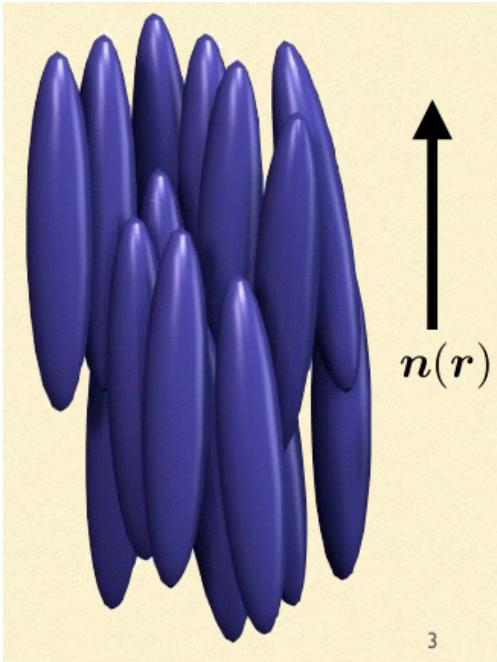


Nematic Order and Biological Function

Jorge Viñals

School of Physics and Astronomy
University of Minnesota

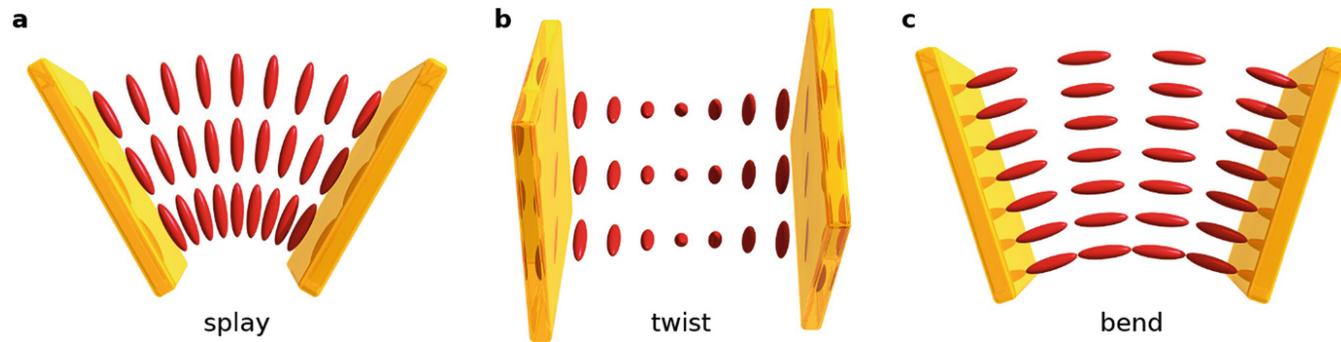
Nematic Order (Liquid Crystal)



Nematic director

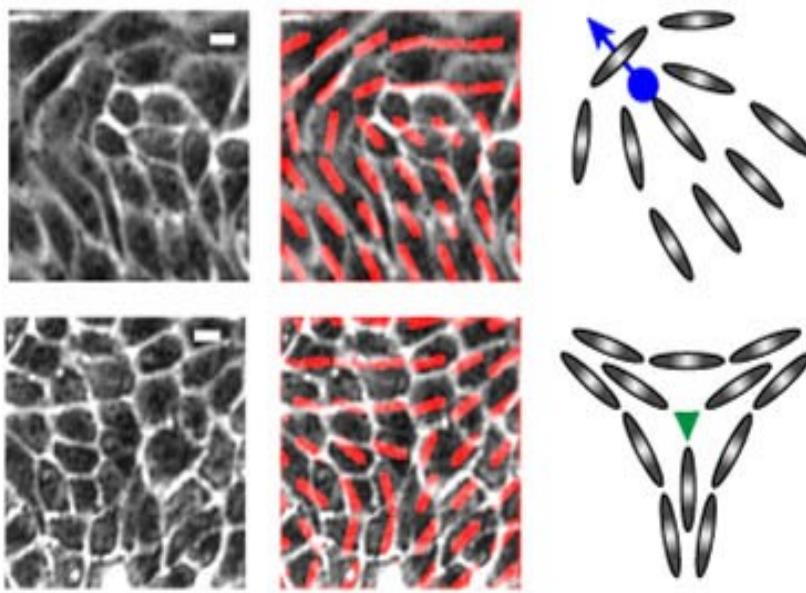
No positional order - it flows like a liquid
Orientational order - generalized elasticity

Elastic energy of deformation – three modes:



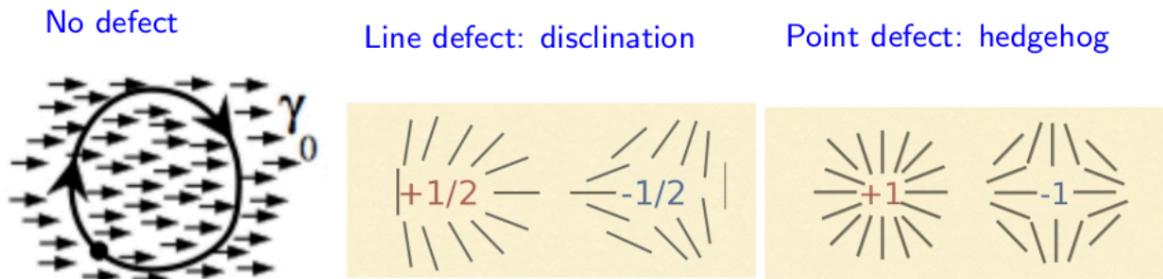
$$\mathcal{F}_d = \frac{1}{2} K_1 (\nabla \cdot \hat{\mathbf{n}})^2 + \frac{1}{2} K_2 (\hat{\mathbf{n}} \cdot \nabla \times \hat{\mathbf{n}})^2 + \frac{1}{2} K_3 (\hat{\mathbf{n}} \times \nabla \times \hat{\mathbf{n}})^2.$$

With order come defects



Nematic defects in epithelial monolayer. Phase contrast images of MDCK monolayer. The nematic field is superimposed to show the location of +1/2 defect (top) and -1/2 defect (bottom). Scale bars, 10 μ m.

[TB Saw et al., Nature 544, 212 (2017)]



$$\oint d\theta = \oint \frac{d\theta}{ds} ds = 2\pi m, \quad m = \pm 1/2, \pm 1, \dots$$

Are defects just an annoyance ?

Mechanobiology: Can one control cell shape, tissue development and repair by manipulating defects ?

Do they have any biological function ?

Topology

Classify manifolds: two manifolds are in the same class if they can be continuously deformed into each other



A sphere ...

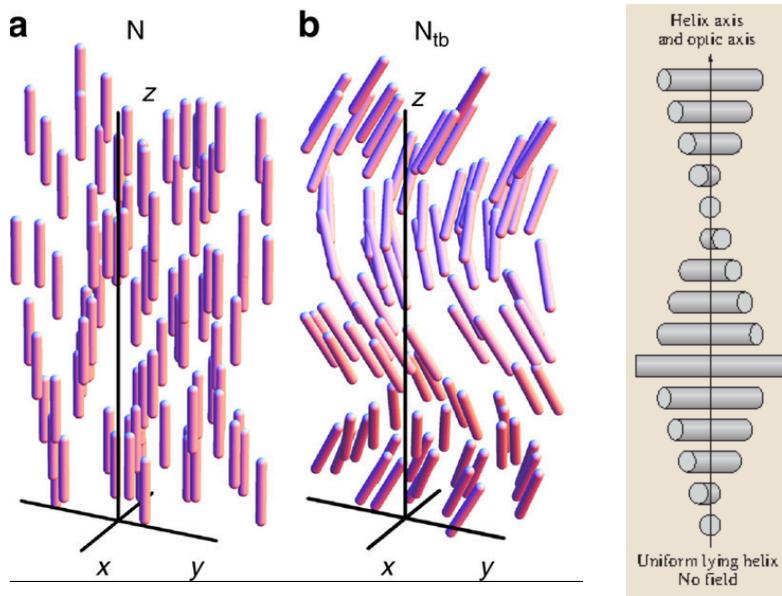


A spherical cow

A lot in Physics relies on continuity

Defect Classes in Nematics

Trivial class (no defect)



