

Self-organization of active epithelial mechanics

Fridtjof Brauns · MPI-PKS & MPI-CBG

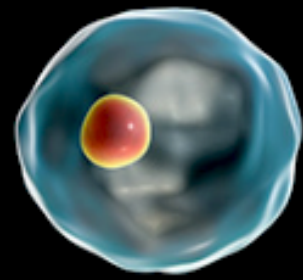


UC SANTA BARBARA
Kavli Institute for
Theoretical Physics

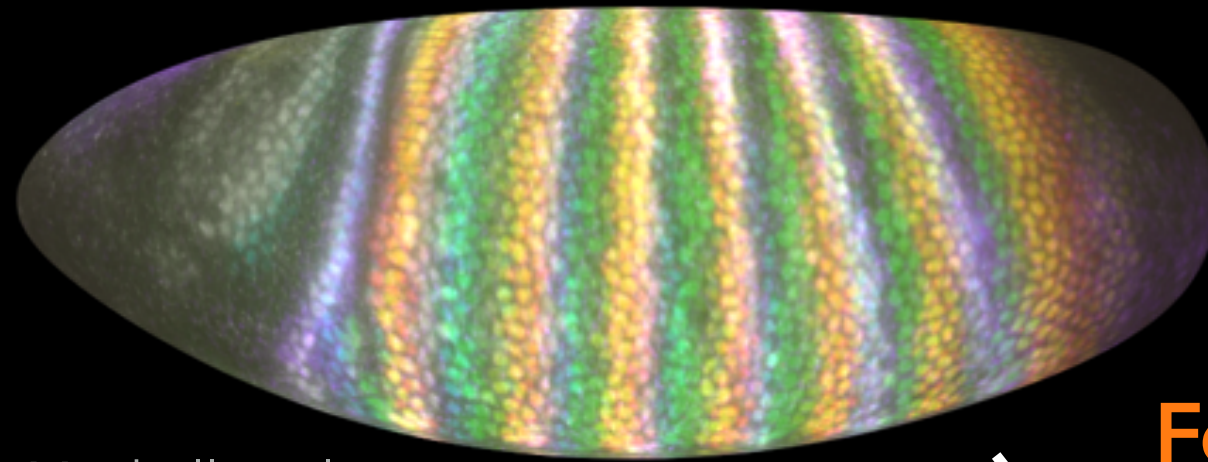
GORDON AND BETTY
MOORE
FOUNDATION

Development: from cell to organism

Oocyte



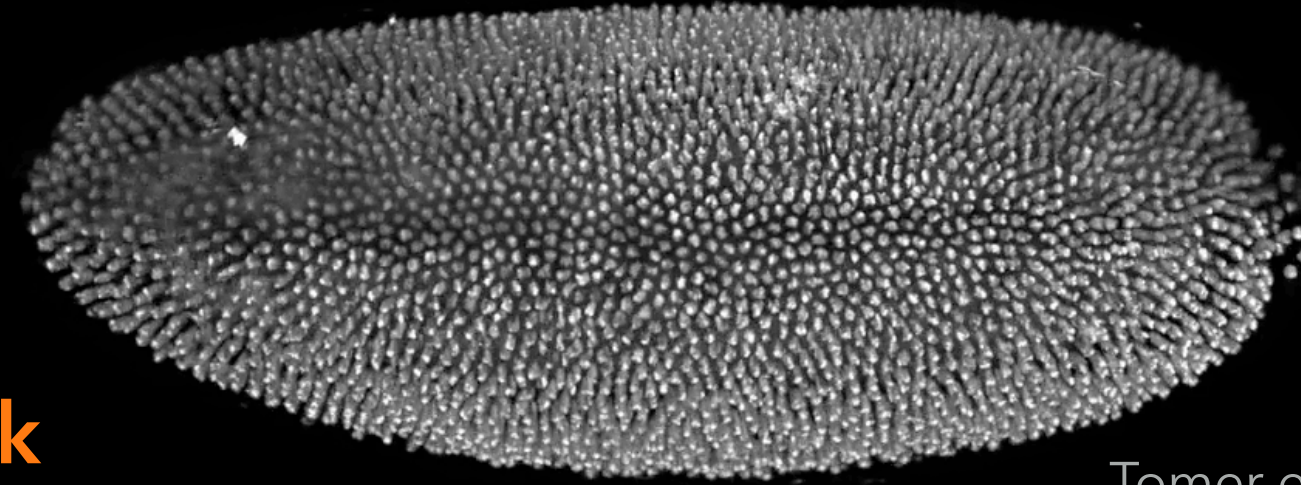
Genetic patterns



Mitchell et al.
bioRxiv (2022)

Morphogenesis: Growth and shape change

ventrolateral view



02:52:30

Tomer et al.
Nat. Methods (2012)

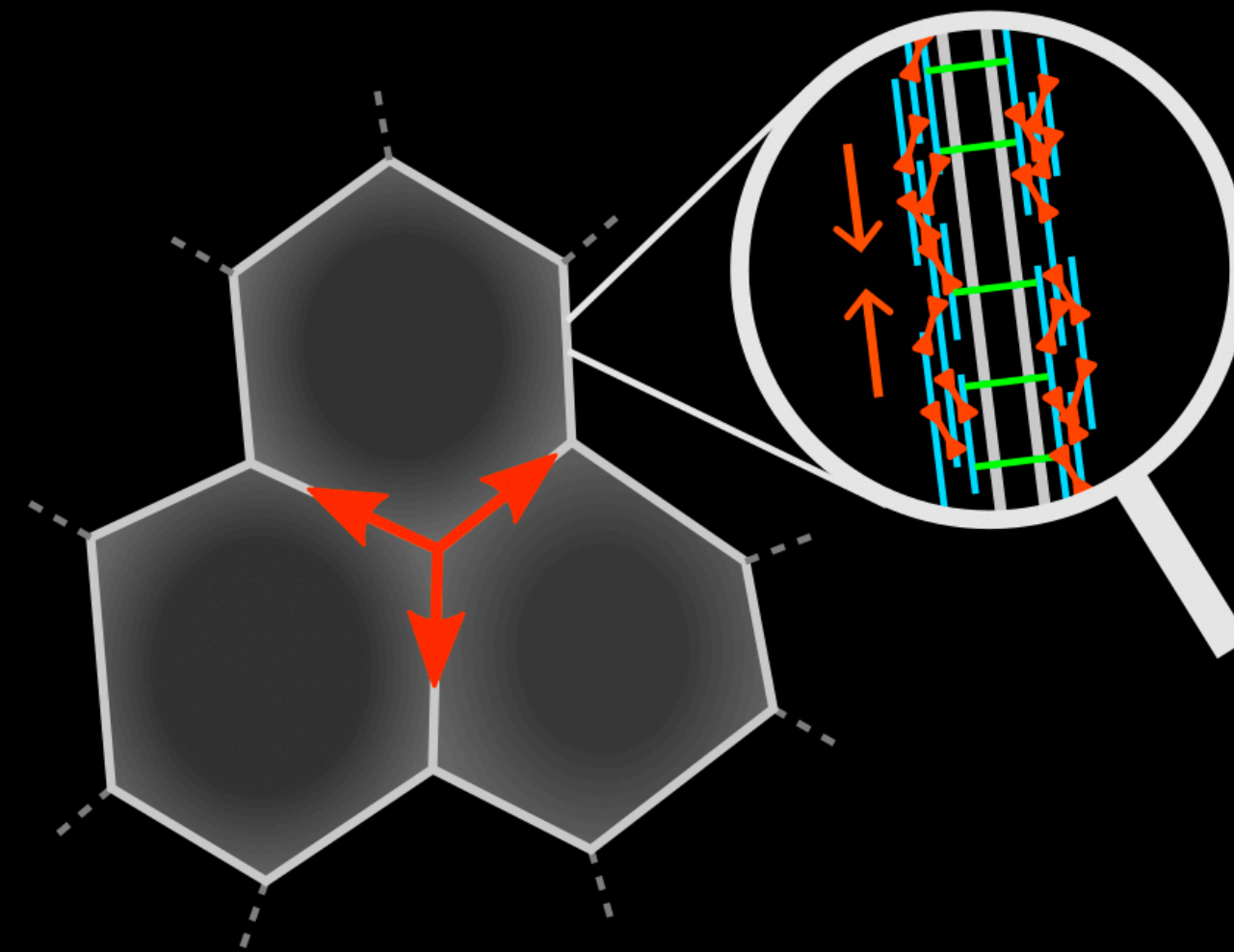
Adult organism



macrogiants

Feedback loops

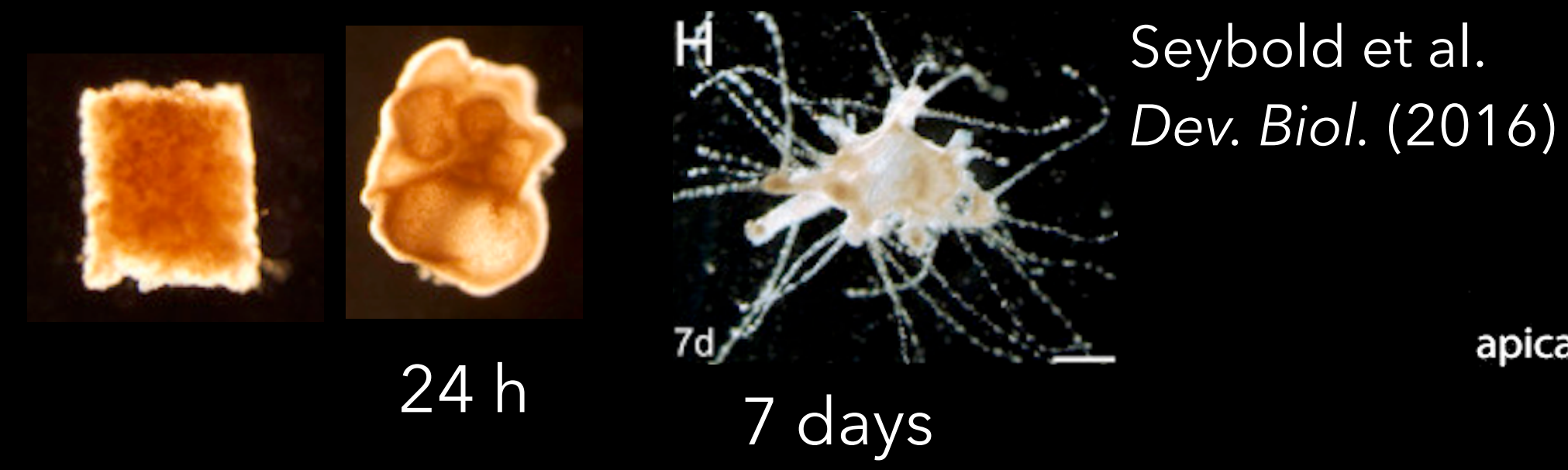
Adhesion & motor molecules, and ...



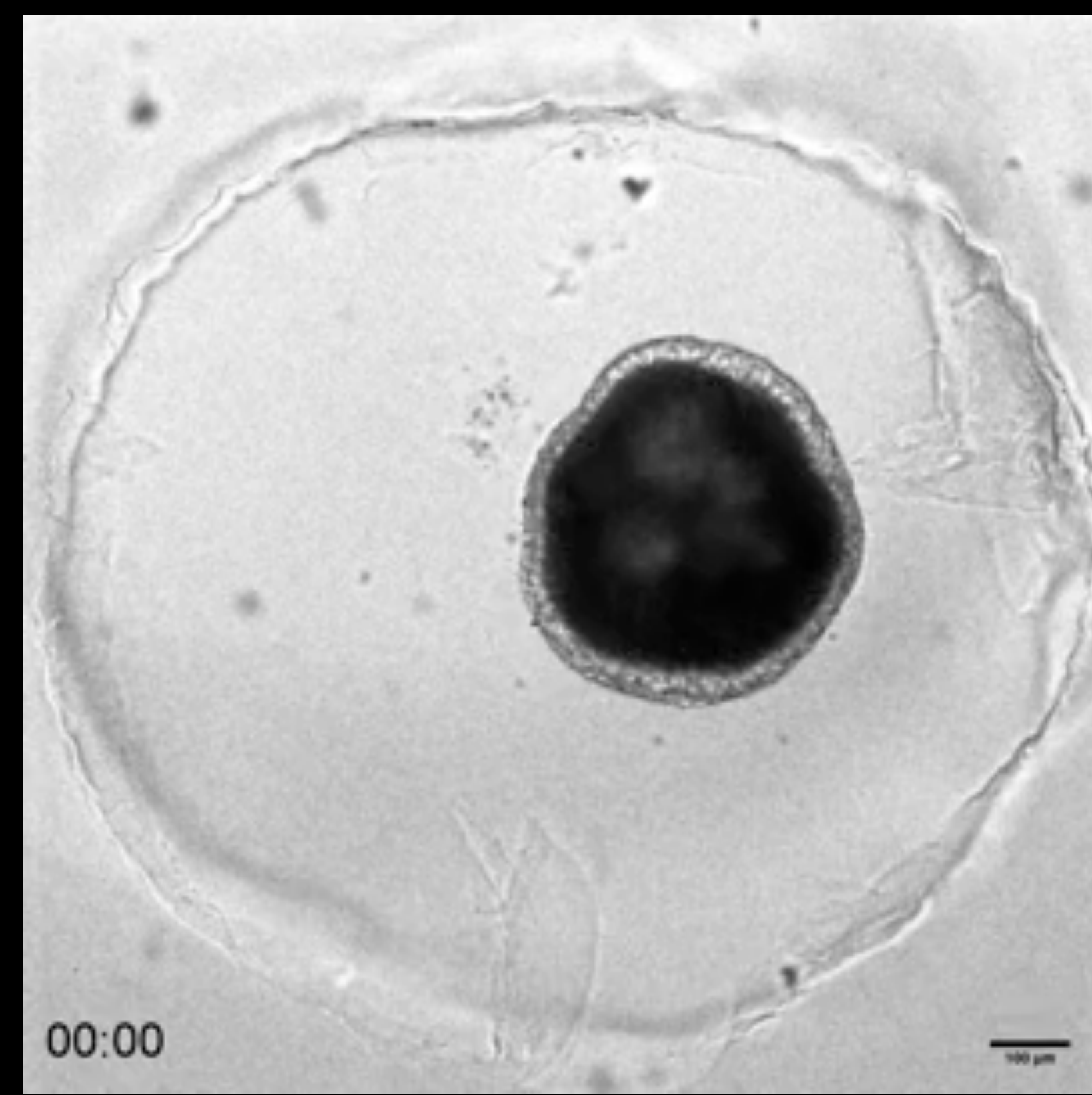
Living tissue = material that shapes itself through collective dynamics of 1000s of cells



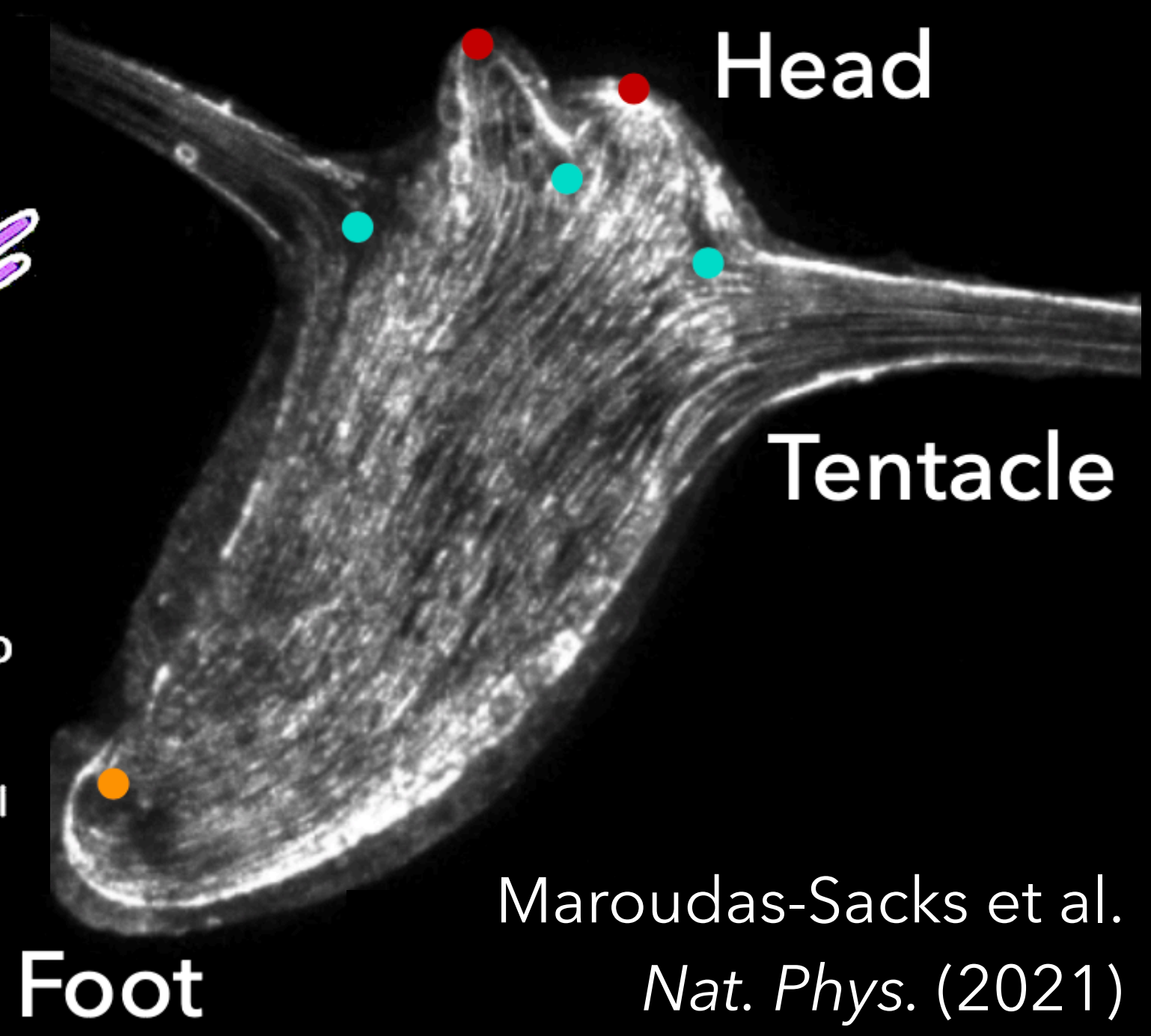
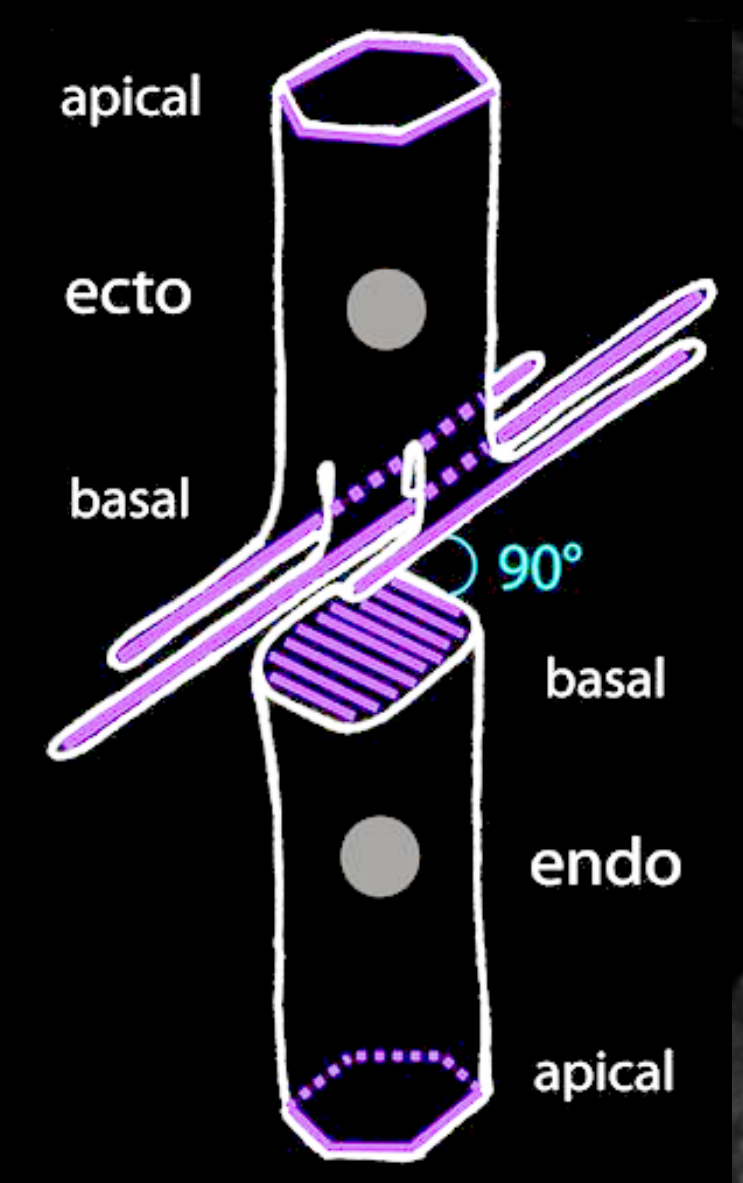
Hydra



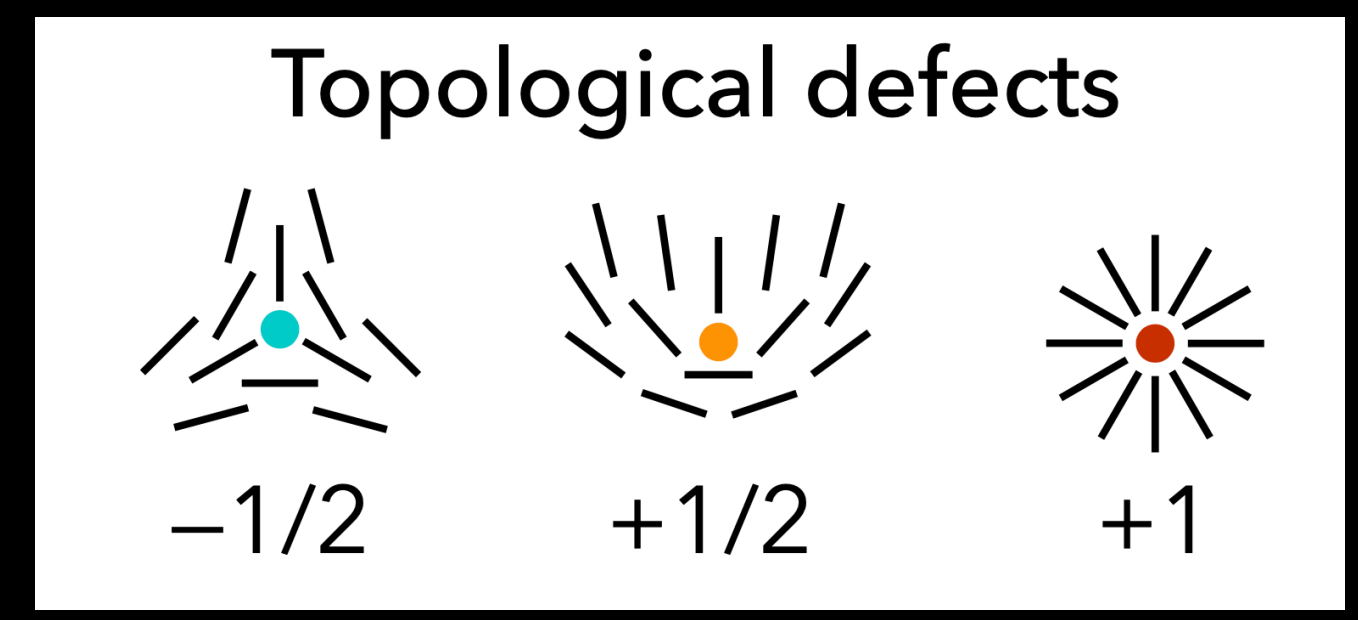
Seybold et al. *Dev. Biol.* (2016)



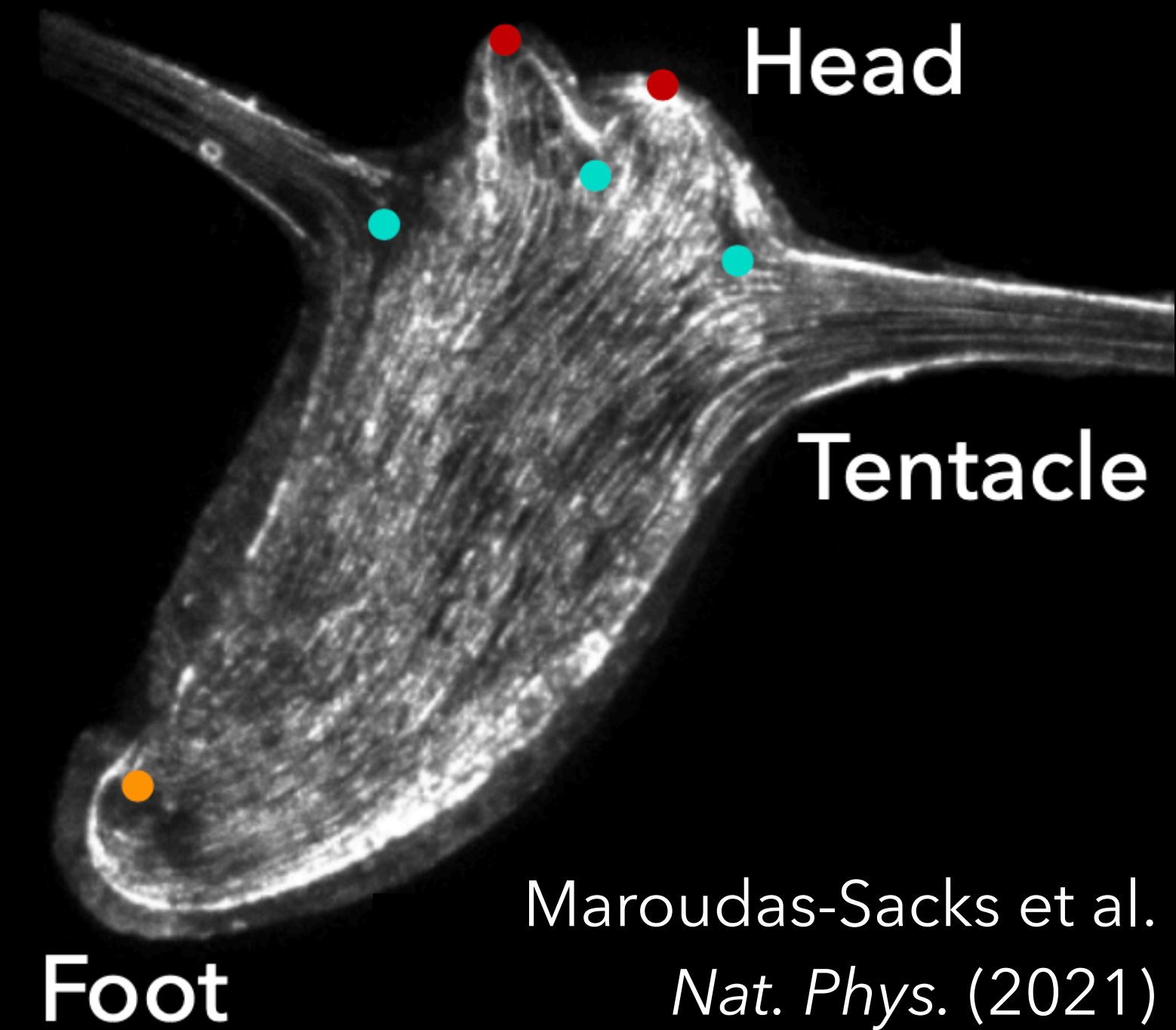
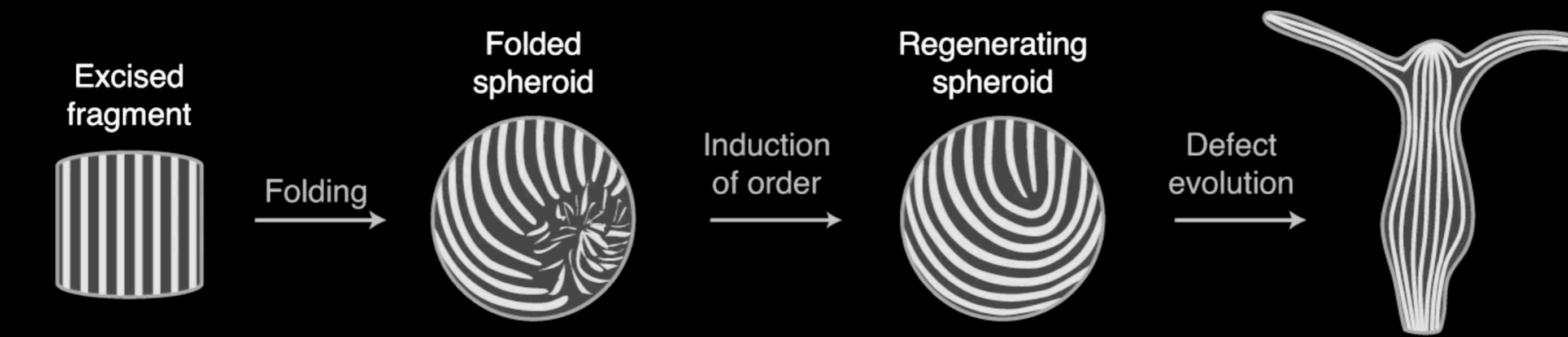
Ferenc et al. *Sci. Adv.* (2021)



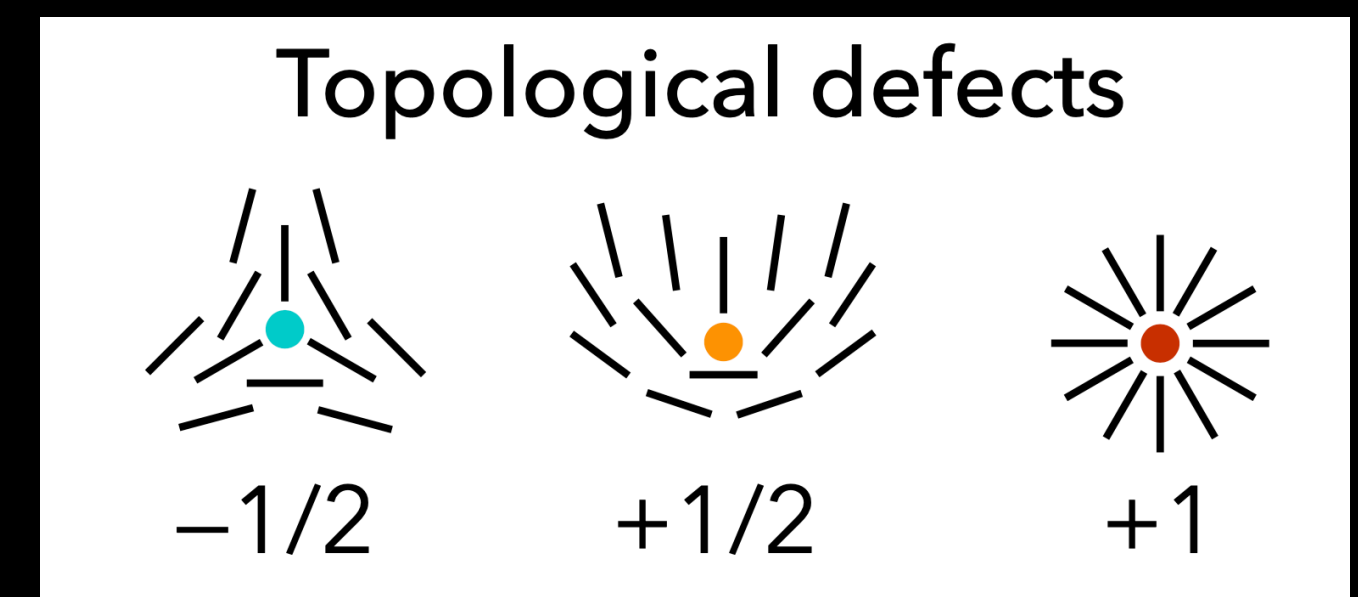
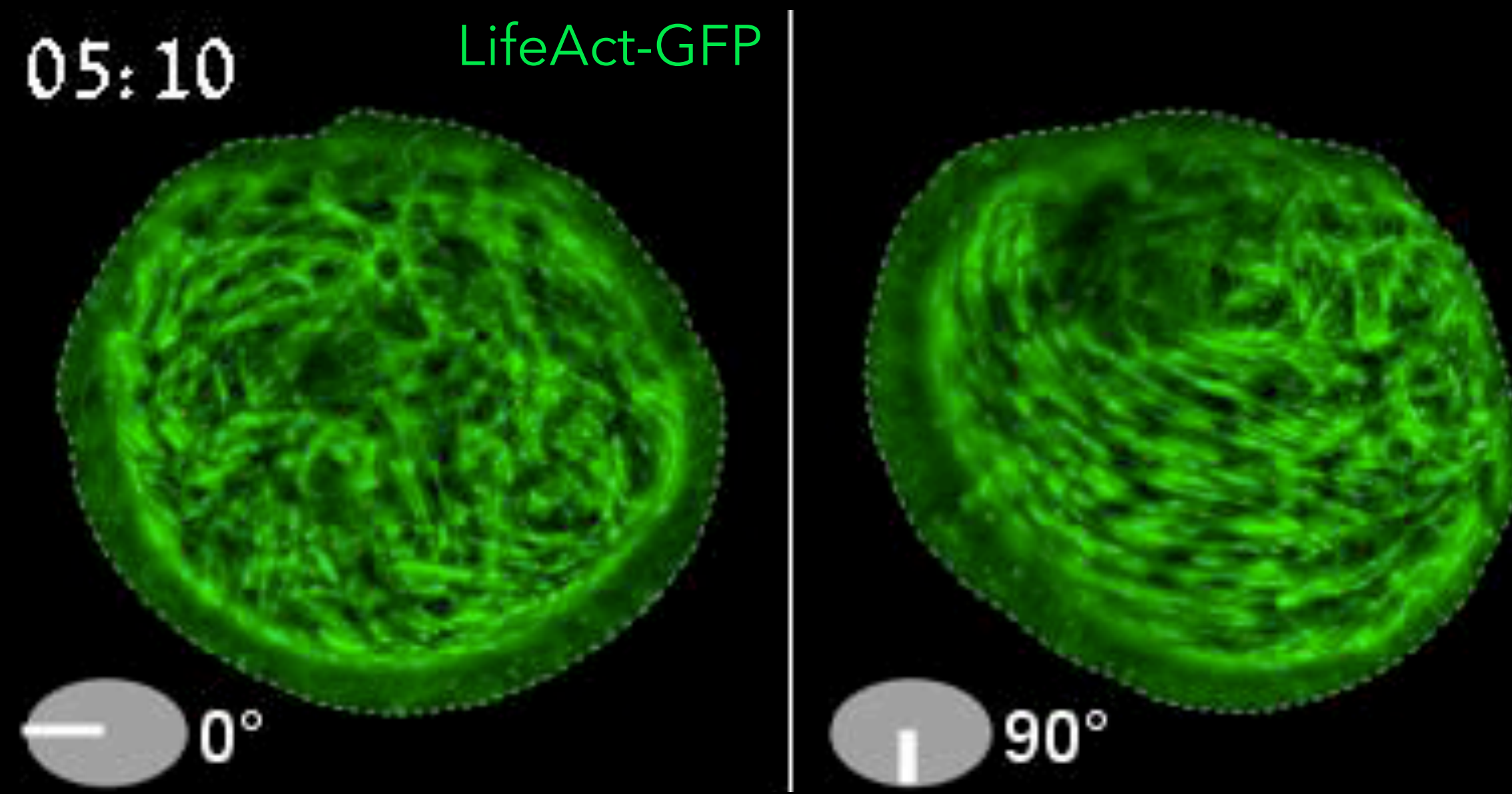
Maroudas-Sacks et al. *Nat. Phys.* (2021)



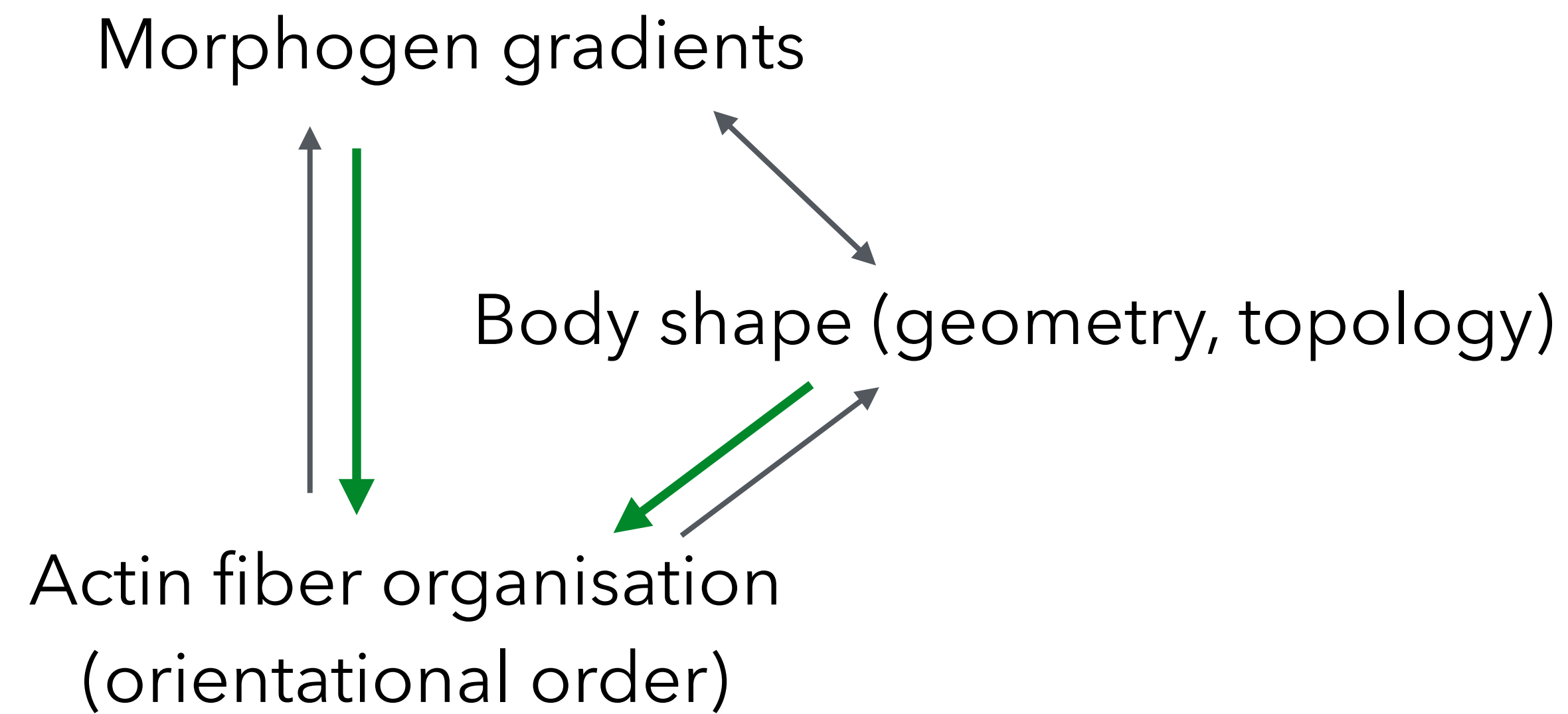
Reorganization of nematic order during regeneration



Maroudas-Sacks et al.
Nat. Phys. (2021)



How do the actin fibers (re-)organize during development and regeneration?



