Bioinspired liquid crystal patterns to command living matter

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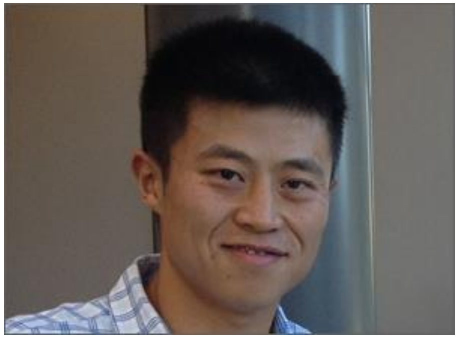
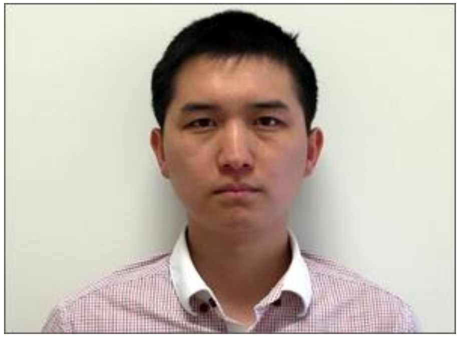
APS March Meeting 2020

Session F18: Non-equilibrium bioinspired modes of assembled materials, March 3, 2020

Contributing graduate students, Chemical Physics Interdisciplinary Program



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

Bingxiang Li, PhD 2019,
now a PDF at AMLCI

Runa Koizumi,
current PhD student

Taras Turiv,
current PhD student

Collaborators

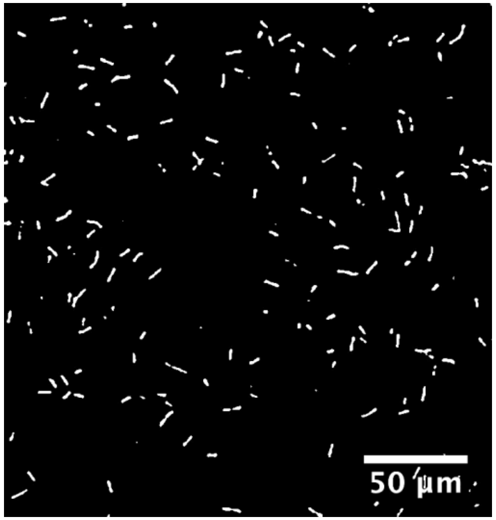
Kent State University:

- Dr. Sergij Shiyanovskii, AMLCI
- Dr. Hao Yu and Prof. Qi-Huo Wei, AMLCI, Physics and CPIP
- Miss Jess Krieger and Prof. Min-Ho Kim, Biological Sciences
- Mr. Robert Lastowski, REU student

Our colleagues:

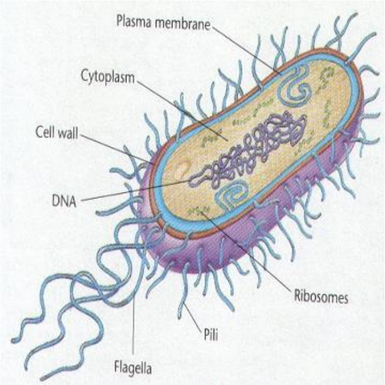
- Prof. Igor Aranson, Department of Biomedical Engineering, Pennsylvania State University
- Kristian Thijssen and Julia M. Yeomans, The Rudolf Peierls Centre for Theoretical Physics, Clarendon Laboratory, University of Oxford, UK
- Amin Doostmohammadi, University of Oxford, now at The Niels Bohr Institute, University of Copenhagen, Denmark
- Mikhail M. Genkin, Cold Spring Harbor Laboratory

Motivation No.1: Swimming bacteria: Can we extract a useful work from them?



Swimming Bacillus Subtilis

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

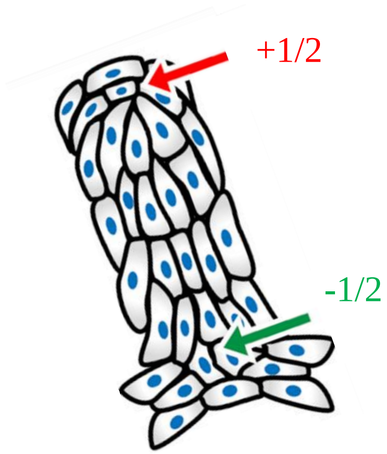


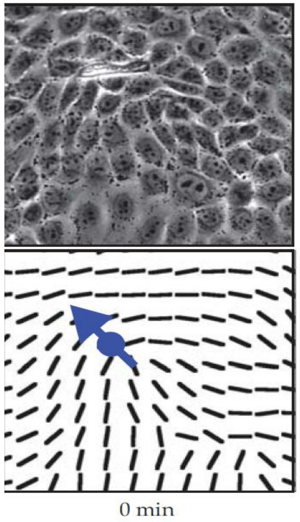
Can we force the swimming bacteria to deliver cargos, drugs, to run micromachines, to transform them into horses of microcosm?

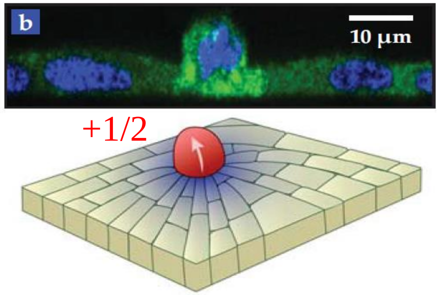
Problem: Visual, audio and tactile communication channels are not available

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
Sanchez et al, Nature **491**, 431 (2012), Zhou et al, PNAS 111, 1265 (2014)

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?

Liquid crystals as guiding and templating medium

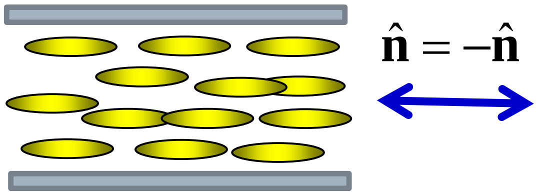
This work:

Replace an isotropic aqueous environment natural to many biological microsystems by an orientationally ordered liquid crystal;

Use patterned liquid crystals as a “communication channel” to command swimming bacteria and epithelium patterns

Why liquid crystals are different from water

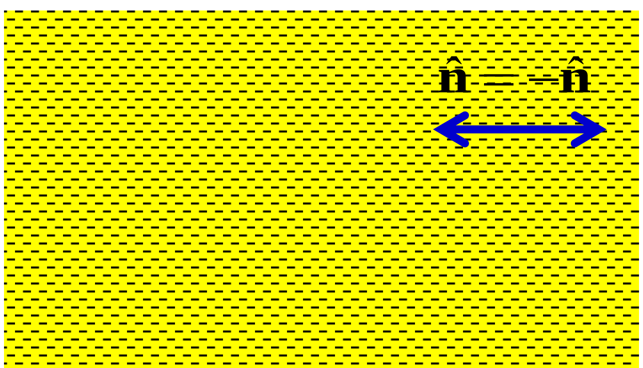
- Anisotropy:

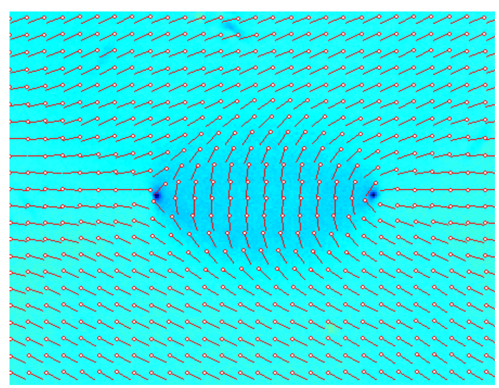


anisotropy axis of dielectric permittivity, viscous drag, birefringence, etc.

- Patterning capabilities

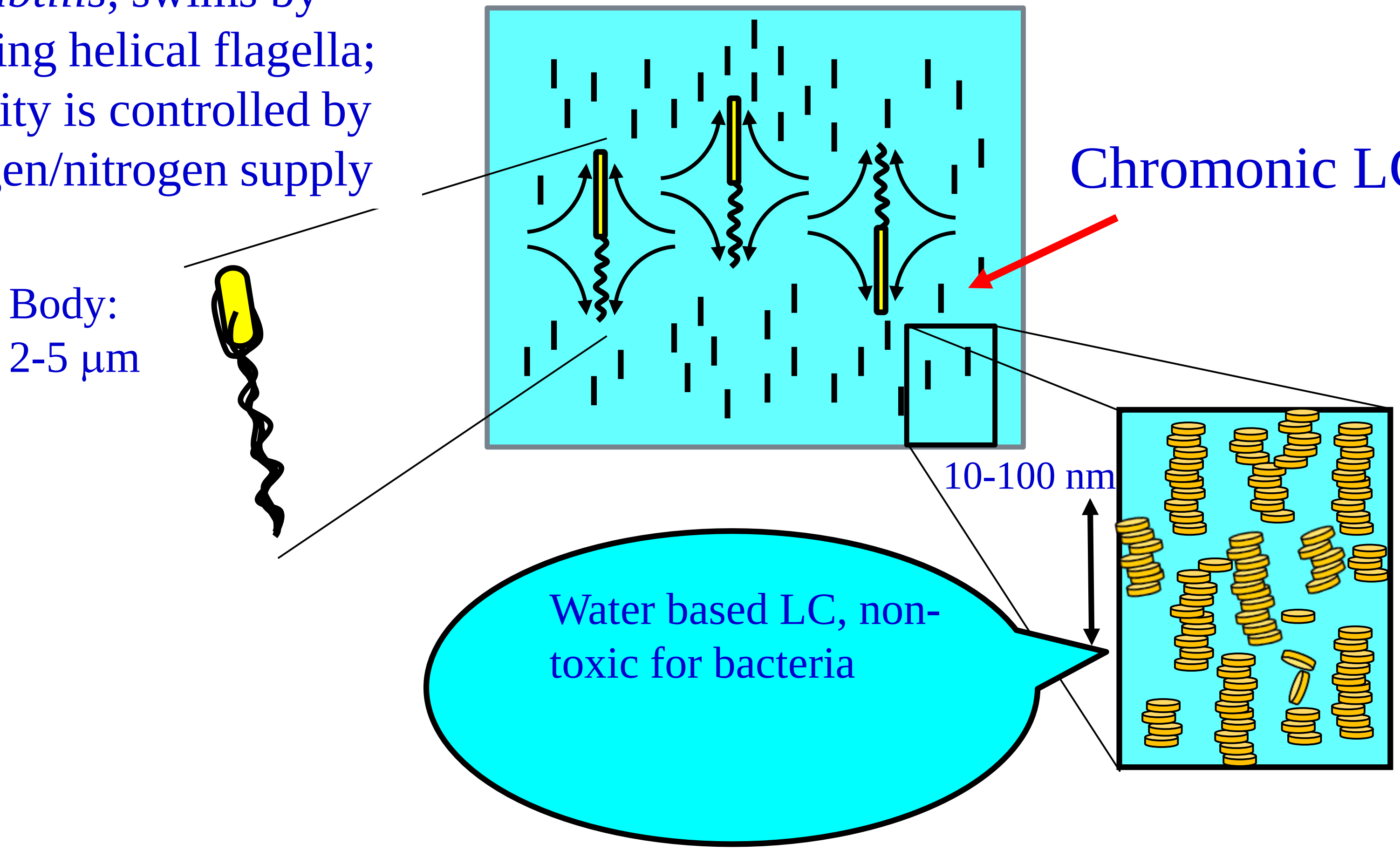
Can be prepared as uniformly aligned or as a pattern, using a photoalignment technique





