Chapter 9

Models for cell shape

9.1 The Grimm Model for actin distribution

This model is based loosely on Grimm et al [1] and was later revised and presented in Lacayo et al [2]. The goal was to understand the basis for the distribution of actin at the leading edge of a keratocyte.

$\rho^+(x,t) = $ right facing filaments
$\rho^-(x,t) = $ left facing filaments

$$\frac{\partial \rho^+}{\partial t} = -\frac{\partial}{\partial x}(v^+ \rho^+) + \text{branching} - \text{capping} \tag{9.1}$$

$$\frac{\partial \rho^-}{\partial t} = \frac{\partial}{\partial x}(v^- \rho^-) + \text{branching} - \text{capping} \tag{9.2}$$

Assume constant velocity, and $v^+ = v, v^- = -v$.
Create + tips from - filaments by branching and vice versa so

$$\frac{\partial \rho^+}{\partial t} = -v\frac{\partial}{\partial x}\rho^+ + \beta b_{1,2}(\rho^-) - \gamma\rho^+ \tag{9.3a}$$

$$\frac{\partial \rho^-}{\partial t} = v\frac{\partial}{\partial x}\rho^- + \beta b_{1,2}(\rho^+) - \gamma\rho^- \tag{9.3b}$$

where $b_{1,2}$ is one of two types of branching rates considered, described below.

The above equations are hyperbolic and need two different BC's:

For (9.3a), need BC at left boundary since tips are moving towards the right. Similarly for (9.3b), need BC at right boundary since tips are moving towards the left, so they assume

$$\rho^+(-L) = 0, \quad \rho^-(L) = 0$$

This means "no actin filaments emanate from domain ends".

Local competition for Arp2/3

$$b_1(\rho^\pm) = \frac{\rho^\pm}{\rho^+ + \rho^-}$$

This means that the branching rate depends on the proportion of local filaments that are facing in the opposite direction and also note that

$$b_1(\rho^+) + b_1(\rho^-) = 1.$$

This case holds when the Arp2/3 diffusion timescale is much smaller than that Arp2/3 actin association timescale.

Global competition for Arp2/3

$$b_2(\rho^\pm) = \frac{\rho^\pm}{\bar{\rho}/L}$$

where $\bar{\rho}$ is the average filament density across the edge, i.e.

$$\bar{\rho} = \int_{-L}^{L} (\rho^+(x,t) + \rho^-(x,t))dx$$

This case holds when the Arp2/3 diffusion timescale is much larger than that Arp2/3 actin association timescale.

Exercise 9.1.1 (Scaling the model)

Scale the equations as follows:

$$x = x^*\bar{x}, \quad t = t^*\tau, \quad \rho_i = \rho_i^*\bar{\rho}$$

$$\bar{x} = L, \quad \tau = L/v, \quad \bar{\rho} = \beta L/v$$

Show that dimensionless equations become

$$\frac{\partial \rho^+}{\partial t} = -\frac{\partial}{\partial x}\rho^+ + b_{1,2}(\rho^-) - \epsilon\rho^+ \tag{9.4a}$$

$$\frac{\partial \rho^-}{\partial t} = \frac{\partial}{\partial x}\rho^- + b_{1,2}(\rho^+) - \epsilon\rho^- \tag{9.4b}$$

9.2   Steady state filament distribution

It is assumed that the front edge is roughly flat, and that the cell moves with steady state velocity.

