Active Self-Organizing Matter

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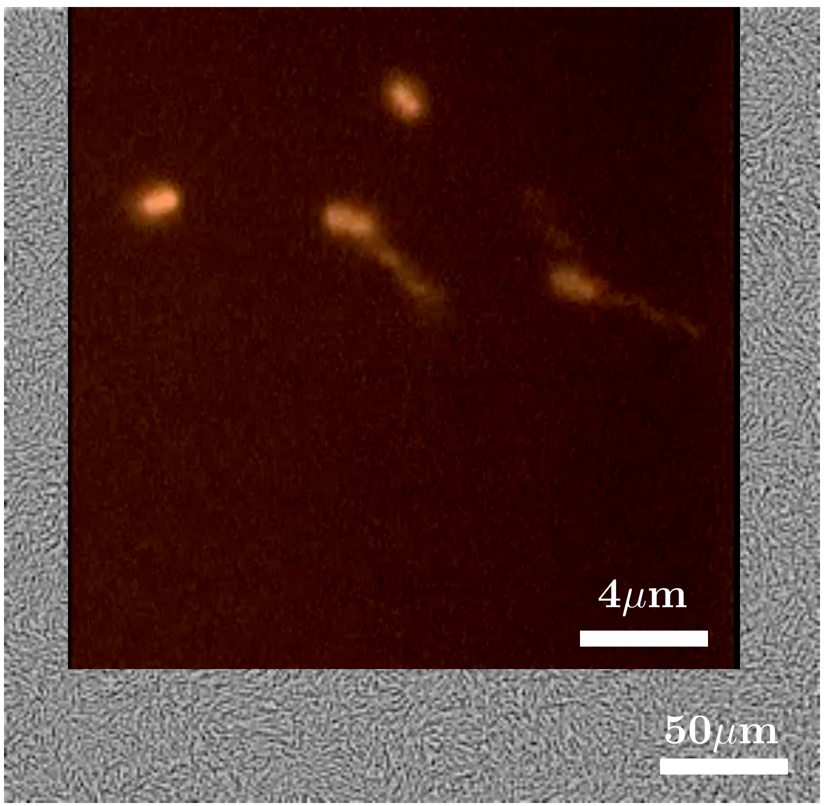
NBIA MSc day, October 2019

Active matter: nature's engines that power life

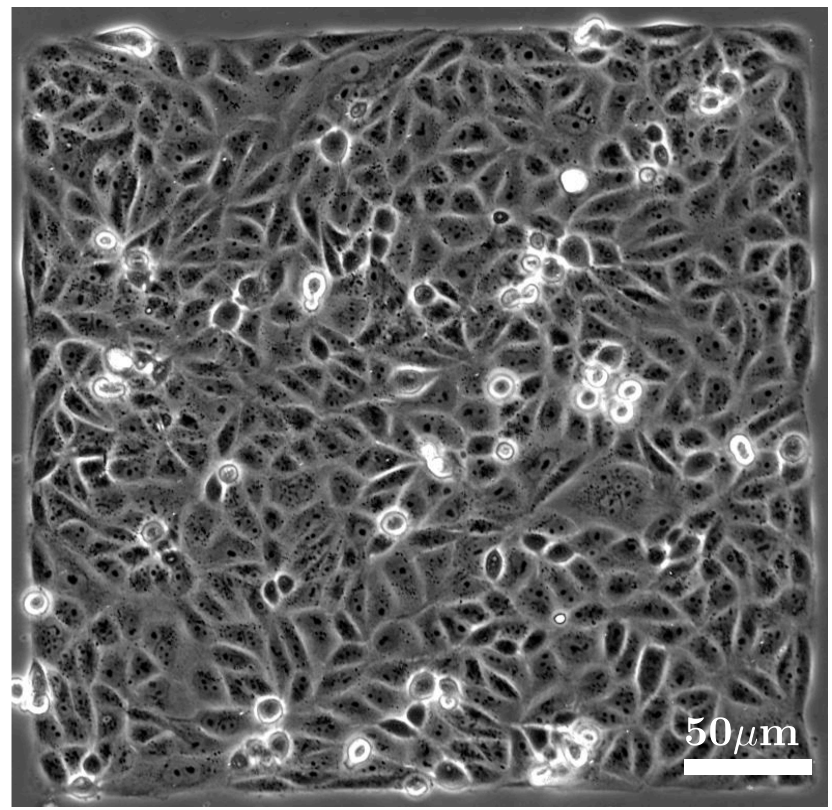
- Out of thermodynamic equilibrium
- Local energy injection
- Collective Motion

E. coli bacteria



Bacterial swarm, Wensink et al, PNAS (2012)

Human skin cell
Cellular tissue



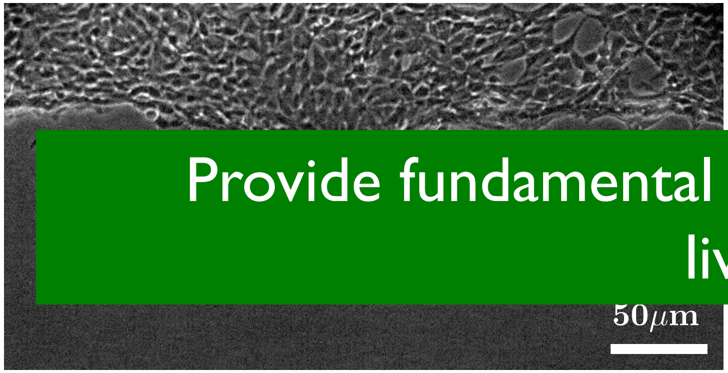
Benoit Ladoux's Lab, CNRS, Paris

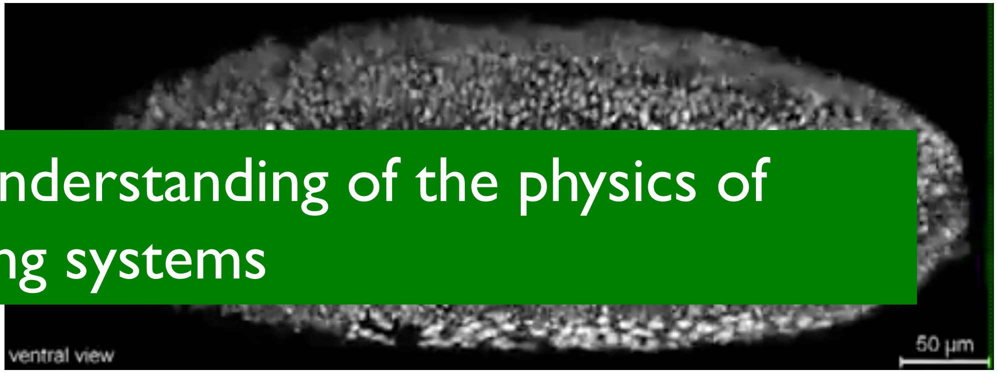
Significance

- **Biology and Health**

Cell invasion

Organ development (morphogenesis)





