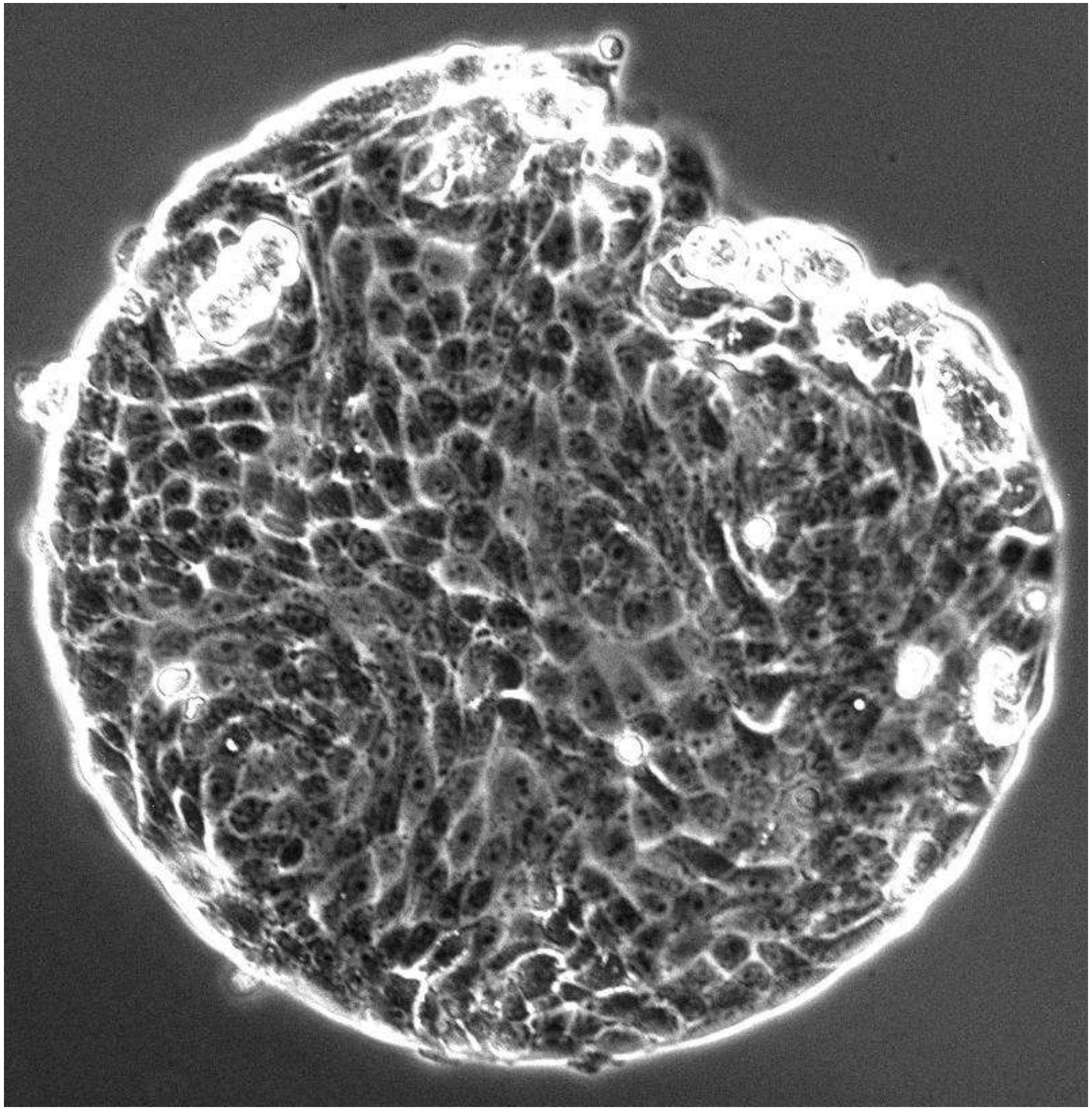
Active Matter 3

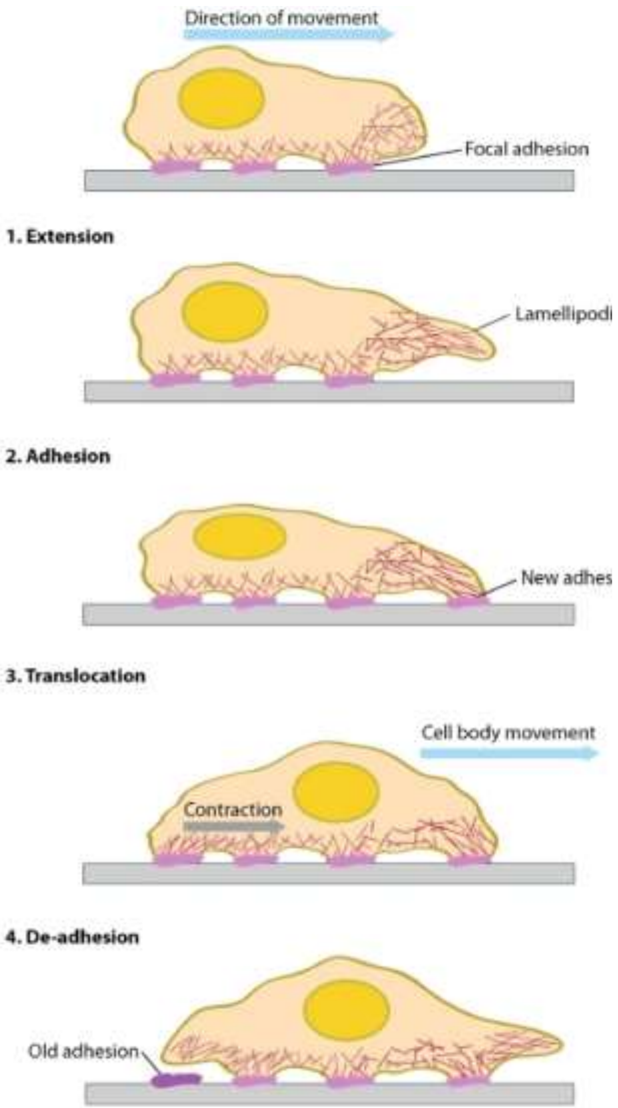
Julia Yeomans
University of Oxford

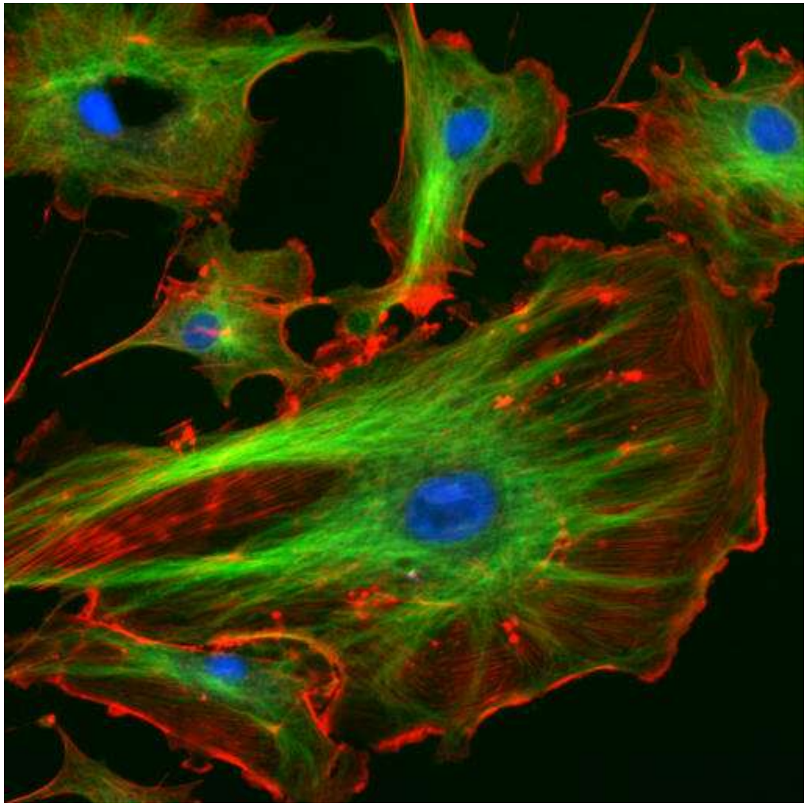
1. What is active matter and why is it interesting?
2. Background 1: nematic liquid crystals
3. Background 2: low Reynolds number hydrodynamics
4. Active nematics and active turbulence
5. Self-propelled topological defects
6. Confining active turbulence
7. Bacteria: the hare and the tortoise
8. Eukaryotic cells as an active system

(Epithelial) cells: which are the important forces?