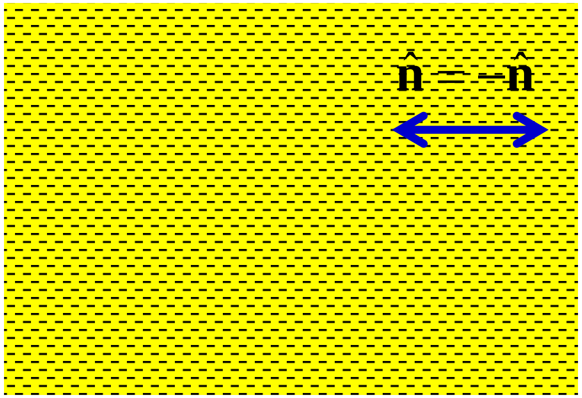
Liquid Crystals to Command Swimming Bacteria

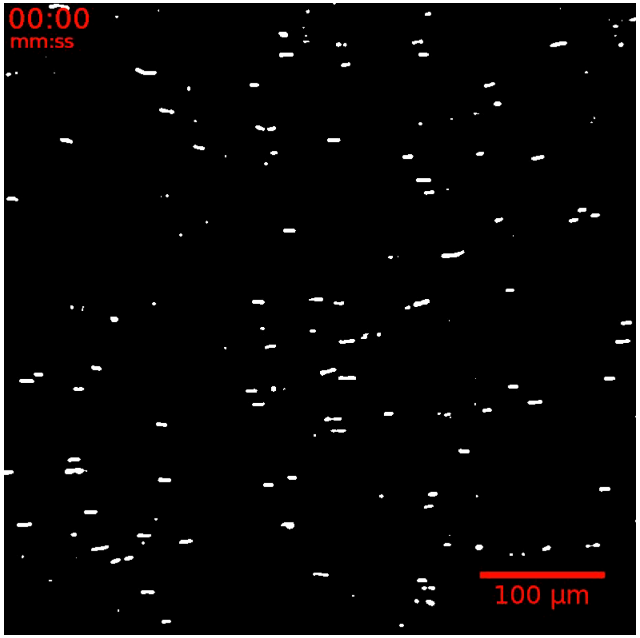
B. Subtilis, swims by rotating helical flagella; activity is controlled by oxygen/nitrogen supply



Main feature: an independent control of orientational order and activity

Uniform alignment: bacteria follow the director

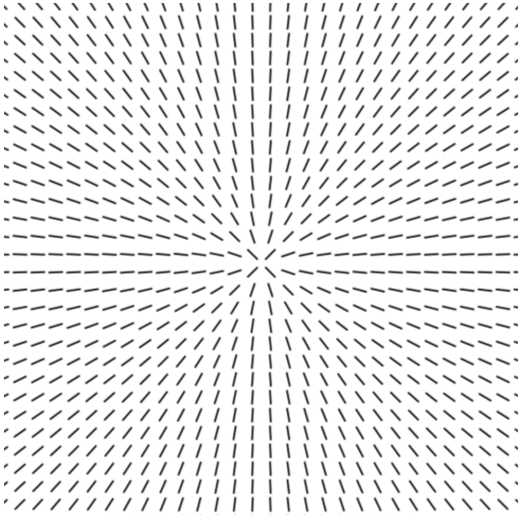




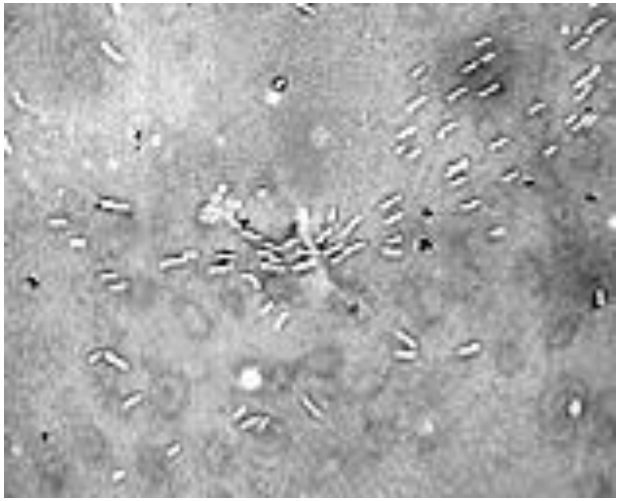
Swimming parallel to the director;
no distinction between right and left,
thus no useful work…

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

Pure splay: Bacteria swim || director; bipolar motion



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

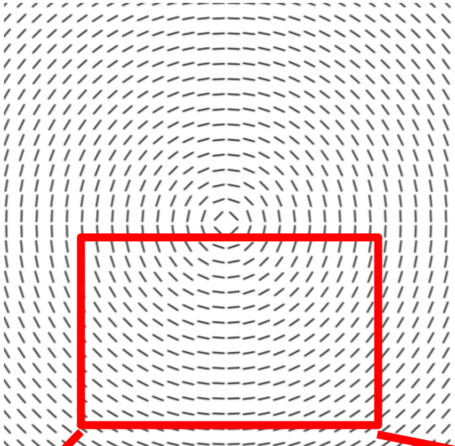


$c_B = 10^{14}$ /m^3

Number of bacteria swimming towards and away from the core is about the same at low c_B

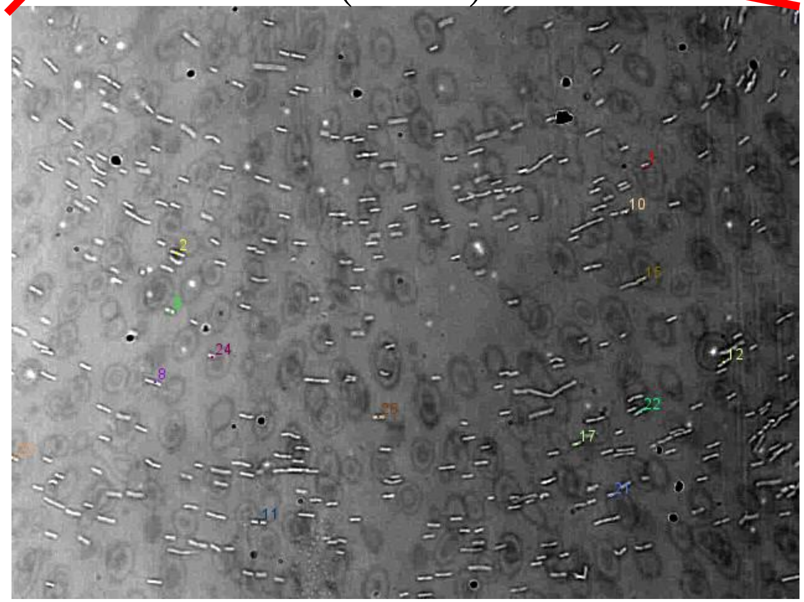
Chenhui Peng, Taras Turiv et al, *Science* **354**, 882 (2016)

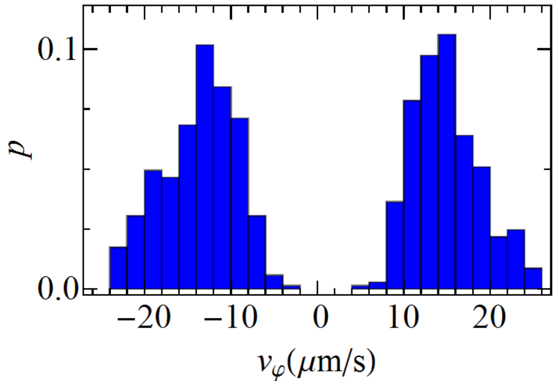
Pure bend: Bacteria swim || director; bipolar motion



$c_B = 10^{14}\ /m^3$

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

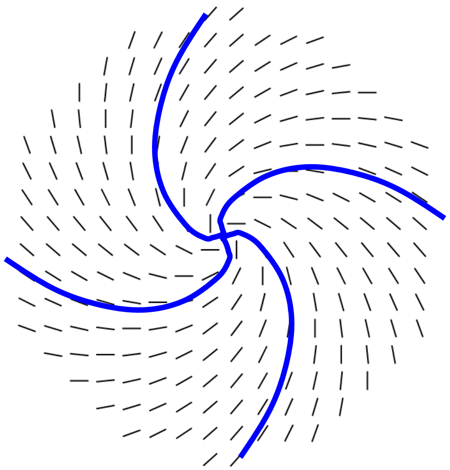


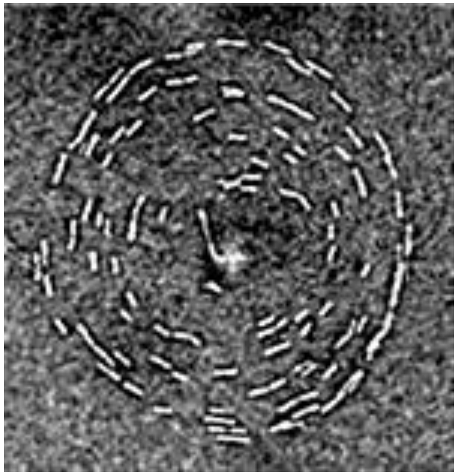


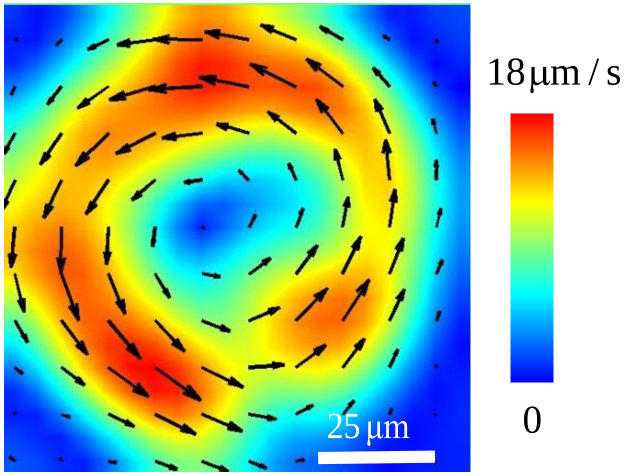
Number of bacteria swimming to the right and to the left is the same, as expected

