BE/APh 161: Physical Biology of the Cell, Winter 2014
Homework #2
Due at the start of lecture, 1PM, January 22, 2014.

Note from JB: For the dimensional analysis problems, it might help to have a table of physical quantities and their dimensions. I put one on the website for you here:
`http://beaph161.caltech.edu/2014/handouts/physical_quantities_and_their_dimensions.pdf`.

Problem 2.1 (Comments on *Cell Biology by the Numbers* part 2, 10 pts)**.**
As in the first homework, we again ask you to read a chapter of *CBBTN* and give us your thoughtful comments. This time, please read chapter 5, pages 273–296, 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 2.2 (Magnetic particles and gravity, 20 pts)**.**
In 1950, Francis Crick published work (Crick and Hughes, *Exp. Cell Res.*, **1**, 37–80, 1950) in which he probed the properties of the cytoplasm of cells. He took cells from the frontal bone of an 11 or 12 day old chick. He then allowed the cells to intake magnetic particles made out of iron by phagocytosis. The particles have a characteristic size, a, of 2 and 10 µm. He then applied a magnetic field and watched how the particles twisted and translated. If you remember your electromagnetism, you will recall that for an applied magnetic field $\mathbf{B}$, the translational force and torque acting on the particle are respectively

$$\mathbf{F} = \mathbf{m} \cdot \nabla \mathbf{B} \tag{2.1}$$

$$\boldsymbol{\tau} = \mathbf{m} \times \mathbf{B}, \tag{2.2}$$

where $\mathbf{m}$ is the magnetic dipole moment, which is permanent and proportional to the volume of the particle. I.e., $\mathbf{m} \sim a^3\mathbf{M}$, where a is the characteristic size of the particle and $\mathbf{M}$ is the pre-volume magnetic dipole moment, set by the material properties of the particle.

a) Assume the cytoplasm is a viscous fluid. Justify why inertia can be neglected in this study.

b) In the text of the paper, Crick was concerned that gravity might affect his results. He therefore did a test. He took a sample with cells that had iron particles in them, turned it on its side for one or two days, and then investigated if the particles settled toward the bottom in the absence of magnetism. The particles did not settle to any substantial degree. Use dimensional analysis or other physical reasoning to estimate a lower bound on what the viscosity of the cytoplasm had to be in order to observe this. (*Hint*: The density of the cytoplasm is irrelevant, as shown in part (a), but the difference in density between the iron and cytoplasm, $\Delta\rho$, is relevant, as this is responsible for the (negative) buoyant force.) Does this result make sense? If not, do you have an explanation?

c) From the experimental set up, the magnetic moment $\mathbf{m}$ and field $\mathbf{B}$ are known, as is the field gradient, $\nabla\mathbf{B}$. Use dimensional analysis to derive a scaling relation for $M \equiv |\mathbf{M}|$, $\delta B \equiv |\nabla \mathbf{B}|$, a, the translation speed of particle motion v, and the cytoplasmic viscosity η. In particular, how does the velocity of a particle for a given magnetic field vary with particle size? Remember, these are scaling relations; you need not include multiplicative constants.

d) Derive a similar scaling relationship involving the observed angular velocity ω. How does ω depend on the particle size, a?

e) Use dimensional analysis to show that if the cytoplasm is elastic (characterized by elastic modulus E as opposed to viscosity η), that the force and torque cannot depend on the velocity or angular velocity, respectively. Nonetheless, the particles will be displaced and rotated by application of the magnetic field. Let's say they are translated by a distance x. Use dimensional analysis to derive a scaling relationship between the force F and the displacement x.

Problem 2.3 (Mathematizing a cartoon for ciliar growth, 8 pts)**.**
In lecture, we mathematized a cartoon describing ciliar growth (Fig. 1). We wrote the following equations

$$\frac{\mathrm{d}c}{\mathrm{d}t} = -kc \tag{2.3}$$

$$\frac{\mathrm{d}\ell}{\mathrm{d}t} = k_g c(x = \ell) \tag{2.4}$$

$$x = vt, \tag{2.5}$$

where c is the concentration of active growth factors in the cilium, k is the rate constant for dephosphorylation of the growth factor, ℓ is the length of the cilium, k_g is the rate constant for growth at the tip of the cilium, and v is the speed of the motors proteins. Note that in writing the mass action expression for dephosphorylation of the growth factors, we have taken advantage of the fact that the phosphatase concentration is constant throughout the cilium and absorbed it into the decay constant k. We solved these equations to get

$$\ell = \frac{v}{k} \ln\left(1 + \frac{k\,k_g c_0}{v}\,t\right), \tag{2.6}$$

where c_0 is the concentration of active growth factor at the base of the cilium.

a) Compute the growth rate, $\mathrm{d}\ell/\mathrm{d}t$ of the cilium as a function of time. Sketch the function. Be sure your axes have the proper dimensionless growth rate and time.

b) Based on our expression for ℓ, the cilium never stops growing, but it slows drastically. How much time τ does it take to slow to one-tenth of the initial growth rate? How long is the cilium at this time?

c) The results from part (b) may be thought of as the characteristic length and growth time of the cilium. Derive scaling relations for these using dimensional analysis. I.e., find a characteristic length ℓ and time τ from the parameters k, k_g, c_0, and v.

