2.797/20.310/3.0536.024 Fall 2006
MOLECULAR, CELLULAR, & TISSUE BIOMECHANICS

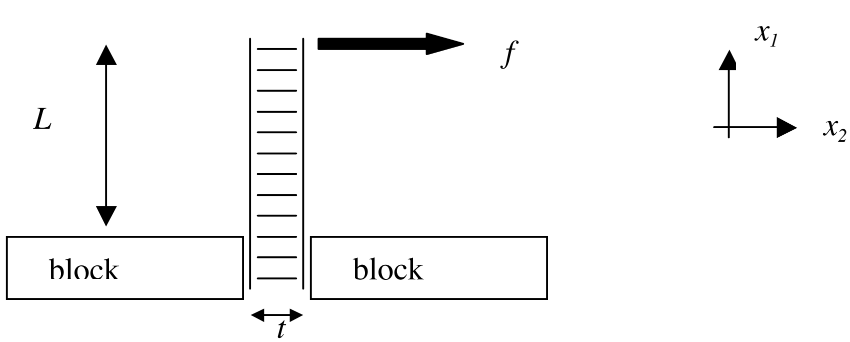
Problem Set #9

Solutions to these problems will either be distributed or discussed in recitation. You do NOT need to hand in a solution for grading.

Problem 1: A test for membrane bending stiffness

Some cell membranes experience bending as a routine matter. For example, red blood cells have to bend in order to fit through a capillary that's slightly smaller than the cell. White blood cells sometimes have to squeeze through small cracks between endothelial cells (lining the blood vessels) to reach a site of infection. Axons of some nerves that run through joints get folded whenever the joint is bent.

In order to test the bending response of a cell membrane, one could isolate a small section of the cell membrane, clamp one end, and then apply a load at the other end. This is not readily done in real life, but for this question, ignore those technical details.



The blocks are immobile and do not deform so that both the displacement and slope of the membrane at that point is fixed and equal to zero. The thickness of the membrane is *t,* and the force applied to the membrane per unit length perpendicular to the page is *f*. The membrane can be assumed to be two-dimensional, with infinite length perpendicular to the page. Thermal fluctuations are also to be ignored in parts (a) and (b).

a) Derive the equation of deformation of the membrane $u_2 = u_2(x_1)$, assuming the membrane is a uniform solid with elastic modulus E and total length L.

b) Compare this solution to an order-of-magnitude solution obtained by *approximating* the governing equation used in (a). Are they similar in form?

c) Now consider the effects of thermal fluctuations on the behavior of the membrane. Assuming that the dimension of the membrane perpendicular to the page in the diagram is $w = 10L$, and using the following expression for the area moment of inertia for a plate of rectangular cross-section:

$$I = \tfrac{1}{12} t^3 w$$

estimate the persistence length of the membrane given the following dimensions: $t = 5$ nm, $L = 100$ nm. How does this influence your answers in parts (a) and (b)?

Problem 2: Indentation

A spherical bead of radius R is rigidly attached to an atomic force microscope (AFM) tip and used to probe the mechanics of a single cell having a membrane characterized by a bending stiffness K_b under uniform surface tension N, and a cytoskeleton of shear modulus G. Both the cell and membrane can be assumed to be homogeneous, isotropic and linearly elastic materials.

a) In interpreting the experimental results, it is assumed that the force-displacement (F-δ) curve obtained in an indentation experiment provides a measure of the cytoskeletal shear modulus, and that the effect of the membrane can be ignored. Given the following parameter values,

$\delta \sim R = 0.5$ μm

$G = 1$ kPa

$\nu = 0.3$

$K_b = 10^{-18}$ N·m

$N = 10^{-3}$ N/m

and neglecting the membrane, estimate the resulting force-displacement curve. (You can either use the exact result or scaling analysis from class.)

b) Now consider the effects of the cell membrane. First, given the parameter values above, is tension or bending dominant?

c) Based on your answer in (b), do you expect the membrane to have a significant influence on the measurement?

d) How might you modify the experiment so that you minimized the influence of the membrane in your result?