Single cell motility

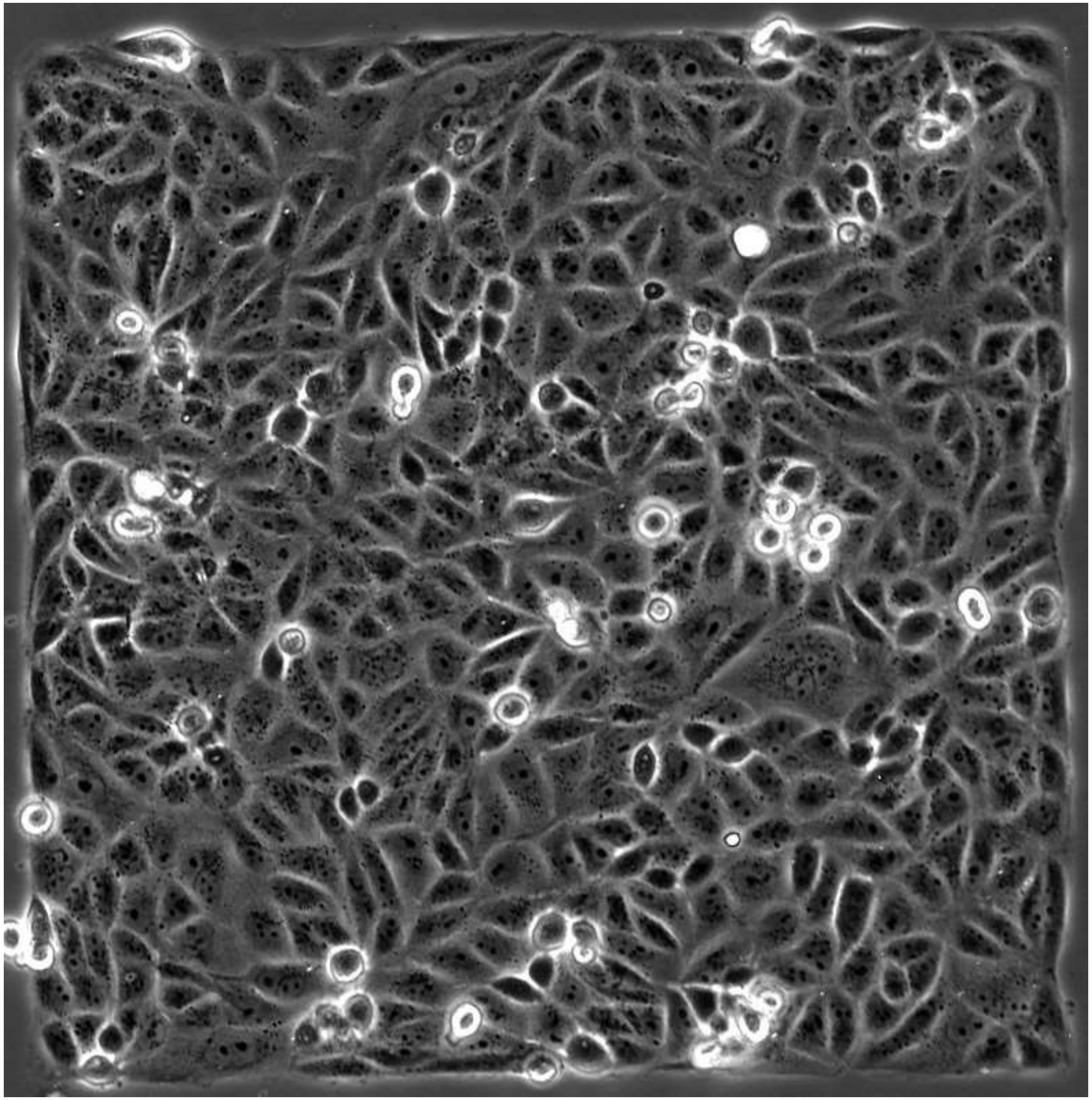




Ladoux and Nicholas Rep Prog Phys 2012

Fritz-Layn,
Riel-Mehan, UCSF

Active turbulence: eukaryotic cells



Thank You



Amin Doostmohammadi

Guanming Zhang

Romain Mueller

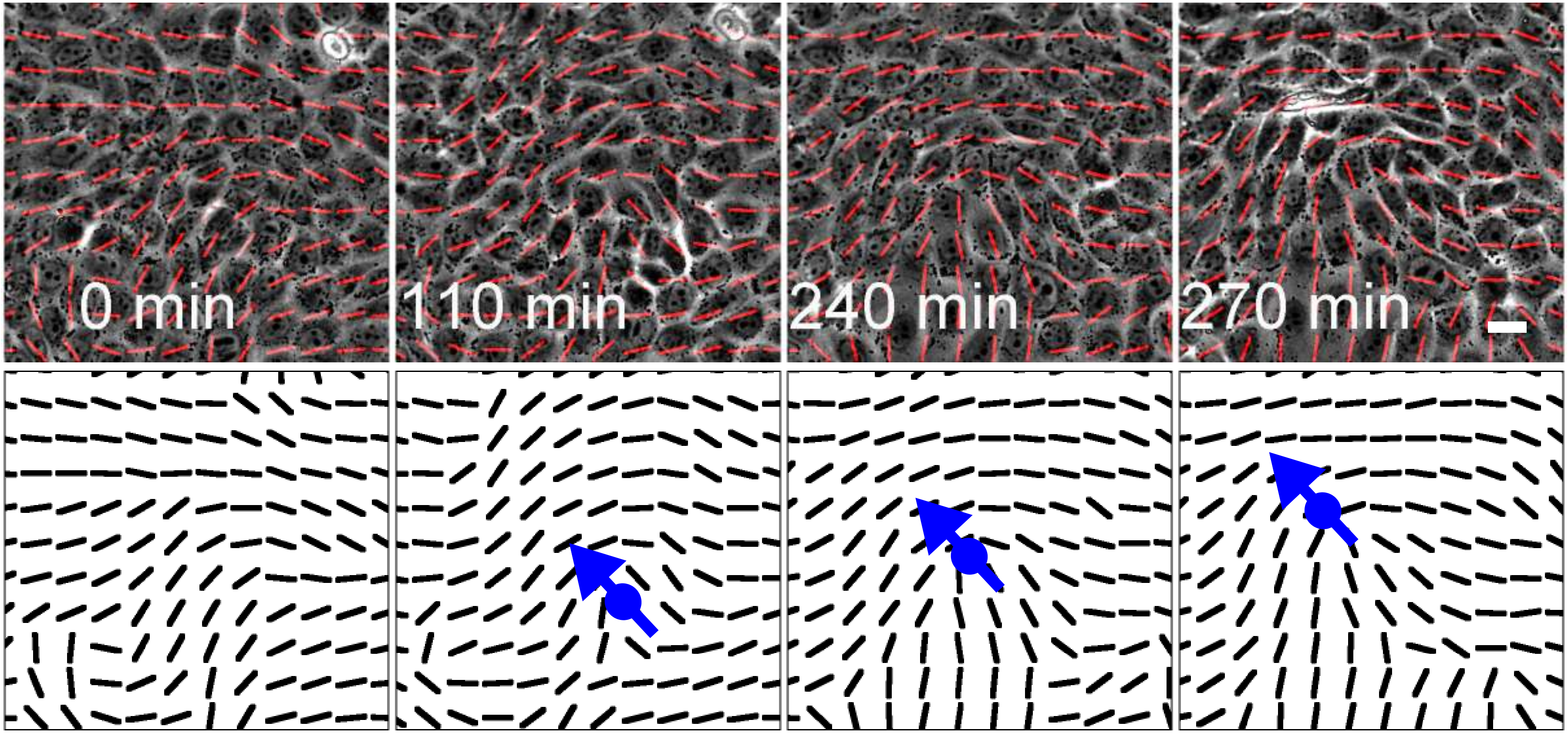
Sumesh Thampi

Mehrana Raesian Nejad

Sreejith Santhosh



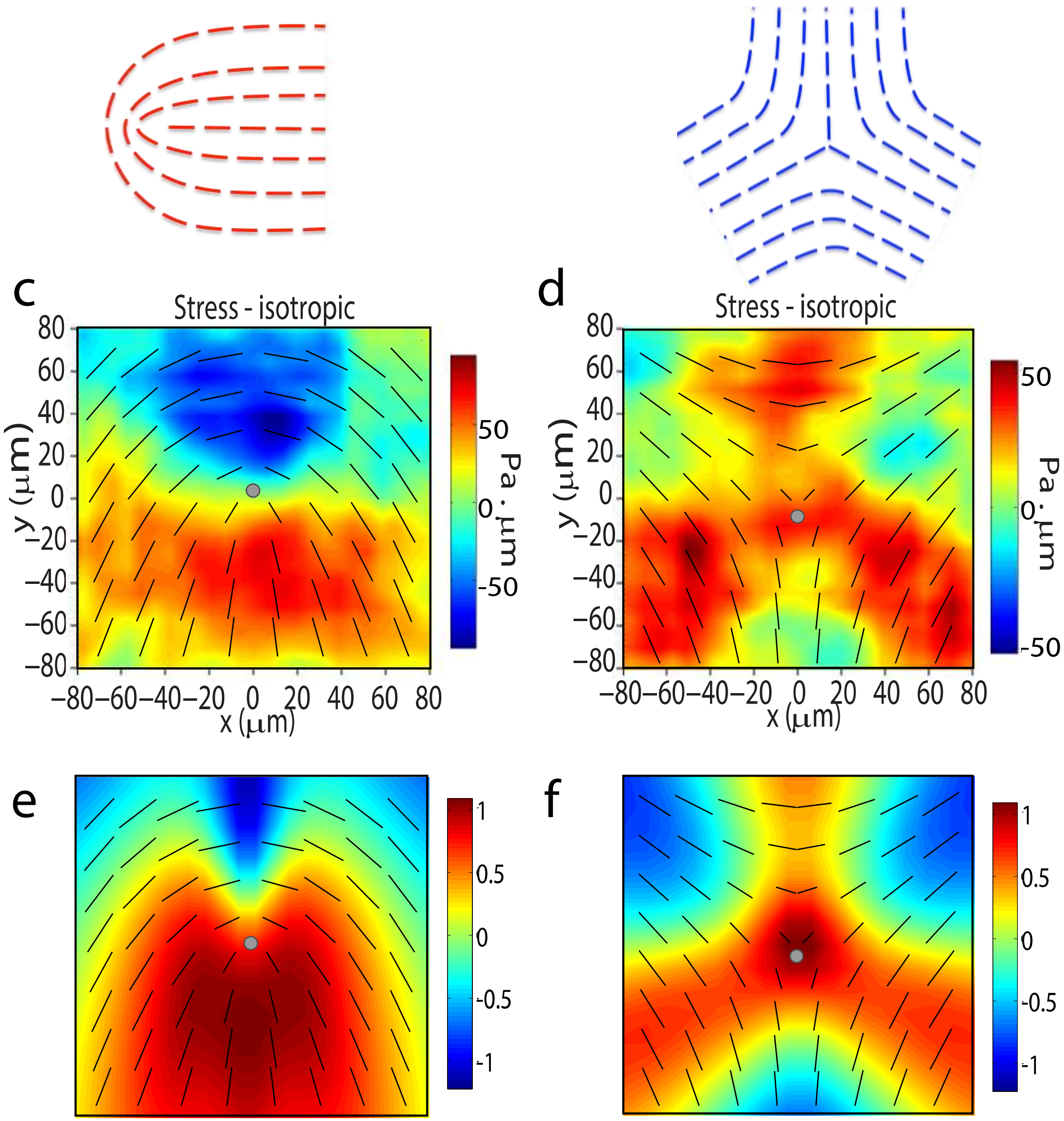
Topological defects in cell layers



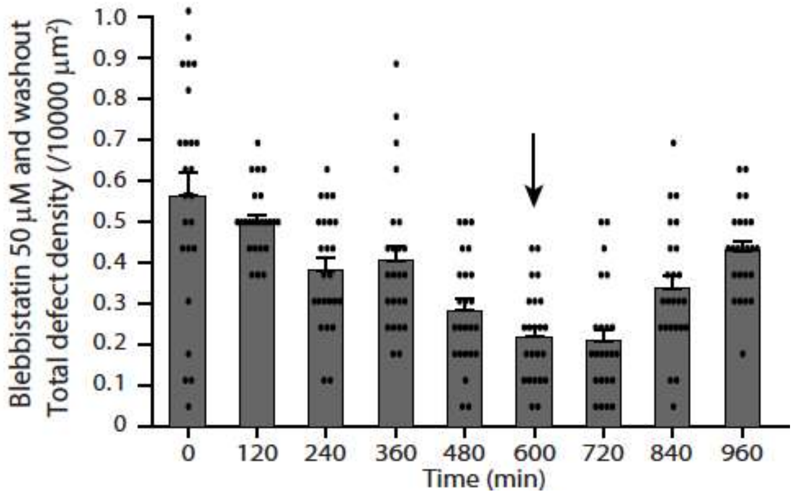
Isotropic stress around a topological defect

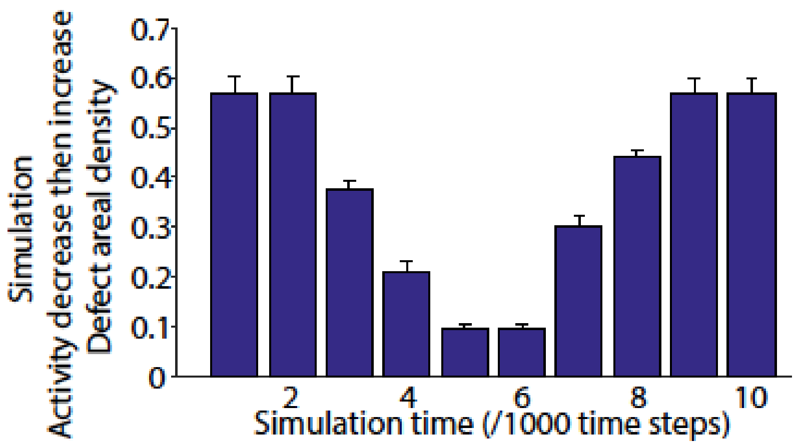
experiment

simulations



‘Turning off’ motility

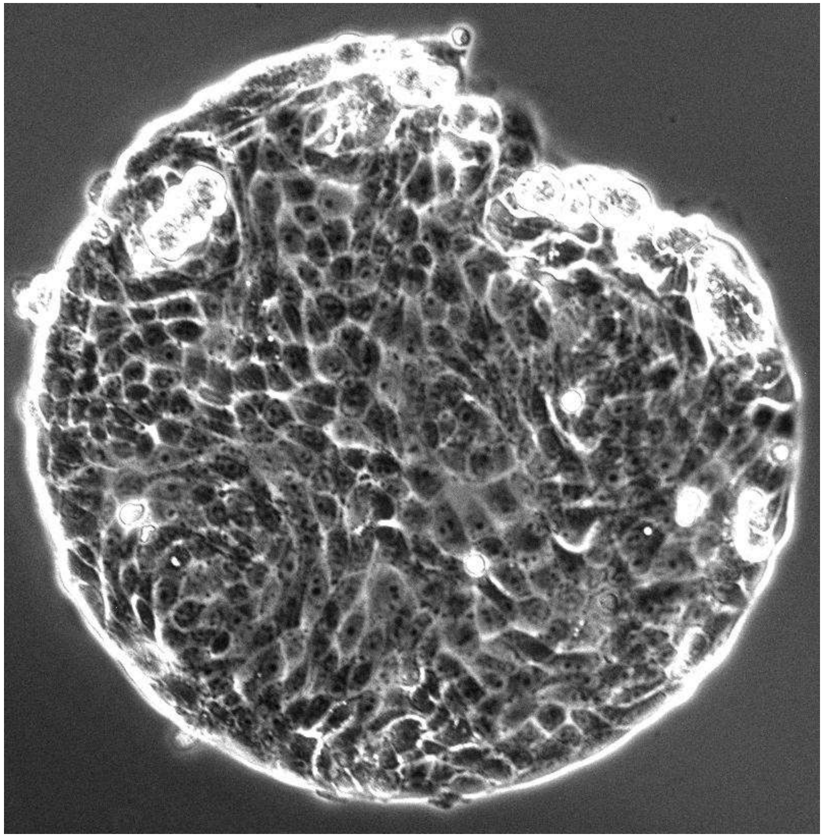




Topological defects in epithelia govern the extrusion of dead cells

T. Beng Saw, A. Doostmohammadi et al, Nature 544 212 (2017)

Topology in biology?



Positions of apoptosis correlated with +1/2 topological defects

High stress drives YAP from nucleus to cytoplasm which is a signal for cell death

Cell dies and is ejected from the monolayer

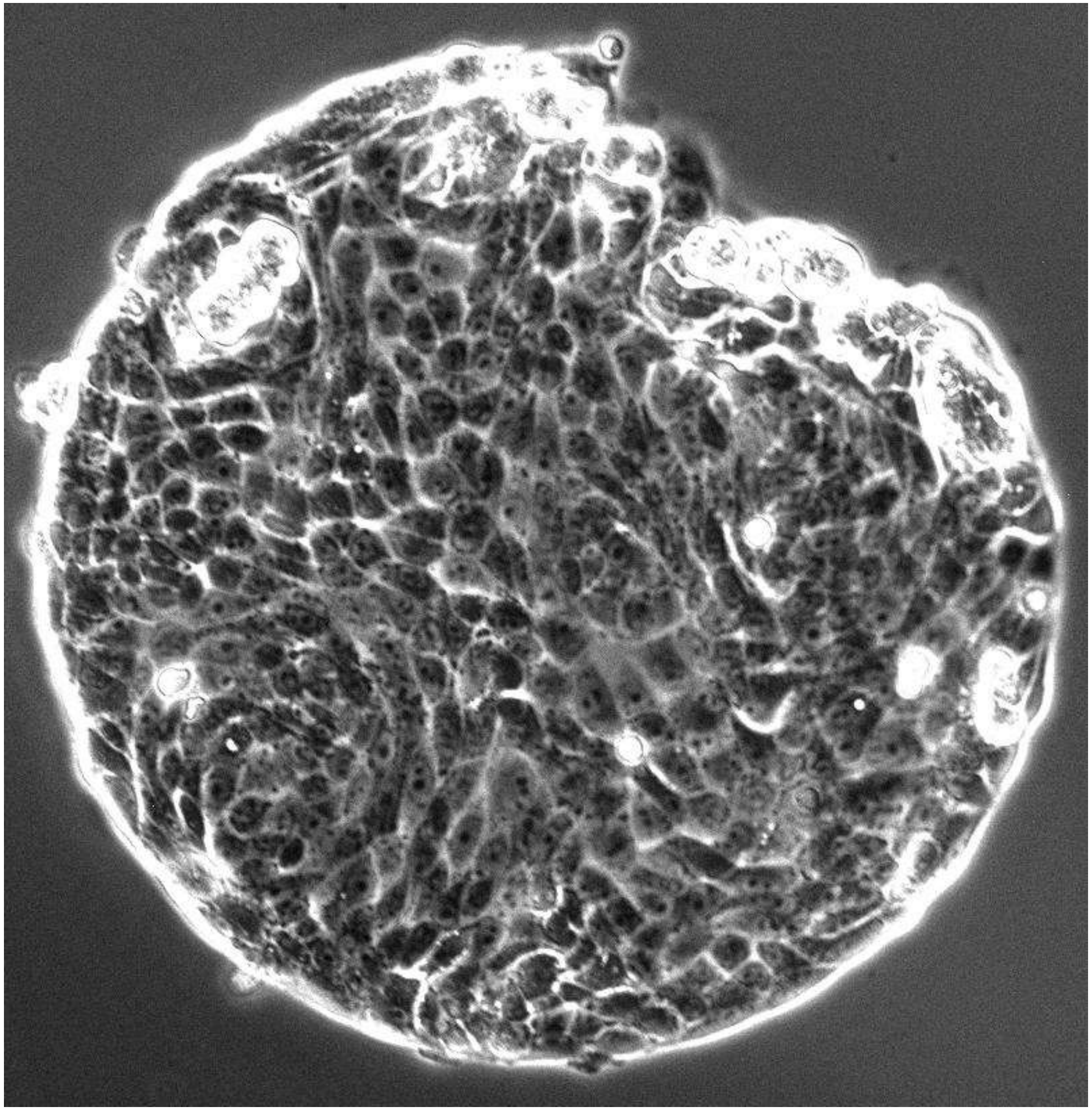
Questions

Why do isotropic cells give nematic defects?