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

Mixed splay-bend: counterclockwise polar motion





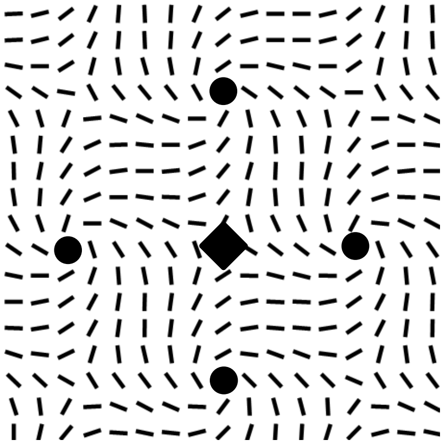


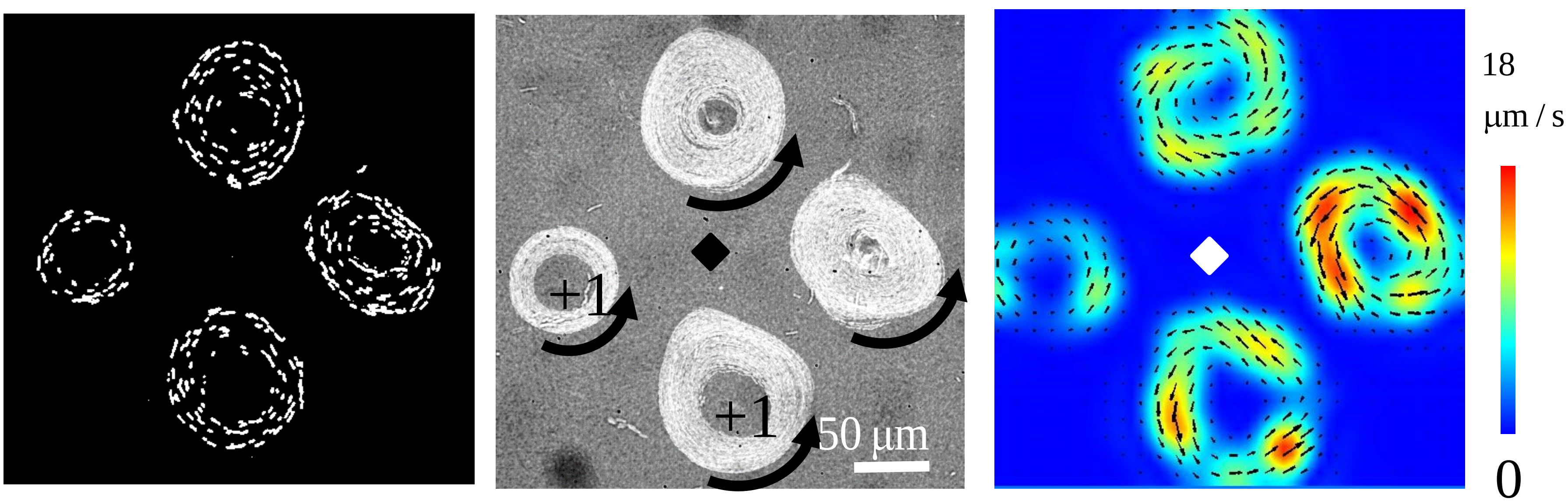
$c_B = 10^{14}$ /m^3

Spiral vortex:
Counterclockwise collective
circular swimming; strictly polar

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

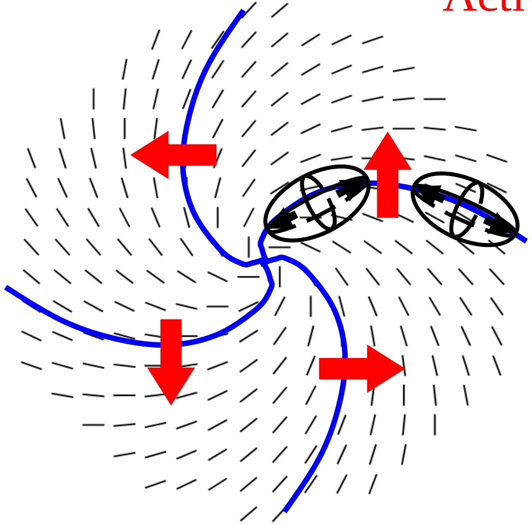
Periodic pattern of -1 and +1 defects: Bacteria gather and circulate around each +1, avoid -1





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

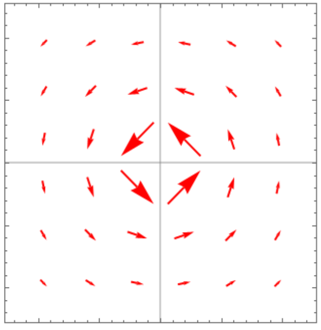
Mechanisms?



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

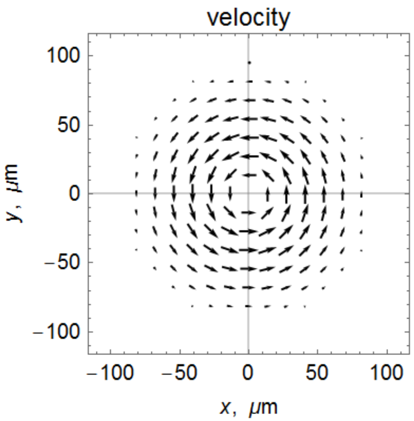
$$\hat{\mathbf{n}} = \left(n_x, n_y, n_z\right) = \left(\cos\theta, \sin\theta, 0\right) \qquad \theta(x,y) = \tan^{-1}\frac{y}{x} + \frac{\pi}{4}$$

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

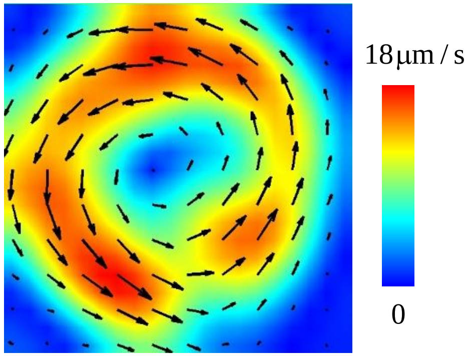


Opposing viscous force $\mathbf{f}_{drag} = \eta\nabla^2\mathbf{v}$

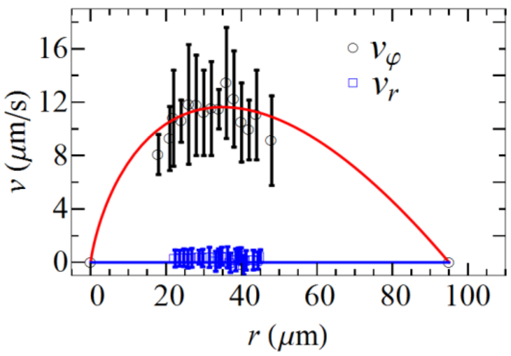
Balance of drive and drag: $\mathbf{v} = \left\{0, \frac{\alpha r}{2\eta}\log\left(\frac{r}{r_0}\right)\right\}$



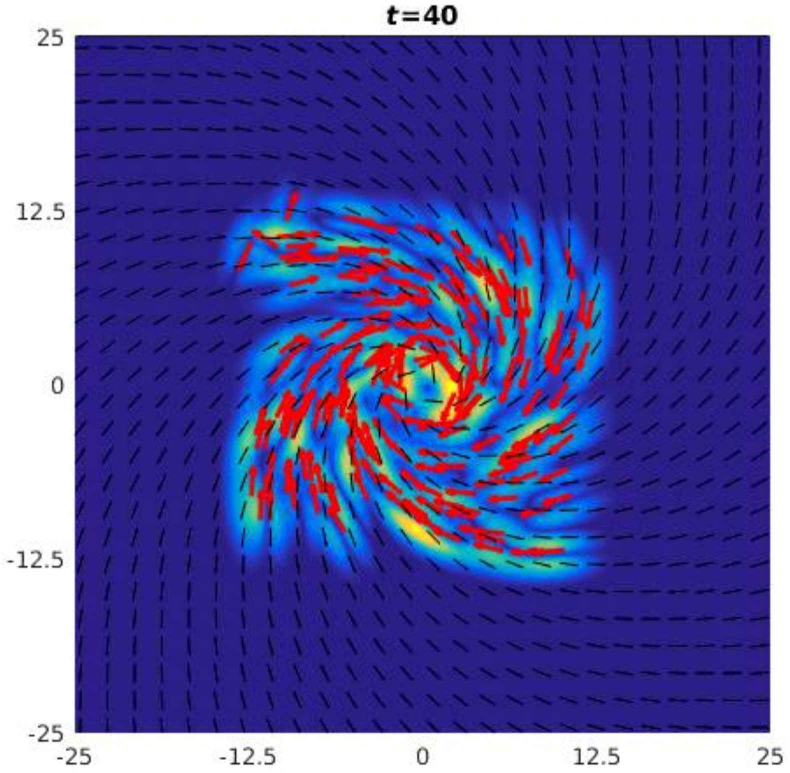
model



experiment

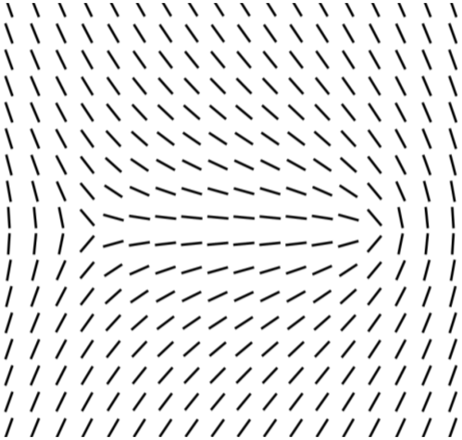


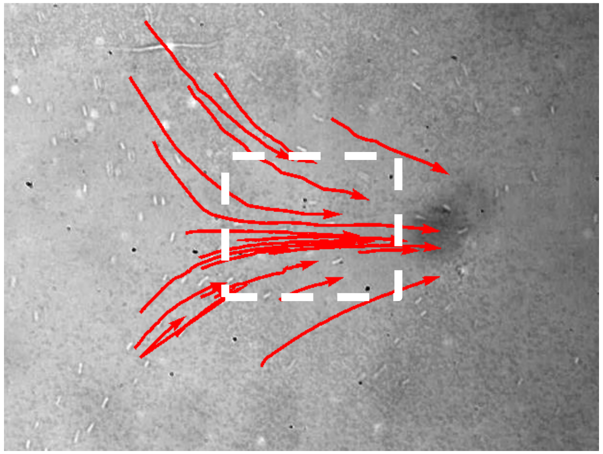
Mixed splay-bend: Forces unipolar circulation

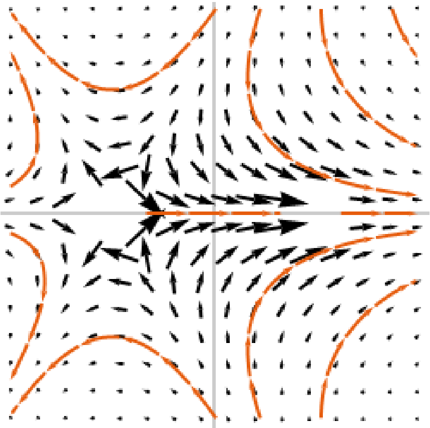


Numerical simulations: Bacteria concentrate into toroidal swirls, concentration varies in space, I. Aranson, T. Turiv, R. Koizumi et al, submitted