Provide fundamental understanding of the physics of living systems

Breast cancer cells, Lene Oddershede, NBI

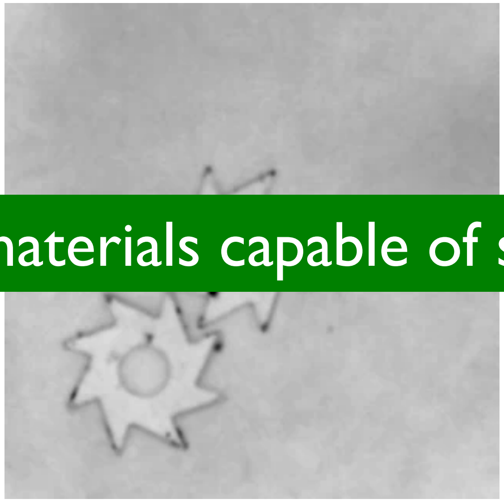
Fly embryo, Tomer, et al., Nature. Meth.,2012

- **(bio) Technology**

Biomimetic design / micromachines

Mi

Emulate nature to make materials capable of self-organisation



Microgears in bacterial bath, Sokolov et al., PNAS, 2010

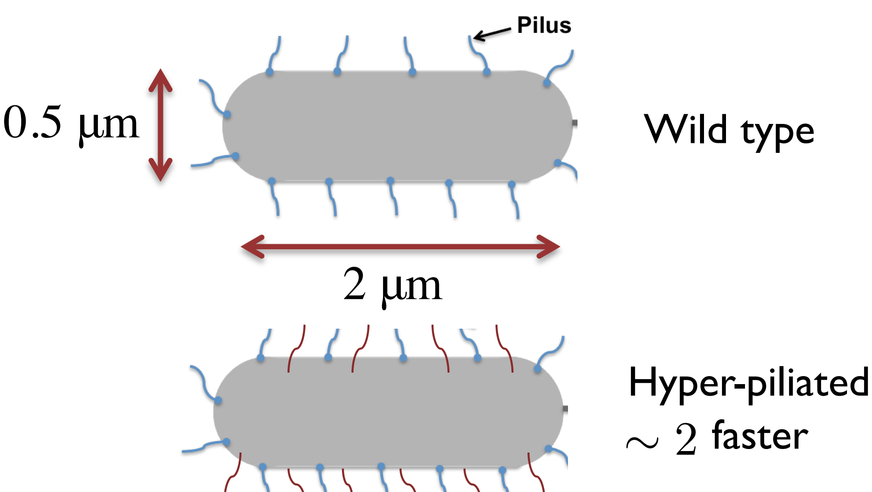
Self-deforming droplets, Keber et al., Science, 2014

Cell Competition

with Oliver Meacock (Oxford Zoology)
William Durham (University of Sheffield)

Two competing bacteria types

- Make fast moving and slow moving bacteria, which one spreads faster?
- Pseudomonas. aeruginosa: infectious, antibiotic resistant bacteria



Nasty picture of Pseudomonas infection

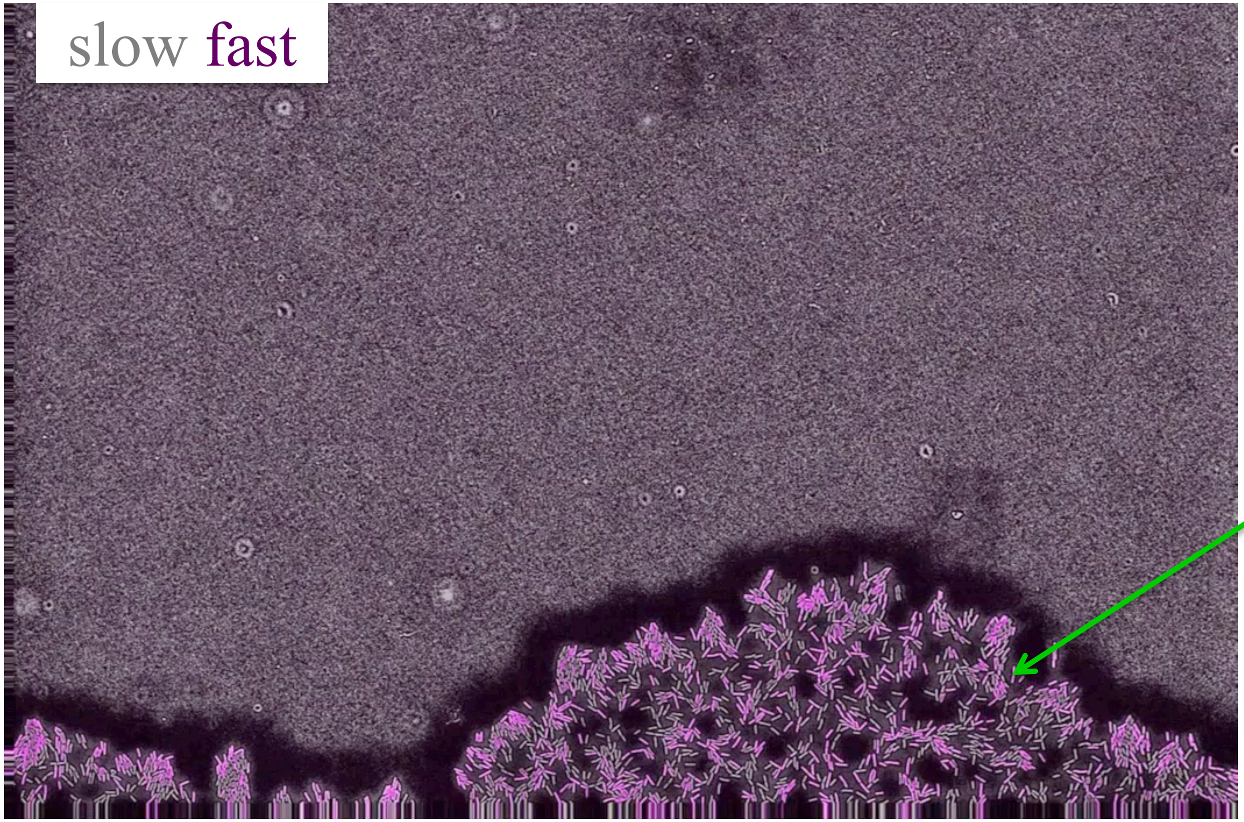
Slow vs fast bacteria: collective invasion

- Individual $\Delta pilH$ cells are ~ 2 times faster than individual WT cells

Slow moving bacteria (normal) outcompetes the
fast (hyper-mutated) one !