Why are the defects extensile?

Can we model cell mechanics as an active system?

(Epithelial) cells: which are the important forces?

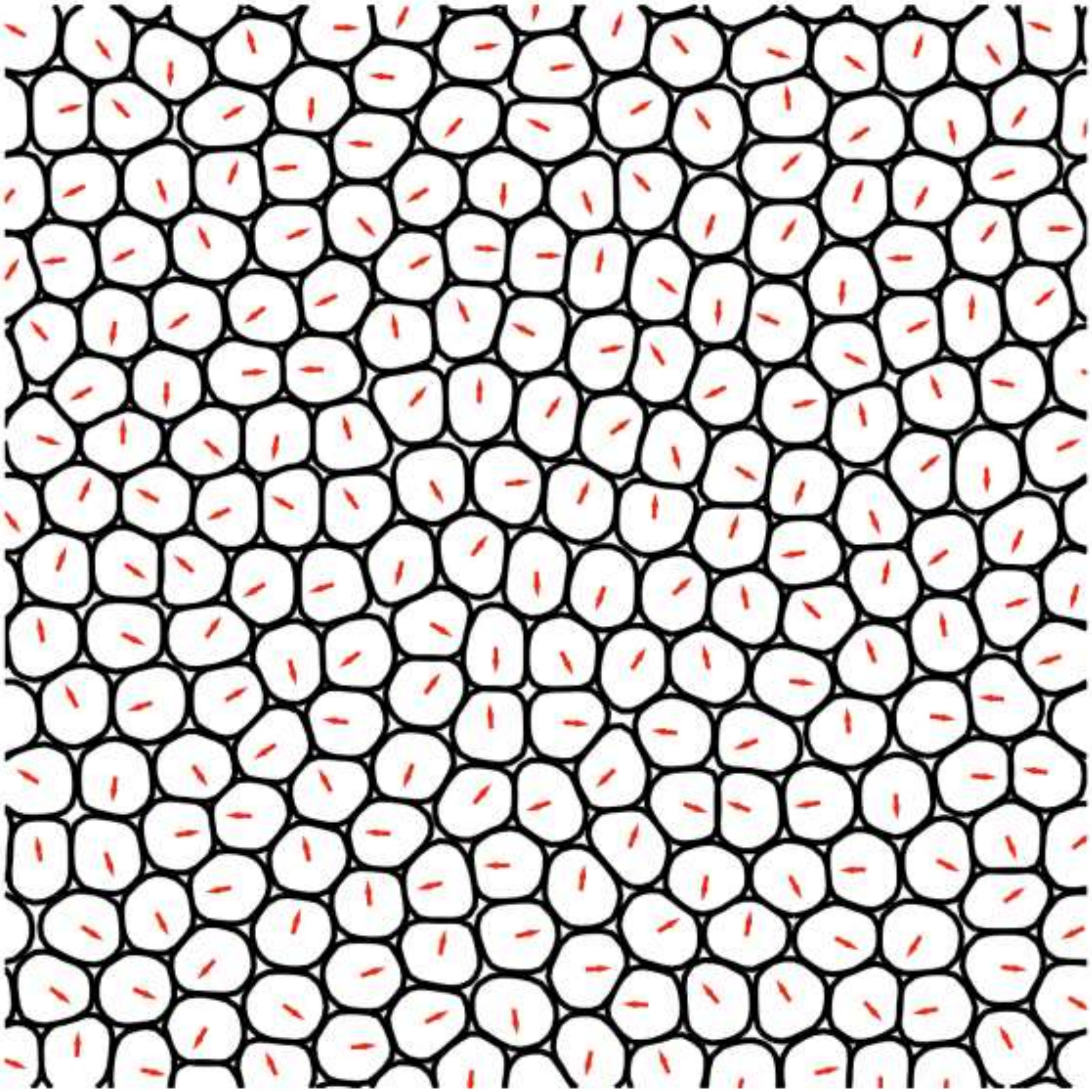


1. Phase field model

2. Unjamming

3. Velocity and flocking

frame index: 30



Grant, Aranson

Equations of motion

Each cell is described by a phase field φ_i

$$\partial_t \varphi_i + \mathbf{v}_i \cdot \nabla \varphi_i = -\frac{\delta \mathcal{F}}{\delta \varphi_i}$$

$$\xi \, \mathbf{v}_i(\mathbf{x}_i) = \mathbf{f}_i^{\mathrm{tot}}(\mathbf{x}_i)$$

Passive forces => relax to minimise free energy

Cahn-Hilliard term: fixes φ_i to 1 inside a cell and 0 outside and imposes a surface tension

$$\mathcal{F}_{CH} = \sum_i \frac{\gamma}{\lambda} \int d\mathbf{x} \left\{ 4\varphi_i^2 (1 - \varphi_i)^2 + \lambda^2 (\nabla \varphi_i)^2 \right\}$$

Soft constraint on the area

$$\mathcal{F}_{\text{area}} = \sum_i \mu \left\{ 1 - \frac{1}{\pi R^2} \int d\mathbf{x}\ \varphi_i^2 \right\}^2$$

Passive forces => relax to minimise free energy

penalises overlap between cells

$$\mathcal{F}_{\text{rep}} = \sum_i \sum_{j \neq i} \frac{\kappa}{\lambda} \int d\mathbf{x}\, \varphi_i^2 \varphi_j^2$$

favours cell-cell adhesion

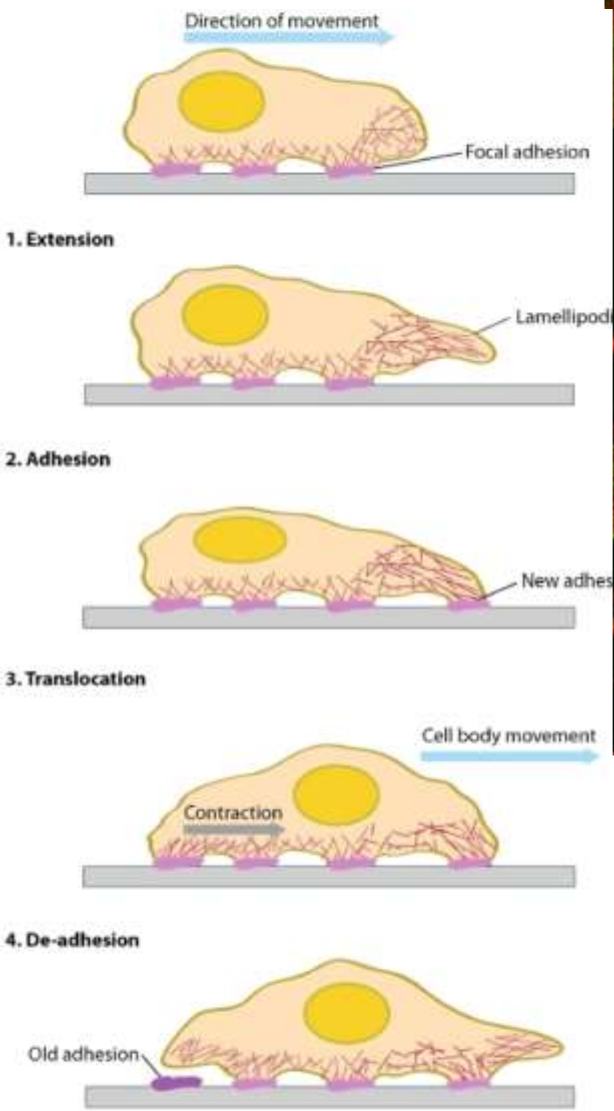
$$\mathcal{F}_{\text{adh}} = \sum_i \sum_{j \neq i} \omega\lambda \int d\mathbf{x}\, \nabla\varphi_i \cdot \nabla\varphi_j$$

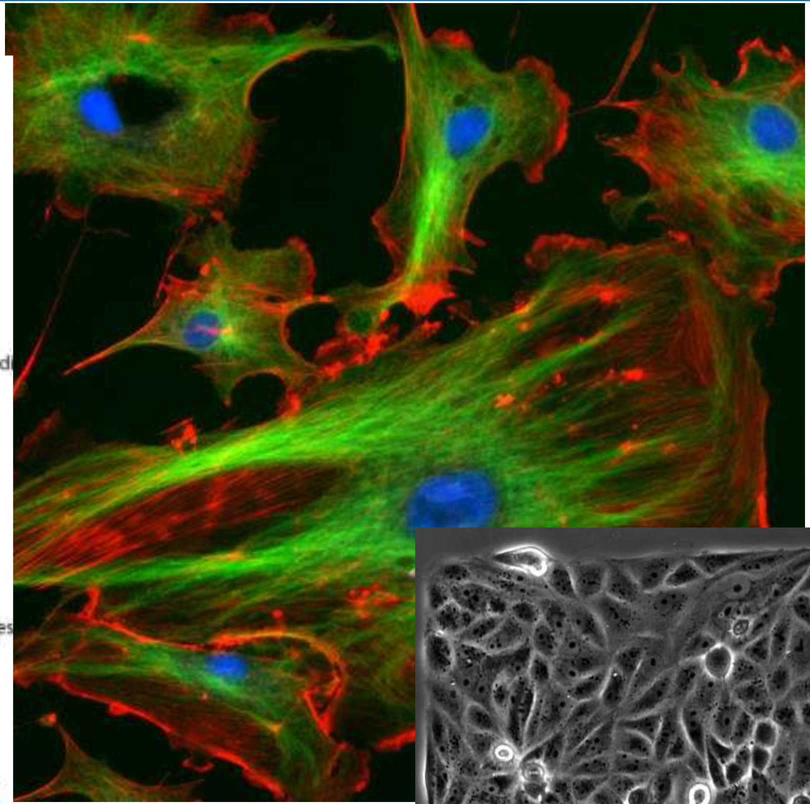
Passive forces => relax to minimise free energy

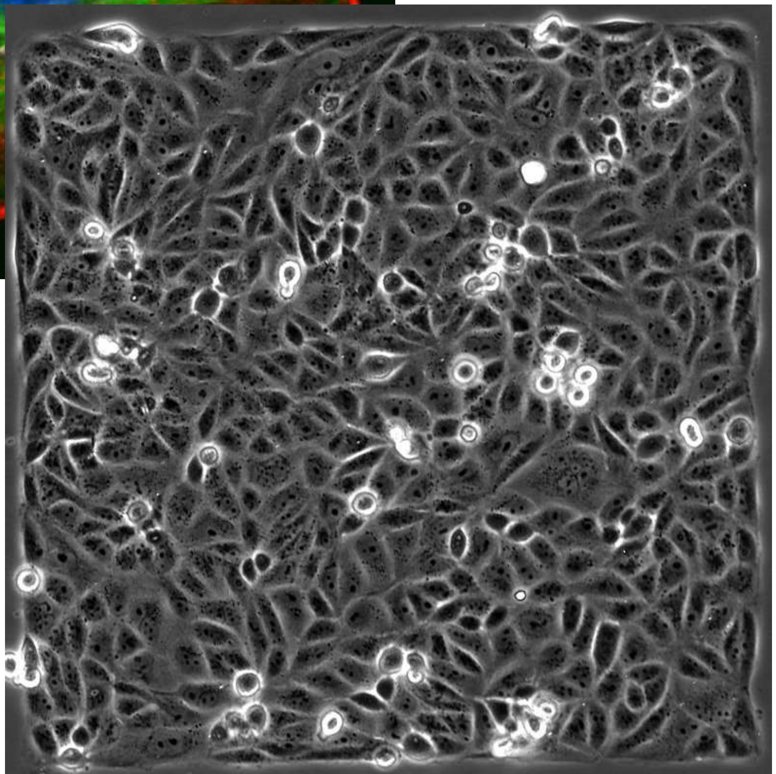
$$\mathbf{f}_i^{passive}(\mathbf{x}) = \frac{\delta \mathcal{F}}{\delta \varphi_i} \nabla \varphi_i$$

Equilibrium is identical hexagons, but the system can get stuck
In a jammed state.

Active forces

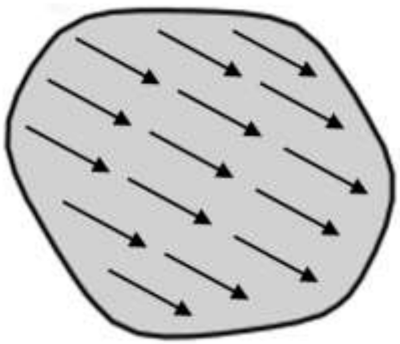


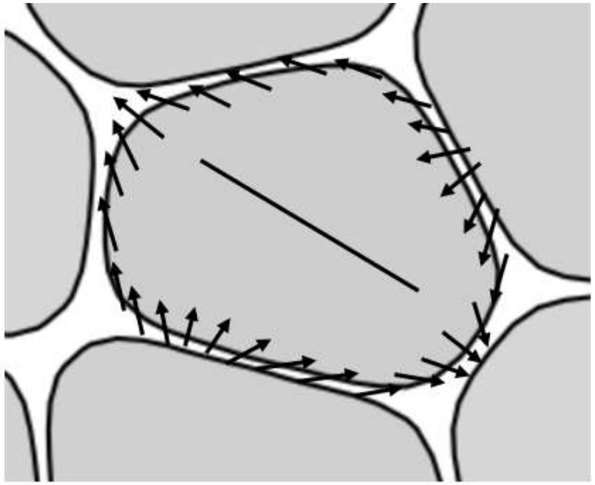




Ladoux and Nicholas Rep Prog Phys 2012

Active forces



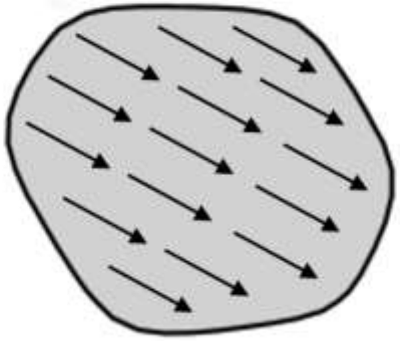


(a) extensile

Polar

intercellular forces

Polar force

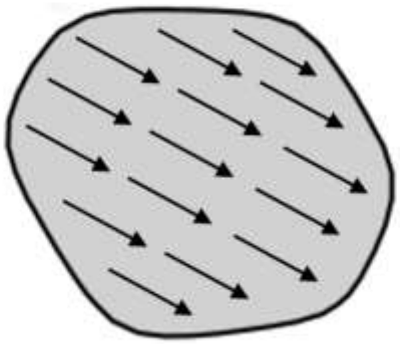


$$\mathbf{f}_i^{\text{pol}}(\mathbf{x}) = \alpha \varphi_i(\mathbf{x}) \mathbf{p_i}$$

Choice of polarisation?