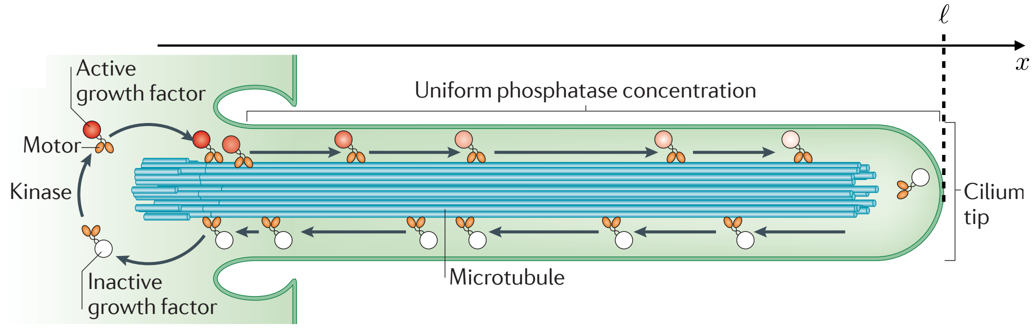

Figure 1: A cartoon describing a possible mechanism for ciliar growth adapted from Howard, et al., *Nature Rev. Mol. Cell Biol.*, **12**, 393–398. The text from the caption in the paper reads as follows. "Schematic of an advectionreaction model, a hypothetical mechanism for the length control of cilia and microvilli. Cargoes, for example growth factors, carried along cilia and microvilli are inactivated over time by phosphatases, which may provide a length-dependent signal to the growing tip."

Problem 2.4 (Growth curves, based loosely on page 103 of *PBoC2*, 24 pts)**.**
In chapter 3 of *PBoC2*, we considered growth curves of *E. coli*. The logistic equation is written as

$$\frac{\mathrm{d}N}{\mathrm{d}t} = rN\left(1 - \frac{N}{K}\right), \tag{2.7}$$

where N is the number of bacteria, r is the growth rate, and K is the carrying capacity, or the maximum number of bacteria that can be present and still have growth. In the analysis in *PBoC2*, the values of r and K were assumed to be constant. For bacteria growing in media, r and K could also be functions of the the concentration of food in the media, which we will call $F(N,t)$ (not to be confused with $f(N,t)$ in equation 3.10 in *PBoC2*).

Since we will be taking N as a continuous variable, and since F is a concentration, we can write the logistic equation in terms of concentration of bacteria, c, by dividing the entire equation by the volume V of the vessel containing the medium.

$$\frac{\mathrm{d}c}{\mathrm{d}t} = rc\left(1 - \frac{c}{K'}\right), \tag{2.8}$$

where $K' \equiv K/V$. We will drop the prime henceforth for notational convenience.

a) Write down an expression for $\mathrm{d}F/\mathrm{d}t$. You should try to keep your expression simple. Give your reasoning for how you chose this expression.

b) Sketch functional forms that you think are reasonable for $r(F)$ and $K(F)$. Again, try to keep them simple.

c) Based on what you know about bacterial growth, give reasonable values of the parameters you defined in your expressions for $\mathrm{d}F/\mathrm{d}t$, $r(F)$ and $K(F)$. Also give reasonable values for the initial bacteria concentration, c_0, and the initial food concentration, F_0. Explain how you came up with these values. *Hint*: Working through problem 2.5 of *PBoC2* will help you.

d) Numerically solve the differential equations and plot the results. You can use whatever numerical integration software you like. If you would like to use Python with NumPy/SciPy, it might help to go through the tutorial found here:
http://beaph161.caltech.edu/2014/handouts/scipy_odeint_tutorial.tar.gz.

e) Explain the shape of the curves.

f) Comment on any enhancements you would propose to this model for bacterial growth.

Problem 2.5 (Boltzmann's grave, 5 pts)**.**
Boltzmann's grave is in Zentralfriedhoff in Vienna, a beautiful cemetery that also contains the graves of some of the world's greatest composers, including Beethoven, Brahms, Schubert, Strauss, Ligeti, and Falco. On Boltzmann's impressive grave stone is inscribed the equation

$$S = k \log W. \tag{2.9}$$

Here, S is entropy, k is the Boltzmann constant, log refers to the natural logarithm, and W is the number of microstates. In class, we derived the famous Boltzmann distribution by maximizing the Shannon entropy, given that we knew an average energy of our system of interest. Derive the equation on Boltzmann's grave using the same technique. To do so, assume we do not know anything about the energy of the system.