Liquid crystals to control microswimmers and tissues

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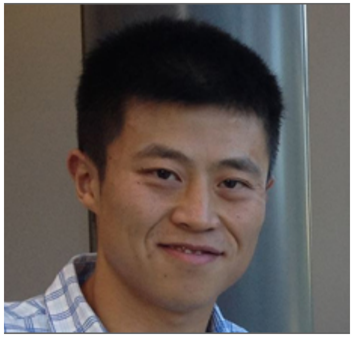
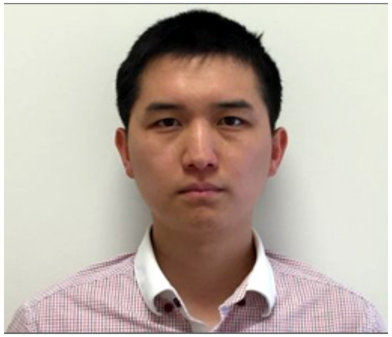
Symmetry, Thermodynamics and Topology in Active Matter, April 21, 2020

Contributing graduate students:



Shuang Zhou, PhD 2016; now Assistant professor at U Mass, Amherst



Chenhui Peng, PhD 2016; now Assistant professor at University of Memphis

Greta Babakhanova, PhD 2019, now a researcher at NIST

Taras Turiv, current PhD student

Runa Koizumi, current PhD student

Mojtaba Rajabi, current PhD student

Hend Baza, current PhD student

Collaborators

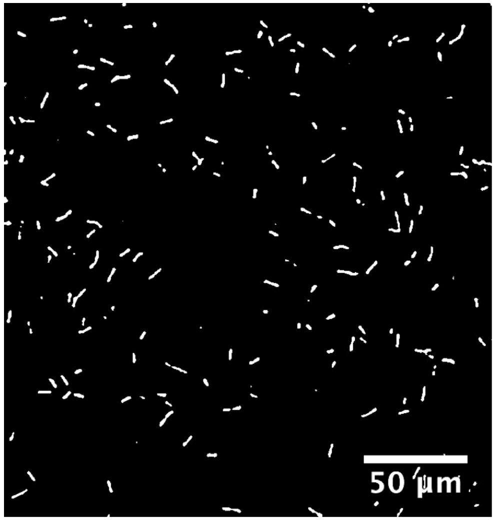
Kent State University:

- Qi-Huo Wei
- Min-Ho Kim and Jess Krieger
- Sergij Shiyanovskii

Our colleagues:

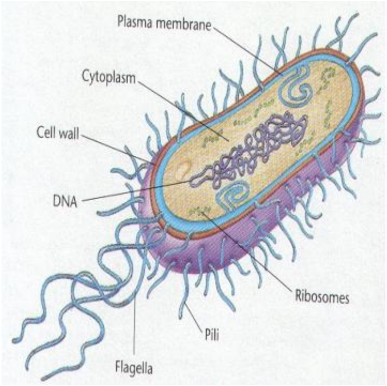
- Igor Aranson, Mikhail Genkin
- Julia Yeomans, Kristian Thijssen, Amin Doostmohammadi

Motivation. Swimming bacteria: Can we extract useful work from them?



Bacillus Subtilis swimming in water

Effective swimmers at microscale, bacteria are “ready-to-use” for microtransport, delivery, mixing



Problem: Visual, audio, and tactile communications are not available

Liquid crystals controlling medium

Our approach:

Replace isotropic or amorphous environment with a liquid crystal as a communication medium to control microscopic active units

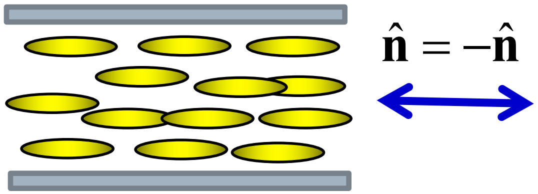
Content:

Three examples united by LC/active coupling theme, little else

- How liquid crystals differ from water
  - Orientational order, elasticity, surface anchoring
  - Life at low Reynolds number in a nematic
- Liquid crystal medium to control swimming bacteria
  - Swimming along the director; instabilities
  - Patterned director: unipolar circulation and translation
- Liquid crystal elastomer substrates to guide tissues
  - Tissue with predetermined locations of topological defects

How liquid crystals differ from water

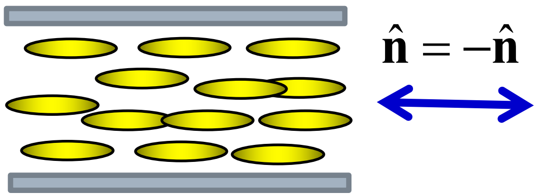
- Anisotropy:



anisotropy axis of dielectric permittivity,
viscous drag, birefringence, etc.

How liquid crystals differ from water

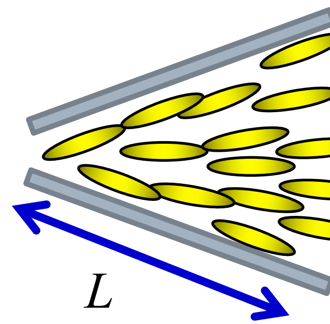
- Anisotropy:



anisotropy axis of dielectric permittivity, viscous drag, birefringence, etc.

- Elasticity:

Director gradients cost energy

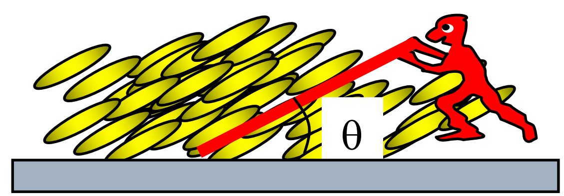


elastic constant

$$U_{elastic} = K\int(\nabla\hat{\mathbf{n}})^2\, dV \sim KL$$

- Surface anchoring

Preferred director orientation



surface anchoring coefficient

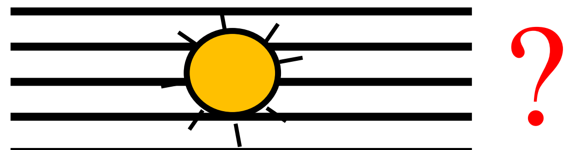
$$U_{anch} \sim WL^2$$

KL *vs* WL^2 : *Surface anchoring wins at* $L > K/W$

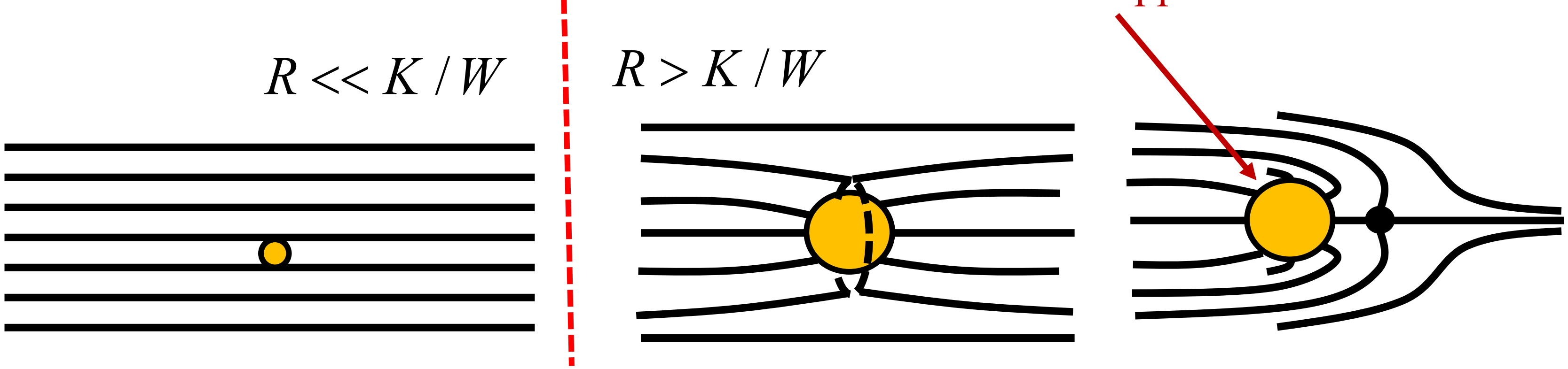
K/W~0.1-10 μm

Water droplet in a thermotropic liquid crystal:

The molecules align perpendicularly to the droplet's surface; the radial distortion competes with the uniform director away from the droplet



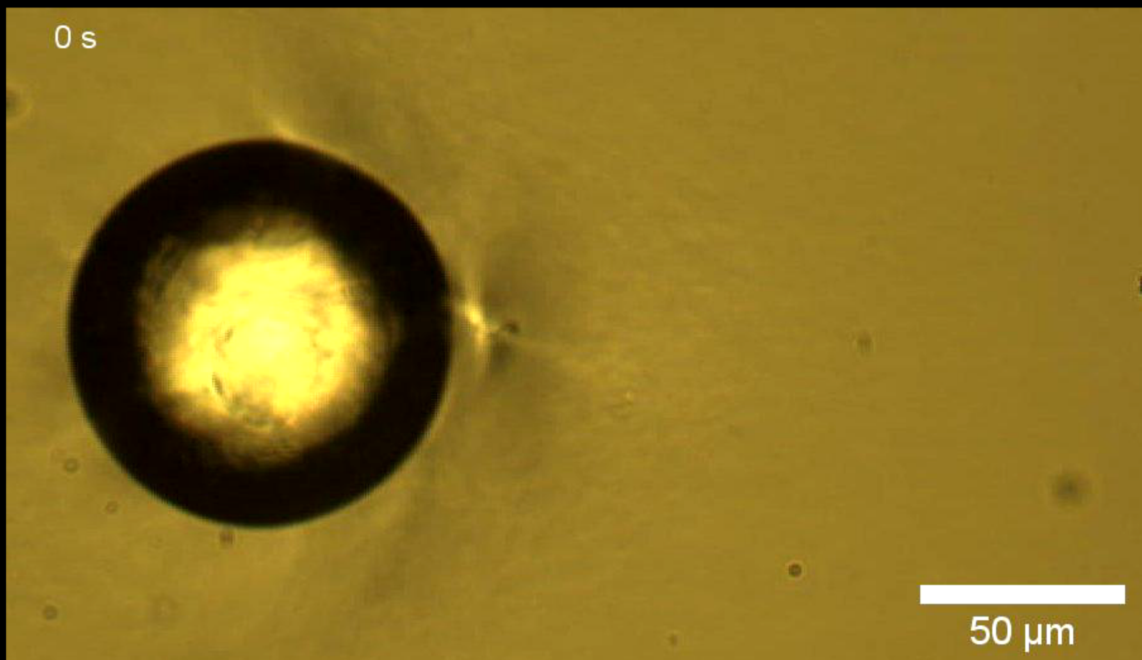
Imagine that this droplet is "active", crowded with swimming bacteria. What would happen?

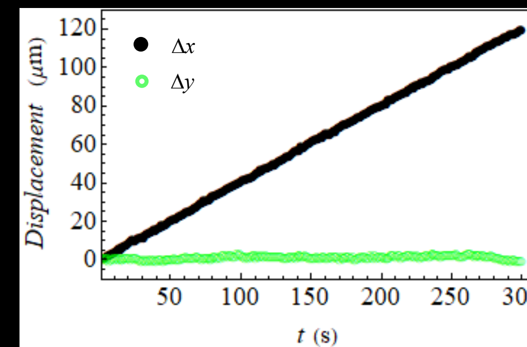


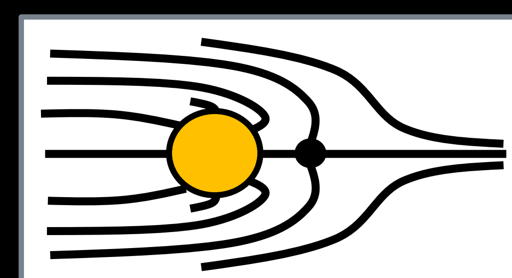
Poulin et al, *Science* **275**, 1770 (1997)

Active droplet in liquid crystal:

B. Subtilis-crowded droplet in a nematic 5CB (the one in LCDisplays)







M. Rajabi, H. Basa, T. Turiv et al, *submitted* (2020)

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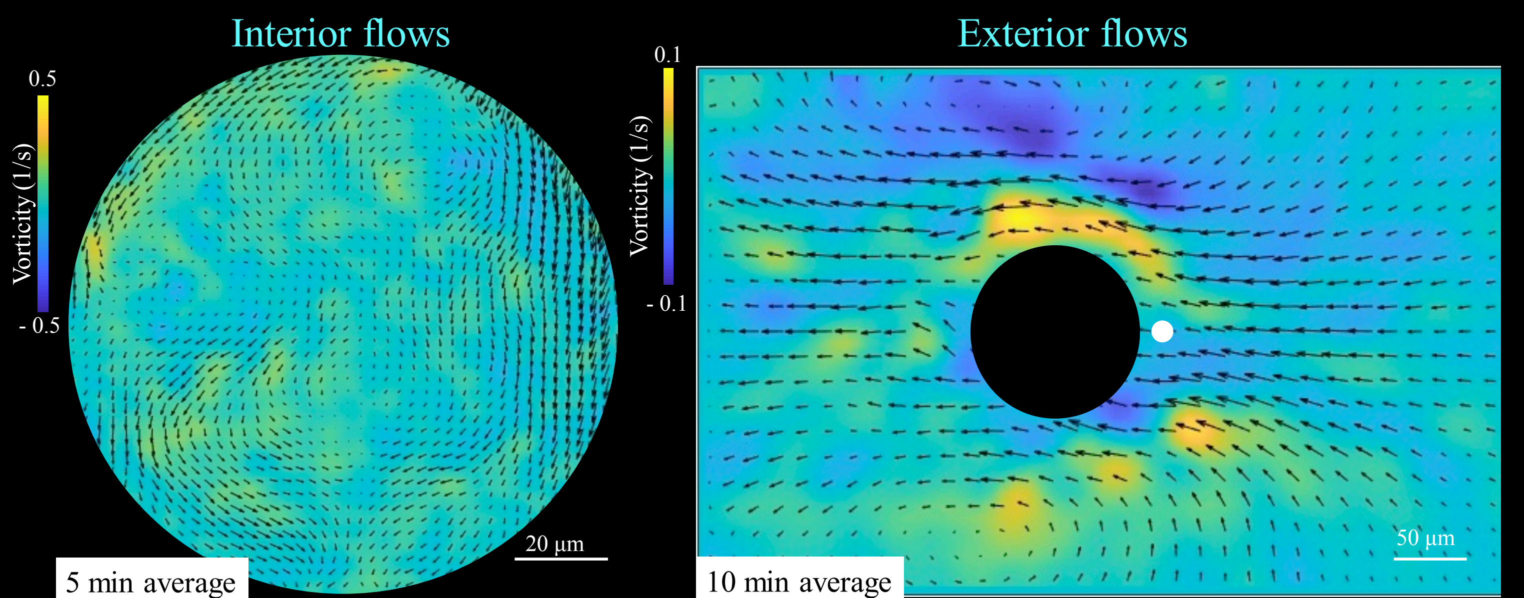

Liquid crystal breaks the symmetry of surrounding, rectifies Brownian motion into directional self-propulsion of drops at low Reynolds number $\sim 10^{-5}$

M. Rajabi, H. Basa, T. Turiv et al, *submitted* (2020)

Conclusion-I

- Anisotropic environment offers a mechanism of microscale propulsion based on broken symmetry of orientational order

Content

- How liquid crystals differ from water
  - Orientational order, elasticity, surface anchoring
  - Life at low Reynolds number in a nematic
- Water-based liquid crystal to control swimming bacteria
  - Swimming along the director; instabilities
  - Patterned director: unipolar circulation and translation
- Liquid crystal elastomer substrates to guide tissues
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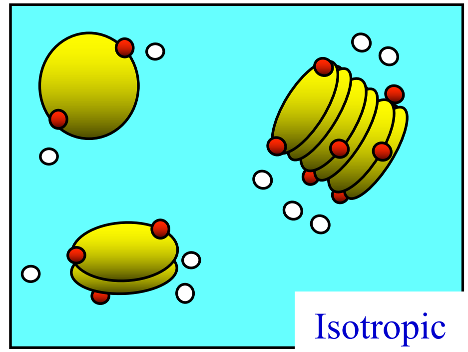
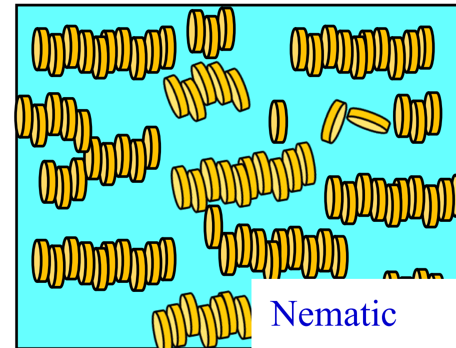
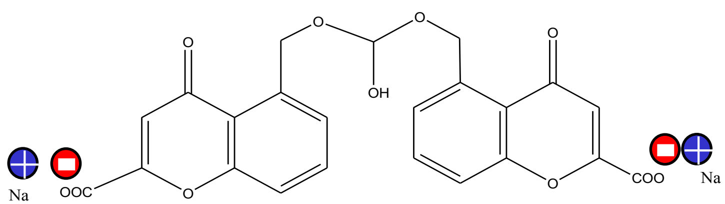
Lyotropic Chromonic Liquid Crystals

- LCLCs are formed by disk-like polyaromatic molecules that assemble face-to-face in water, forming elongated aggregates; the absence of aliphatic tails makes them non-toxic

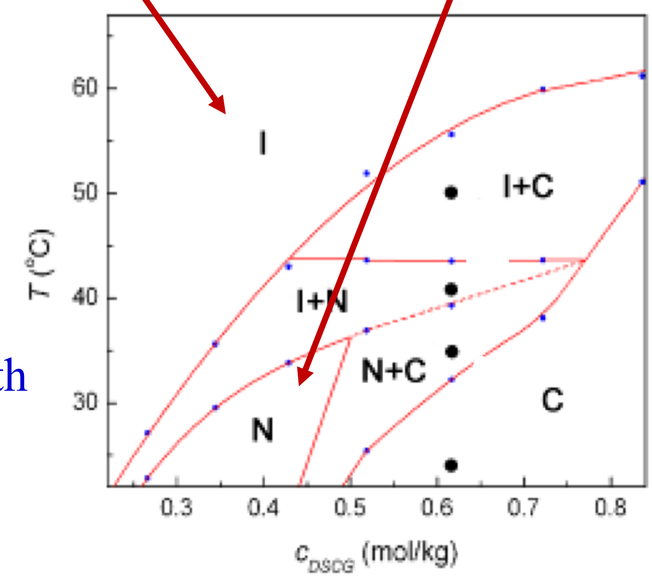






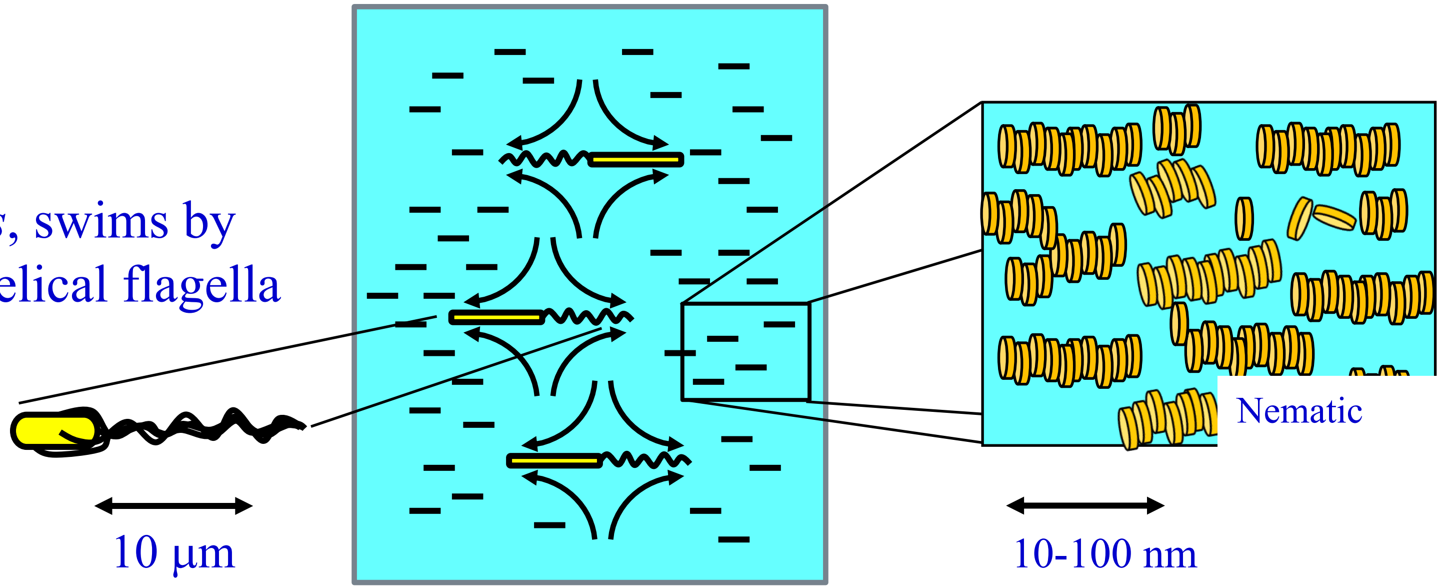
Disodium cromoglycate, a.k.a. cromolyn

Phase diagram: Controlled by both concentration and temperature; nematic exists at 10-15 wt% of DSCG; everything else is water+nutriens (if needed)



Liquid Crystals to Command Swimming Bacteria

B. Subtilis, swims by rotating helical flagella



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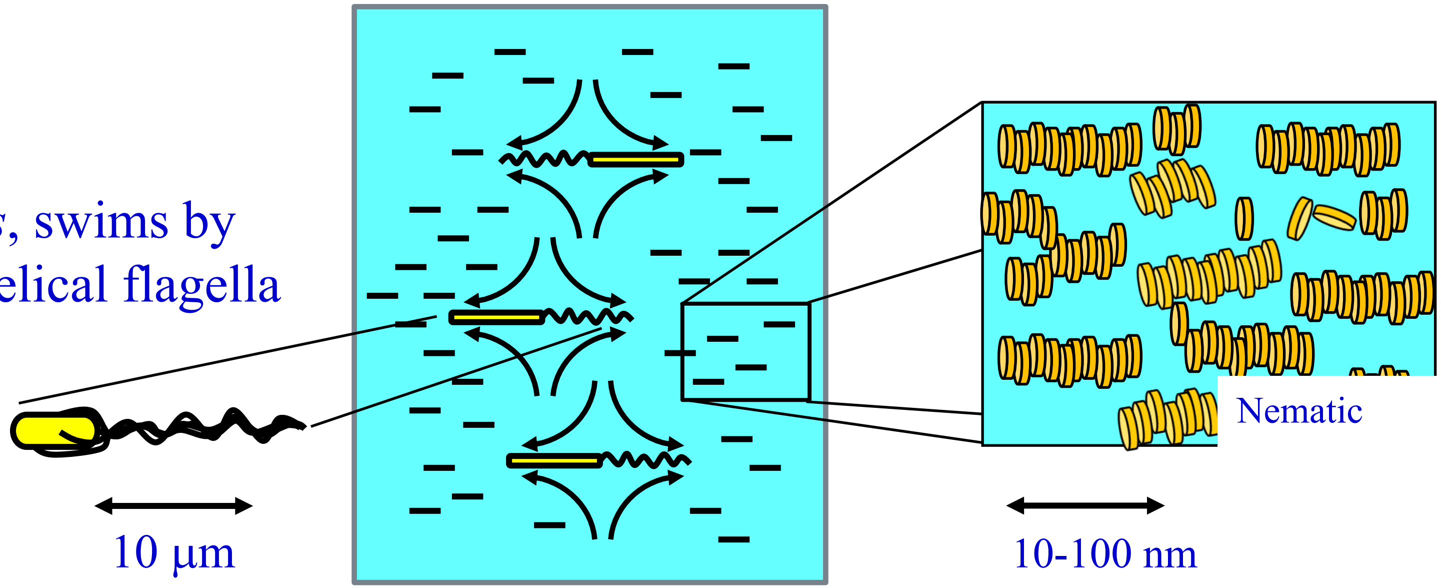
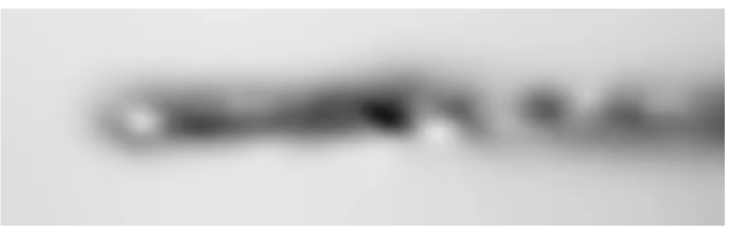
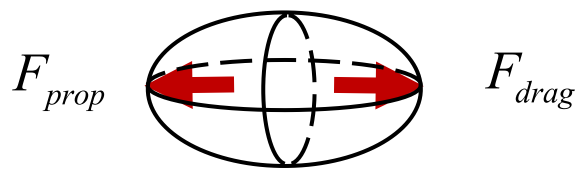