1. Gaussian noise
2. Aligns with velocity of cell (+noise)
3. Aligns with long axis of cell (+noise)

Polar force



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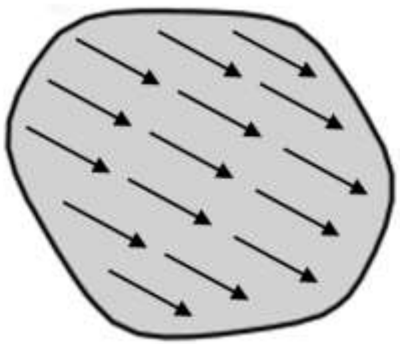


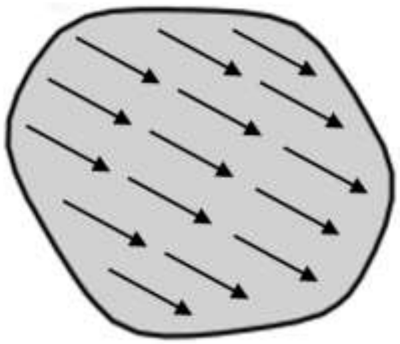
$$\mathbf{f}_i^{\mathrm{pol}}(\mathbf{x}) = \alpha\varphi_i(\mathbf{x})\mathbf{p_i}$$

Choice of polarisation?

alignment time ~ time to move a cell diameter

1. Gaussian noise
2. Aligns with velocity of cell (+noise)
3. Aligns with long axis of cell (+noise)

Polar force



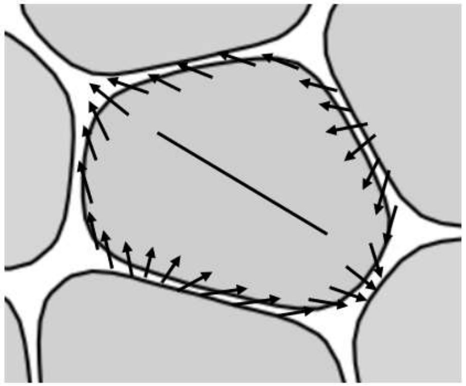
$$\mathbf{f}_i^{\mathrm{pol}}(\mathbf{x}) = \alpha \varphi_i(\mathbf{x}) \mathbf{p_i}$$

Choice of polarisation?

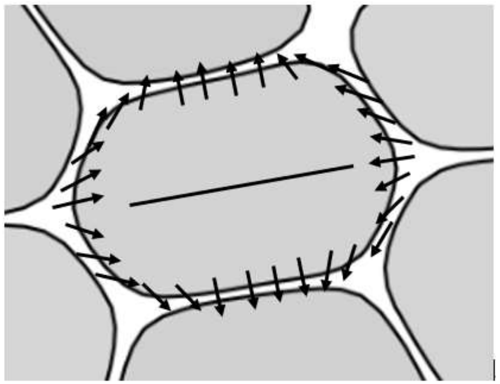
So far we have found little difference except that 2 gives flocking.

1. Gaussian noise
2. Aligns with velocity of cell (+noise)
3. Aligns with long axis of cell (+noise)

Inter-cellular force



(a) extensile



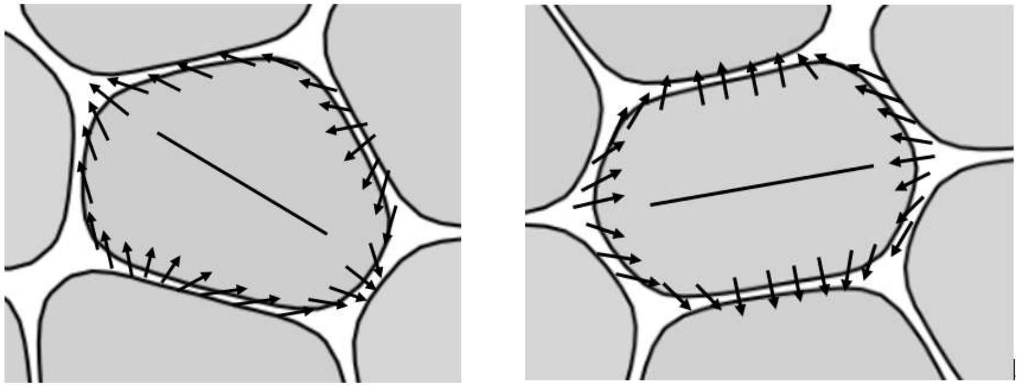
(b) contractile

Deformation tensor $$\mathcal{D}_i = -\frac{1}{2}\int d\mathbf{x}\left\{\nabla\varphi_i\nabla\varphi_i^T - \mathrm{Tr}(\nabla\varphi_i\nabla\varphi_i^T)\right\}$$

Nematic stress $$\sigma_D = -\zeta\sum_i \varphi_i(\mathbf{x})\mathcal{D}_i$$

Nematic force $$\mathbf{f}(\mathbf{x})^{\mathrm{nem}} = \nabla\cdot\sigma_D$$

Inter-cellular force



(a) extensile (b) contractile

Deformation tensor

$$\mathcal{D}_i = -\frac{1}{2}\int d\mathbf{x}\left\{\nabla\varphi_i\nabla\varphi_i^T - \mathrm{Tr}(\nabla\varphi_i\nabla\varphi_i^T)\right\}$$

Nematic stress

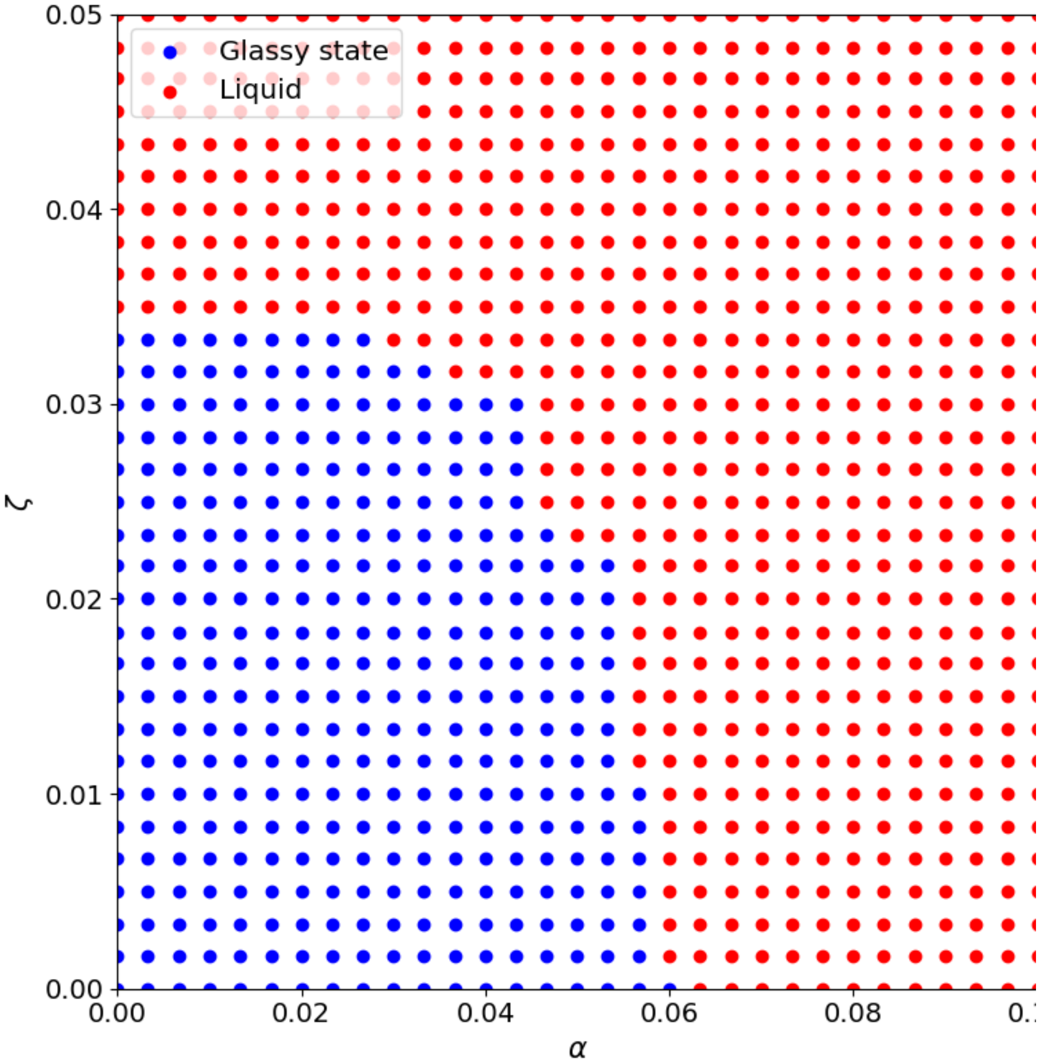
$$\sigma_D = -\zeta\sum_i \varphi_i(\mathbf{x})\mathcal{D}_i$$

