APh161: Physical Biology of the Cell
Homework 1
Due Date: Tuesday, January 27, 2009

"Chance only favours the mind which is prepared." – Louis Pasteur

In my view, homeworks are one of the primary tools at a teacher's disposal to push an educational agenda. I am big on sports analogies, and the simple fact is this: if you want to shoot free throws like Kobe Bryant you have to practice your craft. It isn't always amusing, but it pays off later. As a result, I put lots of time into both thinking up problems and in writing text that goes along with those homeworks that I think will give you the opportunity to practice things that will help you do science better later when it is "for real". The reading that goes along with my homeworks is a key part of the course material, so please read my commentaries (and argue with them if you have an alternative perspective).

   This first homework has as its main objective the development of a feel for the numbers associated with various biological problems and the beginning of an ability to use software for visualizing biological structures and examining biological sequence information. This particular homework will probably involve more searching around on the web than others. Please make sure to report your sources.

Reading: Read the paper entitled "Prokaryotes: the Unseen Majority" that is posted on the course website.

1. Manipulating Atomic Coordinates

This is basically prob. 2.4 of PBoC.

Visualization of the various structures populating the cell is a key part of fulfilling the objective of structural biology to connect structure and function. In addition, having a sense of the sizes of the various molecular actors in the cell will permit us to make the kinds of estimates that will run through the course. For example, later, we will consider gene regulation and will be interested in how large a DNA sequence serves as the regulatory site for genes of interest. Part of our answer to that problem will depend upon the relative sizes of proteins and base pairs. 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 the atoms in ATP, phosphatidylcholine, B-DNA, and the green fluorescent protein (GFP) provided with this homework. More generally, you can do this by visiting sites such as:
   "http://www.rcsb.org/pdb/home/home.do" (i.e. the Protein Data Bank).
Give a brief description of each one of these molecules and its role in cellular life.

(b) Download a structural viewing code such as VMD (University of Illinois), Rasmol (University of Massachusetts) or DeepView (http://www.expasy.ch/spdbv/) and create a plot of each of the molecules you downloaded above. You can download one of these programs under the "General Interest" part of the APh161 webpage. Experiment with the orientation of the molecule and make sure you print out pictures of each and every molecule. In each drawing, use the tools provided within the software to provide relevant scale bars that characterize the size of these molecules.

(c) Later we will see that phosphatidylcholine is one of the molecules that can self assemble to form a lipid bilayer.. 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. Make sure you get the coordinates for this molecule and plot it as well. Now, revisit the cyanobacteria shown in class and do your own version of the estimate of the number of lipids in the membranes of these cells. Make sure to take into account the fraction of the surface taken up by membrane proteins (see the attached paper by Mitra *et al.* and the attached paper by Takamori *et al.*). Also, see the paper by van de Meene *et al.* that shows the multilayer structure of cyanobacterial membranes.

2. Energy scales for nuclei, atoms, molecules and beyond.

In class, I argued that the particle in a box/electron gas model is a very useful tool for exploring the quantum effects that are in play in a given problem. One of the simplest quantities to emerge from this model is an energy scale. Repeat the derivation of the solution for the one-dimensional particle in a box and use your result to make a plot of the energy scale as a function of the size of the region where the electron (or proton, in the case of the nucleus) is confined and use it to comment on the energy scales for nuclei, atoms, molecules, quantum dots and metallic solids. Make sure you give a sentence or two commenting on the energy scale and whether or not you believe it is the correct scale for that problem.

3. A two-dimensional electron gas model for a "porphyrin" ring.

In this problem, we are going to use the same electron gas ideas developed in class to see whether we can construct a toy model of a porphyrin ring.

(a) The porphyrin ring structure can be modeled as a circular box of radius R. Using the schematic in Fig. 1 and the facts that carbon-carbon single bonds are about 1.5 Å and double bonds about 1.3 Å, estimate the area of this circular box, and from that the radius R. Next use software for molecular viewing as in Problem 1 to make a picture of chlorophyll (coordinates posted with the homework) and directly measure the radius of the porphyrin ring.
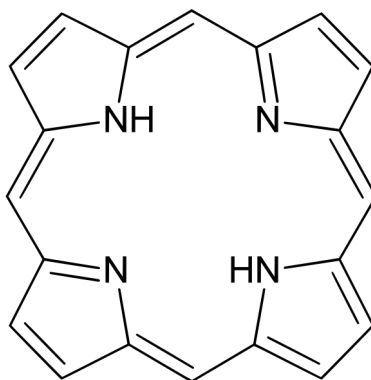
Figure 1: Structure of the simplest porphyrin, porphine.

