Massachusetts Institute of Technology

Biological Engineering Division
Department of Mechanical Engineering
Department of Electrical Engineering and Computer Science

BEH.410/2.798J/6.524J/10.539J
Molecular, Cellular & Tissue Biomechanics, Spring 2003

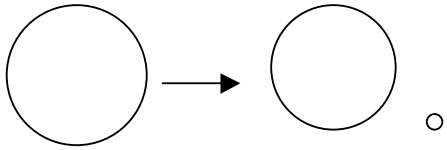
Second quiz **Distributed: Friday, May 9, 2003**
Due: 5:00 PM, Wednesday, May 14, 2003

You are to complete this quiz on your own, without any consultation anyone except for the two instructors or the course TA.
If you have any questions, don't hesitate to ask us. If anyone raises questions that we feel would be of general interest, we will post the question and our response on the class website, so be sure to check periodically.
You are free to use any resource materials you feel might be useful.

There are three problems on the exam with the points as indicated.
Please be sure to explain your reasoning as fully as possible.
Write everything in the exam booklet, not on the exam or on separate pages.
Solutions will be available at the time you turn in the exam.

Problem #1 MEMBRANE MECHANICS (35 Points)

The lipid membrane of a large vesicle in solution will fluctuate due to thermal motion. It is possible that such fluctuations could result in a "pinching off" of the membrane to form two smaller vesicles as shown in the figure below.

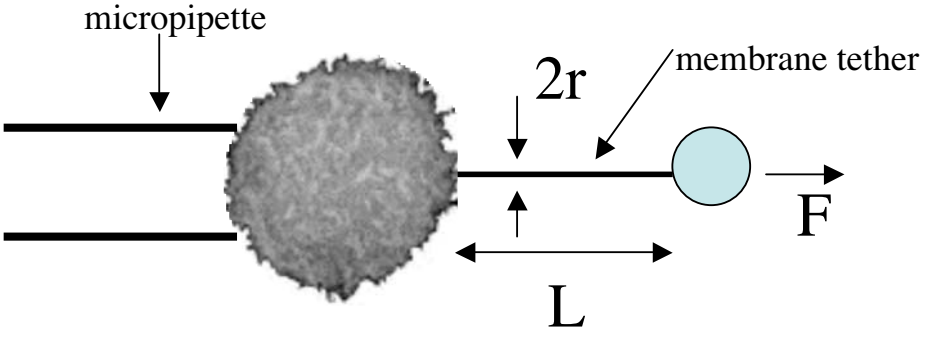


a) (10 pts) What is the change in the *total bending energy* in going from a system containing one large vesicle (radius = 30 μm) to a system containing a slightly smaller vesicle and a very small vesicle (radius = 1 micron)? Assume a value of K_b = 10 kT and negligible change in total volume during the pinching process.

b) (5 pts) Do you expect to find many small vesicles in an ensemble if the system above is at *thermal equilibrium* and the pinching process is reversible? Assume that there is a small change in total volume which is just enough to prevent the membrane from being in a state of tension after the pinching process (ie only bending energy is important).

Lipid membrane tethers can be created by exerting a force at a point on the surface of a cell. The lipid bilayer *separates* from the associated cortex and forms a thin (much smaller radius than the cell itself), long cylindrical shaped tether. The tether is composed of mostly lipids and does not contain a cortex or cytoskeleton.

In the experiment shown in the figure below a small bead is attached to the surface of neutrophil cell held immobile by a micropipette and a force is exerted on the bead using optical tweezers. This type of experiment can be used to measure the adhesion energy *per unit area* (*J*) between the lipid bilayer and the cortex.



c) (5 pts) First develop a simple expression for the energy cost dU to create extra surface dA for a system with *constant* tension N. You can neglect contributions from thermal undulations and effects of adhesion.

d) (15 pts) Using the experimental setup described above one can apply a force F to the bead and measure the change in length of an existing tether by an amount dL. Develop an expression which relates the quantity FdL to *J* and other *dominant* mechanical properties of the neutrophil for this type of deformation. You can neglect any contribution from the cytoskeleton and thermal undulations of the membrane. Assume the radii of the neutrophil, R, and the tether, r, do not change during the course of the experiment. Typical values for these quantities are R=5 μm and r = 50 nm.

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PROLEM 2: TISSUE MECHANICS (<u>35 Points</u>)

As the wall of an artery expands and contracts due to arterial pressure variations, there is a tendency for fluid to be periodically drawn into and expelled from the tissue comprising the wall. In this problem, you will model the arterial wall as a poroelastic material and analyze this fluid motion. This is of special interest in the context of arterial disease since this represents one method by which lipids normally found in the blood plasma might enter the arterial wall where they could react with extracellular matrix proteins and form the nucleus for lipid aggregation (see e.g., Yin et al., A model for the initiation and growth of extracellular lipid liposomes in arterial intima. Am J Physiol. 1997 Feb;272(2 Pt 2):H1033-46.).