Nematic force

$$\mathbf{f}(\mathbf{x})^{\mathrm{nem}} = \nabla\cdot\sigma_D$$

Phase diagram

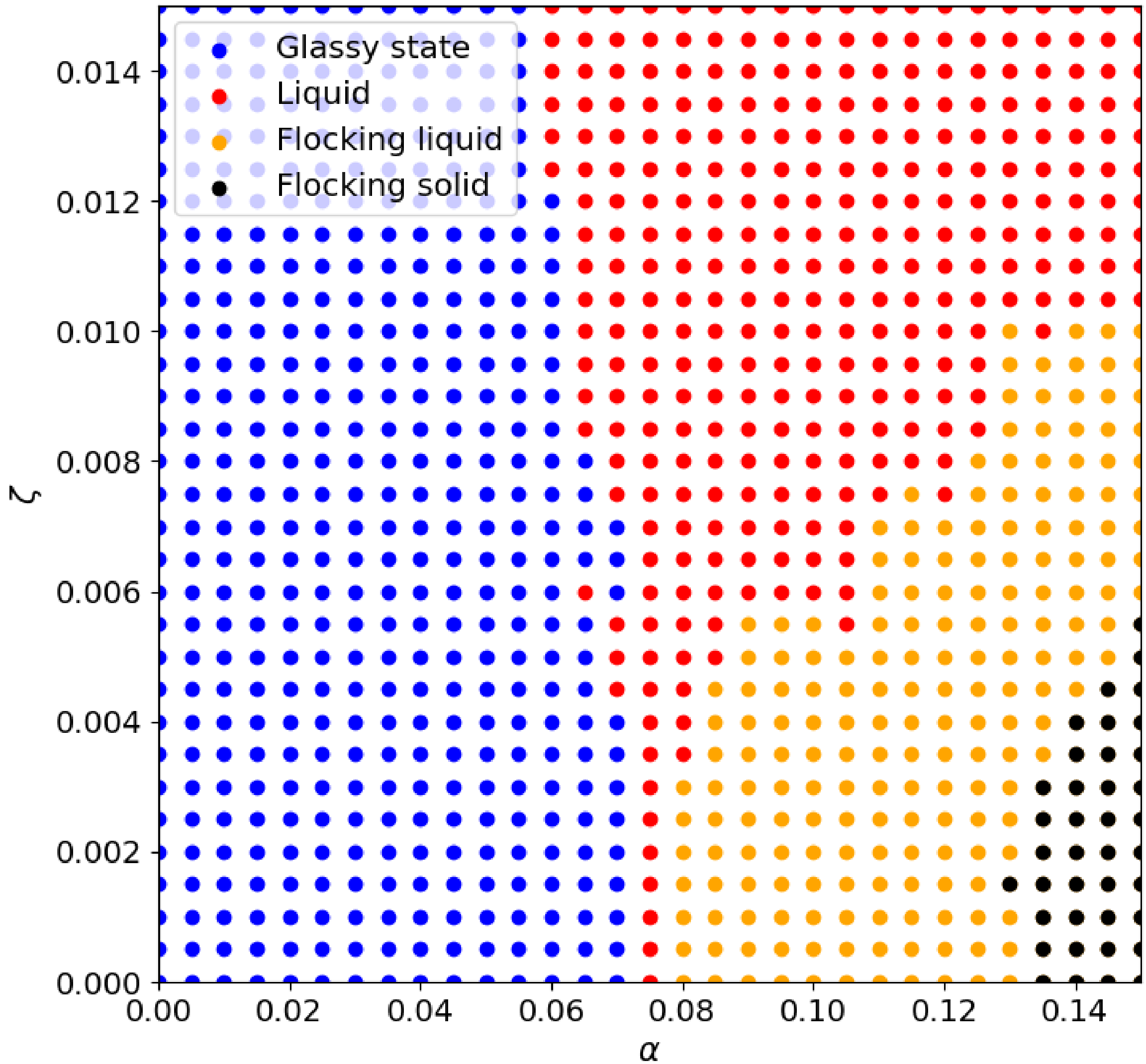
strength of inter-cellular force



strength of polar force

Phase diagram: polar force in direction of velocity

strength of
inter-cellular
force



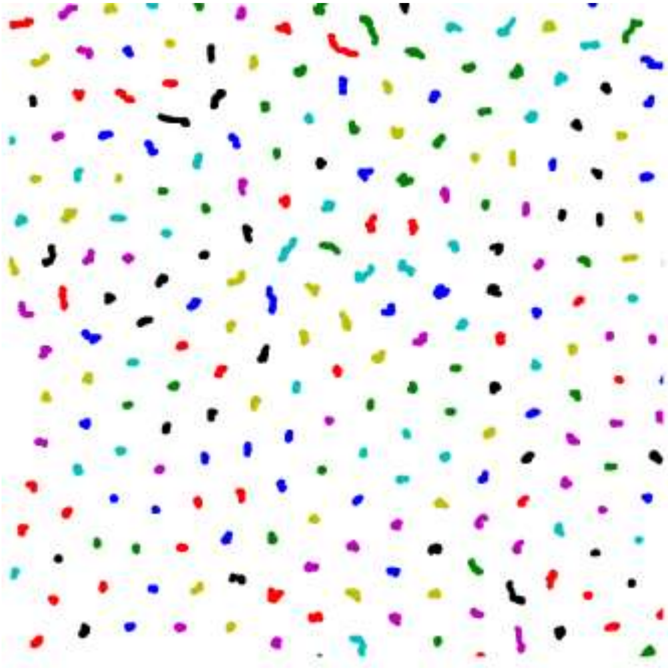
strength of
polar force

1. Phase field model

2. Unjamming

3. Velocity and flocking

unjamming

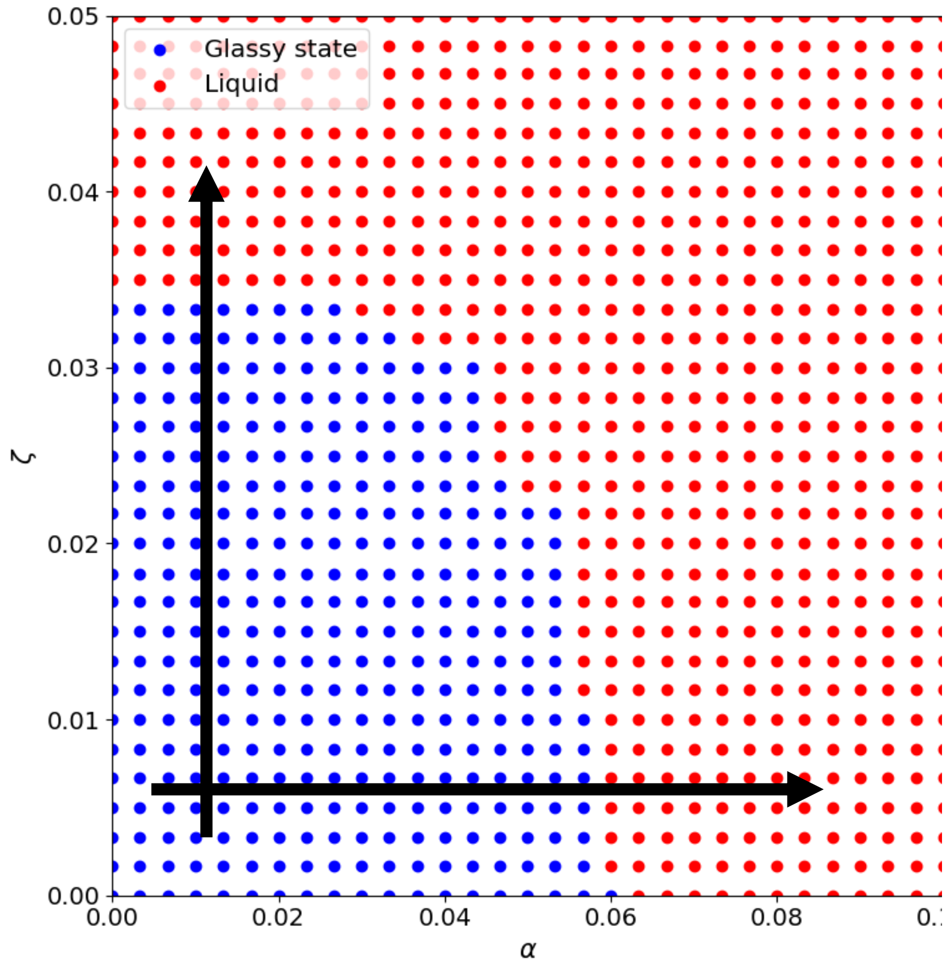


jammed state

liquid

centre of mass trajectories of the cells

unjamming



strength of
Inter-cellular
force

strength of
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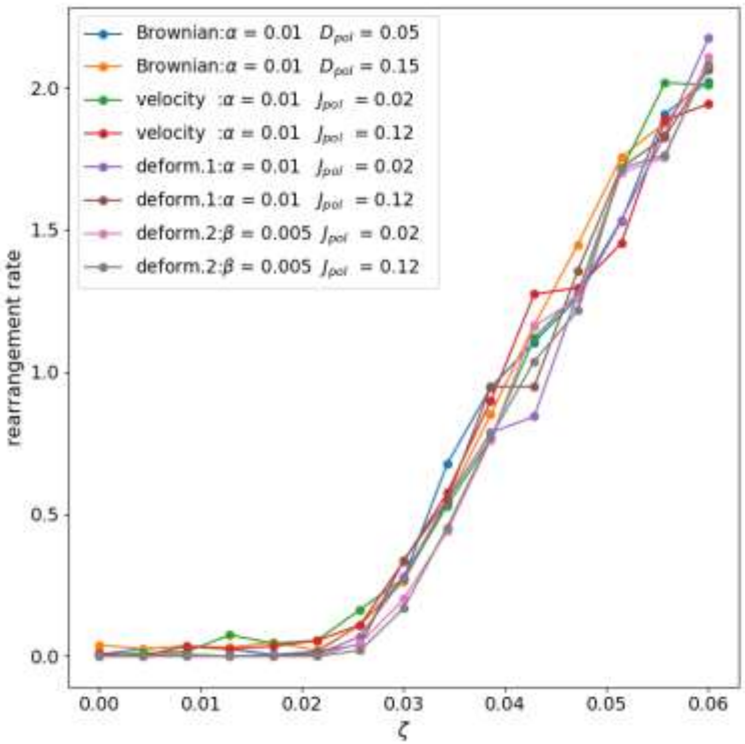
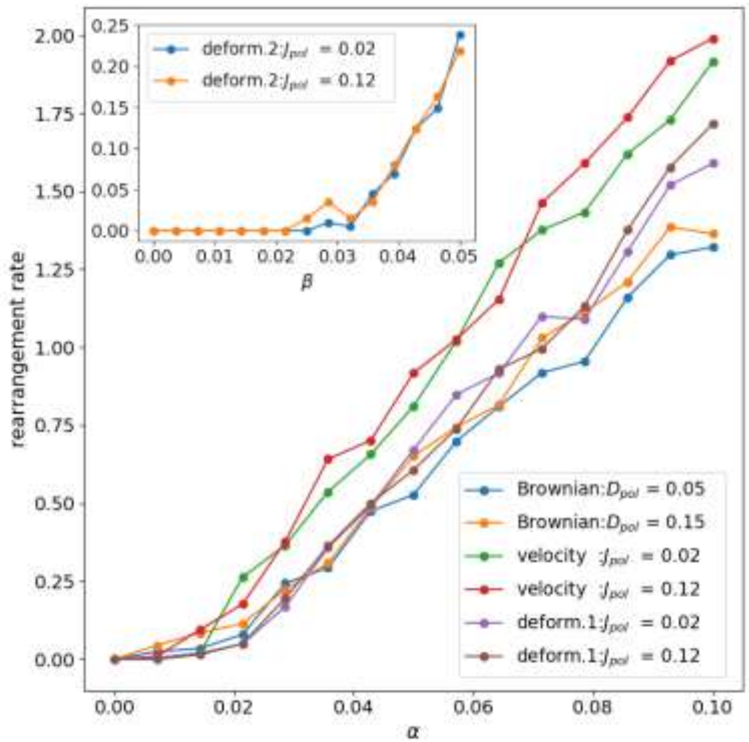
unjamming

Inter-cellular

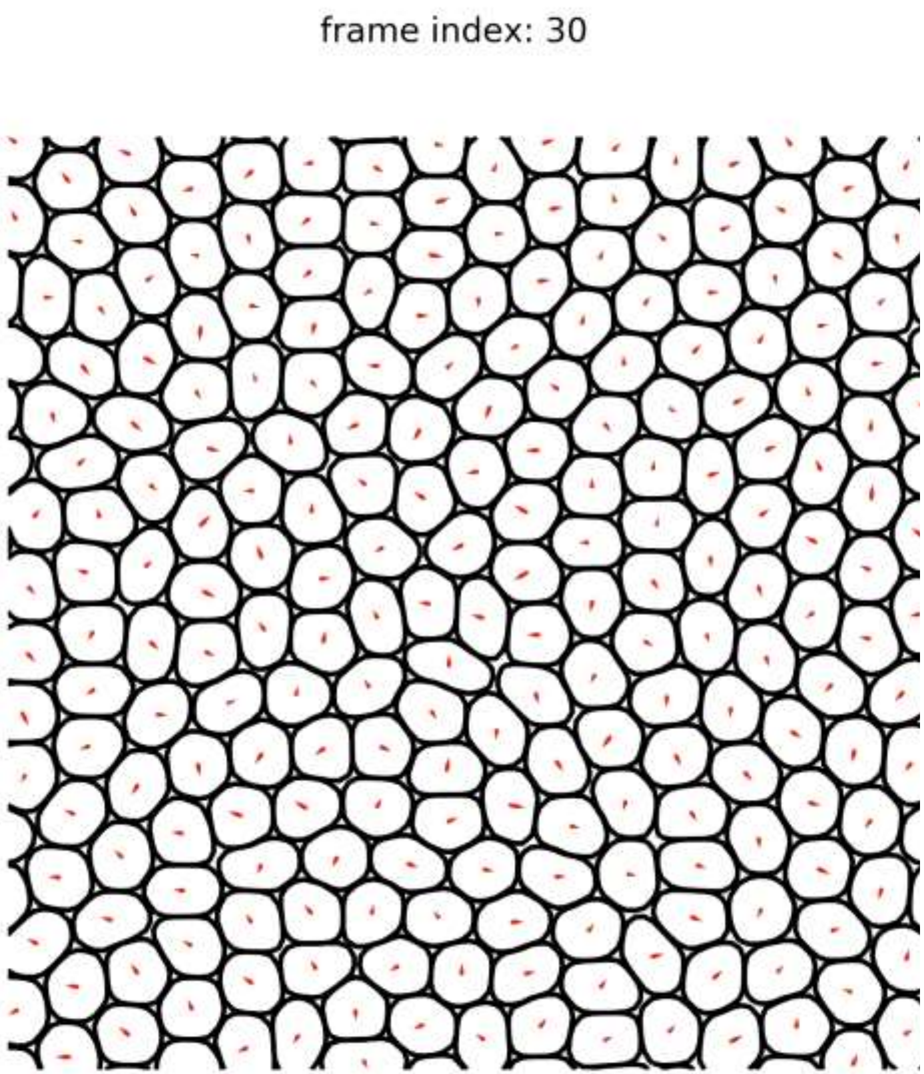


polar

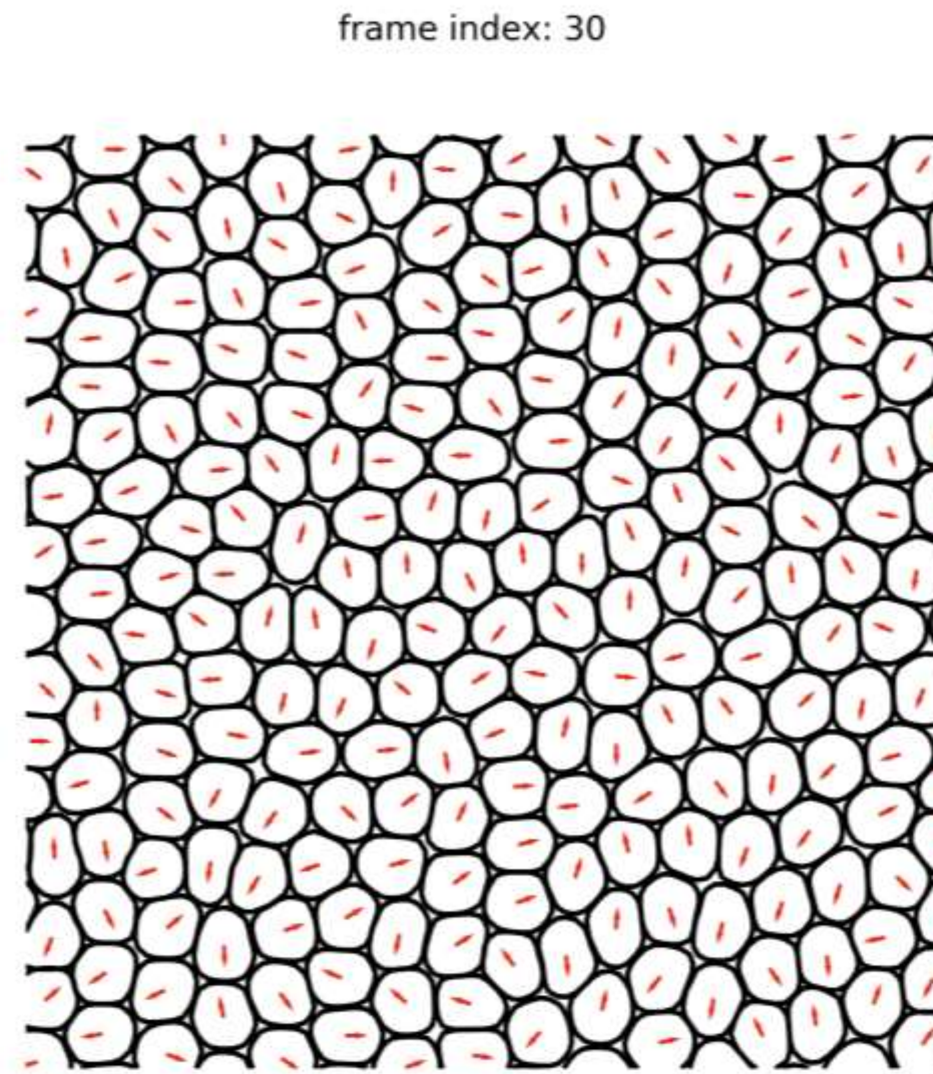


rearrangement rate: average number of cells that change neighbours at each time step