A minimal model for actin fiber orientation

Nematic director field $\mathbf{n}(x, y, t)$

$$\mathcal{F}[\mathbf{n}] = \int dx^2 \frac{K}{2} |\nabla \mathbf{n}|^2 - \beta (\mathbf{n} \cdot \nabla c)^2$$

fibers align with
their neighbors

alignment to
morphogen gradient

$$\partial_t \mathbf{n} = -\gamma \frac{\delta \mathcal{F}[\mathbf{n}]}{\delta \mathbf{n}} \quad \text{Relaxational dynamics minimizes free energy}$$



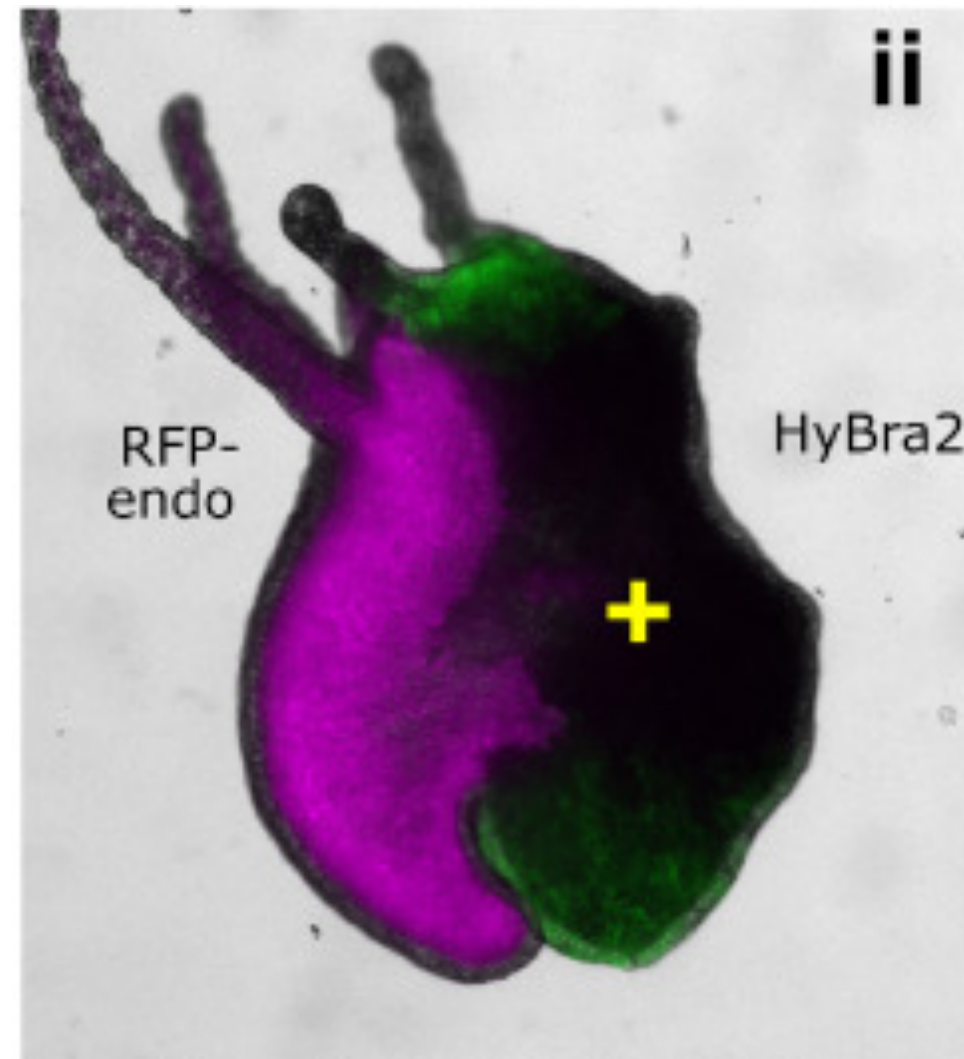
Cristina Marchetti
(UCSB)



Zihang Wang
(UCSB)

Actin aligns with morphogen concentration gradient

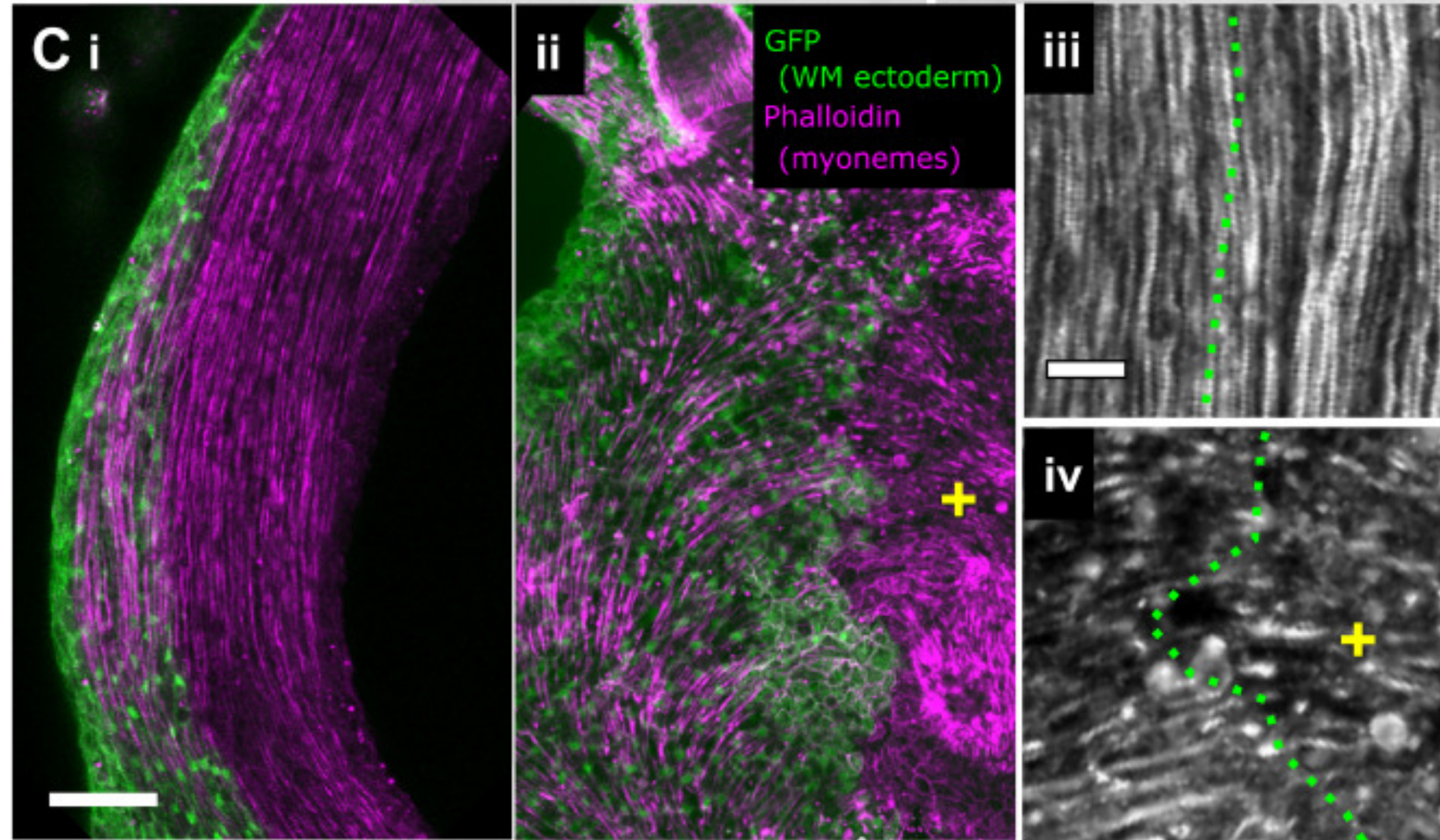
Grafted animal



Wild type



Wnt
overexpr.



Wang, R. et al. *Developmental Biology* **467**, 88-94 (2020).

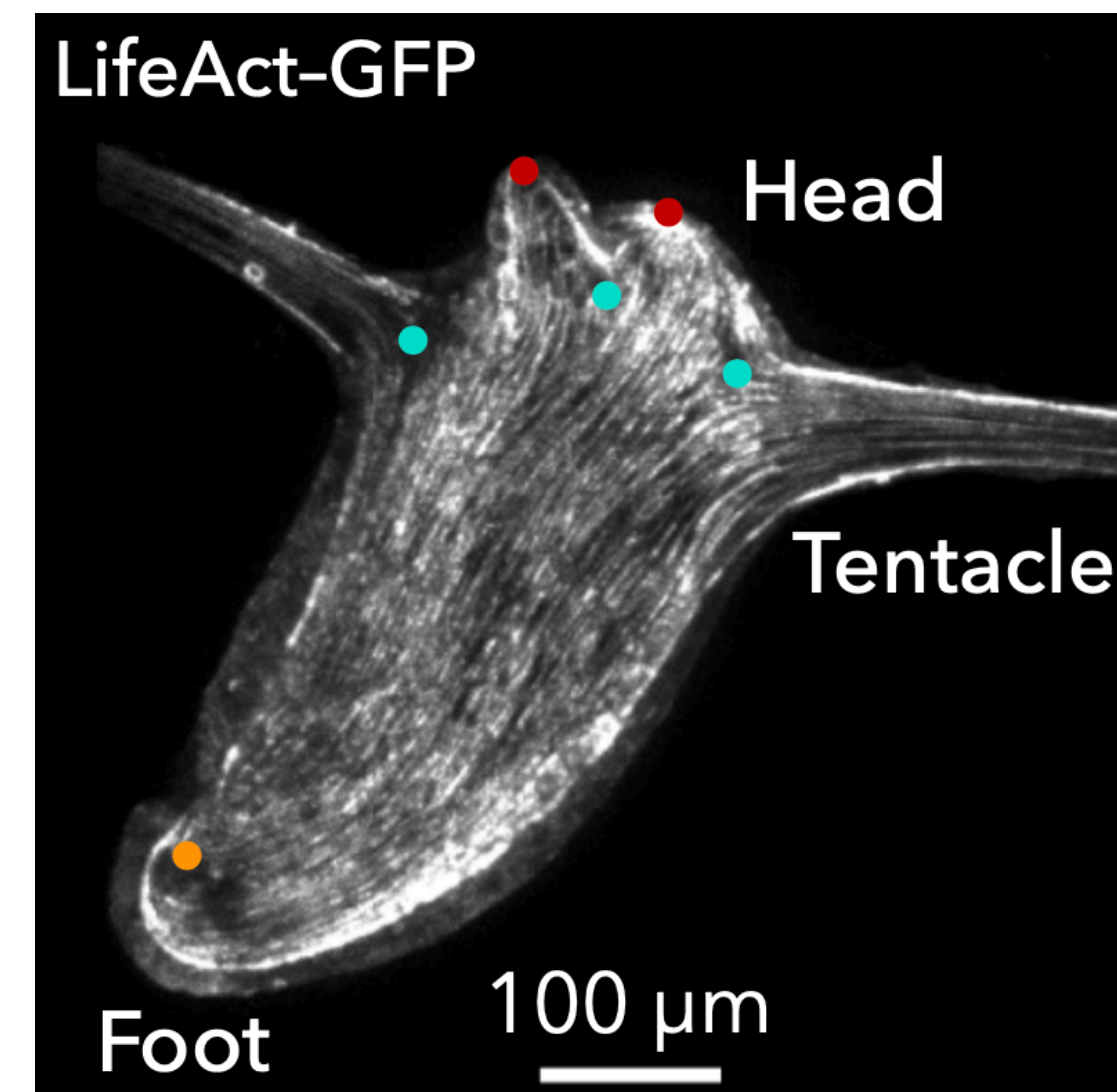
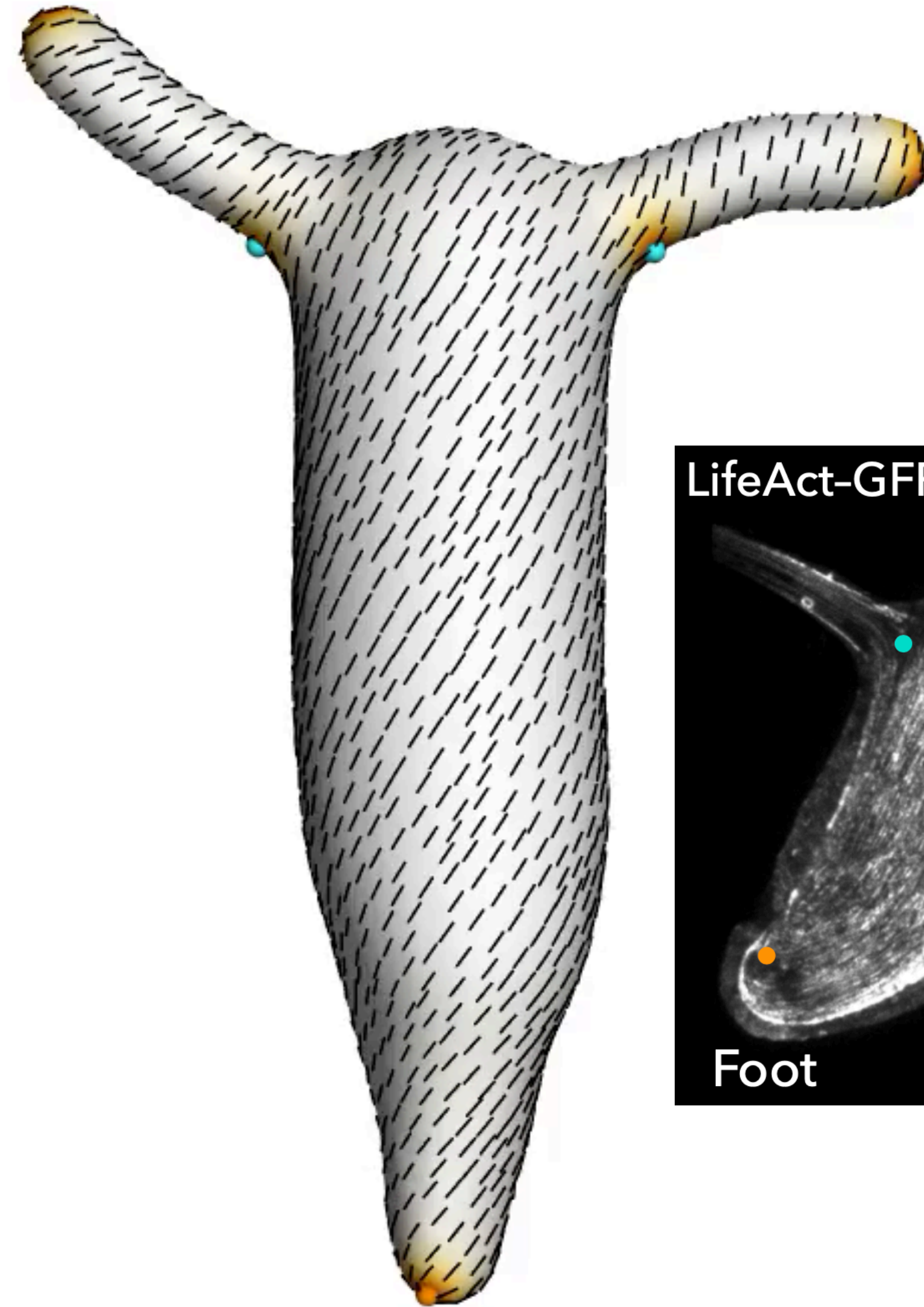
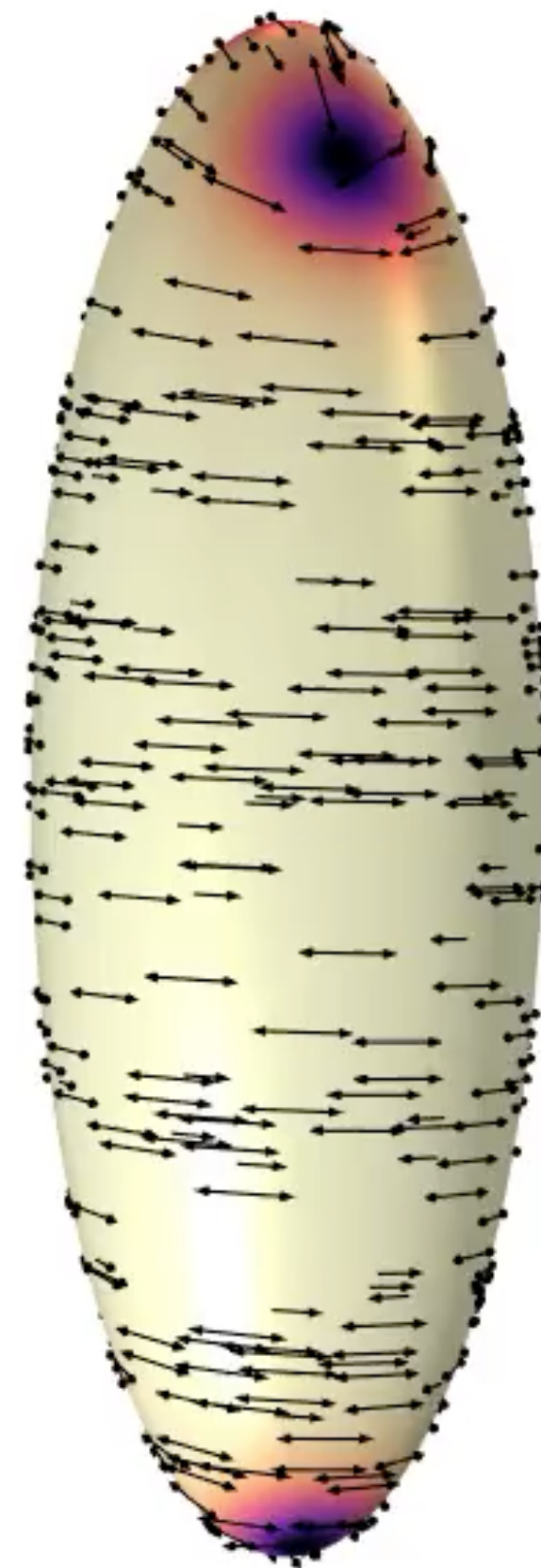
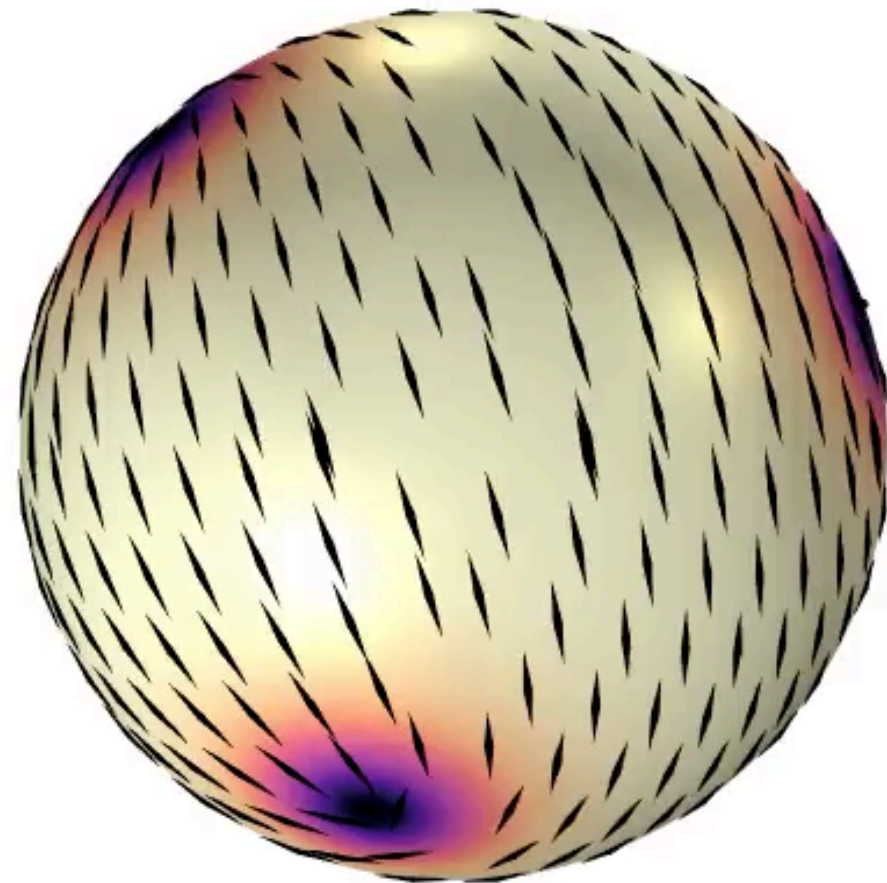
The effect of shape on orientational order

Nematic director field $\mathbf{n}(x, y, t)$ ($\mathbf{n} \equiv -\mathbf{n}$)

$$\mathcal{F}[\mathbf{n}] = \int dx^2 \left[\frac{K}{2} |\nabla \mathbf{n}|^2 - \beta (\mathbf{n} \cdot \nabla c)^2 \right]$$

fibers align with
their neighbors

alignment to
morphogen gradient



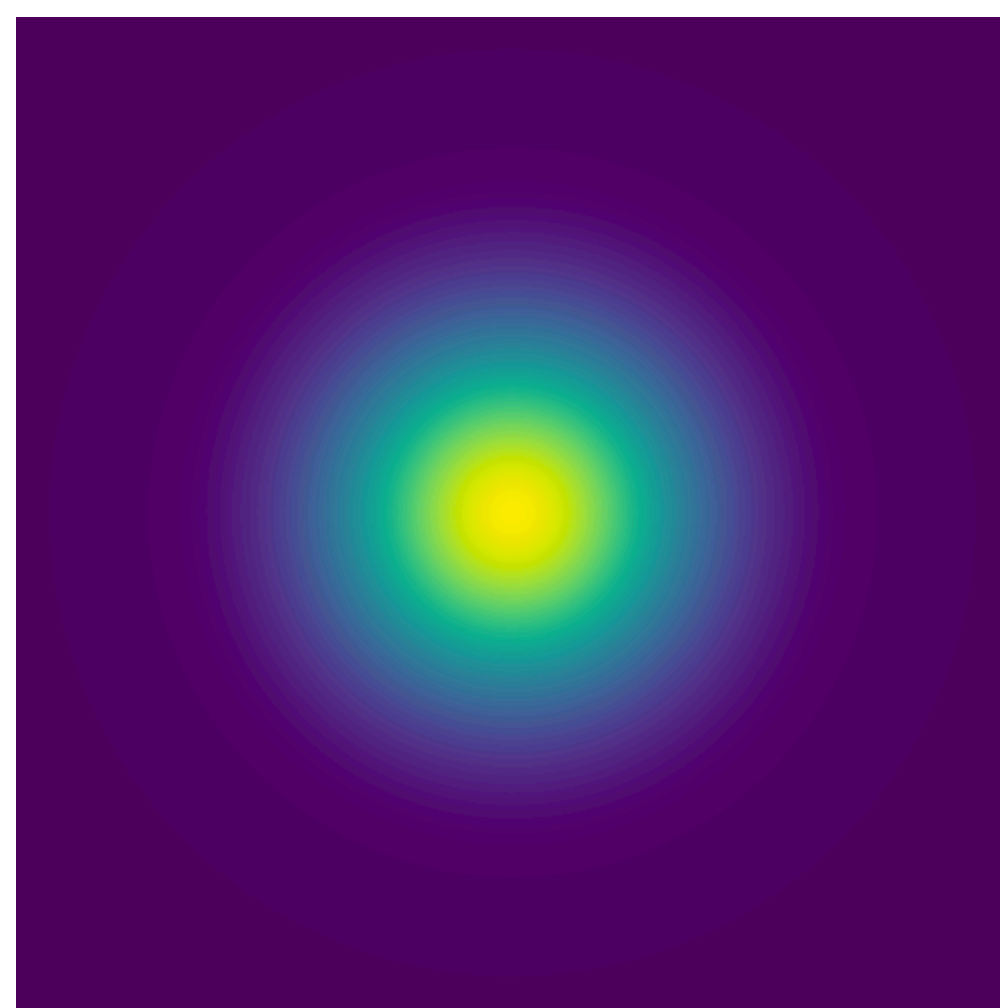
Defect unbinding

Nematic director field $\mathbf{n}(x, y, t)$ ($\mathbf{n} \equiv -\mathbf{n}$)

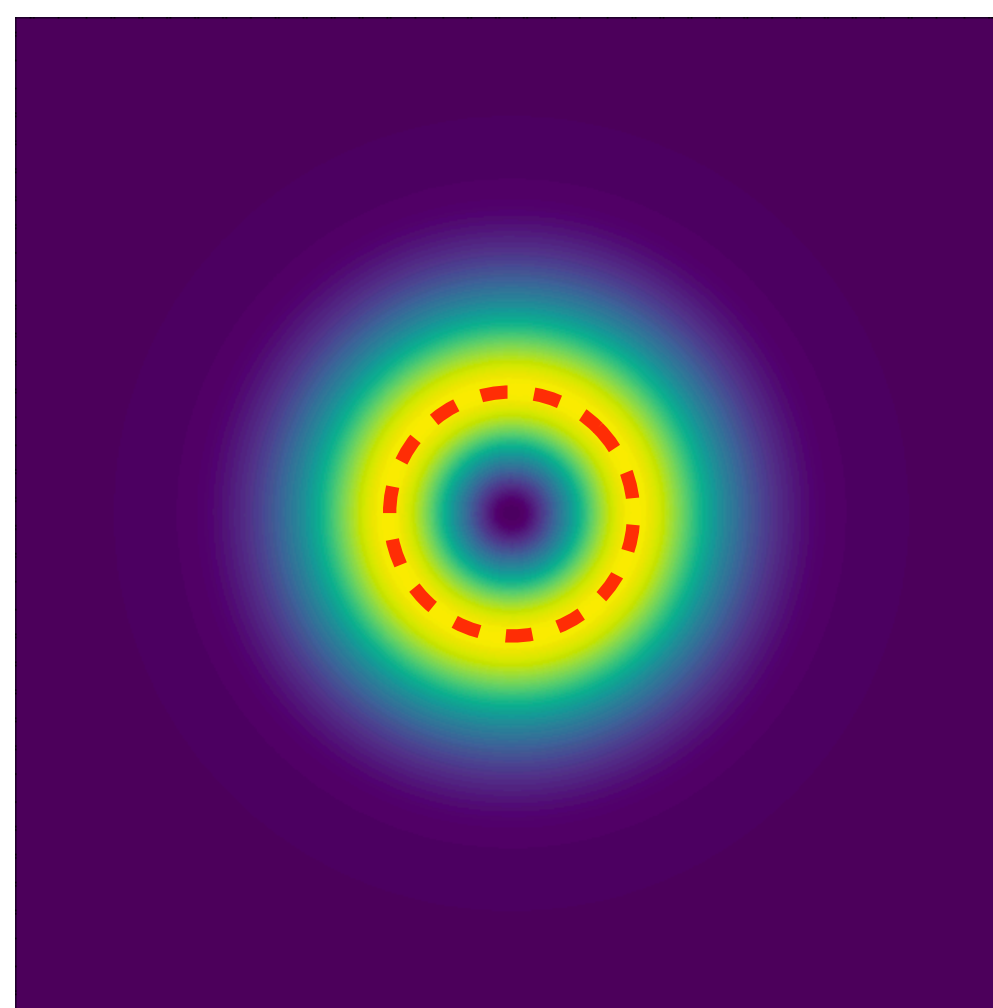
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their neighbors

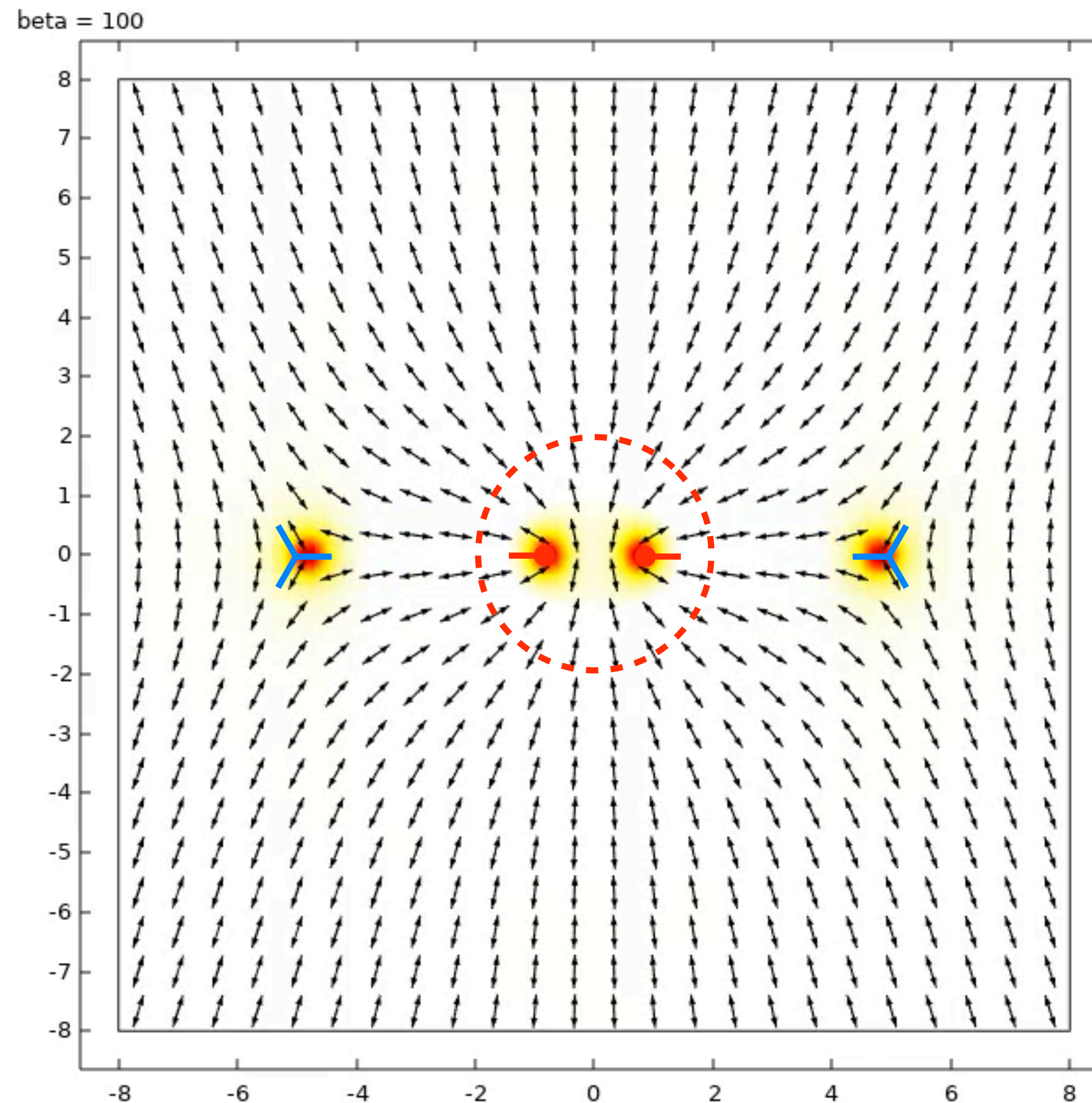
alignment to
prescribed gradient



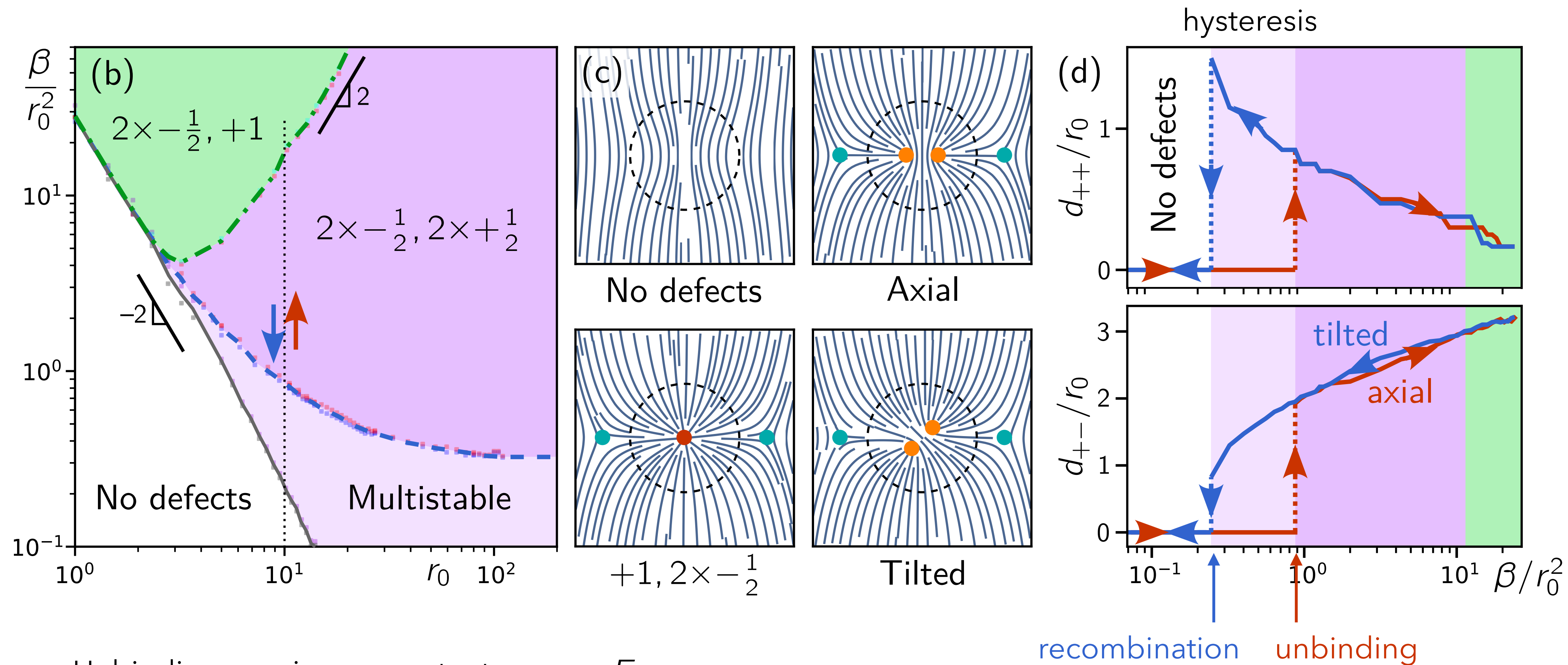
$$c(r) = e^{-r^2/(2r_0^2)}$$



Gradient magnitude $|\nabla c|$



Defect-unbinding phase diagram



Unbinding requires a constant energy E_{unbind}

Alignment energy from defect region $\xi^2 \frac{\beta}{r_0^2} \sim E_{\text{unbind}} \Rightarrow \beta_{\text{unbind}} \sim E_{\text{unbind}} \frac{r_0^2}{\xi^2}$ (ξ = defect core size)

Competition of neighbor- and gradient alignment

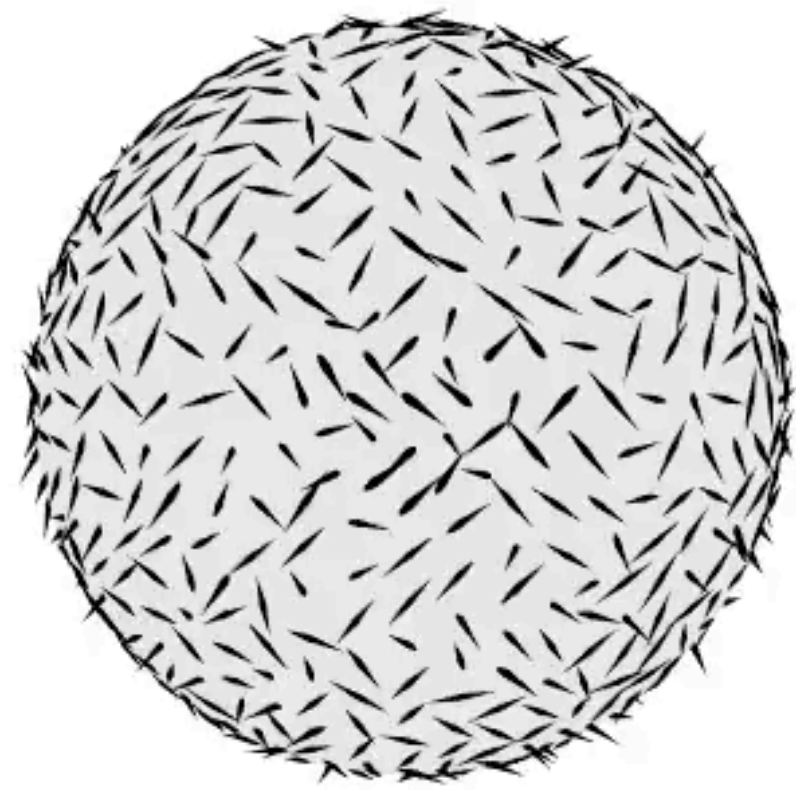
Nematic director field $\mathbf{n}(x, y, t)$ ($\mathbf{n} \equiv -\mathbf{n}$)

