UNIVERSITY OF CAMBRIDGE

MATHEMATICAL TRIPOS Part III

Tuesday 3 June 2003 9 to 11

PAPER 71

MOLECULAR AND CELLULAR BIOPHYSICS

Candidates may attempt **ALL** *questions.*

There are **seven** *questions in total.*

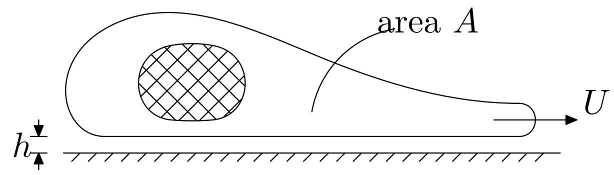
Questions 4 - 7 carry approximately twice the marks of questions 1 - 3.

You may not start to read the questions printed on the subsequent pages until instructed to do so by the Invigilator.

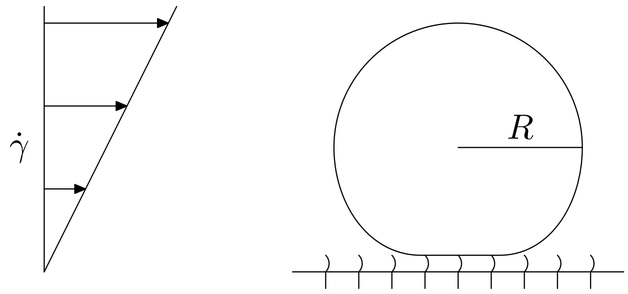
1 (a) Consider the problem of DNA being translocated through a long narrow capillary of diameter D. Assuming that the length L of the DNA molecule is much longer than its persistence length l_p (with $l_p << D << L$), determine the equilibrium length of the DNA in the channel.

(b) Briefly discuss the case when the capillary is replaced by a 2-dimensional channel ?

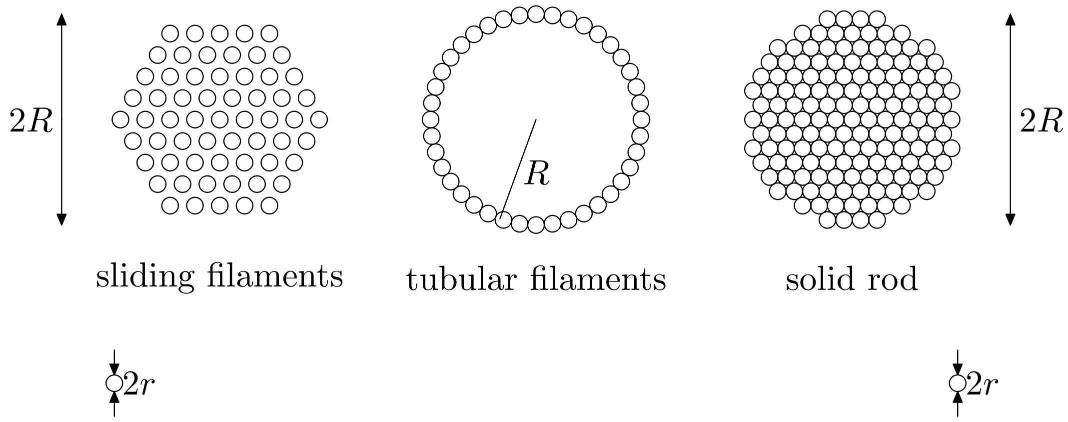
2 (a) Gliding bacteria move by generating a shear flow between themselves and a substrate. The flow is thought to be generated by forcing their membrane to undergo rhythmic peristaltic contractions. As a simple estimate of the efficiency of this type of motion, calculate the energy required to propel a gliding bacterium $0.1\mu m$ above a surface as shown, at a velocity of $1\mu m/s$. You may assume that the surrounding liquid medium is water (viscosity $0.001 Pa\ s$) and that the typical area of the sheared zone is $100\mu m^2$.



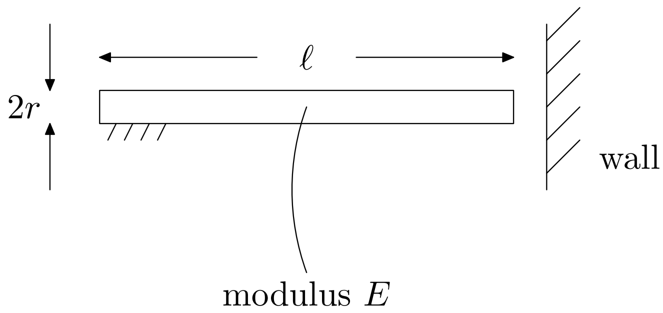
(b) Neutrophils move by rolling, while still adhering to a substrate such as the endothelial layer. Using a simple model of the cell as an elastic sphere of radius R and modulus G that interacts with the substrate (with an interfacial energy per unit area J), estimate the shear rate $\dot{\gamma}$ when the neutrophil will just start to roll.



3 (a) Consider the following different arrangements of slender filaments: filaments that are packed hexagonally but free to slide relative to each other, filaments that are glued into a circular tube, and filaments that are glued together. In each case estimate the bending and twisting stiffnesses in terms of the filament radius r and the bundle tube radius R, as well as the Young's modulus of the material of the filament E.



(b) If the microtubule grows from a seed via polymerization until it contacts a rigid wall, determine a simple scaling relation for the force that it will exert on the wall before it buckles. Will the force increase or decrease as the microtubule grows further ? How might you quantify this ?



