

Active contractility of adherent cells

Ulrich Schwarz

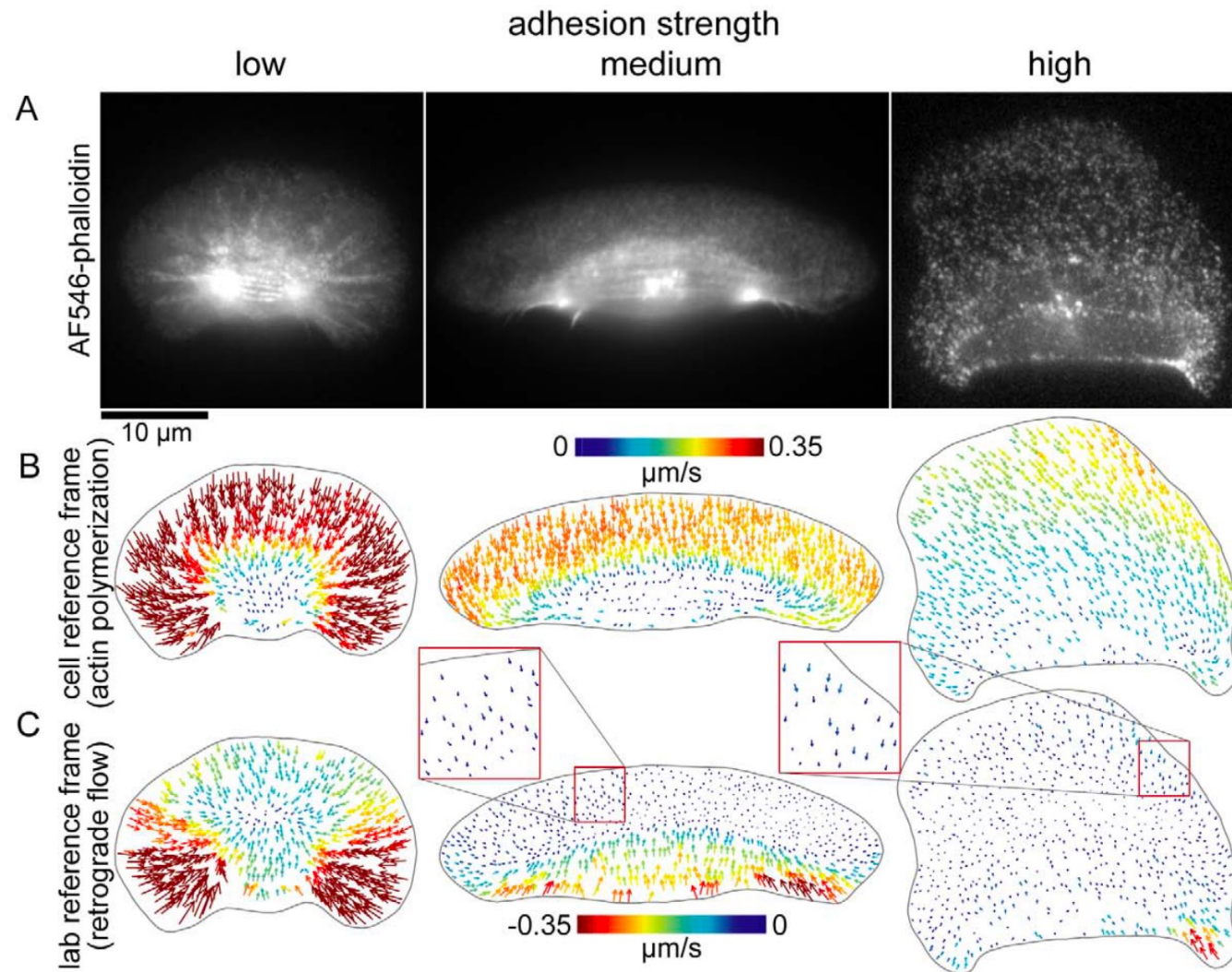