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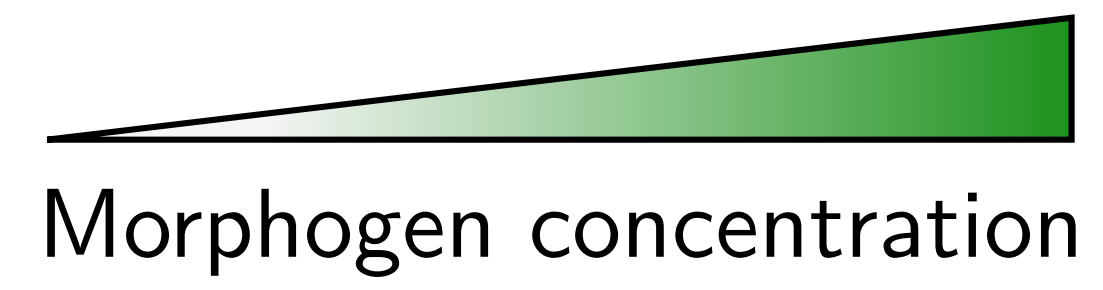
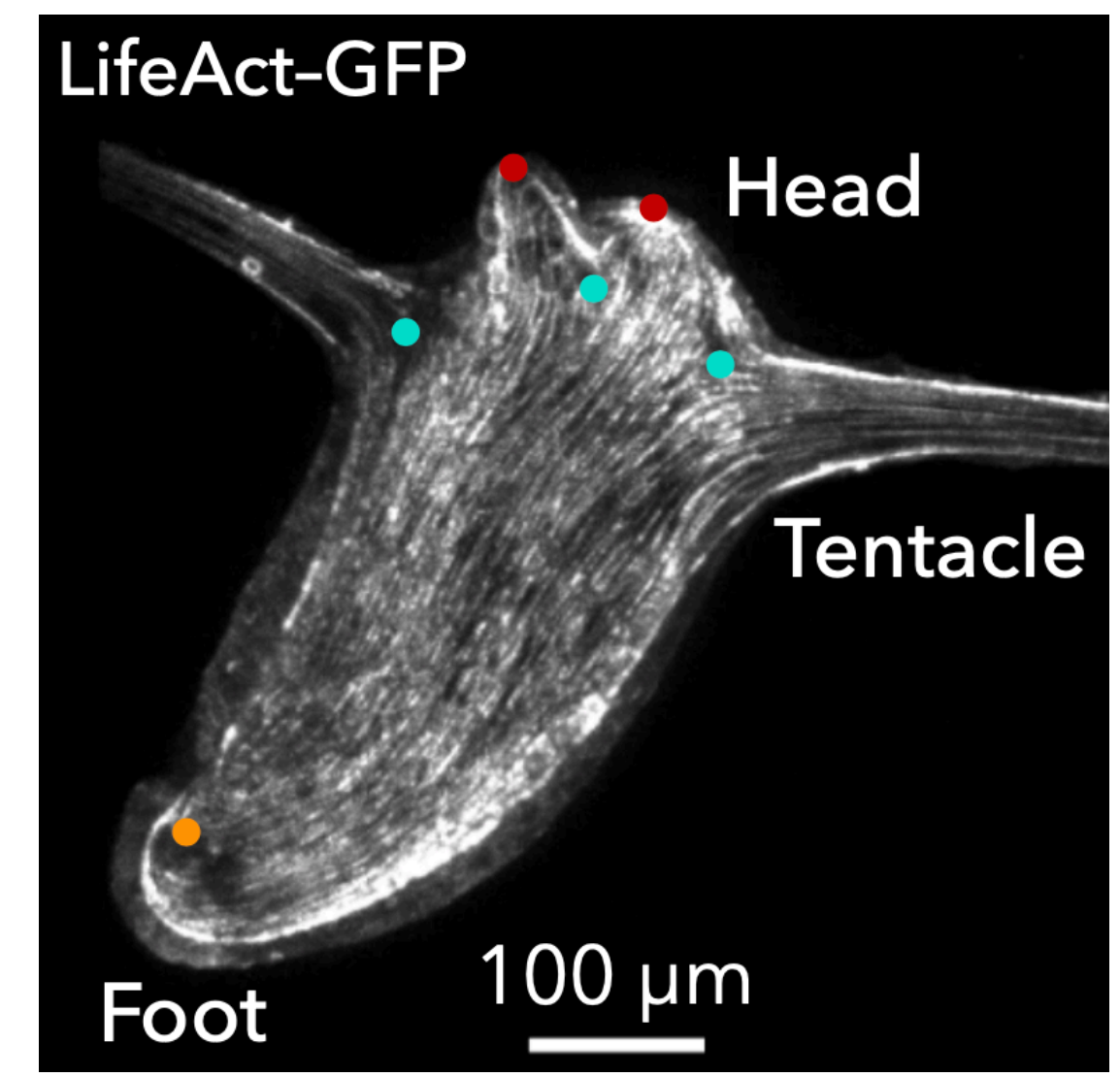
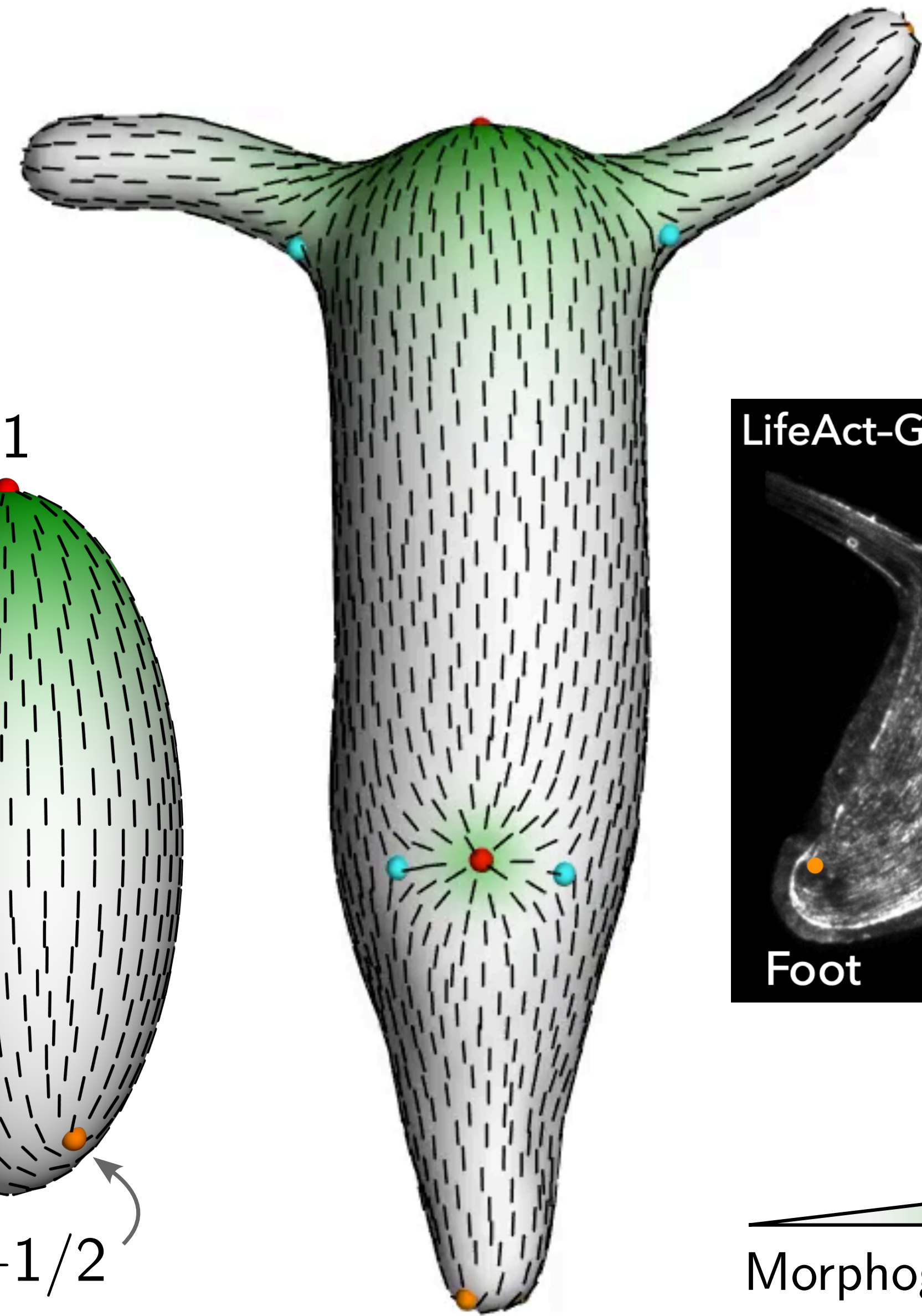
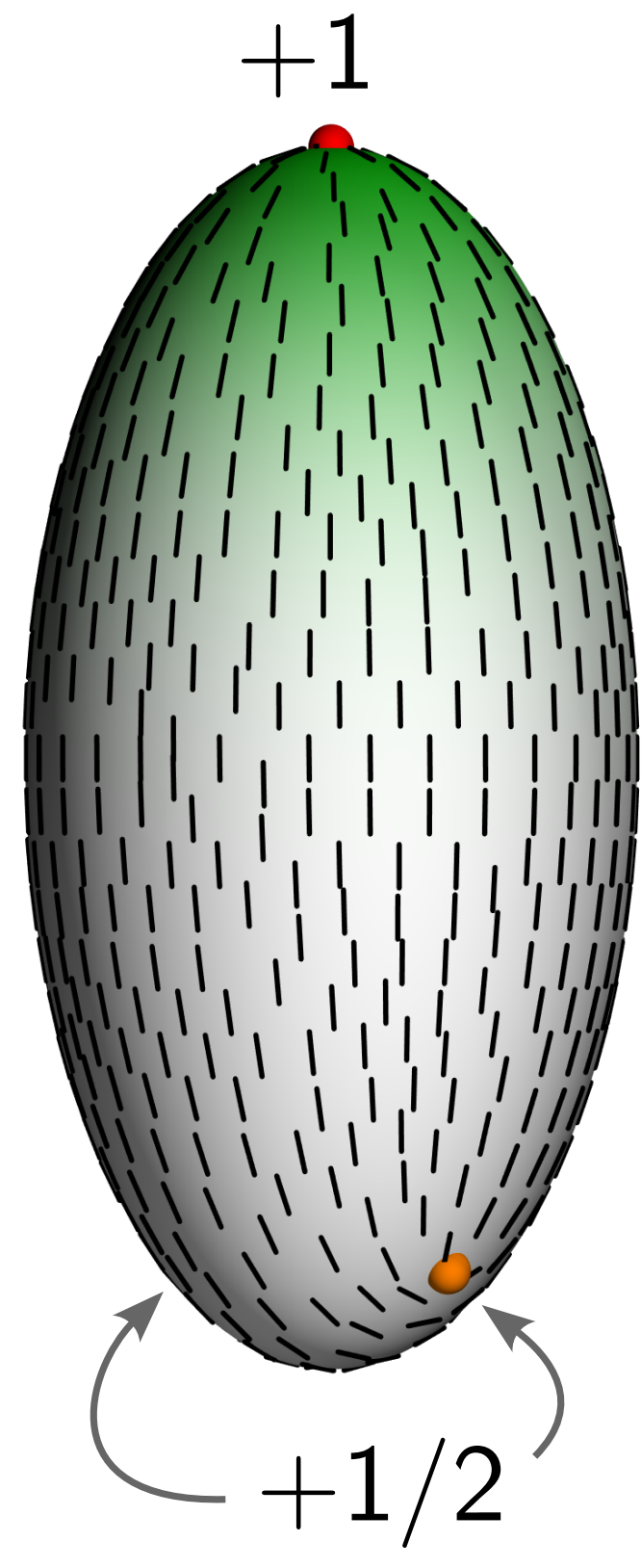
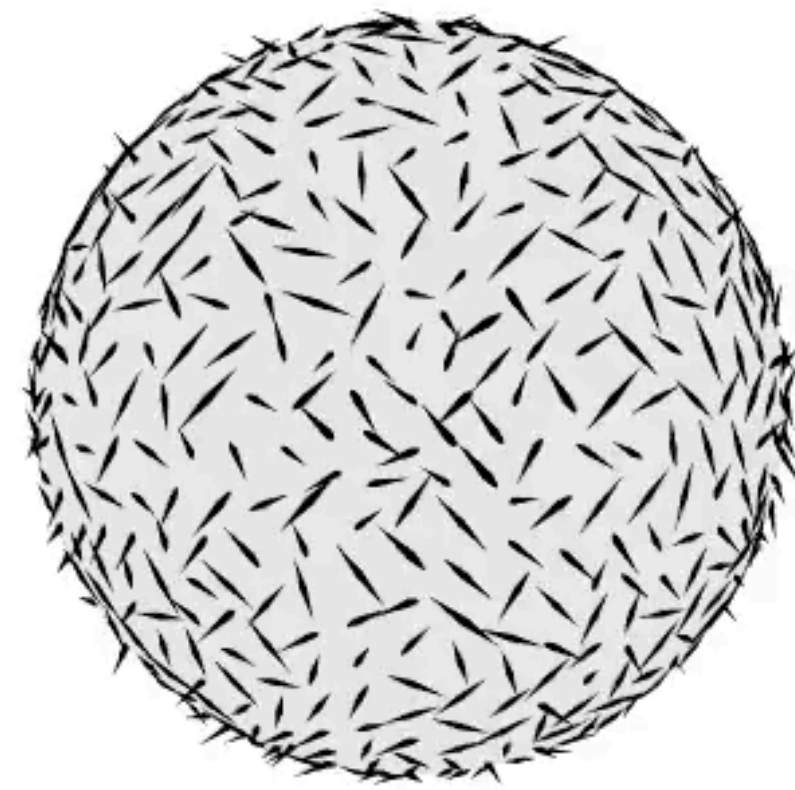
fibers align with their neighbors

alignment to prescribed gradient

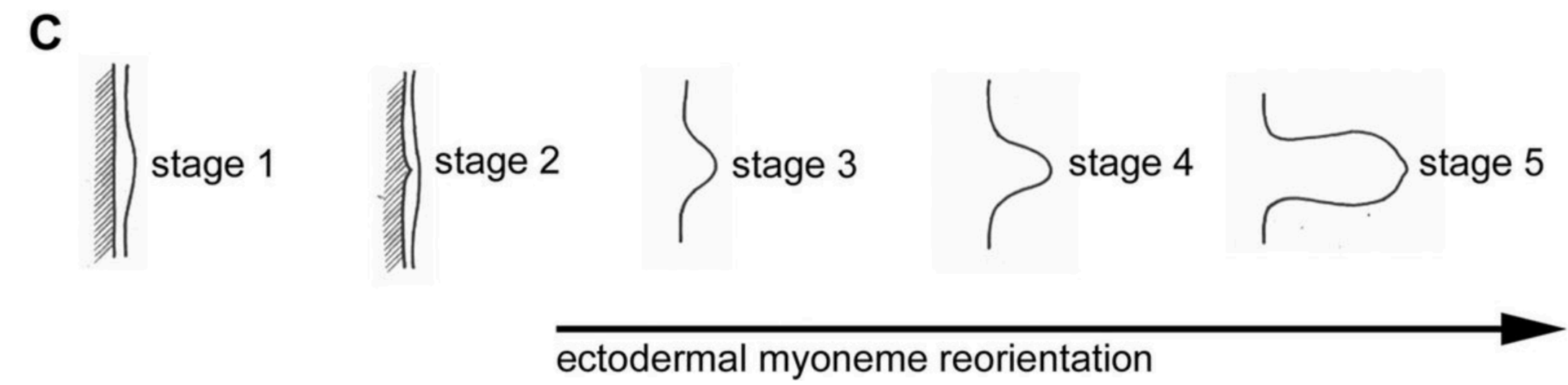
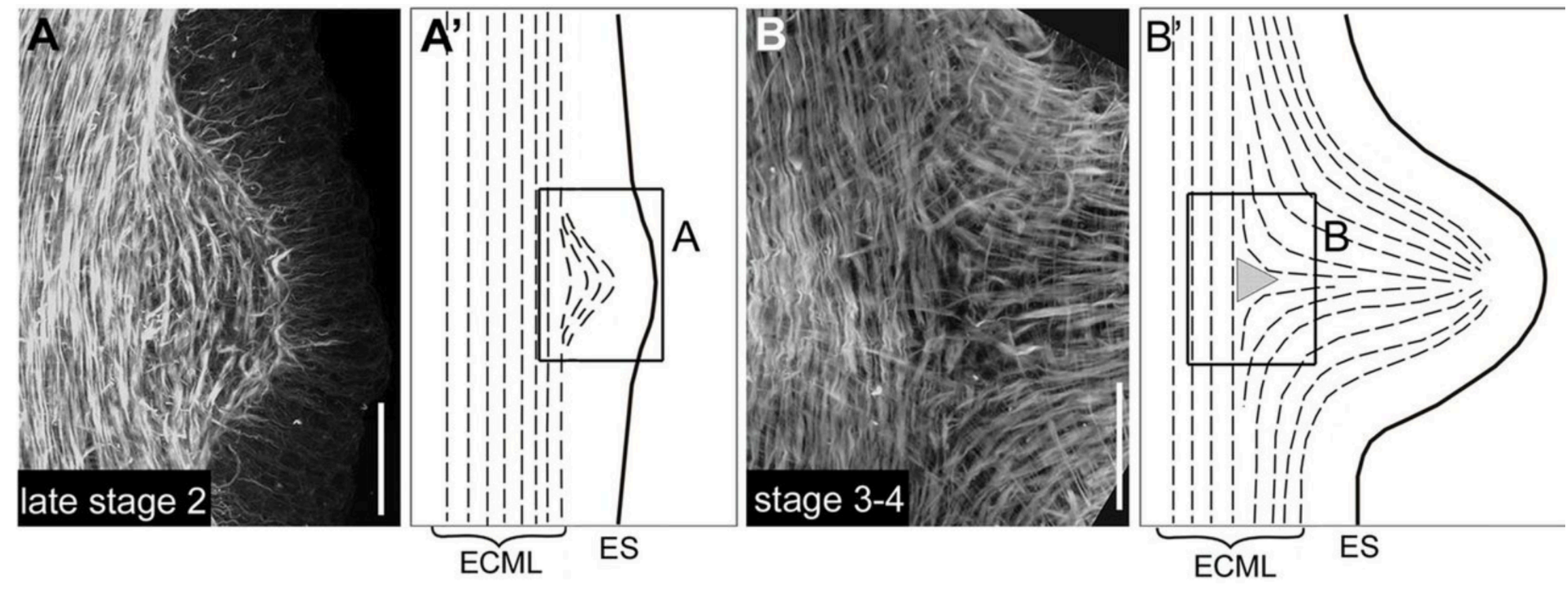
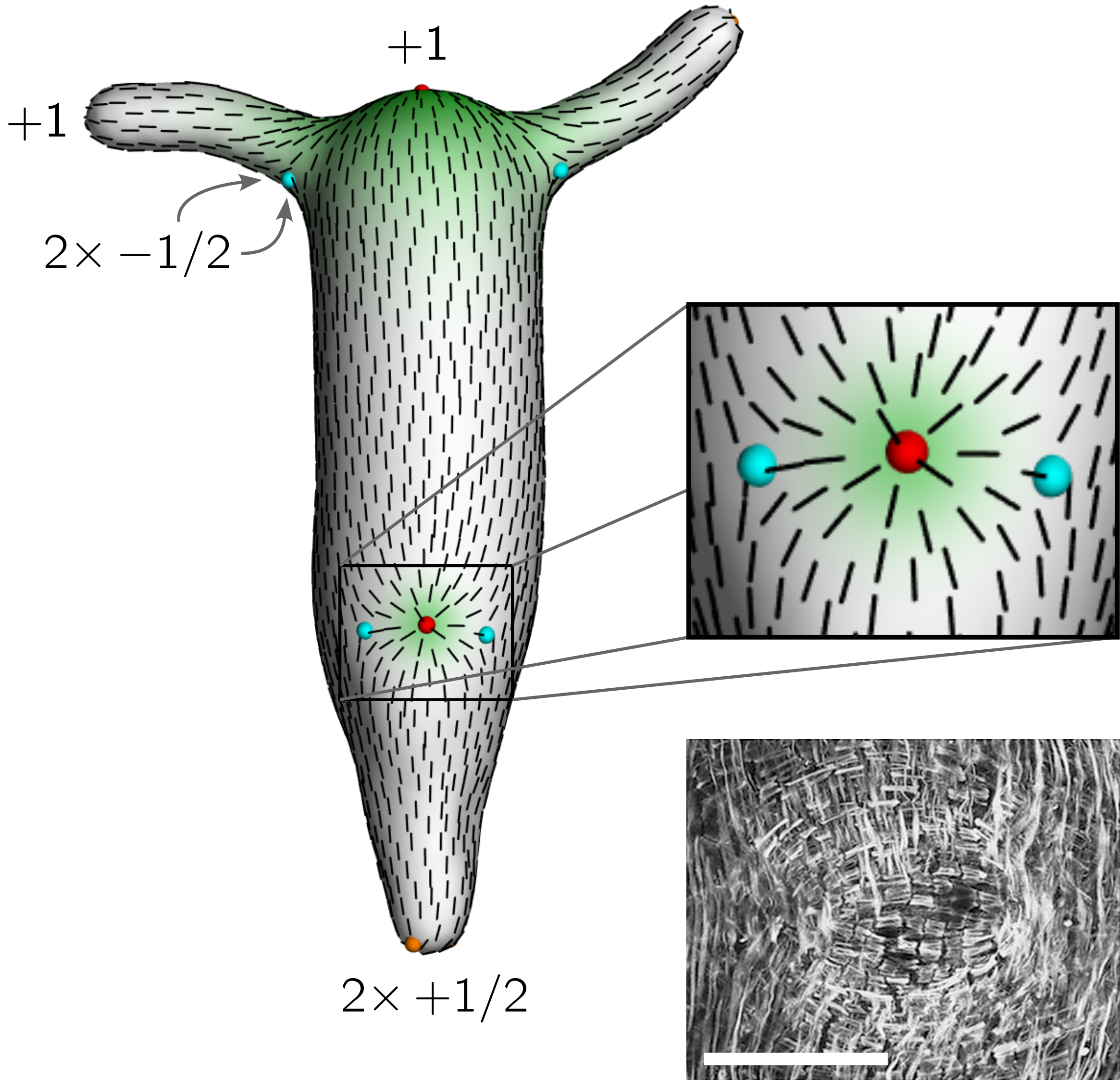
Top view



Bottom view



Actin fiber reorganization during budding

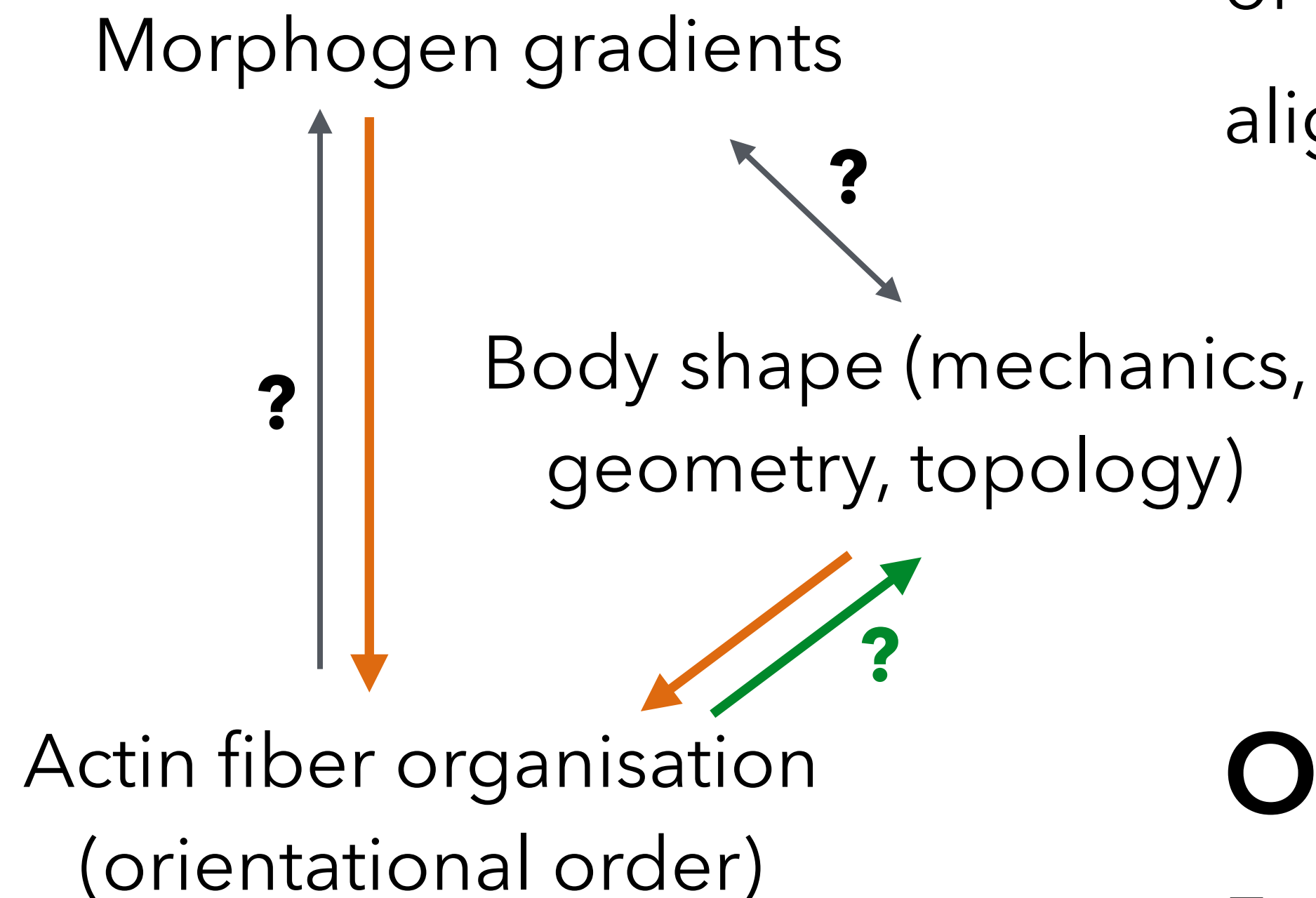


Aufschnaiter et al. *Biology Open* (2017)

Wang, Marchetti & **FB**, *PNAS* (2023)

Summary

Self-organization of orientational order by the competition of two mechanisms: *local* alignment to neighbors and alignment to *large scale* morphogen gradient.



Outlook

Emergence of the tissue-scale gradient (symmetry breaking, mechanochemical feedback)

Alignment of actin fibers on the cell scale

How can tissue change shape, like a fluid,
while resisting external forces, like a solid?



Nikolas Claussen
(now Princeton)



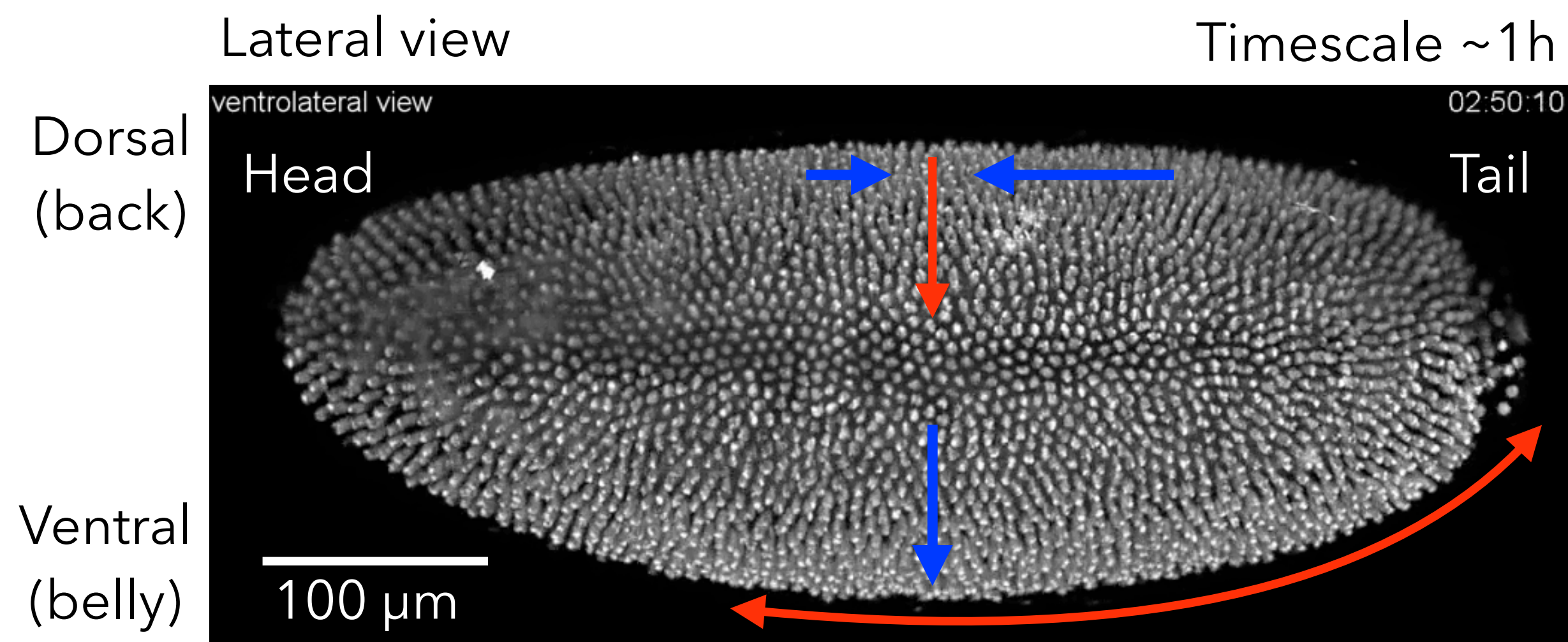
Eric Wieschaus
(Princeton)



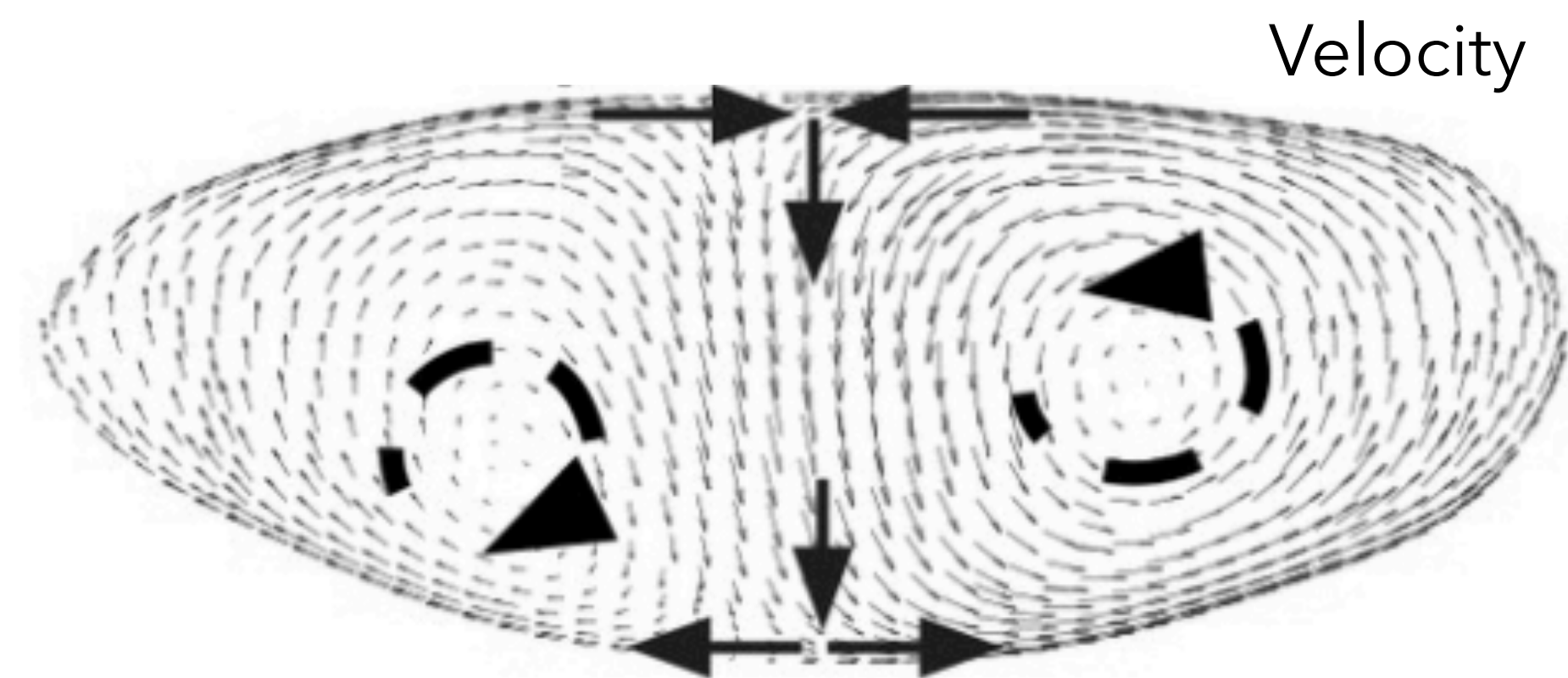
Boris Shraiman
(KITP)

How can tissue change shape, like a fluid,
while resisting external forces, like a solid?

