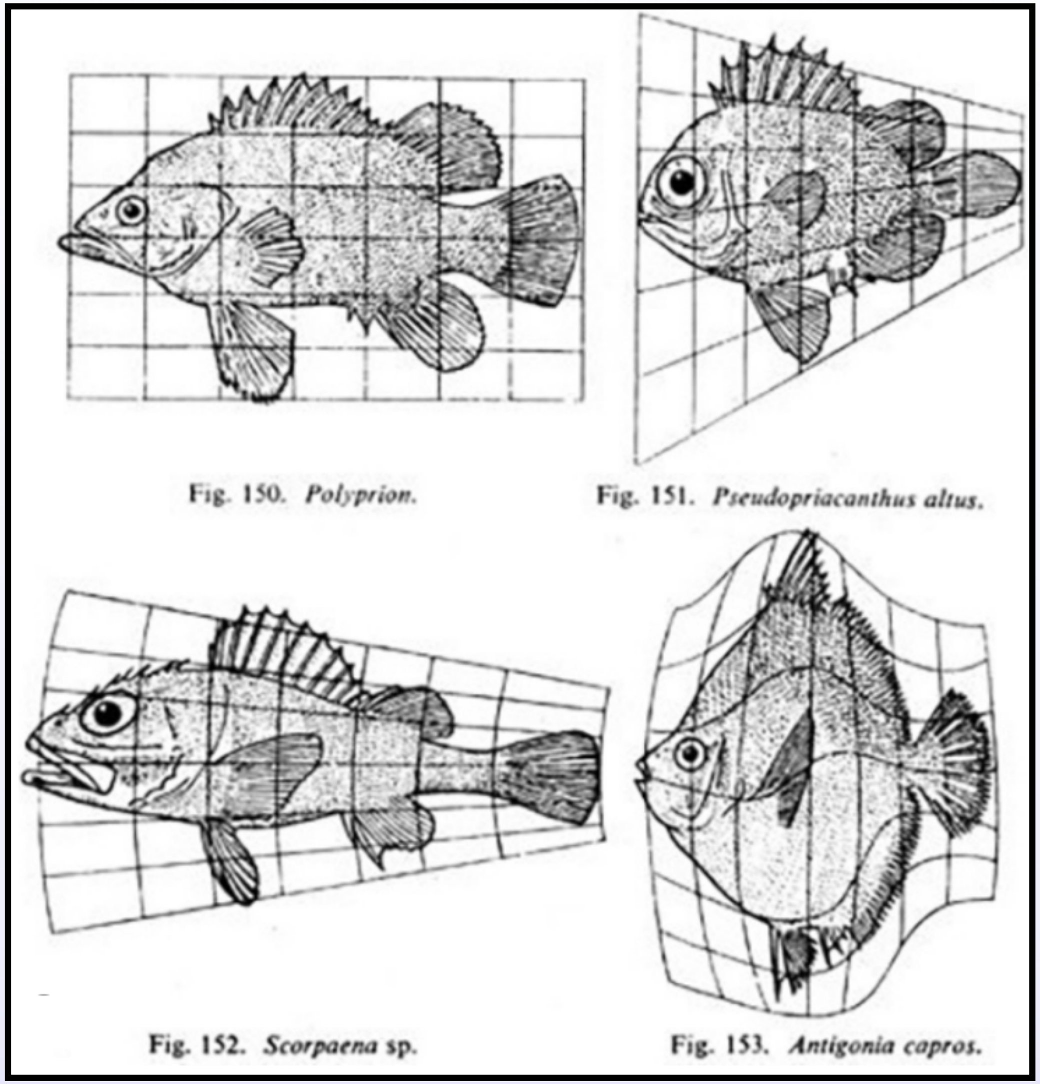
UNIVERSITÉ DE GENÈVE
FACULTÉ DES SCIENCES

