

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

Molecular, Cellular and Tissue Biomechanics  
BEH.410 / 2.978J / 6.524J / 10.537J

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**Problem Set #6**

**Issued: 4/29/02**

**Due: 5/6/02**

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READING ASSIGNMENT:

Articles handed out and on the course website regarding motors and Brownian ratchets.

Chapter 2.1: Cell Membrane Mechanics and Adhesion (R.D Kamm): pp 1-26

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**Problem #1: 2-State Motors**

Consider the 2-state model for a molecular motor discussed in class (in the handouts from 4/24/02) where the state 1 is a spatially periodic asymmetric saw-tooth potential and in state 2 the potential is a constant, independent of position. The motor is modeled as a Brownian particle moving in these potentials.

- a) Using these potentials (see notation from handouts) calculate a force field and show that its spatially averaged value is zero if we integrate (spatially) over an integral number of periods.
- b) You have just shown that the spatially averaged force field is zero and hence why people sometimes call these ratchets “force free motion”. However, we know the Brownian particle can move in this field and so there must be some net force acting on it! Resolve this *apparent* paradox.

## Problem #2: Dynamics of actin polymerization.

Consider the polymerization of an actin filament using the rate laws shown in class. Actin is a polar filament and so we would expect that rate constants  $k_{on}^+ \neq k_{on}^-$  where the plus and minus refer addition to end of the chain considered. Furthermore, polymerization is more rapid when the actin monomers have ATP bound. Sample data for actin containing ATP *in vitro* are:

$$k_{on}^+ = 11.6 \text{ } (\mu\text{M s})^{-1}$$

$$k_{on}^- = 1.3 \text{ } (\mu\text{M s})^{-1}$$

$$k_{off}^+ = 1.4 \text{ s}^{-1}$$

$$k_{off}^- = 0.8 \text{ s}^{-1}$$

a) Plot  $dn/dt$  for the +end and –end as a function of concentration of monomers. Identify the 3 regimes of growth for the filament.

b) At what concentration of monomers will the *total* filament length be constant in time ?

Draw a sketch of a simple filament of length  $n=6$  as a function of time and position in this regime to explain why this is called “treadmilling”.

c) How fast is the leading edge (positive end) of the filament moving forward in time when the filament is treadmilling ?

Compare this to the typical velocity of a keratocyte cell ( $\sim 0.1 \mu\text{m/s}$ ) where treadmilling has been observed.

d) The slow velocity found in c) is due to the fact that we have neglected to account for proteins with change the polymerization process:

- some bind monomeric actin and modify its polymerization properties.
- capping proteins can bind to the ends of filaments and prevent monomers from being added to them.
- severing proteins.

Severing proteins may increase  $k_{off}^-$  by two orders of magnitude or more (Pollard et al. 2000)! How would this change your answer for part c) ?

e) In class we said that the equilibrium force  $F_{eq} = \frac{kT}{\delta} \ln\left(\frac{[M]}{K_c}\right)$  where  $\delta$  is the length change in the filament (5.5/2 nm for actin) when a monomer is added,  $[M]$  is the concentration of monomers and  $K_c$  is the critical dissociation constant in the absence of an external force. We also considered rates processes for the dynamics and at the end of class on 4/24/02 said that for the diffusion limited model the velocity of an end of the filament ( $v = \frac{dn}{dt} \delta$ ) was equal to  $\frac{2D}{\delta^2} \delta$  in the limit that there is no external force. We then said that drag force on the particle is  $-\zeta v$  so the filament must be exerting a force of  $\frac{2kT}{\delta}$ . Why is this value different than  $F_{eq}$ ? What speed does this give for actin pushing a 10  $\mu\text{m}$  particle (bacteria) versus a 100  $\mu\text{m}$  particle?

### Problem # 3 Cell Squishing

An initially spherical cell with membrane tension, but no significant bending stiffness is squeezed between two flat surfaces (see figure). When deformed, the cell membrane behaves as a linearly elastic material with Young's modulus  $E$ , thickness  $t$  and Poisson's ratio  $\nu$ .

- a) If the cell has an initial volume  $V_0$  that remains constant during the experiment, and has an internal pressure equal to external pressure when spherical, what is the internal pressure when the cell is partially flattened so that the contact area on top and bottom is  $A$ ? You may assume that the interior of the cell is a liquid and that the membrane slides freely along the two surfaces.
- b) What force  $F$  must be applied to produce this deformation?

