Supporting Methods

Construction of the mathematical model

In formulating the equations governing the evolution of the local cell density we take the following view. Cells tend to align with one another and with the underlying slime field. That is, cells extrude slime as they move, and prefer to glide on preexisting slime. The cell densities at each location, **x**, are specified by the density functions $n^{s,r}_{+,-,0} = \left(n^s_+, n^r_+, n^s_-, n^r_-, n_0\right) \equiv \vec{n}$ (see Figure 3). The slime field is specified by a unit vector field, **T**(t, **x**) that specifies the local cell velocity: $\mathbf{v} = v_0\mathbf{T}$, where the cell speed, v_0, is assumed constant. The cell density and orientation fields are coupled: cells orient to the local slime direction, and can remodel the slime so as to reorient it.

The evolution of density vector $\vec{n}$ is governed by Equation 1 where the diffusion and gliding fluxes are defined as:

$$\vec{\mathbf{J}}_D = \begin{pmatrix} D\nabla n^r_+ \\ D\nabla n^s_+ \\ D\nabla n^r_- \\ D\nabla n^s_- \\ D_s\nabla n_0 \end{pmatrix}, \qquad \vec{\mathbf{J}}_G = \begin{pmatrix} v_0\mathbf{T}n^r_+ \\ v_0\mathbf{T}n^s_+ \\ -v_0\mathbf{T}n^r_- \\ -v_0\mathbf{T}n^s_- \\ 0 \end{pmatrix} \tag{A.1}$$

States with subscript (+) are gliding in the direction of +**T**, states with subscript (-) glide in the opposite direction (-**T**). In the jammed state the convective gliding velocity $v_0 = 0$. Transitions between states are given by the rate matrix

$$\hat{K} = \begin{pmatrix} -K_a - \underline{K_s} & 0 & 0 & \underline{K_r}^- & 0 \\ K_a & -\underline{K_r}^+ - \underline{K_s} & 0 & 0 & K_m \\ 0 & \underline{K_r}^+ & -K_a - \underline{K_s} & 0 & 0 \\ 0 & 0 & K_a & -\underline{K_r}^- - \underline{K_s} & K_m \\ \underline{K_s} & \underline{K_s} & \underline{K_s} & \underline{K_s} & -2K_m \end{pmatrix} \tag{A.2}$$

Underlined rate constants are assumed to be functions of total cell density, $n_{tot} = n^s_+ + n^r_+ + n^s_- + n^r_- + n_0$. The reversal frequency (rate of reversal in the sensitive state) is a sigmoid function of the density of opposite moving cells (29). Cells in the stop state also signal, so that

$$\underline{K_r^{\pm}} = K_0 + \underbrace{\Delta K_c\left[\frac{\left(n_{\mp} + n_0\right)^q}{\left(n_{\mp} + n_0\right)^q + n_c^q}\right]}_{\text{C-Signaling}} - \underbrace{\Delta K_{str}\left[\frac{n^p_{\pm}}{n^p_{\pm} + n^p_{str}}\right]}_{\text{Streaming Signaling}} \tag{A.3}$$

where $n_+ = n^r_+ + n^s_+$ and $n_- = n^r_- + n^s_-$. The first term refers to the low density limit of reversals, the second term refers to the high density signaling during rippling, and the third term refers to

the decrease in reversal frequency during streaming. The stopping rate, $\underline{K_s}$, is a function of total density, n_{tot}, according to:

$$\underline{K_s} = k_s \frac{n_{tot}^{q_s}}{n_{tot}^{q_s} + n_s^{q_s}} \tag{A.4}$$

Numerical calculations were carried out in Matlab™.

Relationship with previous models

Note that our treatment of the reversal cycle differs from our previous model (29) where we modeled the reversal cycle by a continuous phase variable, ϕ, defined on the circle. To compare two descriptions consider the situation where cells are not dense enough to jam (no-stop state). We discretize the phase circle into 4 Markov states corresponding to four phase domains: **+T** (refractory, sensitive), and **−T** (refractory, sensitive). Markov jump transitions replace the convective flow around the circle. Since the residence time in each Markov state is exponential, the refractory state is necessary to ensure that no cells reverse again immediately upon reversing. Figure 5a shows that the model results that look nearly identical to the experiments, so the 4-Markov state model reproduces the rippling patterns modeled in (29). The reason this discretization works can be seen as follows. Starting with Master Equation for the continuous model (Equation 3 of 29) with no phase dispersion, $D_\varphi = 0$:

$$\frac{\partial n(x,y,\phi,t)}{\partial t} = \underbrace{-\frac{\partial}{\partial x}\left(-D_x \frac{\partial n}{\partial x} \pm v_x n\right) - \frac{\partial}{\partial y}\left(-D_y \frac{\partial n}{\partial y}\right)}_{\text{Spatial Flux}} - \frac{\partial}{\partial \phi}\underbrace{\left(-\omega_\pm n\right)}_{\substack{\text{Phase}\\ \text{flux}}} \tag{A.5}$$

Integrate (A.5) over the four domains of phase and define the phase average densities

$$n_+^r(x,y,t) = \int_0^{\Delta\phi_R} n(x,y,\phi,t)d\phi, \quad n_-^r(x,y,t) = \int_\pi^{\pi-\Delta\phi_R} n(x,y,\phi)d\phi$$

$$n_+^s(x,y,t) = \int_{\Delta\phi_R}^{\pi} n(x,y,\phi,t)d\phi, \quad n_-^s(x,y,t) = \int_{\Delta\phi_R}^{2\pi} n(x,y,\phi)d\phi$$