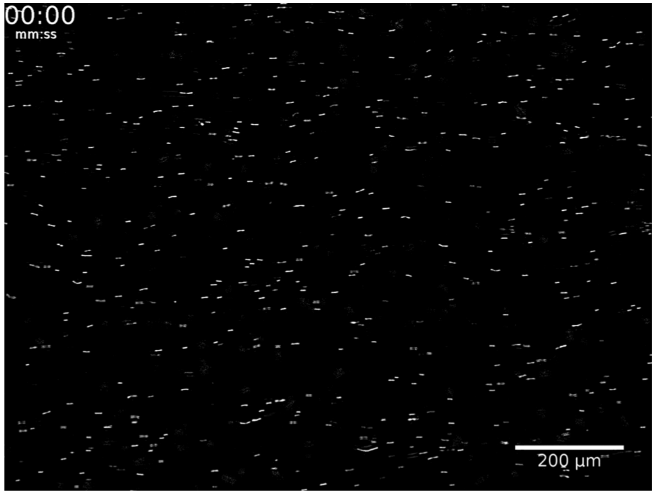


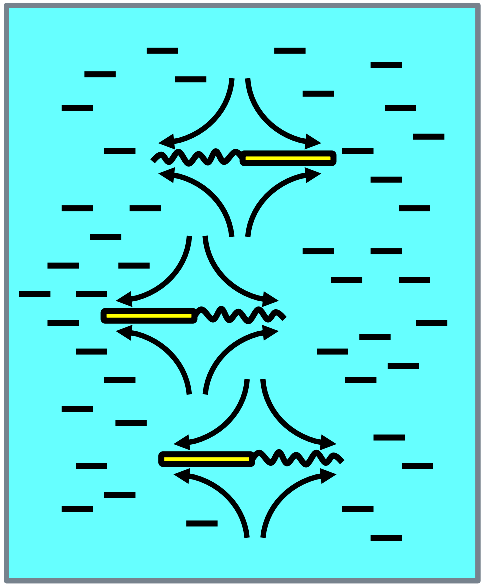


A simple view of a bacterium:
An ellipsoid with two forces at the end, a “pusher”

Uniform alignment: bacteria follow the director

$\hat{\mathbf{n}} = -\hat{\mathbf{n}}$





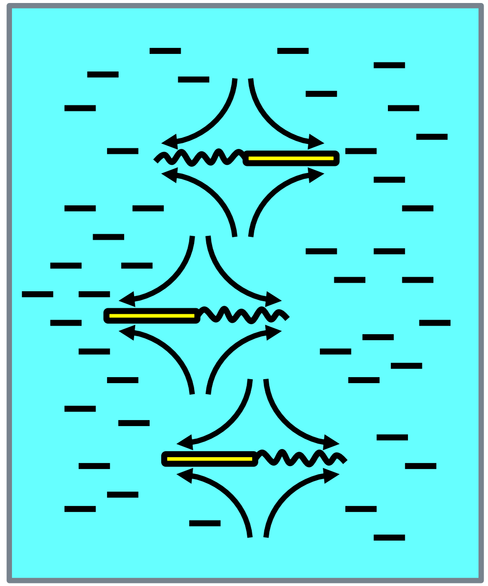
$c < 10^{14}\ \text{m}^{-3}$

Swimming parallel to the director; no distinction between right and left, thus no useful work…

S. Zhou et al, *PNAS* **111**, 1265 (2014)

Uniform alignment: Undulations

$\hat{\mathbf{n}} = -\hat{\mathbf{n}}$



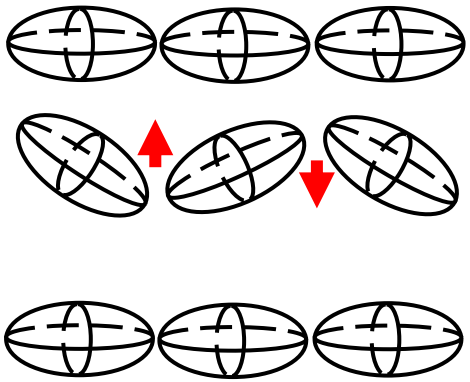
$c > 10^{14}\ \mathrm{m}^{-3}$

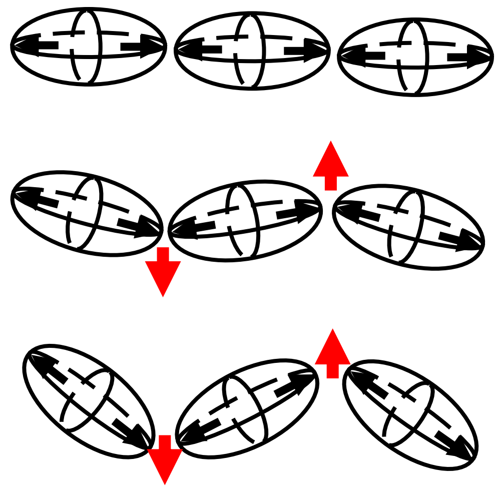
More bad news: Increased activity (concentration, speed) results in bend instability

S. Zhou et al, *PNAS* **111**, 1265 (2014)

Equilibrium nematic vs active extensile nematic:

Equilibrium nematic: Elasticity quenches fluctuative bend



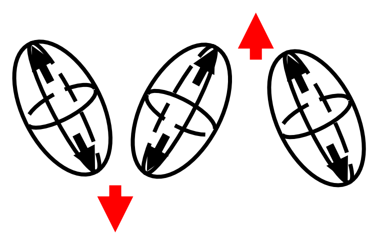


Active forces enhance fluctuative bend

$$bend = \hat{\mathbf{n}} \times (\nabla \times \hat{\mathbf{n}})$$

Simha, Ramaswamy *PRL* **89**, 058101 (2002)

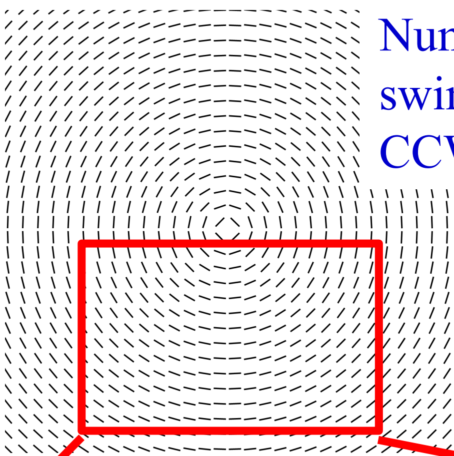
$$splay = \hat{\mathbf{n}} \nabla \cdot \hat{\mathbf{n}} \neq 0$$



Splay should remain stable

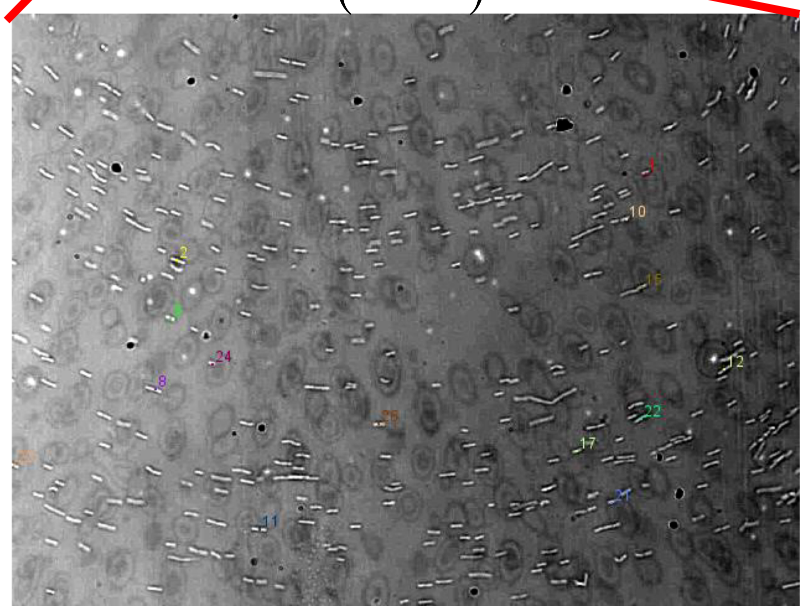
Splay and bend are expected to interact differently with activity, which motivates the next step: Explore activity vs geometry

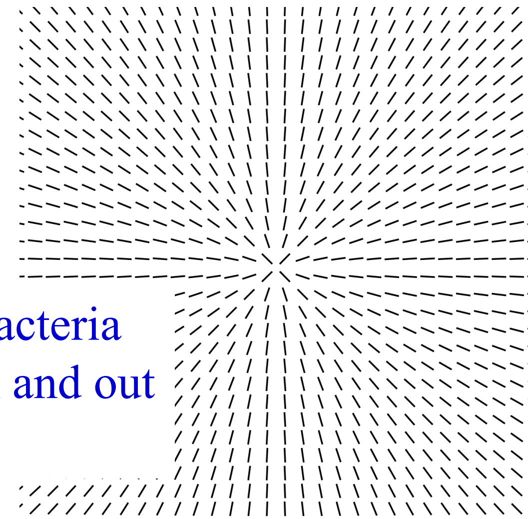
Pure bend and splay : Bacteria swim || director; bipolar motion



Number of bacteria swimming CW and CCW is the same

$$bend = \hat{\mathbf{n}} \times \left(\nabla \times \hat{\mathbf{n}}\right)$$

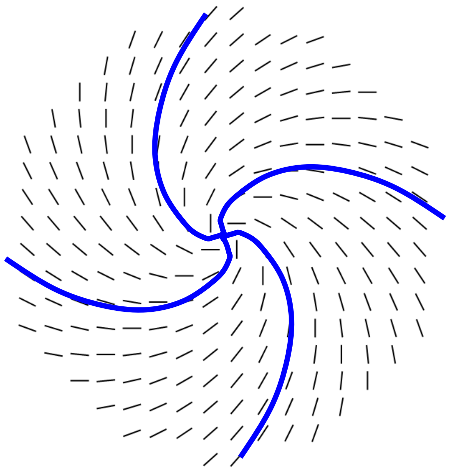


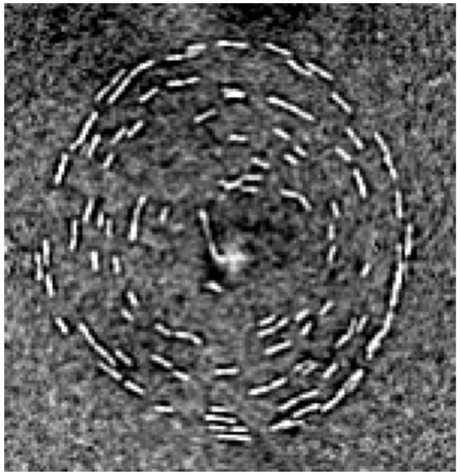


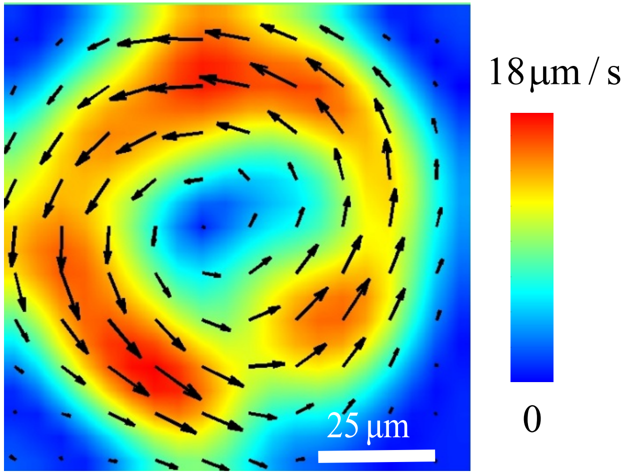
Number of bacteria swimming in and out is the same

$$splay = \hat{\mathbf{n}}\nabla \cdot \hat{\mathbf{n}} \neq 0$$

50:50 splay-bend: counterclockwise polar circulation





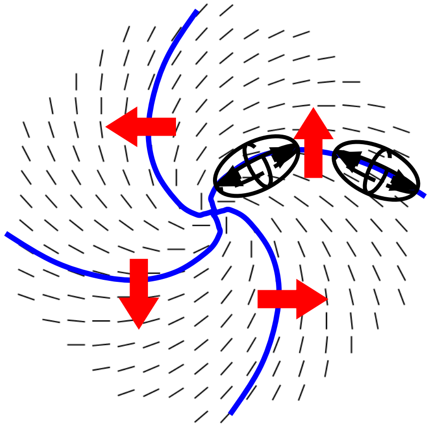


$c = 10^{14}\ \text{m}^{-3}$

Spiral vortex:
Counterclockwise collective circular swimming; strictly polar

Chenhui Peng, Taras Turiv et al, *Science* **354**, 882 (2016)

50:50 splay-bend: Forces unipolar circulation



Bacteria close to each other produce an active force related to director gradients; for the shown pattern, it is directed CCW