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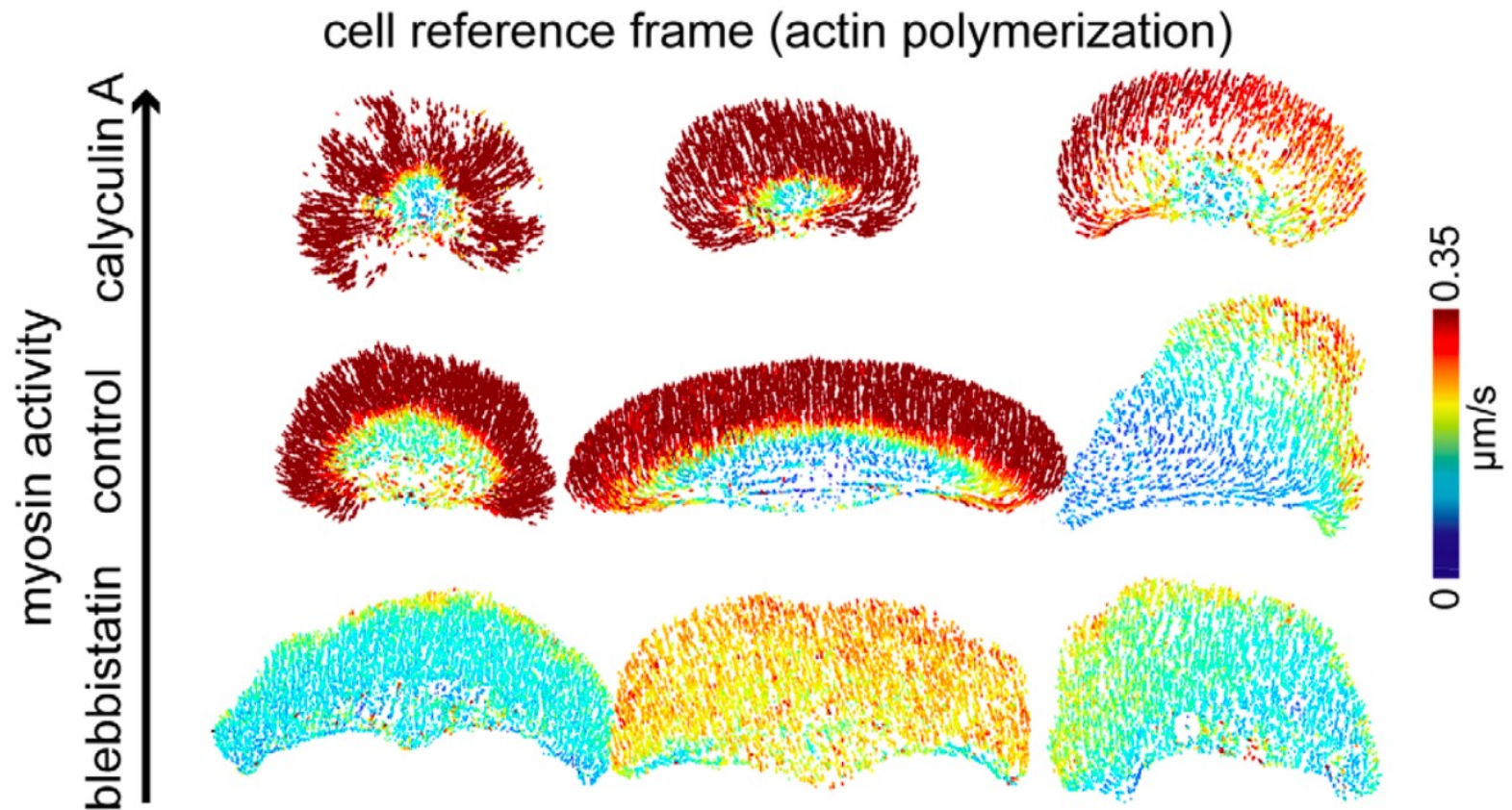
BioQuant
MODEL base of LIFE

