 2. Scanning electron micrograph of human erythrocytes, or red blood cells (left). Micrograph of cells of the bacteria *Staph aureus*. Sizes are indicated by scale bar at the bottom of each image.

Red blood cells are much smaller than normal human cells (look in your text book or on the web). There are typically 2 to 3 x 10^{13} red blood cells, accounting for ¼ of all human cells in the body. The cells, as shown above, are disk shaped with a diameter of 6 to 8 microns and a thickness of 2 microns. Red blood cells are largely responsible for transport of O_2 to the tissues and removal of CO_2, the end product of cellular metabolism from tissues. There is no nucleus in these cells and the predominant protein is hemoglobin (Hb) that can reversibly bind O_2 by its heme cofactor. You will be introduced to hemoglobin and heme in the coming week. *Staph aureus* are gram positive bacteria found in the nostrils of 30% of us. They are of interest in that these bacteria in some cases carry plasmids that contain genes that code for antibiotic resistance. Many of you have probably heard about methicillin-resistant *S. aureus* (MRSA) that infect 500,000 patients per year during their hospital stay. *S. aureus* are spherical and have a diameter of 0.6 microns.

Questions:

a. Calculate the volume and the surface area of a red blood cell.

b. Calculate the volume and surface area of the bacterium, *S. aureus*.

c. Now compare the S/V ratios of the eukaryotic and prokaryotic cell. *S. aureus*, in contrast to human cells, do not have reversible O_2 binders (Hb in red blood cells and myoglobin (Mb) in muscle cells). Does the S/V difference between the eukaryote and prokaryote cells make sense from a physical chemical point of view? Why?

d. Hb accounts for 95% of the protein in RBCs. If you Google the number of Hb molecules in the cell you get two different numbers: in one case the number is 300 million molecules and in another it is 300 molecules. [You need to have/obtain intuition about numbers (within an order of magnitude) in biology. A back of the envelope calculation is always useful.] Hb is a globular protein that has a molecular weight of 67,000 Da. Which number is approximately correct? Show your calculation. What is the concentration of Hb in RBCs? Show your calculation— pay attention to units.

e. The Hb molecule is nearly spherical with a diameter of 55 Å (see Figure 3 below). What is its volume and can the number of Hb molecules you calculated above fit in one RBC? Show your calculations.

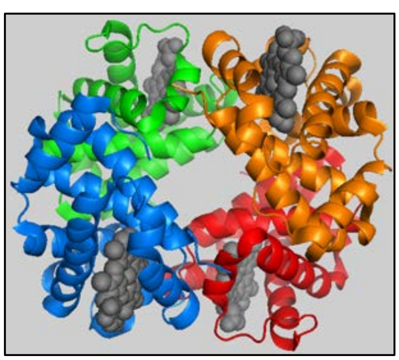

Figure 3. Hemoglobin is composed of 4 polypeptide chains. Each

chain is shown in a different color with the heme group for all shown in grey.

Adapted from PBD ID: 1HHO. Shaanan, Boaz. "Structure of human oxyhaemoglobin at 2· 1resolution."*Journal of molecular biology* 171, no. 1 (1983): 31-59.

Problem 2.

As noted above, a main function of RBCs is to remove the CO_2, the end product of metabolism, from the tissues and bring it to the lungs where it is exhaled. You will learn in the lecture on hemoglobin that H^+ play a key role in both uptake of O_2 from the lungs and in CO_2 release. Both involve the equilibria in RBCs shown below.

$$CO_2 + H_2O \underset{}{\overset{K_1 = 1.7 \times 10^{-3}}{\rightleftharpoons}} H_2CO_3 \underset{}{\overset{K_2 = 2.5 \times 10^{-4}}{\rightleftharpoons}} HCO_3^- + H^+$$

K_1 is the hydration equilibrium constant for CO_2 at 25°C and K_2 is the dissociation constant for H_2CO_3 to HCO_3^- and a H^+.

$$CO_2 + H_2O \overset{K_3 = ???}{\rightleftharpoons} HCO_3^- + H^+$$

a. Using this information, calculate the K3: the equilibrium constant between CO_2 and HCO_3^-. (Hint: this information is important in solving the following problem.)

You are walking on Memorial Drive with your Cairn Terrier, McEnzyme (also known as Zyme). You have recently developed a nanosensor in your UROP lab that allows you to instantly measure the pH of your blood. At the start of the walk, it was 7.35. All of a sudden as you pass MIT President Reif's residence, his pitbull Charlie, bounds out the front door and starts chasing you and Zyme toward the MIT campus. Your fear triggers rapid breakdown of your glycogen (a polymer of glucose) to glucose and the glucose is rapidly converted to lactic acid ($CH_3CH(OH)CO_2$-). You escape the pitbull's jaws by seconds as you jump into Building 18 and slam the door shut. You immediately measure the pH of your blood using your sensor and despite the lactic acid produced as an end product of glycolysis, the pH remains at 7.35. You then go into the lab and draw 10 cc (ml) of blood and measure the total amount of CO_2 by acidification of the blood to pH 1.0. The analysis reveals the sample contains 5.6 cc of CO_2. Recall that 1 mole of gas occupies 22.6 L.

b. Why do you acidify your blood to measure CO_2? (Hint: examine the equilibria above). Calculate the number of moles and the concentration of CO_2 in the acidified blood sample.

c. Given that the pH of your blood has not changed, the blood sample at that time was actually a mixture of CO_2 and HCO_3^-. From the information in **a** and **b**, calculate the concentrations of CO_2 and HCO_3^-.

d. Provide an explanation for the lack of change in pH of the blood despite the large amounts of lactic acid produced.