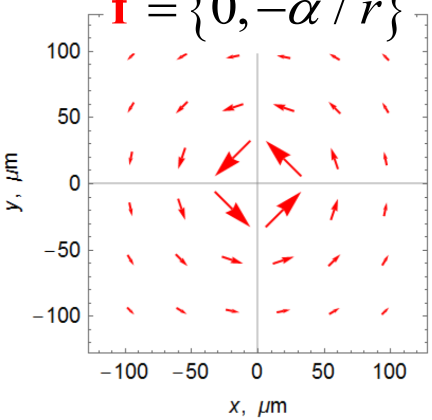
Active force (Simha, Ramaswamy (2002)) $f_i = \alpha \partial_j n_i n_j ; \alpha = const$

Invariant form (eg Green, Toner, Vitelli, PRFluids **2**, 104201 (2017))

$$\mathbf{f} = \alpha \left[\hat{\mathbf{n}} \nabla \cdot \hat{\mathbf{n}} - \hat{\mathbf{n}} \times \left(\nabla \times \hat{\mathbf{n}} \right) \right] ; \alpha = const$$

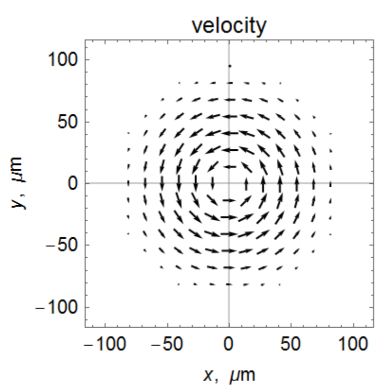
$$\hat{\mathbf{n}} = \left(n_r , n_\varphi \right) = \left(\cos \pi / 4 , \sin \pi / 4 \right)$$

$$\mathbf{f} = \left\{ 0, -\alpha / r \right\}$$

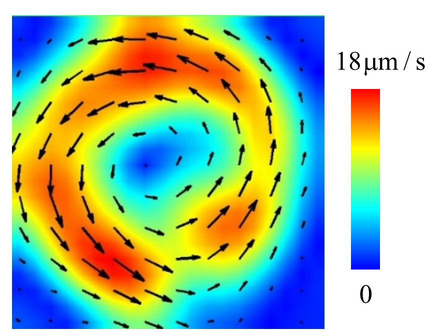


$$\mathbf{f} = \left\{ 0, -\alpha / r \right\} \qquad \mathbf{f}_{drag} = \eta \nabla^2 \mathbf{v}$$

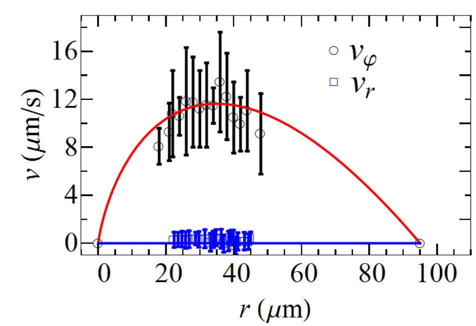
$$\mathbf{v} = \left\{ 0, \frac{\alpha r}{2\eta} \log \left(\frac{r}{r_0} \right) \right\}$$



model

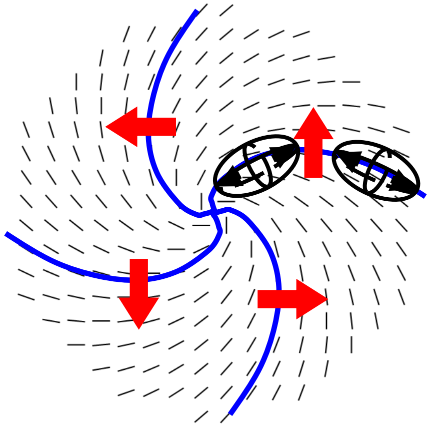


experiment



Deduce $\alpha / \eta \approx -0.7\ \mathrm{s}^{-1}$

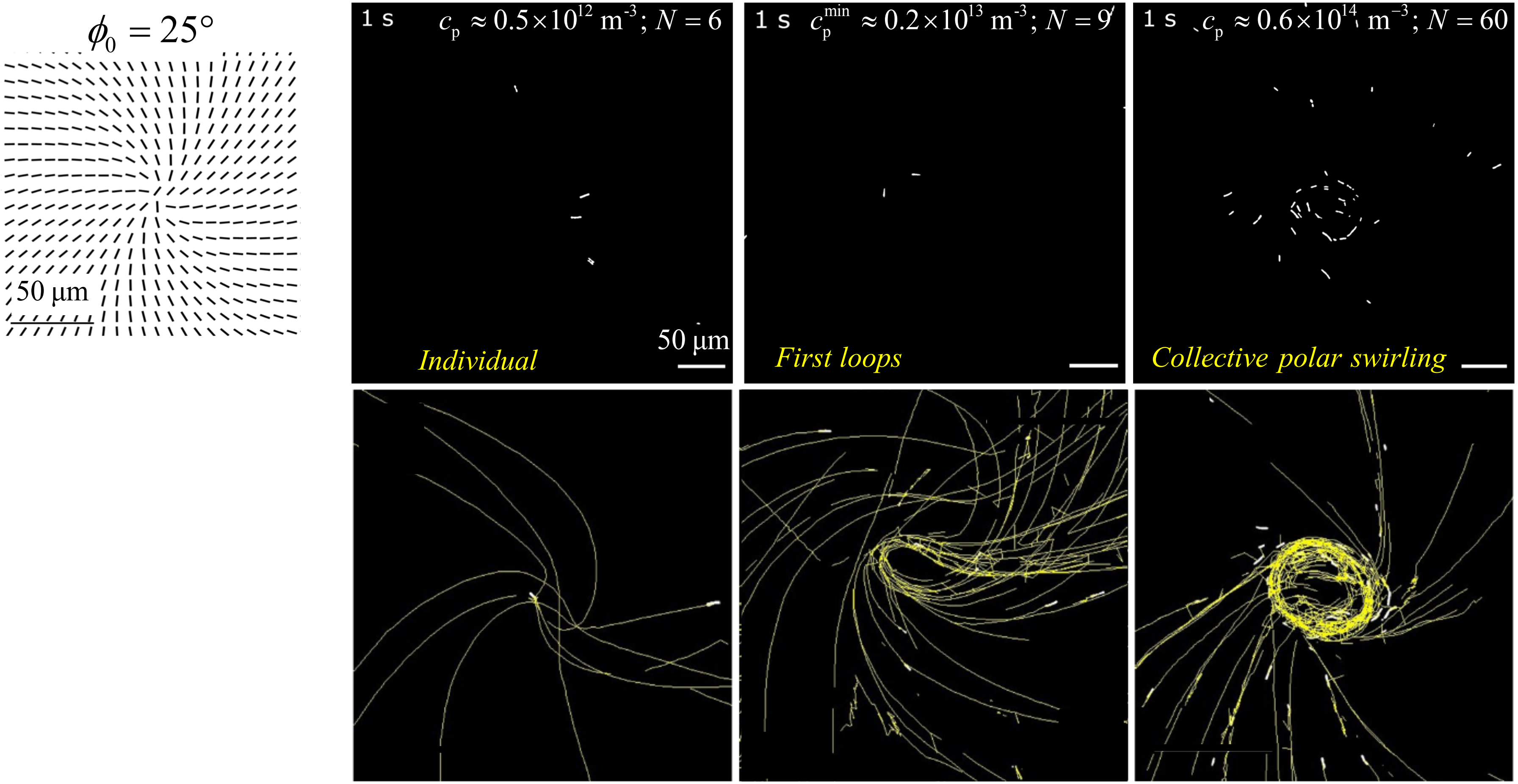
50:50 splay-bend: Forces unipolar circulation



Bacteria close to each other produce an active force related to director gradients; for the shown pattern, it is directed CCW

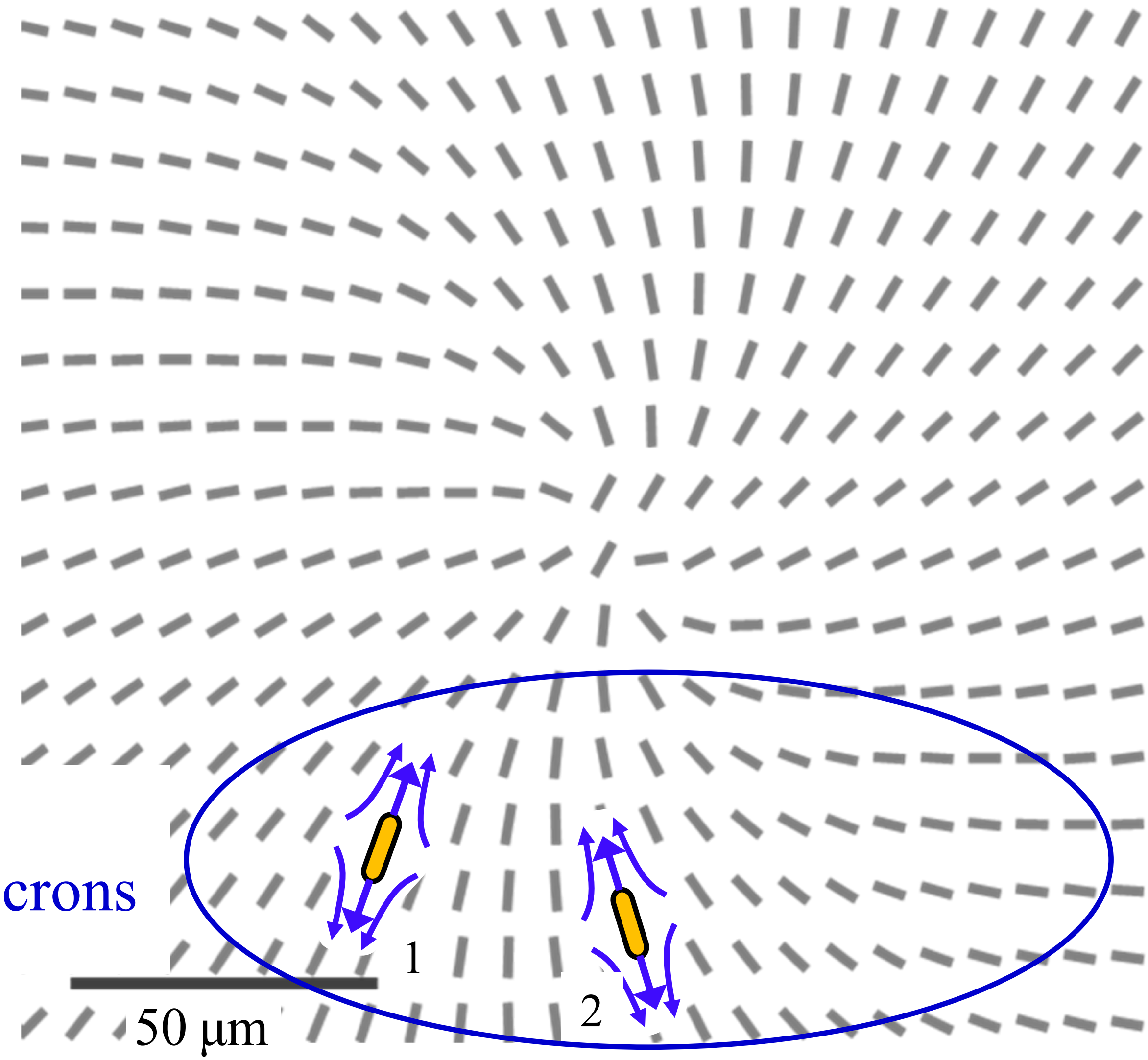
Next step: Increasing bacterial concentration as a trigger of individual-to-collective motion transition