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





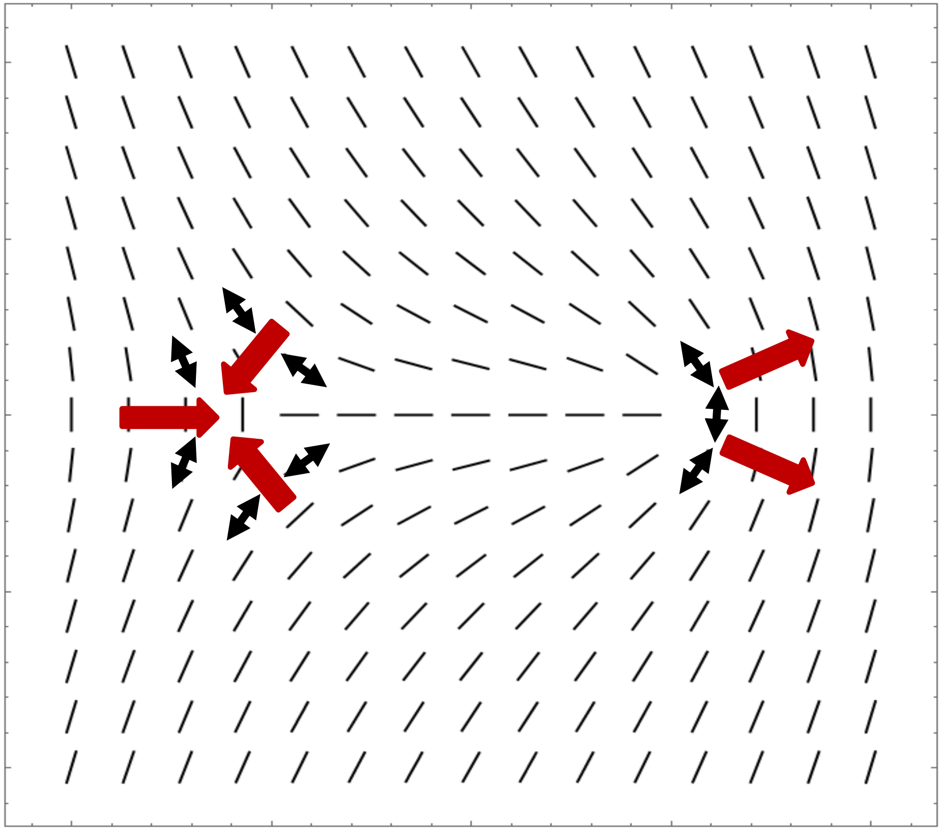


Bacteria concentrate at the cores of +1/2 defects; avoid -1/2 defects

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

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

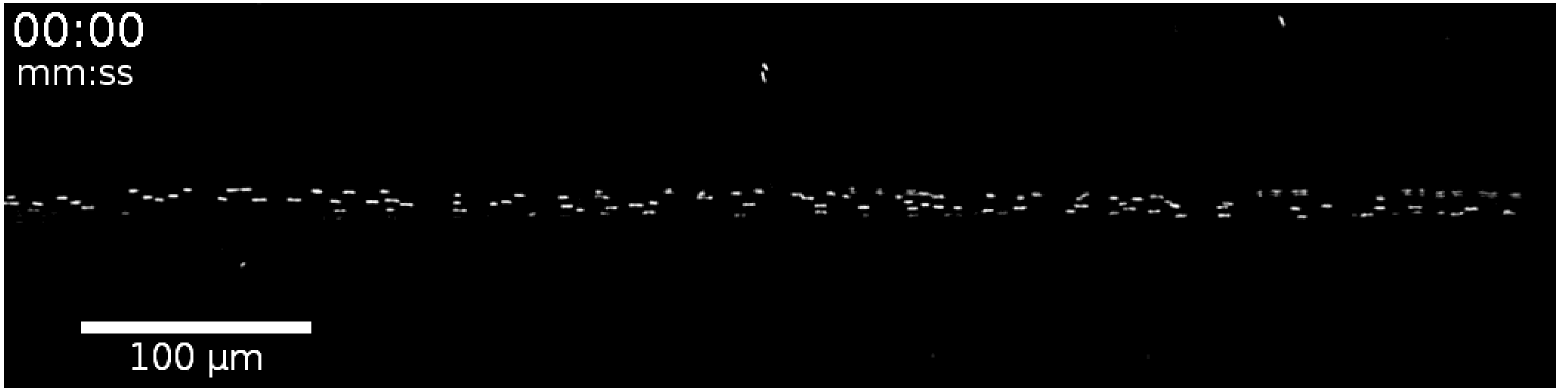
Pumping from -1/2 defect to +1/2 defect

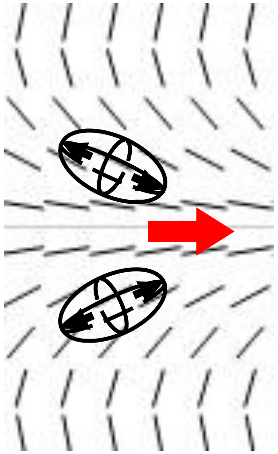


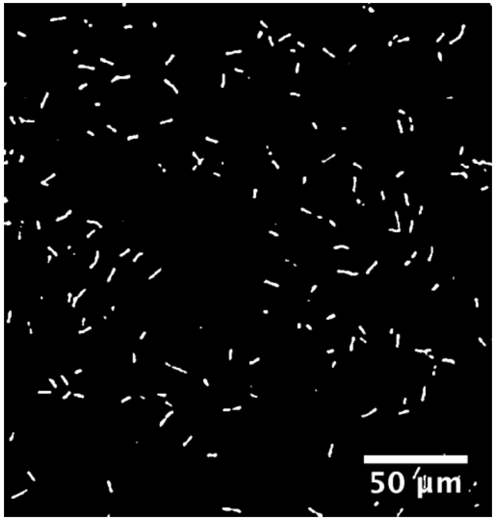
$$\mathbf{f} = \alpha\left[\hat{\mathbf{n}}\nabla\cdot\hat{\mathbf{n}} - \hat{\mathbf{n}}\times\left(\nabla\times\hat{\mathbf{n}}\right)\right]$$

Activity tends to shift the +1/2 defect to the right-hand side

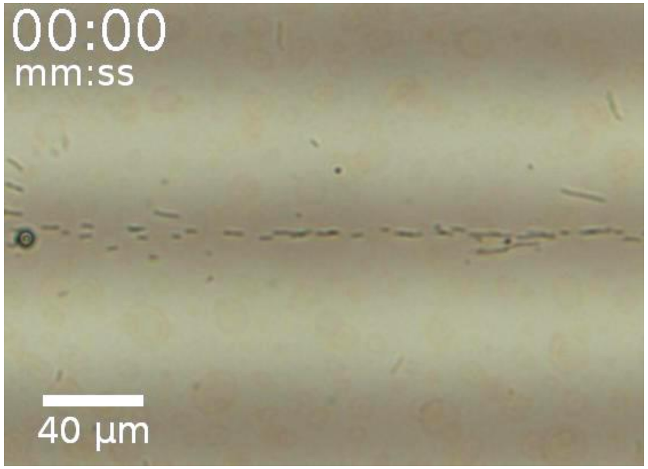
Unipolar swimming in concentrated jets:





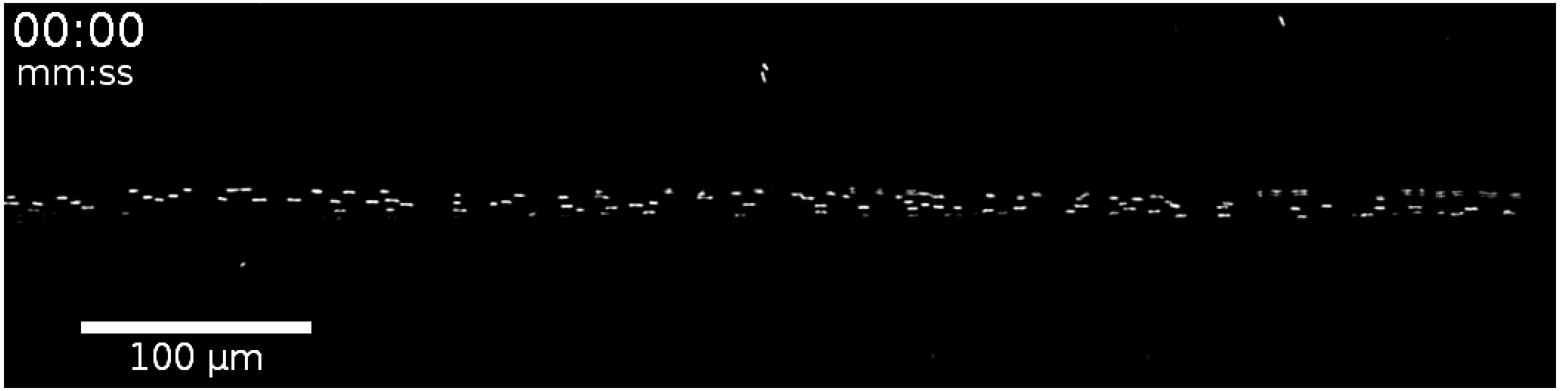


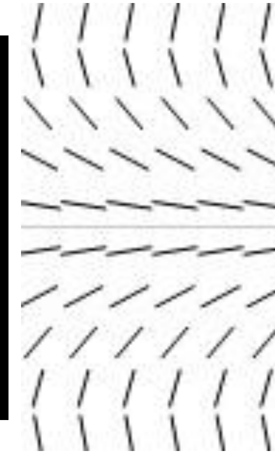
Isotropic phase; few degrees higher temperature