Retrograde flow in keratocytes



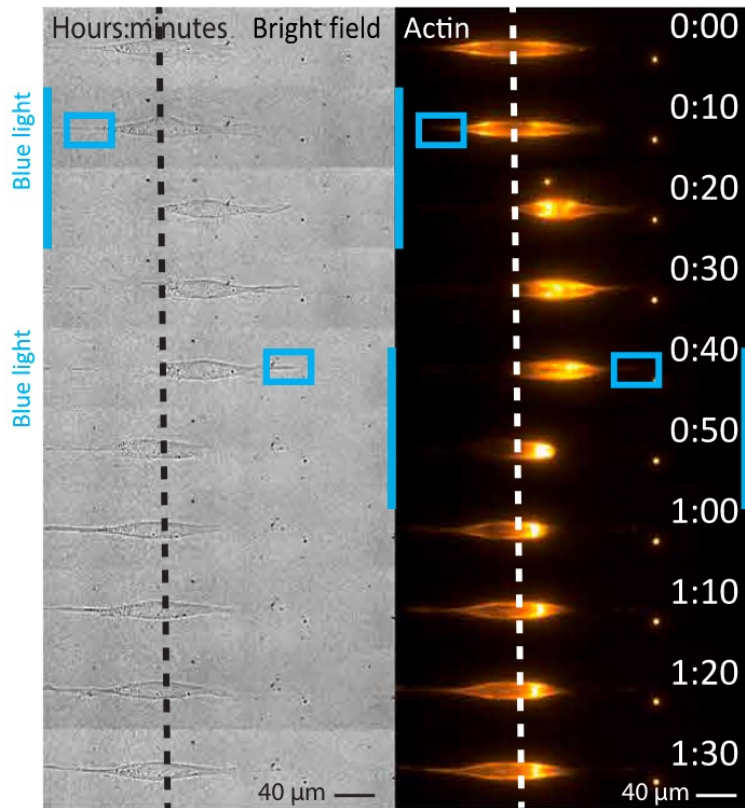
[Barnhart et al. PLoS Biol 2011]

Myosin II drives retrograde flow

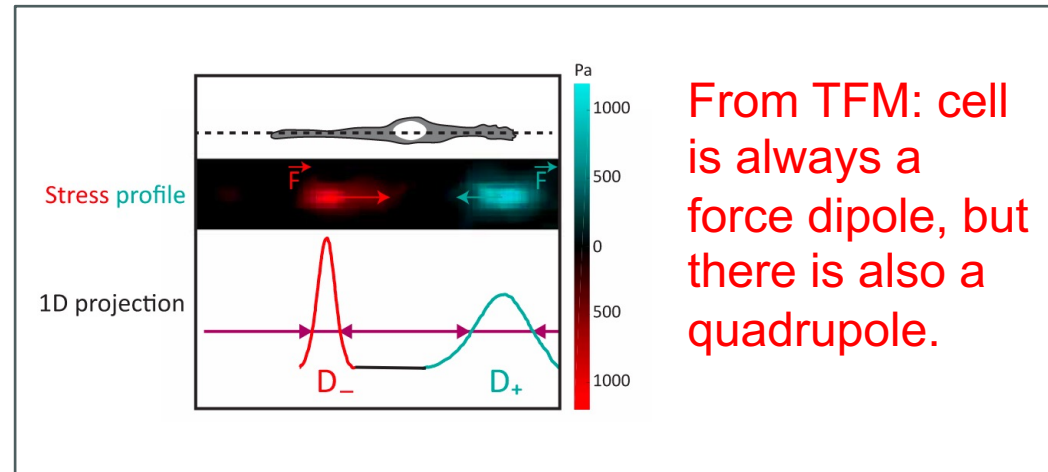


[Barnhart et al. PLoS Biol 2011]