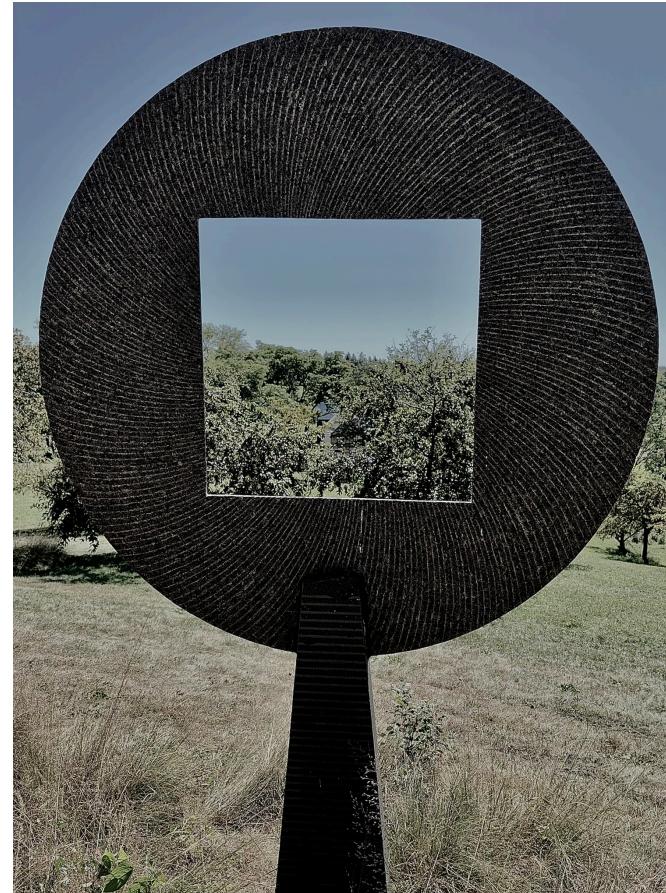
Uniform

Bend

Twist

They can continuously decay
into each other

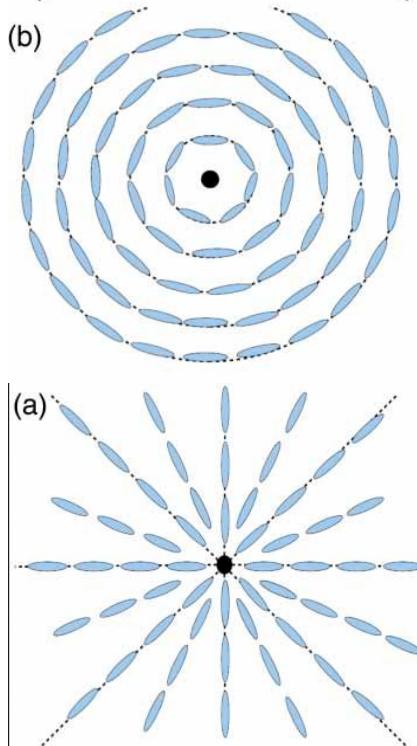
Artist rendition of a defect



- Singular solutions. Angle undefined at core
- Infinite elastic energy at core
- Defects cannot be removed via continuous deformations

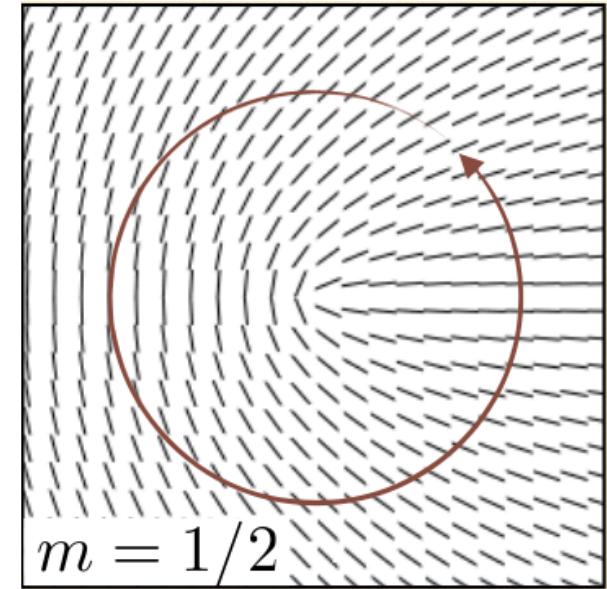
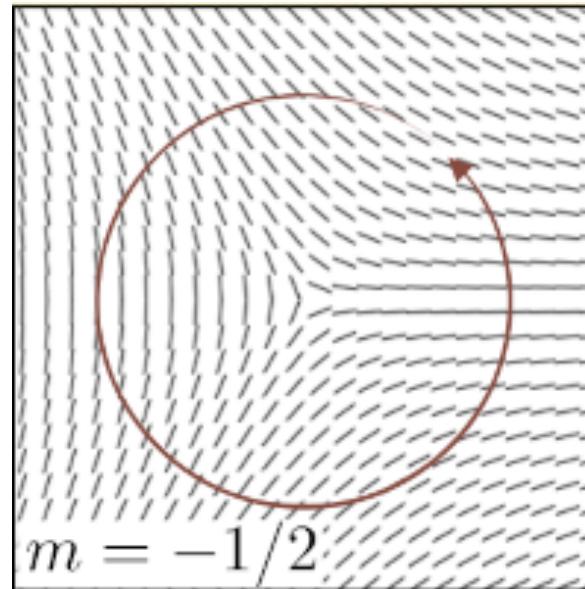
Defect Classes in Nematics

Integer charge ($m = +1$)



Not stable in three dimensions.
“Escape to the third dimension”

Half Integer charge ($m = +/- 1/2$)



They are two different classes in two dimensions

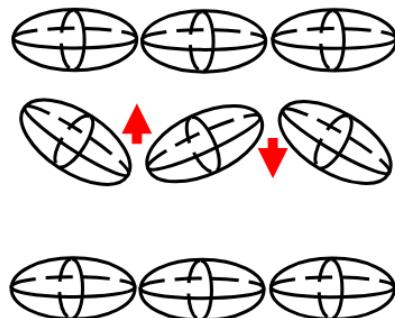
They belong to the same (and only) class in three dimensions ($m = 1/2$)

Active Nematics

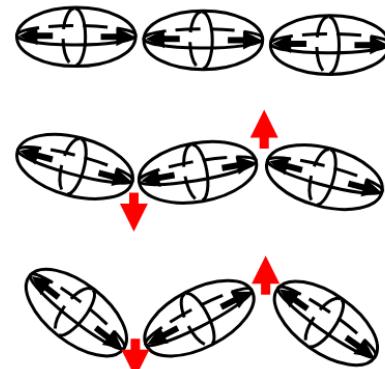
Self propelled objects ("particles") that consume energy and can be modeled as a force dipole

- Energy constantly injected into the system
- No time reversal symmetry. No reciprocity
- Often form nematic phases (elongated units)

