BE 159 Spring 2014
Homework #4
Due at 5pm, June 6, 2014.

Problem 4.1 (The Young-Laplace law and adhering cells (20 pts)).
In class, we derived the Young-Laplace law for a sphere. Specifically, we wrote down an expression for the free energy of a sphere in terms of its surface tension, pressure, and radius and then minimized it to obtain

$$\Delta p = \frac{2\gamma}{R}, \tag{4.1}$$

where R is the radius of the sphere, γ is the surface tension, and Δp is the transmural pressure acting on the surface, the so-called Laplace pressure. We can derive a more general Young-Laplace law using differential geometry as

$$\Delta p = \gamma\left(\kappa_1 + \kappa_2\right), \tag{4.2}$$

κ_1 and κ_2 are the two principle curvatures. These are in general a (possibly complicated) function of position of the surface, but can be obtained easily for simple geometries of homogeneous materials.

In this problem, we will explore use of the Young-Laplace law to obtain information about the surface tension of cells.

a) In class, we discussed experiments in which a cell is squished between two parallel plates and then imaged to assess the surface tension of the cell, as shown in Fig. 1. Show that if a force F is required to hold the plates a distance $2R_2$ apart, the surface tension is

$$\gamma = \frac{F}{\pi R_3^2}\left(\frac{1}{R_1} + \frac{1}{R_2}\right)^{-1}. \tag{4.3}$$

Hint: The principle curvatures for this geometry are $\kappa_1 = R_1^{-1}$ and $\kappa_2 = R_2^{-1}$.

b) Why is it important to wait a long time before measuring the force and radii in the cell squishing experiment from part (b)? What happens if we squish the cell quickly, measure the radii and forces, and then use them to get γ?

c) Derive equation 1 of the Maître, et al. paper.

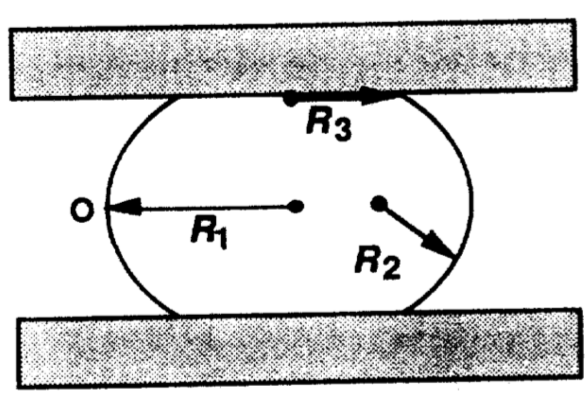

Figure 1: Schematic of cell squishing experiment in a parallel plate compression apparatus. Drawing taken from Foty, et al., *Phys. Rev. Lett.*, **72**, 2298–2301, 1994.

Problem 4.2 (Which papers? (15 pts)).
What paper that we read/discussed did you enjoy the most? Which did you enjoy the least? Please give reasons why you made the choices you did.

Problem 4.3 (What you walk away with (15 pts)).
What aspects of the course were most beneficial to you? Where there things that you think we could cut or change to make better use of time?

Problem 4.4 (Course structure (15 pts)).
Write a brief statement on your thoughts about the way this course was structured. Did you like that it was literature-based with lecture material built around the background for each paper? Would you prefer a more traditional approach? What suggestions for improvement do you have?

Problem 4.5 (Your turn (35 pts)).
Prepare a syllabus for this class if you were to teach it. The syllabus should contain a brief discussion of the topics covered, the approach taken, and a list of lecture topics and/or literature selections. If you want the course to be literature based, you need not identify specific papers (but please do, if you like!), but can instead specify "a paper on topic x."

Problem 4.6 (Simulations of Delta-Notch signaling on a hexagonal lattice (10 pts extra credit)).
I wrote a code to solve the differential equations describing Delta-Notch dynamics on a hexagonal lattice. This would simulate the dynamics, for example, in an epithelial sheet. The code and concept behind this problem are based on a forthcoming paper, Pau Formosa-Jordan and David Sprinzak, Modeling Notch signaling: a practical tutorial. In *Notch Signaling: Methods and Protocols, Methods in Molecular Biology*, ed. H. Bellen and S. Yamamoto, Springer Protocols, 2014, in press.

The differential equations that are simulated on the hexagonal lattice are

$$\frac{\mathrm{d}n_i}{\mathrm{d}t} = \mu\left(\beta_N - k_t n_i \langle d\rangle_i - k_c n_i d_i - n_i\right) \tag{4.4}$$

$$\frac{\mathrm{d}d_i}{\mathrm{d}t} = \nu\left(\frac{\beta_D}{1 + r_i^h} - k_t d_i \langle n\rangle_i - k_c n_i d_i - d_i\right) \tag{4.5}$$

$$\frac{\mathrm{d}r_i}{\mathrm{d}t} = \beta_R\,\frac{(k_t n_i \langle d\rangle_i)^m}{1 + (k_t n_i \langle d\rangle_i)^m} - r_i, \tag{4.6}$$

where n_i is the Notch concentration in cell i, d_i is the Delta concentration in cell i, and r_i is the repressor concentration in cell i. We define $\langle\cdot\rangle_i$ as the average over the neighbors of cell i. The equations are already in dimensionless form. This model takes into account both *cis* and *trans* Delta-Notch interactions, as well as repression of Delta.

Download the code here: http://be159.caltech.edu/2014/protected/delta_notch_code.zip.

a) Explain in a paragraph or two the basic structure of the code.

b) Play with the code. Mess around with parameters, initial conditions, etc. Show a few illustrative plots and describe what you have learned about the Delta-Notch system by playing with it numerically.

Hint: Below is a script to run a simulation on a 24×24 lattice.

```
import numpy as np

import hexagonal_lattice as hex
import delta_notch as dn

t = np.linspace(0.0, 100.0, 50)  # Time points we want

# Set up default parameters, except 24x24 lattice and betaN = 1/2
p = dn.DeltaNotch(n_row=24, n_col=24, betaN=0.5)

p, c = dn.delta_notch_solve(p, t=t)  # Solve it!

hex.show_movie(p.t, c[:,:p.n], p.n_col, 'b') # Show movie of Notch
hex.show_movie(p.t, c[:,p.n:2*p.n], p.n_col, 'k') # Show movie of Delta
hex.show_movie(p.t, c[:,2*p.n:], p.n_col, 'r') # Show movie of repressor
```

Note also that for some parameter values, the differential equations can get extremely stiff, and the solver can fail. If this is the case, you can try different initial conditions. If that still does not work, you can try different parameters. Furthermore, the solution to the differential equations will take a long time for larger lattices, so keep that in mind.