BE/APh 161: Physical Biology of the Cell, Winter 2016
Homework #1
Due at the start of lecture, 1PM, January 11, 2016.

Note from JB: This problem set is largely about estimation. You should be able to do these estimates on a cocktail napkin. Please try to complete this homework without the use of a calculator or computer for calculations. You may refer to any of the material in *PBoC2*. Remember that we're just estimating, so π is about 3, etc. Be sure to comment on what parts of your estimates are most suspect and why. After you come up with your estimates, you may look them up at BioNumbers or elsewhere. And of course, try to have fun!

Problem 1.1 (Exploring biology with numbers, 24 pts)**.**
Spend some time on the BioNumbers website (`http://www.bionumbers.org/`), looking at various numbers. Pick three that are particularly interesting to you, give their BNIDs, and write a few sentences about why you find each one interesting.

Problem 1.2 (Estimations and questions from pictures, based on problems 2.9 and 2.10 of *PBoC2*, 24 pts)**.**
As we will see throughout the course, quantitative imaging techniques play a central role in physical cell biology. Sometimes, the pictures themselves are sources of inspiration. Bill Gelbart (who does really interesting work with viruses at UCLA) once told me that seeing an image is often the source of inspiration for him to start along a path of research. For each of the three images below, make the estimate asked of you and then pose a question that comes to your mind based on the image. The question need not be an unanswered one or one that will win you a big grant; just one that is sparked in your mind after looking at the images. Comment on why the question is particularly interesting to you.

a) Figure 1.16 from *PBoC2* shows an electron microscopy image of an escaped genome from a bacteriophage. As the caption in *PBoC2* suggests, later in the course we will investigate DNA conformations using principles from polymer physics. We can still estimate the total length of DNA in the capsid from the image alone. What is your estimate? Be sure to explain your reasoning. An example question for this image might be: How much energy does it take to pack all of that DNA into that tiny virus?

b) In Figure 2.18(C) from *PBoC2*, we see images of mitochondria of budding yeast. Estimate the volume and surface area of the mitochondria for yeast grown in glycerol. (You can see a similar image in 3D at this website: `http://p3d.in/oYoNV`, posted by Susanne Rafelski's lab at UC Irvine.) Approximately what fraction of the cell volume does the mitochondria occupy?

c) Figure 2.45 in *PBoC2* shows a fluorescent image of immunostained proteins, Bicoid, Even-skipped, and Caudal, in a developing fruit fly embryo. Sketch a plot of the concentration profiles along the long axis of the embryo for each of these three proteins. (Ignore the separation between cells.) Estimate the length scale of gradients in each along the long axis of the embryo. (The gradients are regions where the fluorescent intensity is changing from cell to cell.) Comment on the length scales of the respective gradients. It may help to look at the three channels separately in higher resolution. You can download images of these, taken from the FlyEx Database, from the course website at `http://beaph161.caltech.edu/2016/handouts/flyex_images.tar.gz`.

Problem 1.3 (HIV estimates, problem 2.8 of *PBoC2*, 20 pts)**.**

a) Estimate the total mass of an HIV virion by comparing its volume with that of an *E. coli* cell and assuming they have the same density.

b) The HIV maturation process involves proteolytic clipping of the Gag polyprotein so that the capsid protein CA can form the shell surrounding the RNA genome and nucleocapsid NC can complex with the RNA itself. Using Figures 2.30 and 2.31 from *PBoC2* to obtain the capsid dimensions, estimate the number of CA proteins that are used to make the capsid and compare your result with the total number of Gag proteins.

Problem 1.4 (The replication paradox in *E. coli*, 12 pts)**.**
Given that the typical rate for the motion of the replisome in *E. coli* is roughly 1000 bp/s, and that the replication of the circular bacterial chromosome is carried out by two replication forks, one heading in each direction from the origin of replication, work out how long it takes to copy the *E. coli* genome. How does this time correspond to the *E. coli* cell cycle? For rapidly dividing cells, how is this paradox resolved?

Problem 1.5 (Concentrations and spacing, 20 pts)**.**
Use your skills of estimation to answer the following questions. Comment on the numbers you come up with.

a) Many biochemical studies in test tubes use nanomolar (nM) concentrations of purified proteins. If a protein species inside of an *E. coli* cell has concentration of 1 nM, how many total molecules of that species are there in the cell?

b) What is the typical intercell distance between *E. coli* cells in a saturated LB growth medium? *Hint*: According to BNID 104943, the saturation concentration in LB is 20.5 g/mL.

c) It is estimated that there are of order 10^{30} prokaryotic cells on Earth (BNID ID 104960, see also the beautiful paper by Whitman, et al.). Roughly 10% of these are in the open ocean. Give a rough estimate for the concentration of bacteria in sea water. What is the approximate intercell spacing? *For fun*: If all the bacteria in the sea were lined up end-to-end, how long would the line be?

d) There are approximately 2 to 3 kg of bacteria in your large intestine. What is their intercell spacing?

e) Approximately how many hydronium ions are in an *E. coli* cell?