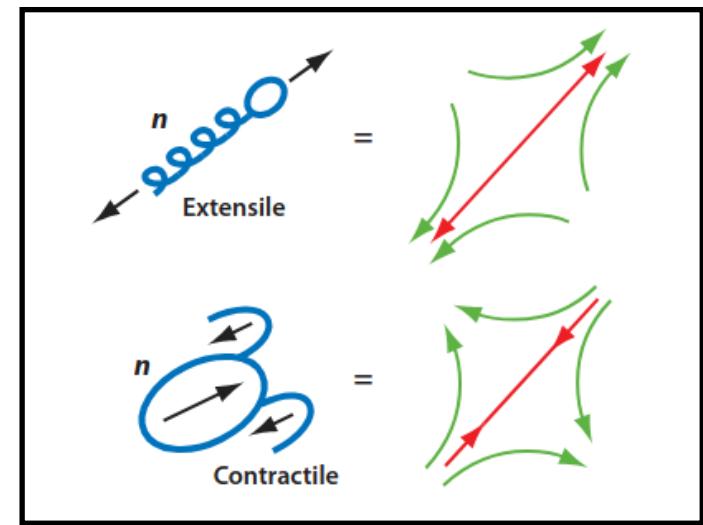
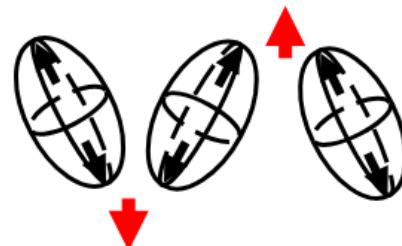
Ordinary nematic.
Restoring force for bend



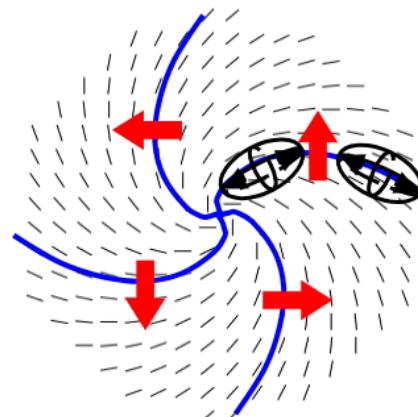
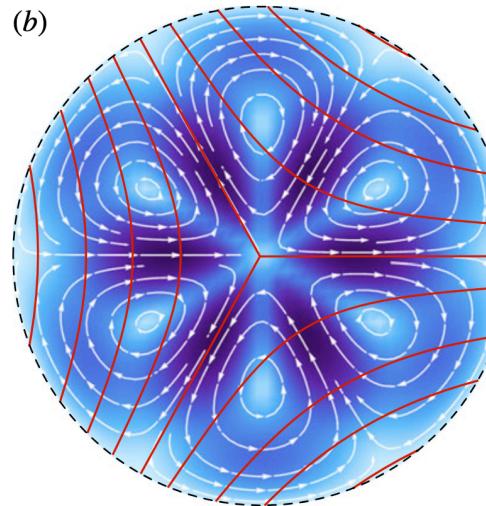
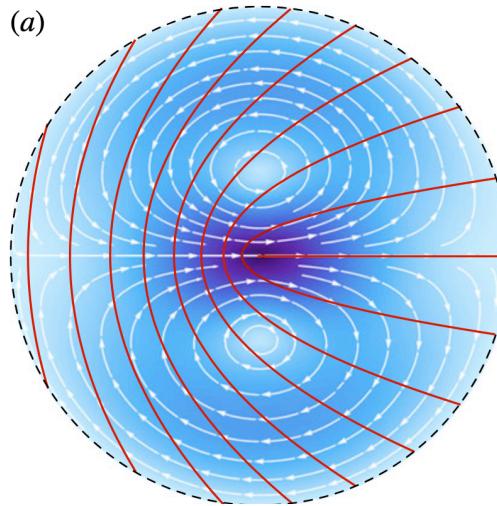
Active, extensile,
nematic. Bend unstable



Active, extensile,
nematic. Splay stable



Disclinations in Active Nematics



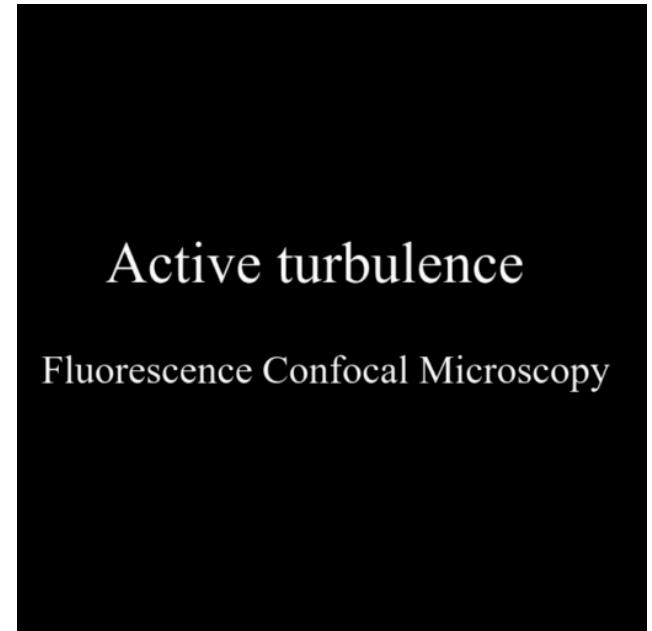
[C. Conklin et al. Soft Matter 14, 4641 (2018)]

[P. Guillamat et al. Nature Comm. 8, 564 (2017)]

Tubulin driven by kinesin-streptavidin motor clusters (an active gel)

(a) $+1/2$ disclination. Self propels with velocity proportional to activity. Extensile and contractile disclinations have opposite velocity
(b) $-1/2$ disclination. Velocity is zero

[L. Giomi et al. Phil. Trans. R. Soc. A 372, 20130365 (2014)]



A Few Questions

Is there nematic order (both passive and active) in Biological systems ?

- Many recent different systems seem to suggest that this is the case
- Caveat: difficulty and accuracy of experiments in living systems

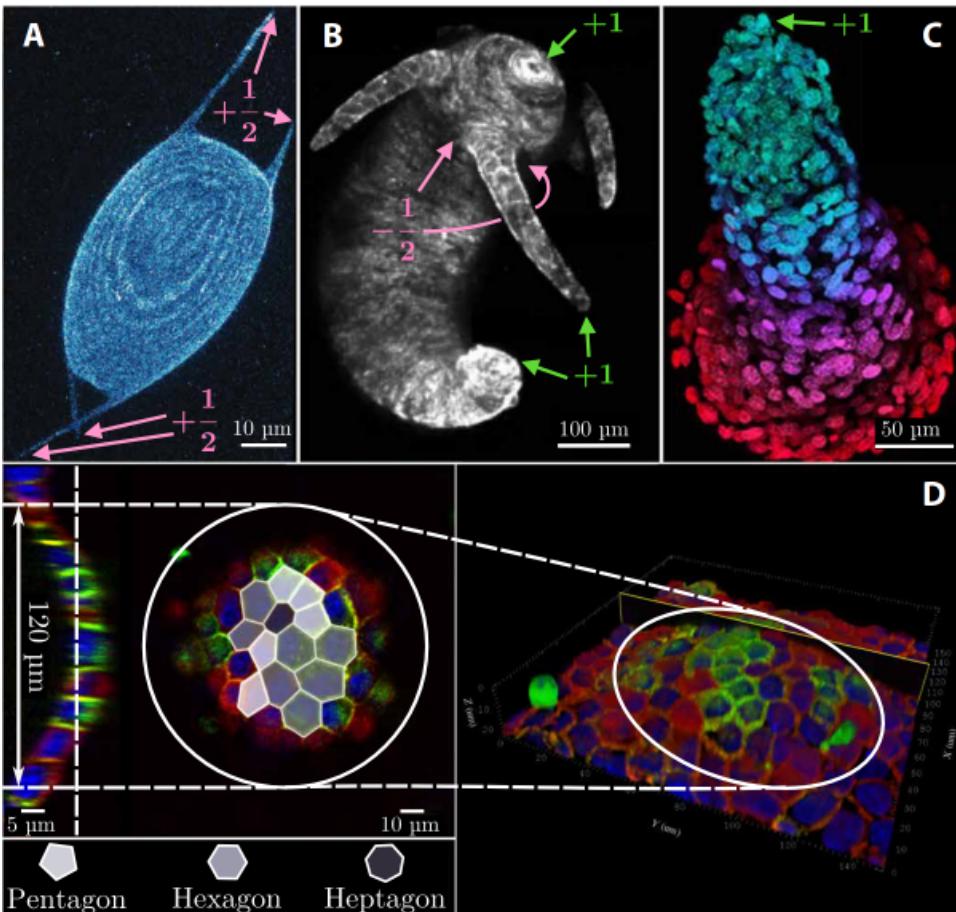
Genetics and biochemistry control/feedback with mechanics (the physical world)

- How Biology controls Mechanics - tissue development and repair
- What is the feedback between mechanics and Biology - remodeling, cell division
- Tissue and organ development modified by mechanical interventions
- Design and build artificial tissue

How does one model the mechanics of living tissue; is it an oriented soft solid ?