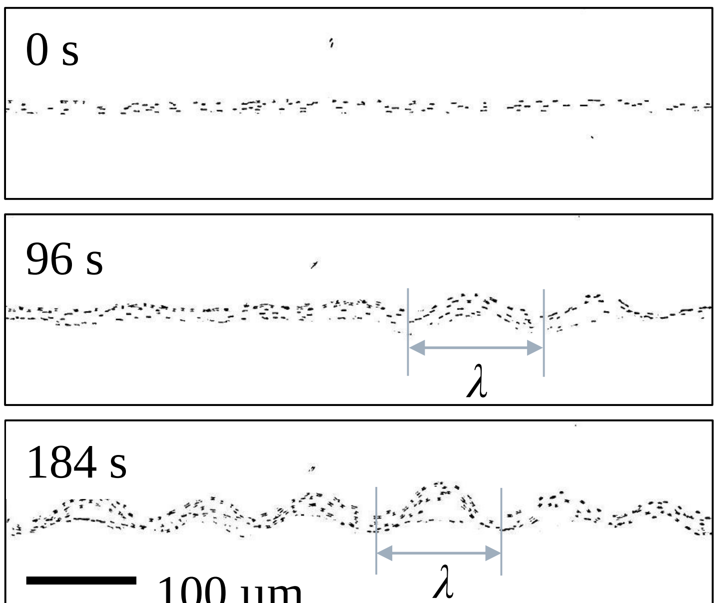


T. Turiv, R. Koizumi et al, *Nature Physics*, March 2, 2020; https://doi.org/10.1038/s41567-020-0793-0

Director bend limits undulations



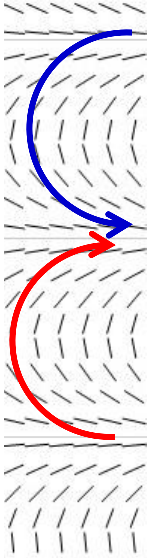


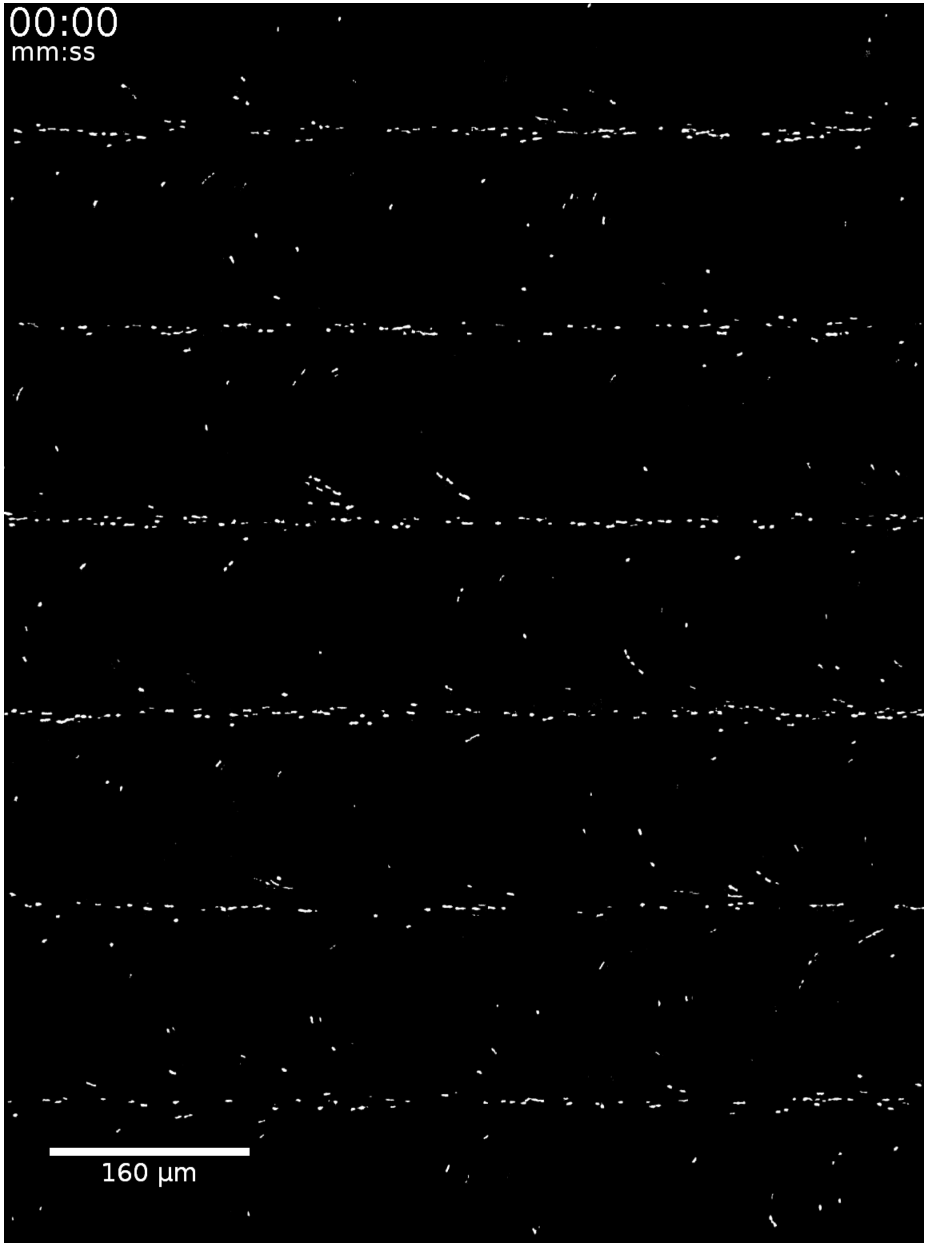


As the jets undulate, the angle between the director and the trajectory increases; viscous drag increases and some bacteria are ejected; it helps to keep the period and amplitude of undulations constant; The jets are stable at $c<7c_{critical}$ where $c_{critical}$ is the critical concentration of instability in a uniform cell

T. Turiv, R. Koizumi et al, *Nature Physics*, March 2, 2020; https://doi.org/10.1038/s41567-020-0793-0

Unipolar transport





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Conclusion-I:

- Bacteria in patterned nematic:
  - Patterns control trajectories, polarity and concentration of bacteria
  - Bacterial swirls and condensed jets are unidirectional and thus perform a useful work
  - Patterns cause unipolar threshold-less flow of bacteria, circular or linear
  - Concentration and thus activity are strongly non-uniform

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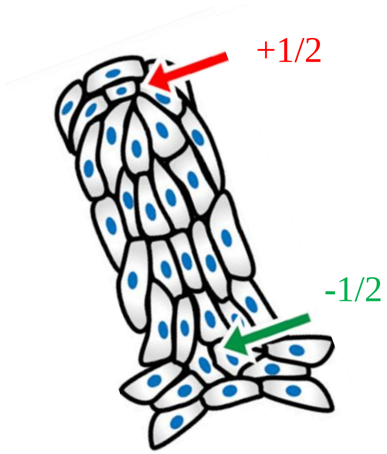

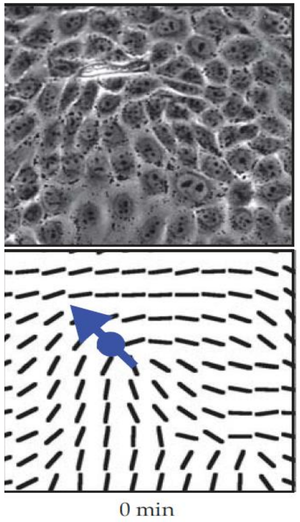

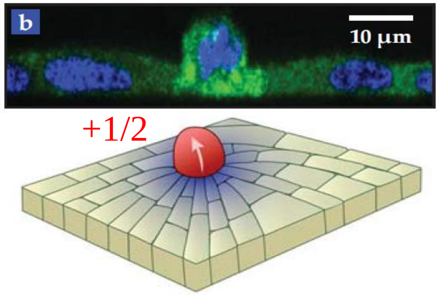

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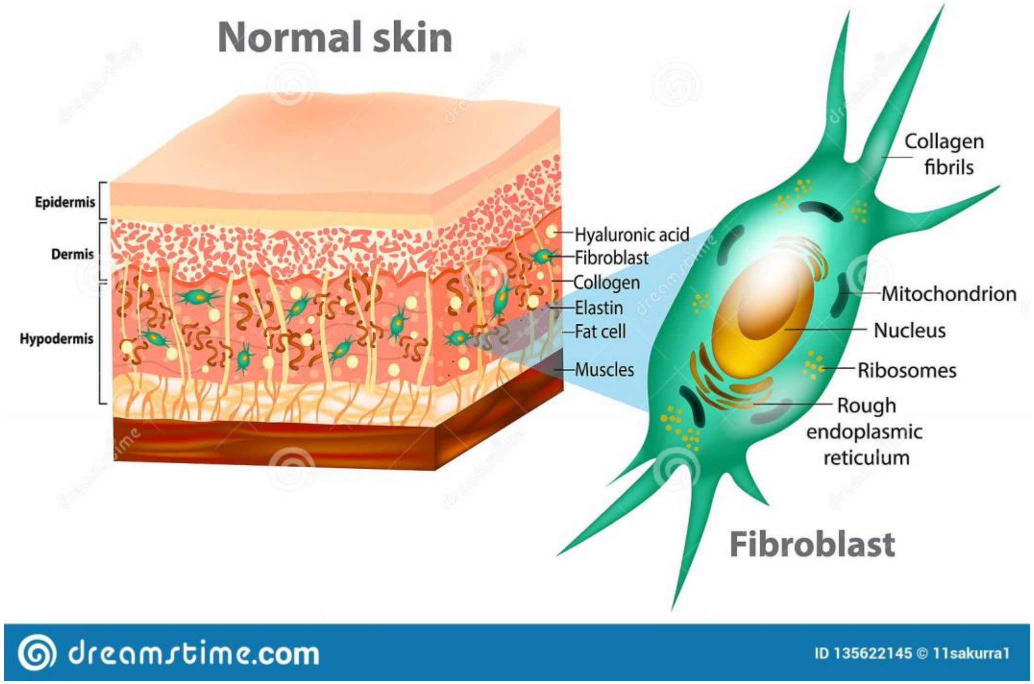
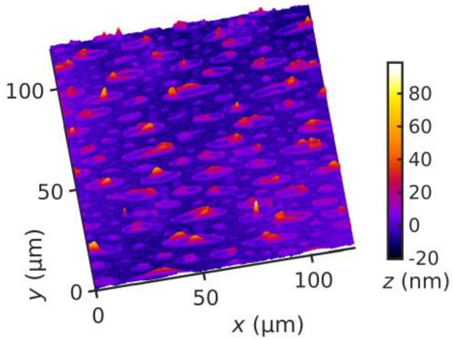
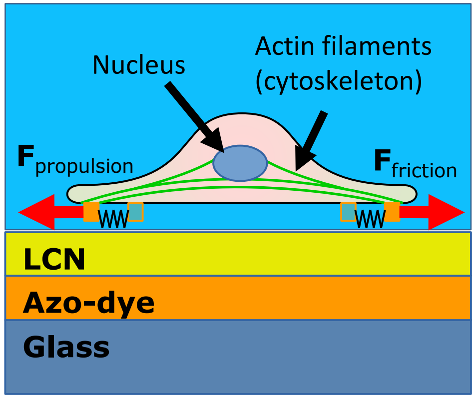
Human dermal fibroblast cells



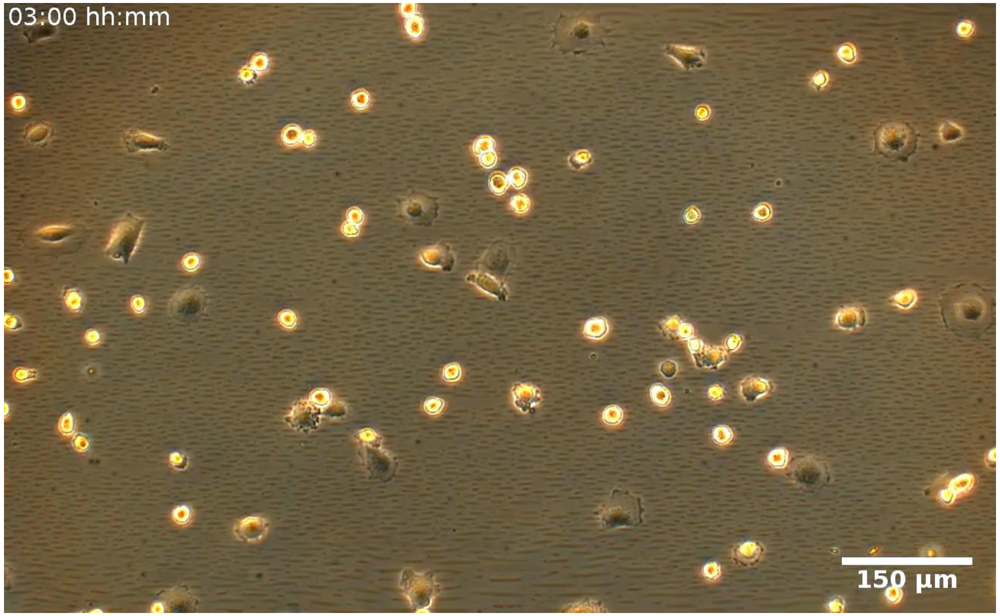
Fibroblast cells are part of skin responsible for generation of connective tissue and healing wounds

Deposition of cells onto LCN substrate from water dispersion



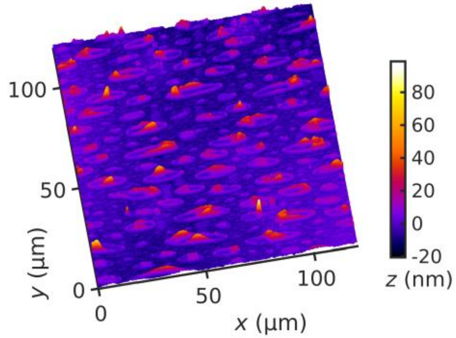


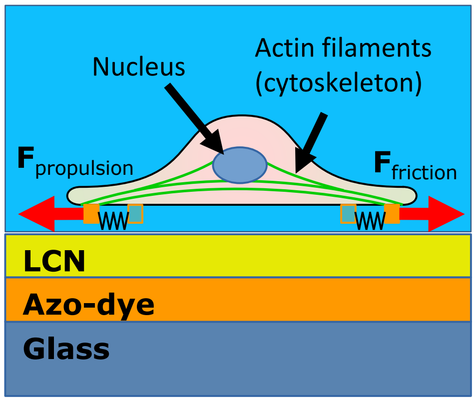
Seeding of human dermal fibroblast cells onto a uniformly aligned LCN substrate, top view



