BE/APh 161: Physical Biology of the Cell, Winter 2016
Homework #6
Due at the start of lecture, 1PM, February 22, 2016.

Problem 6.1 (Active transport vs. diffusion, 20 pts).
Active transport can have various meanings in cellular contexts. The term is often used to describe transport of material by motor proteins along filaments in a cell.

a) In this context, how the the mean square displacement of an actively transported protein scale with time?

b) How does the mean square displacement of a particle moving by thermal diffusion scale with time?

c) Elowitz and coworkers (*J. Bacteriol.*, **181**, 197–203, 1999) found that the diffusion coefficient of GFP in *E. coli* is about 6 $\mu m^2/s$. What is the approximate viscosity of the cytoplasm of *E. coli* in this context. How does this compare to the viscosity of water? If they are very different, comment on why this may be.

d) Use BioNumbers to look up typical motor protein (like kinesin, dynein, and myosin) speeds. At what length scale does it become faster to move cargo shaped like GFP by active transport than by diffusion? How does this length scale compare to typical bacterial and eukaryotic cell sizes?

Problem 6.2 (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 the start-to-end distance of a one-dimensional random walk. 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. *Hint*: You do not actually need to "take" the each walk. Think about how the end-to-end distance is distributed and you can draw random numbers out of that distribution.

Problem 6.3 (Sedimentation, the Einstein-Smoluchowski equation, and the Stokes-Einstein-Sutherland relation, 35 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 $\rho_\mathrm{p}/\rho_{\mathrm{H_2O}} \approx 1.4$ (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 $F_\mathrm{drag} = -fv$. 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, $\rho_{\mathrm{H_2O}}$, a, ω, r, and f. *Hint*: The centrifugal force is given by $F_\mathrm{centrifugal} = m_e\omega^2 r$, where m_e is the effective mass of the protein.

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

$$v = D\,\frac{\mathrm{d}\ln c(r)}{\mathrm{d}r}, \tag{6.1}$$

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) The friction f is given by Stokes's law (applicable for spherical particles),

$$f = 6\pi\eta a. \tag{6.2}$$

This was derived by George Stokes by solving for fluid flow around a spherical object. 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 6.4 (Protein diffusion and temperature, 5 pts)**.**
In what situation might a protein diffuse more *slowly* as the temperature is increased?

Problem 6.5 (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 6.6 (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.