Initiation of cell migration by Rho-optogenetics

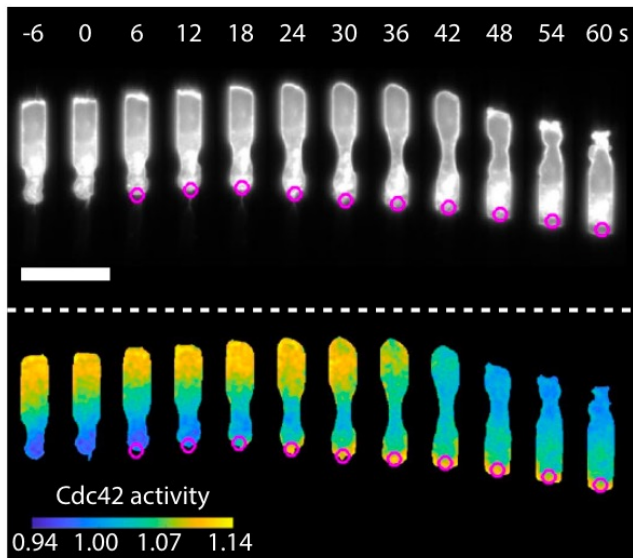
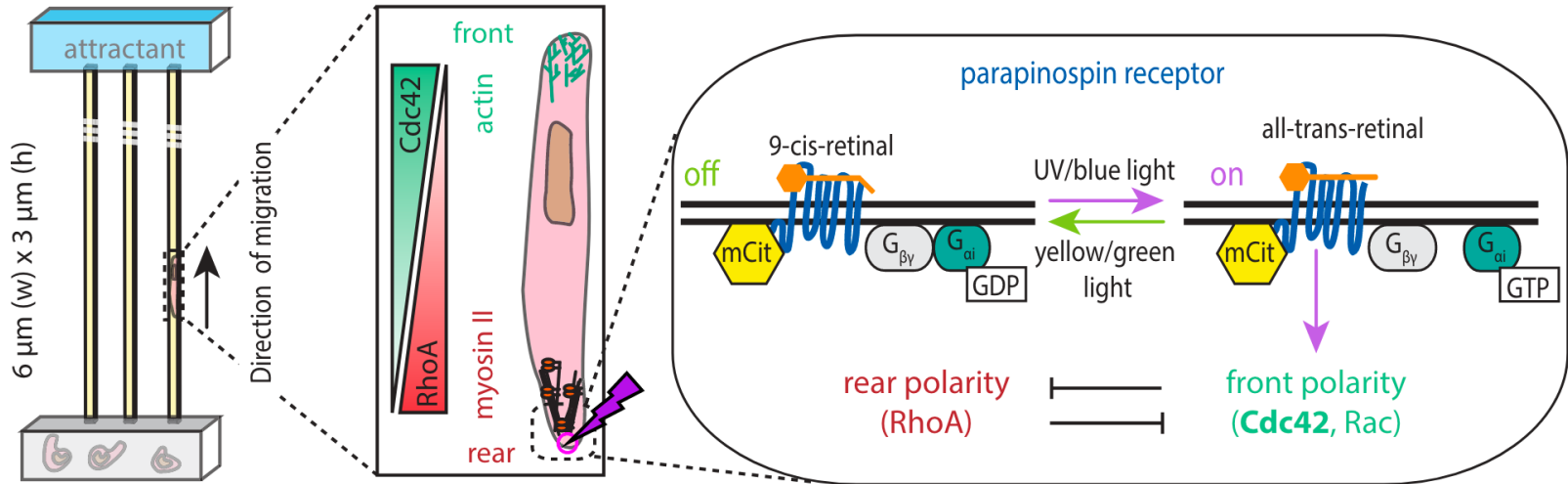


Cells on lines. Activating cell contractility by Rho-optogenetics at one side initiates/reverses cell migration. The contracting side becomes the back of the cell.



From TFM: cell is always a force dipole, but there is also a quadrupole.

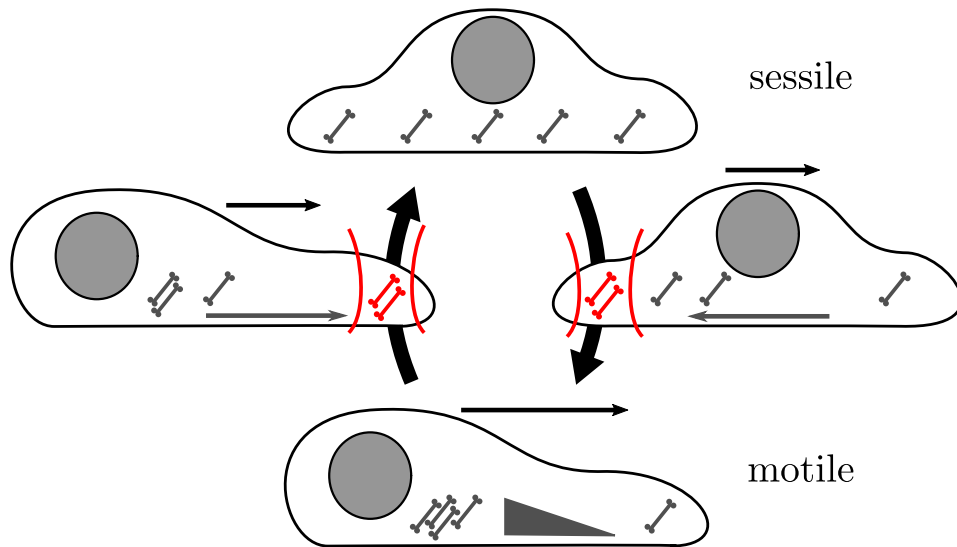
Neutrophil reversal by optogenetics



Optogenetic stimulation of the G-protein downstream of the chemotactic receptor at the back reverses 1D migration in channel. Cells strong in myosin II at the rear do not reverse.