Body axis elongation

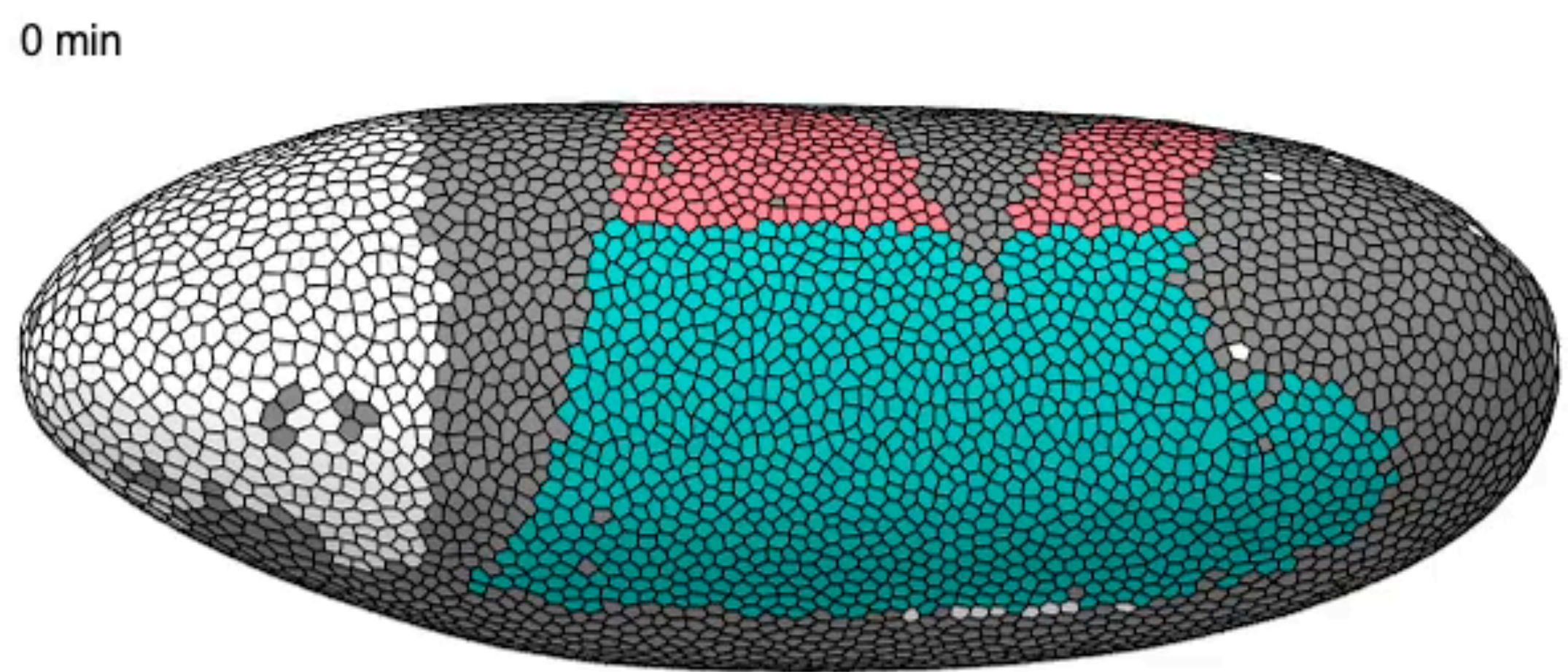


Tomer et al. *Nat. Methods* (2012)



Hyperbolic shear flow (convergent-extension)

Cell-scale kinematics ("tissue tectonics")

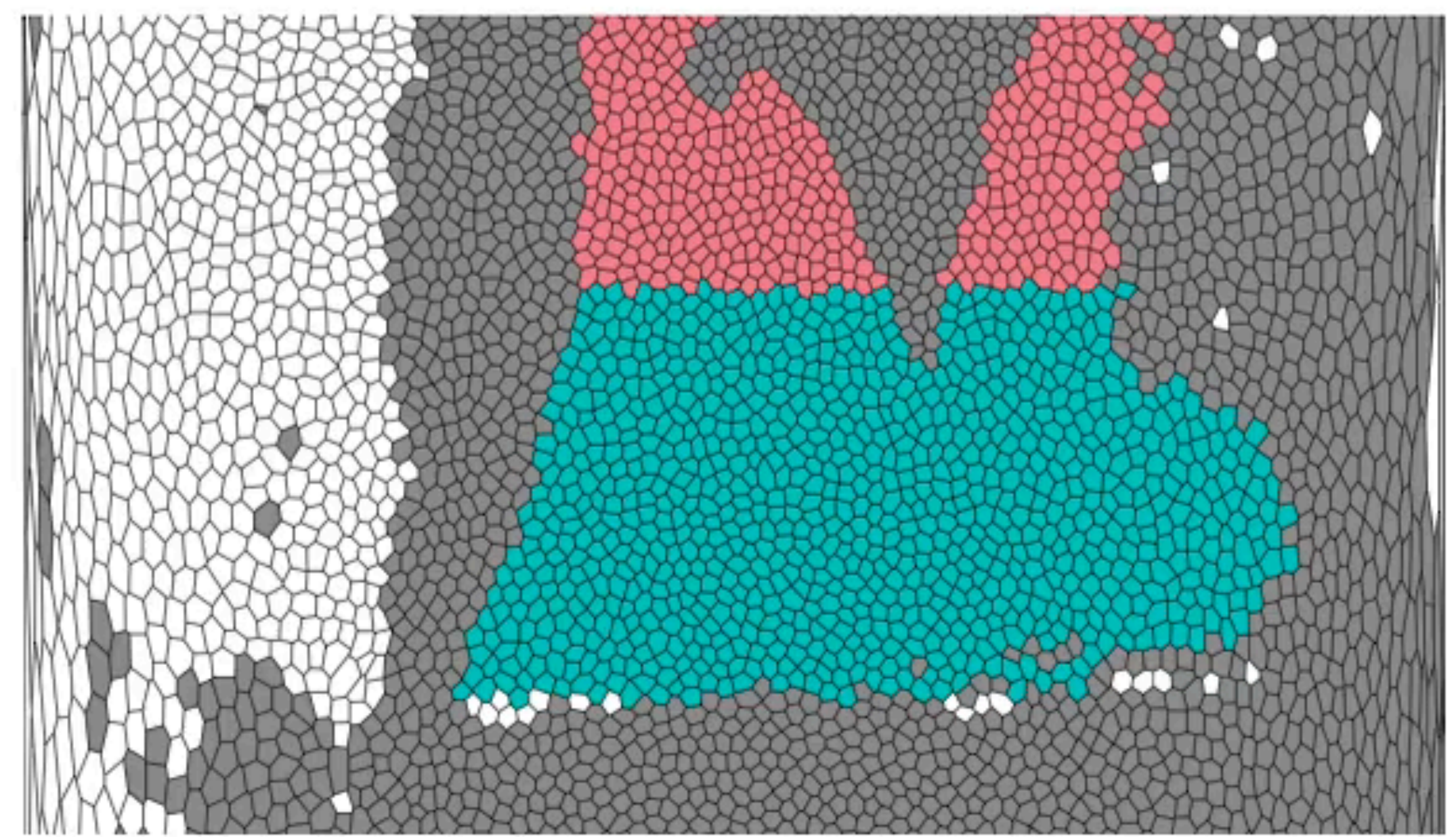


Head

Trunk

Dorsal (back)

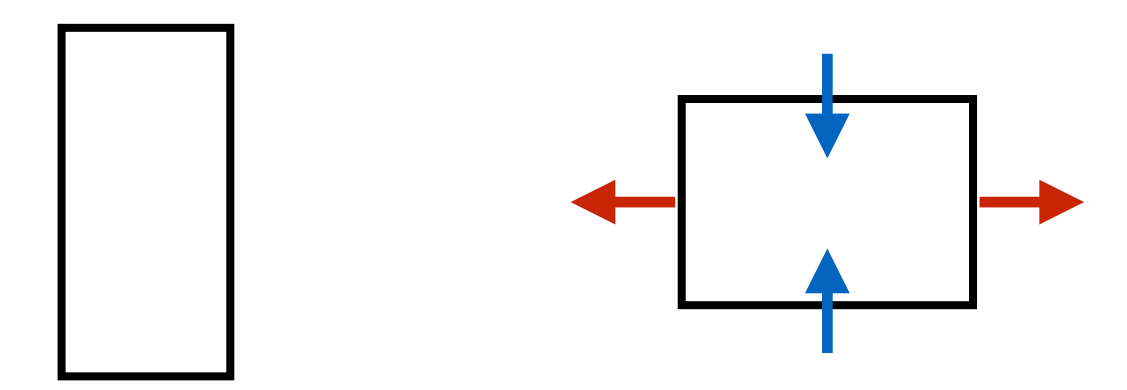
Ventral (belly)



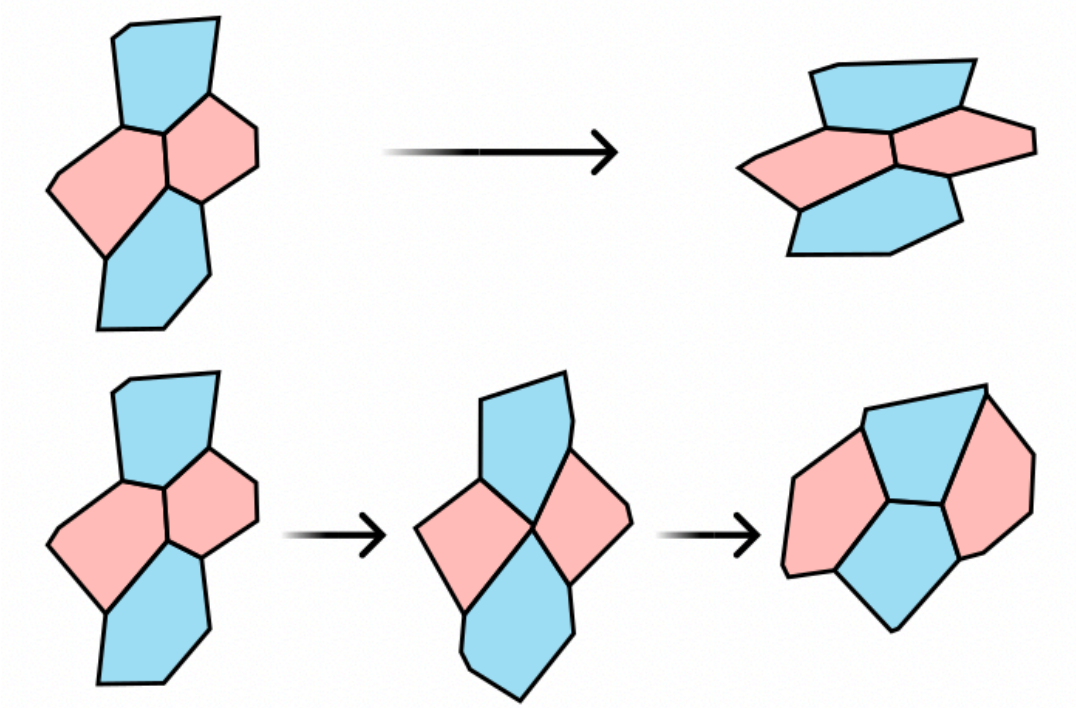
Segmentation data from Stern et al., *Curr Biol.* (2022)

Tissue strain

Convergent-Extension



=
Cell shape changes
+
Cell rearrangements
(T1 processes)

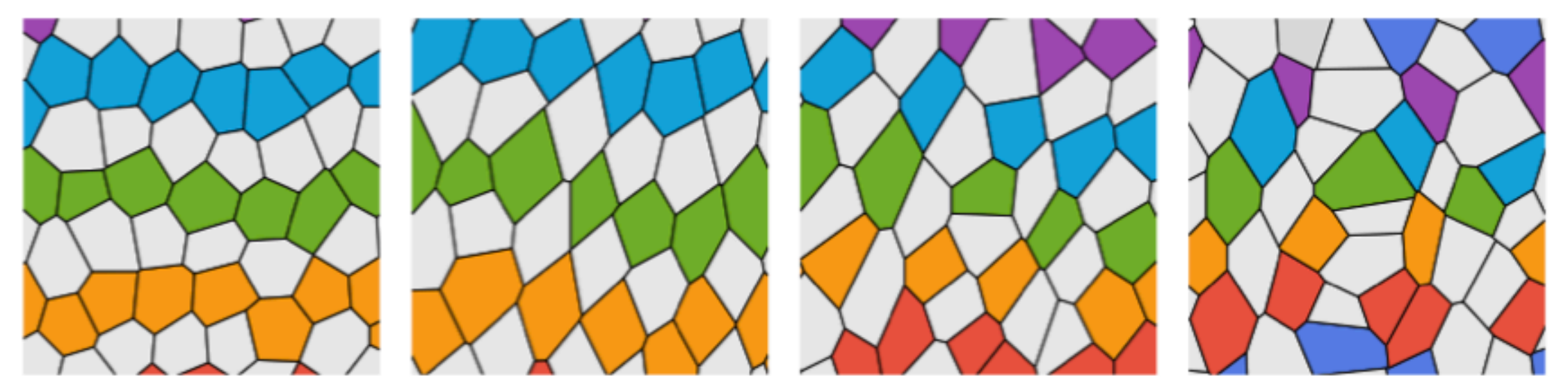


0 min

25 min

37 min

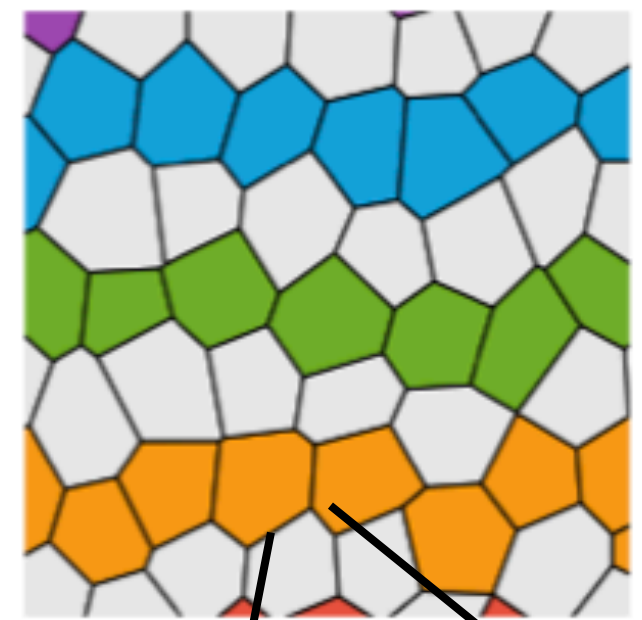
50 min



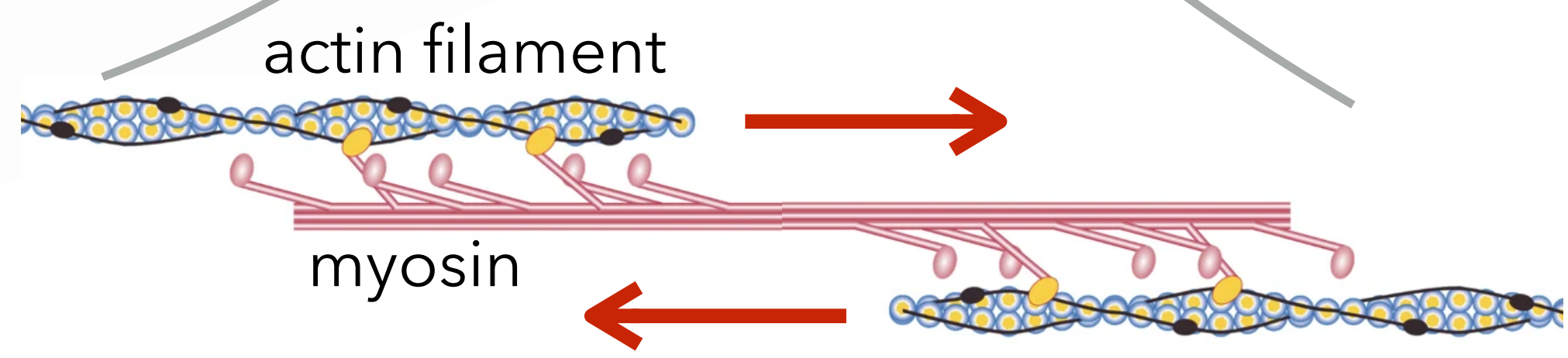
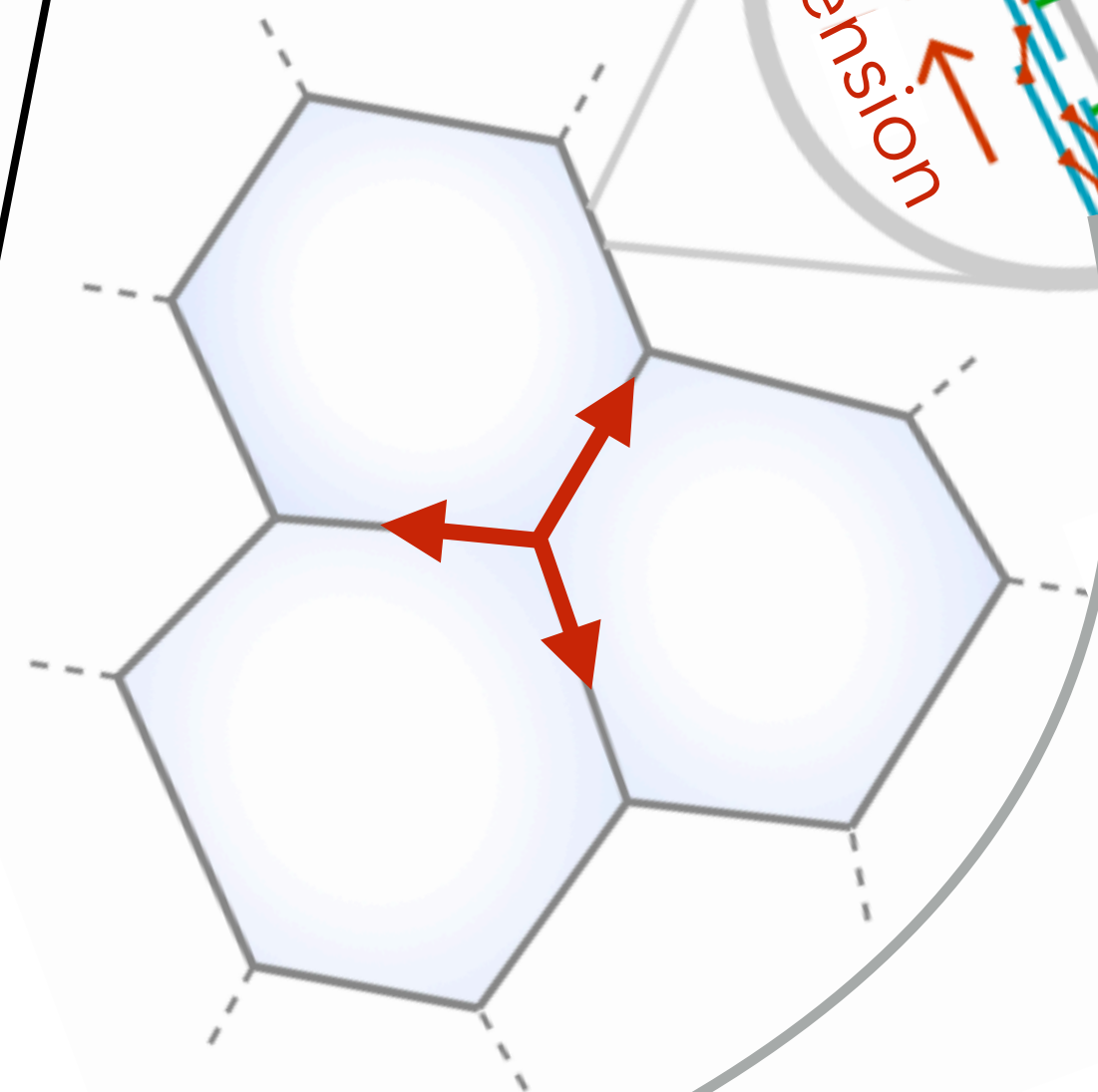
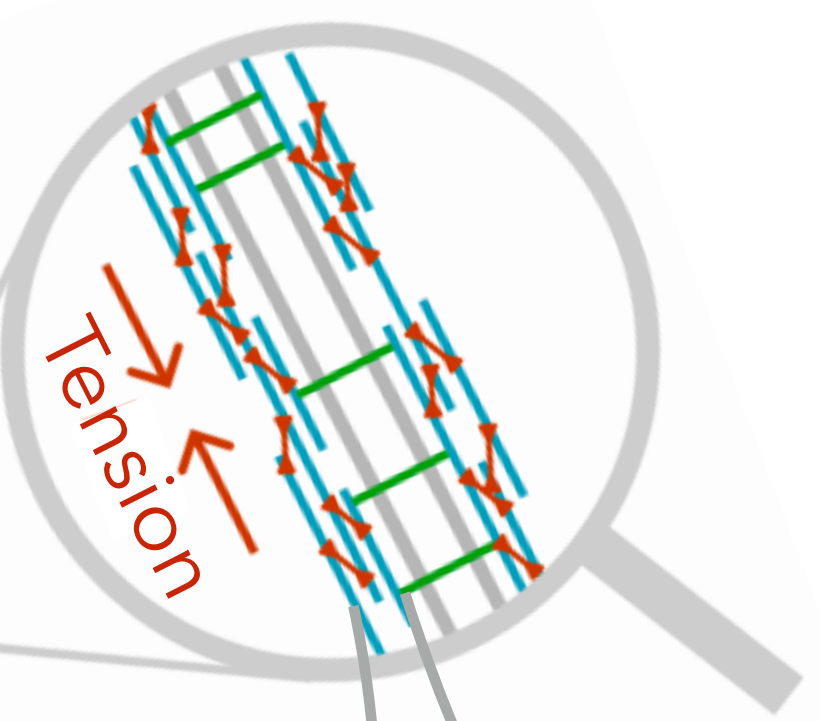
Highly organized cell rearrangements

FB, Claussen, et al, *eLife* (2024)

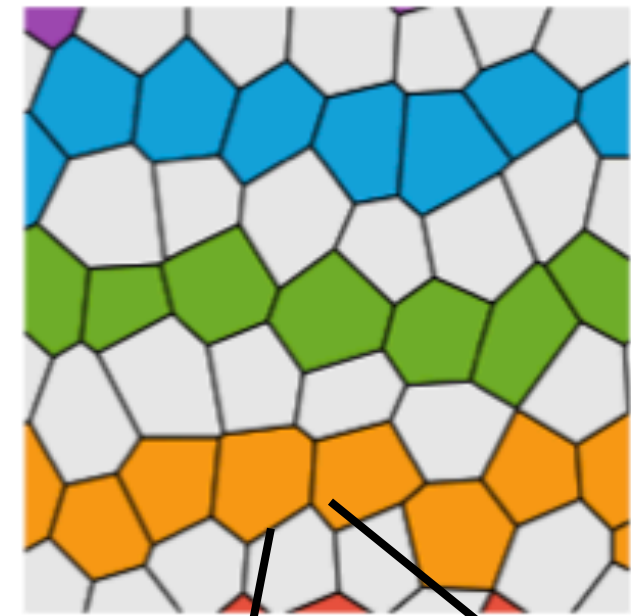
Epithelial tissue forms a tension net in force balance



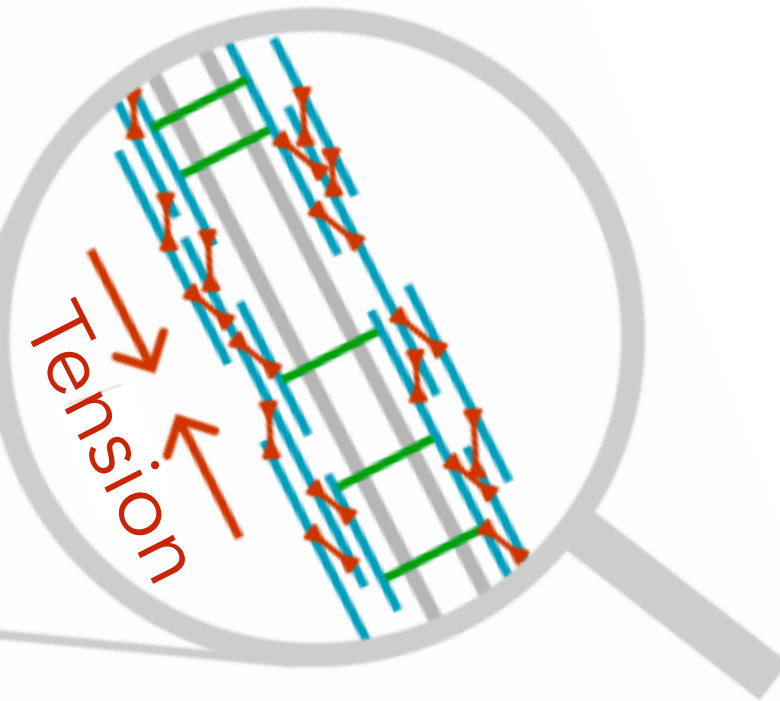
Adhesion- and motor molecules



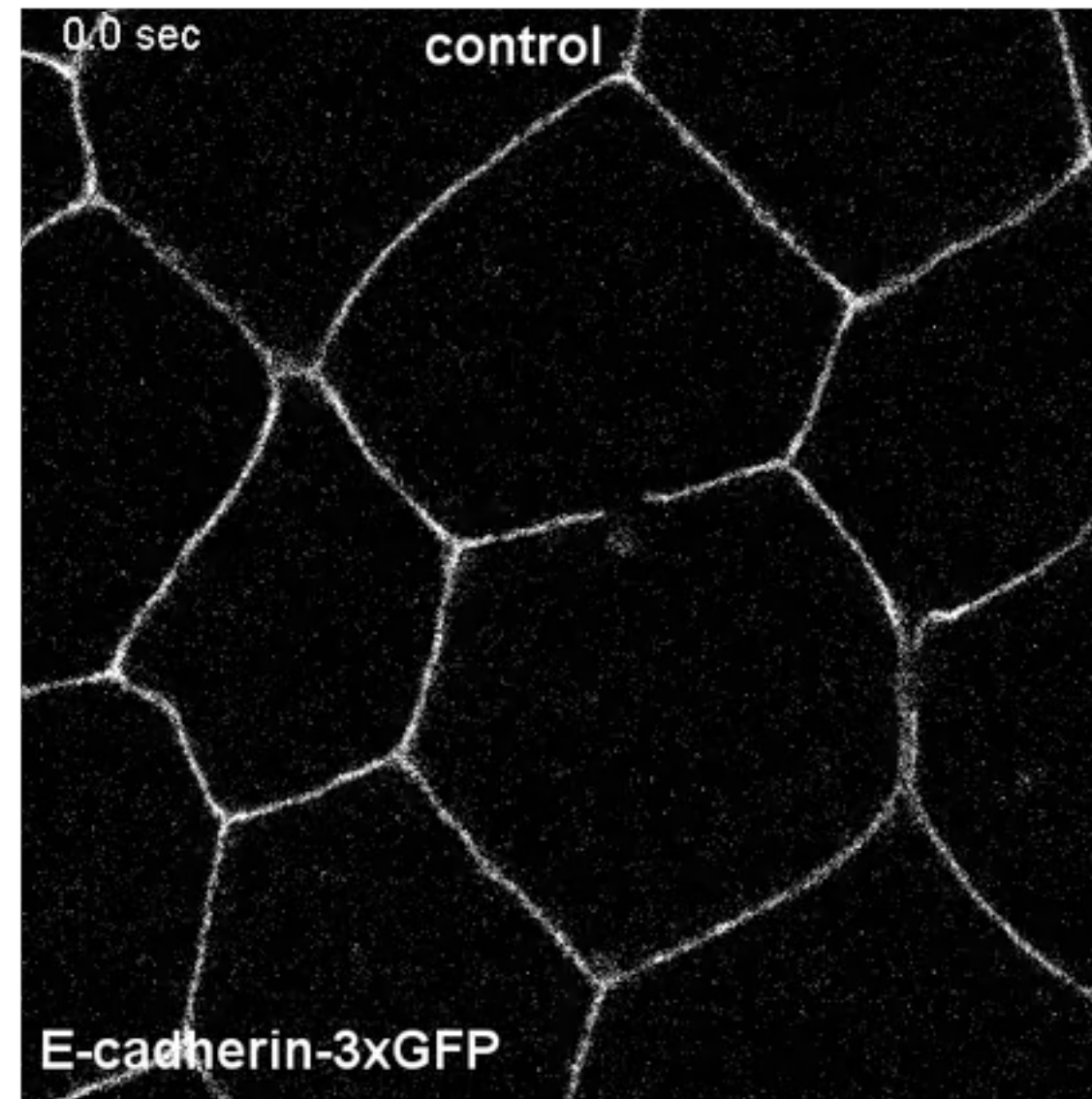
Epithelial tissue forms a tension net in force balance



Adhesion- and motor molecules



Relaxation timescale < 1 min



Arnold et al., *eLife* (2019)

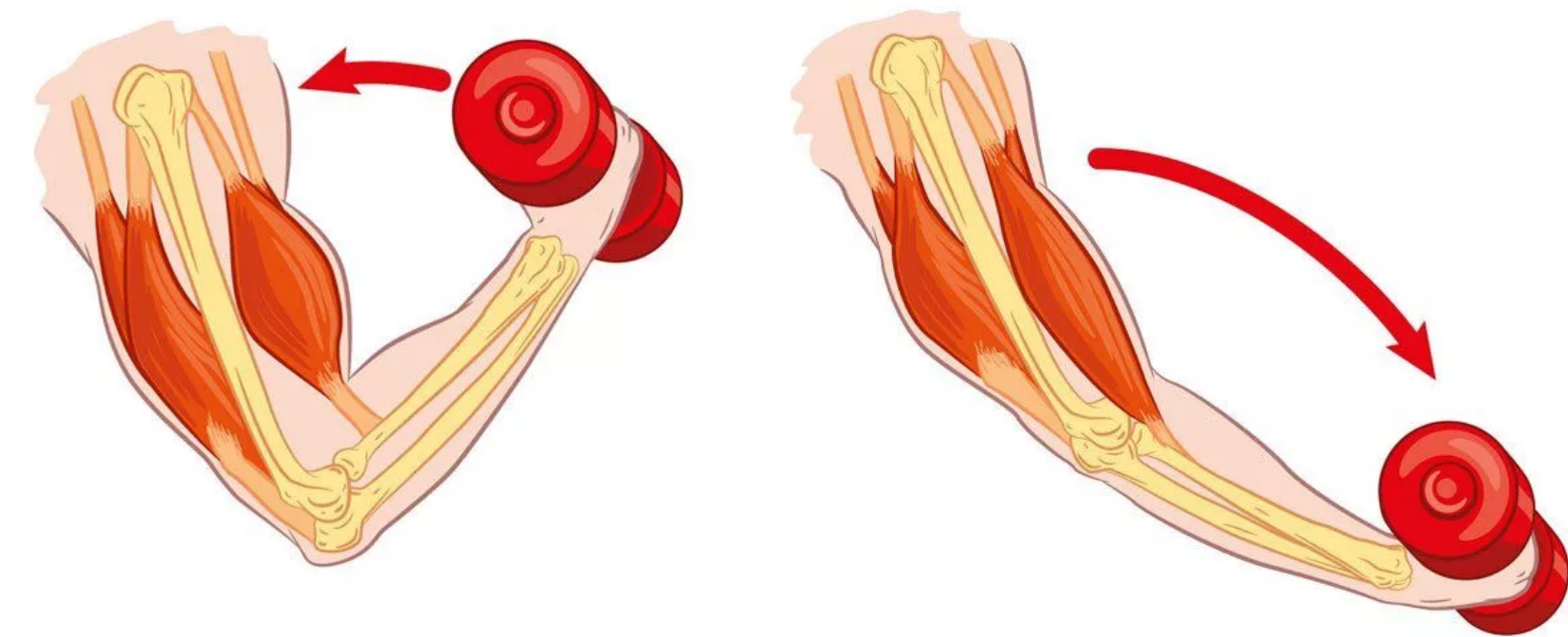
Key observations

- Mechanical relaxation (< 1 min) is much faster than morphogenesis (hours)
- Junctional tensions are the *dominant forces*

Force balance, but *no* constitutive relation between length and tension.



Passive: stress determined by strain
(constitutive relation)



Active: stress regulated *independently* of strain



Fluid



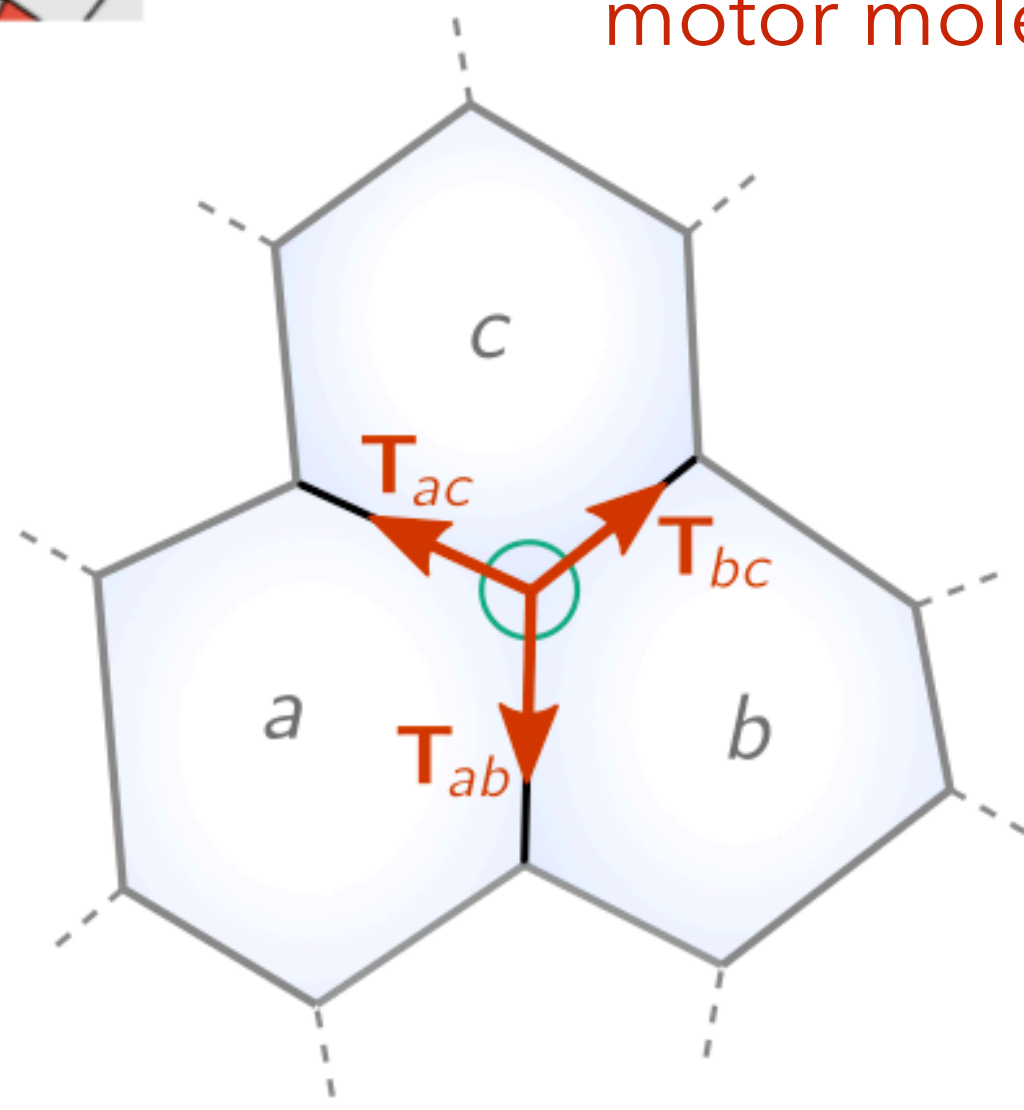
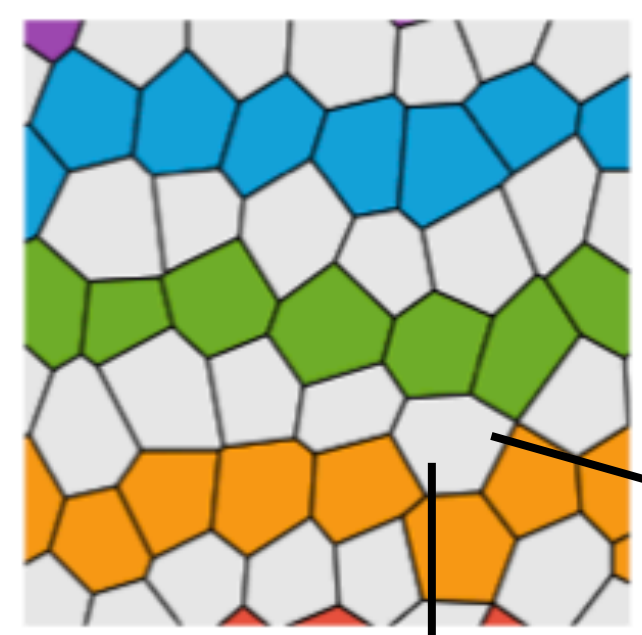
Foam = emergent solid



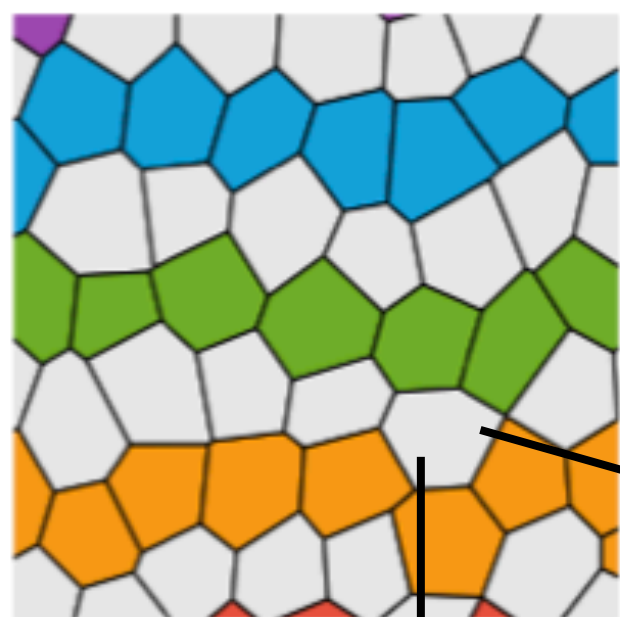
Emergent elasticity

Epithelial tissue = distributed hydrostatic skeleton

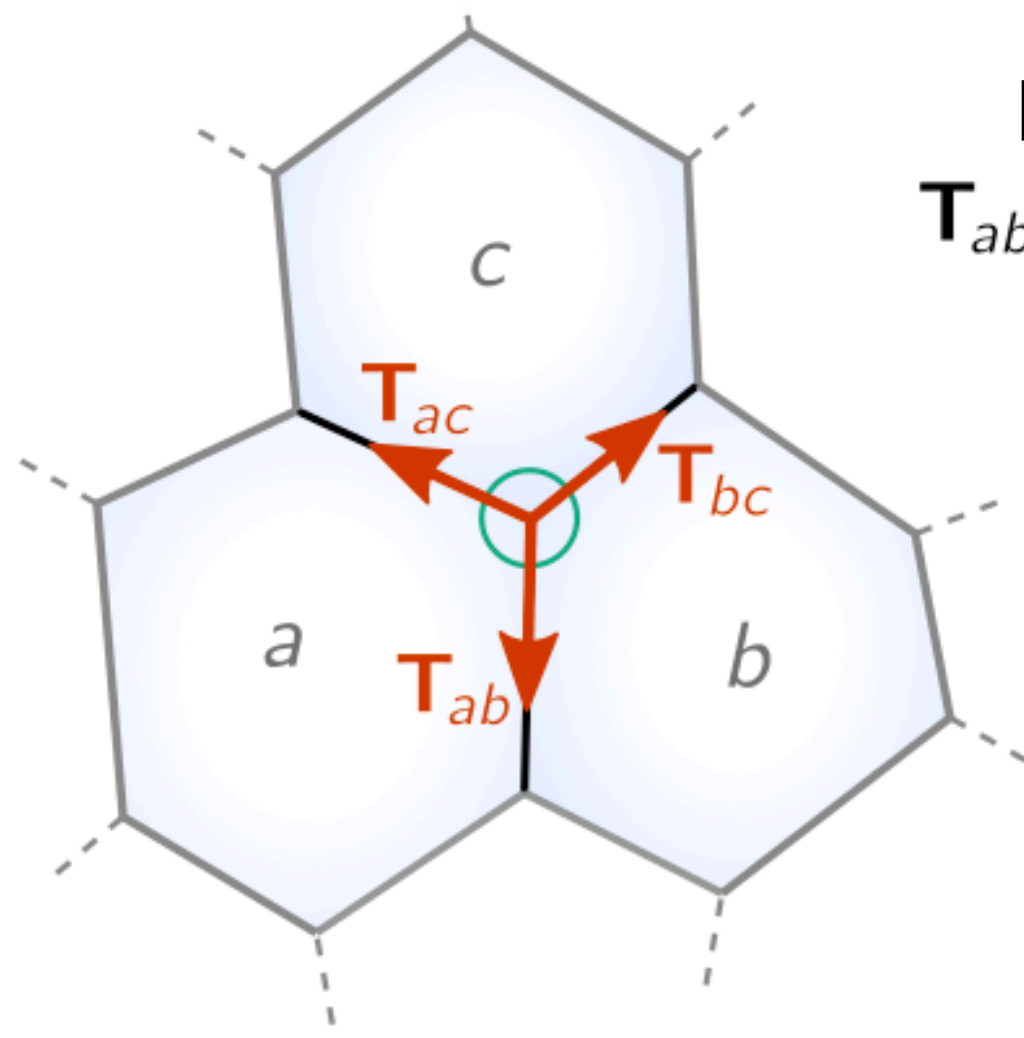
Forces generated by adhesion- and motor molecules