University of Geneva,
Switzerland

From active nematic surfaces to biological morphogenesis

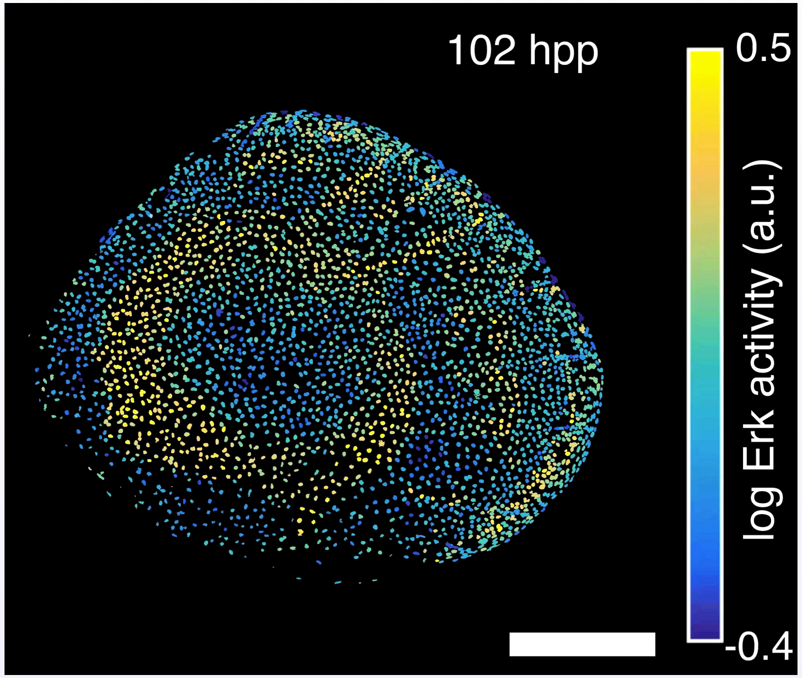
Guillaume Salbreux

Diversity of shapes in biology

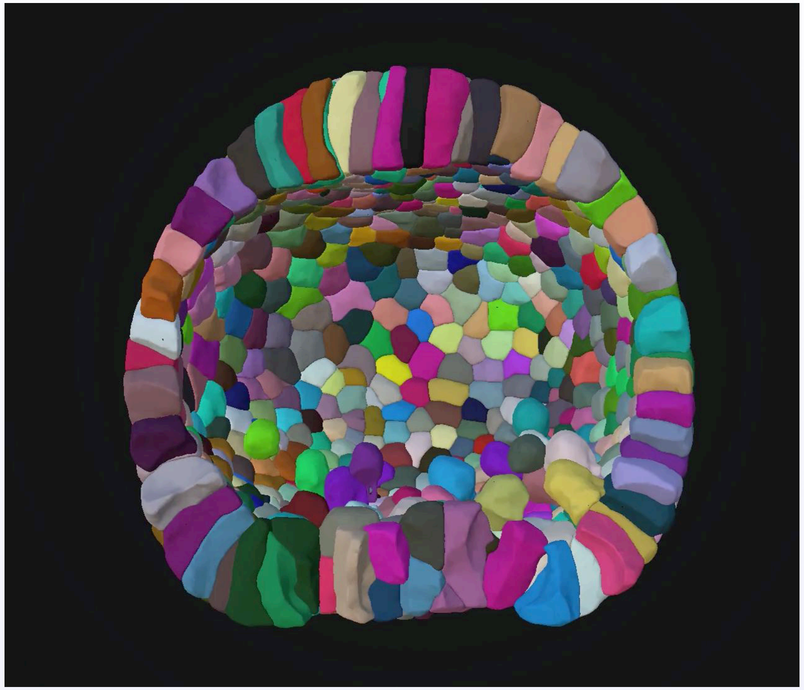


[On growth and form- D'Arcy Thompson - 1917]

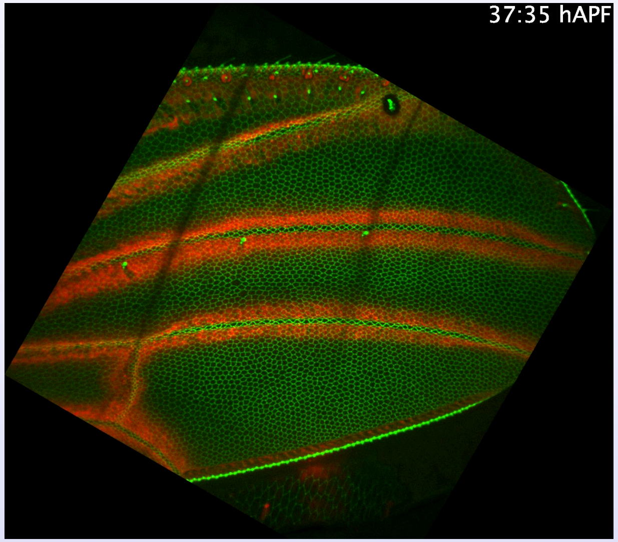
On growth, form and flows



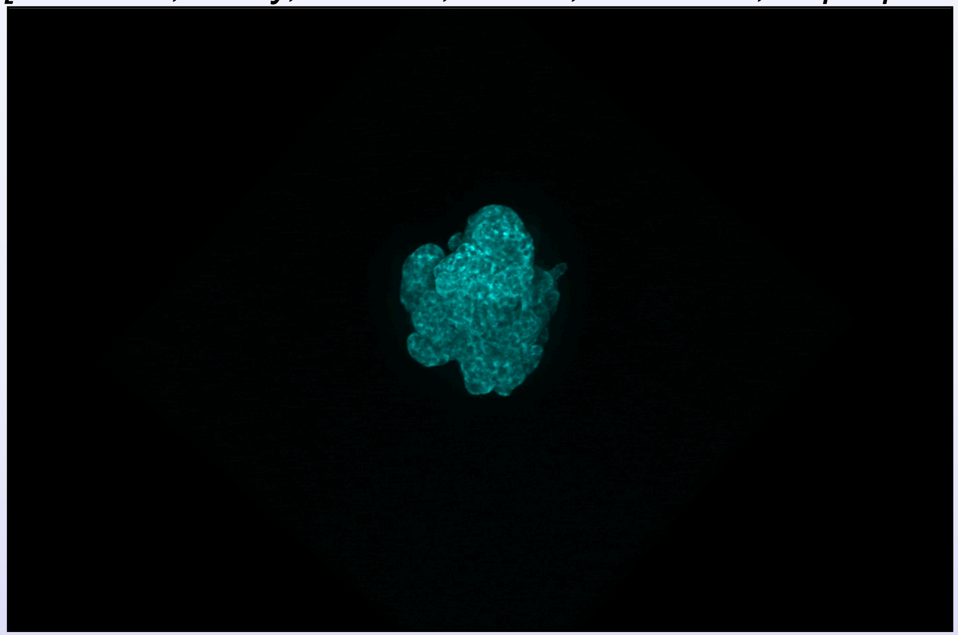
[De Simone&al, Nature, 2021]



[Delorme, Cuny, Mazzei, Rauzi, Salbreux, in preparation]



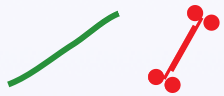
[Herszterg&al, Dev Cell, 2025]