[Hadjitheodorou et al. Nat Comms 2021]

Active gel theory for optogenetic control of migration of contractile cells



- Mesenchymal cell migration requires polarization and retrograde flow.
- This in turn requires a gradient in myosin concentration.
- Can we switch between sessile and motile states by optogenetics of contractility?

Minimal active gel model for migration of contractile cells

Active gel with flow field $v(x,t)$ and myosin concentration field $c(x, t)$

Active stress c -dependent: $\sigma_{act} = \chi c$

Constitutive relation: $\eta \partial_x v = \sigma - \chi c$

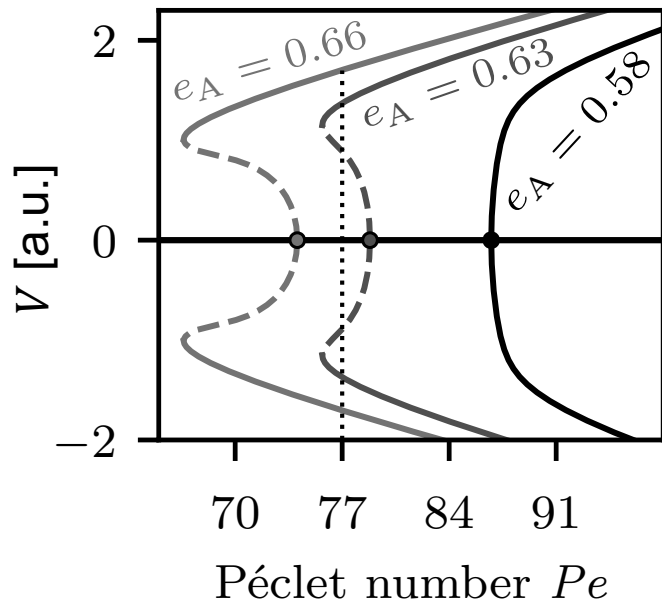
Force balance: $\partial_x \sigma = \xi v$

Active viscous gel: $\frac{\eta}{\xi} \partial_x^2 \sigma = \sigma - \sigma_{act} = \sigma - \chi c$

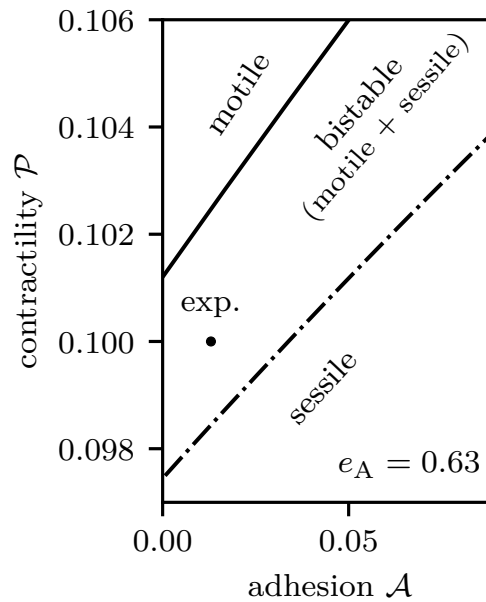
Advection-diffusion of myosin concentration: $\partial_t \mathbf{c} = - \partial_x (\mathbf{v} \mathbf{c}) + \partial_x (\mathcal{D}(\mathbf{c}) \partial_x \mathbf{c})$

Nonlinear diffusion coefficient of vdW fluid: $\mathcal{D}(c) = D \left[\left(1 + \frac{c}{c_\infty - c} \right)^2 - e_A c \right]$

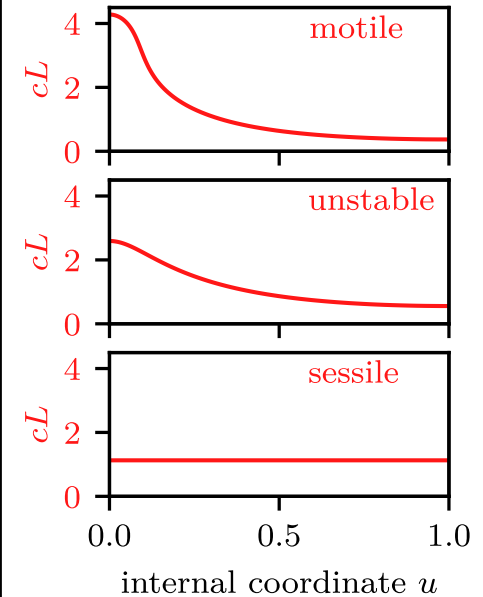
Bistability between sessile and motile solutions