- Why would evolution lead to orientational order. Softer elasticity ?
Topologically induced robustness ?

Morphogenesis



Experimental evidence indicates that topological defects could serve as organizing centers in the morphogenesis of tissue.

- (A) Monolayer of microtubules and kinesin enclosed in a lipid vesicle
- (B) Example of *Hydra* featuring +1 disclinations in proximity of the mouth, the foot, and the tip of each tentacle and two $-1/2$ defects at the base of each tentacle
- (C) Multicellular protrusion in collectively migrating myoblasts under confinement, with a +1 defect at the tip
- (D) Dome formed by a layer of MDCK epithelial cells. Penta/Hepta defects are disclinations of the hexagonal cell structure

Is Topology associated robustness key to the development and maintenance of living structures ?

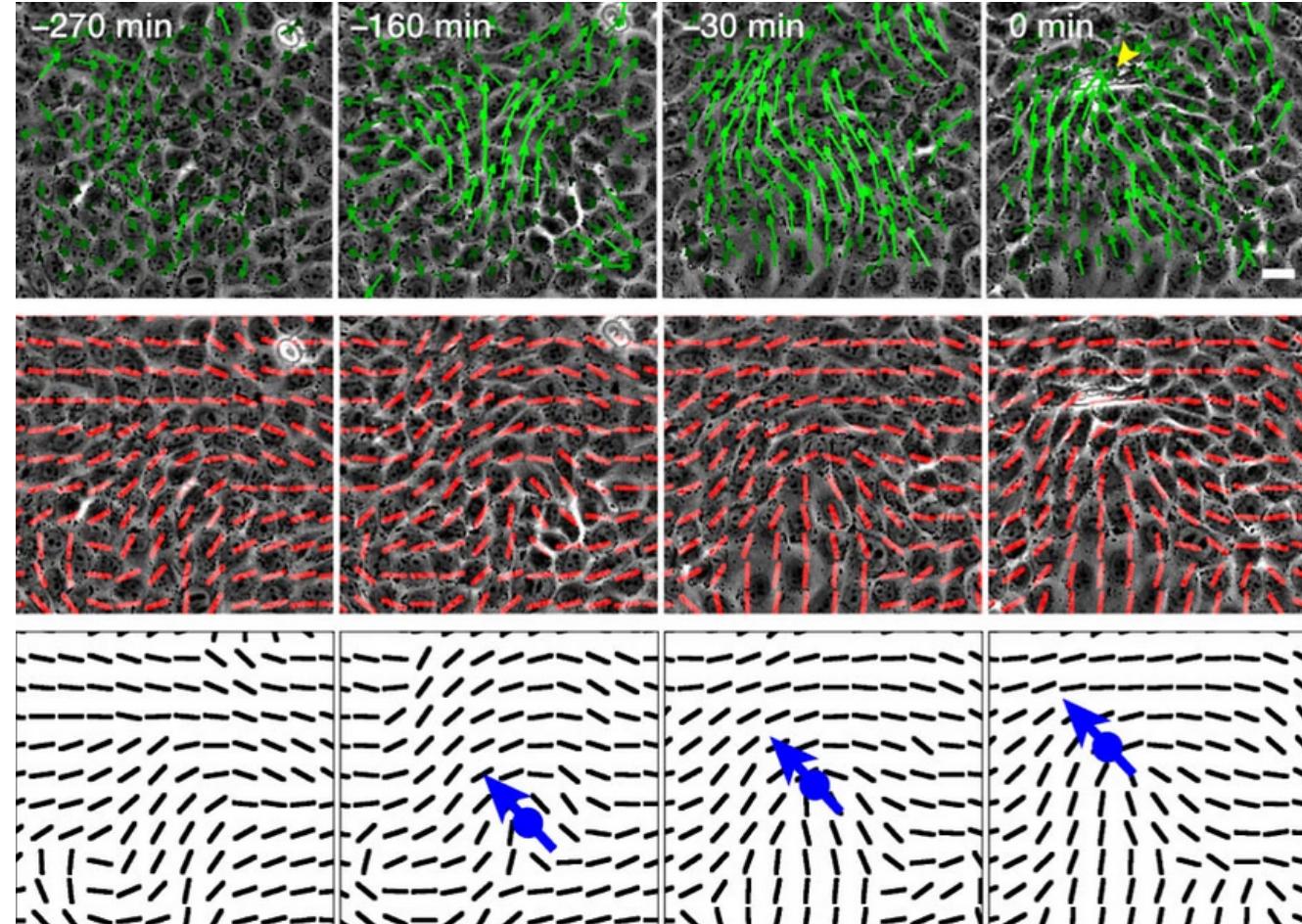
Cell death and extrusion

Epithelial tissues (MDCK) remove excess cells through extrusion, preventing the accumulation of unnecessary or pathological cells.

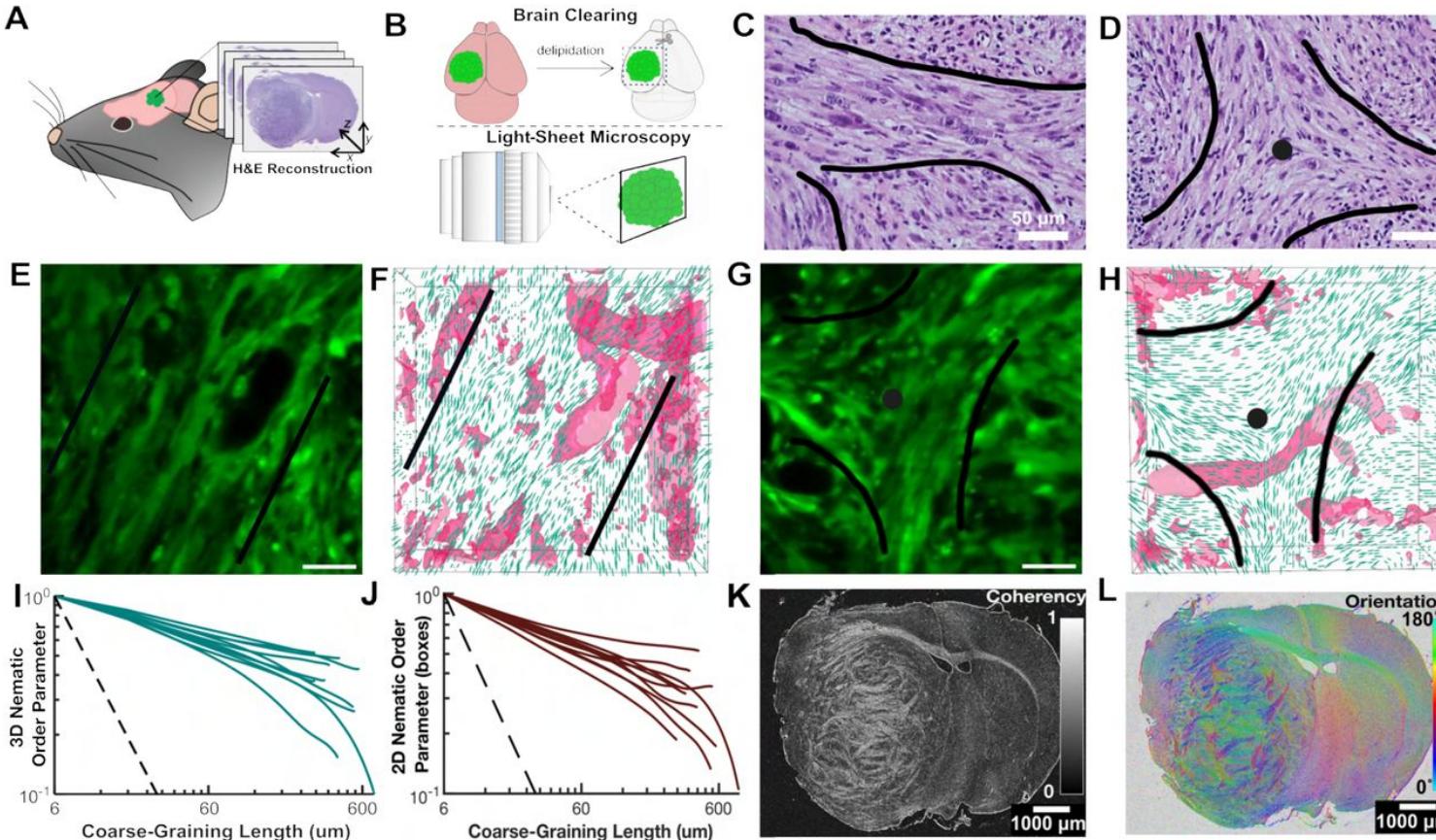
Death and extrusion occur at $\pm 1/2$ disclinations. Defect induced stresses promote apoptosis and extrusion.
Mechano-transduction