Competition in a mixture of fast & slow bacteria

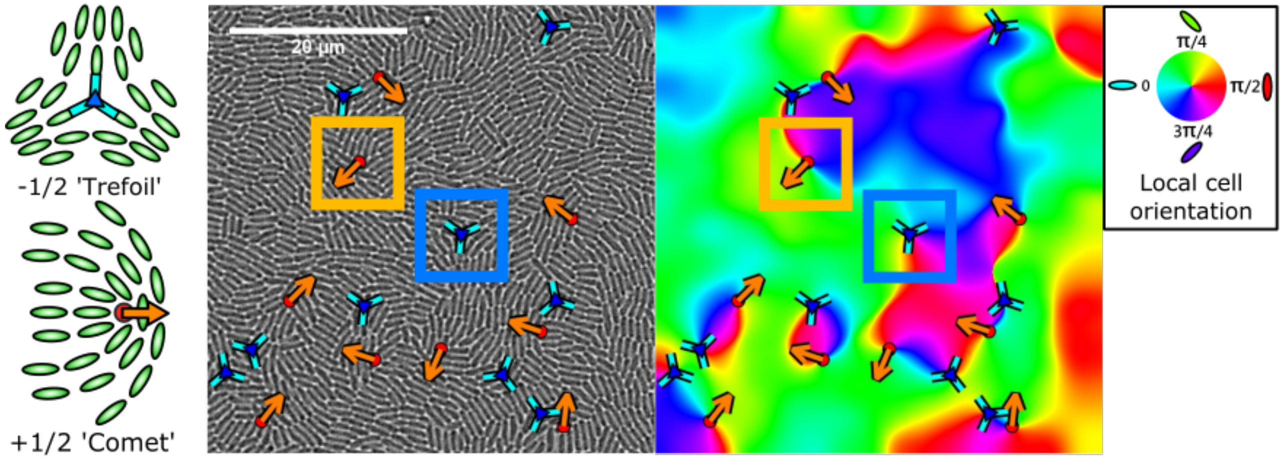
- Mixing fast moving and slow moving bacteria, which one spreads faster?



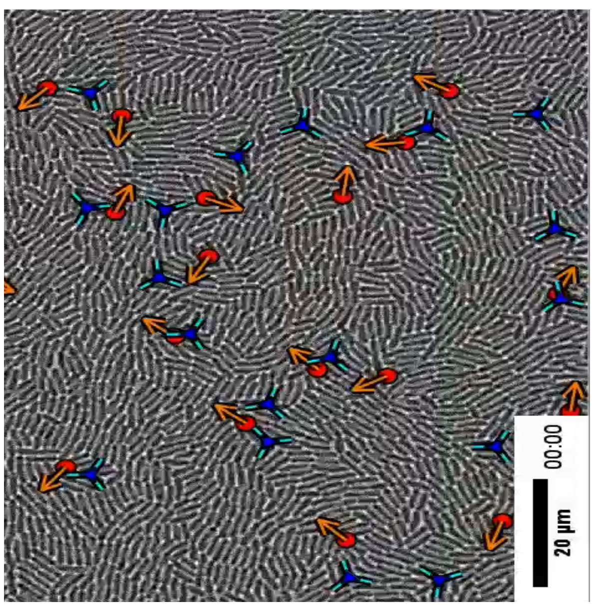
Rosettes from

Slow moving bacteria (normal) outcompetes the fast (hyper-mutated) one !

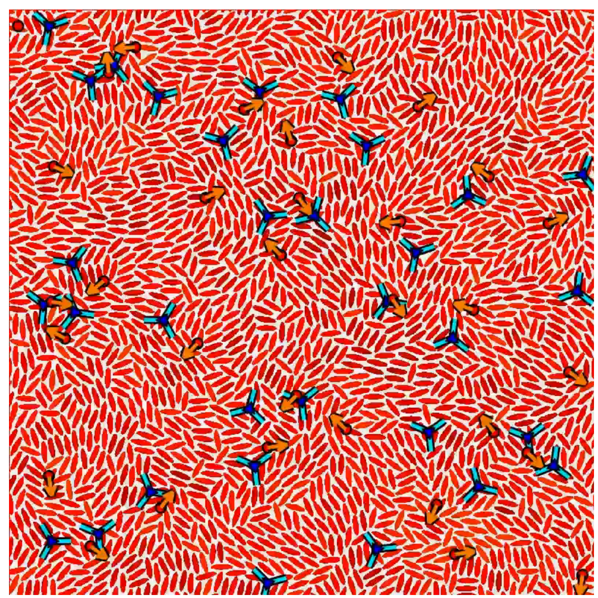
Bacteria show physics of liquid crystals



Experiment



Discrete Model



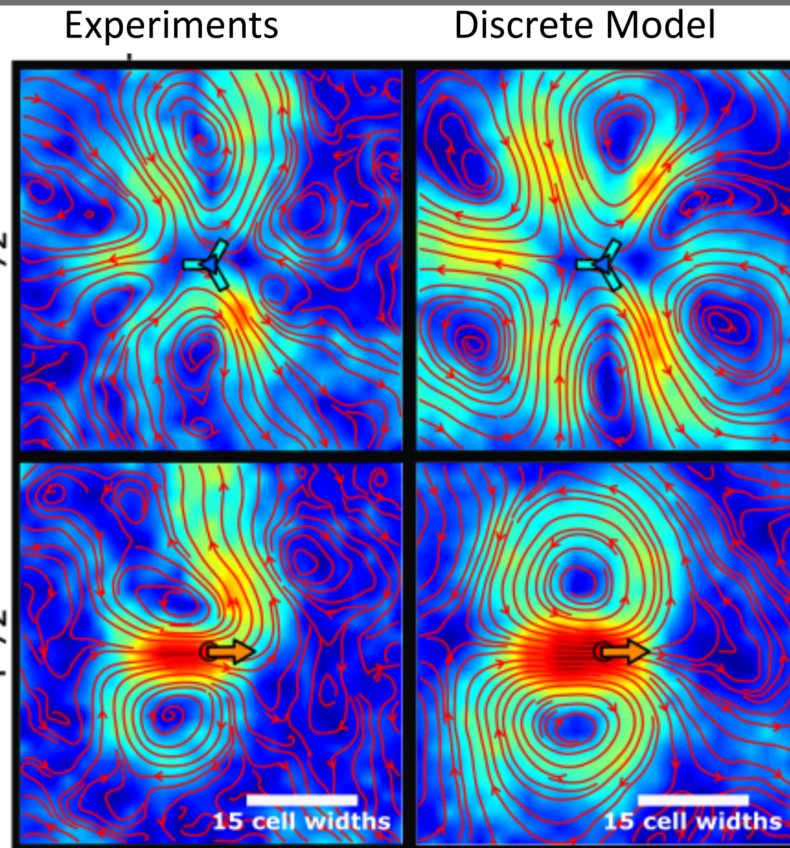
Self-propelled Rods (SPR):

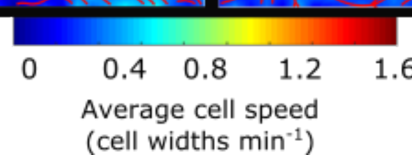
- Hard rods interacting via volume exclusion
- Each rod subject to a driving force

$$f_r \frac{\partial \underline{r}}{\partial t} = -\frac{\partial U}{\partial \underline{r}} + F^{\text{active}}$$

$$f_\theta \frac{\partial \theta}{\partial t} = -\frac{\partial U}{\partial \theta}$$

Topological defects in bacterial colonies





Continuum model:

- Active liquid crystal equations

$$(\partial_t + \underline{u} \cdot \underline{\nabla})\underline{\underline{Q}} - \underline{\underline{S}} = \frac{1}{\gamma}\underline{\underline{H}}$$

$$\rho(\partial_t + \underline{u} \cdot \underline{\nabla})\underline{u} = -\underline{\nabla} p + \underline{\nabla} \cdot \underline{\underline{\Pi}}$$

$\underline{\underline{Q}}$ Orientational order parameter

$\underline{u}$ Velocity

$\underline{\underline{\Pi}}$ Viscous + elastic + active stress

Simha & Ramaswamy, PRL (2002)