Subcritical bifurcation as a function of attraction e_A

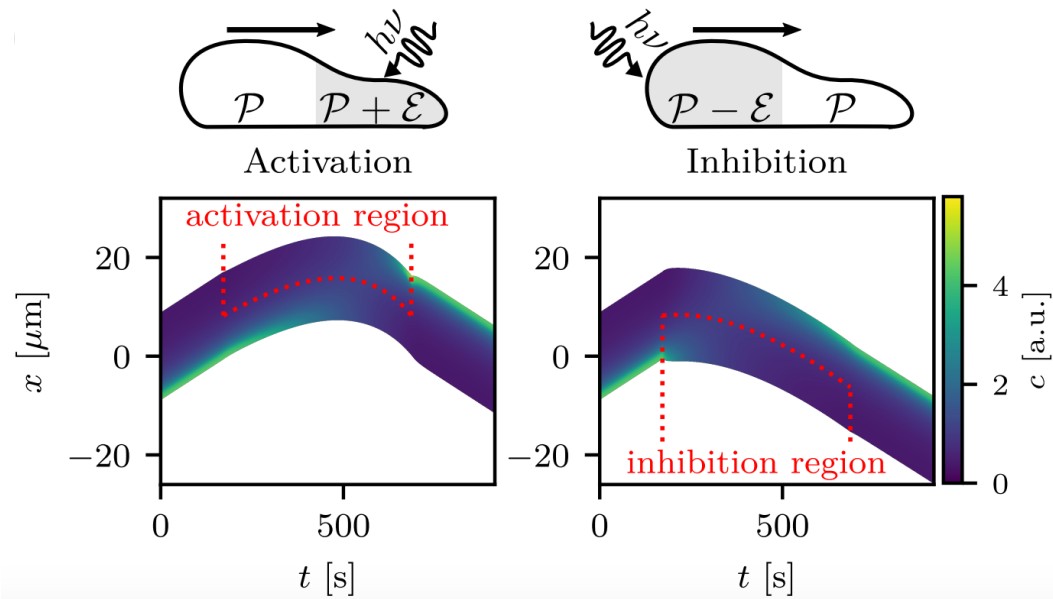


Phase diagram with bistable region



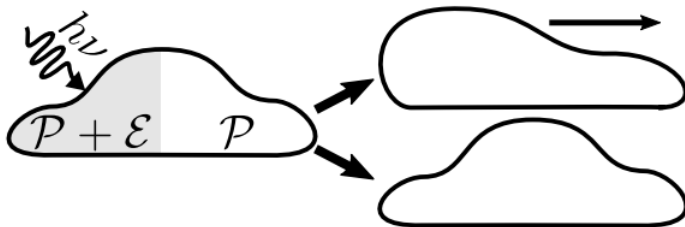
Myosin concentration profiles for different states

Switching migration by optogenetics

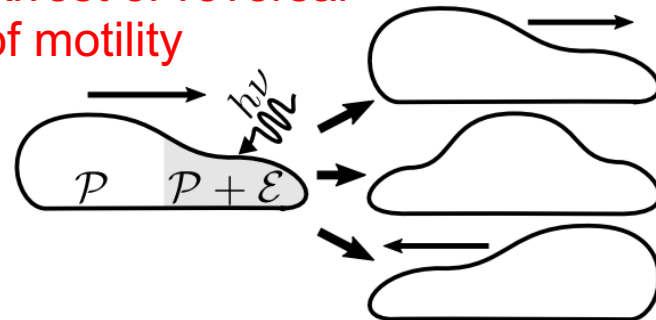


Both activation at front and inhibition at rear can lead to cell reorientation.

Initiation of motility



Arrest or reversal of motility



[Drozdowski, Ziebert and Schwarz PRE 2021 and Comms Phys 2023]