Individual-to-collective motion transition



R. Koizumi, T. Turiv et al, *in preparation* (2020)

Individual-to-collective motion transition



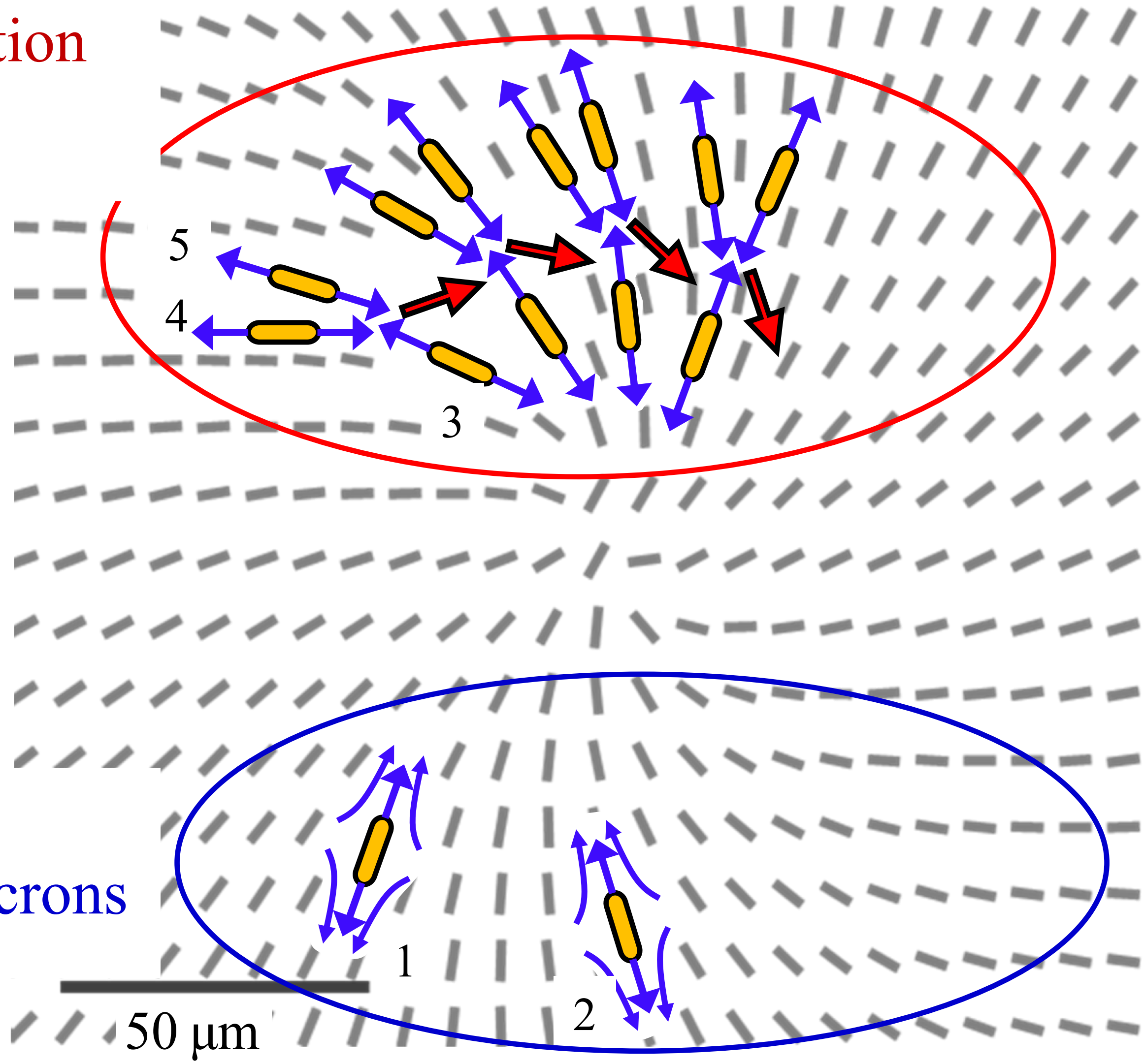
Individual:
Separation >15 microns

Individual-to-collective motion transition

Collective: Separation <15 microns

Increased concentration enables hydrodynamic interactions and leads to collective motion

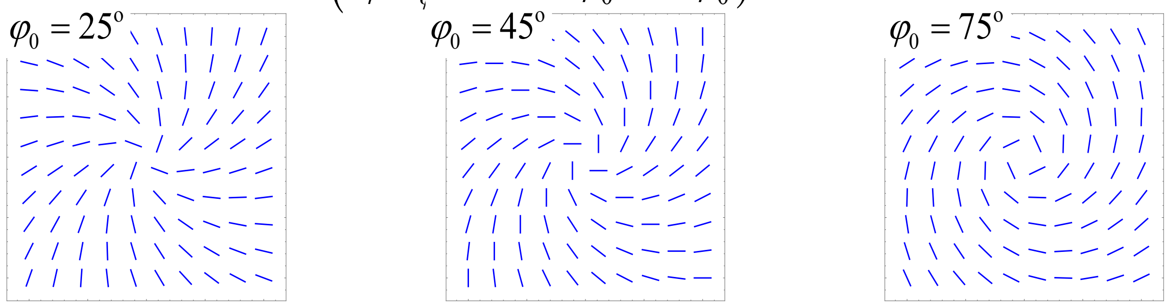
Individual: Separation >15 microns



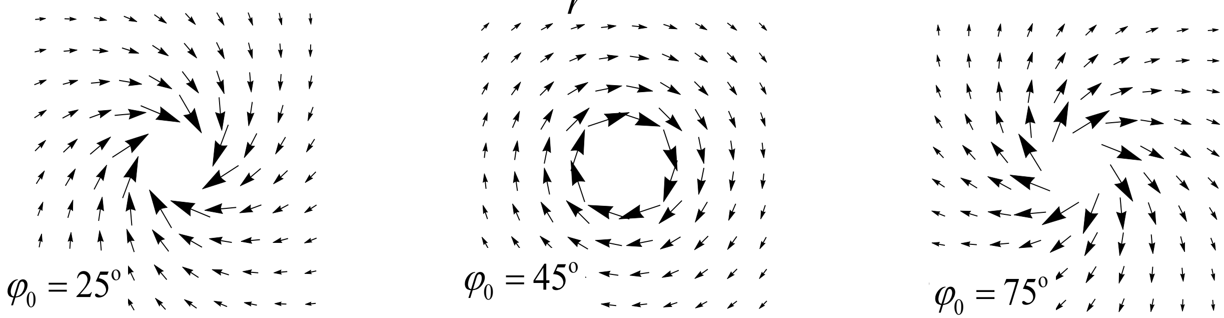
Contraction and expansion of swirls:

Control by spiral angle, qualitative analysis of active force

$$\hat{\mathbf{n}} = (n_r, n_\varphi) = (\cos\varphi_0, \sin\varphi_0)$$



$$\mathbf{f} = \{f_r, f_\varphi\} = \frac{\alpha}{r}\{\cos 2\varphi_0, \sin 2\varphi_0\}$$



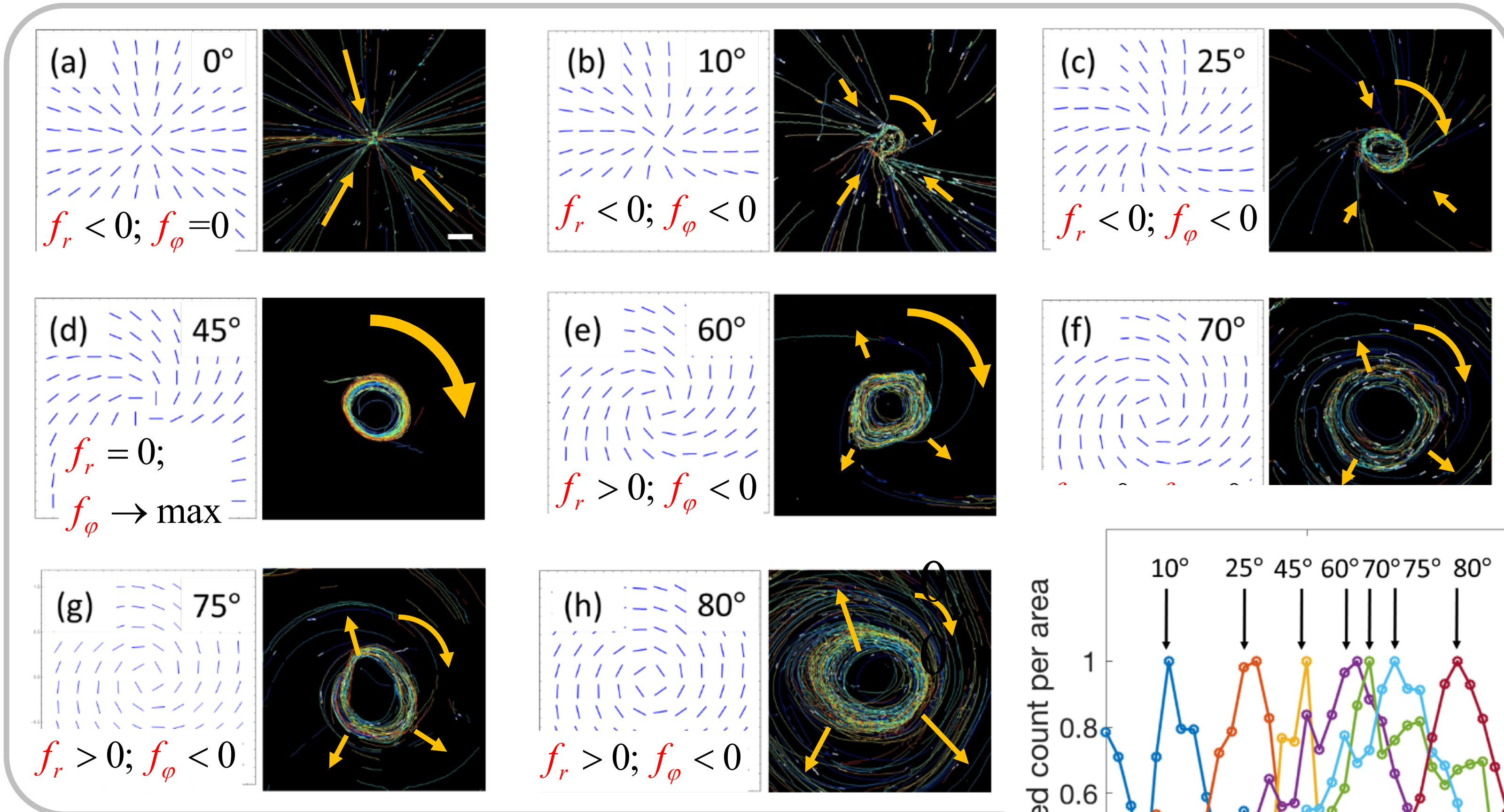
$f_r < 0$ | $f_r = 0$ | $f_r > 0$

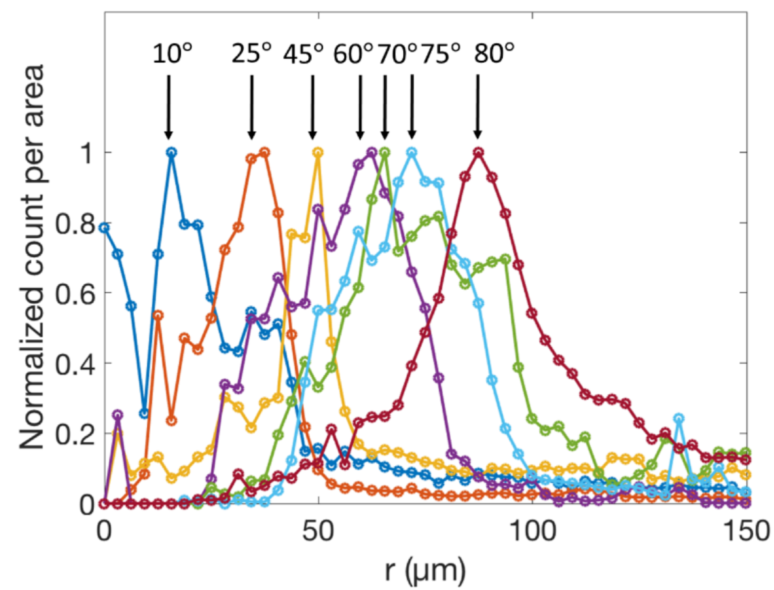
Swirls in vortices with spiral angle <45° should contract

Swirls in vortices with angle >45° should expand

Contraction and expansion of swirls: $\mathbf{f} = \{f_r, f_\varphi\} = \frac{\alpha}{r}\{\cos 2\varphi_0, \sin 2\varphi_0\}$

Control by spiral angle, qualitative analysis of active force

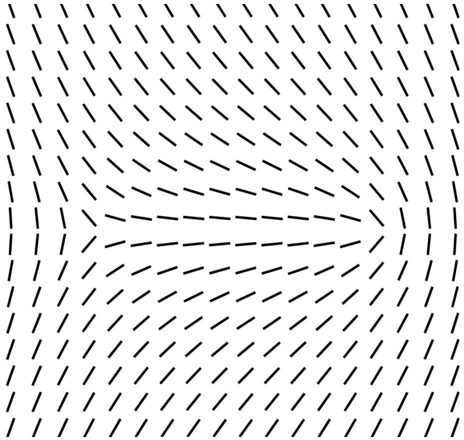
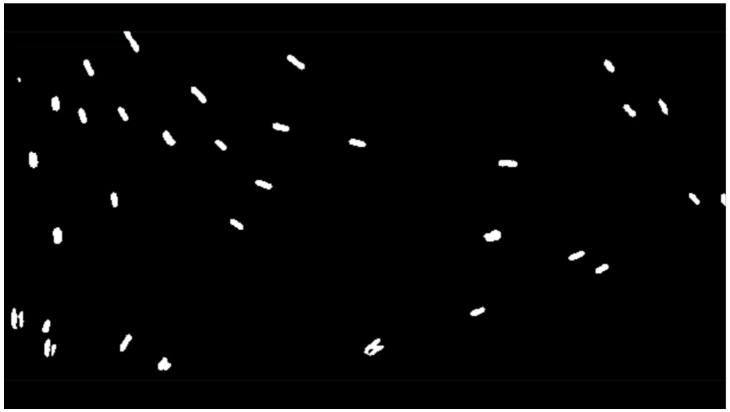




