Master International Centre for Fundamental Physics ICFP

PHYSICS FOR BIOLOGY

Examination (3 hours), December 2014

Based on the article : Cooperative extraction of membrane nanotubes by molecular motors
C. Leduc *etal.* *P.N.A.S.* **101**, 17096–17101 (2004)

1. Experimental section

1.1 Describe *briefly* the phenomenon and the system studied in this article. Why is this interesting from a biological viewpoint. From a physical viewpoint. What are the main experimental findings reported in this work.

1.2 How does a molecular motor like kinesin work. Why should the motor velocity depend on ATP concentration. Give the expected functional form for this dependence (mathematical expression and plot). What are the general features allowing a molecular machine such as kinesin to walk on cytoskeletal filaments.

1.3 What are the main experimental parameters that can be changed to control the number of tubes emanating from a vesicle.

1.4 Derive the force required to pull a membrane tube : $F_0 = 2\pi\sqrt{2\kappa\sigma}$, where κ and σ are the bending rigidity and tension of the membrane. What is the radius R_0 of the tube. Give numerical estimates for these two quantities with the parameters of the article.

1.5 Unlike what is stated in the article, the calculated osmotic pressure difference across the vesicle membrane ($\Delta\Pi = 20$mOsm) does not (at all!) correspond to the membrane tension inferred from the force measurement. Calculate the membrane tension corresponding to the quoted $\Delta\Pi$ and speculate on the possible reasons for the discreapancy, knowing that the rupture tension of a typical lipid membrane is of order 10^{-2}N/m.
Hint : 1Osm is the osmotic pressure of an ideal gas with concentration 1mol/l. the Avogadro number is $\mathcal{N}_A = 6 \times 10^{23}$/mol.

2. Theoretical section

2.1 Explains all the terms appearing in Eq.[1] and in Eq.[3]. Explain the assumptions underlying Eq.[1].

2.2 Explain why the motor velocity to decrease with an applied force. Does the linear approximation given in the text seem reasonable?

2.3 Give the expression for the flux of bound motors $\hat{J}_b(x = 0)$ as a function of the initial surface density of motors in the vesicle ρ_∞. Do this for small tubes, where the motor density in the tube is uniform and matches the initial motor density ρ_∞ in the vesicle. How does the flux depends on the number of bound motor at the tip n_b, and why?
Hint : remember that Eq.[1] is written in the reference frame associated to the tube tip. Remember also that ρ_∞ *is a surface density while* ρ_b *and* ρ_u *are linear densities of motors bound and unbound to microtubules, along the tube length.*

2.4 Explain qualitatively why one can expect the motor unbinding rate under load to be given by Eq.[2]. What does the length scale a represent in Kramer's rate theory. Use a sketch to illustrate your explanation.

2.5 Write the differential equation for the number of bound motors at the tip (n_b) that in such a way that the parameter ν of Eq.[4] appears in this equation. Give a graphic representation of this equation for different values

of ν.
Hint : Instead of directly representing dn_b/dt, it might be easier to represent $n_b \times dn_b/dt$.

2.6 What is a saddle-node bifurcation. Derive the condition on ν for the existence of a stationary solution for n_b. What is the number of bound motors in the tip at the threshold ? Explain why there is a stable and an unstable solution if this condition is satisfied, and qualitatively explain Fig.3 of the paper.
Comment : a qualitative explanation should be given, even short of the precise expression of ν_c given in the paper.

2.7 Why is there two possible criteria (Eq.[5] and Eq.[6]), corresponding to two different regimes for the existence of a stable tube. Derive both equations. Why is the critical motor density on the vesicle independent on the membrane bending rigidity ? how can one determine experimentally in which regime a given system is.

2.8 For longer tubes, and assuming quasi-stationarity (a constant density profile in the reference frame of the tube), why should the motor density in the tube be characterised by an exponential function. Derive eq.[7].
Hint : The motor profile is exponential in the reference frame of the moving tube tip

3. Discussion

3.1 What would have been your first guess for the critical number of motors required to pull a membrane tube. How does this compare the critical number of bound motor found experimentally and theoretically ?

3.2 A comment is made in the discussion that fluctuations may play an interesting role in the process. Why is this so. What role could the fluctuations play. How could fluctuations influence the dynamics of tube extraction.

3.3 What type of tube dynamics can one expect if the membrane tension increases with the tube length (it will eventually do for long tubes).

3.4 Do you find this paper convincing. Do you trust the quantitative result of the paper (what is it). Are the experimental approach and the theoretical treatment appropriate. Do you see possible improvement that would test the results.