Minimal active gel model for coupling actin flow and adhesions

Active gel with flow field $v(x,t)$ and with adhesion field $a(x, t)$

Active stress constant:

$$\sigma_{act} = const$$

Constitutive relation:

$$\sigma(x, t) = \eta \partial_x v(x, t) + \sigma_{act}$$

Force balance:

$$\partial_x \sigma(x, t) = \xi v(x, t) (a_0 + a(x, t))$$

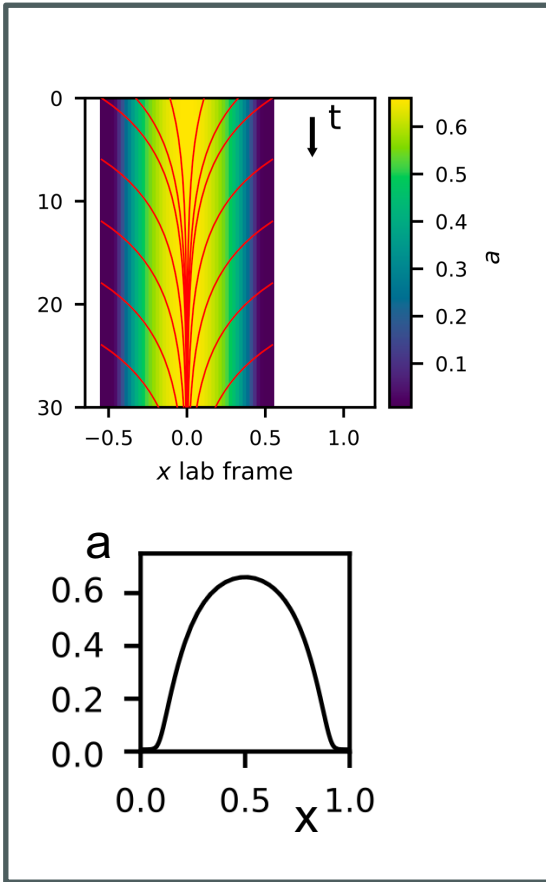
Stress equation:

$$\frac{\eta}{\xi} \partial_x \left(\frac{\partial_x \sigma(x, t)}{a_0 + a(x, t)} \right) = \sigma(x, t) - \sigma_{act}$$

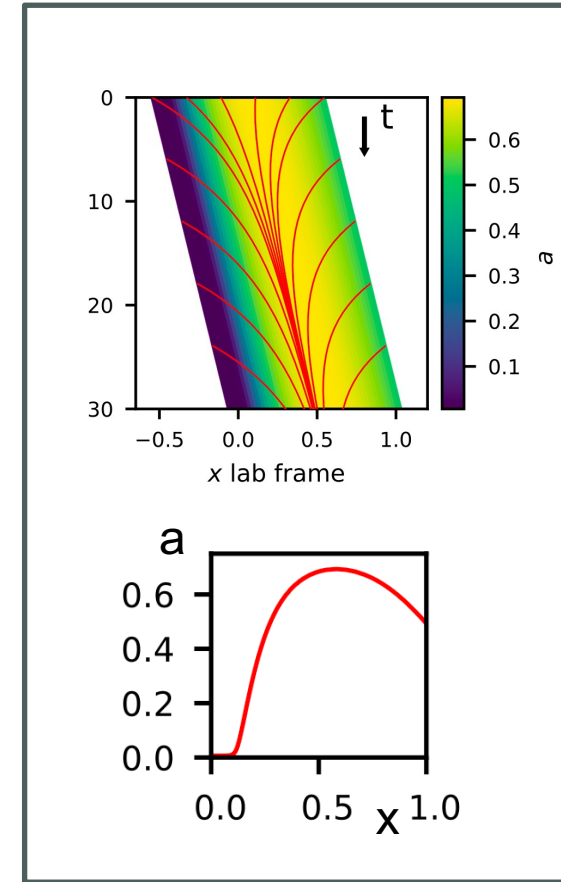
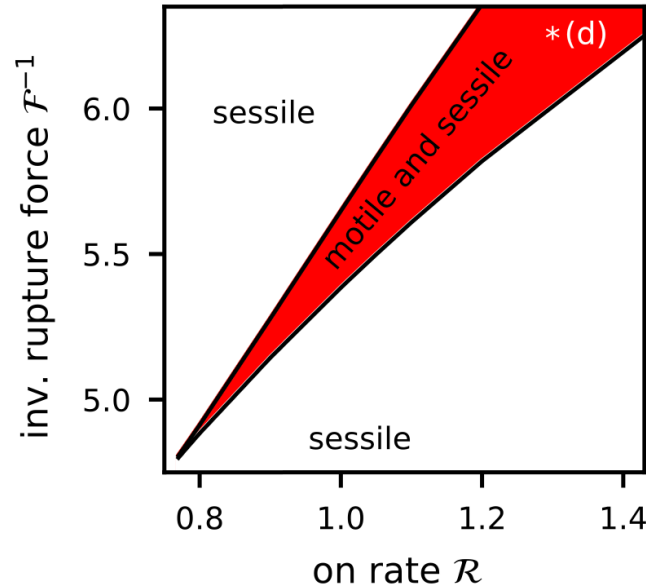
Reaction-diffusion of adhesion field: $\partial_t a(x, t) = r_{on} - r_{off}(x, t)a(x, t) + D\partial_x^2 a(x, t)$