(b) Solve the Schrodinger equation for such a ring and find expressions for the energy eigenvalues as we did for the one-dimensional model in class. Then, assuming that each C and N atom in the ring donates one electron to the pi-orbital system of the ring, work out the excitation energy (and corresponding wavelength) as a function of the size of the ring.

NOTE: on part (b) you will have to separate variables and use the fact that the radial equation is a Bessel equation. Be careful and make sure you impose the boundary conditions correctly (i.e. vanishing of the wavefunction at the boundary). You can use Mathematica, Matlab or a handbook to find the zeros of the Bessel functions which you will need in order to find the energy eigenvalues. We will also post a list of the zeros of the Bessel functions.

4. Sugar Budget.

The discovery of radioactivity revolutionized biology in a huge number of different ways. One way was that it showed that physicist's estimates on the age of the Earth were completely off base and hence that evolution had had far longer to act than originally thought. A second key outcome was that radioactive isotopes provided a means of following the paths of various molecules during their journey through the biochemical life of a cell. Indeed, the famous papers by Calvin on the biochemistry associated with photosynthesis were entitled "The Path of Carbon in Photosynthesis". In addition, radioactivity provided a means of quantifying the number of molecules of interest on the grounds that there is a linear relation between the number of radio labeled molecules and the intensity on a radiogram. Hence, over the years, much effort has gone into counting up the number of molecules of different types in living cells. Ultimately though, there has to be a carbon source and radioactivity has been a reliable tool in tracing the path of carbon (and other elements) in organisms.

(a) Estimate the number of sugars to make an *E. coli* cell. Note that in class, we flirted with these kinds of estimates when we examined the construction of a cyanobacterium. Now, it is your turn to exploit this kind of estimation to see what you come up with. Chap. 2 of PBoC should help you formulate your estimate. Remember to carefully state your assumptions. Also, for the moment, concentrate only on the building materials needed to make a cell and don't worry about the energy needed to assemble them.

(b) LB media is one of the famed growth media for studying bacterial cultures. However, for more controlled experiments, a growth medium with only a single carbon source is used (so-called minimal media) which has 2 g of glucose for every 100 mL of media. A typical experiment involves 5 mL of minimal media which is inoculated with a small number of cells (let's assume one cell) which then grows and divides repeatedly until the culture saturates at roughly 5×10^9 cells per mL. Estimate the number of carbons in the 5 mL of growth media. Also, work out the fraction of these carbons that are used in the fully saturated culture. Extra Credit: use the recipe for LB posted with this homework to carry out a similar estimate for LB.

5. Light From the Sun: A Feeling for the Numbers.

Here we think of the sun as a chemical reactor and make several estimates about it. Use the measured solar energy at the earth and the fact that the distance to the sun is roughly 93 million miles to figure out the *total* power output of the sun. Next, estimate the size of the sun by using your thumb to measure the angular width of the sun (obviously, you have to be careful when doing this and if you want as an alternative, just look up the size of the sun). Once you know the size of the sun, work out the total possible energy output if it were doing chemical burning (use the chemical energy released from combustion of glucose since it will be of interest to think about the free energy liberated in respiration) and how long the sun would last at this power output. If you want, you can also imagine that the sun is burning gasoline. Take a look at the paper by Lord Kelvin on the subject where he himself works out how long the sun could last with chemical reactions as the source of its energy. How does your estimate compare with his?

6. Photons, $k_B T$ and ATP equivalents.

One of the questions we will explore in class (or a future homework) is the number of photons it takes to make a cyanobacterium. To that end, we need to have a sense of the relation between the various energy scales that are in play. In class, we worked out the energy associated with photons of visible light. In this problem, work out the ATP equivalents for photons with wavelengths of 400, 500, 600, 650 and 700 nm. To do this, you will have to figure out the free energy of ATP hydrolysis and convert it to $k_B T$ units using the rule of thumb

that $k_B T \approx 4\ pN\ nm$.