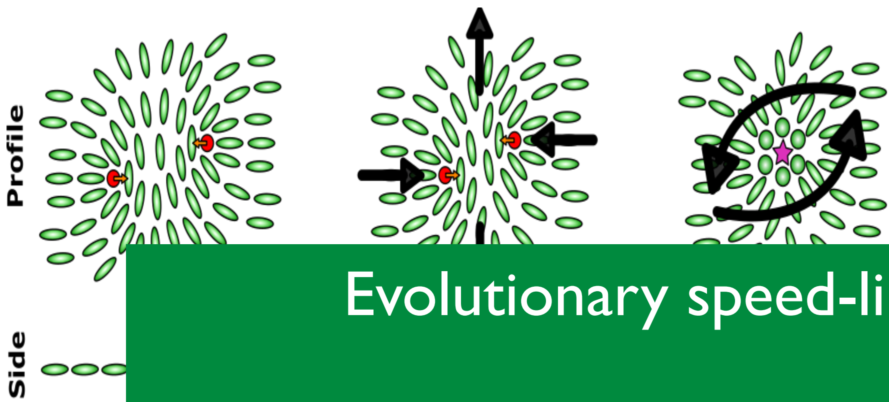
Giomi et al., Phil. Trans. Roy. Soc. A. (2015)

Prost, Julicher, Joanny, Nat. Phys. (2015)

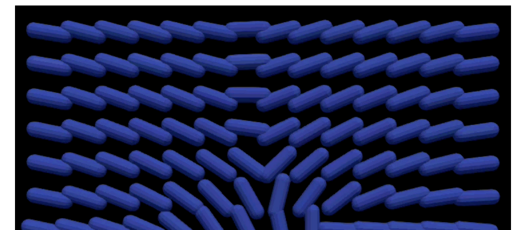
Doostmohammadi, et al., PRL (2016)

Bacteria stand up when two defects collide

Fast defect collision pushes bacteria out of plane

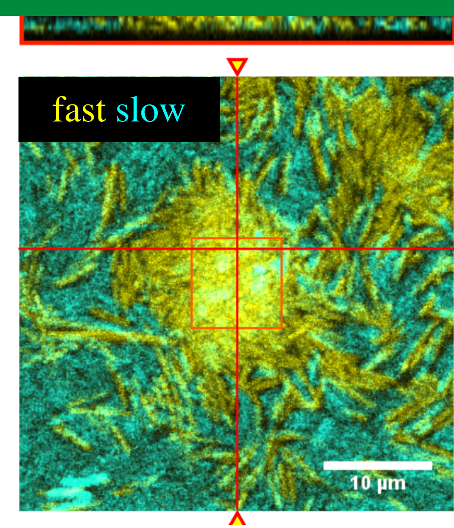


Defects collision in fast moving rods



Evolutionary speed-limit on bacterial colonies

Fast bacteria get trapped in structures of their own creation



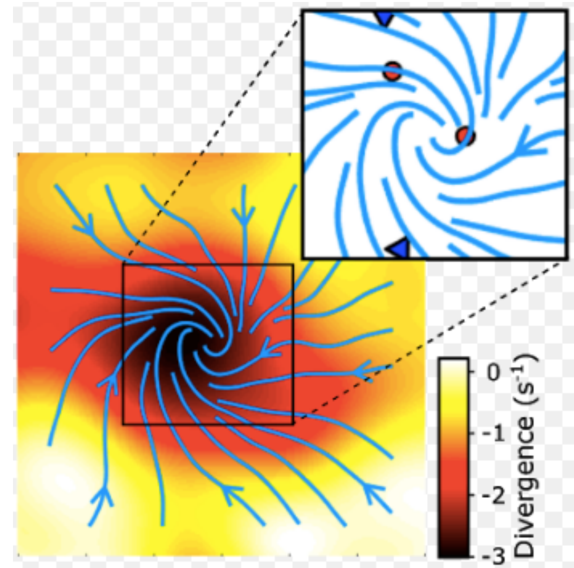
Experiments:
fast moving bacteria (yellow) stand up when two defects approach and once stood up they can not spread anymore

Project: Analytical

Calculating the flow field associated with rosettes

Involves:

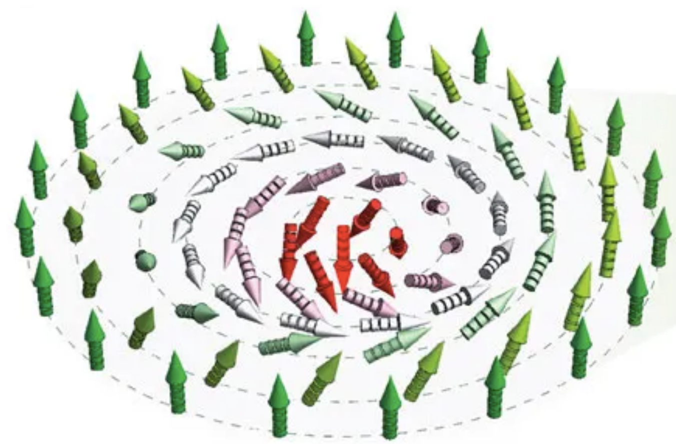
- mean field theory of active liquid crystal
- topological excitations
- Green’s function calculation
- Collaboration with experimental group in Oxford



Experimentally measured flow field

Are they half-skyrmions?

Skyrmions are topological solitons reported in Bose-Einstein condensates, superconductors, thin magnetic films, and chiral nematic liquid crystals.



Cell Decision-making

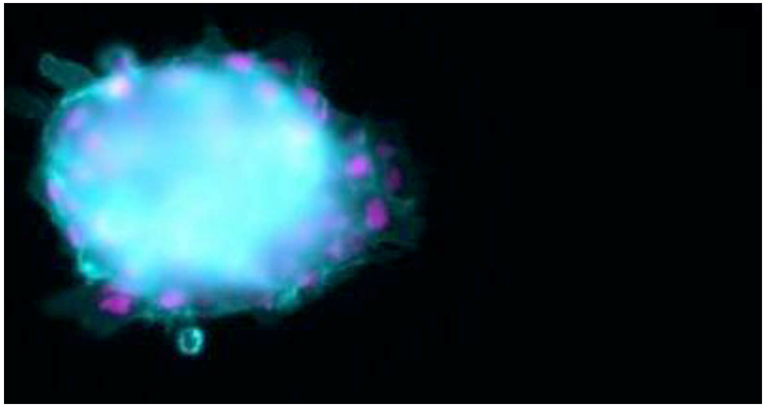
Cells sense mechanical forces

Renaissance in Biophysics

- Force measurement at single cell and at tissue level
- Mechanotransduction:

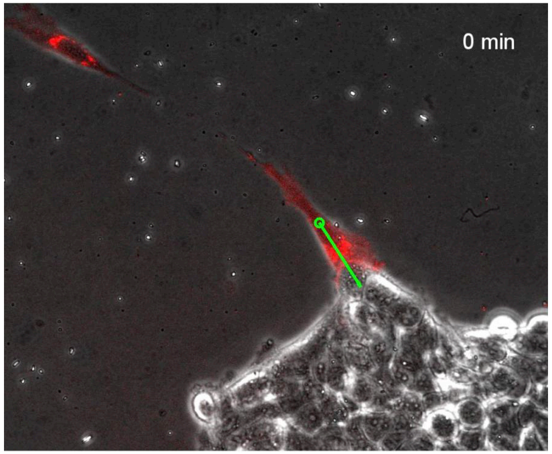
read mechanical cues → translate into cell function (cell division/death, migration)