Near unjamming: inter-cellular vs polar driving



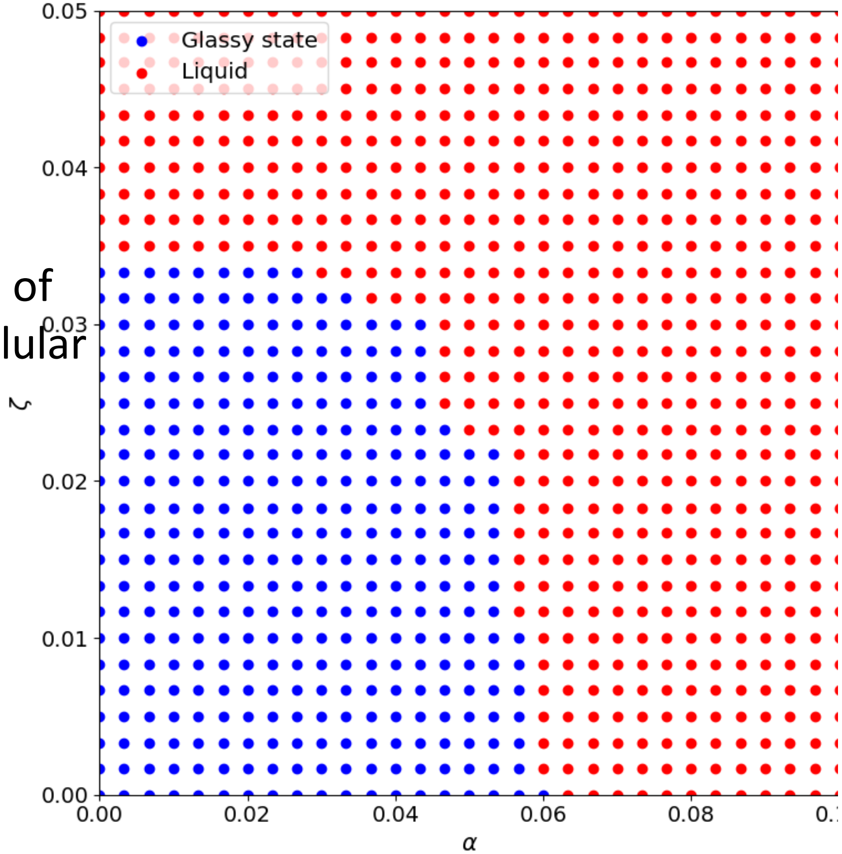
inter-cellular



polar

unjamming

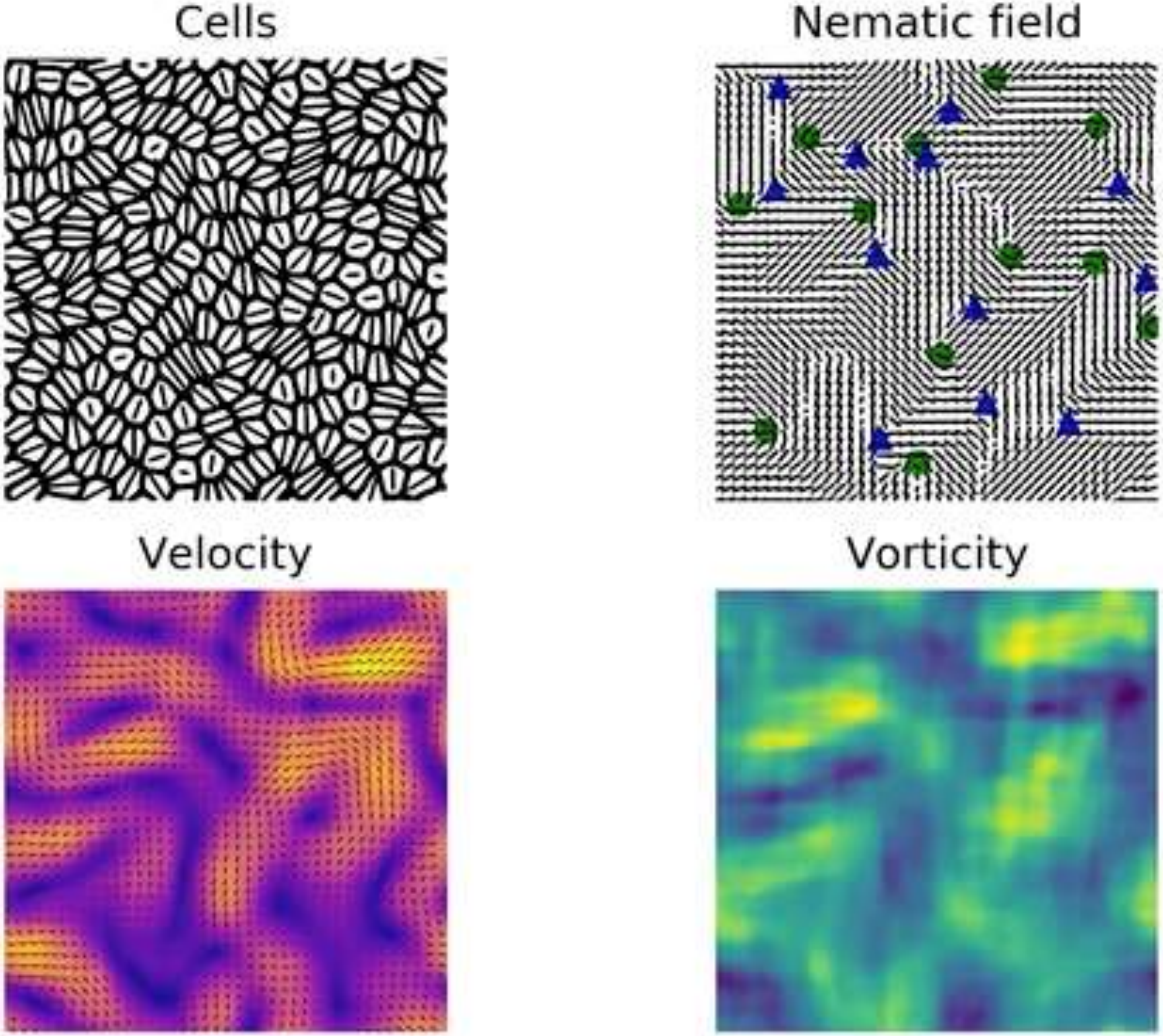
strength of
Inter-cellular
force



strength of
polar force

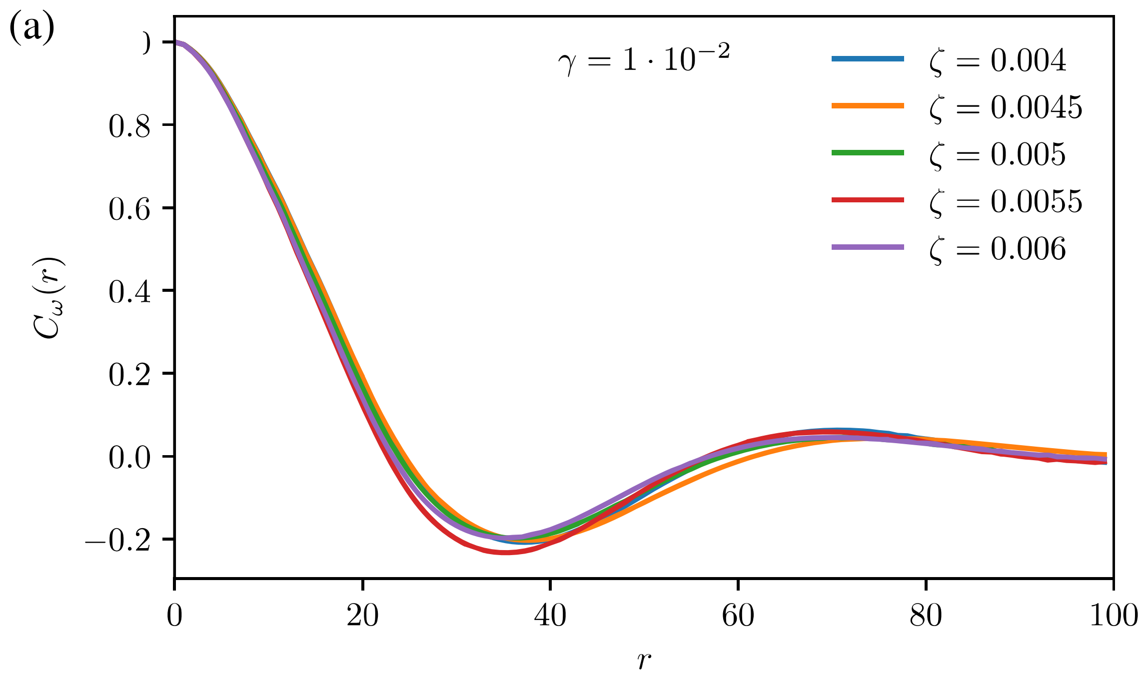
Inter-cellular or polar driving doesn't make much difference

Are we seeing a "liquid" or "active turbulence"?


Cells
Nematic field
Velocity
Vorticity

Active turbulence

vorticity-vorticity correlation function



r

1. Phase field model

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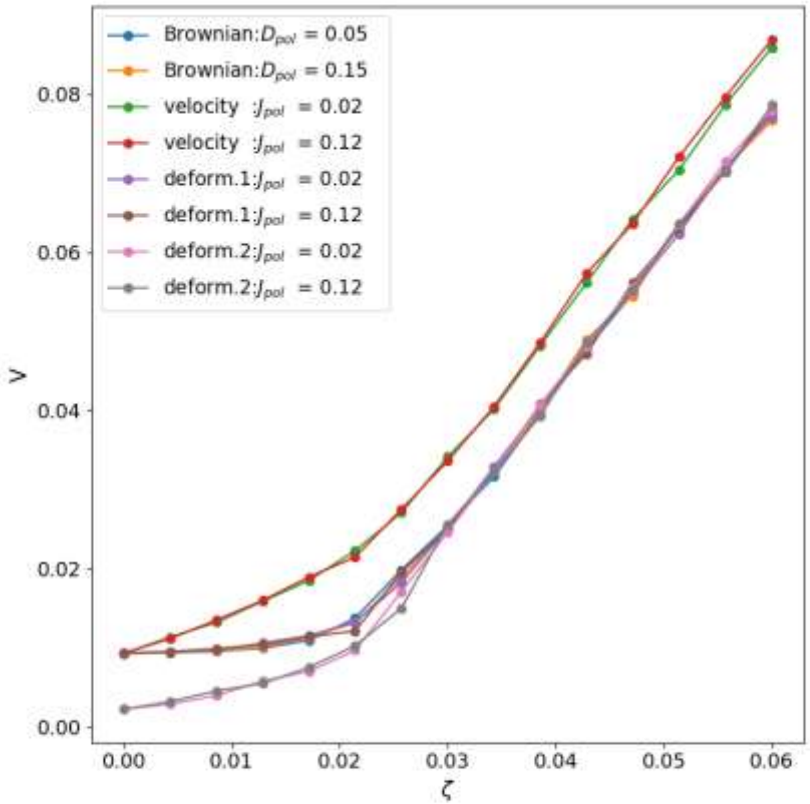
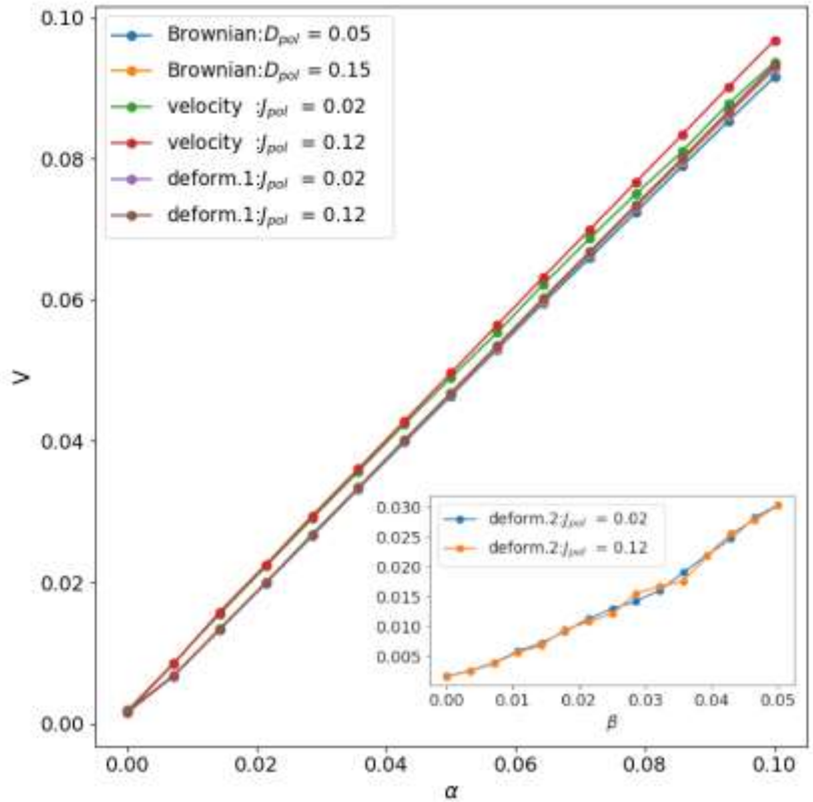
3. Velocity and flocking

