M. Ben Amar

December 18^{th}

Morphogenesis 2017

Only *allowed documents: Personal written notes (courses and TDs), lecture handouts, and bilingual dictionary. The two problems are independent. Duration: two hours.*

1 FIRST PROBLEM:Cell motility on substrate

We consider a living flat cell, on rest on a solid substrate. Its thickness is assumed constant.The interior of the cell is modeled by a fluid containing actin monomers but also actin polymers that can be considered as rigid sticks. The edge of the cell is a lipid membrane, responsible for a surface tension effect. We neglect all other ingredients in the cell and we focus on possible shape deformations. We do not consider global displacement of the cell but only possible deformations. The actin sticks are polarized: it means that each of them has a tip + where monomers adhere (polymerization process) and a tip $-$ where the monomers escape (depolymerization).

- Justify by a drawing that this effect polymerization /depolymerization can induce the displacement on the whole stick and thus can explain the cell deformation.

1.1 Mass-Flux equation

Polymerization requires proteins located at the cell surface, while depolymerization occurs everywhere inside the cell. We call $\vec{v}$ the velocity of the fluid in the laboratory frame.

- Justify the following balance equation giving the density of actin polymers ρ, in the laboratory frame:

$$\frac{\partial \rho}{\partial t} + \nabla \cdot (\rho\ \vec{v}) = -\rho k_d + \rho \mathcal{F} V_p \delta[(\vec{r} - \vec{r}_{int}) \cdot \vec{n}] \tag{1}$$

  where $\delta[]$ is the Dirac's distribution in one dimension, $\vec{r}_{int}$ is the position of an arbitrary point on the interface, obtained by projection, $\vec{n}$ is the normal in the outer direction from the cell border.

- Give the physical significance of k_d and V_p, knowing that $\mathcal{F}$ is a form factor which can depend on the point of the interface in consideration so can be dependent on the curvilinear coordinate s, defined on the cell border $\delta\Omega(t)$

1.2 Relationship between velocities

We assume that the density ρ is constant over space and time and the fluid incompressible.

- By integrating Eq.(1) on the surface of the cell, deduce a relation between k_d, V_p and R_0, the cell radius when the cell is circular.

- Then consider the cell border and deduce that the normal fluid velocity satisfies the following equation:

$$\vec{v}. \cdot \vec{n} + \mathcal{F} V_p = \vec{V}_{\delta\Omega} \cdot \vec{n} \tag{2}$$

$\vec{V}_{\delta\Omega}$ is the speed of a point on the edge of the cell.

1.3 Fluid flow equations

- Write the two-dimensional Stokes equation satisfied by the velocity of the fluid $\vec{v}$ in the cell, taking into account the viscous friction force between the cell and the substrate. ζ is the friction coefficient. We will call μ the viscosity of the fluid inside the cell, R_0 the typical size of the cell and ζ the coefficient of friction.
- Show that in the limit where the coefficient of friction is very large (in a sense to be defined), we find a Darcy-type law for the hydrodynamics of the fluid.

1.4 Summary of the equations for the fluid flow

- Summarize all the equations giving the shape of the cell.
- Introduce the velocity potential ϕ_0.
- Compare these equations with the Saffman-Taylor problem in the same geometry, in an infinite Hele-Shaw cell. Is ϕ_0 Laplacian?

1.5 Particular solution

We will choose $\mathcal{F} = 1$.

- Show that the static round shape is one possible solution.
- Give the expression of the potential ϕ_0 in this case. Recover the relation between k_d, R_0 and V_p.

1.6 Stability analysis

We would like to study the stability of such solution with respect to fluctuations of the interface contour. To do this, we assume that the edge fluctuates around the average position according to:

$$r = R_0(1 + \epsilon_n e^{\Omega_n t} cos(n\theta)) \tag{3}$$

- Deduce that the fluctuations of the velocity potential due to this perturbation can be writen as:

$$\delta\phi(r, \theta) = a_n r^n e^{\Omega_n t} cos(n\theta) \tag{4}$$

- Taking into account the Laplace's law (the surface tension being γ), show that the relation between both small quantities, ϵ_n and a_n, reads:

$$a_n = \frac{\epsilon_n}{R_0^n}\left(\frac{k_d}{2}R_0^2 - \frac{\gamma}{\zeta R_0}(n^2 - 1)\right) \tag{5}$$

We give here the curvature κ of a curve described in polar coordinates:

$$|\kappa| = \frac{|r^2 + 2r_\theta^2 - r \cdot r_{\theta\theta}|}{(r^2 + r_\theta^2)^{3/2}} \tag{6}$$

where r_θ (resp. $r_{\theta\theta}$) is the first derivative (resp. the second) of r with respect to θ.

1.7 Shape stability

- Deduce the growth rate of the perturbation Ω_n. Discuss the stability of the solution?

2 SECOND PROBLEM:Structures in activator-inhibitor system

The aim of this exercise is to explain the pattern observed on shells or animals. The model is due to Meinhardt and collaborators (2012). They consider the following set of equations:

$$\frac{\partial \tilde{a}}{\partial \tilde{t}} = D_a \Delta \tilde{a} + \mu_a (\frac{\tilde{a}^2}{\tilde{h}} - \tilde{a}) + \sigma_a \tag{7}$$

$$\frac{\partial \tilde{h}}{\partial \tilde{t}} = D_h \Delta \tilde{h} + \mu_h (\tilde{a}^2 - \tilde{h}) \tag{8}$$

where Δ is the Laplacian in 2 dimensions, D_a and D_h the diffusion coefficient.

- What is the the physical meaning of the coefficients μ_a, μ_h and σ_a
- Why do the physicists study such equations??

2.1 Dimensionless analysis

We use μ_a to define a time scale and D_h a length scale.

- Show that, written in dimensionless units, the previous equations become:

$$\frac{\partial a}{\partial t} = D \Delta a + (\frac{a^2}{h} - a) + \sigma \tag{9}$$

$$\frac{\partial h}{\partial t} = \Delta h + \mu (a^2 - h) \tag{10}$$

Tildas are dropped for dimensionless variables. Define again a, h, D, σ and μ.

2.2 Homogeneous solution

- The system occupies a domain $\mathcal{D}$ such that $\mathcal{D} = [x, 0 < x < L]$ with imposed border conditions: $\partial_x a = \partial_x h = 0$ in $x = 0$ and $x = L$. Find the homogeneous static solution.

2.3 Spatial perturbations

We consider a perturbation of these solutions with weak amplitude:

- What are the possible values of k?

2.4 Time dependance of the perturbations

- Deduce from the Jacobian of the dynamical system given by Eq.(9) the following dispersion relation:

$$\omega_n^2 + \alpha\,\omega_n + \beta = 0 \tag{11}$$

- Give the value of α and β.

- Discuss the stability of the pattern according to the sign of α and β. Give the conditions for observing oscillating patterns by changing the length of the box.