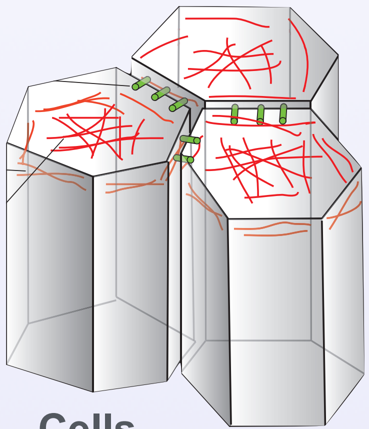
[B.Canales, A. Elosegui-Artola, R. Rollin, G. Salbreux]

Continuum theories of active matter

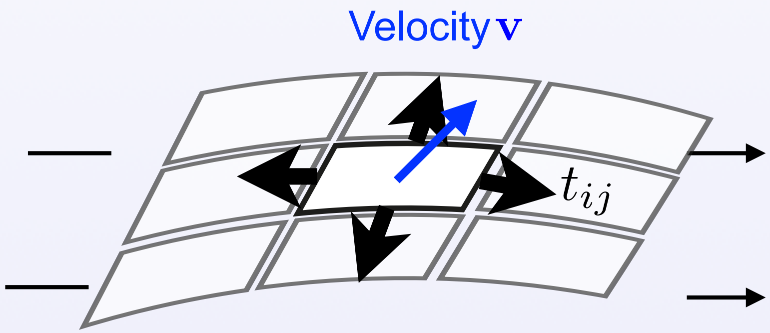
Microscopic *Mesoscopic* *Macroscopic*



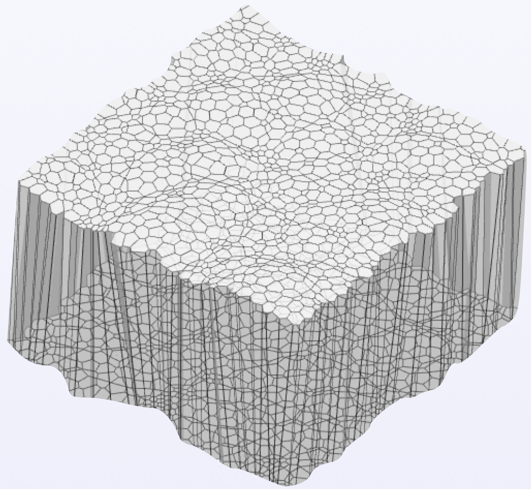
Motor, cytoskeletal filaments,



Cells

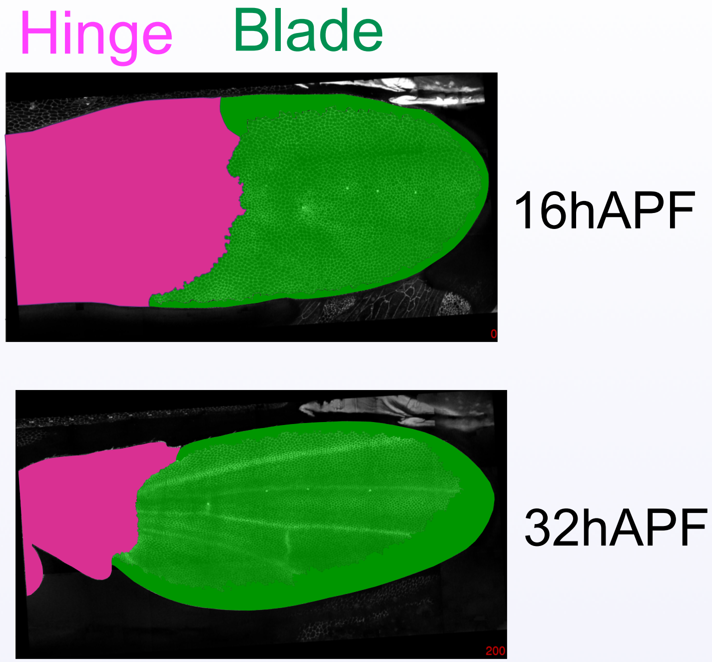