Epithelial tissue = distributed hydrostatic skeleton



Forces generated by adhesion- and motor molecules



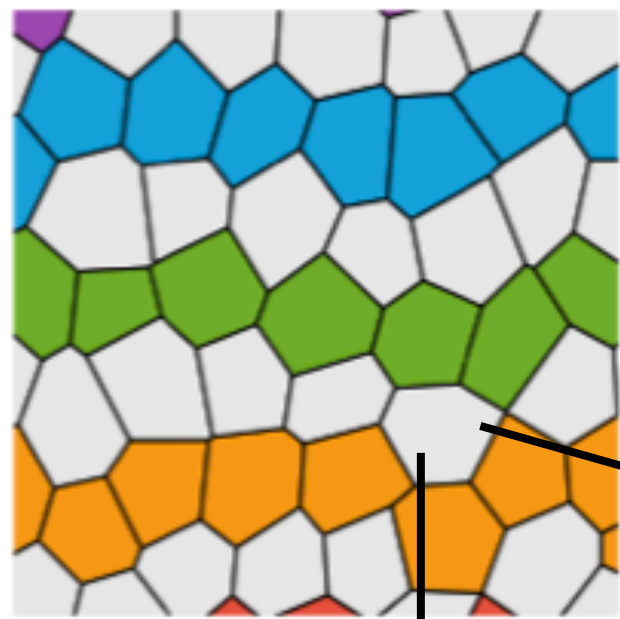
Force balance
 $T_{ab} + T_{bc} + T_{ac} = 0$

$$\frac{\sin \gamma}{\sin \alpha} = \frac{T_{ab}}{T_{bc}}$$

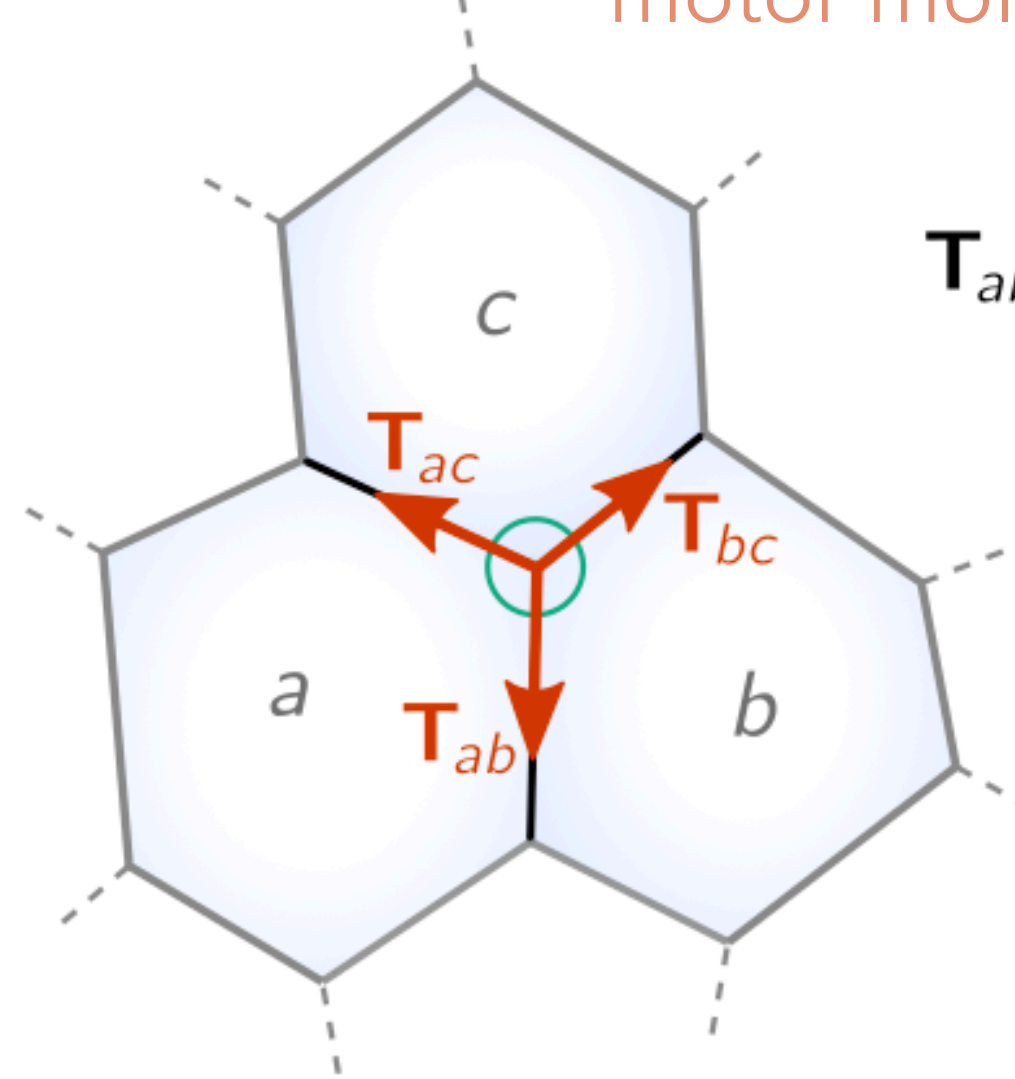
Force balance links **geometry** and **mechanics**:
Angles at vertices \iff **Junctional tensions**



Epithelial tissue = distributed hydrostatic skeleton

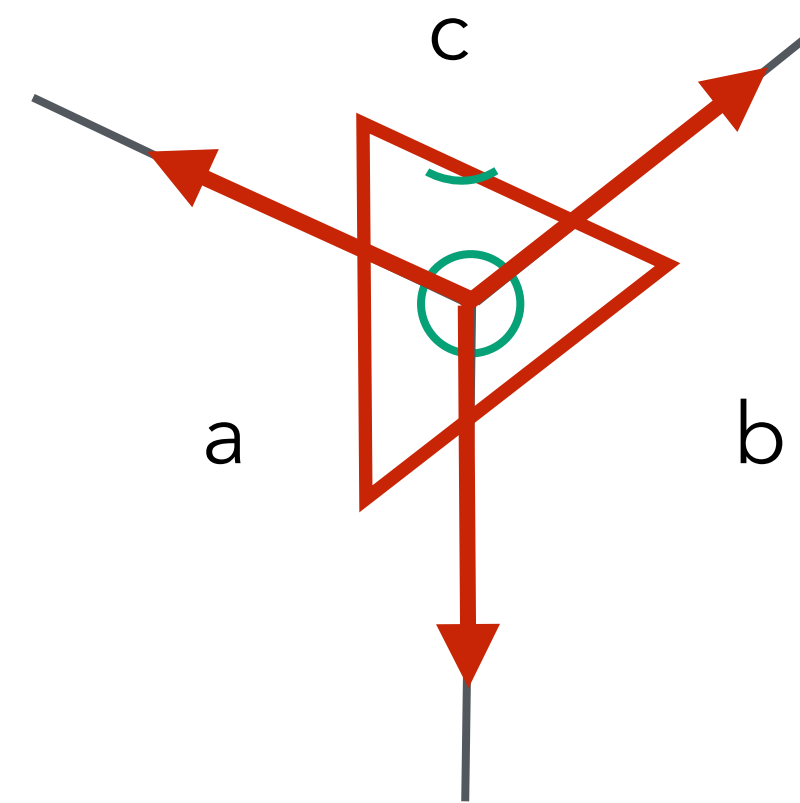


Forces generated by adhesion- and motor molecules

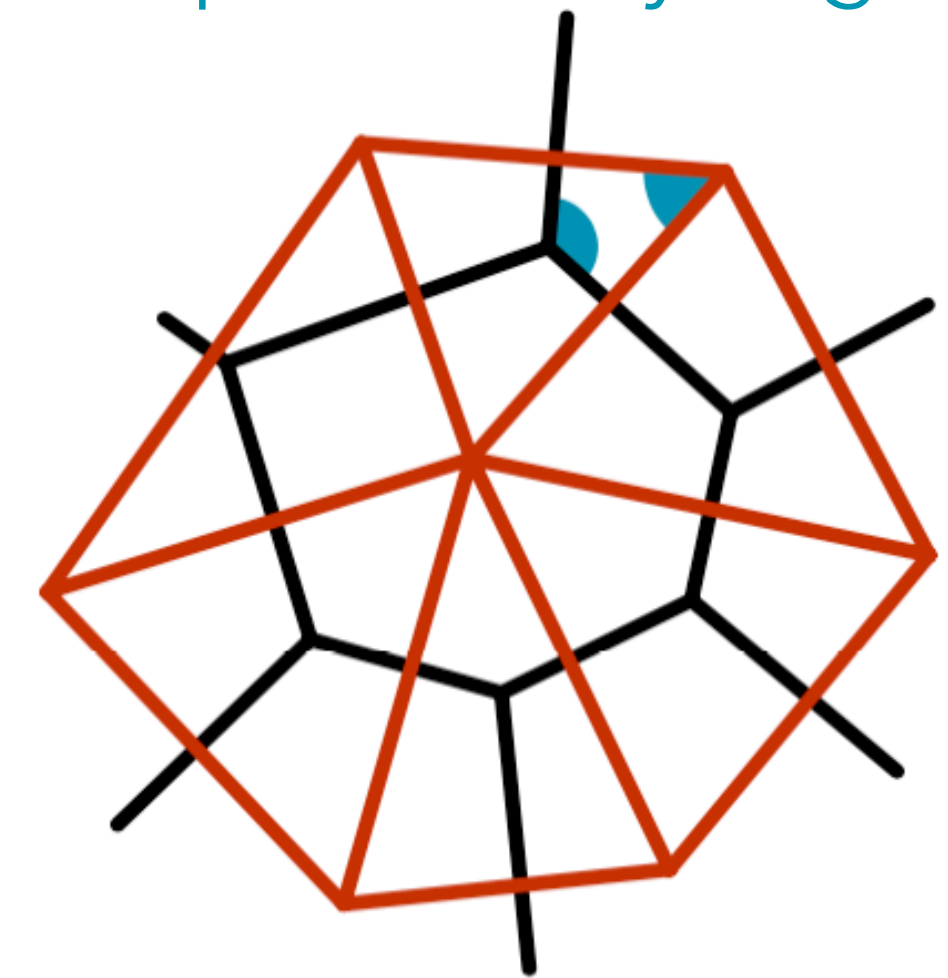


Force balance
 $T_{ab} + T_{bc} + T_{ac} = 0$

$$\frac{\sin \gamma}{\sin \alpha} = \frac{T_{ab}}{T_{bc}}$$



Complementary angles

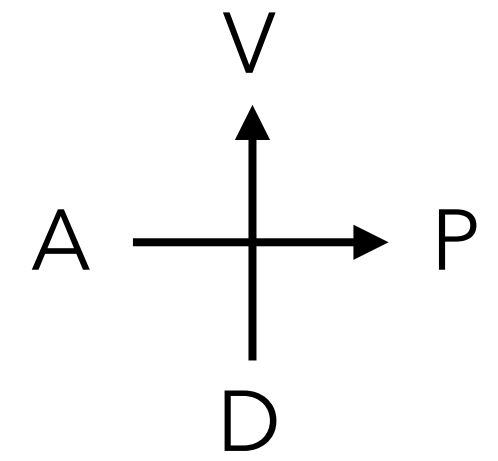
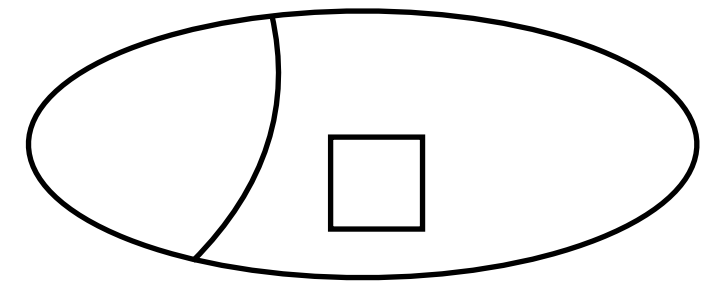
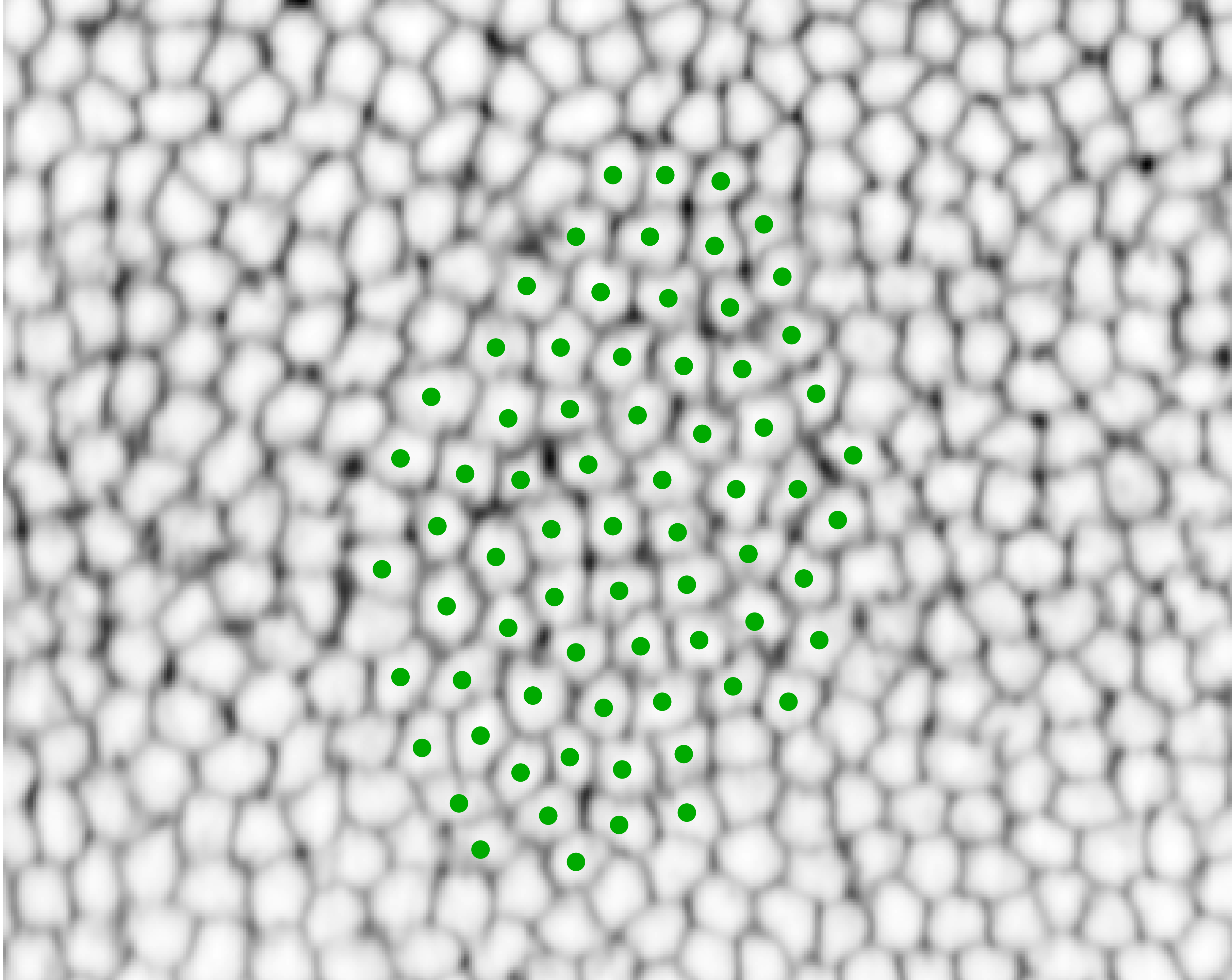


Force balance links **geometry** and **mechanics**:

Angles at vertices \iff **Junctional tensions**

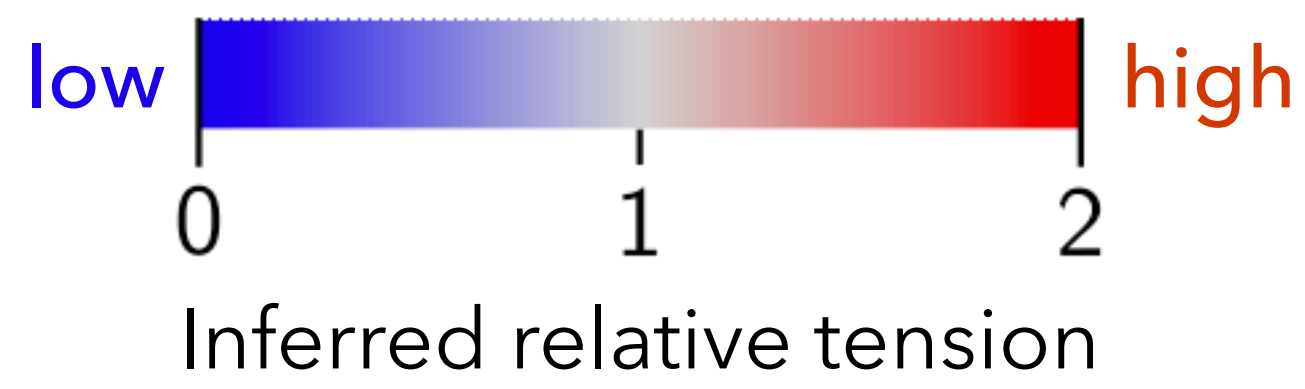
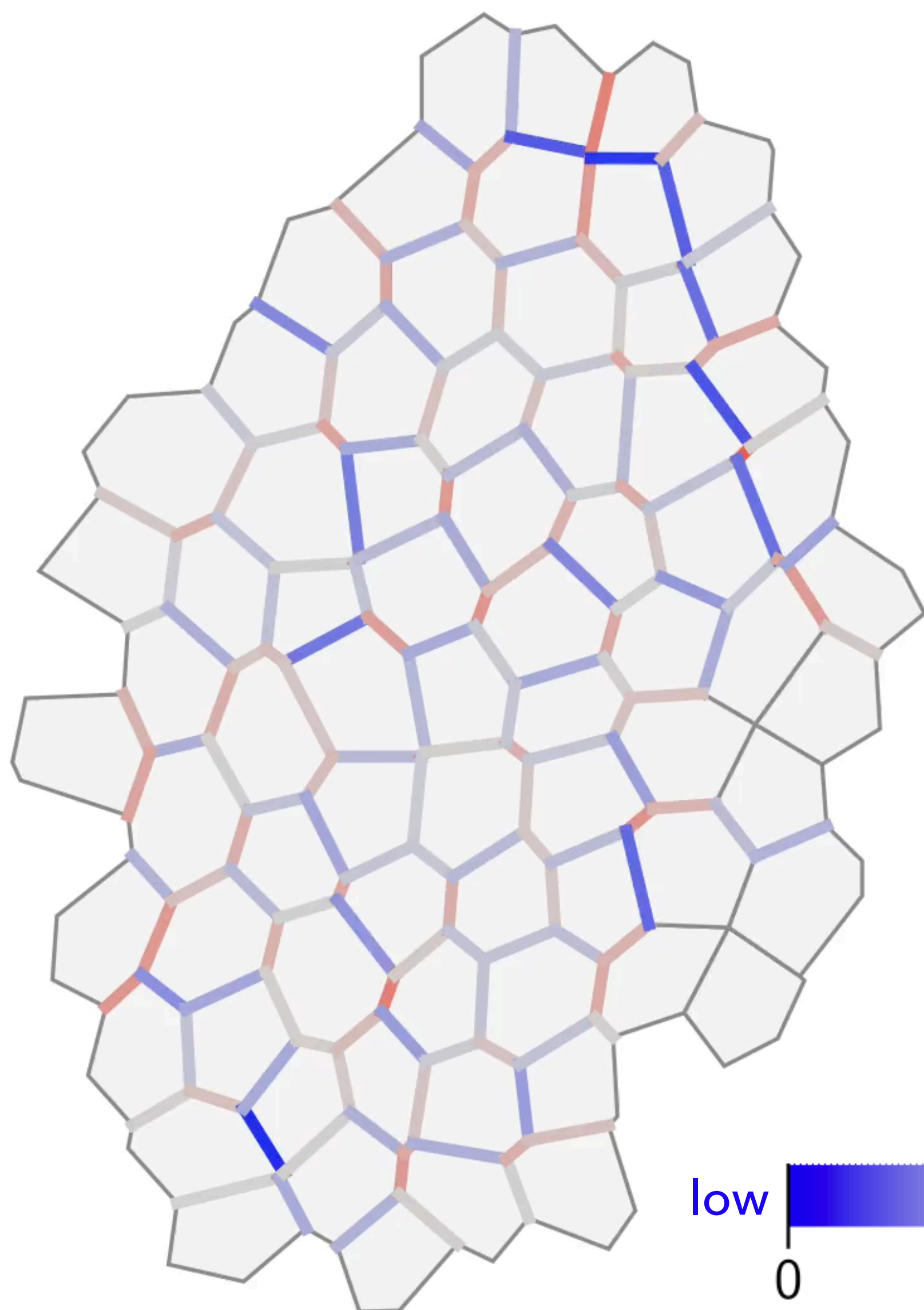


Dual triangulation of tensions represents global force balance



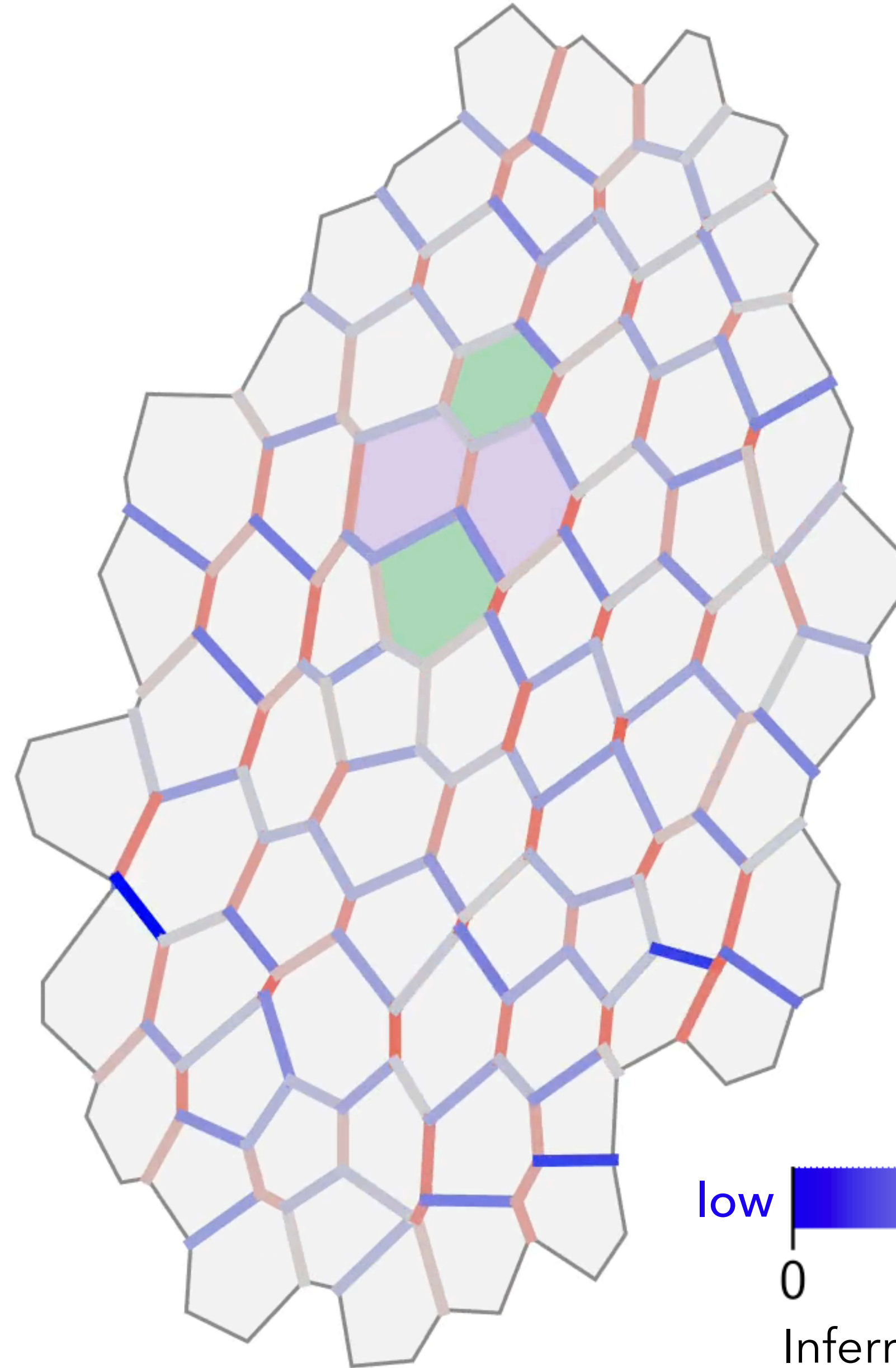
t = 0 min

- 1. Initial hexagonal cell packing
- 2. Alternating pattern of low and high tensions emerges

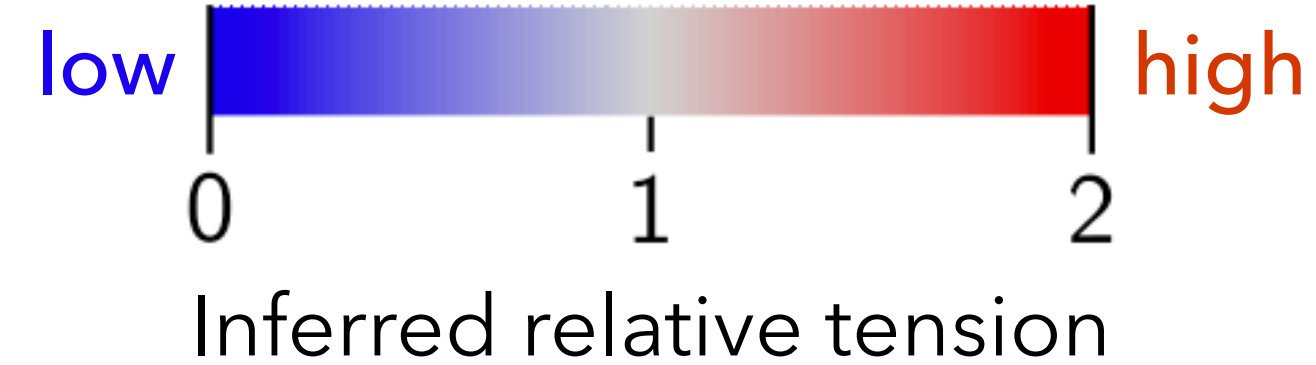


Tension inference on experimental data!

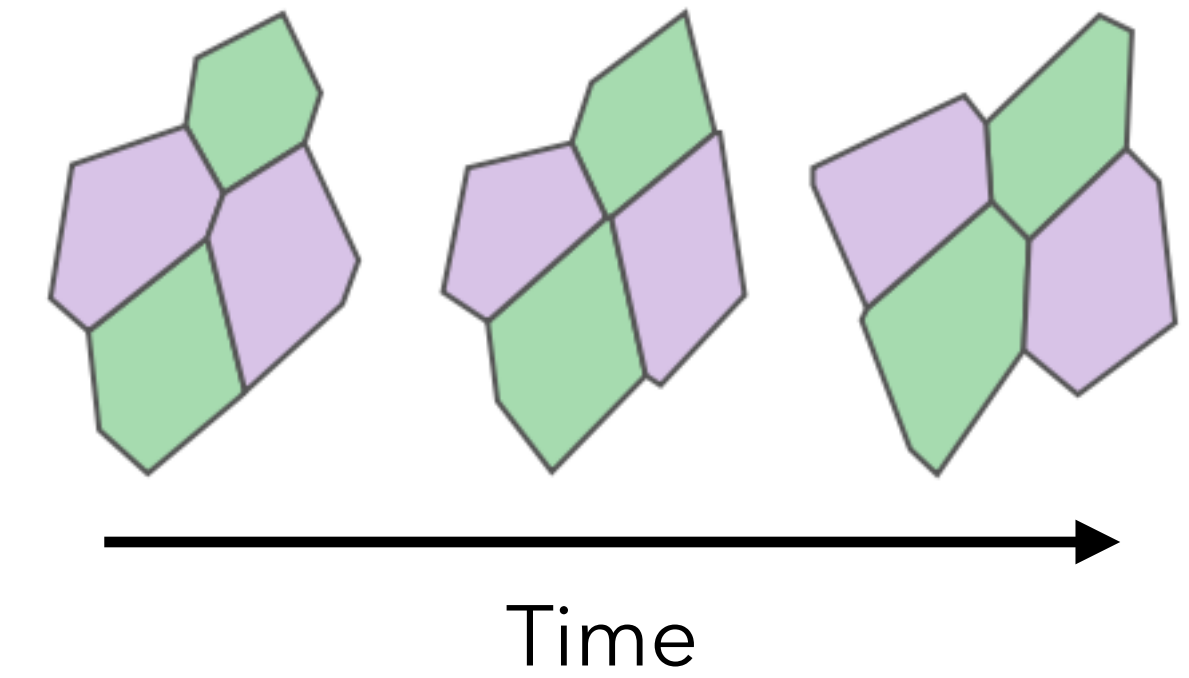
$t = 19 \text{ min}$



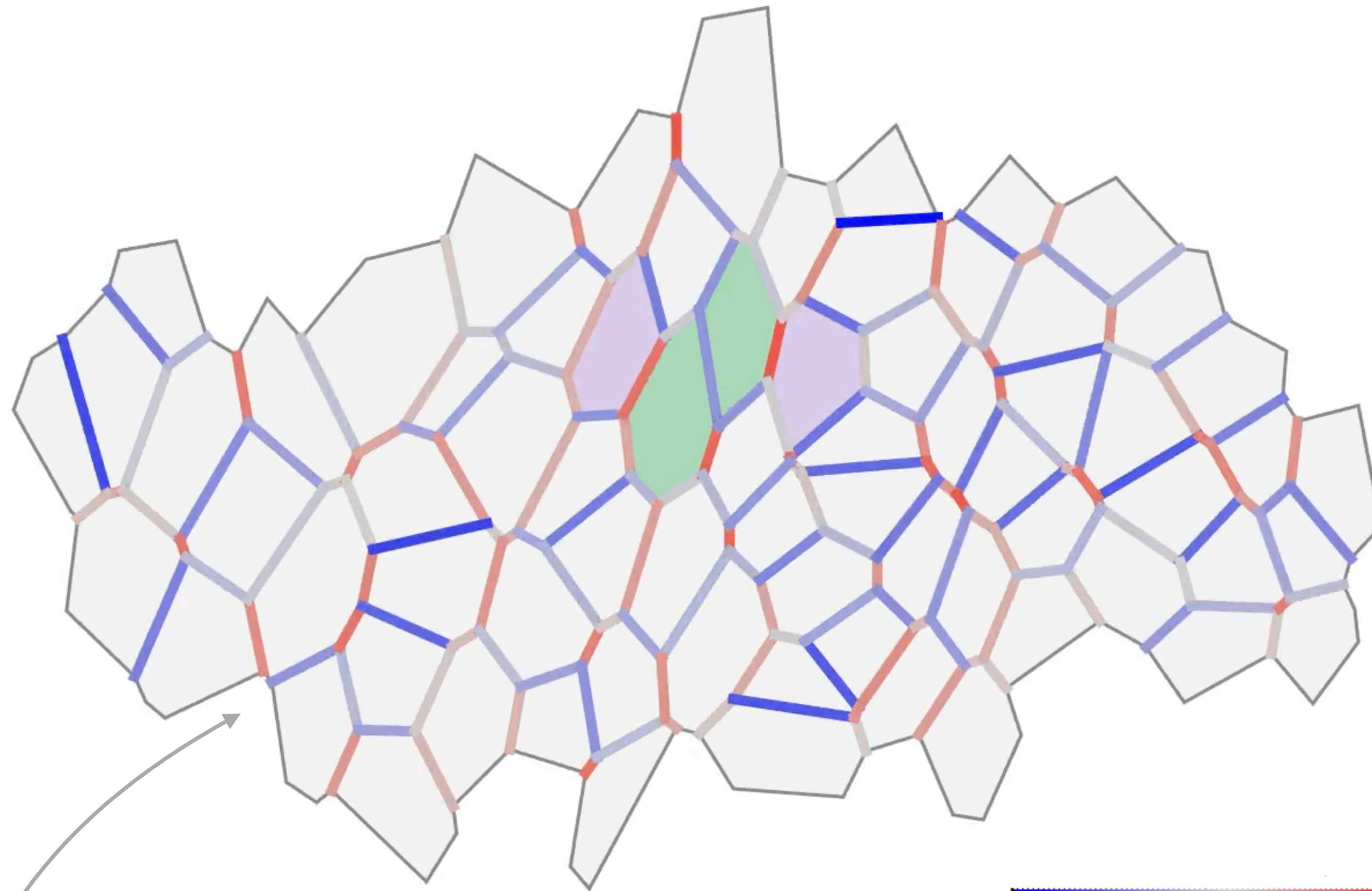
Tension inference on
experimental data!



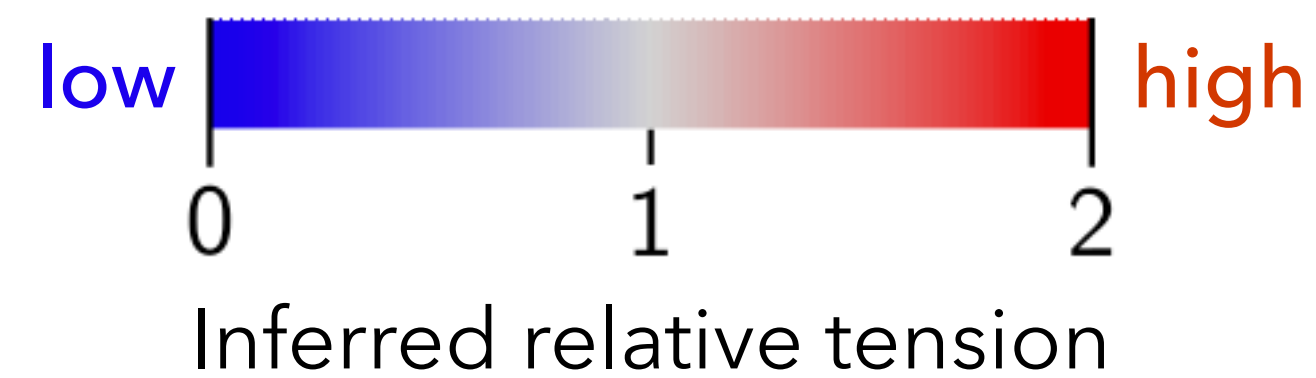
1. Initial hexagonal cell packing
2. Alternating pattern of **low** and **high** tensions emerges
3. **High** tension interfaces contract ...
4. ... leading to oriented, coherent T1s



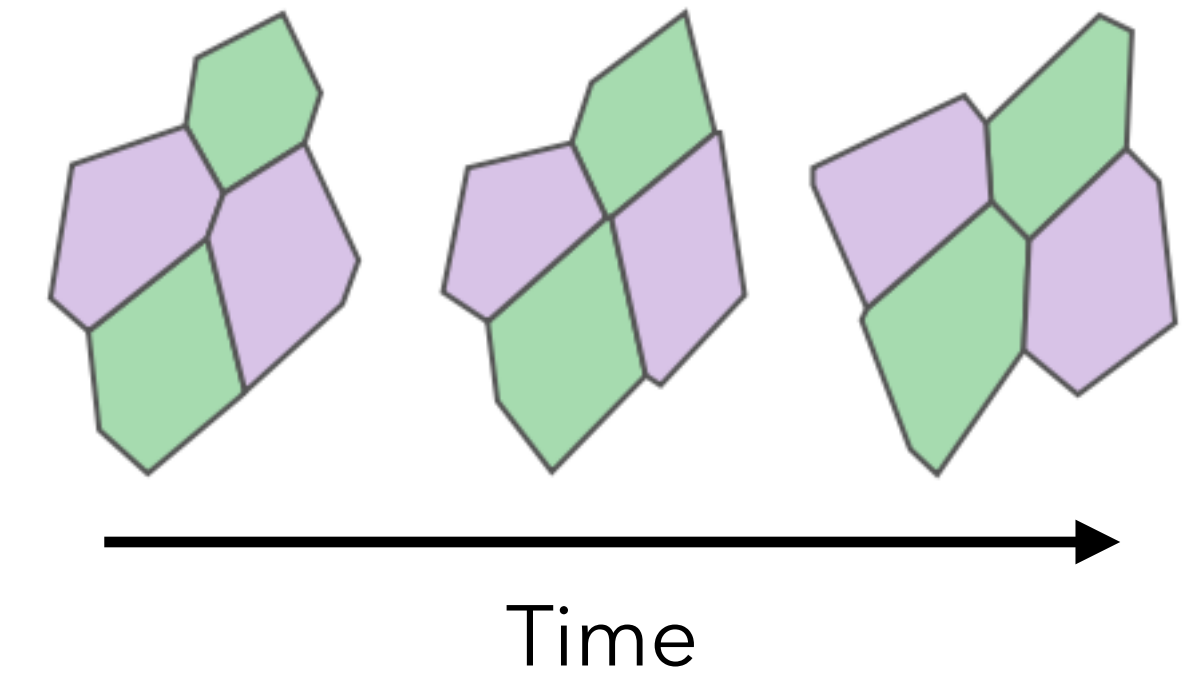
$t = 43 \text{ min}$



Tension inference on
experimental data!