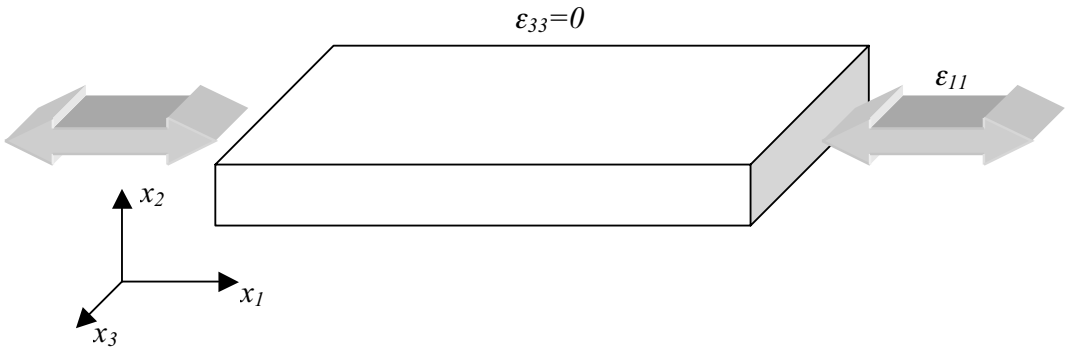
Assume here that:

the wall is thin compared to the radius of the artery, so that you can treat the wall locally as though it were a flat plate. With this assumption, the change in vessel circumference with time can be expressed in terms of a time-varying value of $\boldsymbol{\varepsilon_{11} = \varepsilon_0 \sin(\omega t)}$ (see Fig. 1).

since the total length of the arterial segment does not change during a cardiac cycle, you may assume that $\boldsymbol{\varepsilon_{33} = 0}$. Consequently, there will be a tendency for ε_{22} to vary with time. Note that this does not imply that $\tau_{33} = 0$.

the bottom surface is impermeable, so that all the fluid inflow and outflow occurs through the top surface ($x_2 = h$). The top surface can be assumed to be exposed to a **constant pressure $p = 0$** for all times, so that the fluid flow into and out of the arterial wall is driven entirely by the imposed time varying strain ε_{11}.

Fig. 1



a) (<u>10 pts</u>) First consider the tissue to be a homogeneous, isotropic, incompressible ($\nu = 0.5$) and **linearly elastic** (not poroelastic) material, and obtain

expressions for $\varepsilon_{22}(x_2,t)$ and $u_2(x_2,t)$. Note, in particular, whether or not ε_{22} depends upon x_2.

b) (10 pts) Now treat the tissue as a **poroelastic** rather than an elastic material, with known values for the shear modulus G and Lame' constant λ. **Show** that u_2 satisfies the following relationship:

$$\frac{\partial u_2}{\partial t} = Hk\frac{\partial^2 u_2}{\partial x_2^2}$$

(which is the same as that which governs one-dimensional confined compression as was discussed in class) where $H = 2G+\lambda$ and k is the hydraulic permeability.

c) (5 pts) Consider the limit of $\omega \to \infty$ and obtain an expression for $u_2(x_2,t)$. (Hint: Think in physical terms what happens in this limiting case, and **do not** simply set $\partial u_2 / \partial t$ to zero!)

d) (5 pts) Consider the limit of $\omega \to 0$ and obtain an expression for $u_2(x_2,t)$. (Hint: What boundary condition must be satisfied at $x_2 = h$?)

e) (5 pts) What are the two boundary conditions needed to solve the equation you obtained in (b)? Sketch (but **do not solve**) the solution $u_2(x_2,t)$ for the intermediate case, when ω is neither very large nor very small.

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PROLEM 3: CELL MECHANICS (<u>25 Points</u>)

Several recent studies have shown that subtle mutations in lamin, a protein whose primary role is in providing structural stability to the nuclear membrane, are implicated in a variety of pathologies. In order to investigate these structural changes, experiments are to be conducted on nuclei isolated from normal and lamin-deficient cells. The isolated nuclei are allowed to settle onto a rigid surface, then probed using the tip of an atomic force microscope (AFM). In the interpretation of the force-displacement (F-δ) relationship obtained from these experiments, two different models are proposed. In both, the nucleus is assumed to be initially spherical with radius R. You may assume that in all cases, deformations are small and linearity can be assumed.

a) (<u>15 pts</u>) In the first model, the nucleus is treated as a homogeneous, isotropic, linear elastic material (the membrane is neglected) with shear modulus G and Poisson's ratio ν. Recognizing that the total displacement of the AFM tip represents deformations both on the top and bottom of the nucleus, obtain an expression that shows how the tip displacement δ depends on the applied force F and the properties of the elastic sphere.

b) (<u>10 pts</u>) Now consider the nucleus to be modeled as a spherical shell that deforms exclusively due to bending. That is, the membrane exhibits no intrinsic surface tension, and its extensional modulus is sufficiently high that there is no significant areal strain. Thus, the only structural parameter of interest is the membrane bending stiffness K_B. Obtain a second expression for the relationship between the applied force F and the displacement of the AFM tip. In your analysis of the bending deformations in the vicinity of the AFM tip, you will need to assume that the characteristic distance over which bending occurs scales with the radius of the cell, R. **For this part of the problem only**, you can neglect the deformation on the bottom surface relative to that on the top. Be sure that your answer makes physical sense!