Problem 3: Chondrocyte deformation in a matrix or gel

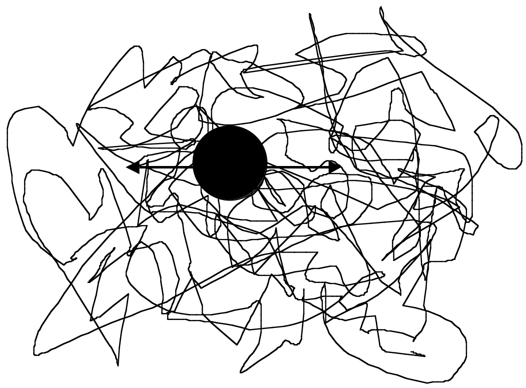
a) A chondrocyte embedded in extracellular matrix material deforms with the matrix from an initially spherical shape of radius R to an ellipsoid with a major axis of approximately $1.5R$. If the elastic modulus (Young's modulus) of the cytoskeleton is E, provide an order of magnitude estimate for the magnitude of stresses induced within the cell due to the deformation.

b) Given the chondrocyte mentioned above, list four potential biologic responses that have been observed in cell culture experiments on various cell types (not just chondrocytes) following mechanical stimulus.

c) List and describe three different mechanisms by which a cell might <u>transduce</u> the forces acting on it from the mechanical stress to a biological signal.

Problem 4 – Microbead assay for cytoplasmic measurements

Various types of experiment have been designed to measure the elastic and viscous characteristics of the cytoskeleton (CSK). One that has recently become possible through the development of optical or magnetic traps involves the oscillation of a microbead (diameter d) as shown in the sketch below. In the following, you can assume that the bead experiences an oscillatory force $F = F_0\sin(\omega t)$ and undergoes an oscillatory displacement of amplitude u_0 (the phase relationship between F and u will depend on the characteristics of the CSK) and that $d \sim u_0$ >> the typical inter-filament spacing in the CSK.



a) First, treat the CSK as a purely elastic medium, characterized by a Young's modulus, E. What is the phase relationship between the applied force and the bead displacement?

b) Assuming that the deformations extend a distance of order d from the bead, estimate (order of magnitude) the strain experienced by the CSK.

c) Obtain a *scaling relationship* between the magnitude of the applied force (F_0) and the displacement amplitude (u_0).

Now treat the CSK as a viscous fluid of viscosity μ.

d) What is the phase relationship between the applied force and the bead displacement? Assuming that the fluid motions extend a distance of order d away from the bead, estimate (order of magnitude) the relationship between the amplitude of the applied force and the bead displacement (or velocity, du/dt).

e) Form a ratio of the force estimates in a) and b) to estimate the relative importance of elastic and viscous effects given the following values:

- $E = 100$ Pa
- $\mu = 100$ kg m^{-1} s^{-1}
- $d = 1$ μm

- $u_0 = 1$ μm
- $\omega = 1$ rad/s

Problem 5: Viscoelastic measurement by laser tracking micro-rheometry

The rheology of a dilute polymer solution, actin for example, can be measured using either single particle tracking techniques or diffusing wave spectroscopy (Pine et al., 1988). These methods provide a measure of the displacements of a passive microsphere due to thermal fluctuations from an initial position as a function of time. These displacements average to zero, but nevertheless lead to an excursion of the particle with time. Using the graph shown below for the mean-square displacement of a 0.48 μm particle as a function of time, determine the viscosity and elasticity of the solution (Palmer et al., 1999). Concentration of actin is expressed in μM and the temperature of the system is 300 ^{o}K. What is the intrinsic relaxation time of the material?