Modeled as extensile active nematic

Control extrusion hotspots by inducing defects through micros contact printing



Nematic order in gliomas



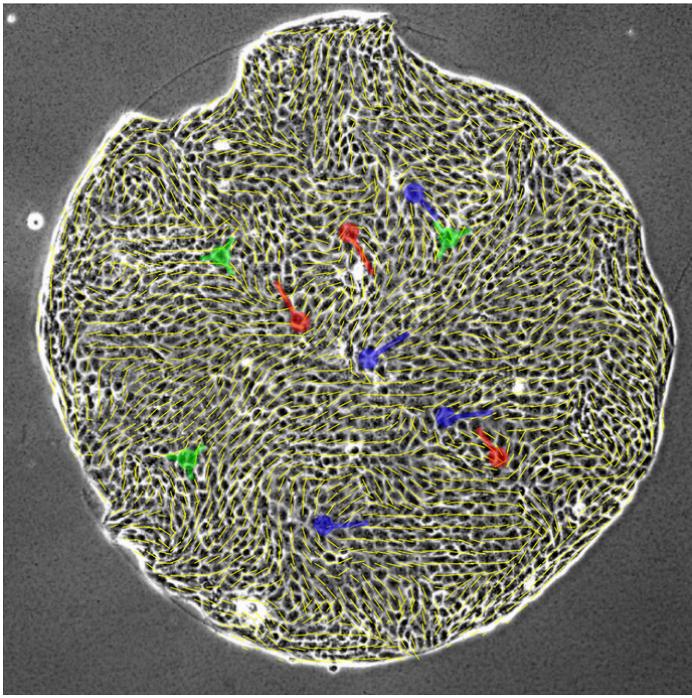
Oncostreams: gliomas (*in vivo*, mouse and human) exhibit self-organized, aligned, multicellular structures - active nematic.

Disclinations clearly visible in stained tissue and laser images

Nematic correlations are long ranged 300-3000 microns

Degree of nematic order correlates with tumor aggression. Order contributes to malignancy

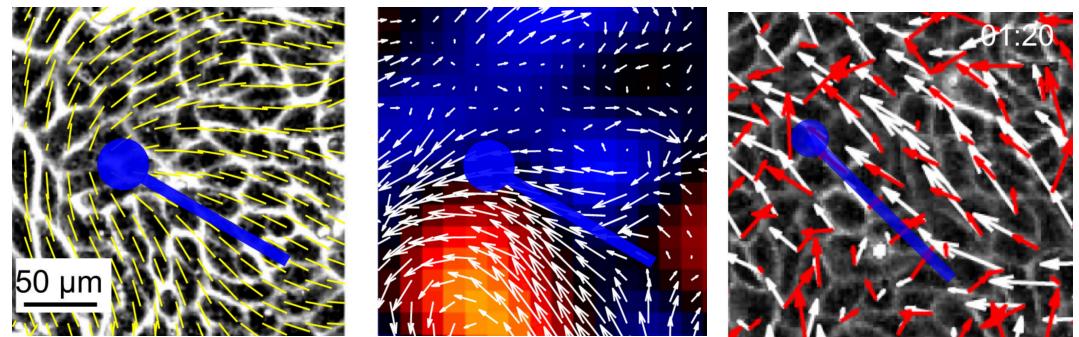
Biomechanics of MDCK tissue



[P. Bera, ..., J. Notbohm, Newton 1, 100231 (2025)]

Madin-Darby canine kidney (MDCK) epithelial tissue

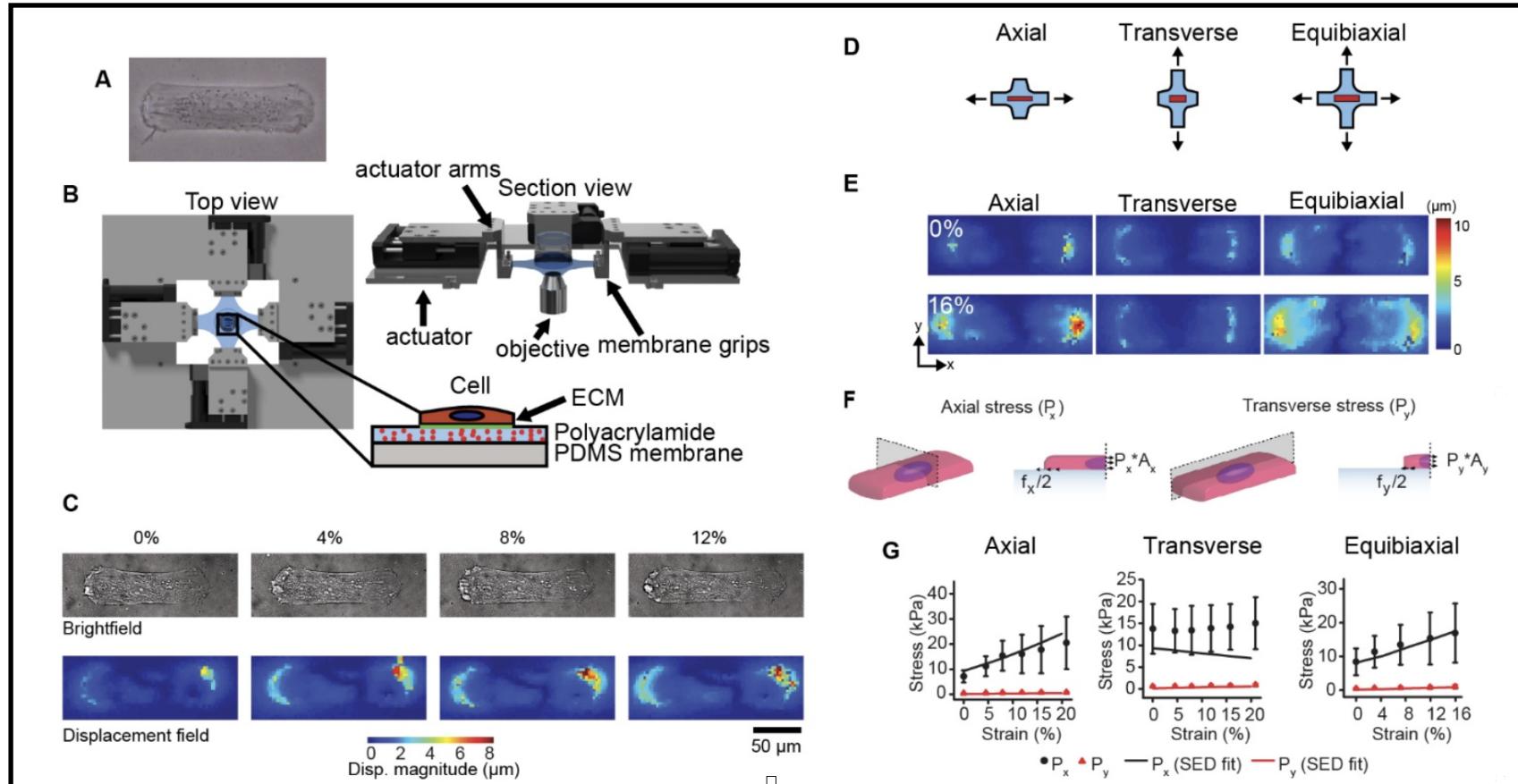
Easy to keep alive, manipulate, and pattern