speed

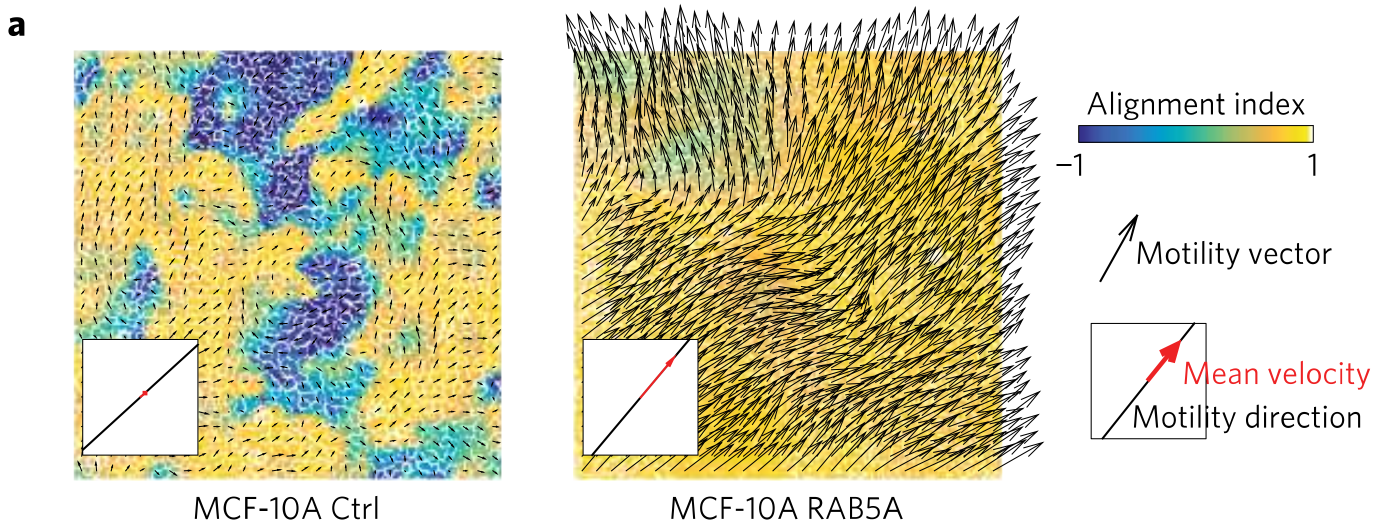
Inter-cellular

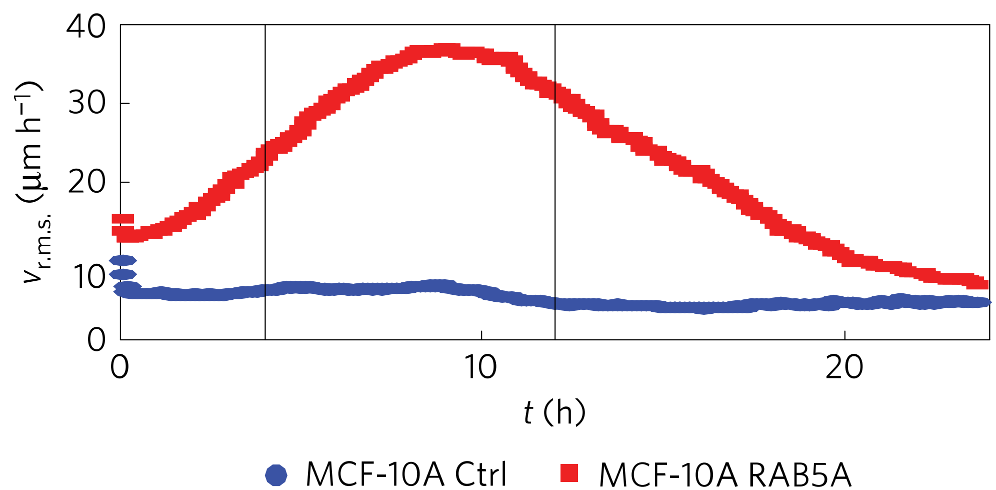
polar

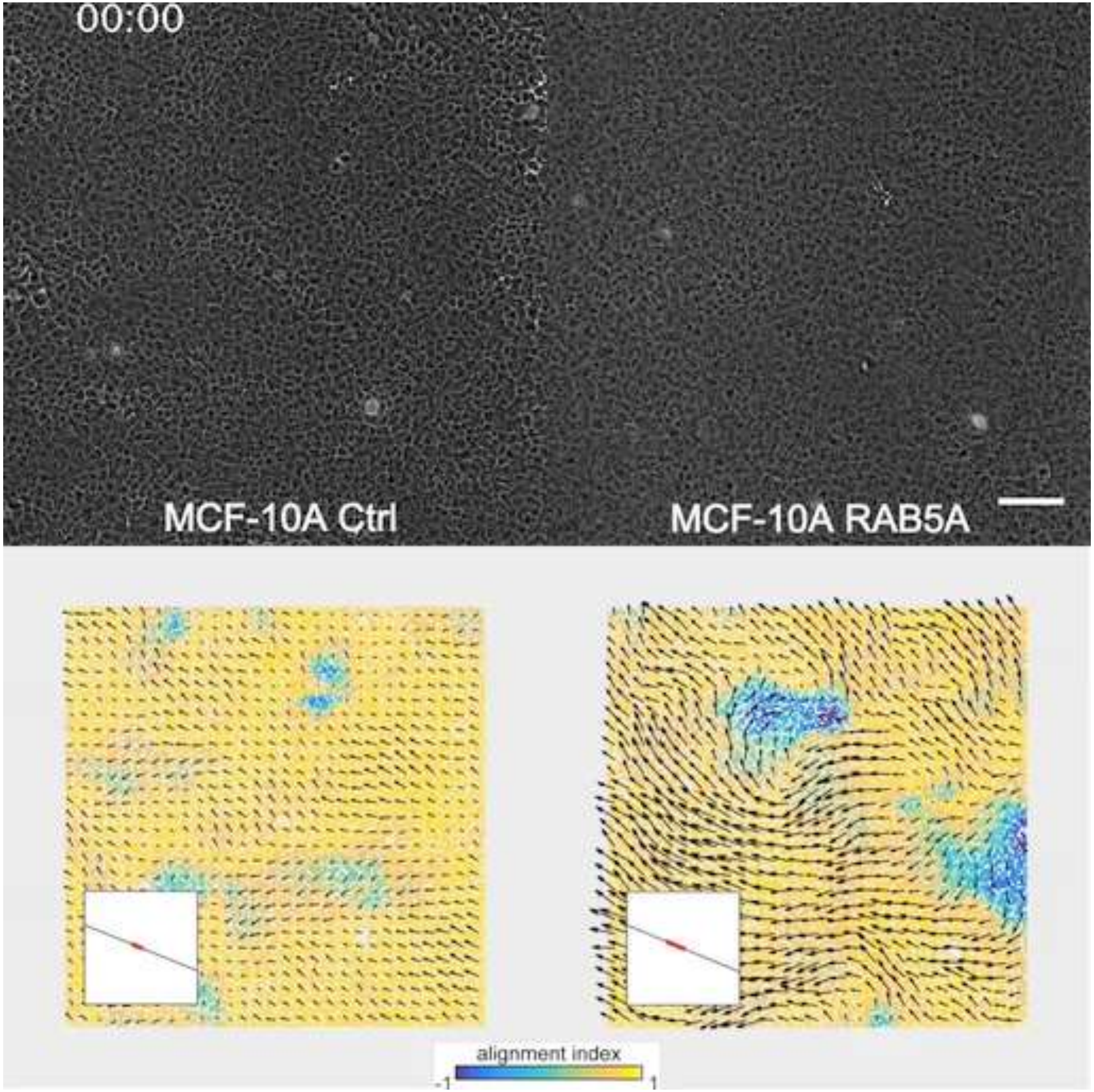




Malinverno et al Nature Materials 16 (2017)



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alignment index
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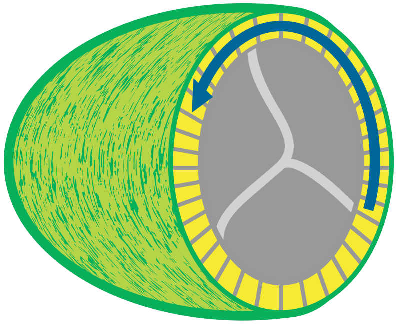
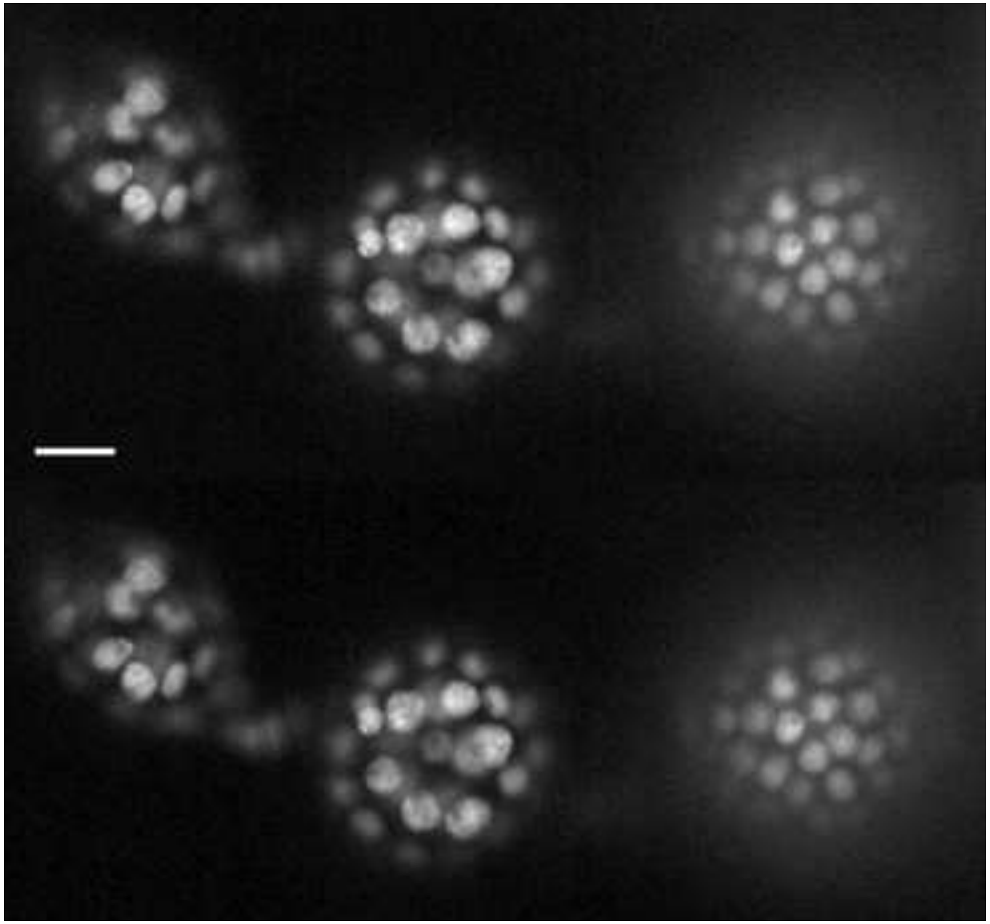
1

Drosophila egg chamber

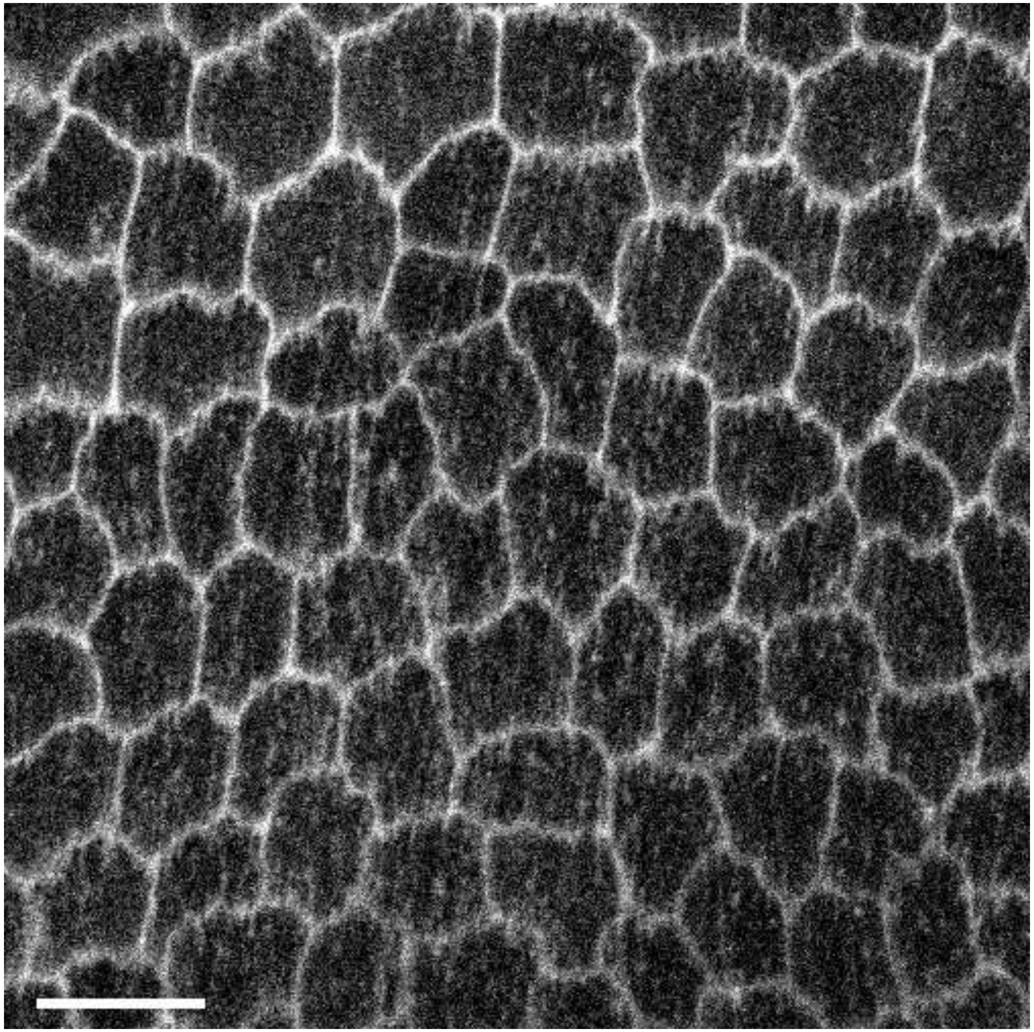
Egg chamber rotation





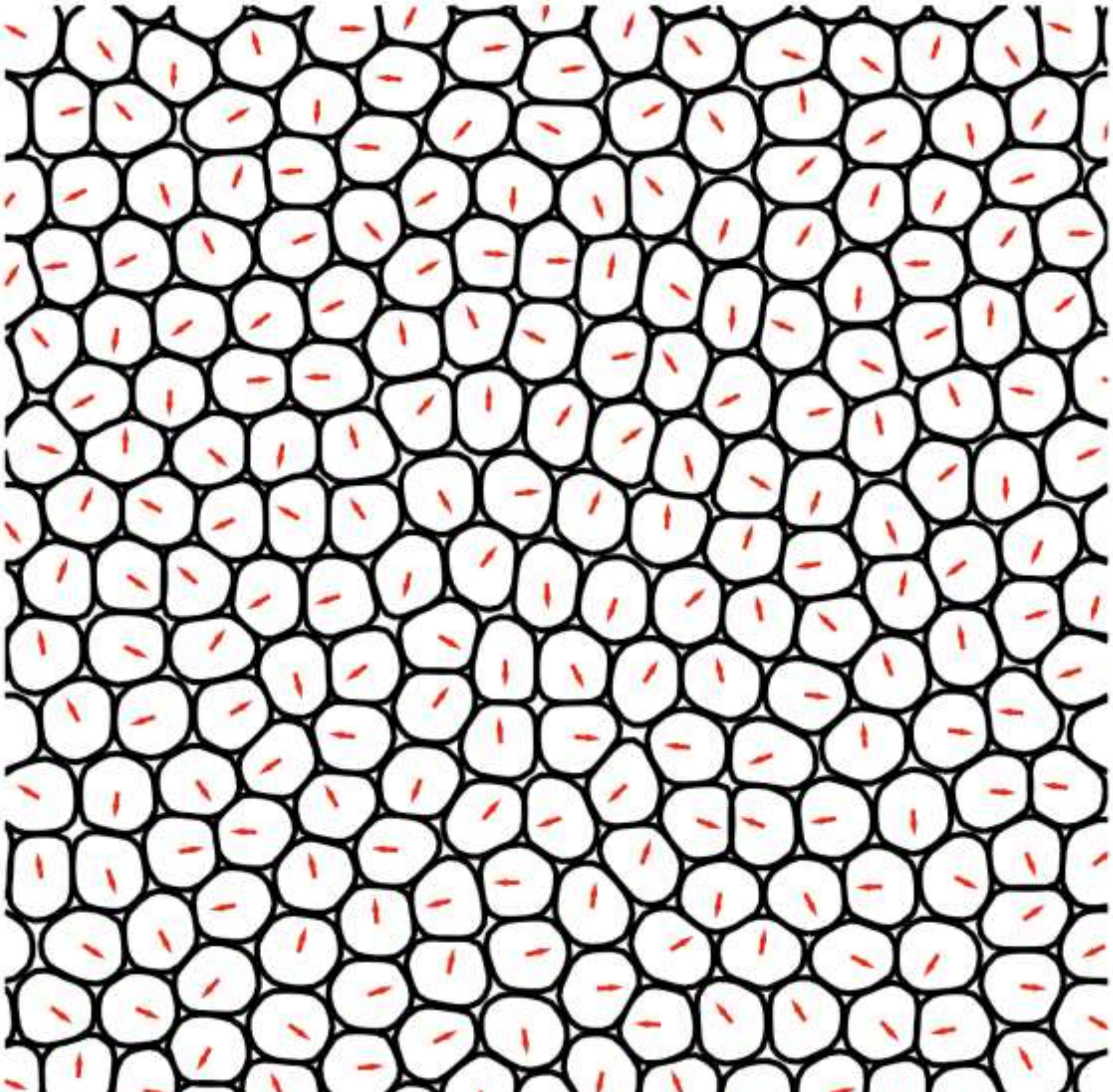
From Sally Horne-Badovinac's lab:
Cetera et al. Nature Comms. 5, 5511 (2014)