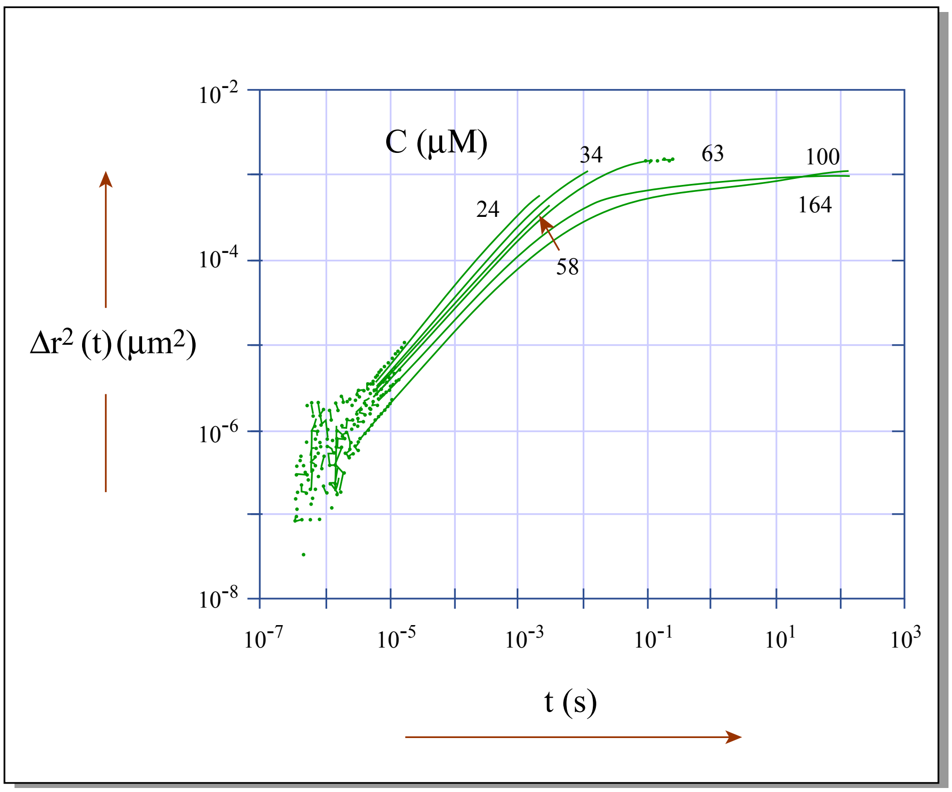


Figure by MIT OCW.

Problem 6: Microstructural model

Consider a very simplified model for a random network of macromolecules, in which we represent the network as an array of molecules arranged in a cubic lattice, as schematically shown in the figure. The molecules are cross-linked at the junction points (the small circles at the corner) and this single unit cube of molecules is repeated in space to make up the molecular network. Assume that all the molecules have the same properties: *N* links of Kuhn length *b*, and can be modeled as Gaussian chains at temperature T. The equilibrium length, r_0, of each molecule is $r_0 = b\sqrt{2N/3}$.

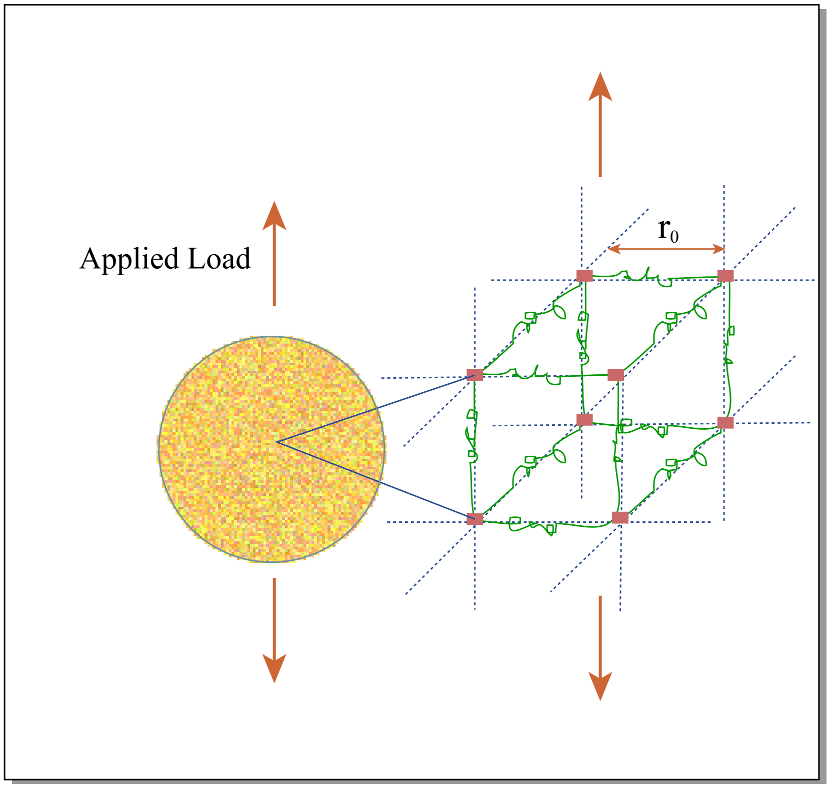


Figure by MIT OCW.

a) If we load this molecular network along the vertical direction indicated in the figure, what will be the measured macroscopic Young's modulus, E? What will be the Poisson ratio, ν?

b) What happens to the Young's modulus if we increase the temperature? Why?