- Master regulator: YAP (yes-associated protein)

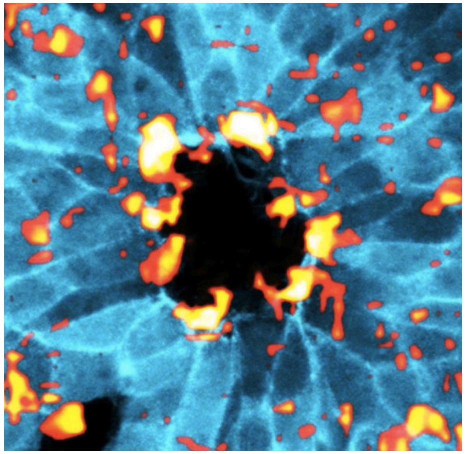


substrate stiffness

Tissue stiffening coordinates cell migration in organ development



Cell-level force guiding tumour mass

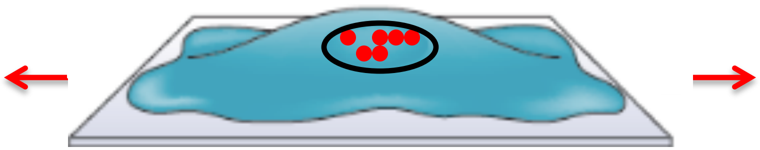
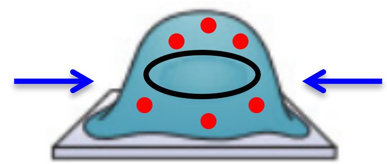


Tissue level forces driving wound healing

Mechanical forces determine cell response

- Reading forces by shuttling protein (YAP) between nucleus & cytoplasm:

Physical deformation of cell

Stretching	compression
	
Protein in nucleus	Protein in cytoplasm
↓	↓
active (ON)	inactive (OFF)
↓	↓
cell division cell migration	cell death impaired motility

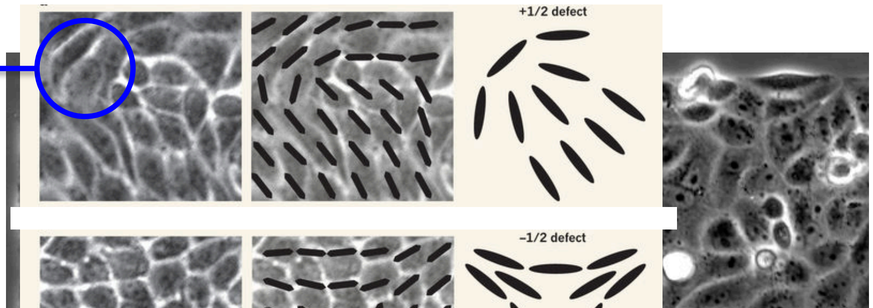
Regulation of signaling ➔ shapes organ during development

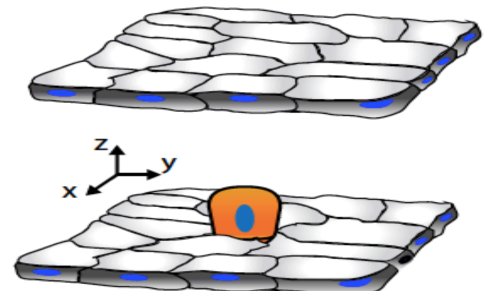
Deregulation of signaling ➔ leads to multiple diseases

Excessive force ➔ signal overactivation ➔
- Unrestrained division
- Cancer development

Defects control cell death

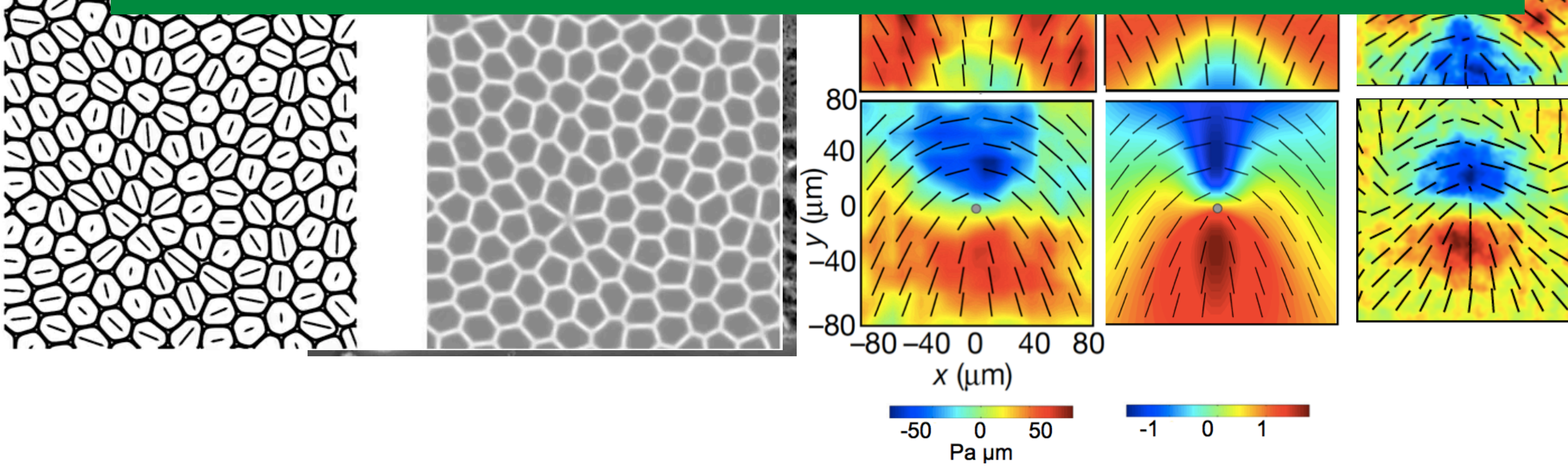
cells die and expelled in this area





High levels of mechanical stress at topological defects

This makes topological defects hotspots for cell death & extrusion in epithelia



Saw*, Doostmohammadi*, et al., "Topological defects in epithelia govern cell apoptosis and extrusion", Nature (2017)

Mueller, Yeomans, Doostmohammadi, "Emergence of active nematic behavior in monolayers of isotrorpic cells", PRL (2019)