The evolution of the average densities differs from Equation 1 since the flux from one phase domain to the other is determined by the density values at the phase boundary rather than an average over the phase domain. However, assuming a homogeneous phase distribution of density in each domain (i.e. n is not a function of φ within each interval) one can obtain Equation 1 with the rates related to phase velocity (29)

$$\omega_\pm(x,\phi,n,q) = \underbrace{\omega_0 + \omega_n\left(\frac{n_\mp^q}{n_\mp^q + n_w^q}\right)}_{\omega_c} \cdot F(\phi), \quad \text{where } F(\phi) = \begin{cases} 0 \text{ for } \phi \in \Delta\phi_R \\ 1 \text{ for } \phi \in \Delta\phi_S \end{cases}$$

as follows

$$K_a = \frac{\omega_0}{\Delta\phi_R}, \quad K_0 = \frac{\omega_0}{\pi - \Delta\phi_R}, \quad \Delta K_n = \frac{\omega_n}{\pi - \Delta\phi_R}$$

Equation (A.2) describes evolution of the local average cell orientation, which is the same as the orientation of the slime field (This is analogous to the method used in 33).

Orientation dynamics

Equation 2 describes the evolution of the slime orientation field, **T(x,** t). The coefficient, α describes the tendency of neighboring cells to align. We chose this coefficient to increase linearly with the total density of cells:

$$\alpha = \alpha_0 n_{tot} \tag{A.6}$$

At sufficiently high densities the torque, τ, rotates cells perpendicular to the direction of the local density gradient. This results in circulation of cells around aggregates that are too dense to penetrate. We chose the following form (the justification is below)

$$\tau = -\beta(n_{tot}) \frac{(\mathbf{T} \cdot \nabla n_{tot}) \nabla n_{tot}}{|\nabla n_{tot}|^2} \tag{A.7}$$

where $\beta(n_{tot})$ is an increasing function of density, e.g.

$$\beta = \beta_0 \frac{n_{tot}^{q_T}}{n_{tot}^{q_T} + n_T^{q_T}} \tag{A.8}$$

It is clear that the right hand side of Equation 2 is not perpendicular to $\mathbf{T}$ and so does not conserve the magnitude of $\mathbf{T}$. To maintain the normalization, one can either renormalize the orientation vector each time step, or add an additional term to maintain its magnitude close to 1. The specific form of these terms corresponds to different ways of deriving and interpreting Equation 2. Below we present two alternative approaches that lead to similar results.

First, we introduce an energy functional describing the evolution of the orientation field:

$$E[\mathbf{T}] = \underbrace{\alpha |\nabla \mathbf{T}|^2}_{\text{Alignment}} + \underbrace{\beta (\mathbf{T} \cdot \frac{\nabla n_{tot}}{|\nabla n_{tot}|})^2}_{\text{Turning}} + \underbrace{C(1 - (\mathbf{T})^2)^2}_{\text{Preserving magnitude}} \tag{A.9}$$

Taking the functional derivative of this energy with respect to $\mathbf{T}$ results in

$$\frac{\partial}{\partial t}\mathbf{T} = \frac{\delta E[T]}{\delta \mathbf{T}} = \alpha^2 \nabla^2 \mathbf{T} - \beta \frac{(\mathbf{T} \cdot \nabla n_{tot}) \nabla n_{tot}}{|\nabla n_{tot}|^2} + 2C\mathbf{T}(1 - \mathbf{T} \cdot \mathbf{T}) \tag{A.10}$$

The first two terms in Equation (A.10) correspond the two first two terms of Equation 2; the last term maintains the normalization $|\mathbf{T}| = 1$ in the limit $C \to \infty$. Numerically, it is sufficient to renormalize $\mathbf{T}$ at each time step.

Alternatively, one can introduce a velocity field $\mathbf{V}_+ = v_o \mathbf{T}$, and adopt Vicsek's approach to describe its evolution (34). Thus

$$\frac{\partial}{\partial t}\mathbf{V}_+ = \underbrace{\frac{v_0\mathbf{V}_+}{\tau_1|\mathbf{V}_+|}}_{\text{Propulsive force}} - \underbrace{\frac{\mathbf{V}_+}{\tau_1}}_{\text{Viscous force}} + \underbrace{\alpha\nabla^2\mathbf{V}_+}_{\text{Alignment}} + \underbrace{\mathbf{F}_T}_{\text{Turning}} \qquad \text{(A.11)}$$

The first term represents a self-generated propulsive force which is countered by the viscous resistance force in the second term. The timescale, τ_1, can be estimated as $\tau_1 \sim \xi/m$, which is very small. So the purpose of the first two terms of Equation (A.10) is to insure $|\mathbf{V}_+| = v_0$; therefore, one can take the limit $\tau_1 \to 0$ and renormalize $\mathbf{V}_+$ at each time step. The third term in Equation (A.10) is responsible for alignment; and is obtained by taking the lowest order gradient expansion of the local aggregation rule specifying that each cell adapts the average local orientation. The last term represents turning due to cell-cell interactions at high densities.

There are several important differences between our approach and the one developed in (34). First, since the slime is stationary, there is no $(\mathbf{V}_+\cdot\nabla)\mathbf{V}_+$ term corresponding to convection of orientation. That is, cells readjust their orientation to the local slime field orientation rather than carrying their orientation with them. Second, the 'turning force', F_t, need not be conservative (i.e. of the form ∇p) since this force involves interactions between cells and between cells and substrate. Dividing this equation by v_0 and introducing orientation vector $\mathbf{T} = \mathbf{V}_+/v_0$ one obtains Equation 2 in the limit $\tau_1 \to 0$, with renormalization of $\mathbf{T}$ at each time step.