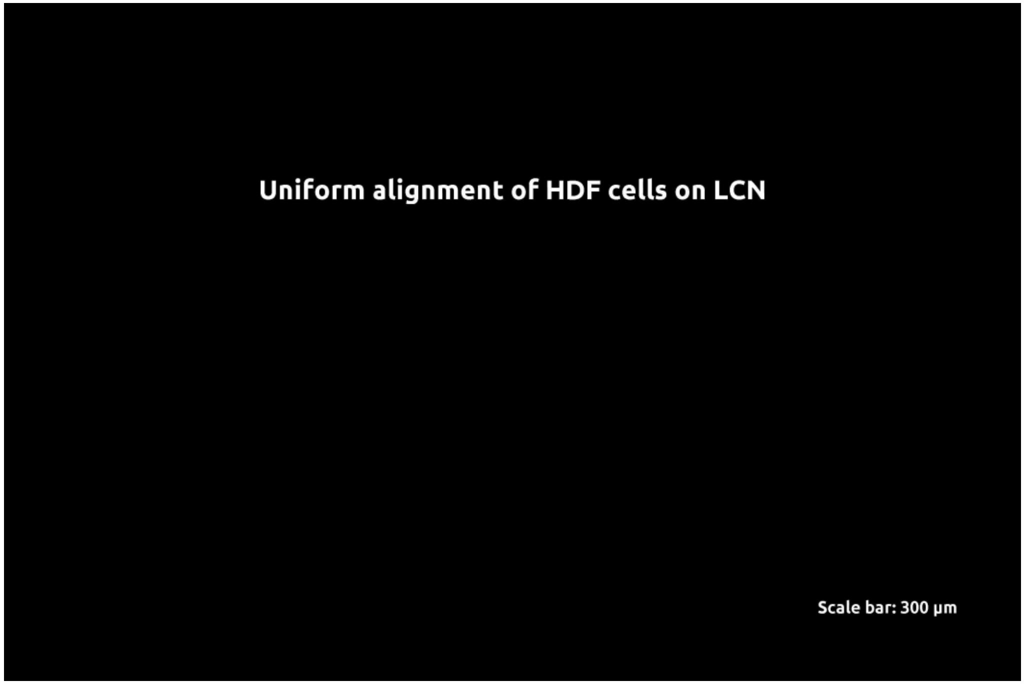
T. Turiv, J. Krieger, G. Babakhanova et al, *Science Advances*, accepted (March 2020)

Alignment of human cells at uniform LCN substrate





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



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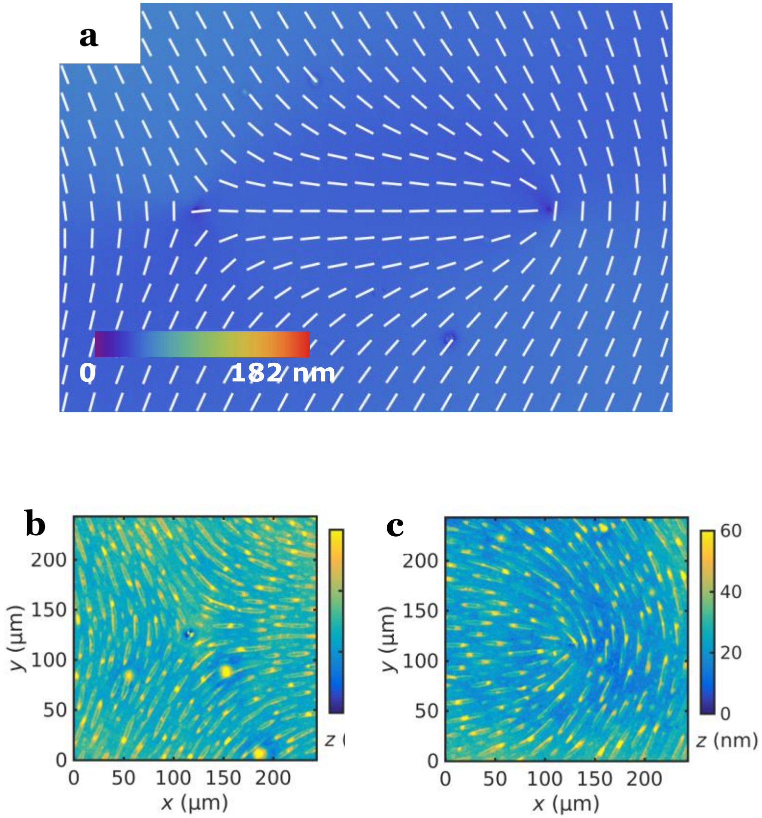
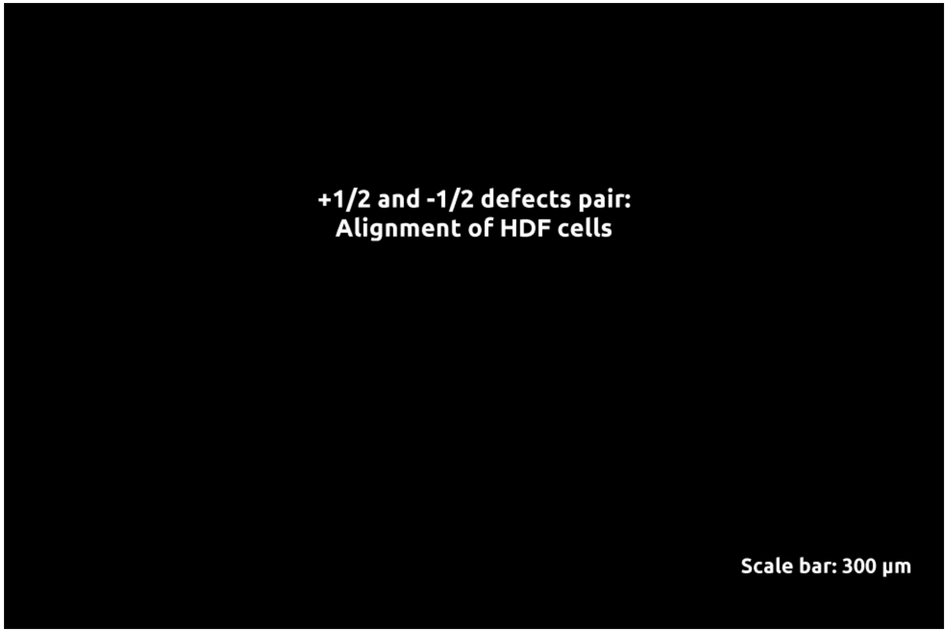
Patterns with +1/2 and -1/2 topological defects

a

b

c





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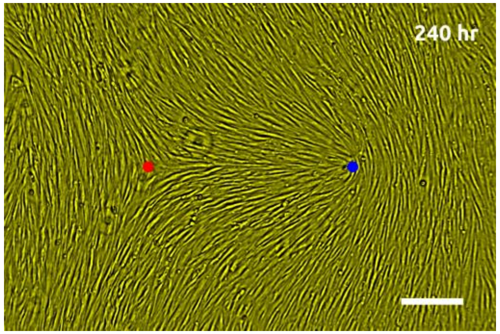
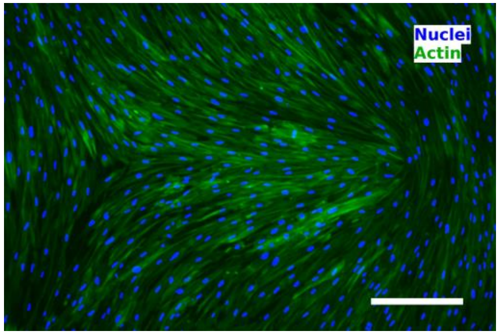
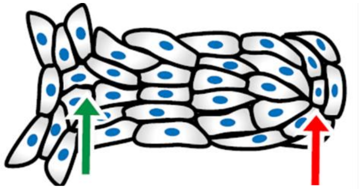
Patterns with +1/2 and -1/2 topological defects

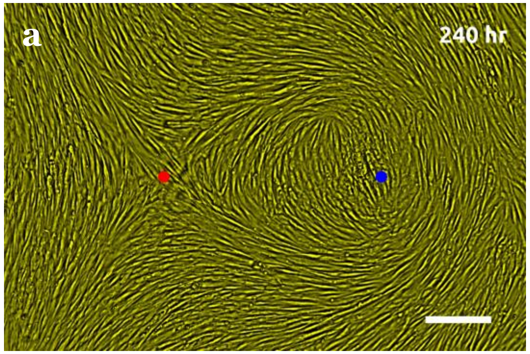


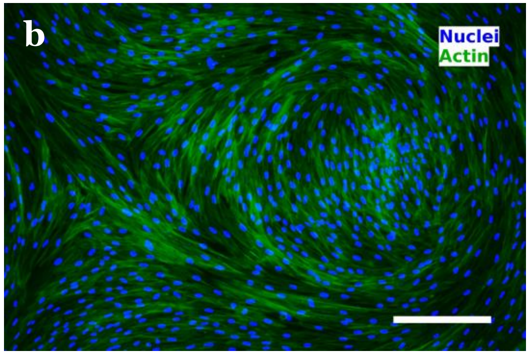




The templated tissue with ½ and -1/2 defects closely resembles the natural epithelium tissue, with that difference that the defects do not leave the predesigned locations.