Drosophila egg chamber

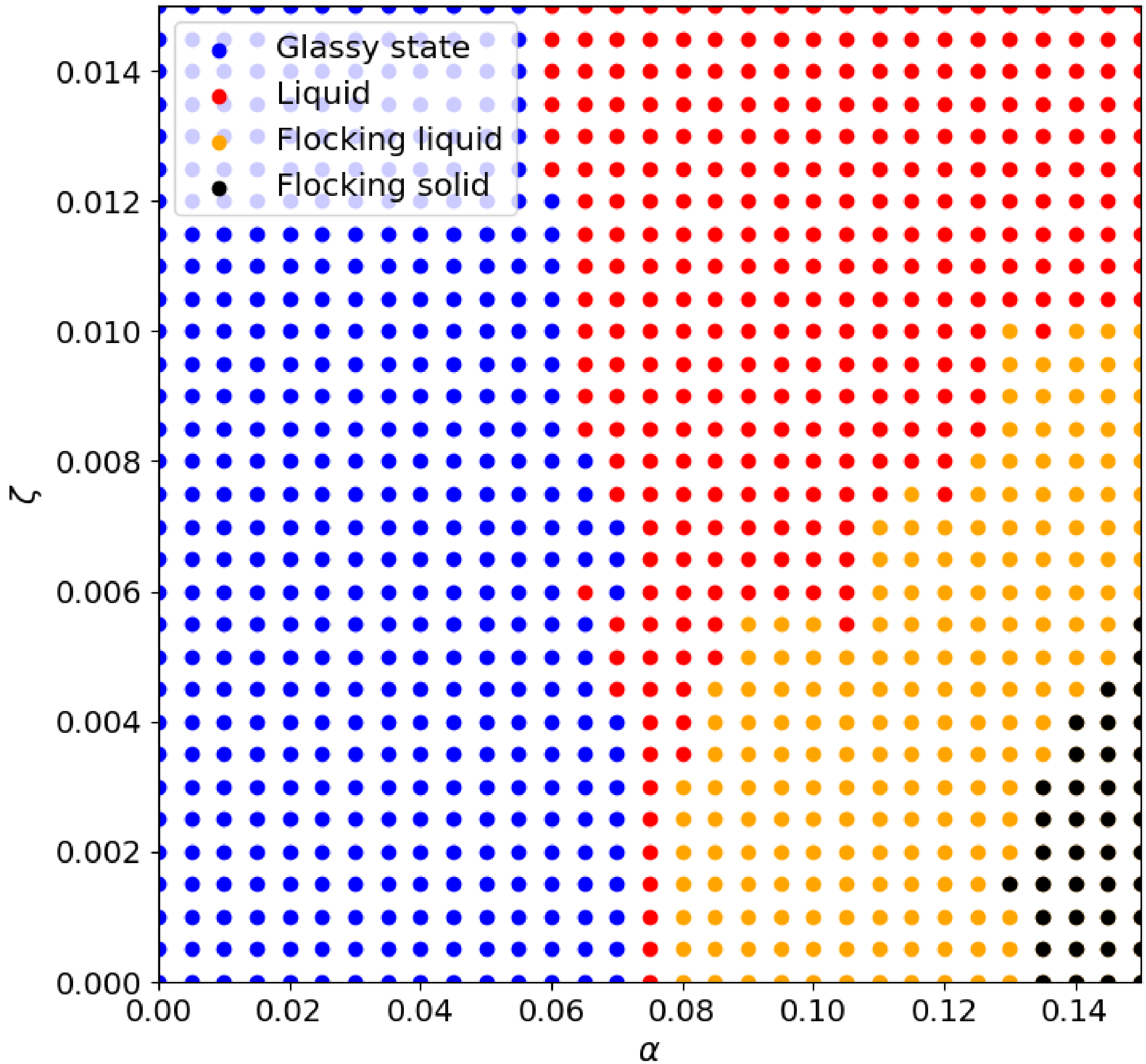


Flocking: polar force slaved to velocity

frame index: 30



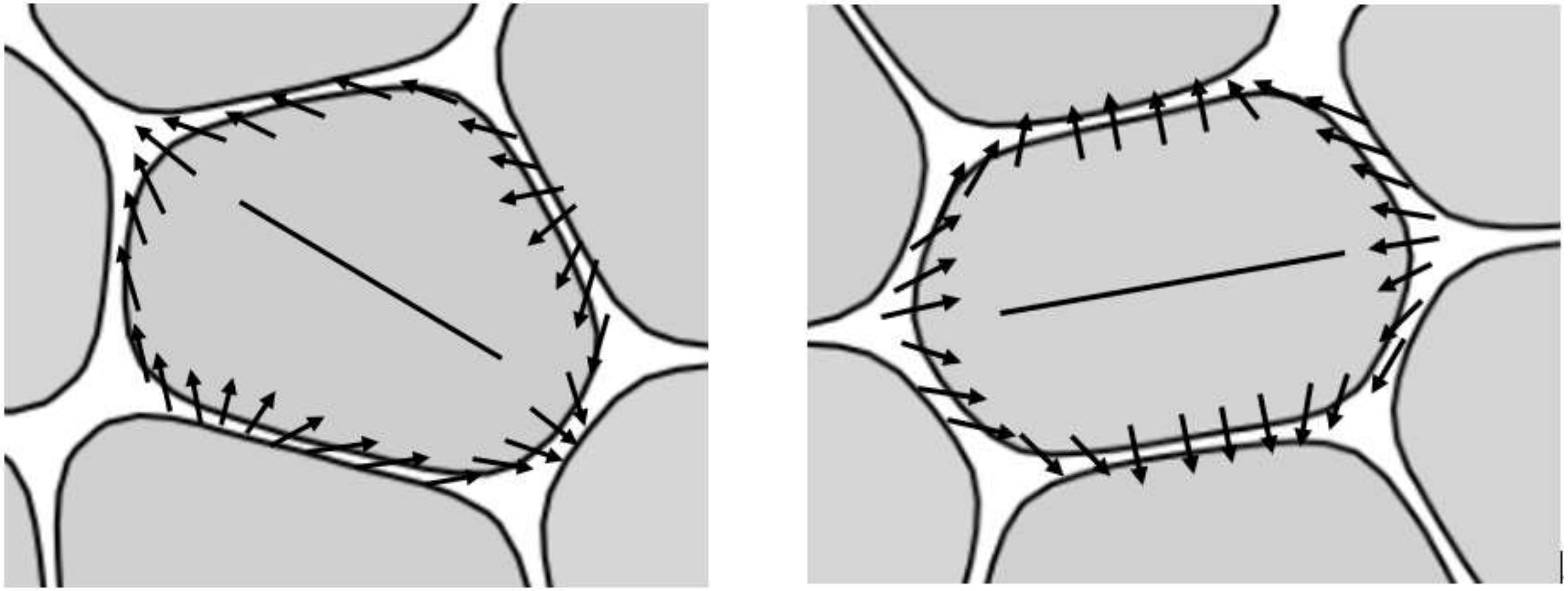
Phase diagram: polar force in direction of velocity



strength of inter-cellular force

strength of polar force

Why can circular cells show topological defects



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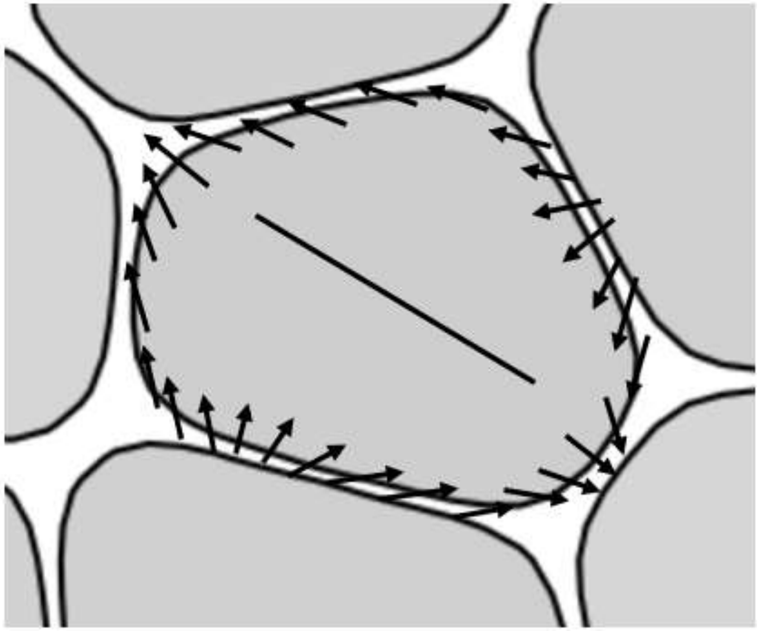
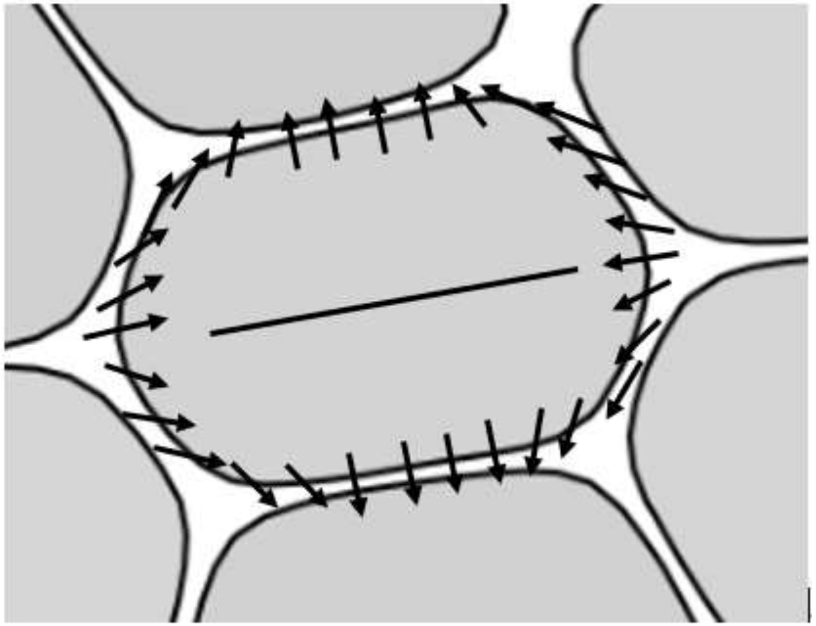


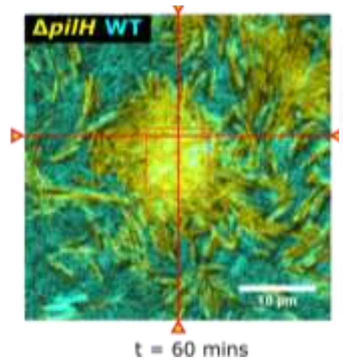


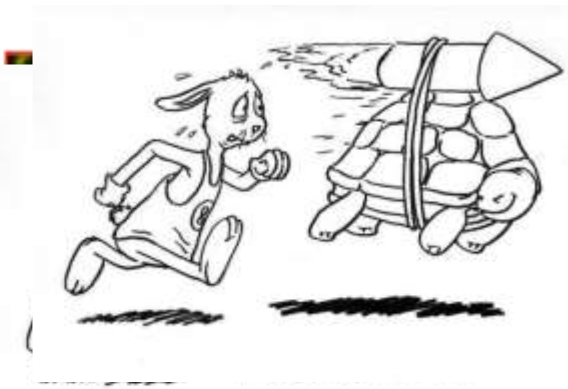
extensile inter-cellular interactions

bootstrapping nematic order => active turbulence

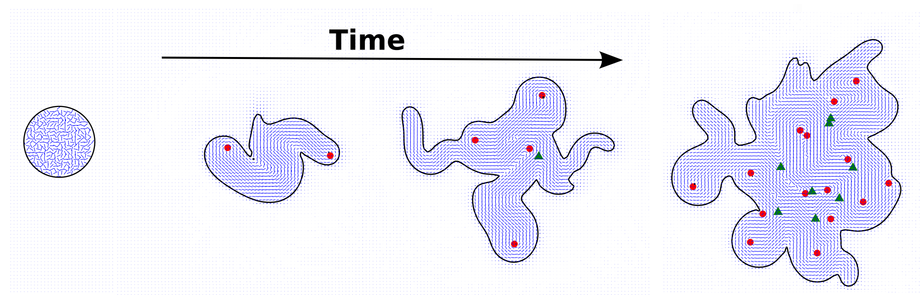
Topological defects turn up in biological systems – and, at least in model systems, have biological relevance

- nucleation sites

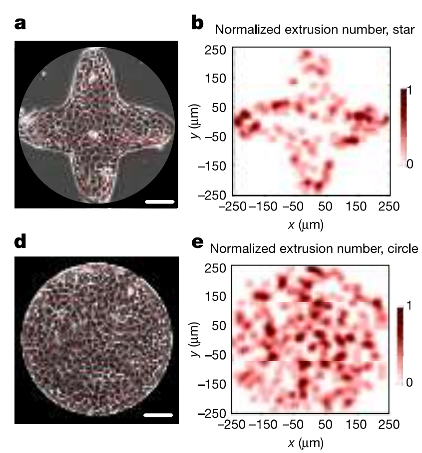




- colony shape



- apoptosis in epithelial cell layers



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THANK YOU FOR LISTENING