BE/APh 161: Physical Biology of the Cell, Winter 2014
Homework #5
Due at the start of lecture, 1PM, February 19, 2014.

Problem 5.1 (Comments on *Cell Biology by the Numbers* part 5, 10 pts)**.**
We continue in our reading in *CBBTN*. This time, please read chapter 4, pages 200–272, and send comments about two vignettes. Remember to email your answers to me and the TAs and indicate whether you would like to be anonymous when I send the comments to the book's authors. Also, please either send your responses as text in an email or as a PDF. Do not send MS Word documents.

Problem 5.2 (Visualizing random walks, 30 pts)**.**
In this problem, we will develop intuition about random walks by exploring them computationally.

a) Write a computer program to generate two-dimensional random walks. Generate five random walks of 10^5 steps with unit step size. Plot these five random walks on the same plot (but space them apart so they do not overlap). Comment on anything you find striking about the plot.

b) Write a computer program to generate one-dimensional random walks. You will generate three sets of random walks, with each walk containing 10^4 steps. The first set has 10 walks, the second has 1000, and the third has 100,000. For each set of walks, plot a normalized histogram of the displacement (the distance from the origin of the last step of the walk). Overlay the corresponding solution to the continuum diffusion equation. Comment on the plots.

Problem 5.3 (Sedimentation, the Einstein-Smoluchowski equation, and the Stokes-Einstein-Sutherland relation, 25 pts)**.**
In this problem, we will derive some landmark results in statistical physics, and learn something about a technique for studying protein structure in the process.

In equilibrium sedimentation experiments, a tube of solution of a protein or protein complex of interest is placed in a centrifuge. The concentration of protein is measured along the tube. The shape of this concentration profile is used to infer information about the size and shape of the protein. For our analysis, let ω be the angular velocity of the rotor of the centrifuge and r describe the distance from the center of the rotor to a given position in the tube of solution. Let ρ_{H_2O} be the density of the solvent and ρ_p be the density of the protein. Note that $\rho_p/\rho_{H_2O} \approx 1.4$ (BNID 104272). Let a be the radius of gyration of the protein.

a) Due to its density being greater than water, the protein will tend to fall toward the bottom of the tube with steady state velocity v. As it falls through the solvent, it experiences a friction f, such that it experiences a drag force of $F_{drag} = -fv$. At steady state, the drag force balances the centrifugal force. Use this fact to compute the velocity with which it falls in terms of ρ_p, ρ_{H_2O}, a, ω, r, and f. *Hint*: The centrifugal force is given by $F_{centrifugal} = \omega^2 r$.

b) Show that at steady state, the sedimentation velocity is given by

$$v = D \frac{\mathrm{d} \ln c(r)}{\mathrm{d}r}, \tag{5.1}$$

where D is the diffusion coefficient of the protein.

c) Now use equilibrium statistical mechanics to derive an expression for the concentration profile of the protein. I.e., compute $c(r)$ as a function of k_BT and the other variables describing the system. Note that if $P(r)$ is the probability density for a given particle being at position r in the centrifuge, $c(r) \propto P(r)$. Assume that in the absence of centrifugation, the solution has a uniform concentration of c_0. *Hint*: In part (a), you used an expression for the centrifugal force. Recall that a force $F(r)$ acting on a particle in a potential $U(r)$ is given by $F(r) = -\mathrm{d}U(r)/\mathrm{d}r$.

d) Use your expressions from parts (b) and (c) to derive an expression for D in terms of f. This is the Einstein-Smoluchowski equation, an example of a fluctuation-dissipation theorem. It has this name because it relates equilibrium fluctuations to response to applied perturbations. This is a profound and important concept in statistical physics.

e) Recall that the friction f is given by Stokes's law (applicable for spherical particles),

$$f = 6\pi\eta a. \tag{5.2}$$

Insert this result into your result in part (d) to get the Stokes-Einstein-Sutherland relation.

f) The sedimentation coefficient S is the ratio of the sedimentation velocity to the acceleration applied to it. It therefore has units of time. Derive an expression for S.

g) Ribosomes are often named by their sedimentation coefficient. A typical unit is a svedberg, which is equal to 10^{-13} s. The 70S ribosome has a sedimentation coefficient of approximately 70 svedbergs. Estimate the diameter of the 70S ribosome. Compare this estimate to what is reported on BioNumbers and explain any discrepancies.

Problem 5.4 (Protein diffusion, 5 pts)**.**
In what situation might a protein diffuse more *slowly* as the temperature is increased?

Problem 5.5 (Diffusion along a polymer, 5 pts)**.**
Some proteins, such as polymerases, diffuse along DNA prior to finding their binding sites. If a protein diffuses along DNA, its root mean square displacement along the filament scales as $\sqrt{t}$. How does the root mean square displacement *in space* scale with time?

Problem 5.6 (Genomes in cells, 6 pts)**.**
In this problem we consider how genomes take up space in cells.

a) If your genome were a single strand of DNA, what would its approximate radius of gyration be if it were free in solution? What implications does this have for the design of a cell?

b) Estimate the radius of gyration of the *E. coli* genome if it were not confined in a cell. How does that compare to the size of an *E. coli* cell?

Problem 5.7 (Effects of temperature on pulling polymers, 5 pts)**.**
If I hold the ends of a flexible polymer at a fixed length from each other and then raise the temperature, will it require more or less force to keep the ends at the same distance from each other? Explain.

Problem 5.8 (The WLC in the stiff limit, 5 pts)**.**
In class, we derived the mean squared end-to-end distance of a wormlike chain to be

$$\langle \mathbf{R}^2 \rangle = 2L\xi_p \left(1 - \frac{\xi_p}{L} \left(1 - \mathrm{e}^{-L/\xi_p} \right) \right). \tag{5.3}$$

We showed that if $L \gg \xi_p$, $\langle \mathbf{R}^2 \rangle \approx 2L\xi_p$. I wrote without proof that in the other limit of $L \ll \xi_p$, $\langle \mathbf{R}^2 \rangle \approx L^2$. Show that this is the case. Specifically, show that in the $L \ll \xi_p$ limit,

$$\langle \mathbf{R}^2 \rangle = L^2 \left(1 - \mathcal{O}\left(\frac{L}{\xi_p} \right) \right). \tag{5.4}$$

Problem 5.9 (Viral packaging, 10 pts)**.**
In this problem, we explore estimates of the energetics of viral packaging of $\phi 29$, which we introduced in lecture.

a) (Based on problem 10.6 of *PBoC2*) Estimate the entropy penalty for packing the genome in the viral capsid. You can assume that the entropy of the packed state is nearly zero, since it features almost crystalline packaging. Compare this entropy contribution to the free energy (equal to the entropy times the temperature) to the total bending free energy of packing given by equation 10.42 of *PBoC2*. *Hint:* In computing the entropy of the unpacked state, remember that each configuration of the unpacked state has the same energy, since it is a flexible chain on the length scale of the entire genome.

b) Compare the force required to pack the last bits of genome into the capsid as given by equation 10.43 of *PBoC2* and by the experimental result of ≈ 50 pN discussed in lecture and in Figure 10.19(B) of *PBoC2*. What factors might account for any discrepancy you may notice? Make sure you know how equation 10.43 of *PBoC2* is derived.