Cell shapes consistent with nematic order and active nematic flows (vorticity shown). Also measured tractions (red arrows), with Traction Force Microscopy

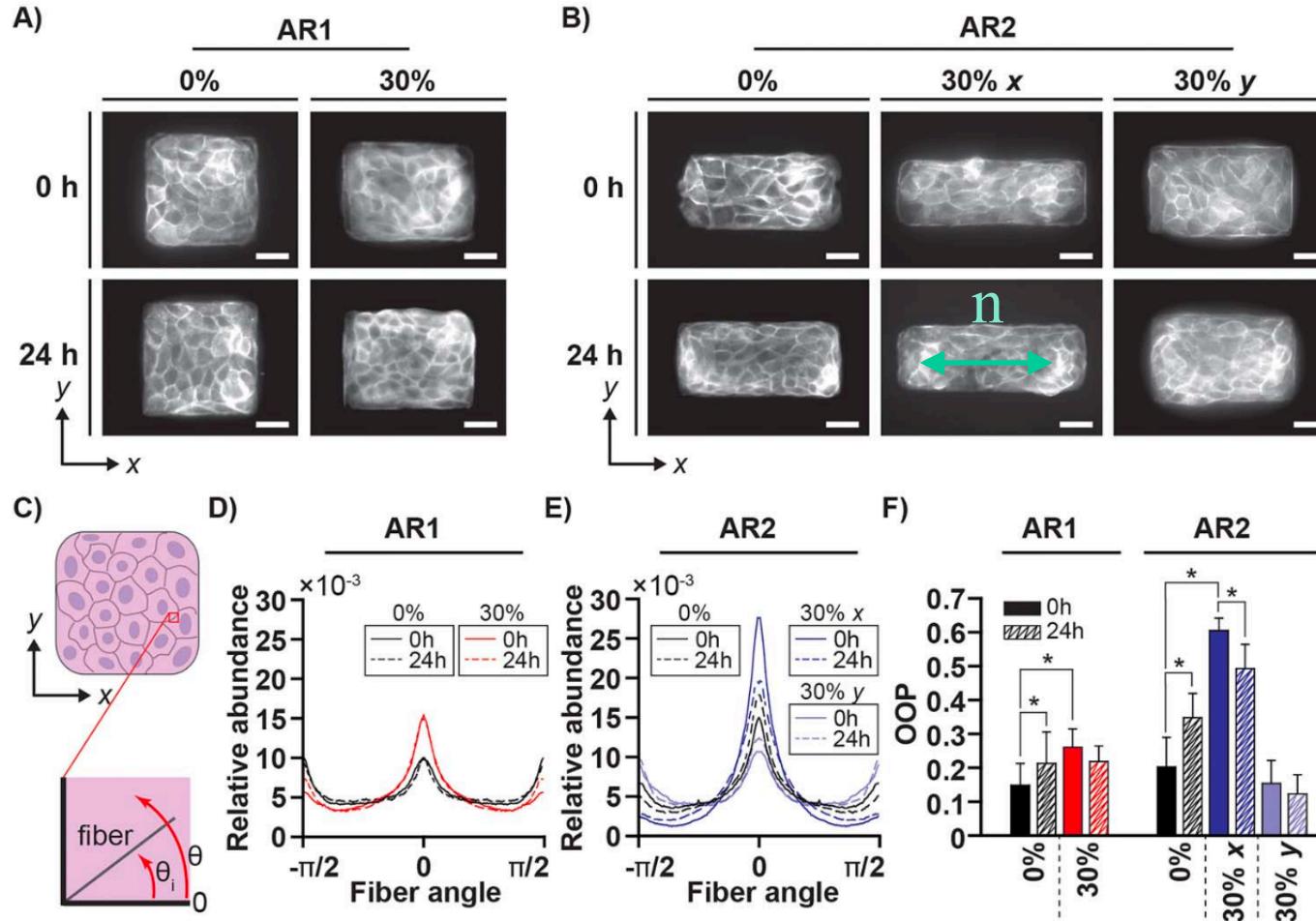
There has to be more to tissue mechanics than a flowing, active, nematic fluid. Tissues also respond elastically

C μ BS (UofM)



Pat Alford, Department of Biomedical Engineering

Tissue has long range nematic order



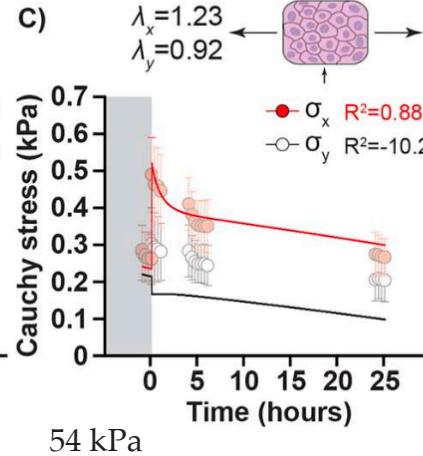
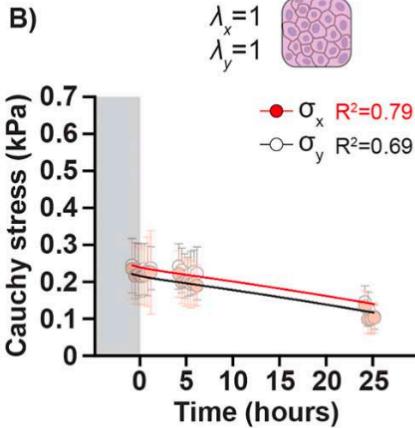
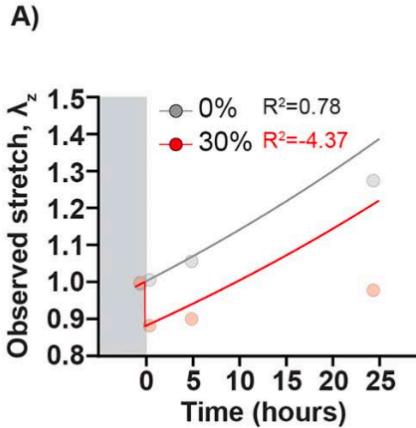
Lithographically micro patterned tissue. Square (AR1), and rectangular (ARn) shapes

Tissue stained for actin fibers
n is the “director”

Biomechanics:

- Degree or order changes under stretching
- Change depends on relative orientation of director and stretch
- Order changes over time - mechano adaptation

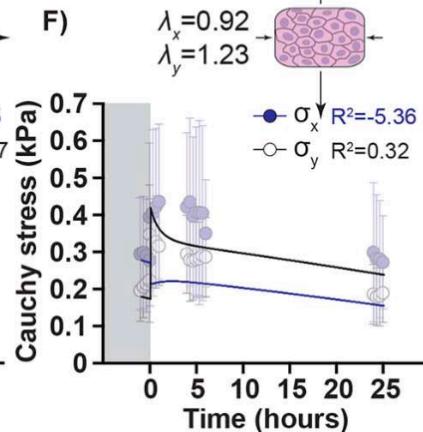
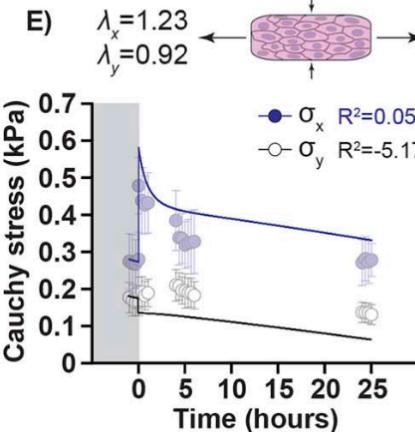
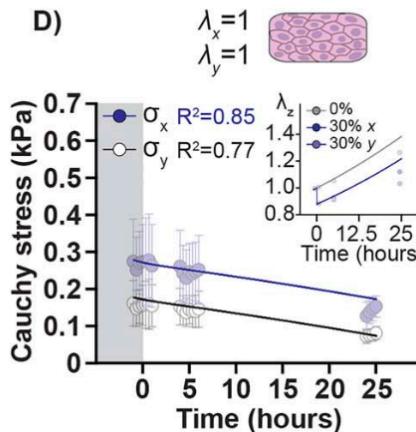
AR1



