"The finest fruits are the highest hung and few there are who can reach them." – Michael Faraday

**Reading:** Read chap. 7 of Alberts et al., chap. 2 of Boal and chap. 2 of Howard.

1. **A feeling for the numbers: macromolecular crowding**

   (a) Estimate the number of cells in a human body.

   (b) Assume that a given cell is 20% by volume protein. Using this estimate, for a typical bacterium like E. coli, estimate the number of protein molecules in the bacterium. Then, estimate the mean spacing between the proteins and comment on the nature of the unoccupied space in the cell.

   (c) Assuming the remainder of the volume of the cell is occupied by water, estimate the number of water molecules in the cell.

   (d) I have given you a paper by Zimmerman and Trach in which they attempt to measure the crowding in the cellular interior. In table 3 they tell us their estimated macromolecular concentrations in the cellular interior. Use these numbers to make an estimate of the mean protein spacing using the same sort of logic as earlier in the problem. In addition, express the macromolecular concentration in the cellular interior in mM (millimolar). Compare the two results.

2. **A Feeling for the Numbers: Kilodaltons and Beyond**

   The description of proteins is partially advanced by referring to the number of kilodaltons (i.e. number of atomic mass units) making up that protein.
For example, G-actin is a 42kD protein, while the motor molecule myosin is an enormous 520kD protein (made up of several different domains). The goal of this problem is to develop some rules of thumb for thinking about these numbers and to use these rules of thumb to generate a feel for protein size (both mass and geometry).

(a) Generate an estimate for the size of a "typical" amino acid in daltons. Justify your estimate by explaining how many of each type of atom you chose. Also, to quantify the goodness of your estimate, consider the actual masses of several key amino acids such as glycine, proline, arginine and tryptophan. Report these masses in daltons also.

(b) On the basis of your result for part (a), deduce a rule of thumb for converting mass of a protein (reported in kD) into a corresponding number of residues. Apply this rule of thumb to myosin, G-actin, hemoglobin and hexokinase. How well does the rule of thumb compare to the exact values for the number of residues in each of these proteins?

(c) Generate an estimate for the spatial size of a typical amino acid. You may choose to work either in Å³ or nm³. Similarly, work out a rule of thumb that allows for a conversion between a statement of the mass of a protein in kD and its volume.

(d) Apply the rule of thumb from part (c) to the same set of proteins you considered in part (b).

(e) As a point of amusement, provide brief explanations concerning the function of each of the proteins you have considered in this problem.

3. A Feeling for the Numbers: The Scales of Things

In class, I tried to convey a sense of the meaning of some of the key length scales that will be on constant duty during this course. The goal of this problem is to try and get a sense of the relative sizes of the various length scale units we have introduced.

For the purposes of this problem, scale up a typical protein so that it is
the size of an apple. In such a world, use familiar objects or distances from
everyday life (i.e. the size of a house, the distance between New York and
LA, etc.) to characterize the sizes of:
(a) the ribosome
(b) a bacteriophage
(c) an E. coli bacterium
(d) a typical Eukaryotic nucleus
(e) a Eukaryotic cell
(g) a fruit fly
(h) a human

4. Manipulating Atomic Coordinates

Visualization of the various structures populating the cell is a key part of ful-
filling the objective of structural biology to connect structure and function.
In this problem, you will learn how to manipulate pdb files from the Protein
Databank and to view them using one of the various plotting programs.

(a) Obtain coordinates for ATP, phosphatidylcholine, B-DNA and myo-
globin. You can do this by visiting sites such as “http://chemistry.gsu.edu/glactone/PDB/pdb.html”
and the Protein Databank itself. You may have to search around a bit.

(b) Download a structural viewing code such as VMD (University of Illi-
nois), Rasmol (University of Massachusetts) or DeepView (http://www.expasy.ch/spdbv/)
and create a plot of each of the molecules you downloaded above.

(c) Later we will see that phosphatidylcholine is one of the molecules that
can self assemble to form a lipid bilayer (see chap. 11 of Alberts et al.). Part
of our analysis of such structures will be to consider their geometry. As a
first step down that path, estimate the cross sectional area of the polar head
of phosphatidylcholine.
(d) ATP is the energy currency for many processes in biochemistry. The action of ATP is mediated by ATP binding onto other molecules which then exploit the energy associated with hydrolysis of ATP. Use your coordinates for ATP to estimate the size of the regions in which ATP might bind when it encounters other molecules.

5. Relative Sizes of Enzymes and Substrates

Phosphoglycerate kinase is a key enzyme in the glycolysis pathway (see pg. 112-113 of ECB). One intriguing feature of such enzymes is their enormity in comparison with the sizes of the molecules upon which they act (their “substrate”). Obtain the coordinates for both phosphoglycerate kinase (protein databank) and glucose (for example, at Molecules R Us) and examine the relative size of these molecules. First, use your graphics programs to plot both molecules simultaneously. Next, treat each of these molecules as a sphere and characterize them both in terms of their linear dimensions and also in terms of their relative volumes.