Bell-Dembo dissociation rate: $r_{off}(x, t) = r_0 \exp \left(\frac{|\sigma(x, t)|}{f_0 (a_0 + a(x, t))} \right)$

Bistability between motile and sessile solutions requires balance of association and dissociation

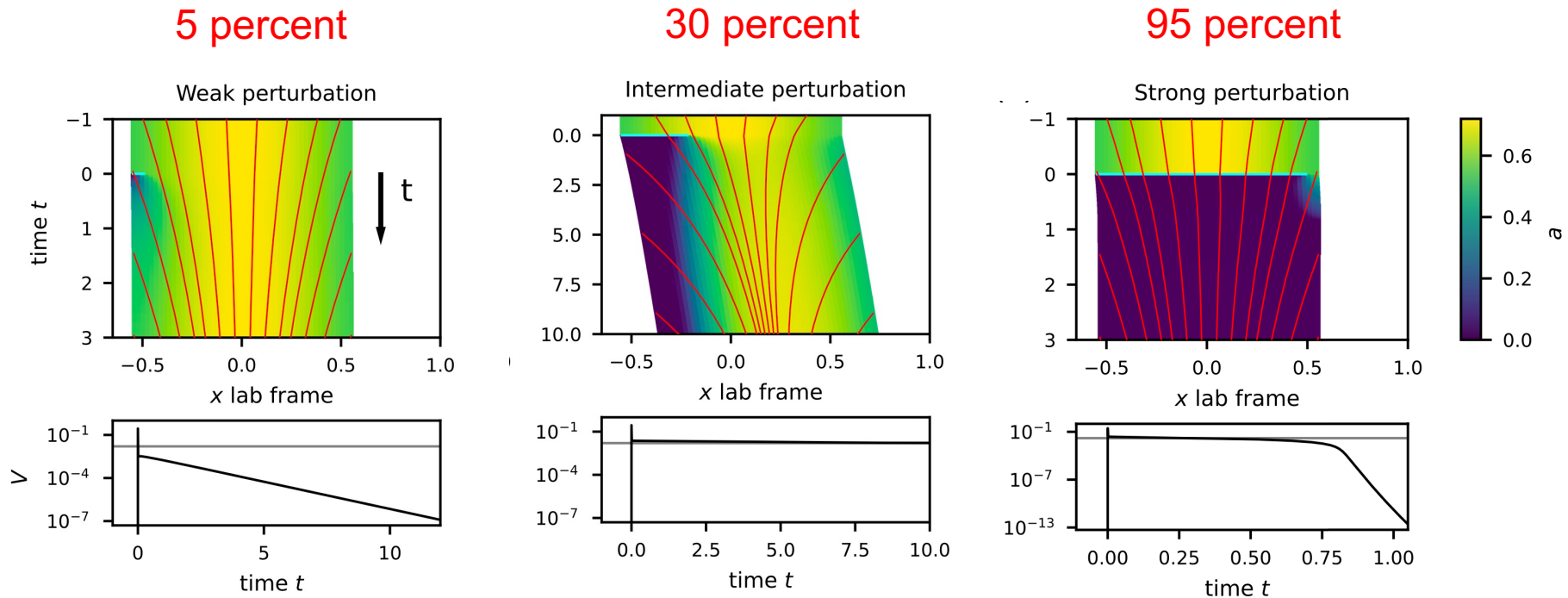


sessile



motile

Changes in adhesion can also switch cell migration



A certain percentage of the adhesion is removed in the sessile state.

For intermediate values, the cell switches into the motile state, as observed experimentally by Hennig et al. Sci Adv 2020.

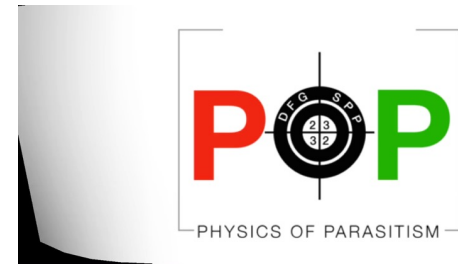
Acknowledgements



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