Isotropic solid response, $\mu \approx 0.54$ kPa

Cell proliferation relieves stress over a scale of hours

AR2



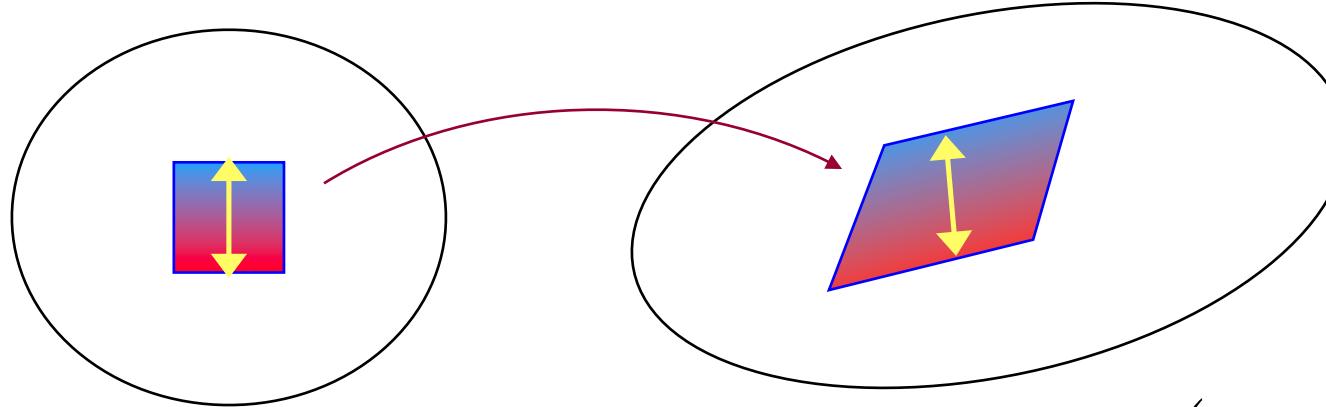
Under longitudinal strain $\delta S \approx 0.25$

Reduction in effective shear modulus relative to isotropic

Reduction in alignment under transverse stretch

$$\text{Elastic distortion } W_{ij} = \delta_{ij} - \partial_j u_i \quad (\mathbf{W} = \mathbf{I} - \mathbf{U}^{el})$$

Lattice kinematics $\dot{\mathbf{W}} + \mathbf{WL} = \mathbf{WG}$, with $L_{ij} = \partial_j v_i$, \mathbf{G} the growth rate tensor



Anelastic growth \mathbf{G} occurs because

- Changes in nematic order $\mathbf{Q} = S \left(\hat{\mathbf{n}} \otimes \hat{\mathbf{n}} - \frac{1}{3} \mathbf{I} \right)$
- Cell proliferation. Cells are largely incompressible, but mass is not conserved.

Free energy $\mathcal{F} [\mathbf{W}(x, t), \mathbf{Q}(x, t), \nabla \mathbf{Q}(x, t)] = \int_{\Omega(t)} dV \rho f (\mathbf{W}(x, t), \mathbf{Q}(x, t), \nabla \mathbf{Q}(x, t)), \quad \text{not } \mathbf{G} !$

$$f (\mathbf{W}(x, t), \mathbf{Q}(x, t), \nabla \mathbf{Q}(x, t)) = f_{el}(\mathbf{W}(x, t), \mathbf{Q}(x, t)) + f_n(\mathbf{Q}(x, t), \nabla \mathbf{Q}(x, t))$$

Use dissipation inequality to obtain evolution equations for distortion, transport, and nematic order

Evolution Equations

Stress includes two contribution from nematic order (if isotropic, otherwise uniaxial elasticity)

$$\mathbf{T} = 2\mu(\boldsymbol{\epsilon} - \alpha\mathbf{Q}) + K \nabla \mathbf{Q} \odot \nabla \mathbf{Q}$$

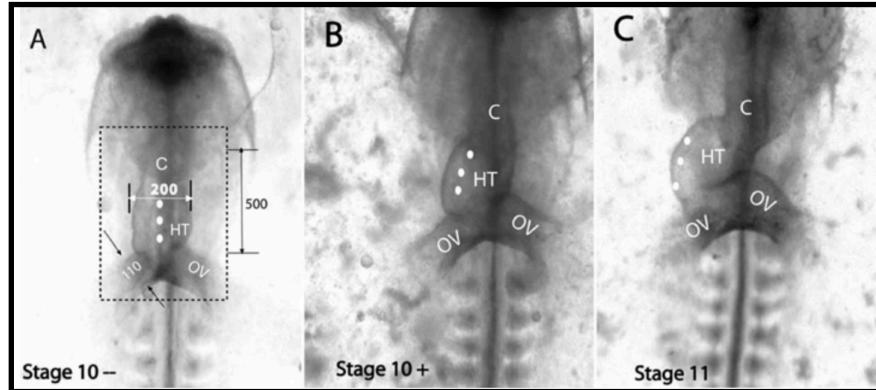
Nematic order affected by stress (also for isotropic elasticity)

$$\dot{\mathbf{Q}} = 2\mu\alpha(\boldsymbol{\epsilon} - \alpha\mathbf{Q}) - \Gamma \frac{\delta \mathcal{F}}{\delta \mathbf{Q}} - \gamma' [\boldsymbol{\sigma}]_{tr}$$

Tissue growth affected by both local stress (homeostasis) and nematic order

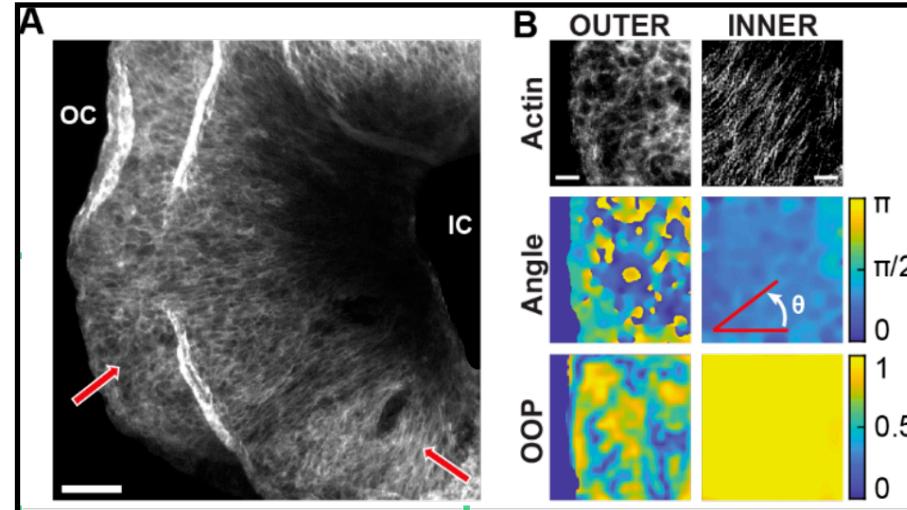
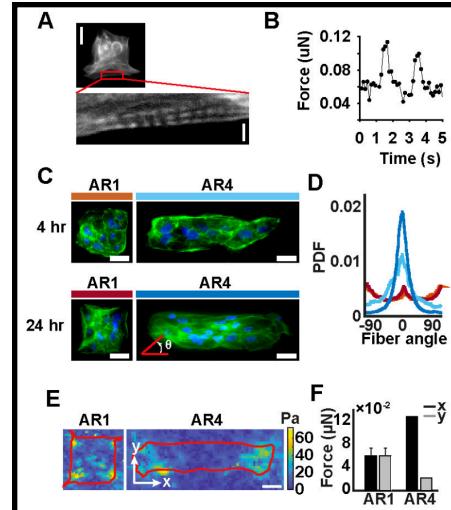
$$\dot{\mathbf{G}} = \gamma \boldsymbol{\sigma} - \gamma' \left[\frac{\delta \mathcal{F}}{\delta \mathbf{Q}} \right]_{tr}$$