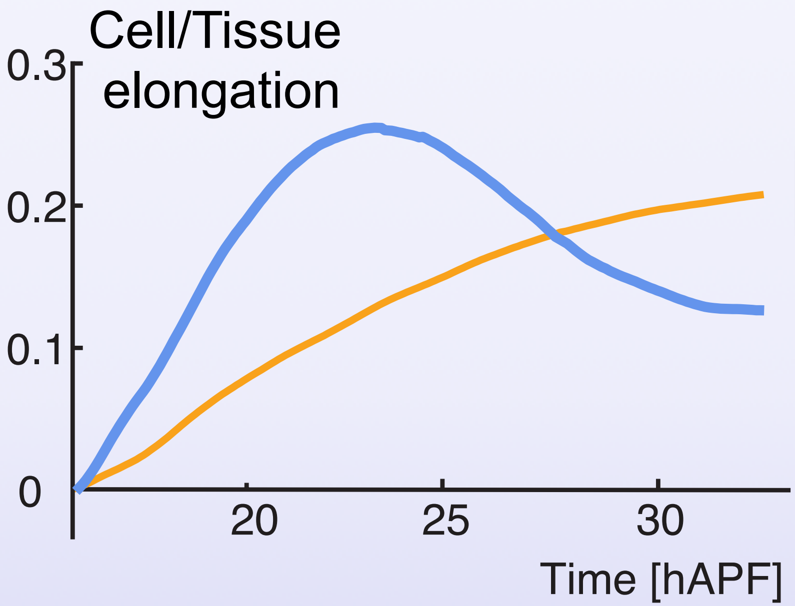
Continuum theory of active matter

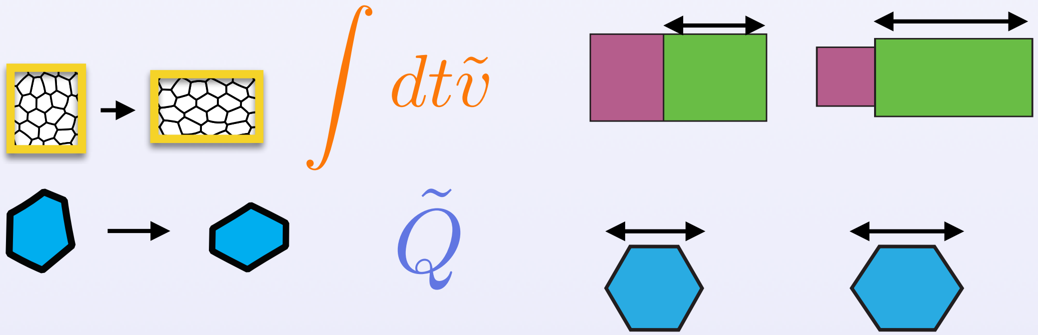


Biological tissue

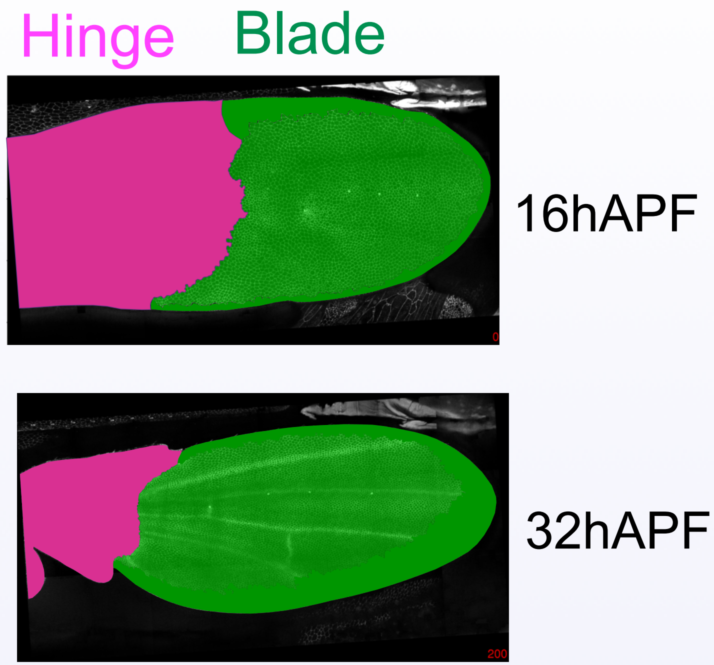
Tissue fluidity



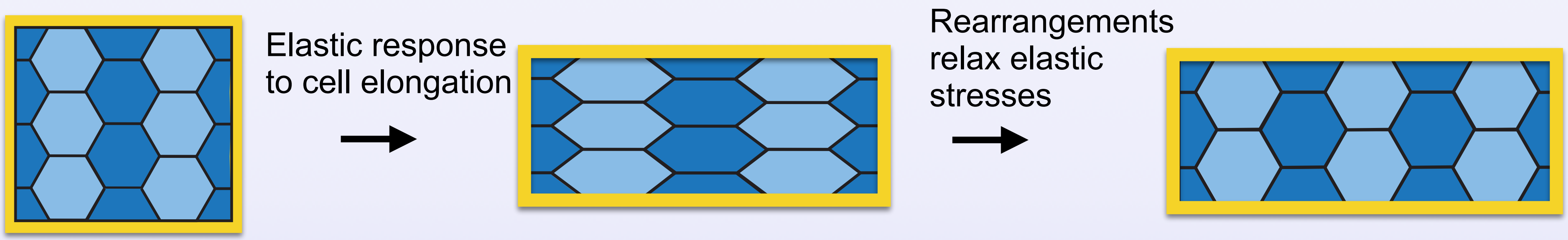




Tissue fluidity



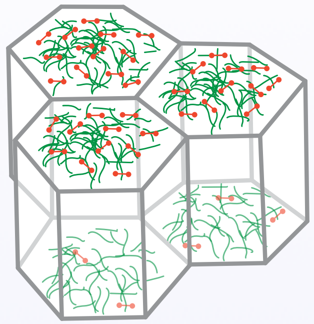
Cellular rearrangements ensure long-time scale tissue fluidity