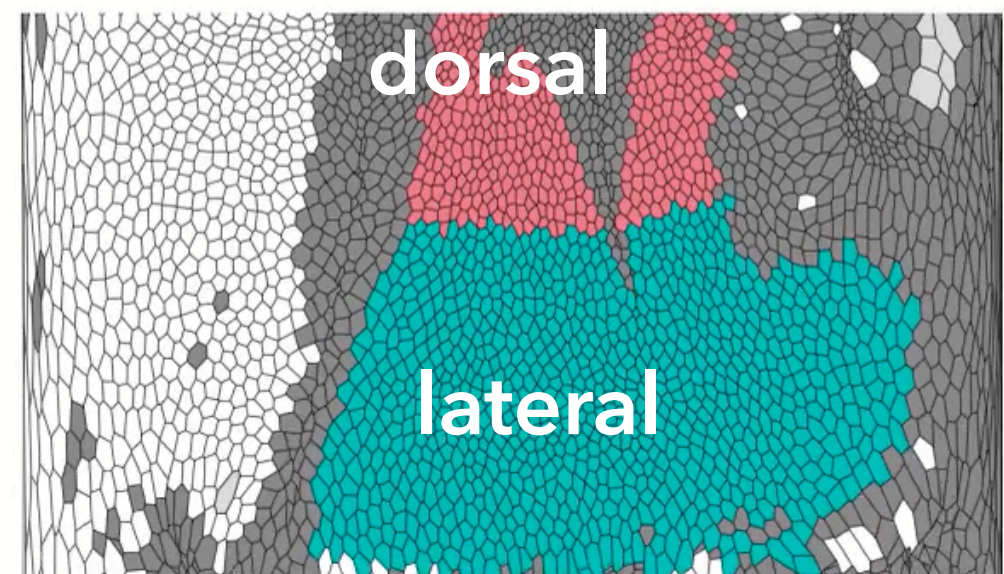
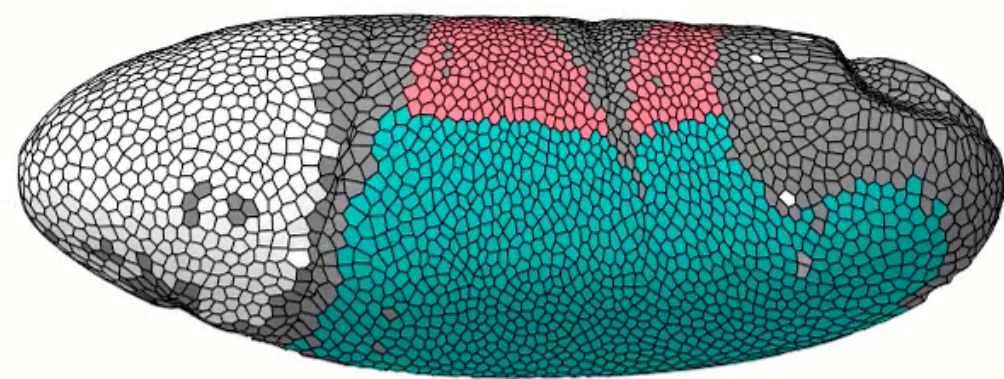
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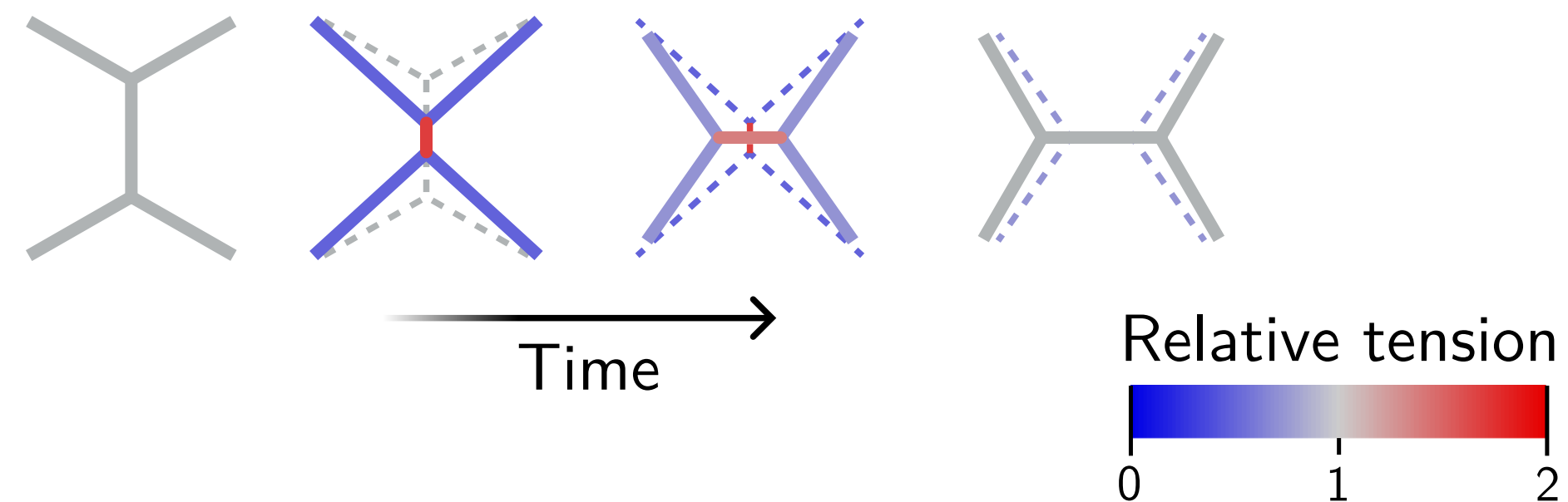
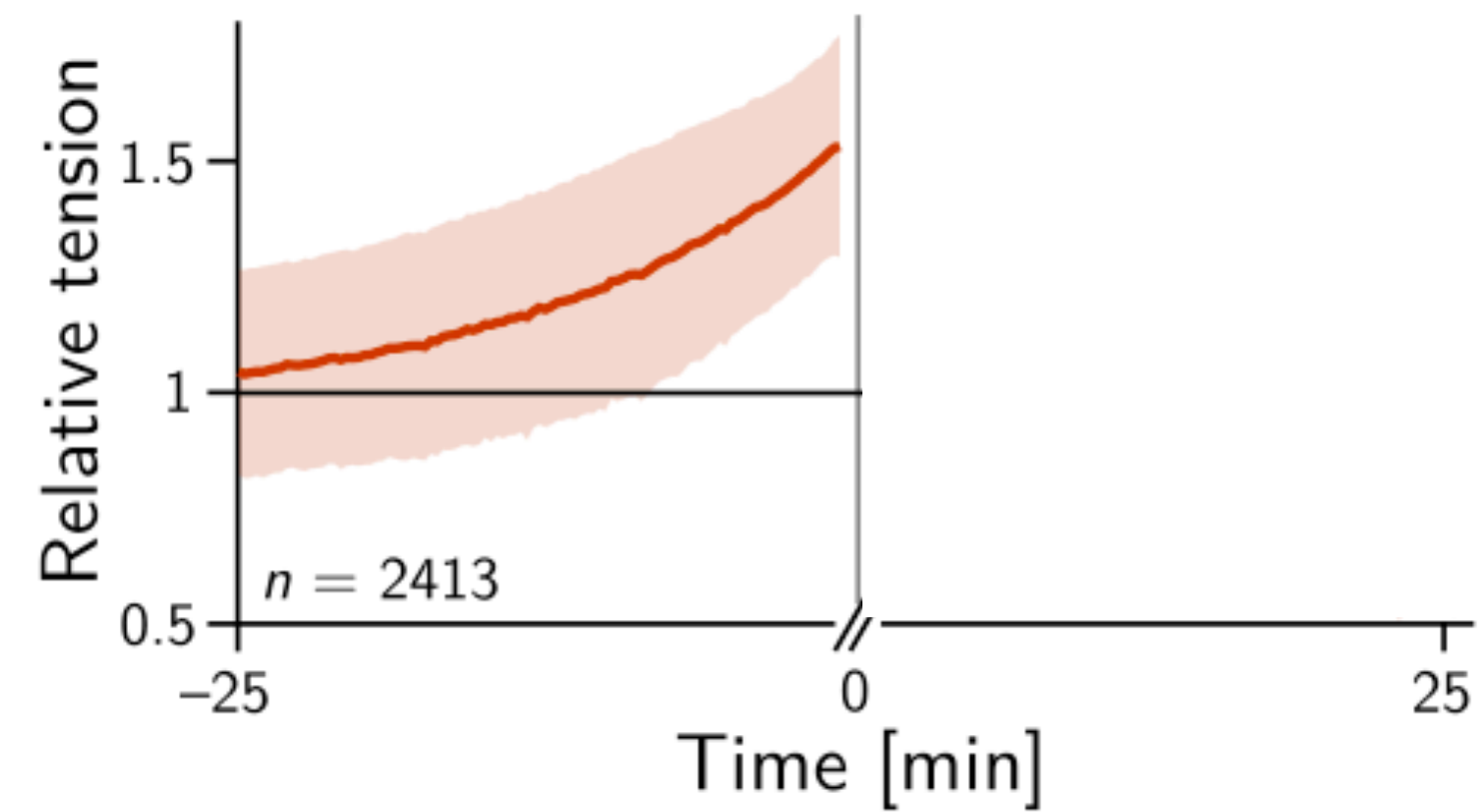
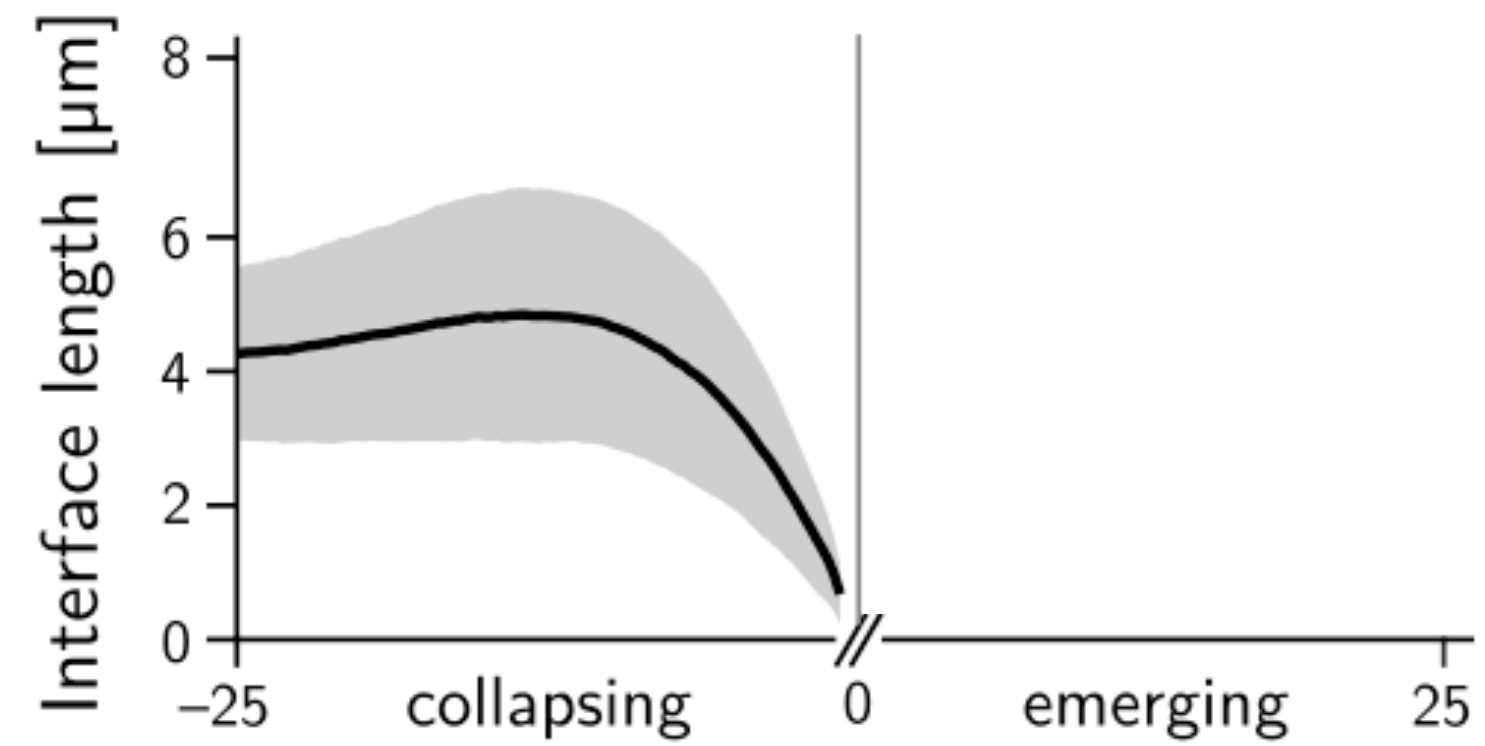
5. T1s destroy order and flow stalls

Conditional analysis: active vs passive T1s

- Identify all T1s
- Align temporally
- Group spatially (lateral vs dorsal)

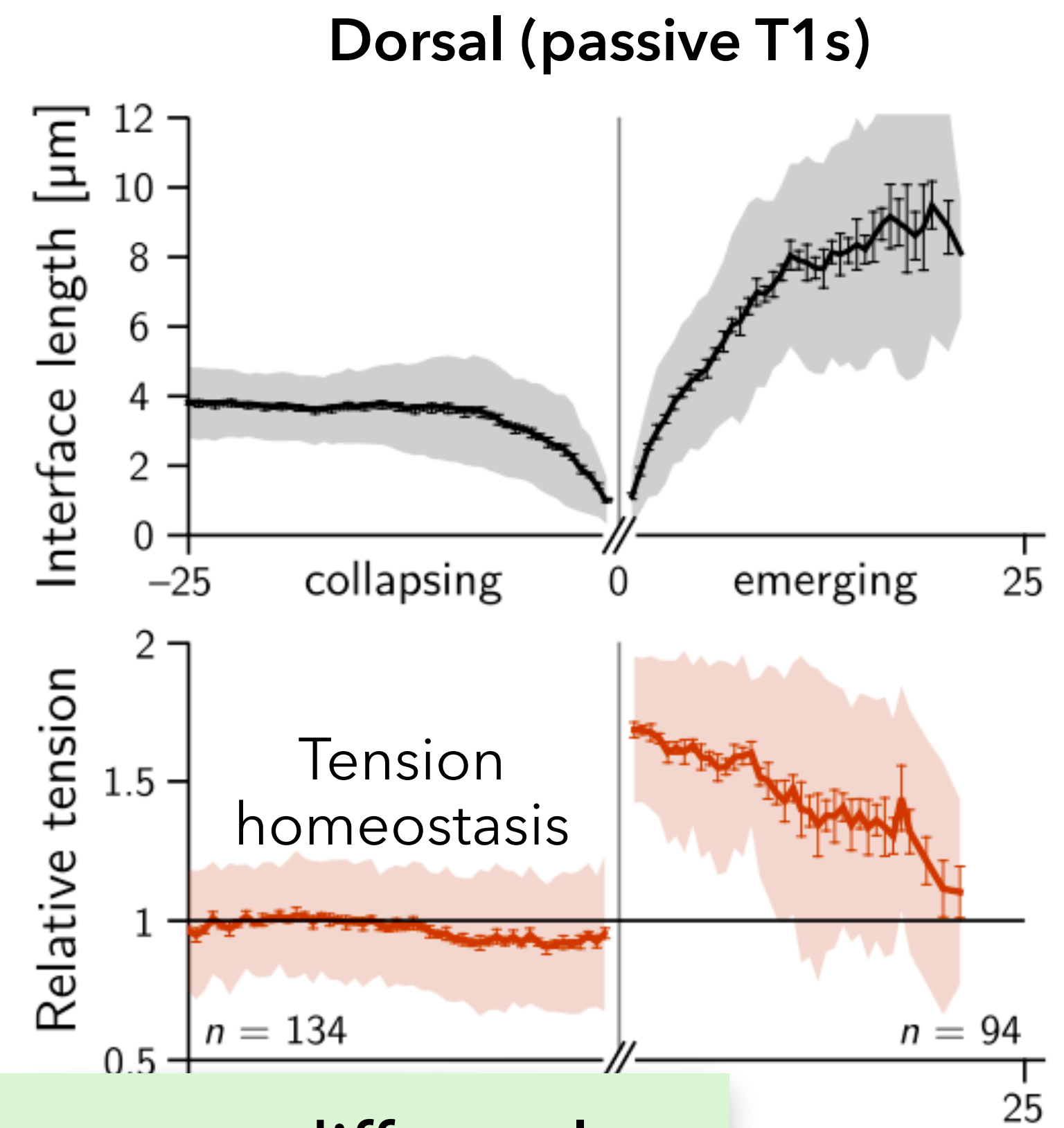
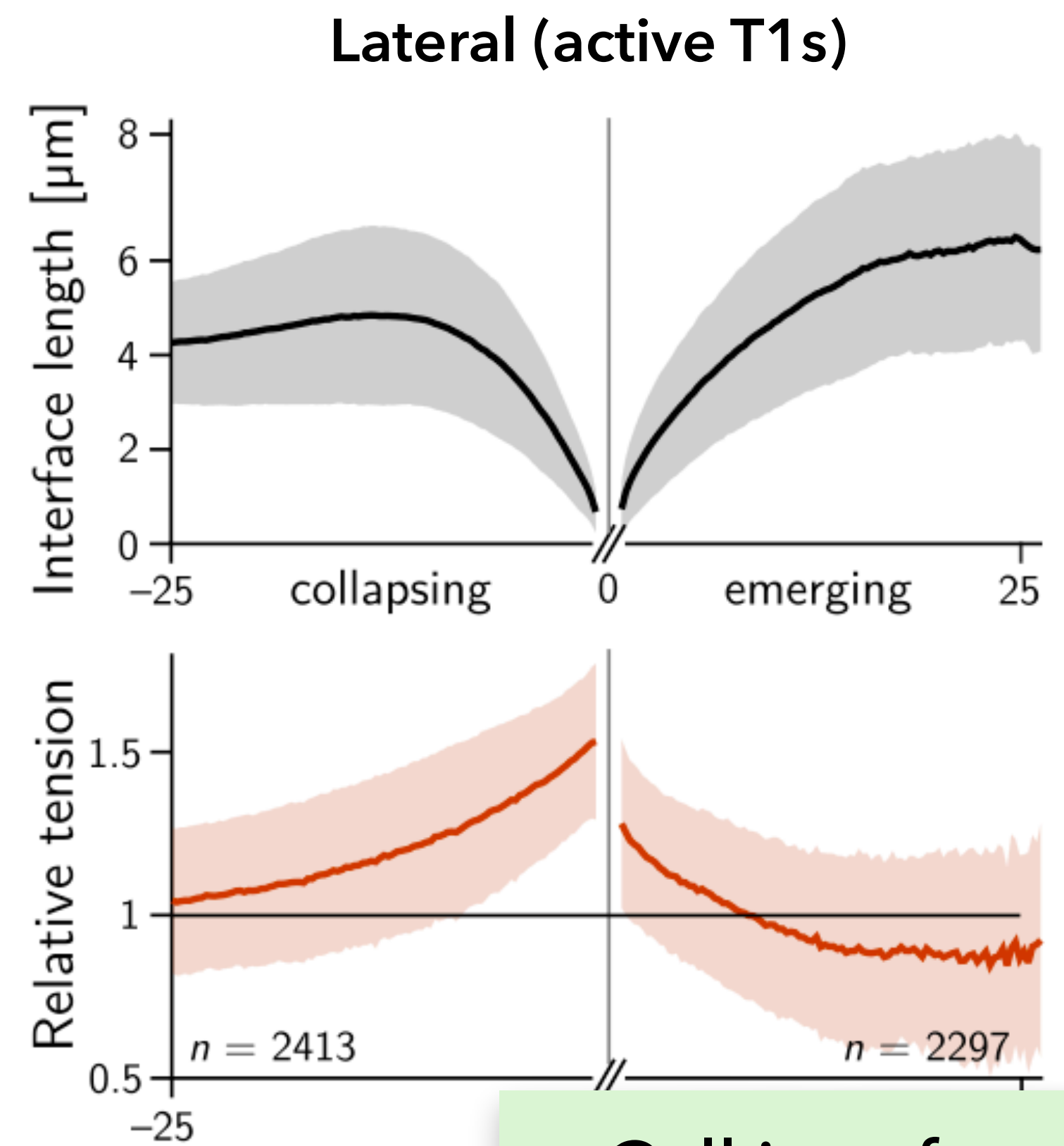
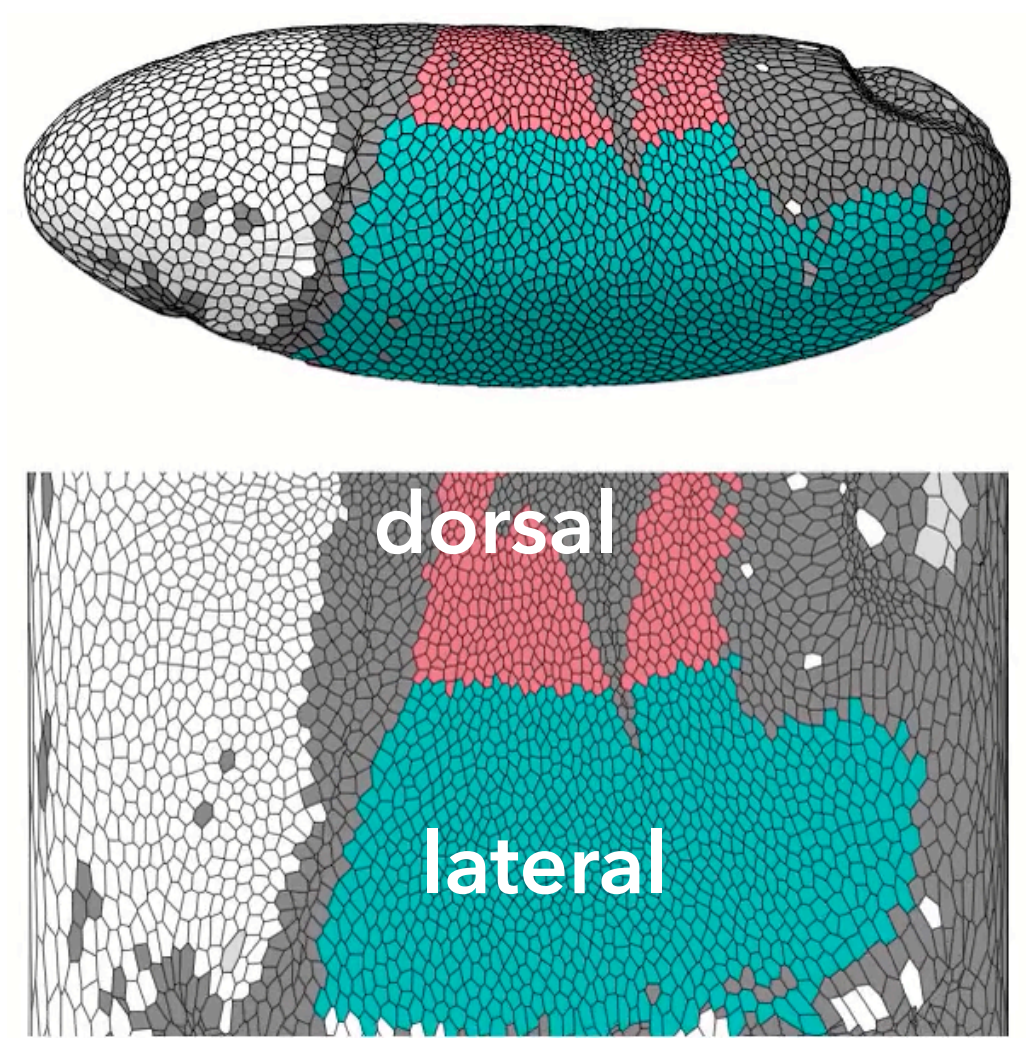


Lateral (active T1s)

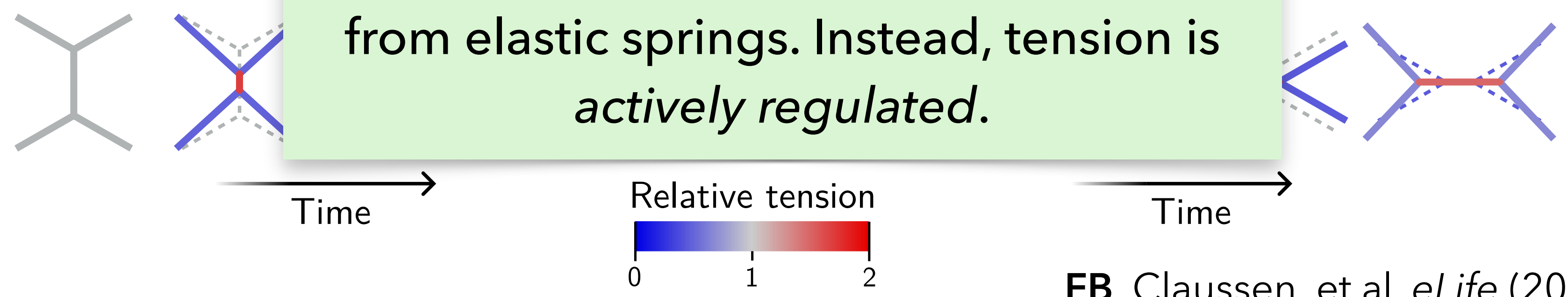


Conditional analysis: active vs passive T1s

- Identify all T1s
- Align temporally
- Group spatially (lateral vs dorsal)

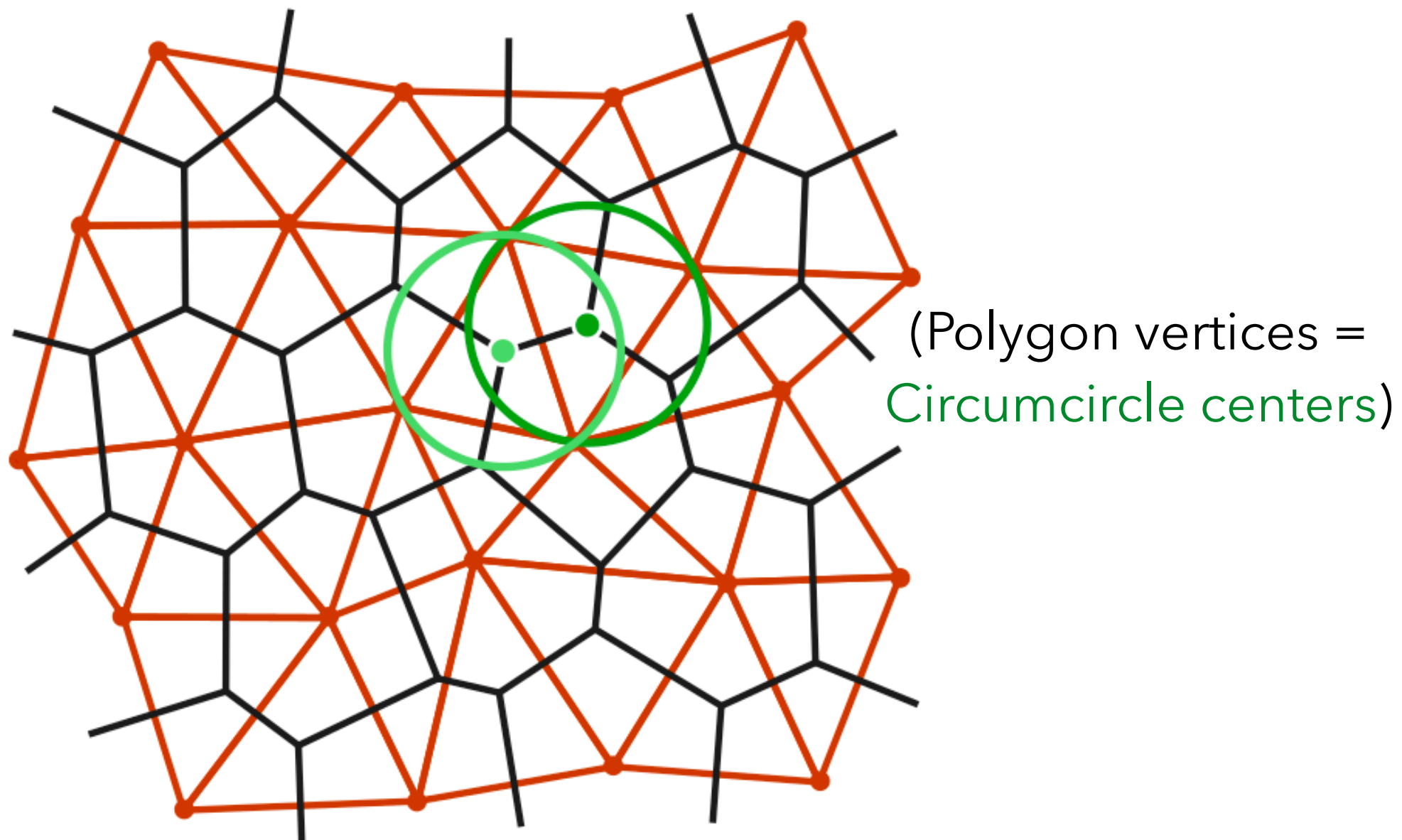


Cell interfaces behave very differently from elastic springs. Instead, tension is *actively regulated*.

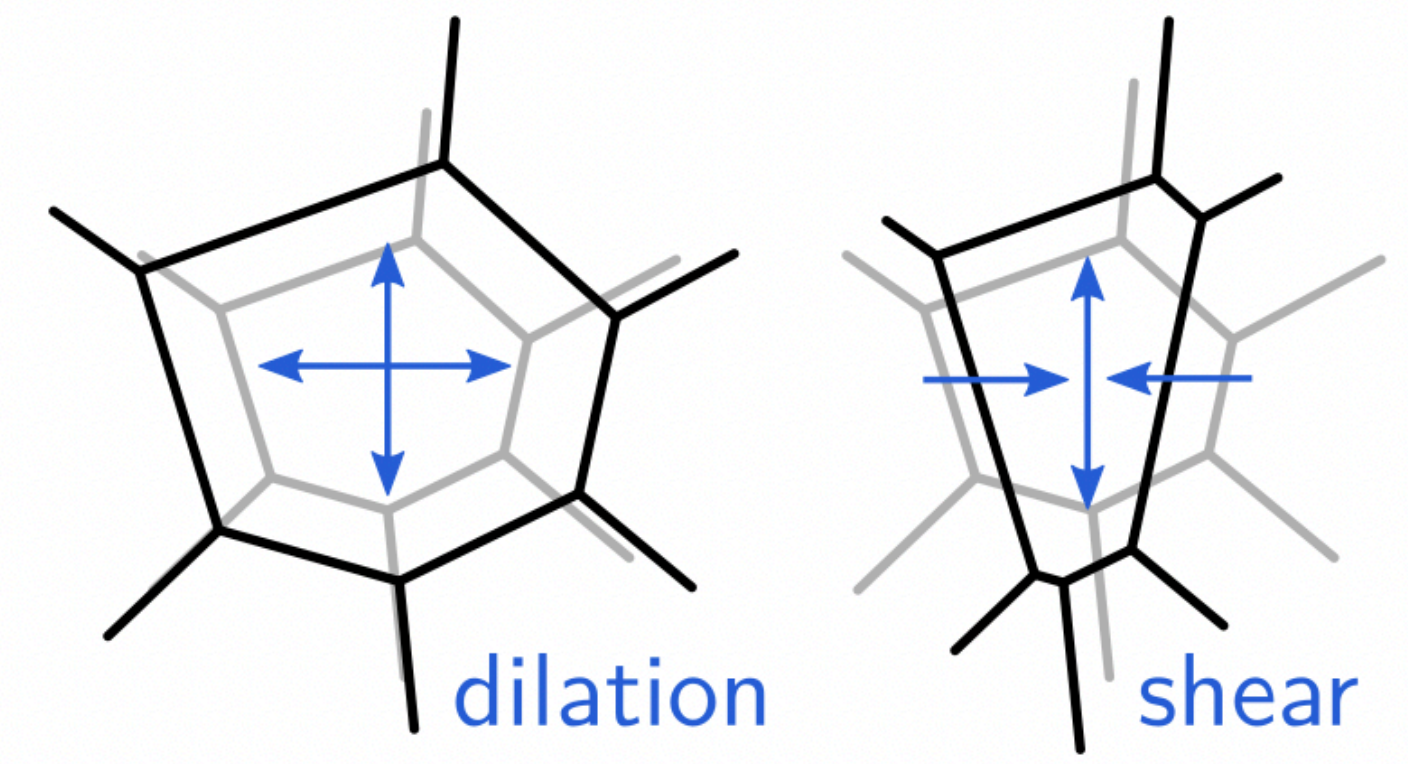


From tension triangulation to cellular tiling

Tensions define an **emergent reference state** via Voronoi-Delaunay duality



External forces act on "isogonal" modes



$\sigma \sim$ isogonal strain

Emergent elasticity

Tensions specify angles but leave *isogonal* (= angle preserving) soft modes

Macroscopic tensile stress:

$$\sigma = \frac{1}{a} \sum_{(ij)} \ell_{ij} \tau_{ij} \hat{e}_{ij} \otimes \hat{e}_{ij}$$

In the Voronoi configuration:

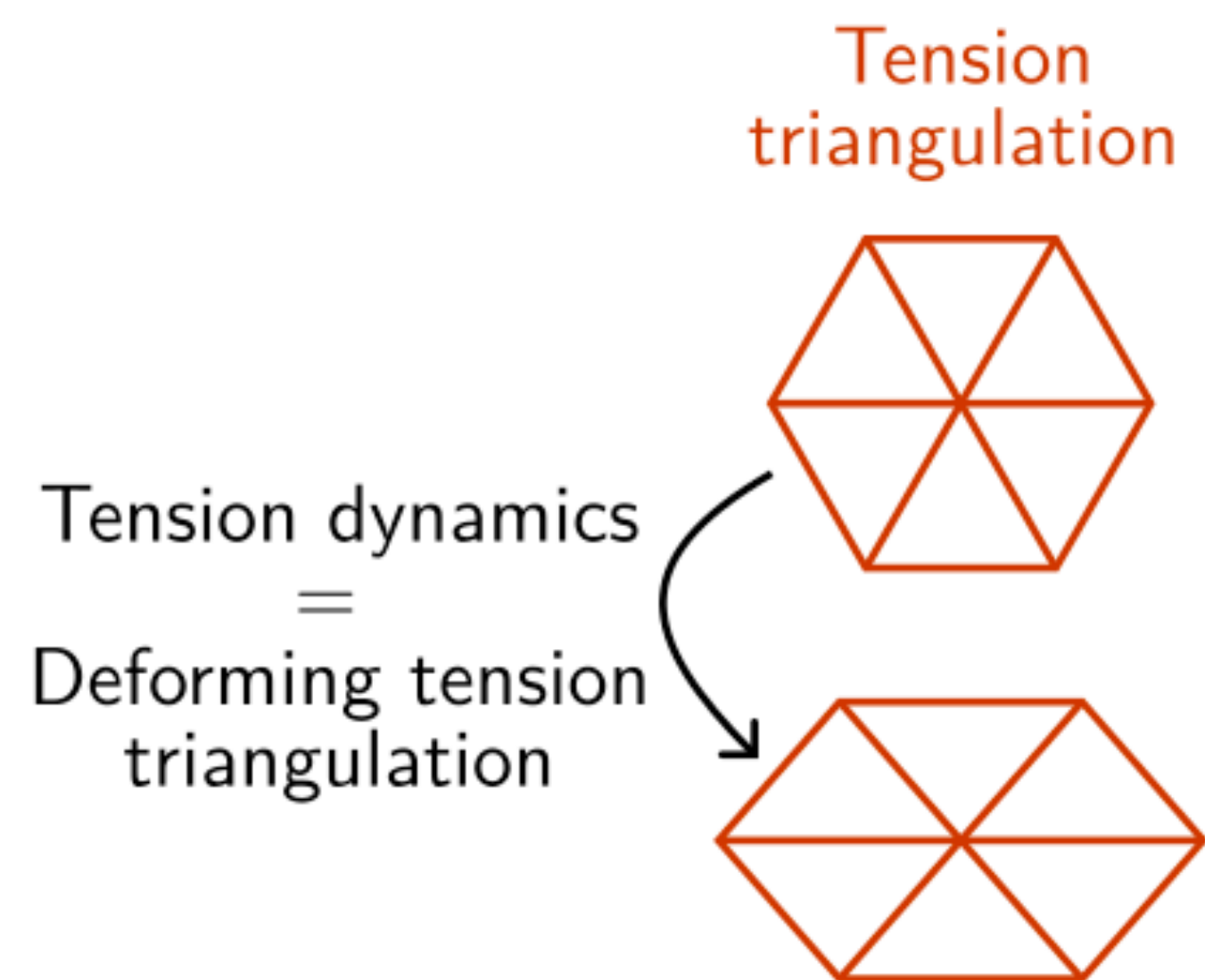
$$\sigma^{\text{tot}} = \sigma - p_0 \mathbb{I} = 0$$



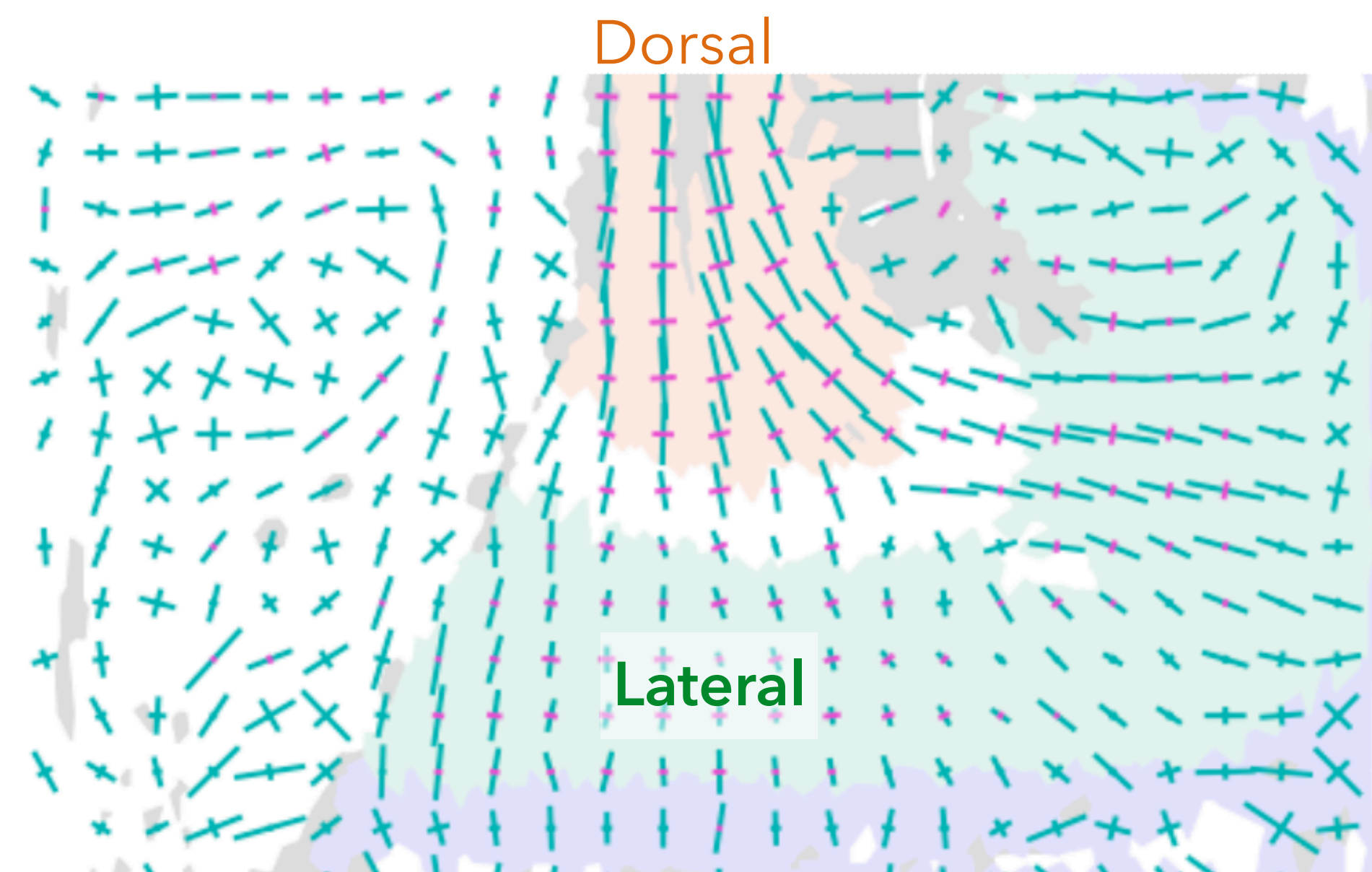
FB, Claussen, et al, *eLife* (2024)