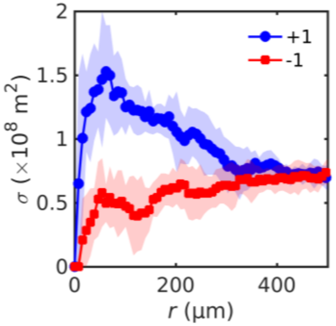
Patterns with +1 circular and -1 defects: Different concentration and phenotype of cells





All scale bars are 300 μm

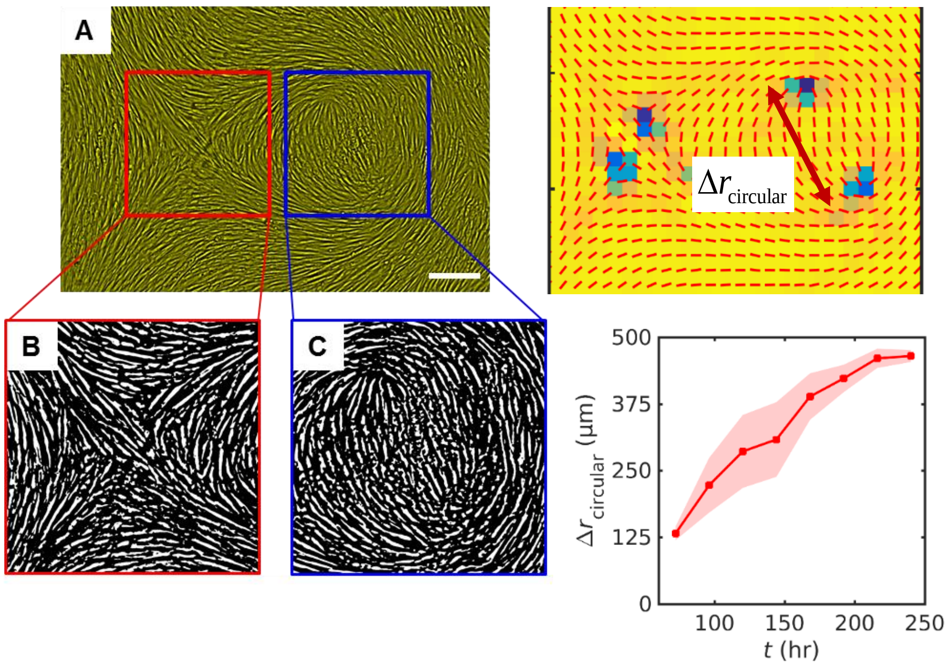
Density of cells vs radial distance from the core

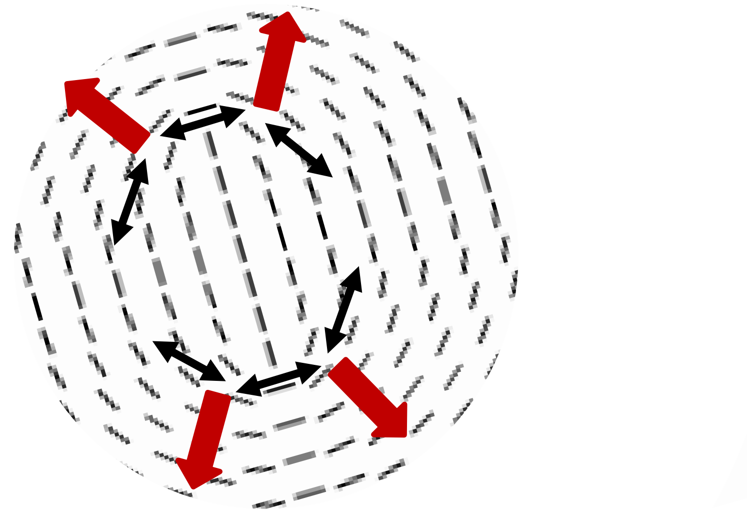


+1 defect core attracts high concentration of cells while -1 core depletes them. Since the cells are in contact with each other, variation of density leads to variation in phenotype/shape: length/width ratio =2.6 near +1 defects and =5.8 near -1 defect.

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

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

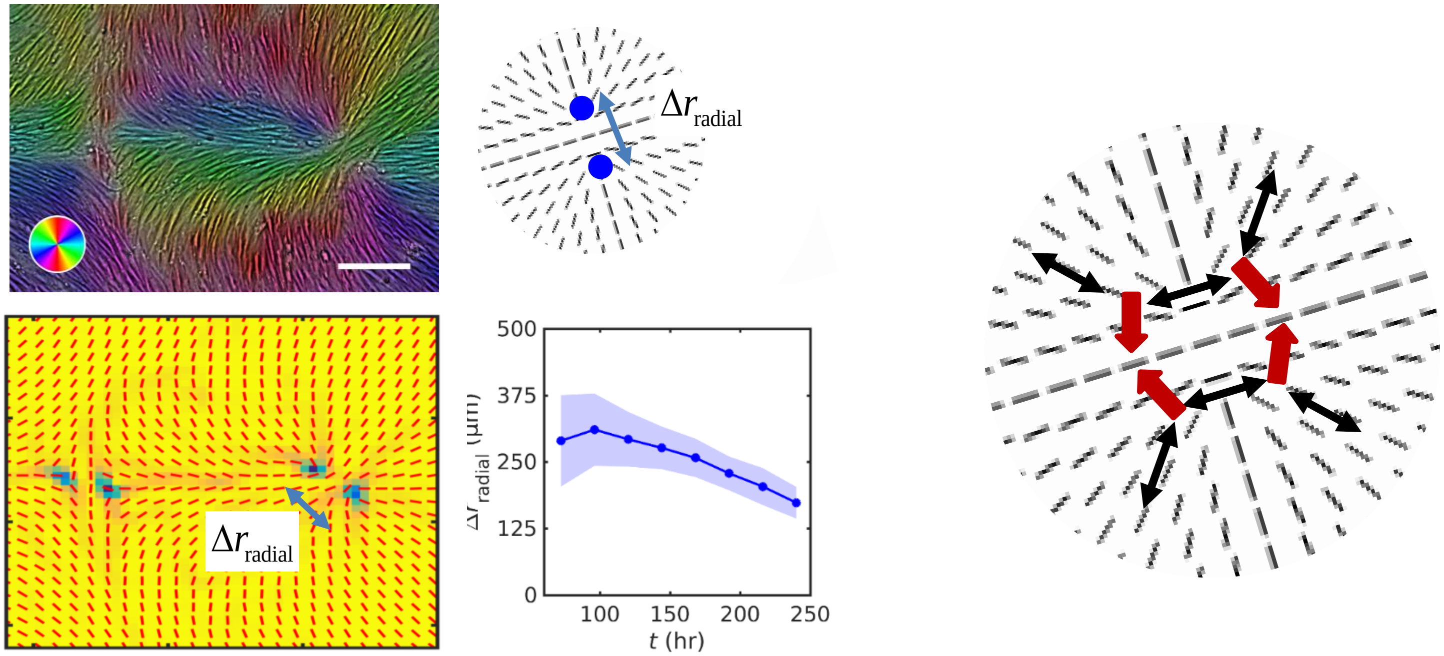




Circular +1 splits into +1/2 defects that move away from each other, which is expected as the elastic energy ~(strength)^2;

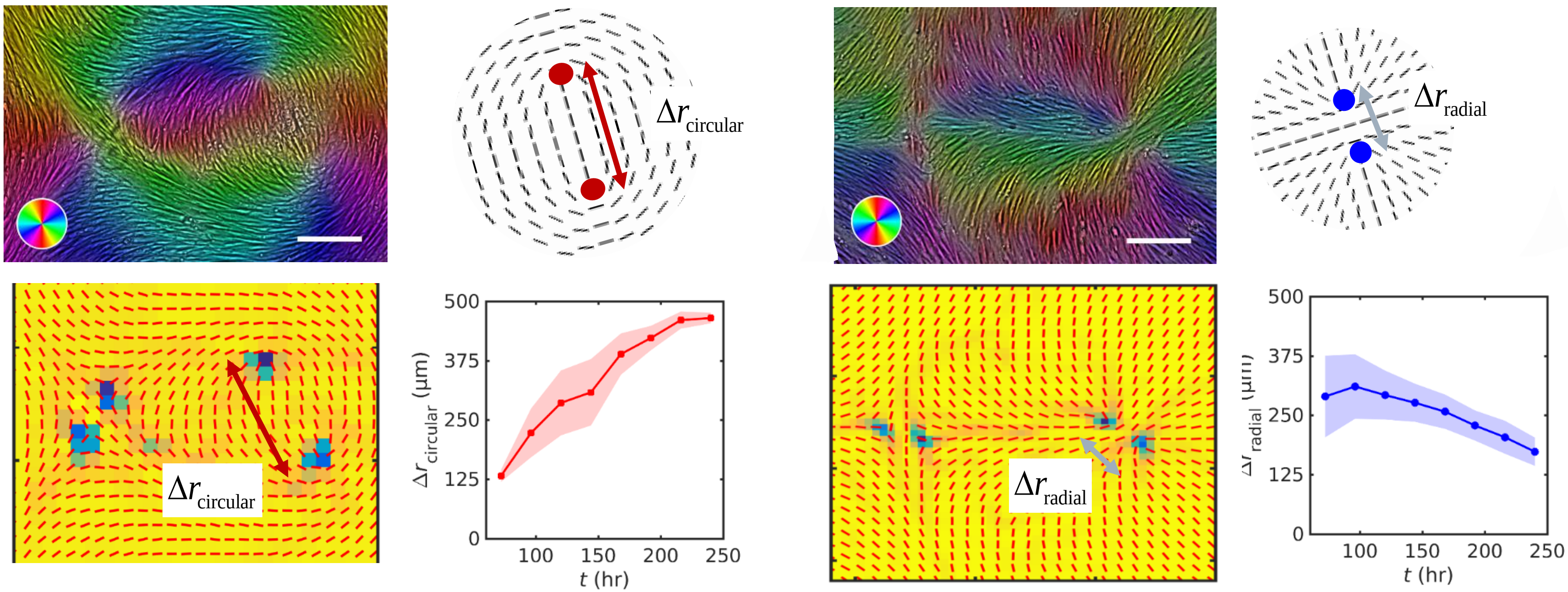
Note that the -1 defect splitting distance is shorter

Core splitting of +1 circular and radial defects into pairs of +1/2s



Radial +1 splits into +1/2 defects that move towards each other, defying elasticity!

Core splitting of +1 circular and radial defects into pairs of +1/2s



Circular +1 splits into +1/2 defects that move away from each other

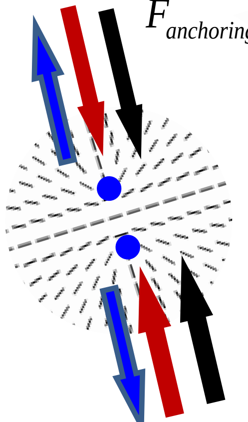
Radial +1 splits into +1/2 defects that move towards each other, defying elasticity!

Side-by-side comparison of splitting of +1 circular and radial defects into pairs of ½ defects shows that the distance of splitting is influenced by active forces, in addition to elasticity and surface anchoring

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

Core splitting of +1 radial and circular defects into pairs of +1/2s

Balance of elasticity, surface anchoring and activity:

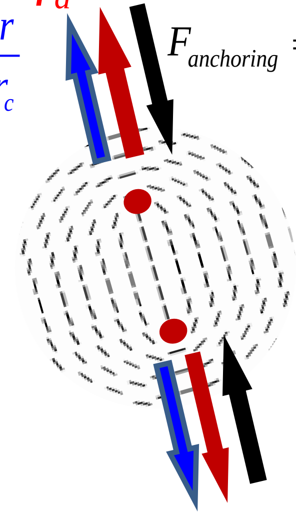


$$\Delta r^{\text{circular}}_{\text{radial}} = \left(\pm |f_a| + \sqrt{f_a^{\,2} + 0.8\pi h K W} \right) / 0.8W$$

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

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

$$f_a \approx K \approx 5\ \text{nN}; \quad W \approx 2.5\times 10^{-5}\ \text{J/m}^2$$