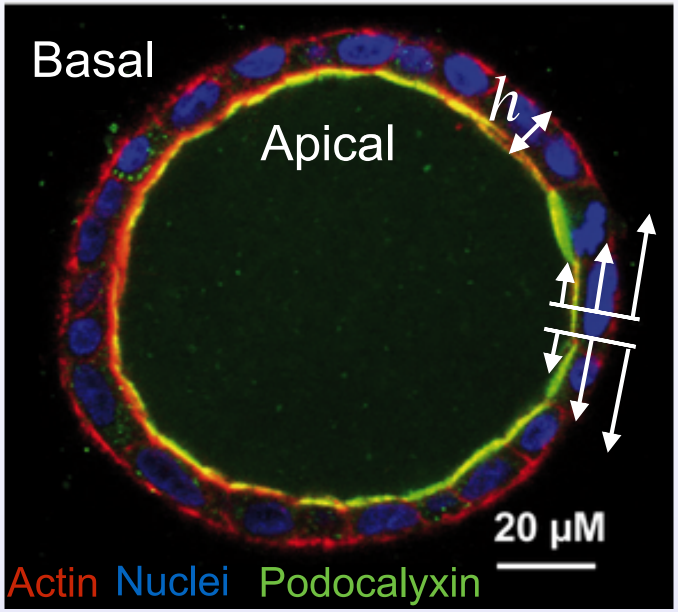
Tissue viscosity ~ $10^4 - 10^5$ Pa.s

Epithelial tissues as thin shells

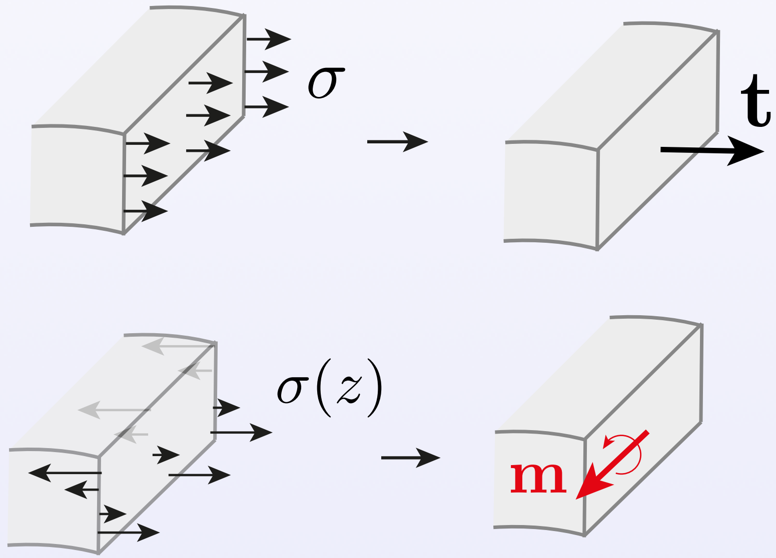
Describing epithelia as « active thin shells »:



MDCK cyst

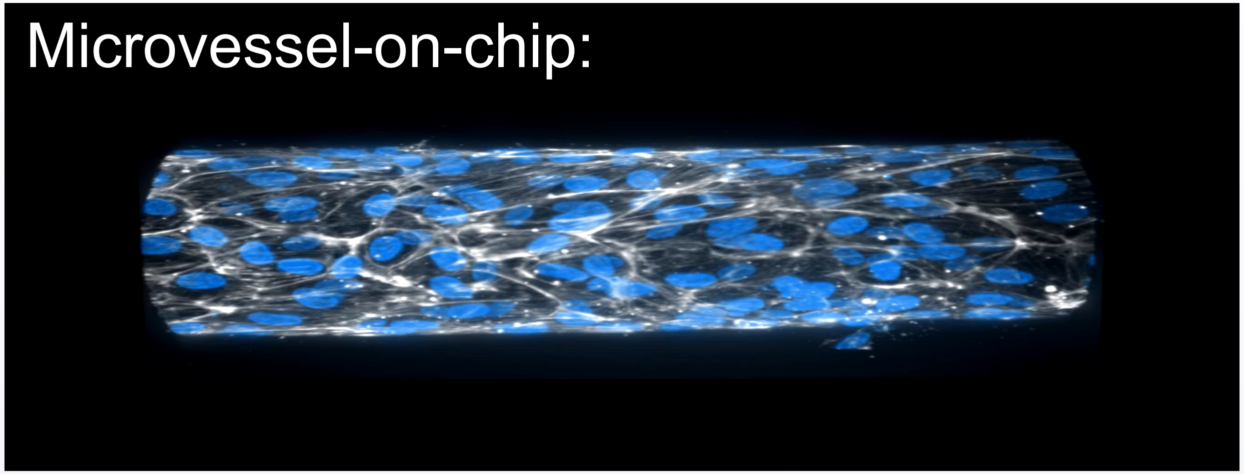


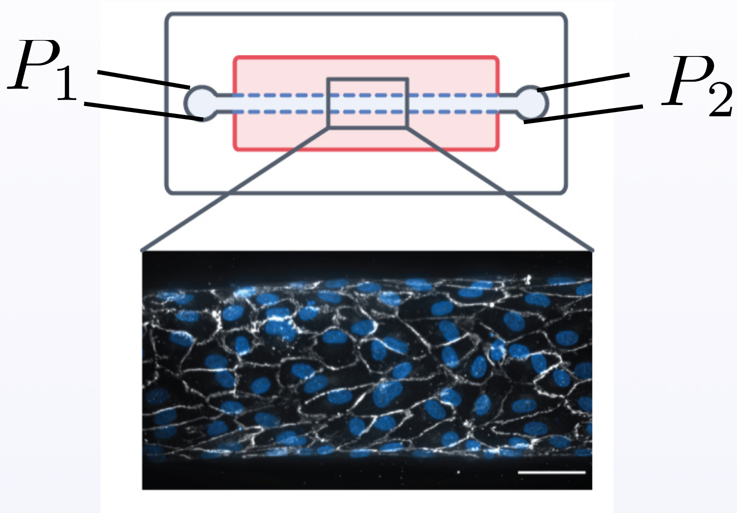
[Engelberg&al, PloS Comp Bio, 2011]



[Salbreux&al, PRE, 2017; Salbreux&al, PRR, 2022]