Project: Analytical + computational

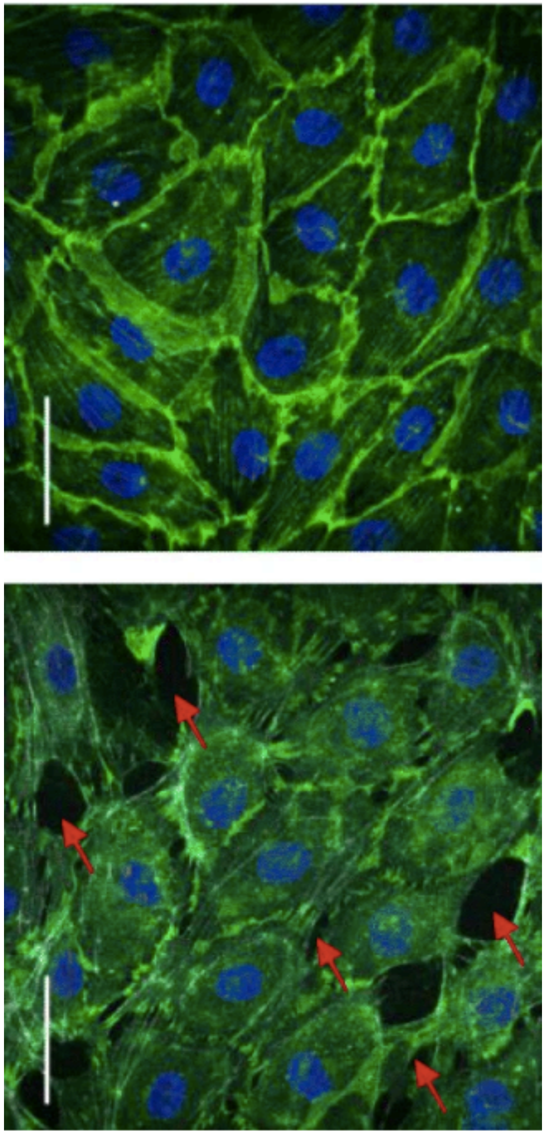
Studying the defects in stress field & their cross-talk with defects in orientation field

Involves:

- mean field theory of active liquid crystal
- topological defects
- Numerical simulations of active matter
- Collaboration with experimental groups in Paris & Japan

Do they have a biological functionality?

We examine a hypothesis that defects in stress field are responsible for gap formation in tissues.

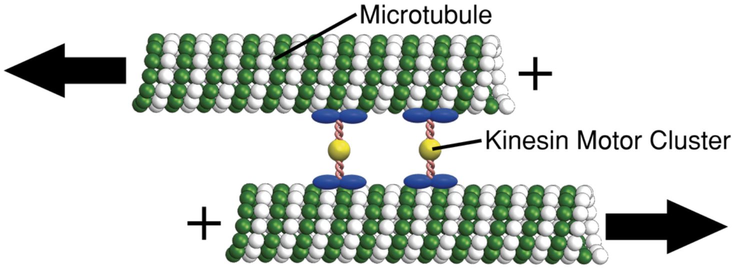


Gap formation in cells lining surface of blood vessels

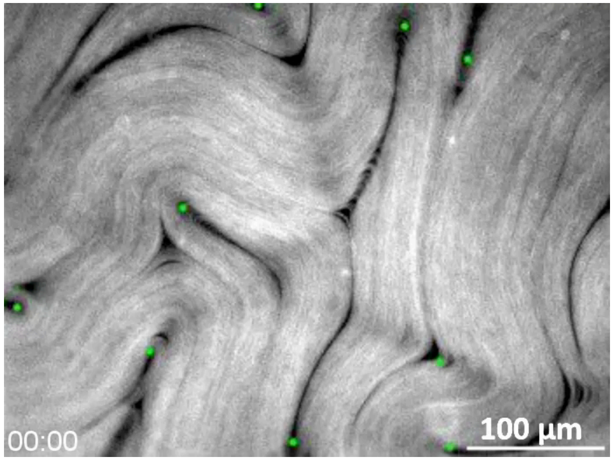
Bioinspired, Self-Pumping Fluid

Bioinspired self-organizing matter

System made of subcellular filaments + motor protein



Sanchez et al., Nature 2012

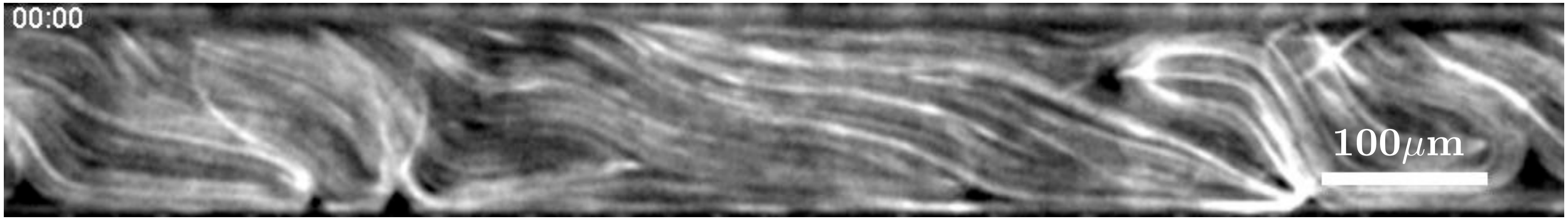


● : +1/2 defects

Doostmohammadi, Ignés, Yeomans, Sagués., "*Active nematics*", Nature comm, 2018

Are active flows always disorderly?