Cardiac Looping in Embryos



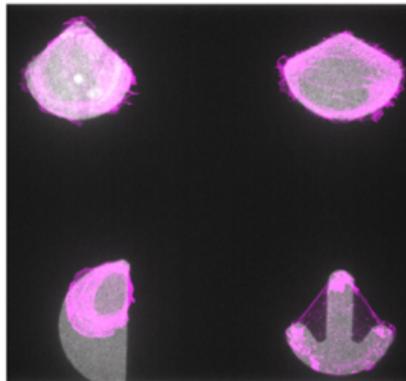
[A. Subramanian,, L. Taber, Ann. Biomed. Eng. 34, 1355 (2006)]

Changes in cell shape driven by actin polymerization in heart tube are responsible for the bending component of c-looping, while unbalanced forces in the OVs (omphalomesenteric vein), due to a combination of cell migration and cytoskeletal contraction, initiate dextral rotation (torsion).

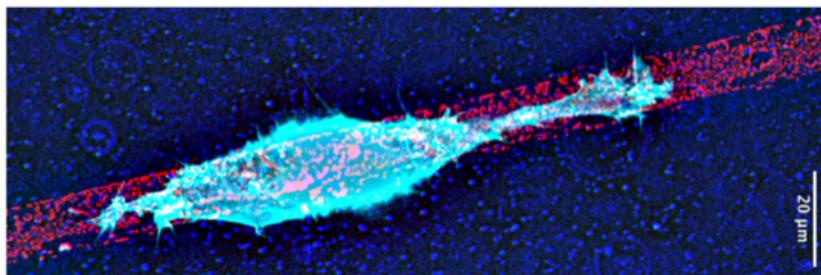


Epithelial Tissue

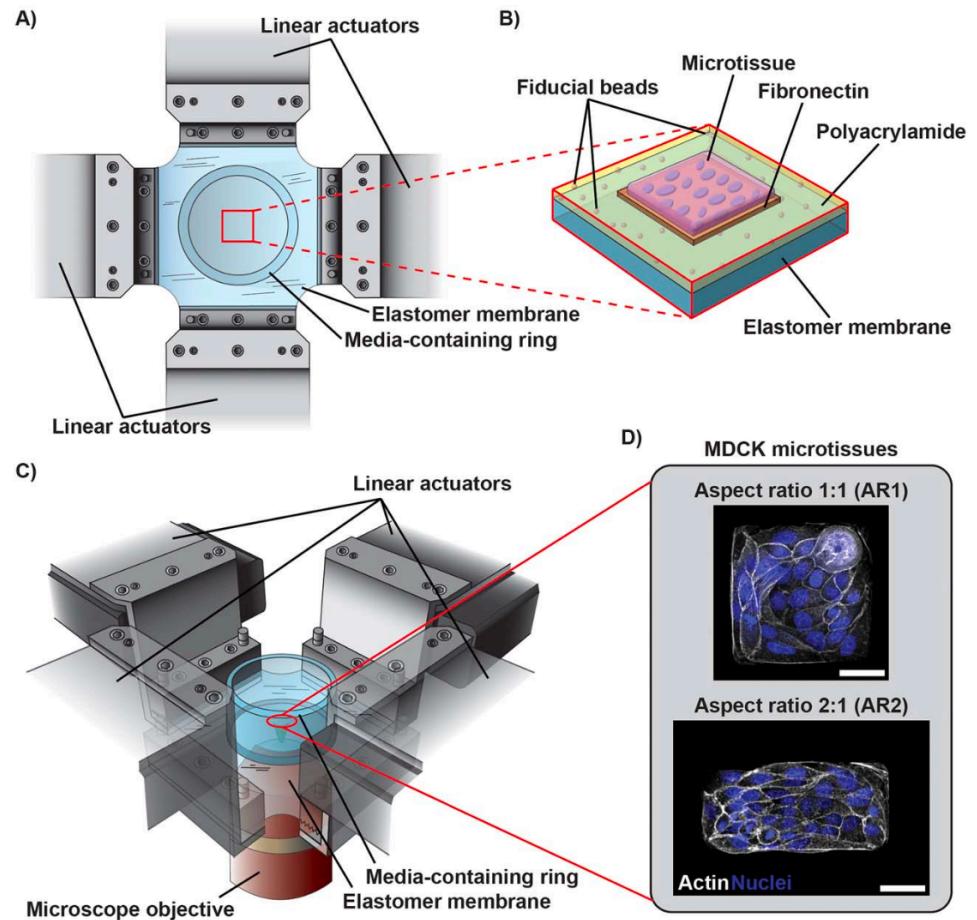
Play with cells in the lab: Fibronectin pattern (grey) and adherent cells (cyan)



Actual tissue with many cells

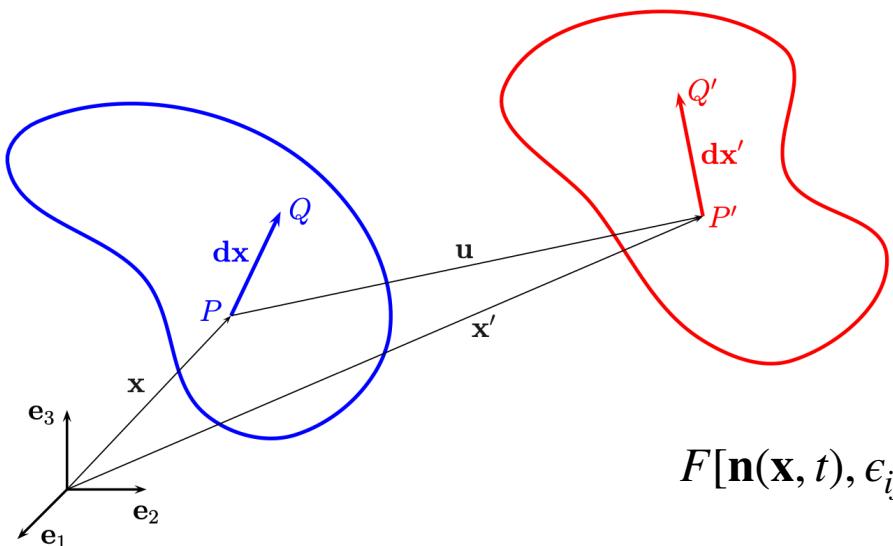


Single cell migrating on a predefined track



Order and defects happen in a deformable manifold

Tissue will change shape during growth or in experiments. Potentially cell differentiation (“creation of space”)



$$(ds')^2 - (ds)^2 = 2\epsilon_{jk}dx_jdx_k$$

$$\epsilon_{ij} = \frac{1}{2} \left(\frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i} + \frac{\partial u_m}{\partial x_i} \frac{\partial u_m}{\partial x_j} \right)$$

$$F[\mathbf{n}(\mathbf{x}, t), \epsilon_{ij}(\mathbf{x}, t)] = F_{el}[\epsilon_{ij}(\mathbf{x}, t)] + F_d[\mathbf{n}(\mathbf{x}, t)] + F_c[\mathbf{n}(\mathbf{x}, t), \epsilon_{ij}(\mathbf{x}, t)]$$

Figure 2.1: Kinematics of deformable bodies