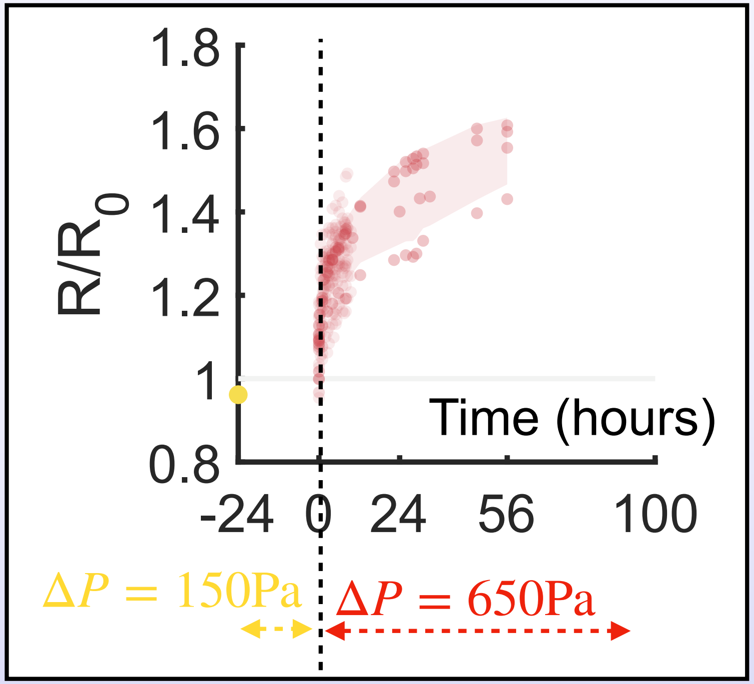
Tissues as nematic liquid crystals

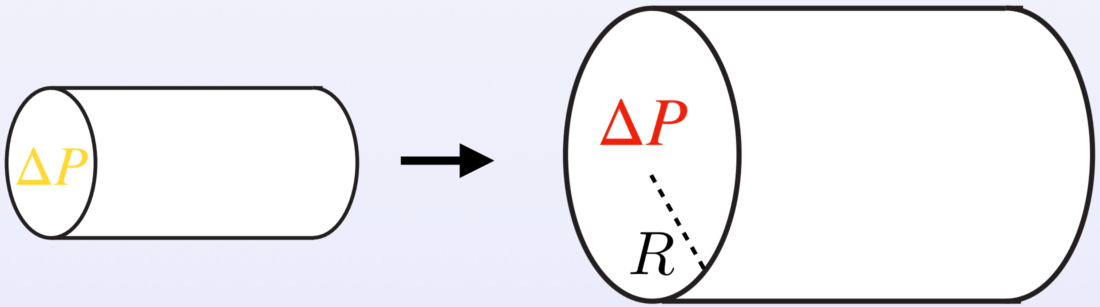




[Dessalles &al, Biofabrication, 2022]

Pressure application leads to endothelial tube slow expansion:

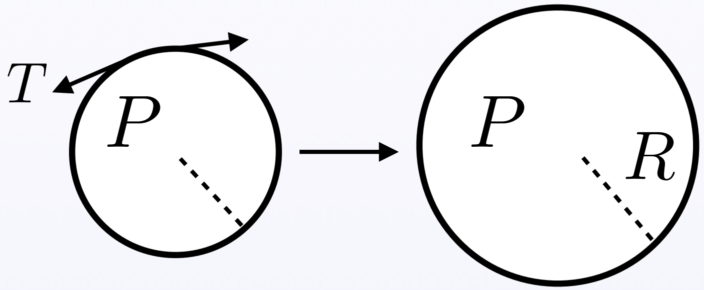




[Dessalles, Cuny &al, Nature Physics, 2025]

How to resist the expansion of a tube?

Surface tension?

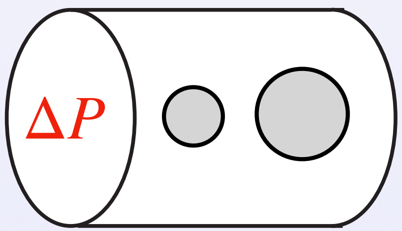


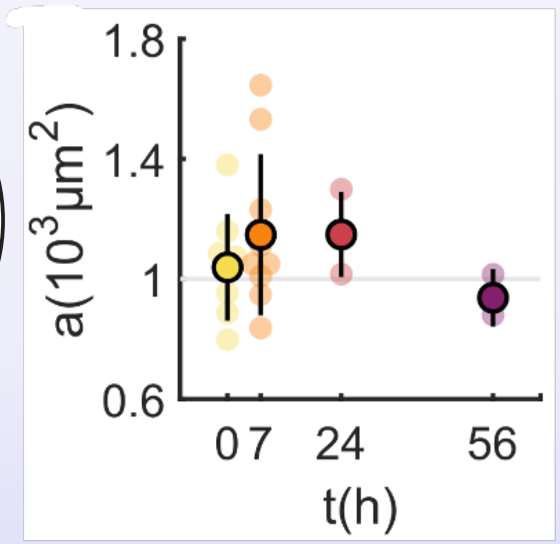
$$P = \frac{T}{R}$$

Unstable by the law of Laplace

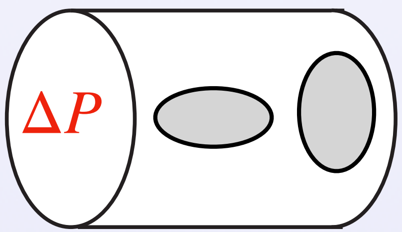
Elastic stresses resulting from cell deformation?