Filaments organise themselves into a shear flow when put under confinement

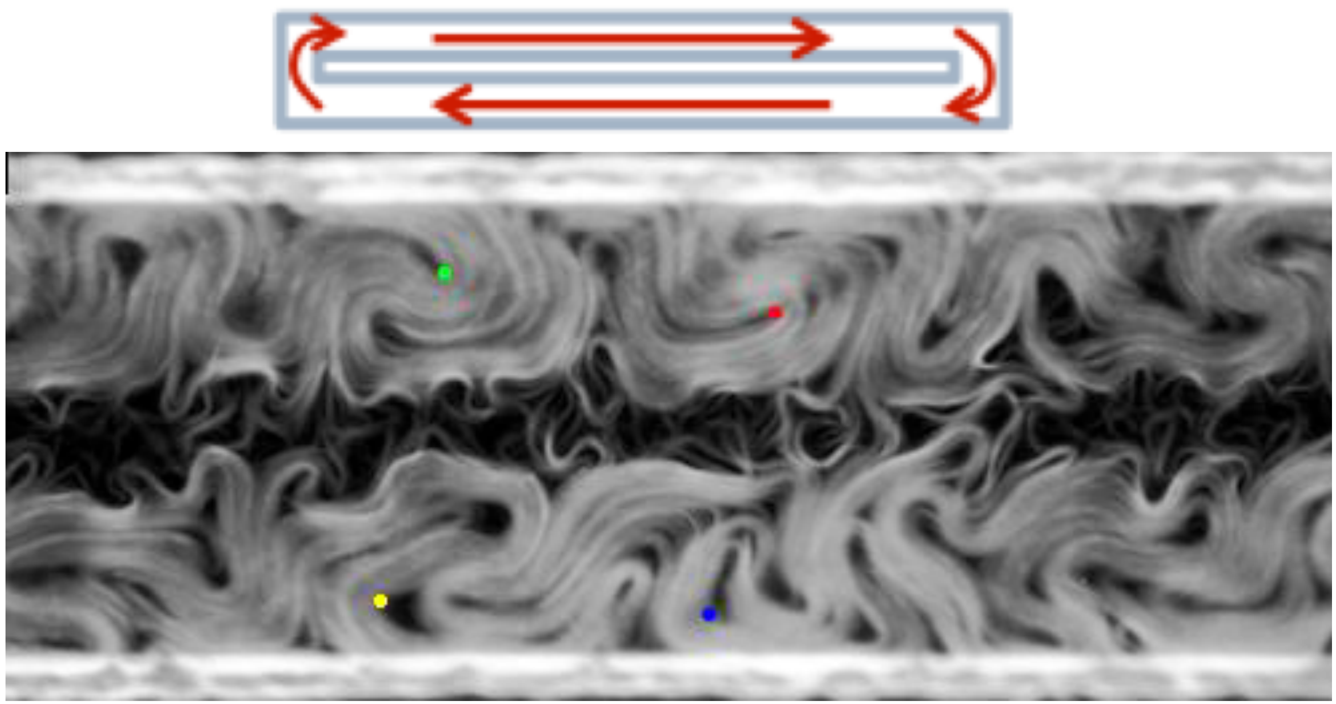


Francesc Sagues's Lab, Barcelona

Self-pumping flows emerge

- Spontaneous symmetry breaking in a racetrack geometry:
  Material moves as one coherent unit
- Universality of self-pumping:
  Occurs in cells, bacteria, subcellular filaments

Microtubules racetrack

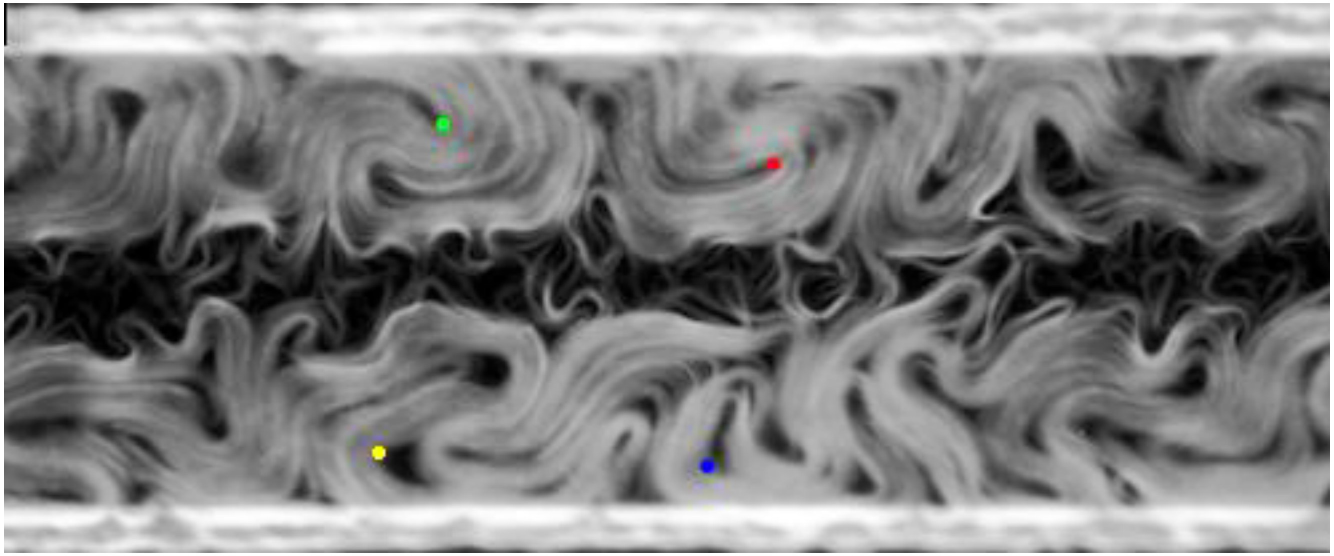


Project: Analytical + computational

Under what physical conditions self-pumping flows can be created?

Involves:

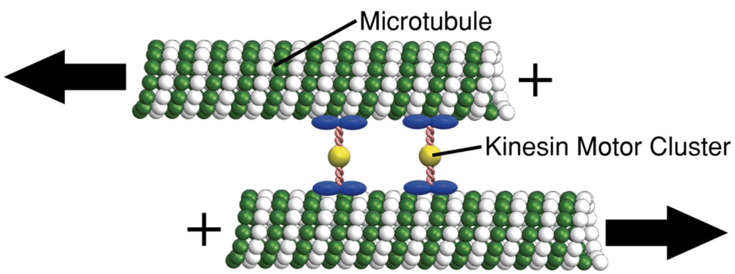
- Lattice-Boltzmann simulations of active fluids
- Examining the effect of boundary properties
- Collaboration with experimental group in Barcelona &theoretical group in Oxford