4 Consider the case of a single particle of mass m moving in 1 dimension (for simplicity), described by its location $x(t)$ at time t, so that its velocity is $\dot{x}(t)$. Assume that the particle is in a thermal bath so that its motion satisfies the Langevin equation

$$m\ddot{x} + 6\pi\mu a\dot{x} = F(t)\,,$$

where $F(t)$ is the random forcing which has zero mean, i.e. $< F(t) >= 0$, and is delta correlated, i.e. $< F(t)F(t') >= \delta(t - t')$.

(a) Derive an expression for the mean velocity $< \dot{x}(t) >$ and the mean-square velocity $< \dot{x}^2(t) >$ and thence derive the fluctuation-dissipation relation in this particular case. (b) Now evaluate the mean-square displacement $< x^2(t) >$. Show that at short times the particle moves ballistically like a free particle, while at long times it behaves like a diffusing particle.

5 Consider a polymer made up of 10^{10} monomers that are each 10 nm long, and 1nm in diameter, sitting in an aqueous environment of viscosity = 0.1 gm/cm.s, and temperature 300 K. The Boltzmann constant is $1.38 \times 10^{-23} J/K$.

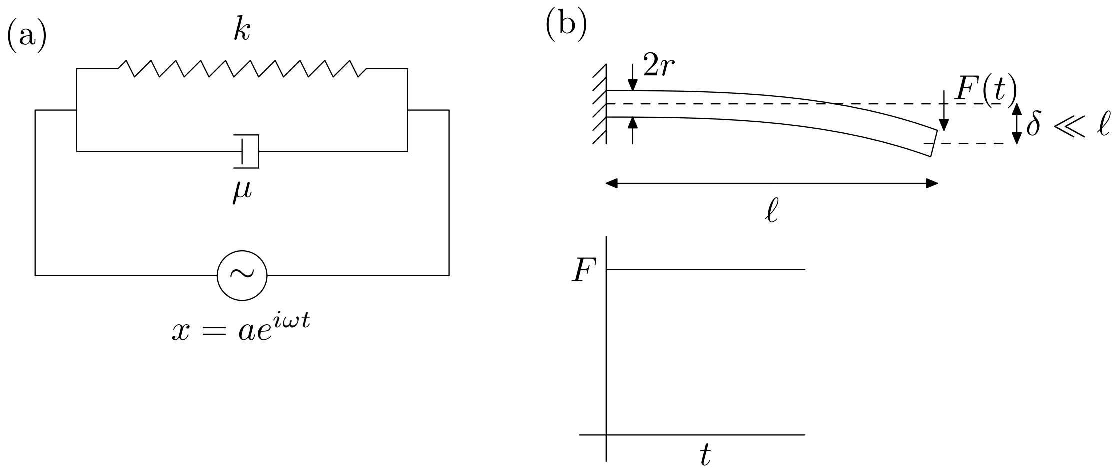
a) Evaluate the polymer's stretching stiffness for small strains. Explain your assumptions in choosing the model for polymer elasticity.

b) Light scattering experiments show that the persistence length of the polymer is actually 20 nm, almost twice the size of the monomer size. Determine the Young's modulus of actin using this experimental result. What is the bending stiffness of an actin filament ?

c) What is the extension of the filament when a 1 microwatt laser is used to pull on one end of the polymer which is attached to a latex bead, with the other end fixed to a substrate. Is your answer reasonable ? The relative refractive index of latex in water is 1.2.

d) What is the power required by a molecular motor to drag the polymer at a velocity of $0.01 \mu m/s$? Justify any assumptions that you may have to make to complete this calculation.

6 A useful paradigm for the deformation of biological materials is the so-called Maxwell model which consists of a spring in parallel with a dashpot, shown below.



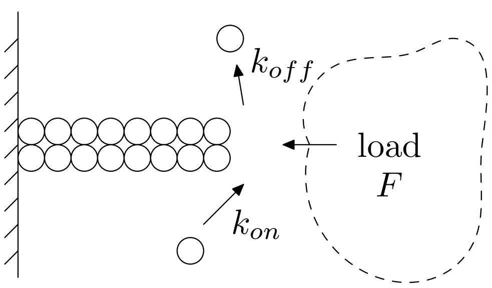
(a) Write down the general relation between force and displacement for this model in terms of the damping μ of the dashpot and the stiffness k of the spring. Determine the complex response function $G(\omega)$ for the system when forced by an applied displacement field $ae^{i\omega t}$, and calculate the elastic and loss moduli.

(b) Now consider the bending of a beam that is made of a viscoelastic material that has a single relaxation time, i.e. a Maxwell solid. Determine the equation of motion for such a beam when it is clamped at one end and subject to a constant transverse force at the other, as shown above.

7 Consider the polymerization of the filament in an aqueous solution of monomers as shown in the figure below.

(a) If the polymerization reaction is very fast compared to the diffusion of the load, calculate the rate of growth of the filament. Now consider the effect of a constant force on the growing filament, and calculate the reduction of the growth rate as a result.

(b) If the polymerization is limited by reaction instead, determine the velocity of the growing end. Outline any assumptions that you have to make in each of these situations to justify your answers.



k_{on} = on rate

k_{off} = off rate

monomer size = δ

2-stranded polymer

μ = viscosity of solvent