Also, a limiting case of slow capping $\epsilon << 1$ is considered. Then the steady state equations in case 1 are:

$$0 = -\frac{\partial}{\partial x}\rho^+ + \frac{\rho^-}{\rho^+ + \rho^-} \tag{9.5a}$$

$$0 = \frac{\partial}{\partial x}\rho^- + \frac{\rho^+}{\rho^+ + \rho^-} \tag{9.5b}$$

The BC's are:

$$\rho^+(-1) = 0, \quad \rho^-(1) = 0$$

9.3 Solving the steady state equations

Define

$$s(x) = \rho^+(x) - \rho^-(x), \tag{9.6}$$

$$p(x) = \rho^+(x) + \rho^-(x) \tag{9.7}$$

Then

$$\rho^+(x) = \frac{p(x) + s(x)}{2} \tag{9.8}$$

$$\rho^-(x) = \frac{p(x) - s(x)}{2} \tag{9.9}$$

Exercise 9.3.2 (Recasting the model)

Determine the equations and BCs satisfied by the new variables. Show that the new equations are

$$\frac{\partial s}{\partial x} = 1 \tag{9.10a}$$

$$\frac{\partial p}{\partial x} = -\frac{s}{p} \tag{9.10b}$$

and that the BCs are

$$s(1) = p(1), \tag{9.11}$$

$$s(-1) = -p(-1) \tag{9.12}$$

This is a much simpler system that can be solved by integration and separation of variables and the solutions (an exercise below) are

$$s(x) = x, \tag{9.13}$$

$$p(x) = \sqrt{2 - x^2} \tag{9.14}$$

Exercise 9.3.3 (Solving the new system)

Solve first for $s(x)$ and use this to find $p(x)$. Then use the BC's to find the full solutions (to obtain the values of the arbitrary constants).

9.4   Putting it all together

Once we obtain the solutions for $s(x), p(x)$, we readily find the densities of the filaments to be

$$\rho^+(x) = \frac{1}{2}\left(\sqrt{2 - x^2} + x\right), \tag{9.15}$$

$$\rho^-(x) = \frac{1}{2}\left(\sqrt{2 - x^2} - x\right) \tag{9.16}$$

The total density is

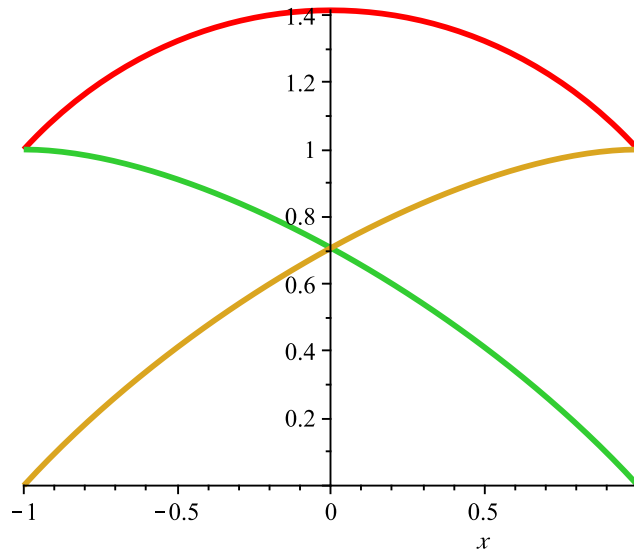$$\rho^+(x) + \rho^-(x) = \sqrt{2 - x^2}$$

Figure 9.1: The resulting actin density distribution. red = total density, green = left moving and yellow = right moving filament distributions.

Exercise 9.4.4 (For further study)

The authors also consider several other cases, including (1a) the case of very fast capping and (2) the case of global Arp2/3 (as described earlier). Consider how this changes the model, find solutions and interpret your results.

Bibliography

[1] HP Grimm, AB Verkhovsky, A. Mogilner, and J.J. Meister. Analysis of actin dynamics at the leading edge of crawling cells: implications for the shape of keratocyte lamellipodia. *European Biophysics Journal*, 32(6):563–577, 2003.

[2] C.I. Lacayo, Z. Pincus, M.M. VanDuijn, C.A. Wilson, D.A. Fletcher, F.B. Gertler, A. Mogilner, and J.A. Theriot. Emergence of large-scale cell morphology and movement from local actin filament growth dynamics. *PLoS biology*, 5(9):e233, 2007.