Claussen, FB, Shraiman *arXiv:2601.08968* (2026)

Emergent elasticity theory

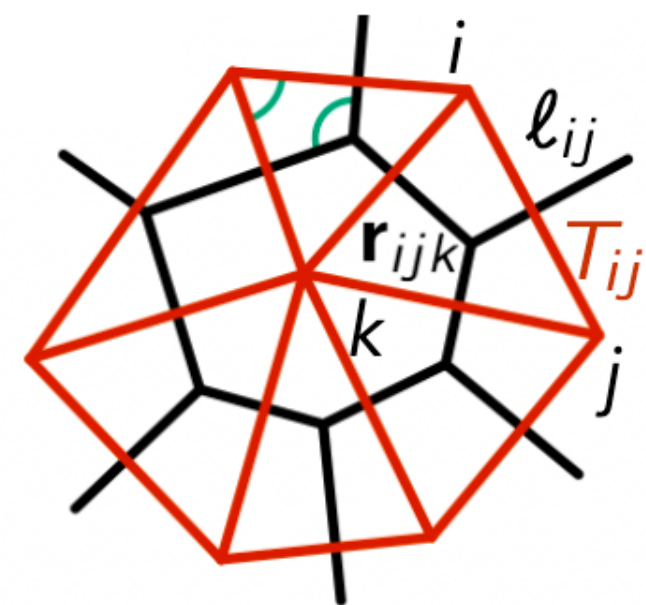


Passive elastic strain can be inferred
from observed cell geometry



FB, Claussen, et al, *eLife* (2024)
Claussen, **FB** & Shraiman (2026)

Statics: geometric constrains from force balance (+ soft modes)

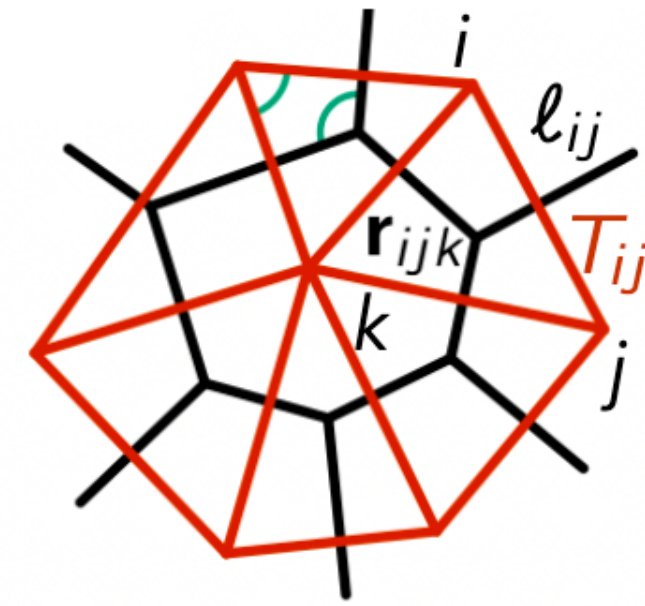


$$dE(\{\mathbf{r}_{ijk}\}|\{T_{ij}\}) = \sum_{ij} T_{ij} dl_{ij} - p \sum_i dA_i + \varepsilon \dots$$

~~Canonical vertex model: area-perimeter elasticity~~

~~$$E = \sum_{i \in \text{cells}} k_p (p_i - p_0)^2 + k_a (a_i - a_0)^2$$~~

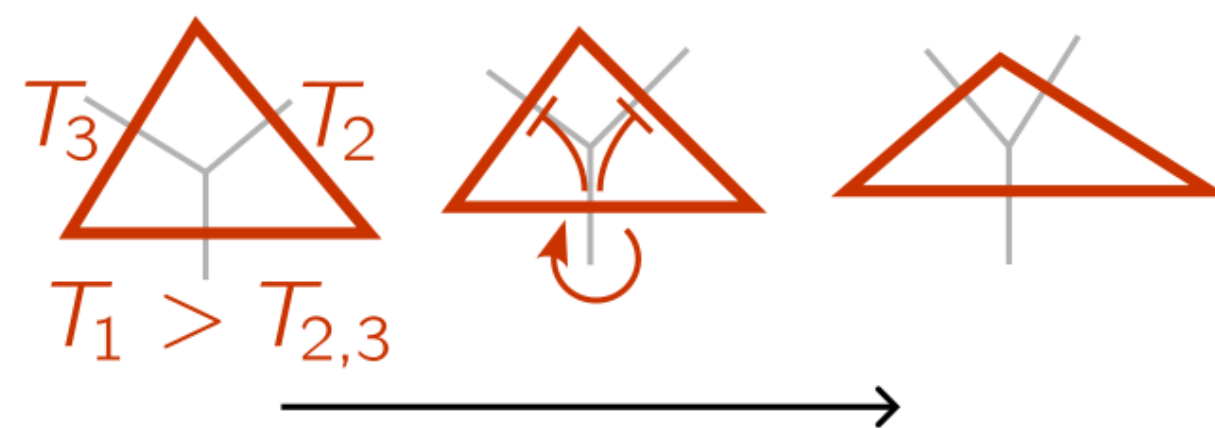
Statics: geometric constraints from force balance (+ soft modes)



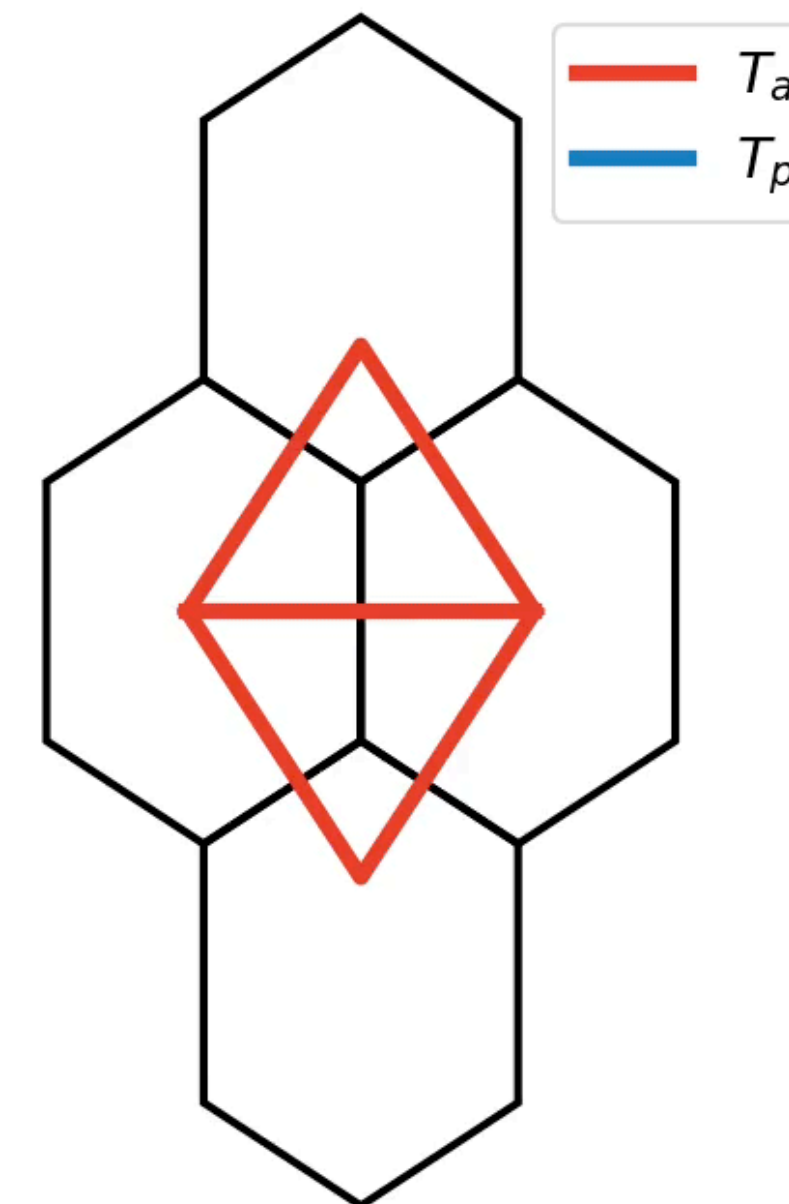
$$dE(\{\mathbf{r}_{ijk}\}|\{T_{ij}\}) = \sum_{ij} T_{ij} d\ell_{ij} - p \sum_i dA_i + \varepsilon \dots$$

Dynamics: adiabatic changes in T_{ij} controlled by feedback loops

$$\tau_T \partial_t T_{ij} = \overbrace{T_{ij}^n}^{\text{local self-amplification}} - \frac{1}{3} \sum_{\alpha \in \Delta_{ijk}} \overbrace{T_{\alpha}^n}^{\text{"limited myosin pool"}}$$



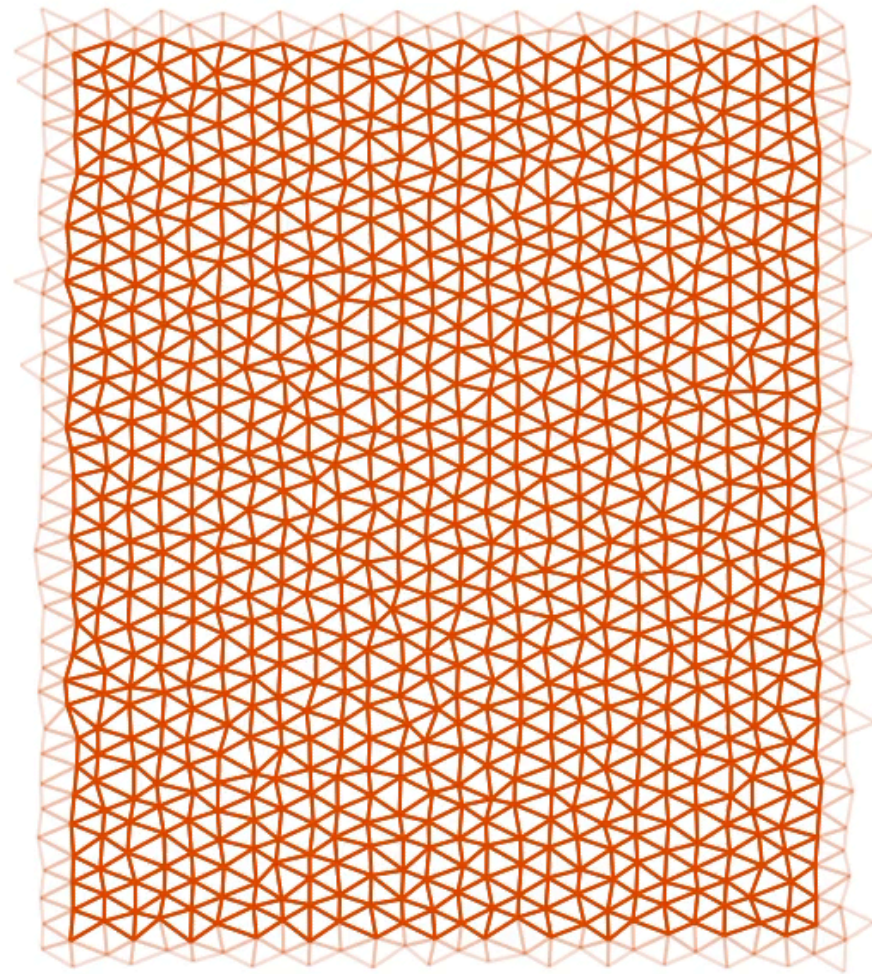
Positive tension feedback drives active T1s



Time: -20 min

Extent of flow depends on initial packing order and anisotropy

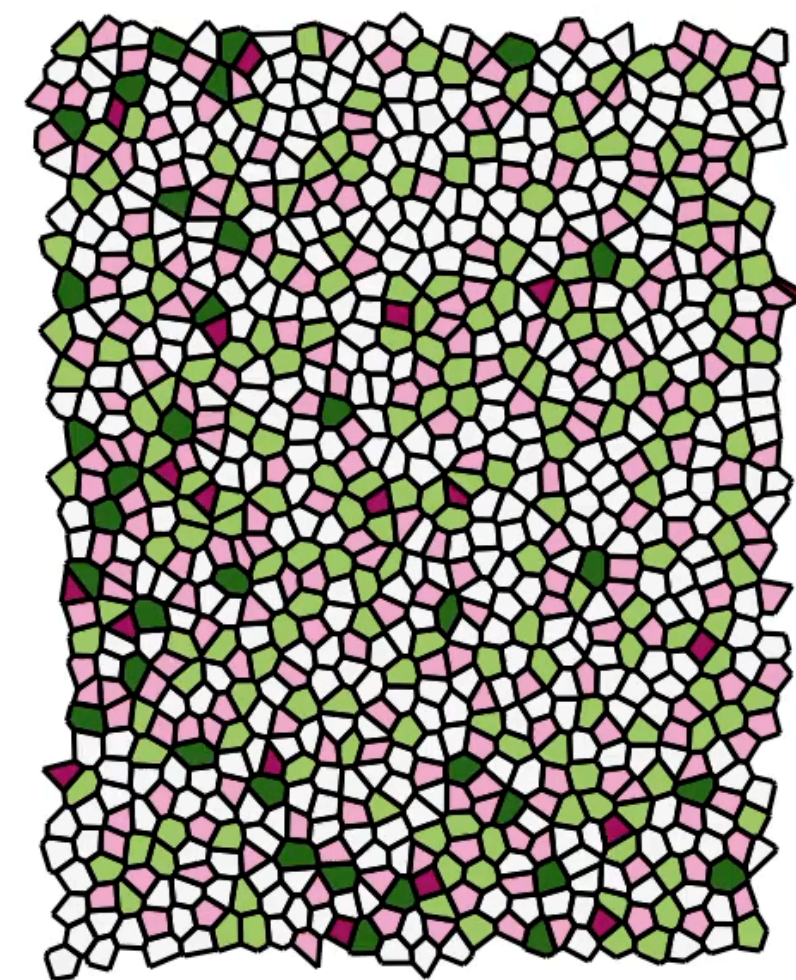
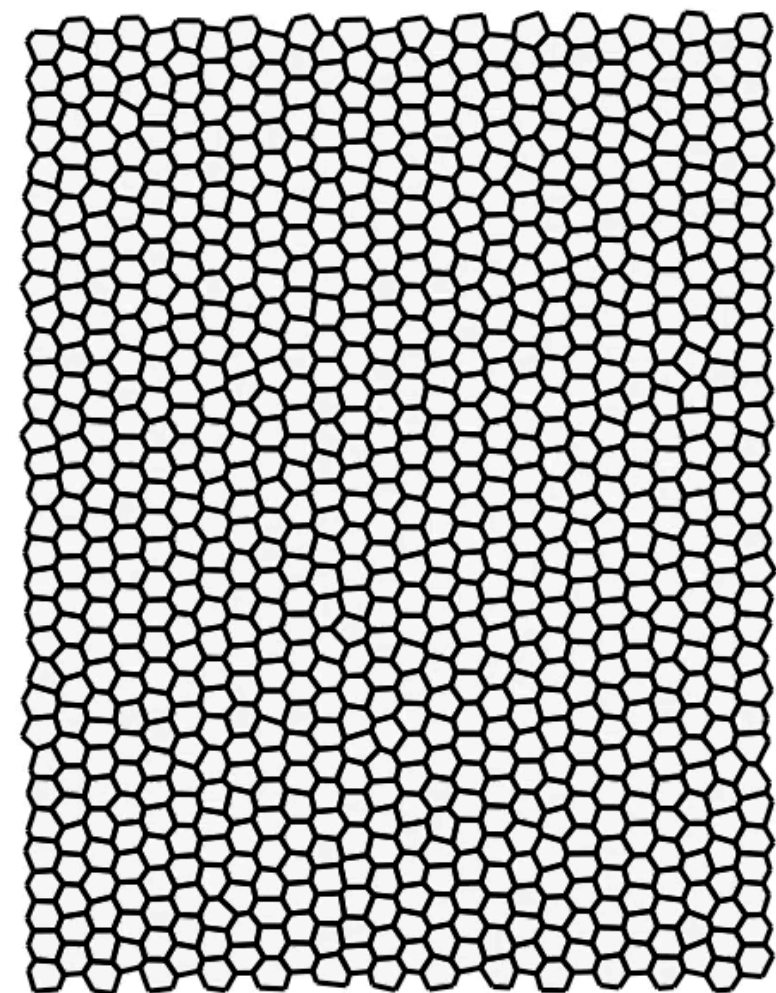
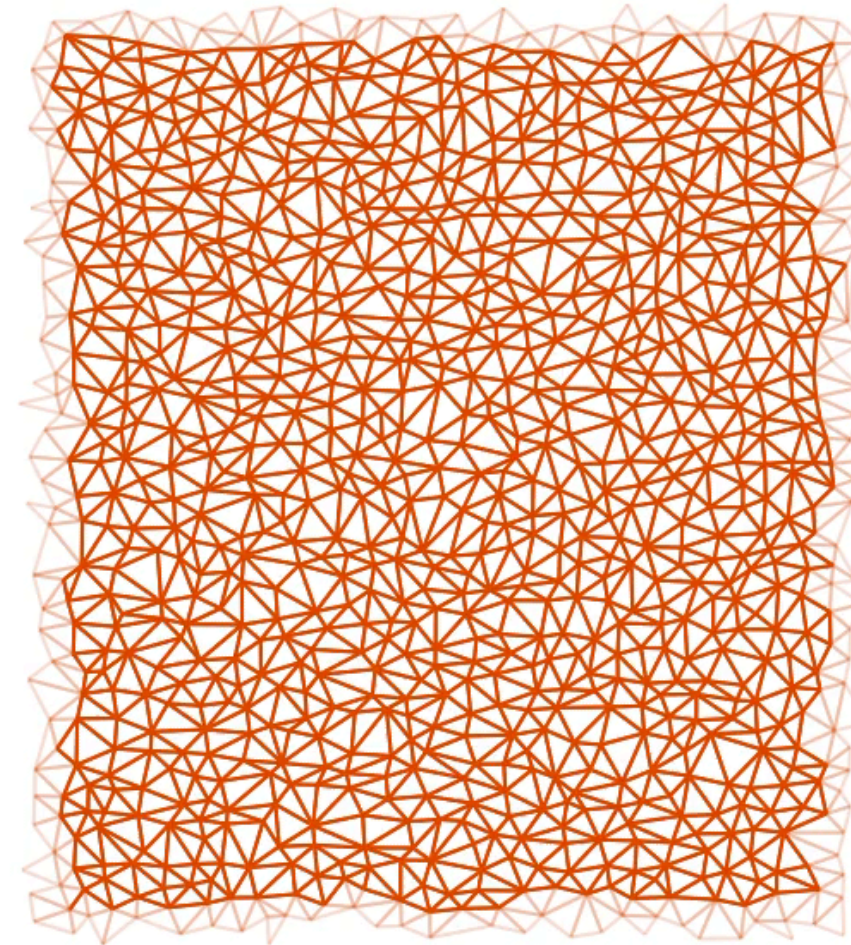
Initially ordered packing



Initial
tension
anisotropy



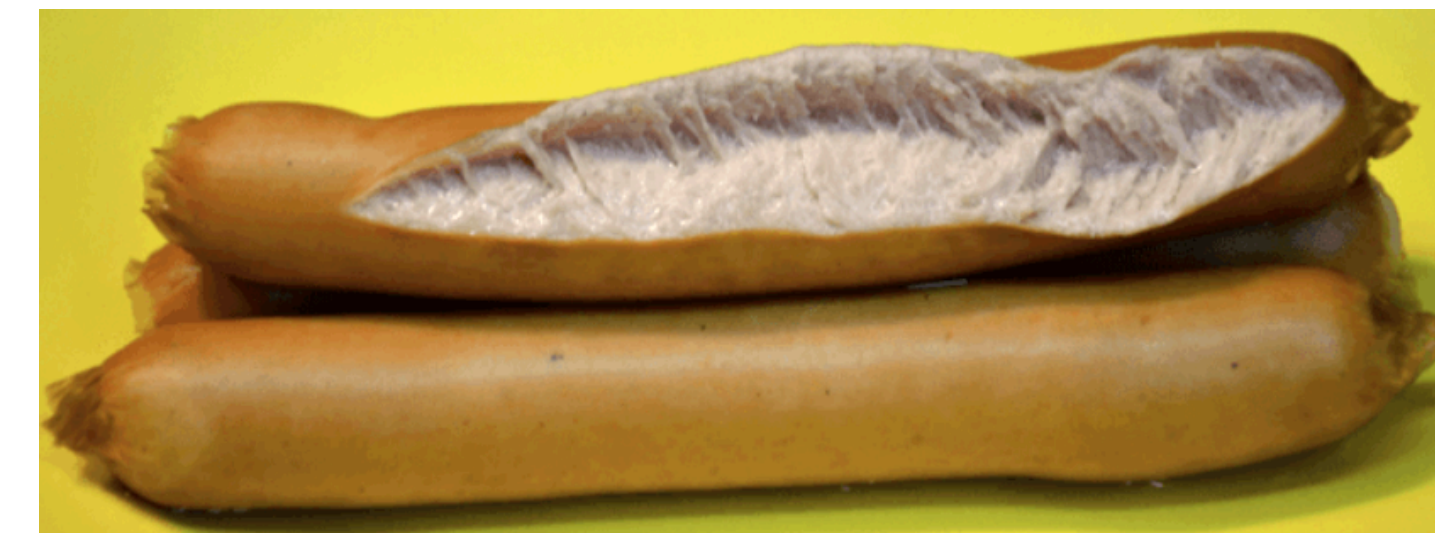
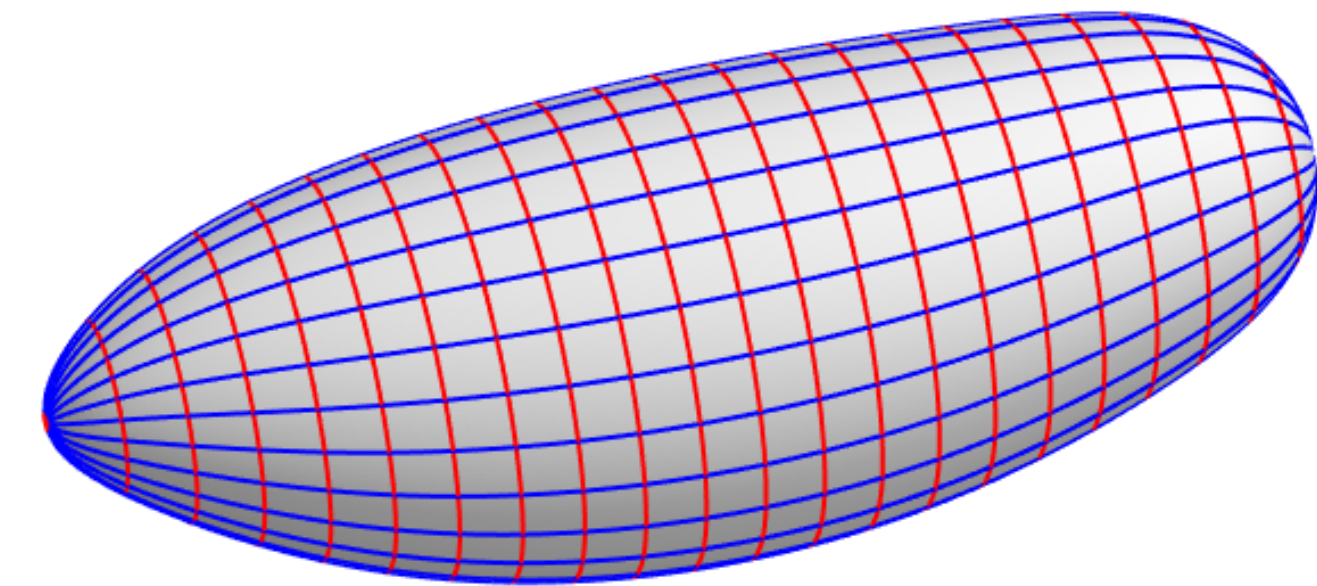
Disordered packing



4 5 6 7 8
Coordination number

Claussen, **FB** & Shraiman, *PNAS* (2024)

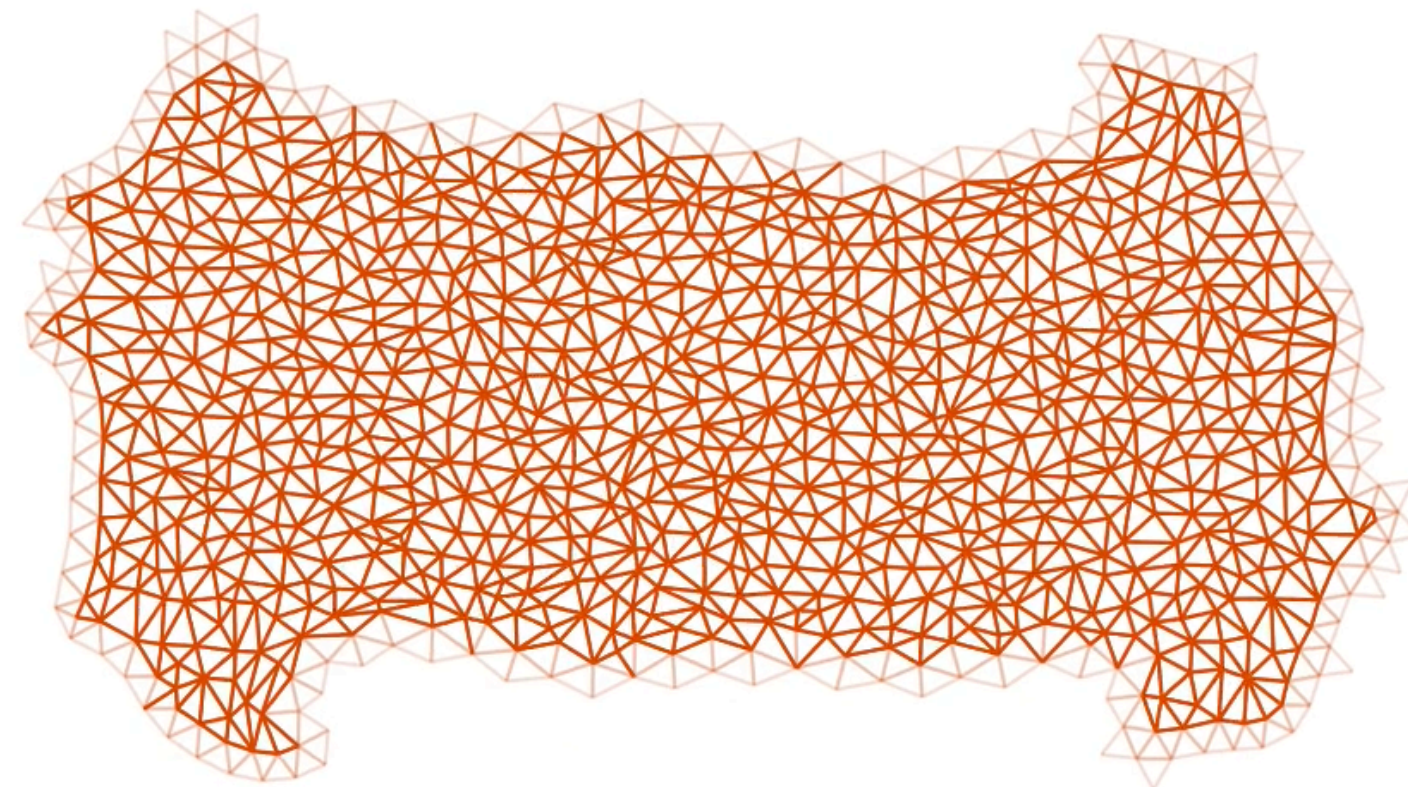
Mechanical feedback can
respond to static pre-stress:
hoop stress = 2x axial stress



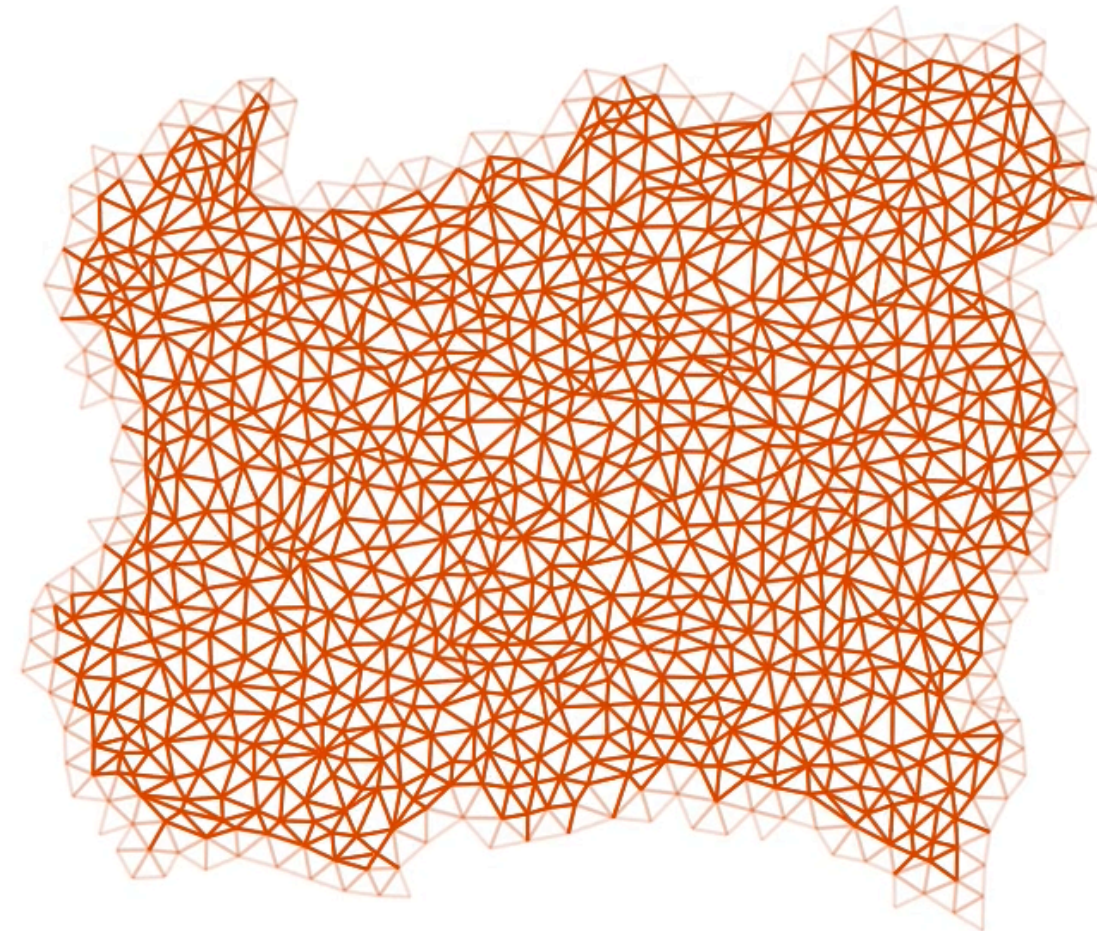
"hot dog effect"