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

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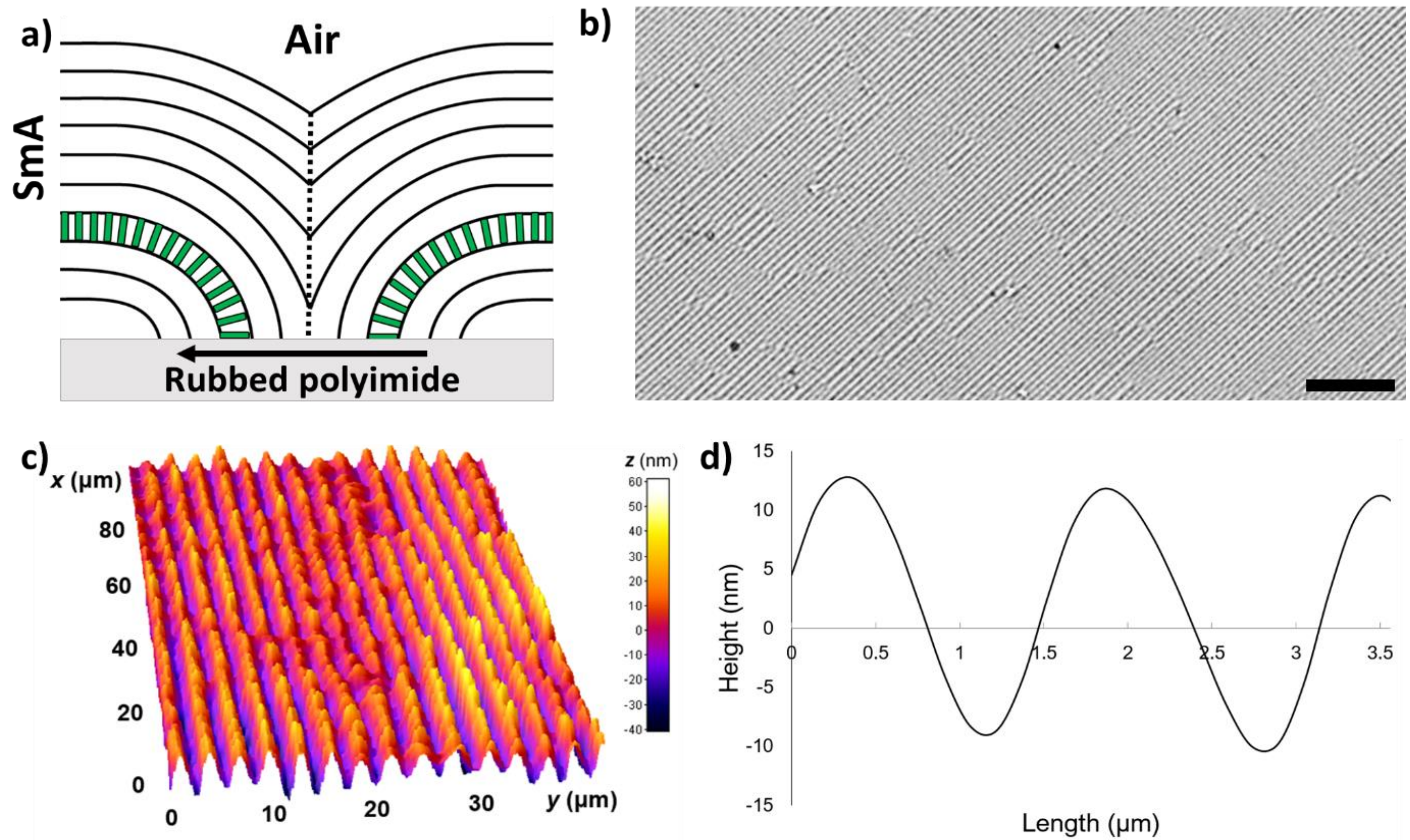
Alignment of human dermal fibroblast cells by smectic elastomers

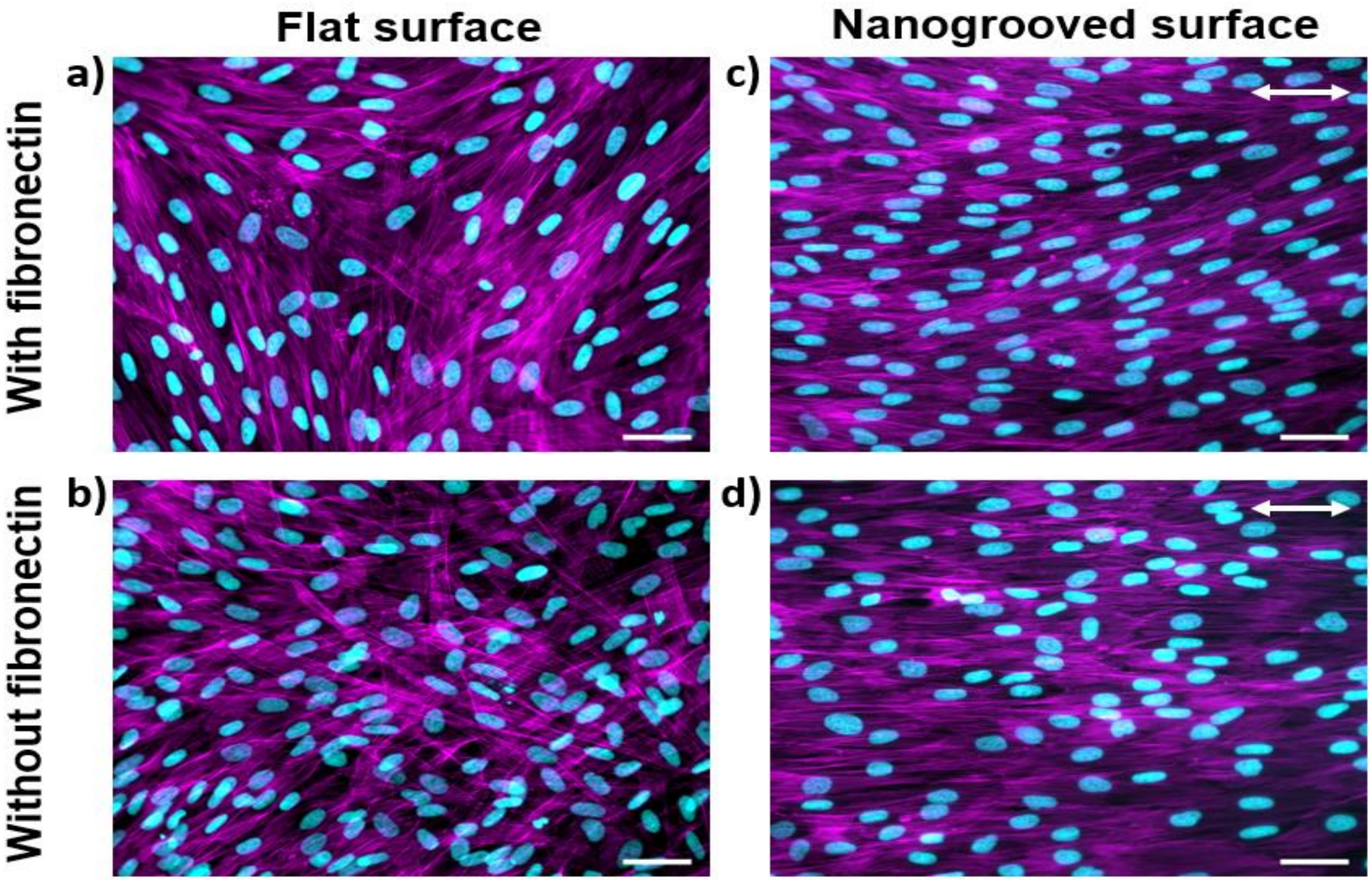
A free surface of a smectic A develops undulations associated with the hybrid character of alignment and the requirement of layers equidistance (a); a mixture of a reactive monomer RM82, smectic A 8OCB and a photoinitiator Irgacure 651 can be polymerized in this undulated state (b,c) with nanogrooves amplitude reaching 25-30 nm (d)



G. Babakhanova, J. Krieger et al, *J. Biomed. Mater. Rec*, DOI: 10.1002/jbm.a.36896 (2020)

Alignment of human dermal fibroblast cells by smectic elastomers

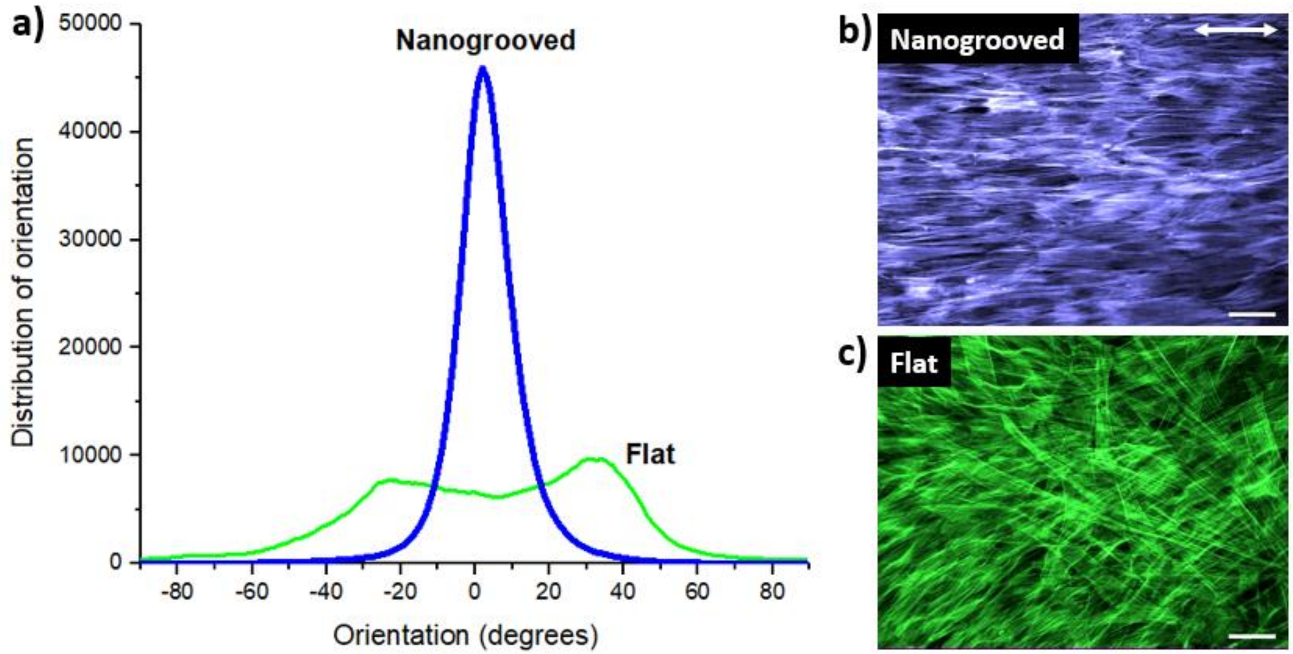
Fluorescent microscopy images of hDF grown on substrate **a,b)** flat glass with fibronectin, **c,d)** glass with nanogrooved smectic A elastomer. Note the uniform alignment of cells by the smectic A elastomer nanogrooves ariented along the arrows. Scale bars 50 μm.



G. Babakhanova, J. Krieger et al, *J. Biomed. Mater. Rec*, DOI: 10.1002/jbm.a.36896 (2020)

Alignment of human dermal fibroblast cells by smectic elastomers

Comparison of actin filament orientation by nanogrooved smectic A elastomer and by flat surface. Scale bars 50 μm.



G. Babakhanova, J. Krieger et al, *J. Biomed. Mater. Rec*, DOI: 10.1002/jbm.a.36896 (2020)

Conclusion-II

- Liquid crystal elastomer coatings of nematic and smectic A type control human dermal fibroblast tissues
  - Patterned LC network in contact with aqueous solution produces elevations that guide patterned growth of cells
  - Undulation instability of smectic A elastomer creates nanogroves for cell alignment
  - Human dermal fibroblast tissues follow the predesigned LC network and behave as extensile active matter with +1/2 defects moving in the plane of the tissue
  - 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

- Patterned liquid crystals can control trajectories, polarity of swimming and concentration distribution of swimming bacteria
- Patterned liquid crystal polymers can be used to design arrays of biological cells with predetermined locations of topological defects