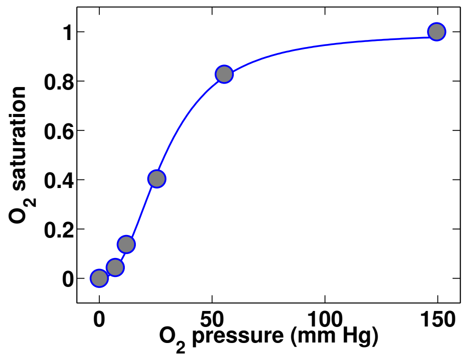
Problem set 3
(Hand in by May 6)

Problem 1

Oxygen binding by myoglobin. In class, we extensively discussed the binding curve of oxygen binding to hemoglobin, shown below. In a coordinate system of oxygen saturation vs. oxygen pressure, schematically draw the hemoglobin binding curve shown below and the oxygen binding curve for **myoglobin**. Your qualitative plot should be guided by the basic facts that we covered about myoglobin in class. Hint: What does the fact that myoglobin is a monomer (as opposed to hemoglobin, which is a tetramer) tell you about the expected shape of the binding curve? What does the fact that myoglobin binds oxygen in the muscle tissue imply about the location of the binding curve relative to hemoglobin?



Problem 2

Estimates of hemoglobin in the body. From a blood test known as complete blood count (CBC), we learn that there are roughly $5 \cdot 10^6$ red blood cells per μl of blood and that there are roughly 15 g of hemoglobin for every deciliter of blood. An average adult has about 5 L of blood in total.

a) Estimate the total number of red blood cells for an average adult.

b) Estimate the total amount (mass) of hemoglobin in the body.

c) Given the molecular mass of hemoglobin, ≈ 64 kDa, how many hemoglobin molecules are in the body?

d) How many hemoglobin molecules are in one cell?

e) What is the average spacing between hemoglobin molecules in the cell? Remember that red blood cells are very small eukaryotic cells. How does this spacing compare to the size of the hemoglobin molecule?

Problem 3

Free vs. bound ligand. In class, we covered the basic expression for the probability or "fraction bound" of a ligand L binding to a receptor R (i.e. a protein), as a function of the *free* ligand concentration $[L]$:

$$Y = \frac{[L]/K_d}{1 + [L]/K_d} \tag{1}$$

where K_d is the dissociation constant. Experimentally, however, the free ligand concentration can be difficult to determine; much more readily available is the *total* ligand concentration $[L]_{tot}$ and the total receptor concentration $[R]_{tot}$.

a) Derive an expression for the fraction bound as a function of $[L]_{tot}$ and $[R]_{tot}$.

b) Take the limit where $[L]_{tot} \gg [R]_{tot}$ and show how the expression given in Equation 1 is recovered.

c) Maeda *et al.*, *Nucleic Acids Research* (2000), measured binding curves for different σ subunits binding to the RNA polymerase core enzyme. The paper and data are available on the course website. Fit the data from their Figure 1A to the binding model derived in subproblem a), assuming a total receptor (σ^{70}, in this case) concentration of 0.4 nM. Compare this to the result obtained by fitting the standard expression, Equation 1.