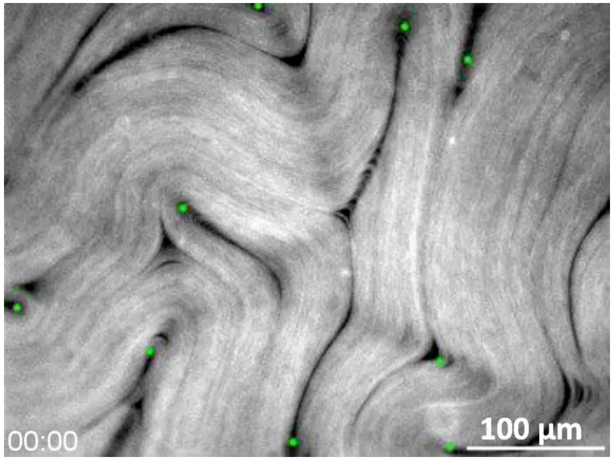
Designing a Material that Evolves

Bioinspired self-organizing matter

System made of subcellular filaments + motor protein



Sanchez et al., Nature 2012
Guillamat et al., PNAS 2016

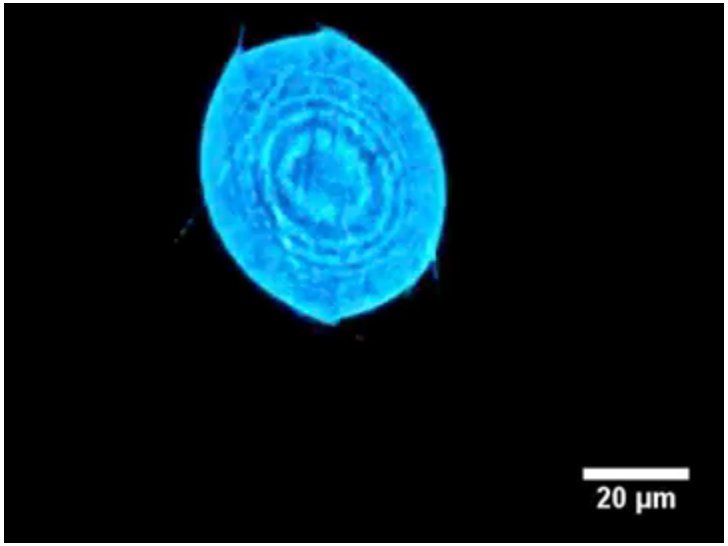


● : +1/2 defects

Doostmohammadi, Ignés, Yeomans, Sagués., "*Active nematics*", Nature comm, 2018

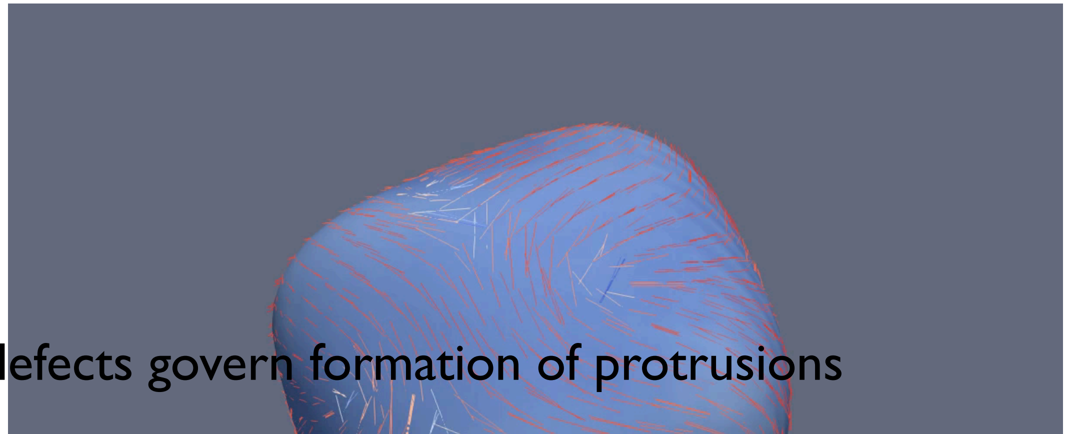
Topological control of active matter?

Self-deforming vesicles

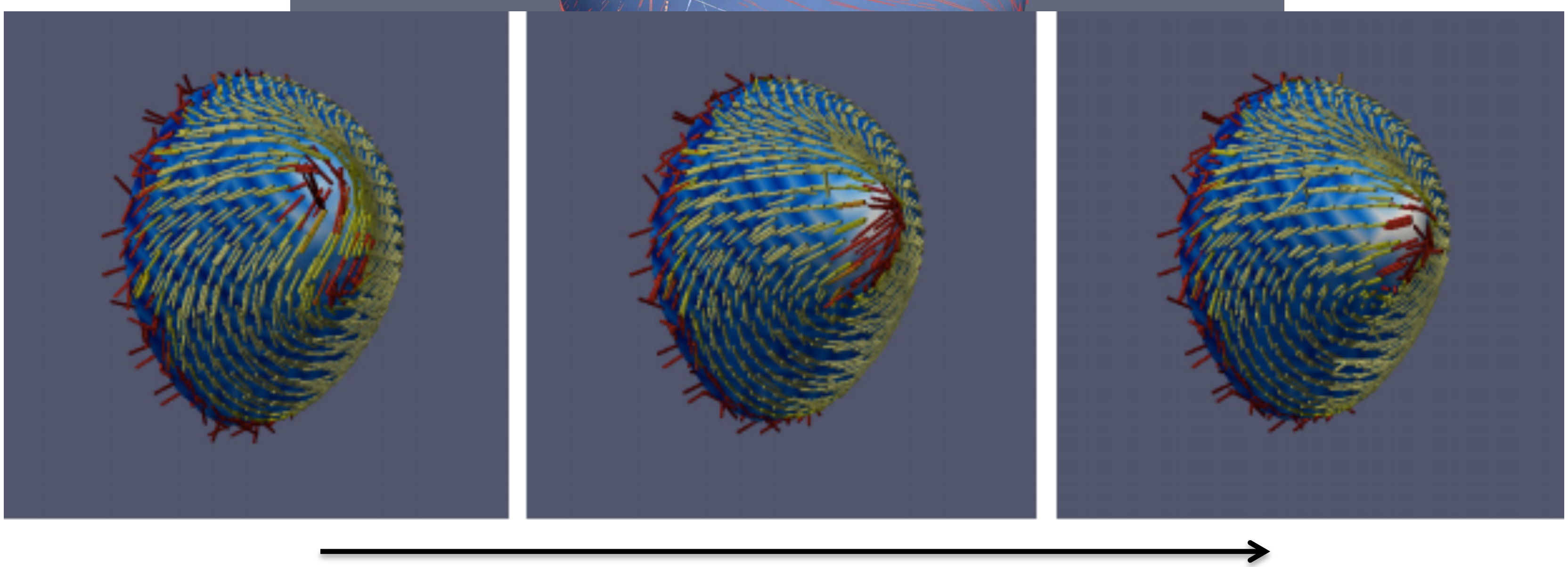


Keber et al., Science (2015)

Activity controls the morphology of the shell



Topological defects govern formation of protrusions



Time

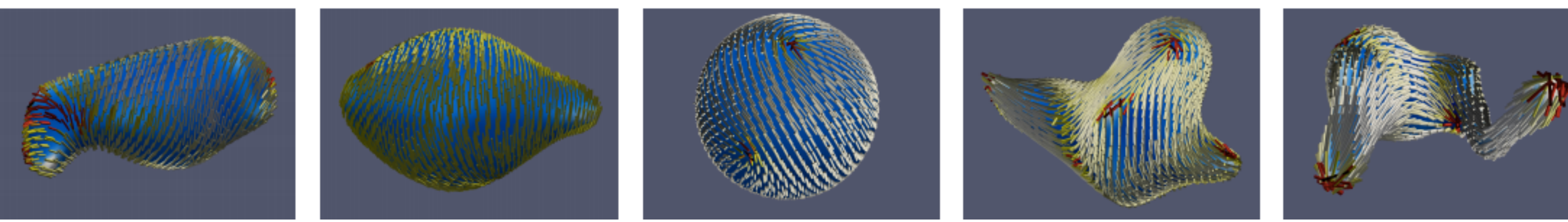
Metselaar, Yeomans, Doostmohammadi, "Topology & morphology of self-deforming active shells", Phys. Rev. Lett. (2019)

Project: Computational

Studying local activity to control the shape

Involves:

- Lattice-Boltzmann method
- Phase-field formulation
- Collaboration with experimental groups in Barcelona and Santa Barbara



Active Self-organizing Matter

What is New

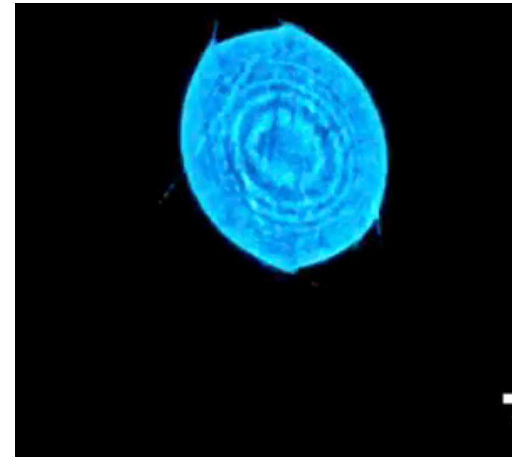
- A physics understanding of fundamental biological processes
- Designing new ways of controlling active materials

What is Exciting

- To predict cell fate based on its mechanical features
- To program materials that are capable of self-organization, self pumping, self-healing
- To work on interdisciplinary projects with international collaborations

Projects

- Cell competition: calculating flow fields of half-skyrmions
- Cell decision-making: studying stress topological defects
- Self-pumping fluids: how they emerge?
- Designing materials that evolve



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