Supporting Material for “Self-Organized Cell Motility from Motor-Filament Interactions” by XinXin Du, Konstantin Doubrovinski, and Miriam Osterfield.

Dimensionless parameters

The dimensionless parameters used in the text can be translated to dimensionful ones using the following formulation:

$$\begin{aligned}
&D = D'\ell^2\nu_d \quad ; \quad D_m = D'_m\ell^2\nu_d \quad ; \quad \alpha = \alpha'\ell\nu_d \\
&v = v'\ell\nu_d \quad ; \quad \eta = \eta'\zeta \quad ; \quad \sigma = \sigma'\ell\nu_d/\zeta \\
&\kappa = \kappa'\ell^3\nu_d/\zeta \quad ; \quad P = P'\nu_d/\zeta \quad ; \quad A_0 = A'_0\ell^2 \\
&F_0 = F'_0\ell\nu_d/\zeta \quad ,
\end{aligned}$$

where the primed variables are dimensionless, and l is the length of a filament, ν_d is the degradation rate of filaments, and ζ is the mobility of the boundary.

Model Assumptions

We make several model assumptions about the processivity of motors, the way filaments nucleate, the nature of motor-mediated attractive interactions between filaments, and the diffusion constants. We will clarify some of these assumptions below.

Processivity of motors

We assume that a motor, when it comes off of a filament, does not travel very far before binding to another filament. Therefore, the only terms that we consider for motors are a current due to being carried by filaments and a term that accounts for local diffusion. Quick unbinding and rebinding would locally lead to a proportional distribution of motors among differently oriented filaments populations. These assumptions may best correspond to motor complexes with multiple heads that remain near the filament network, with individual motor heads rapidly switching between different nearby filaments.

Filament nucleation

We assume that a newly nucleated filament reaches some terminal length on a time-scale much shorter than the time-scale of the evolution of the density fields. In a moving cell with little to no retrograde flow, such as keratocytes, the time it takes for a filament to reach terminal length is the speed of polymerization, roughly equal to the cell velocity, divided by the average length of the filament. The time scale of the evolution of the density fields is the time it takes the cell to crawl its own length. Therefore, in a cell in which the average filament length is substantially shorter than the cell length, this assumption is valid. Filament lengths are difficult to measure precisely in vivo because of the density of the network; although filaments extending the width of the lamellipodium are sometimes seen, the majority appears to be shorter (1).

In many cases, filaments are not nucleated uniformly in living cells. For example, actin filaments are nucleated by Arp2/3 complexes that are themselves activated only near the cell boundaries, and the newly nucleated filaments' orientations depend on the orientations of pre-existing filaments. We use an approximation that ignores this effect and assumes that filaments of all orientations are nucleated at the same rate independent of the densities and orientations of pre-existing filaments. Future versions of this model could explore the angle and density dependence of the nucleation terms. However, the point illustrated in this paper is that attractive motor-mediated forces are sufficient to generate motility even in the absence of any special regulation of filament polymerization.

Motor-mediated filament interactions

The parameter α represents the strength of the attractive interaction between filaments, that is, the strength with which a motor pulls on a pair of filaments to aggregate them. The parameter α may be related to the number of motors in a myosin mini-filament, or the fraction of myosin that is activated by phosphorylation of the regulatory light chain. Changes in these motor properties lead to changes in α in some functionally complicated way, which could be explored experimentally. In principle, α may depend on the difference in orientations of two filaments that are coupled by the same motor. However, for simplicity in the numerical solutions, we take α to be isotropic. Additionally, in this model, motors do not affect the angles between filaments; this is reasonable given the highly entangled nature of the cytoskeleton.

Diffusion

In general, diffusion for the filaments is negligible because they are anchored to the substrate. Motors, in general, would have larger diffusion constants. For this reason, the parameter D may be made arbitrarily small; for the present numerical work, we have taken D to be 0.1 in non-dimensionalized units. We have also performed simulations of cells in which D is taken to be ten times smaller, and this does not have much effect on the shapes of the cells or the qualitative nature of the phase diagram.

Biological comparisons

There are significant similarities between our model results and experimental observations in moving keratocytes, including in features like subcellular myosin localization, cell shape and velocity as a function of adhesion, and cell velocity as a function of myosin activity. However, living cells become rounder when myosin activity is increased while in the model, increasing myosin activity causes the cell to become more elongated (2). One reason for the disagreement between model and experiments may be the presence of the nucleus. In live cells, myosin is distributed at the back of the cell in two spots on either side of the nucleus. Myosin is therefore closer to the sides of the cell, and increasing its activity may efficiently decrease the width of the cell. In the model, myosin forms a single peak at the back of the cell, far from the sides. In this case, increasing myosin activity would compress the rear of the cell, but leave the sides of the cell mostly unaffected; therefore the cell elongates. Another possible reason for the

disagreement between model and experiments is that our model exists in two-dimensions, so that area constraints rather than volume constraints are imposed; in live cells, myosin contraction may pull cytoskeleton off of the contact surface and thus round up the cell, but this is not possible in a two-dimensional model. Therefore, more detailed comparisons to experiments may be difficult due to additional complications of real keratocytes.

Boundary treatment

The boundary in our model is treated as a movable object with realistic physical properties (3). The boundary interacts with the filament populations through direct contact; specifically, we use a "smeared out" potential to simulate the confining effect of the cell boundary on filaments, similar to methods in references (4,5). Using such a potential to replace formal boundary conditions greatly facilitates numerical treatment without affecting the results.

The model captures the ratchet model of actin pushing the front of cells. In the model, all filament-boundary interactions are repulsive, and filaments of any orientation near a boundary push normally on the boundary due to pure contact forces. However, filaments treadmilling in a direction normal to the boundary will appear near the boundary with the greatest density, and due the directionality of treadmilling, push the most. This is captured naturally in the model and most clearly illustrated in the inset filament profiles in Figure 4.

Boundary treatments in related models

There are other models of cell motility that capture the dynamics of the cytoskeleton and cell membrane. A popular set of models determine the time evolution of the cellular domain using phenomenological boundary conditions based on filament polymerization rates and velocities (6,7). In contrast, a cellular Pott's Model (8) for motility has been described in which cell boundaries are time-evolved in a way that is similar to that in our model.

In the Pott's Model, the simulation domain is discretized into many pixels where the pixel type depends on whether it is considered to be inside a cellular domain or outside of it. In the Pott's model approach, an energy functional determined by the boundary's shape, that incorporates the length of the boundary, the area enclosed by it, and the presence and orientations of nearby filaments, is minimized to propagate the boundary dynamically. In both models, there is a second order term related to area constraint for the overall area of the cell (the term proportional to P in the Helfrich energy and the term proportional to λ in equation (22) of the Pott's Model), and a linear term proportional to the total perimeter of the cell (the surface tension proportional to σ in the Helfrich energy and the sum over J_{CM} in the Pott's Model counting the number of pixels on the cell boundary). An additional similarity is that in the description of reference (8),

the boundary Hamiltonian includes linear terms corresponding to pushing by barbed ends of filaments that occupy pixels within the cell; this is analogous to our filament-boundary interactions, where the interaction energy is also linear with the total number of filaments near the boundary. The Helfrich energy includes an additional term energetically punishing regions of high boundary curvature that is not present in the model in reference (8).

Supporting References

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