Extent of flow depends on initial packing order and anisotropy

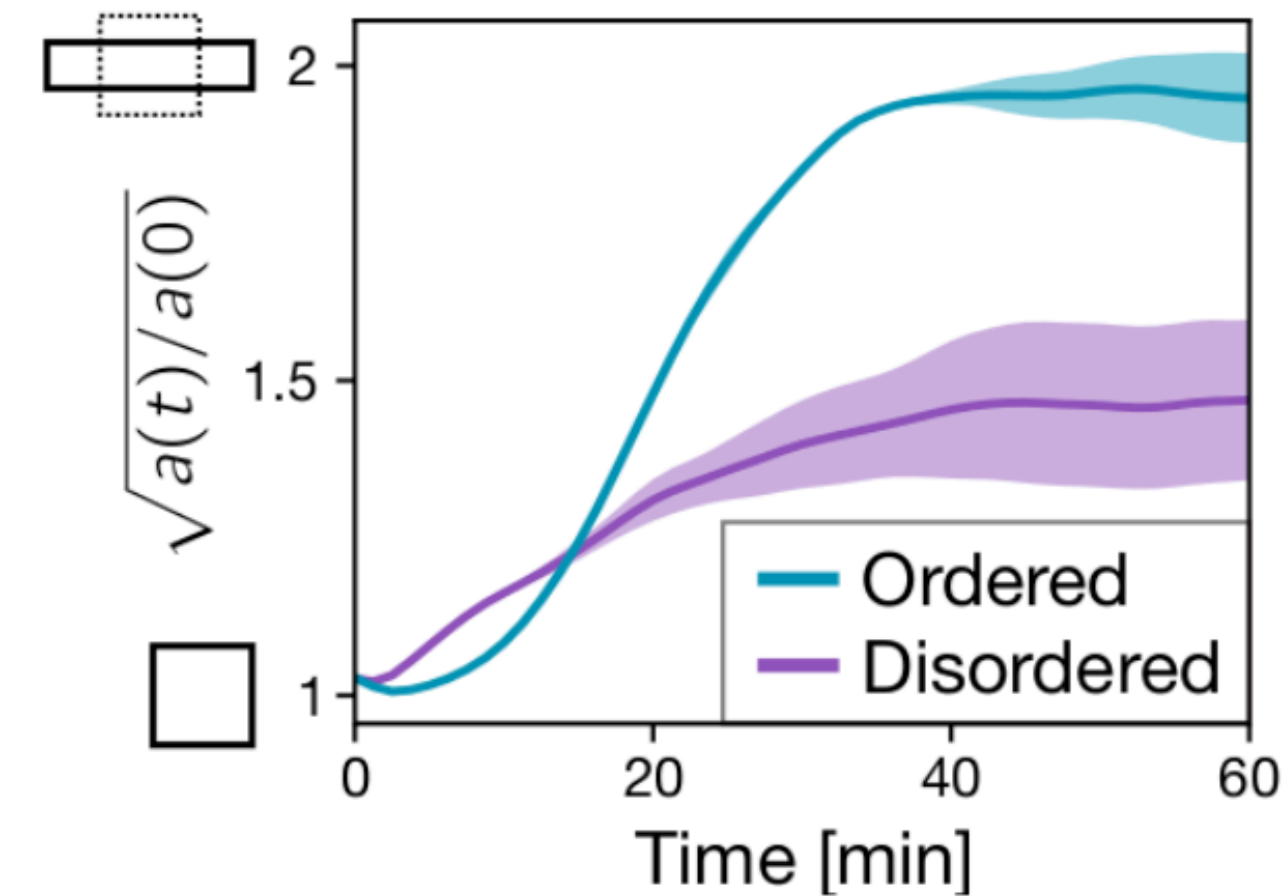
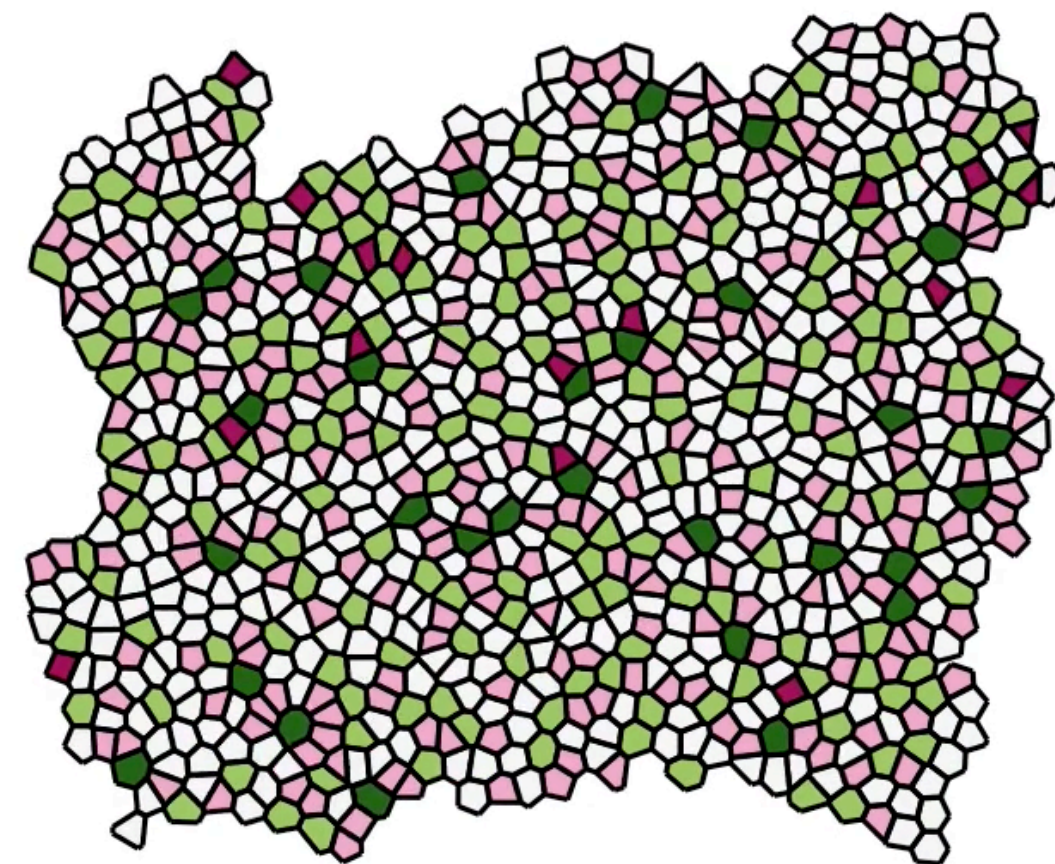
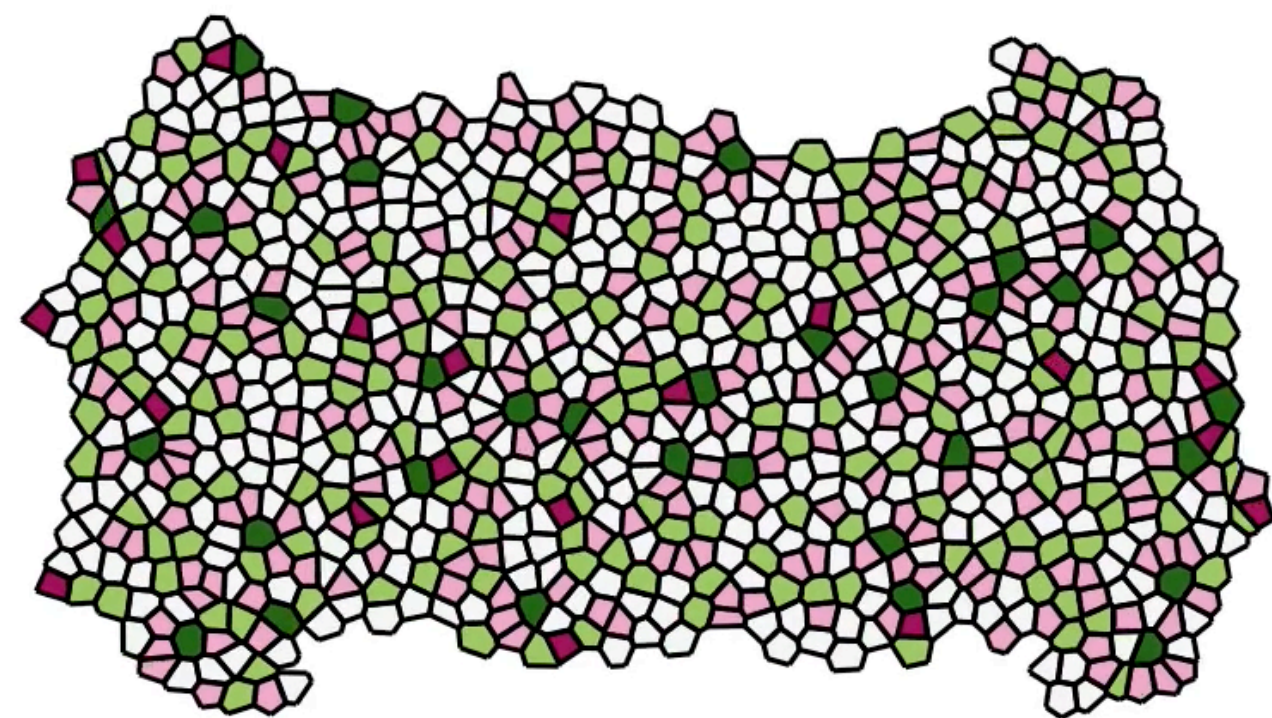
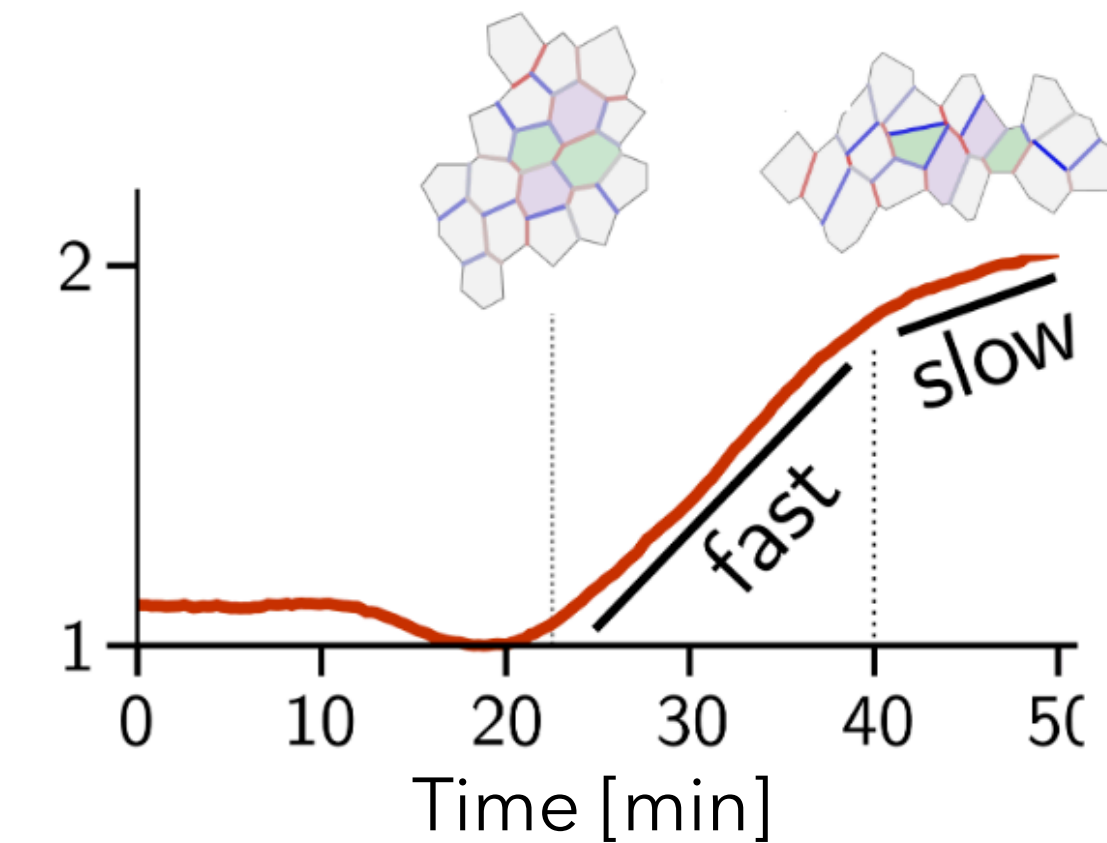
Initially ordered packing



Disordered packing



Theory

Experimental data from *Drosophila*

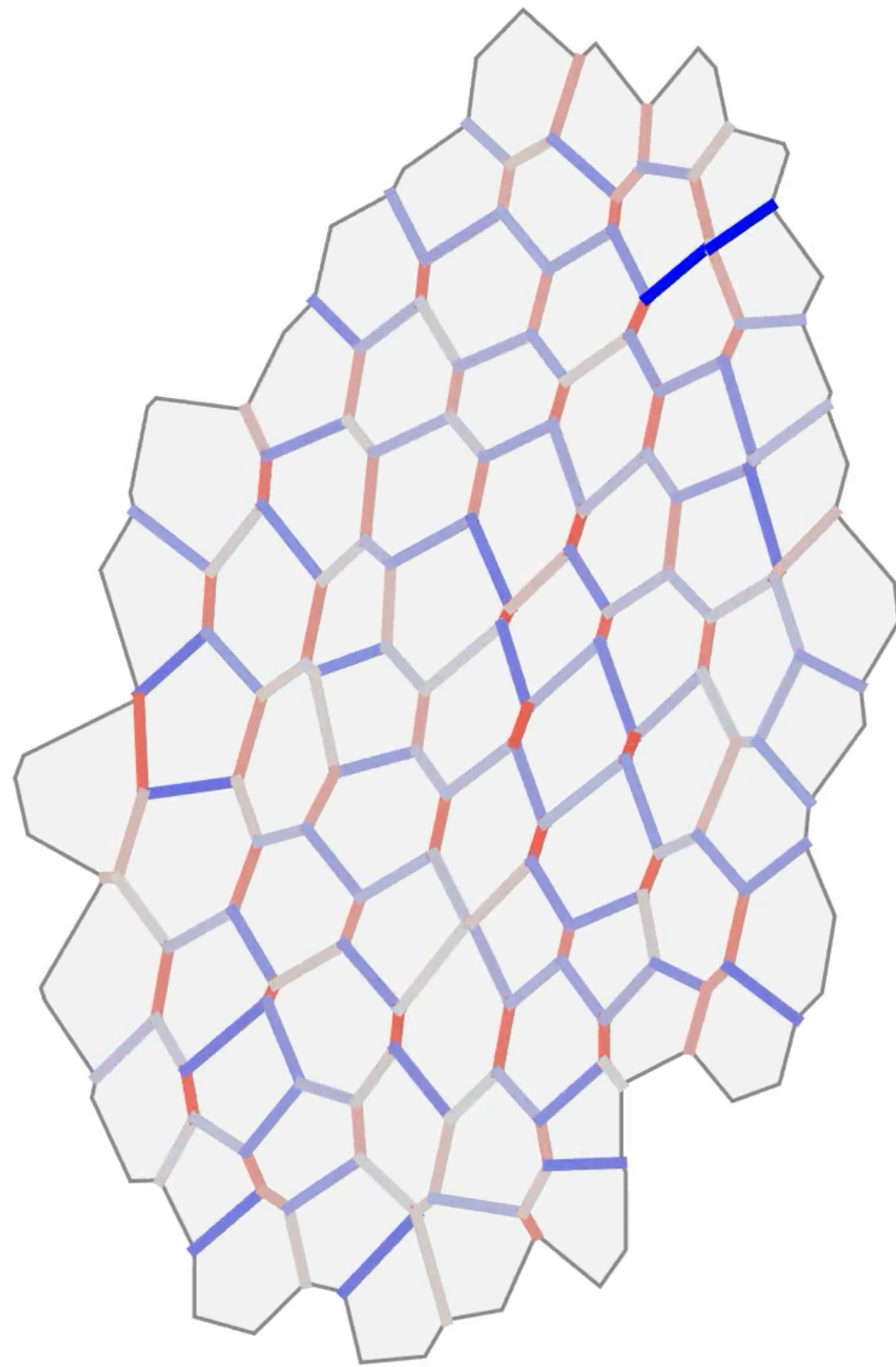
- Cells can remodel solid tissue quasi-statically by controlling balanced tensions ("active plastic flow")
- Strong effect of order in cell packing
=> self-organized flow is self-limiting



Coordination number

Claussen, **FB** & Shraiman, *PNAS* (2024)

t = 20 min



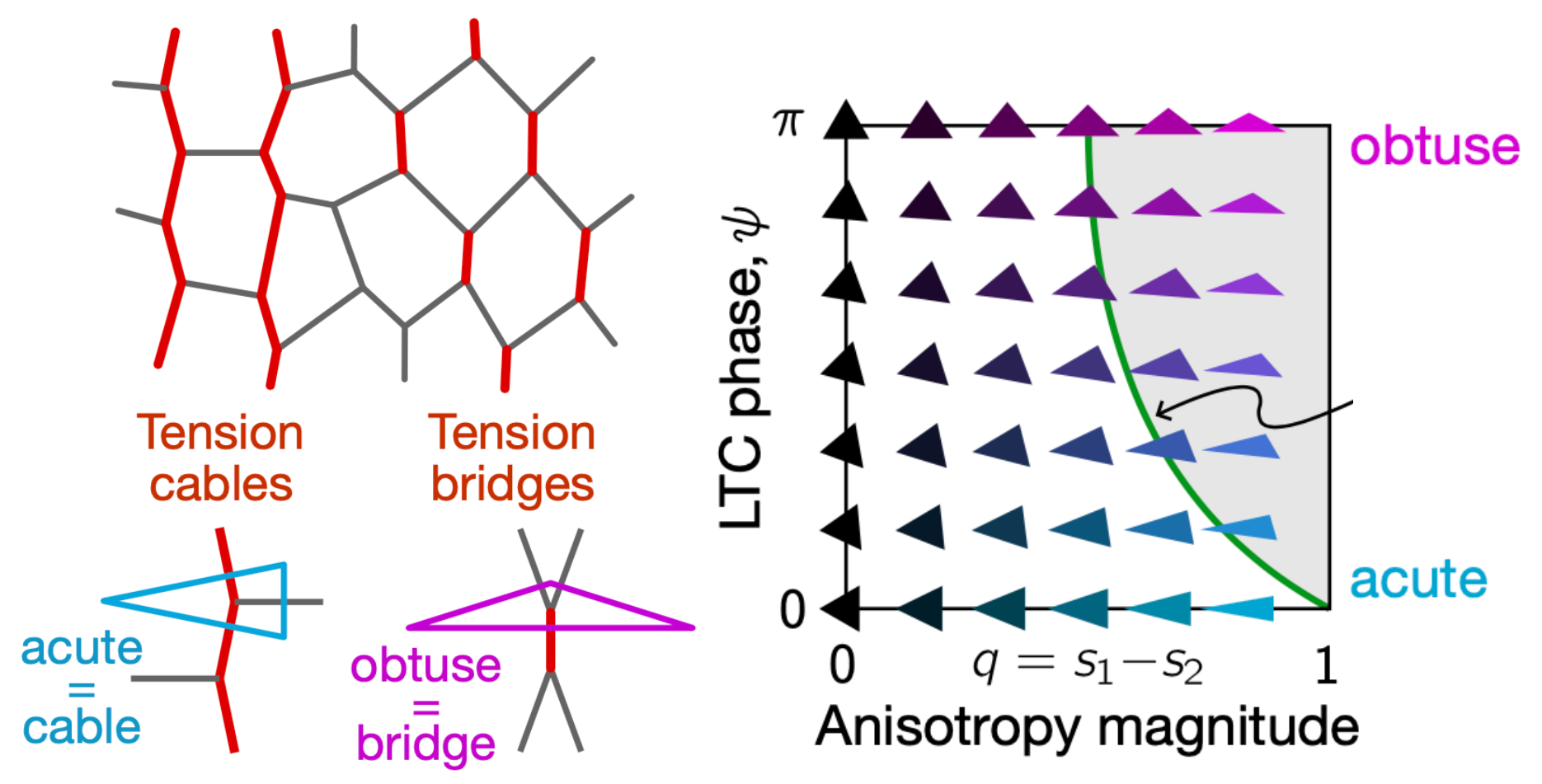
Summary

Epithelial tissue = distributed hydrodynamic skeleton
=> emergent elasticity

Adiabatic changes of tensions drive shape change in
force balance ("active plastic flow")

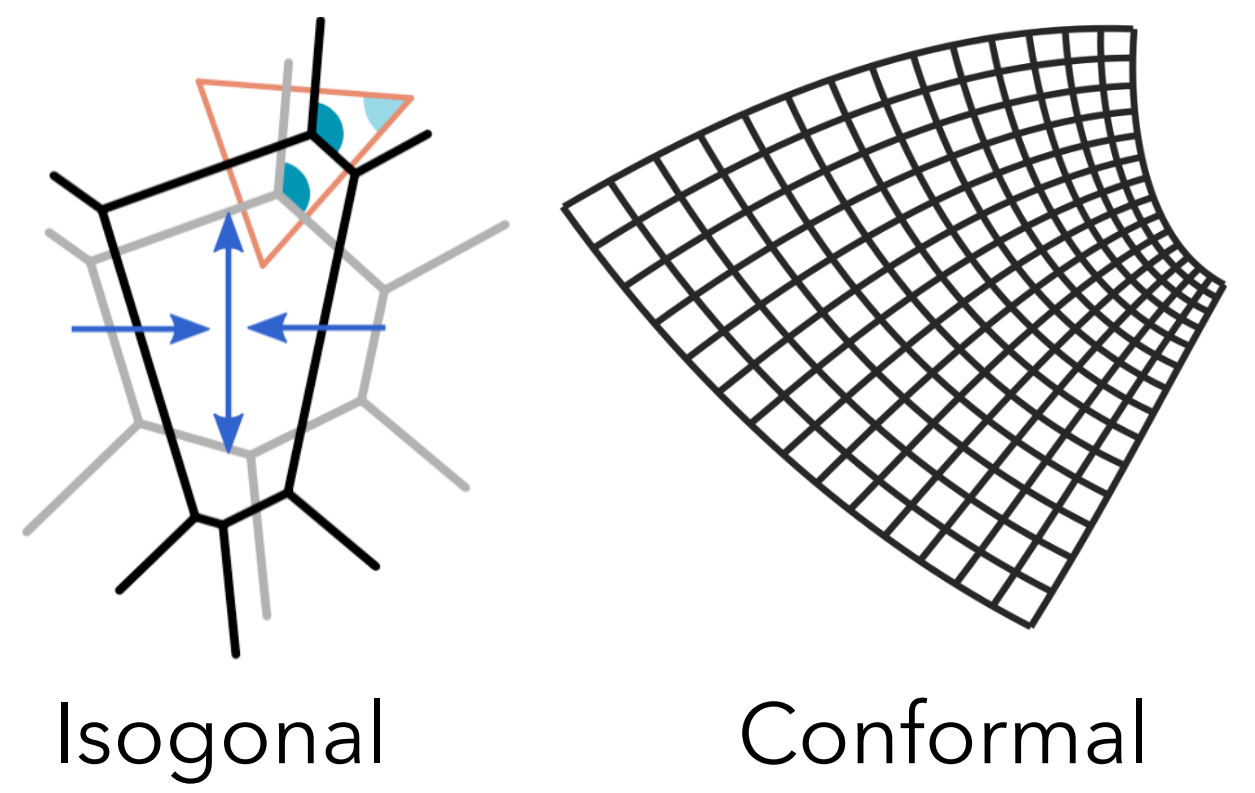
Local positive feedback drives *global* flow

• **Order parameter** for local tension configurations

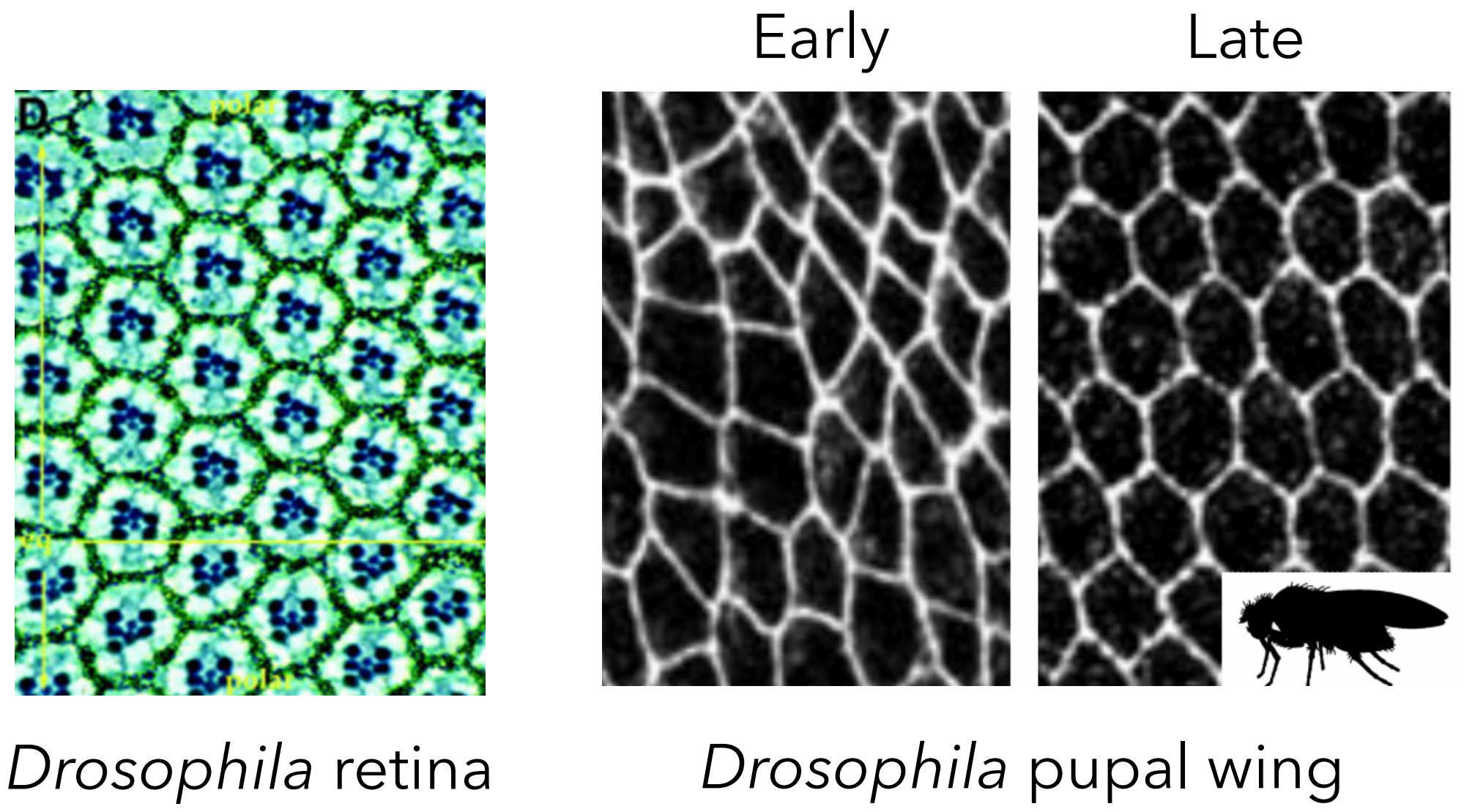


Claussen*, **FB*** & Shraiman (2024)
 Claussen, **FB** (2024)

• Continuum theory for emergent mechanics



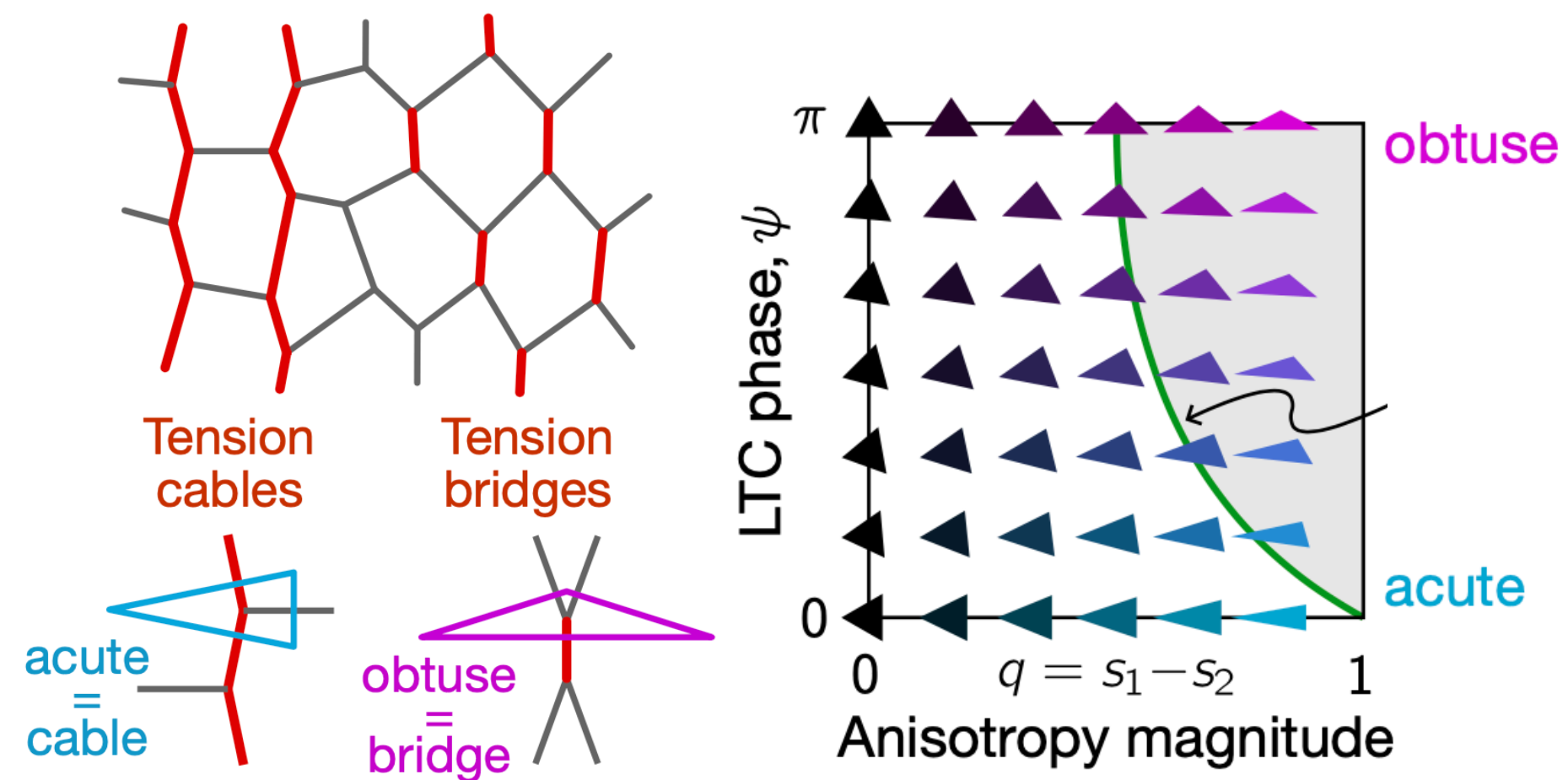
Claussen, **FB** & Shraiman (2026)



Drosophila retina

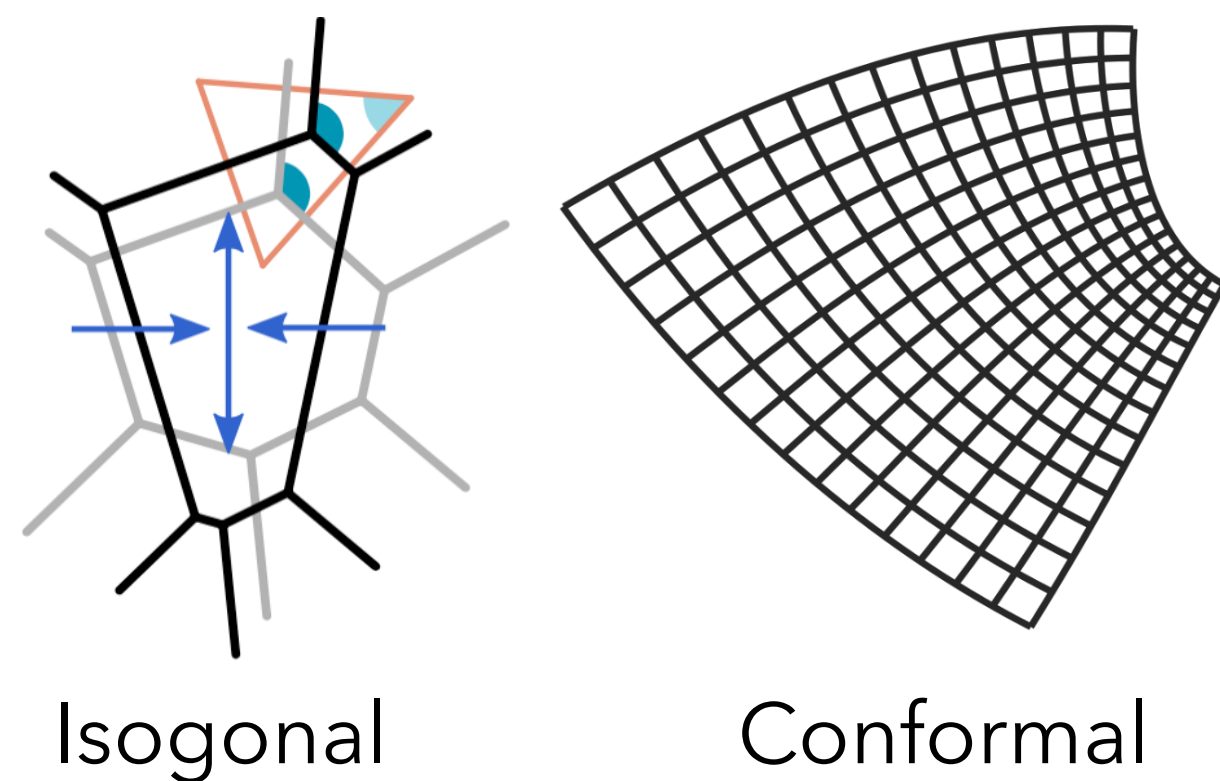
Drosophila pupal wing

• **Order parameter** for local tension configurations



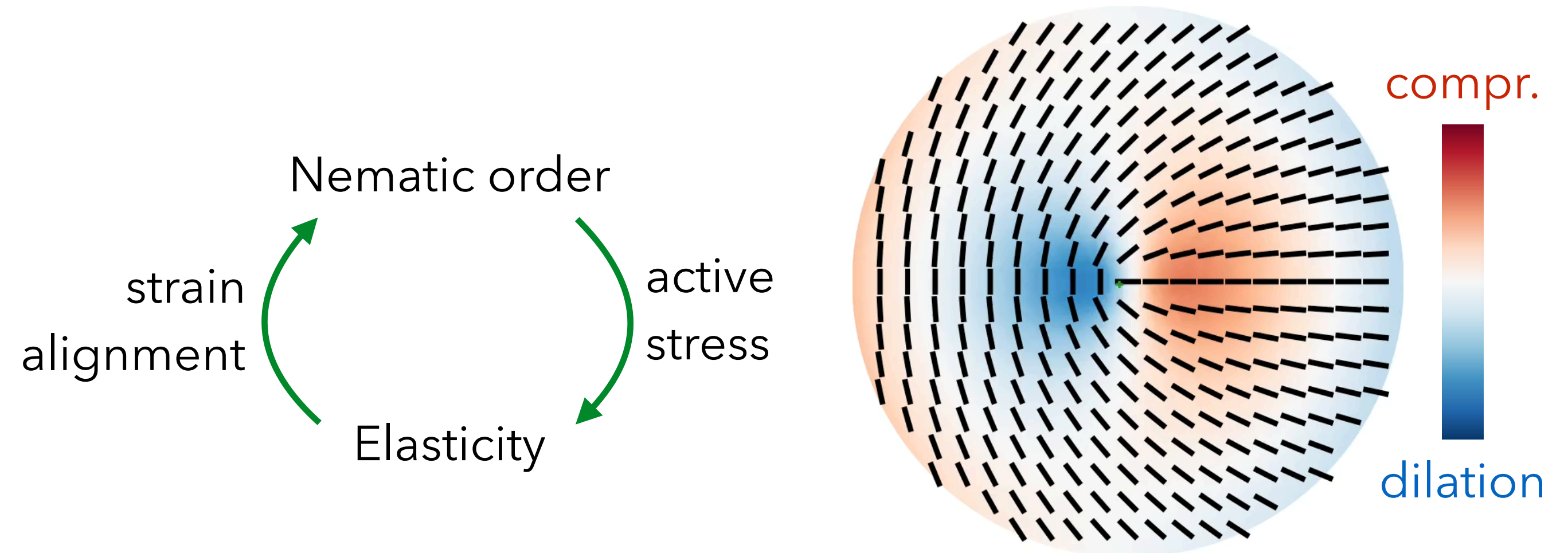
Claussen*, **FB*** & Shraiman (2024)
 Claussen, **FB** (2024)

• Continuum theory for emergent mechanics

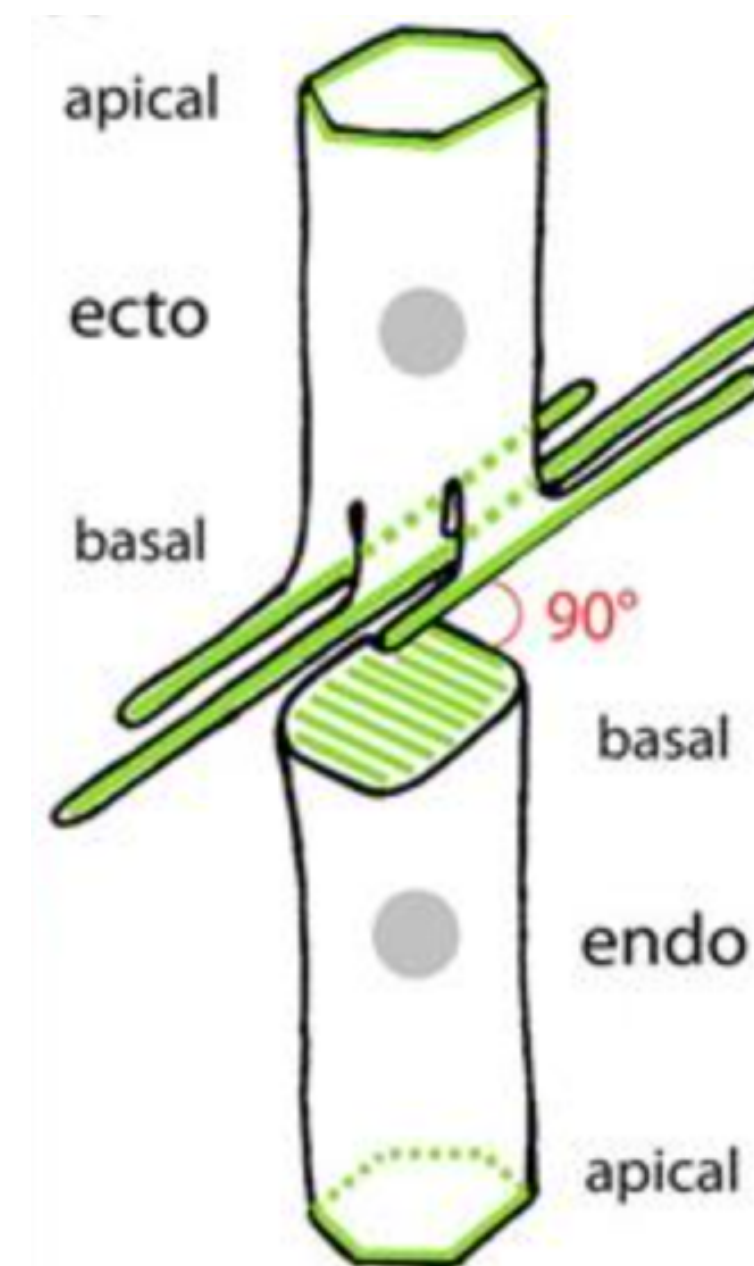


Claussen, **FB** & Shraiman (2026)

• Feedback-controlled active mechanics



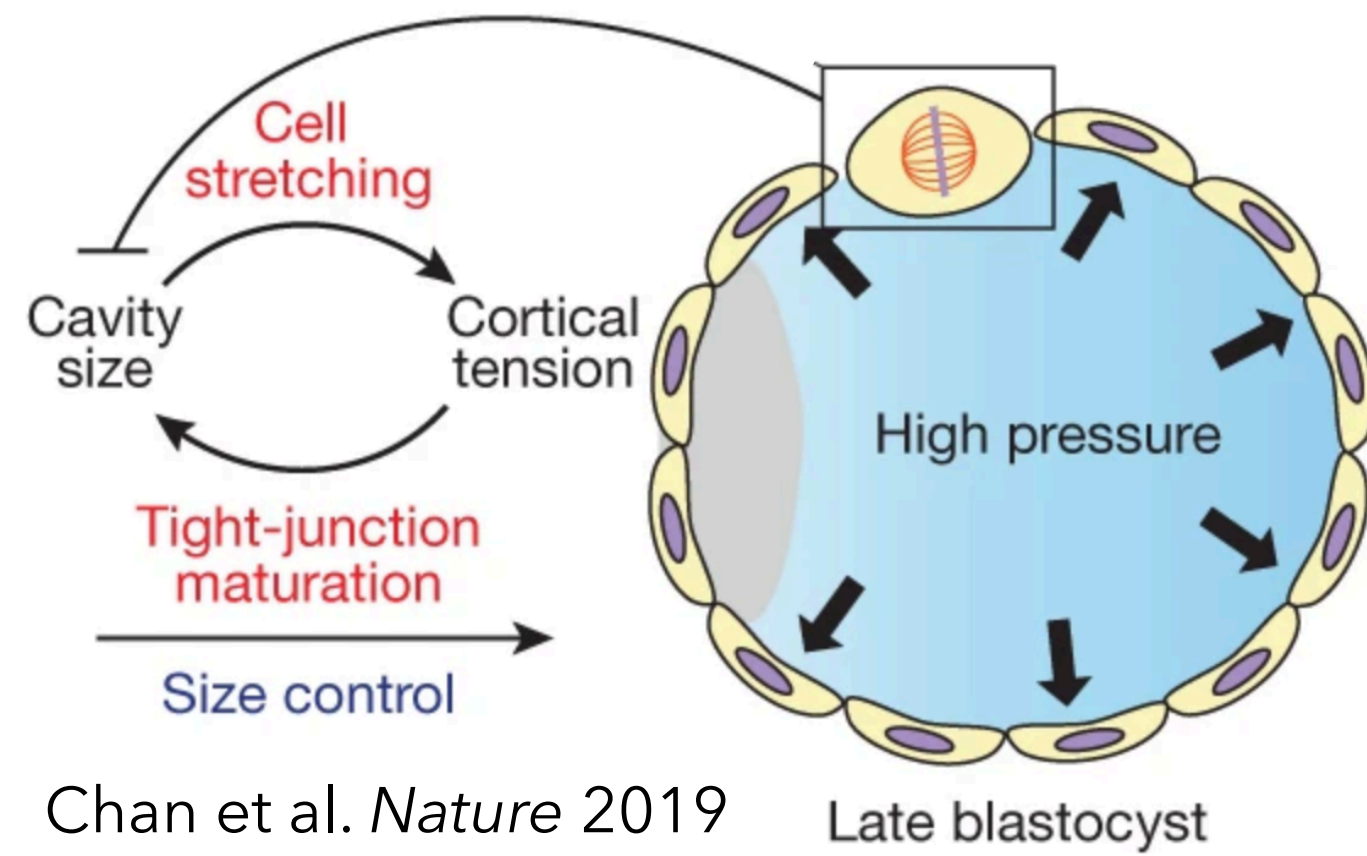
FB, ... Marchetti (2026)
 Yu, **FB** & Marchetti (2026)



Perpendicular alignment of actin fibers

Singh, Weyer, Marchetti & **FB** (in preparation)

Outlook: 3D shape from active surface stress



$$p = T/R$$