R. Koizumi, T. Turiv et al, *in preparation* (2020)

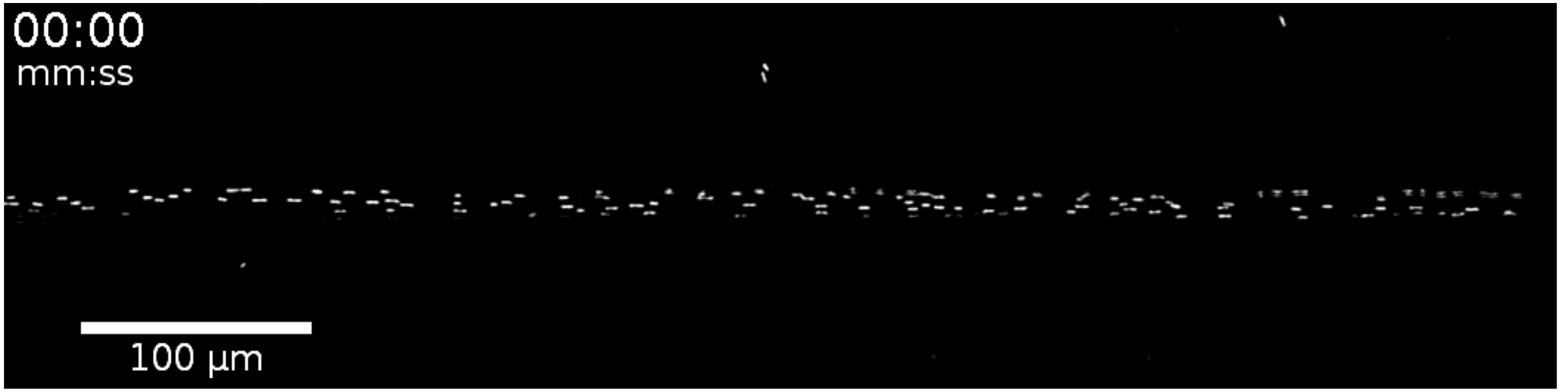
Pumping from -1/2 to +1/2:

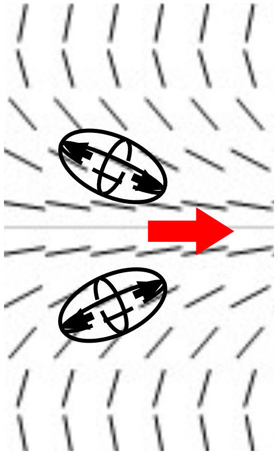
Qualitative analysis of active force

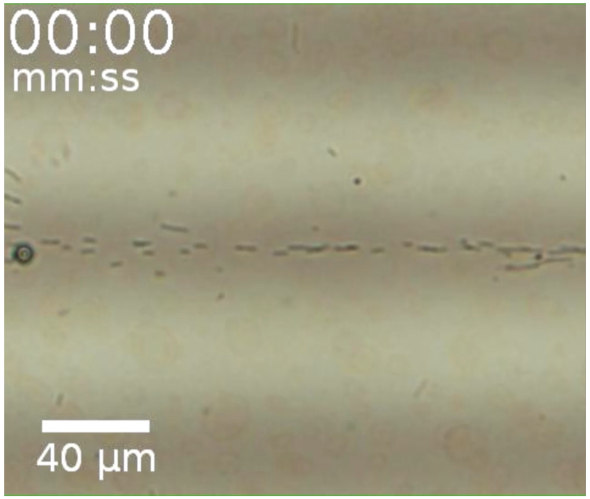
Bacteria concentrate at the cores of +1/2 defects; avoid -1/2 defects

Unipolar swimming in concentrated jets



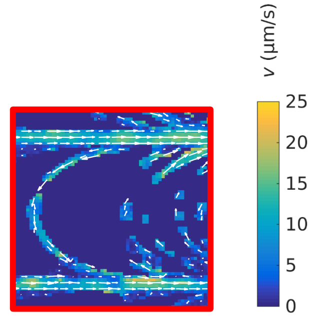


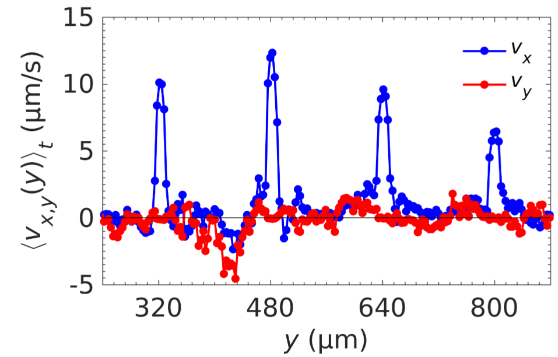
Colloidal transport by bacterial jets



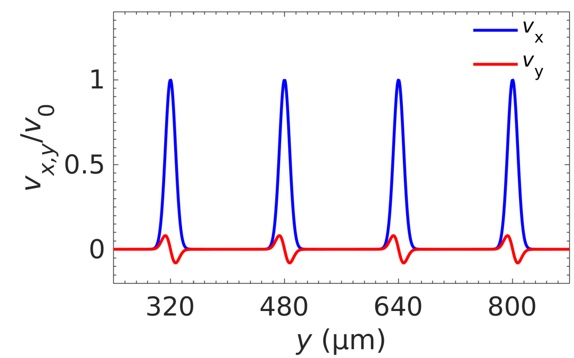
T. Turiv, R. Koizumi et al, *Nature Phys.* **16**, 481 (2020)

Unipolar swimming in concentrated jets





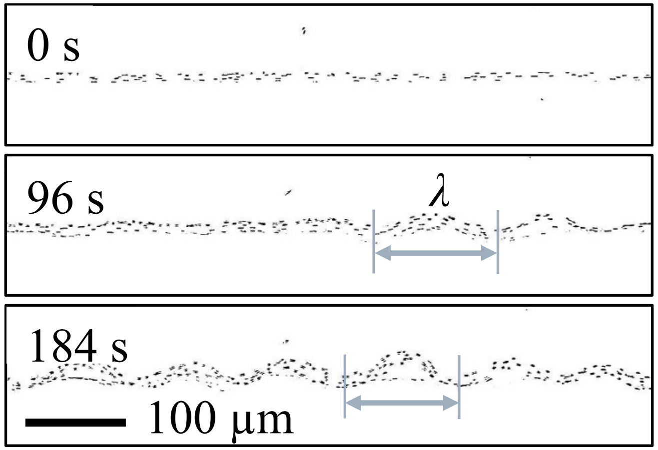
The system cannot be considered as incompressible, as $c, \alpha = f(x,y)$



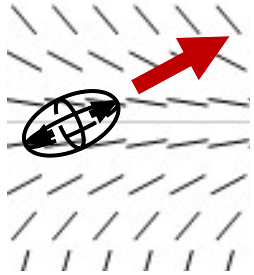
Advection-diffusion model by Genkin and Aranson captures the concentration and velocity distributions

T. Turiv, R. Koizumi et al, *Nature Phys.* **16**, 481 (2020)

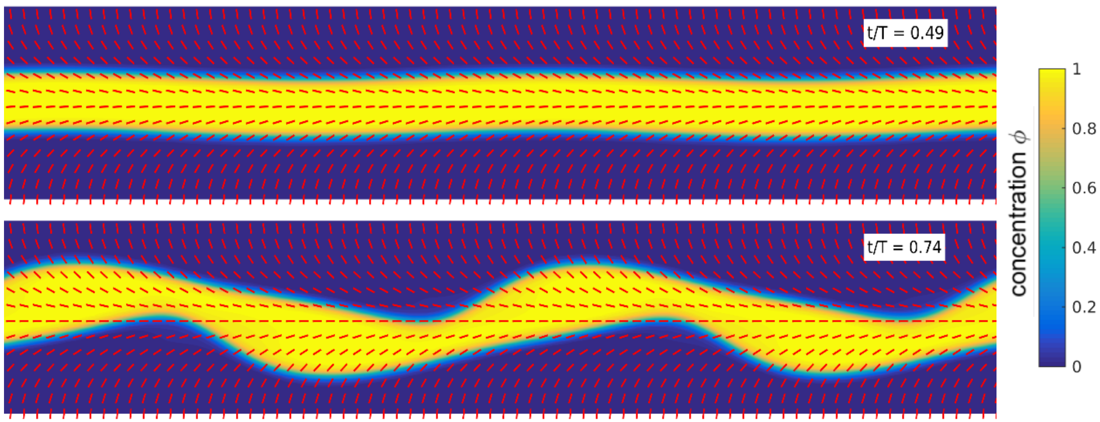
Director bend quenches undulations

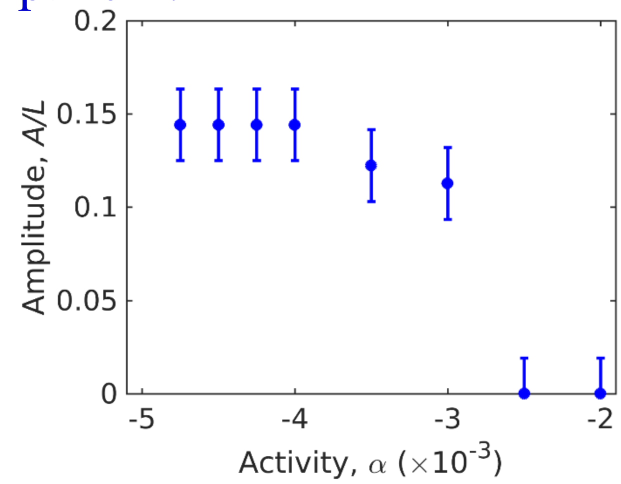


As the jets undulate, the angle between the director and the trajectory increases; it delays undulations up to $c=7c_{critical}$ where $c_{critical}$ is the critical concentration of instability in a uniform cell



Two-phase model by Thijssen, Doostmohammadi and Yeomans and advection-diffusion model capture this stabilizing effect of the pattern:





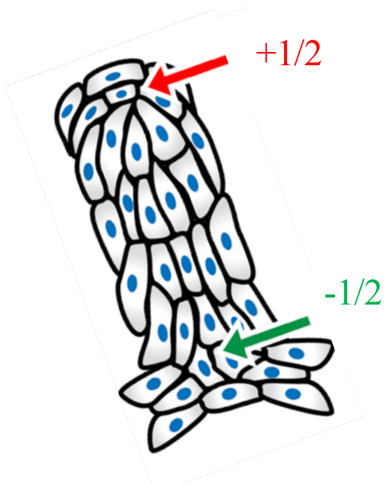
T. Turiv, R. Koizumi et al, *Nature Phys.* **16**, 481 (2020)

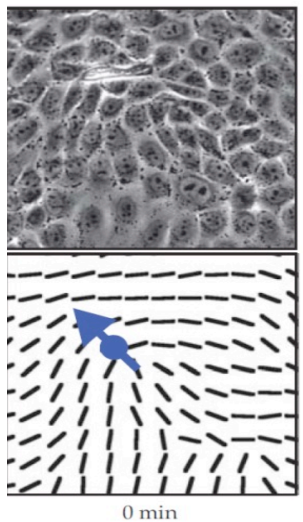
Conclusion-II:

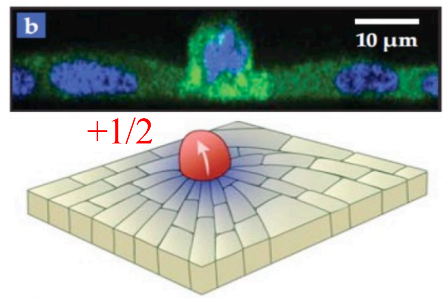
- Bacteria in a patterned nematic:
  - Patterns control trajectories, polarity and concentration of bacteria
  - Patterns cause unipolar threshold-less flow of microswimmers, circular or linear

Motivation No.2: Epithelium: Can we design it?

In epithelia, cells form an orientationally ordered nematic with topological defects, T.B. Saw et al, *Topological defects in epithelia govern cell death and extrusion*, Nature **544**, 212 (2017):







Dead cell are extruded at the +½ cores;
The +1/2's move around in the plane of film

Topological defects are intrinsic to many other active matter systems

We do not know *where* the defects would emerge nor *how to control* them
Can we develop a template to produce and pin the defects at predesigned locations?

Content

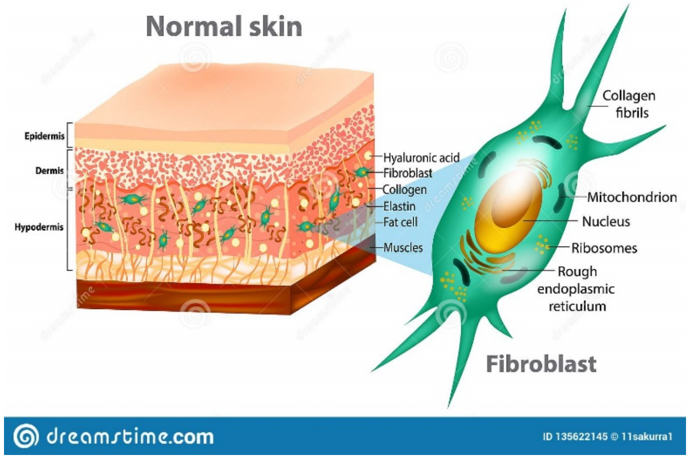
- How liquid crystals differ from water
  - Orientational order, elasticity, surface anchoring
  - Life at low Reynolds number in a nematic
- Water-based liquid crystal to control swimming bacteria
  - Swimming along the director; instabilities
  - Patterned director: unipolar circulation and translation
- Liquid crystal elastomer substrates to guide tissues
  - Tissue with predetermined locations of topological defects

T. Turiv, J. Krieger, G. Babakhanova et al, *Science Advances* **6**, eaaz6485 (2020)

The two ingredients

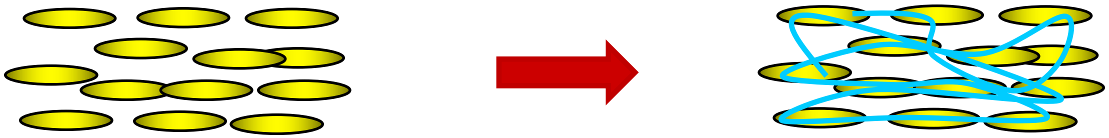
1. Human dermal fibroblast cells

Fibroblast cells are part of skin responsible for generation of connective tissue and healing wounds



2. Liquid Crystal Elastomer as a substrate

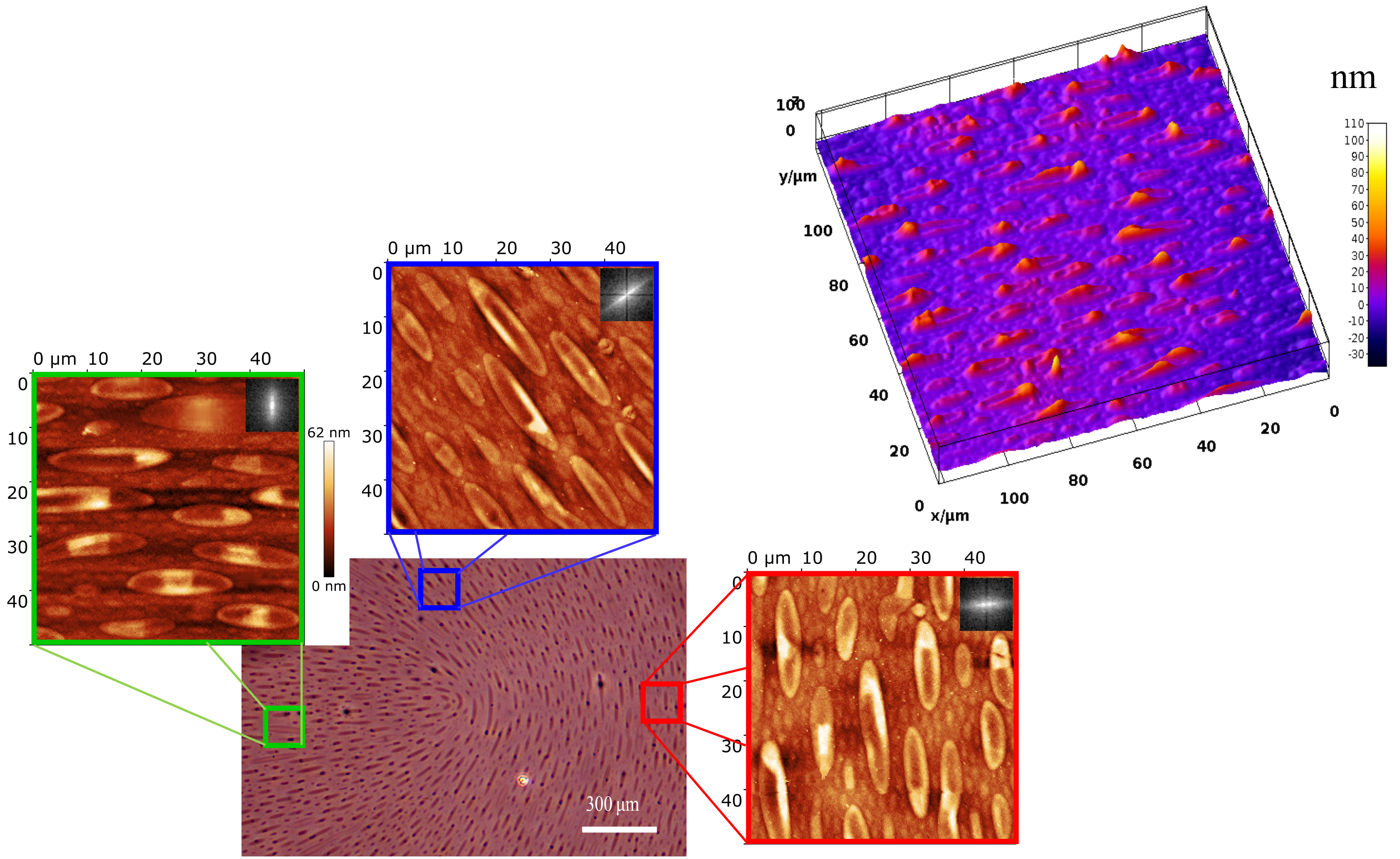
Thermotropic nematic liquid crystal cross-linked by covalent bonds into an anisotropic polymer mesh; used as a substrate, not a medium



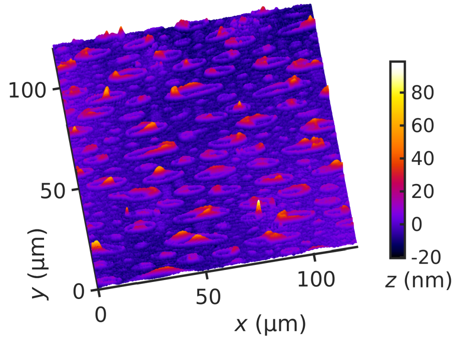
Nematic fluid

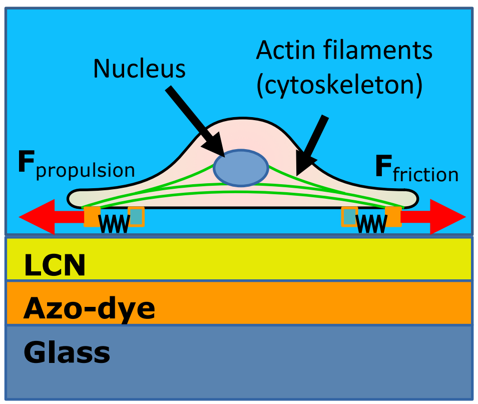
Nematic elastomer

LC Elastomer coating swells and develops grainy profile when in contact with water

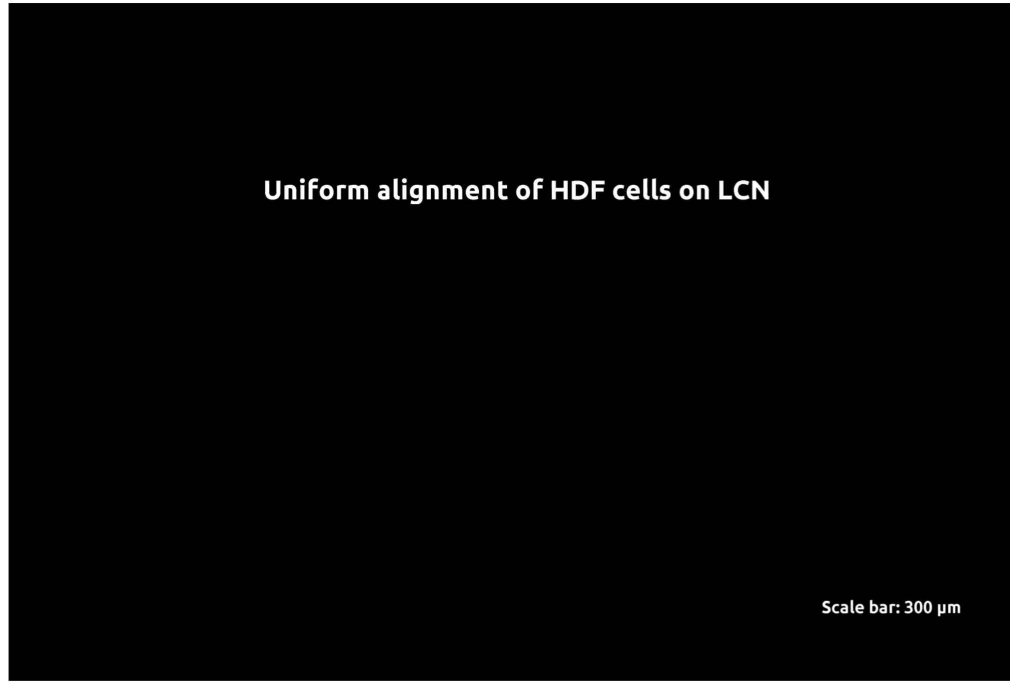


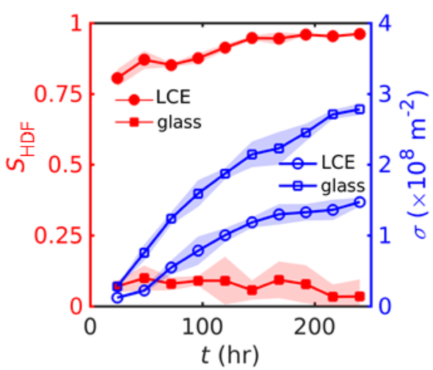
Alignment of human cells at uniform LCN substrate

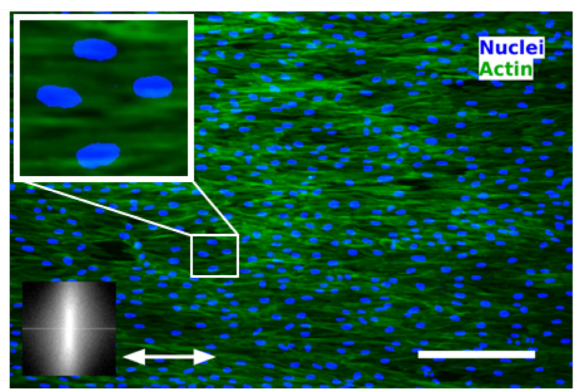




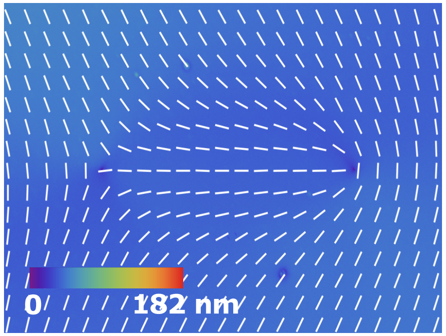
Uniform alignment of human dermal fibroblast cells at a uniform LCN substrate

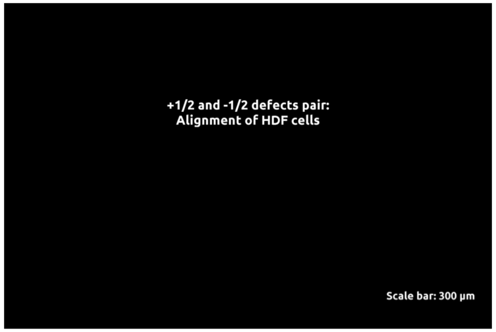




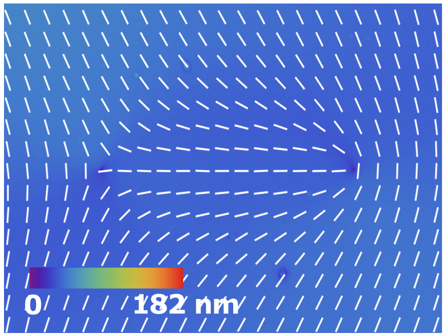


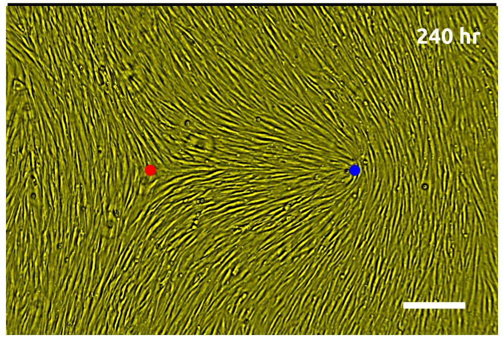
Patterns with +1/2 and -1/2 topological defects

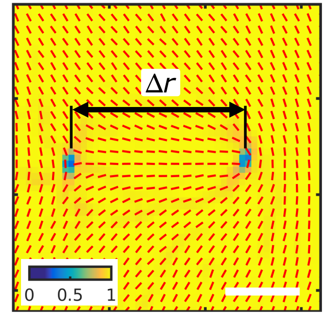


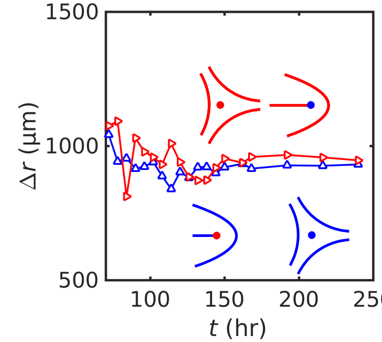


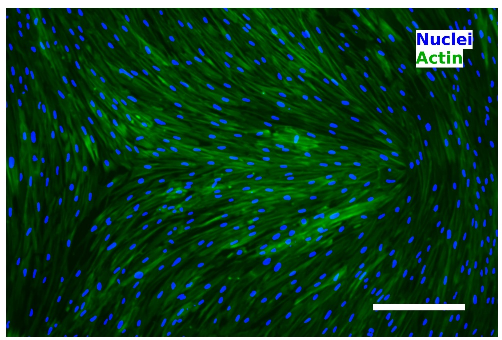
Patterns with +1/2 and -1/2 topological defects



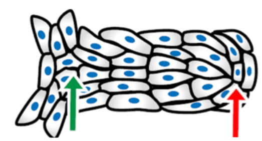




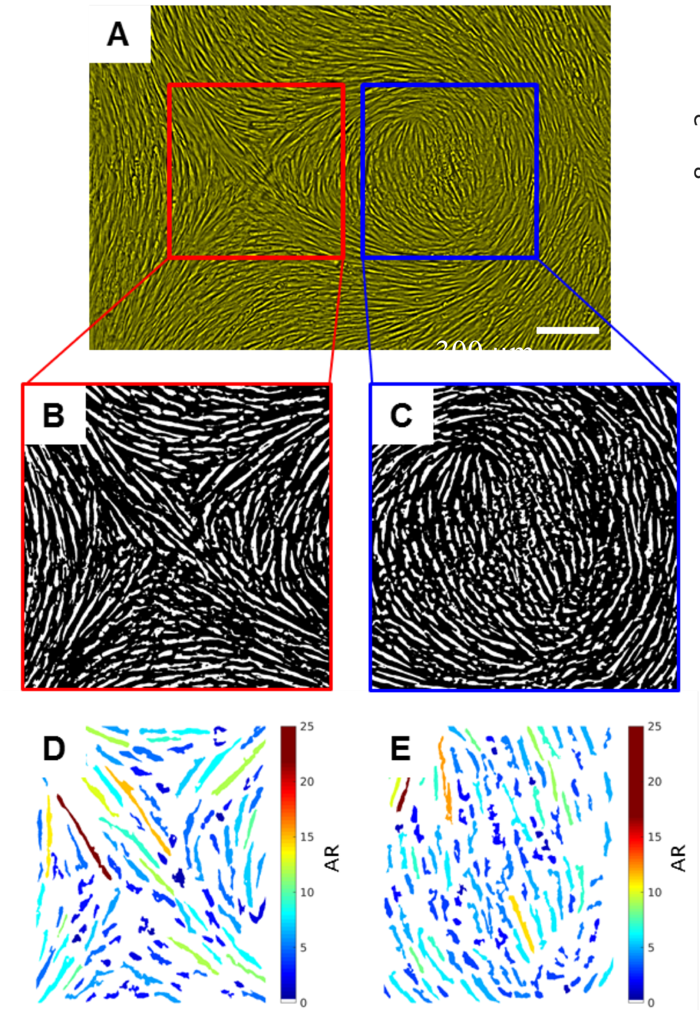


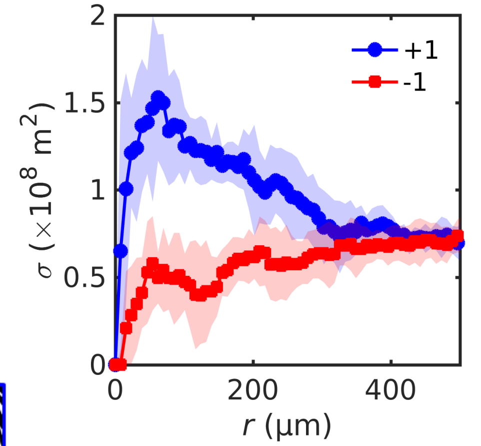


Surface anchoring by the LCE substrate prevents the ½ and -½ defects from moving around

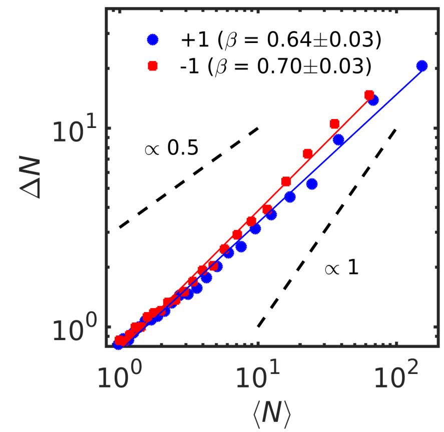


Patterns with +1 circular and -1 defects: Different concentration and phenotype of cells





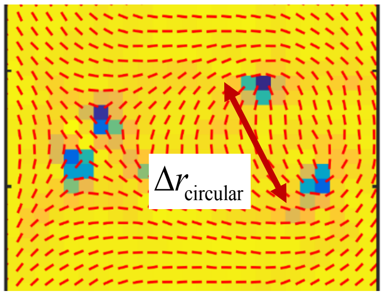
Density of cells vs r

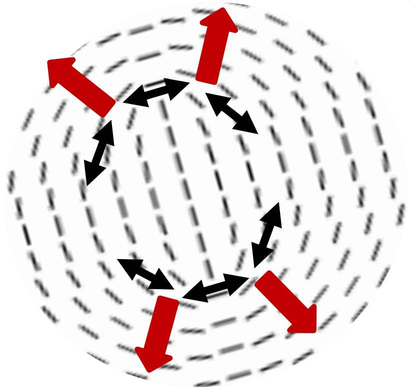


Large density fluctuations

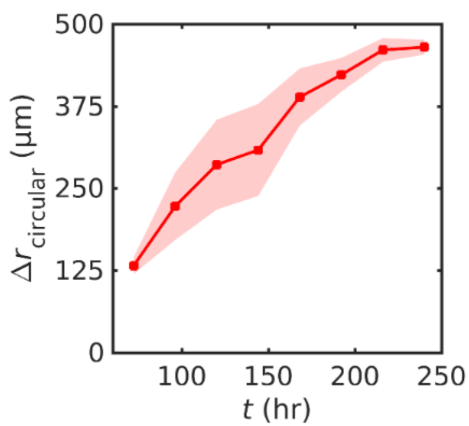
Cells concentrate at +1 cores and avoid -1 cores. Since the tissue is confluent, variation of density leads to variation in phenotype/shape: AR=length/width =2.6 near +1 defects and =5.8 near -1 defect

Core splitting of +1 defects into pairs of +1/2s

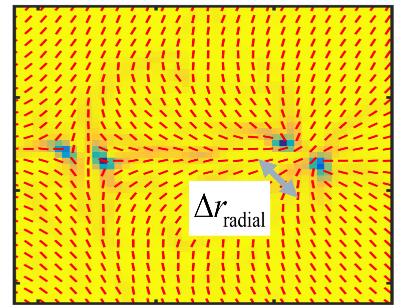


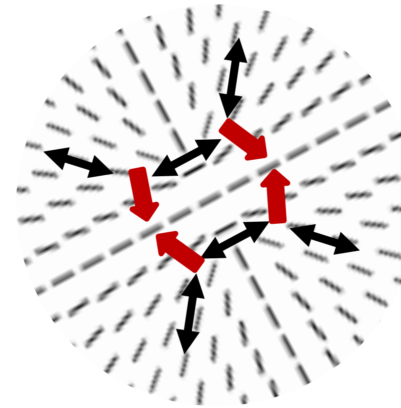


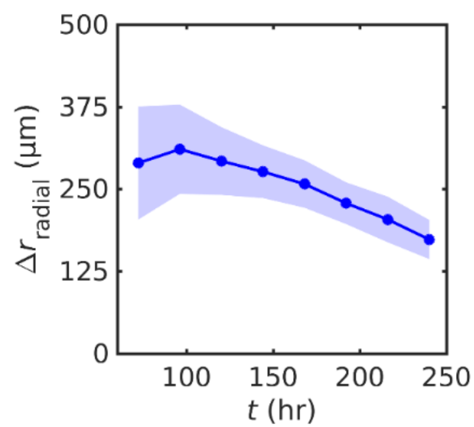
Circular (bend) pattern



+1/2 defects move away from each other in circular pattern





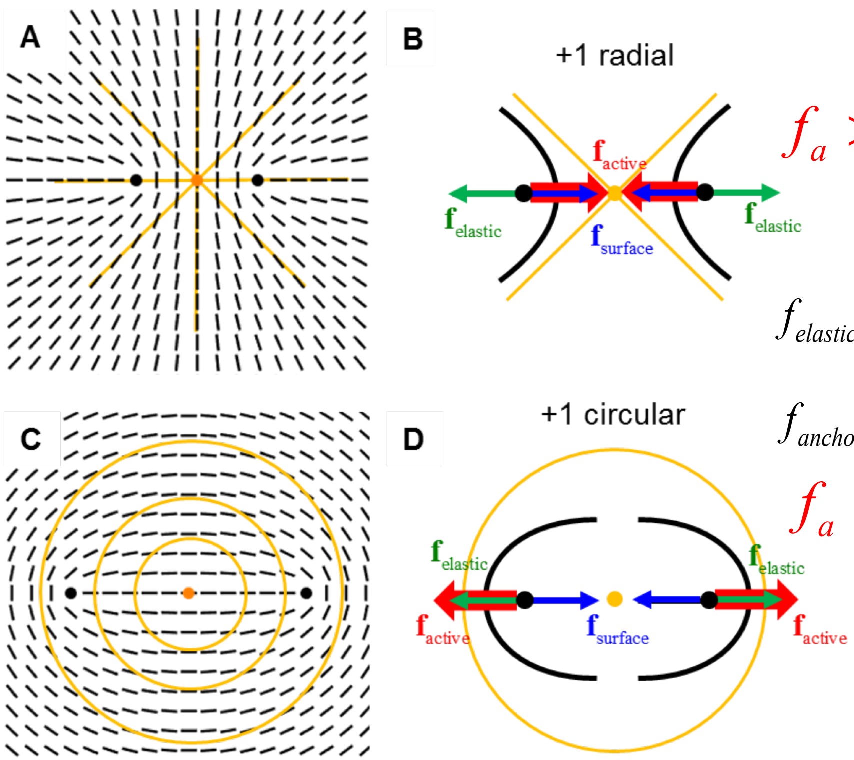


Radial (splay) pattern

+1/2 defects move towards each other in radial pattern

Core splitting of +1 defects into pairs of +1/2s

Defect dynamics suggests that the cells behave as “pushers”; allows one to estimate tissue parameters such as the anchoring strength W, elastic modulus K and the active force f_a



$f_a > 0$

$$f_{elastic} = -\frac{\pi}{2} Kh \ln \frac{\Delta r}{2r_c}$$

$$f_{anchoring} = 0.2W(\Delta r)^2$$

$f_a < 0$

$$\Delta r^{\text{circular}}_{\text{radial}} = \left(\pm|f_a| + \sqrt{f_a^{\,2} + 0.8\pi hKW}\right) / 0.8W$$

$$\Delta r^{\text{circular}} - \Delta r_{\text{radial}} = f_a / 0.4W \Rightarrow f_a / W \approx 140\ \mu\text{m}$$

$$\Delta r_{-1/2} = \sqrt{\pi hK / 0.8W} = 120\ \mu\text{m} \Rightarrow K / W \approx 180\ \mu\text{m}$$

$$f_a \approx K \approx 5\ \text{nN}; \quad W \approx 2.5\times10^{-5}\ \text{J/m}^2$$

Conclusion-III

- Liquid crystal elastomer coatings control human dermal fibroblast tissues
  - Human dermal fibroblast tissues follow the predesigned LC elastomer texture and behave as extensile active matter
  - Patterns define the concentration and phenotype of cells
  - Difference in the splitting distance of the cores of radial and circular defects allows one to estimate the Frank elastic modulus of the tissue, surface anchoring and the active force

Summary

- Anisotropic environment offers a mechanism of microscale propulsion based on broken symmetry of orientational order
- Liquid crystal medium can control trajectories and spatial distribution of microswimmers, guide them into circular and linear polar flows
- Liquid crystal elastomer substrates control alignment of HDF tissues, formation and location of topological defects