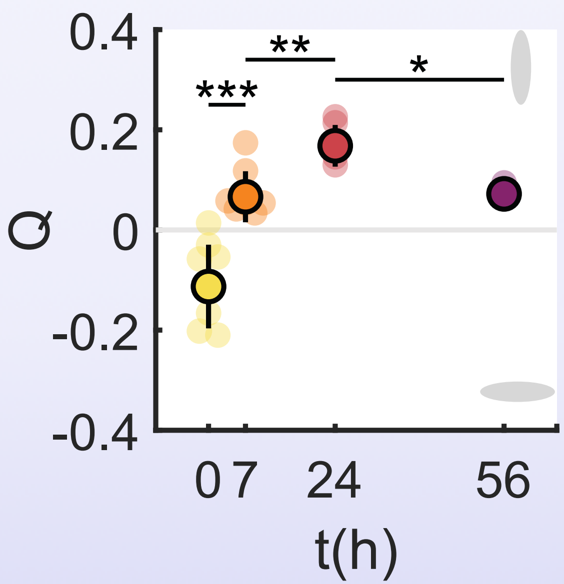
Cell area dynamics



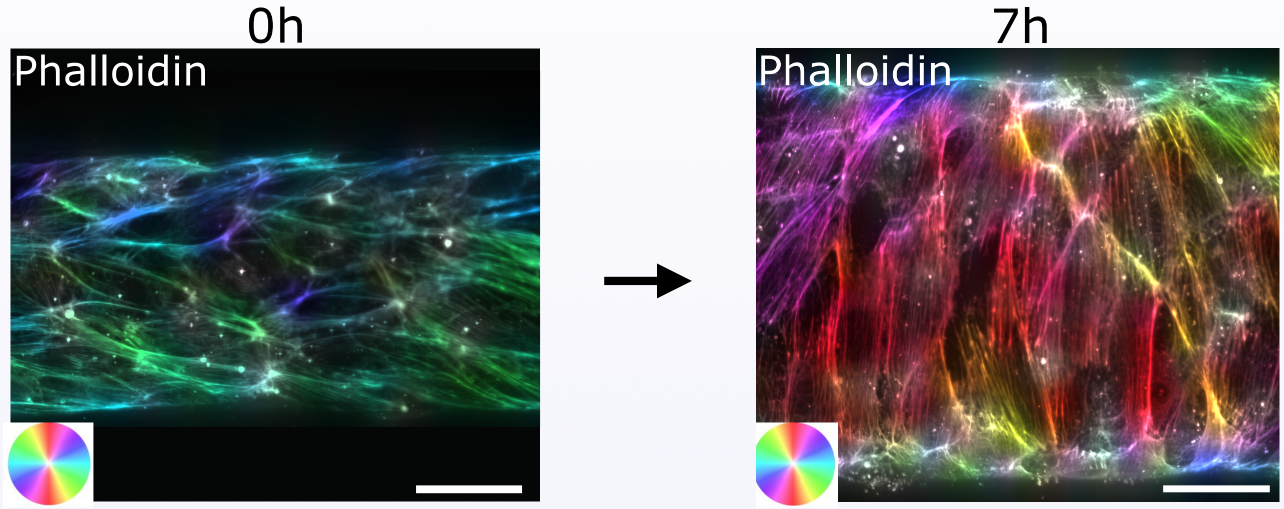


Cell elongation dynamics

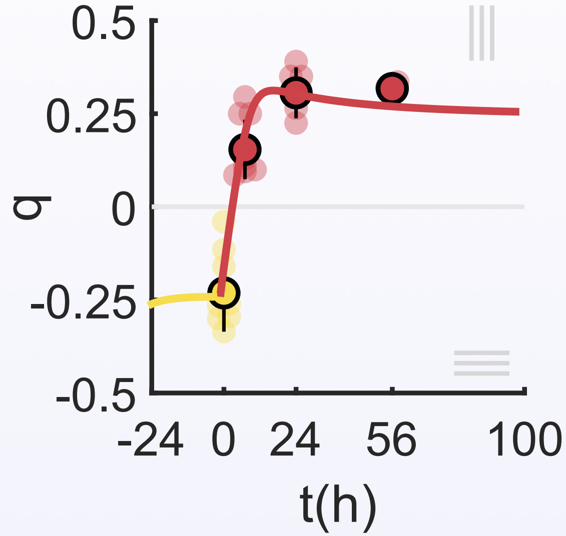




How to resist the expansion of a tube?



$\Delta P = 150Pa$ $\Delta P = 650Pa$

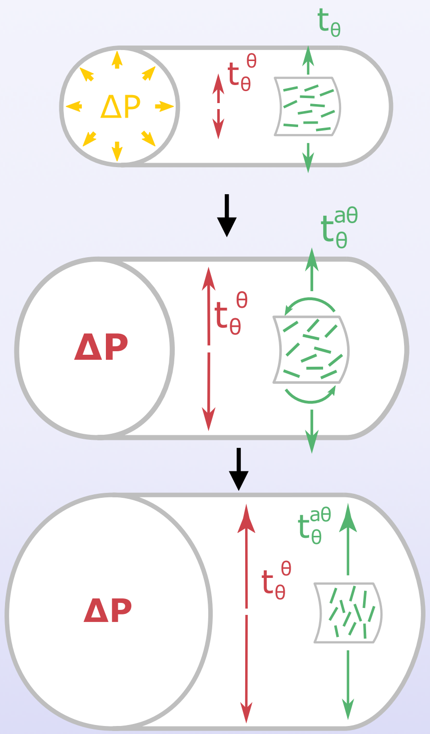


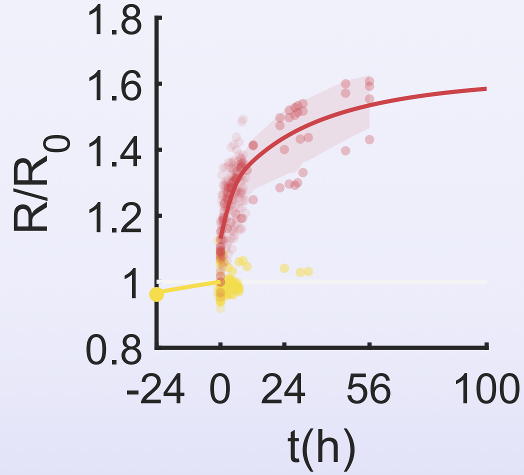
Nematodynamics:

$$D_t q_{ij} = -\frac{1}{\gamma}(q^2 - q_0^2)q_{ij} + \beta t^r_{ij}$$

Tension oriented by nematic order:

$$t^a_{ij} \sim \zeta q^{ij}$$

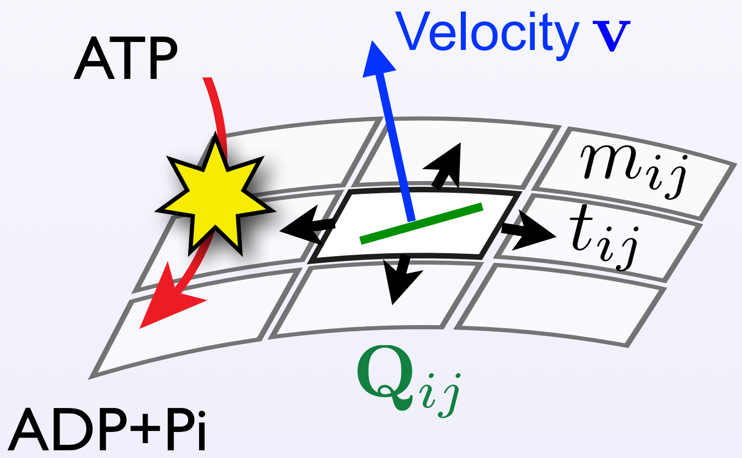




[Dessalles, Cuny &al, Nature Physics, 2025]

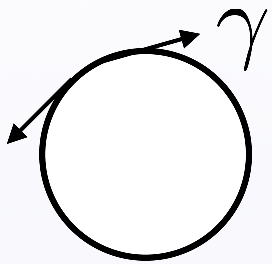
Hydrodynamics of active nematic surfaces

Continuum, coarse-grained description of active surface:

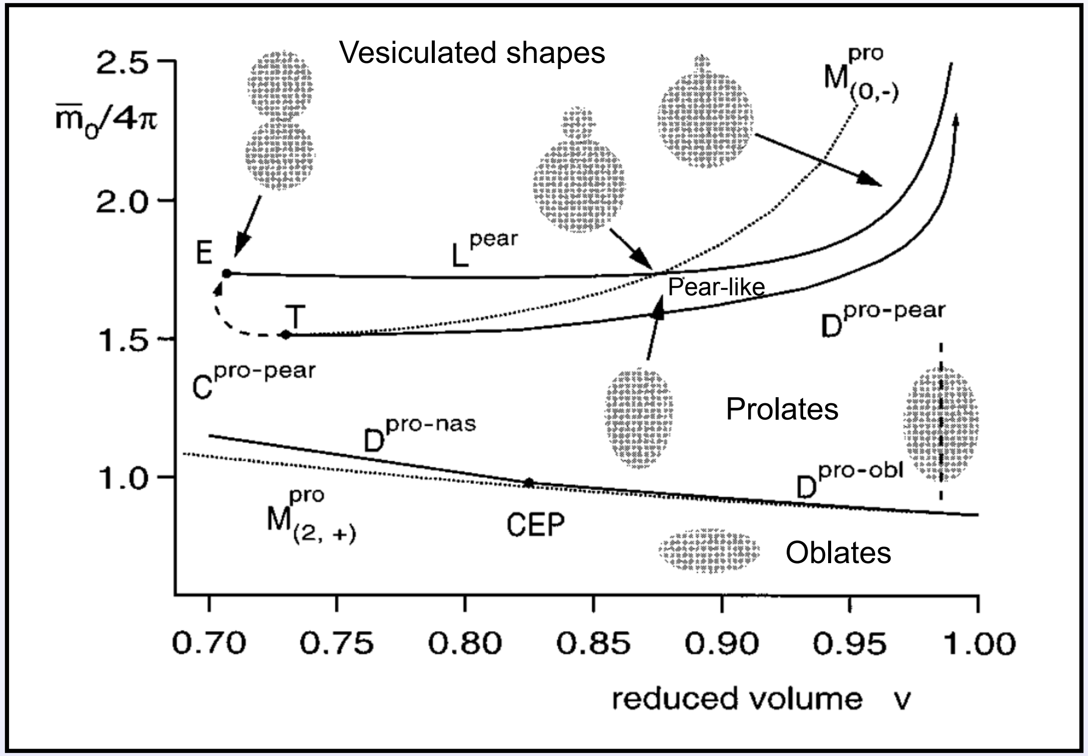


Metric tensor	g_{ij}
Curvature tensor	C_{ij}
Velocity field	$\mathbf{v}$
Nematic tensor	$\mathbf{Q}_{ij}$
Tension tensor	t_{ij}
Bending moment tensor	m_{ij}

Helfrich theory for lipid membranes: a passive fluid surface



$$F = \int dS \left(\gamma + \frac{\kappa}{2}({C_k}^k - C_0)^2\right)$$



[Döbereiner&al, PRE, 1997]

Helfrich theory for lipid membranes: a passive fluid surface

$$F = \int dS \left(\gamma + \frac{\kappa}{2} ({C_k}^k - C_0)^2 \right)$$

<u>Virtual work principle for a surface:</u> $$\delta W = \int dS \left[\bar{t}^{ij} \frac{\delta g_{ij}}{2} + {\bar{m}^i}_j \delta {C_i}^j \right]$$

<u>Tensions and bending moment arising in a Helfrich membrane:</u>

$$\bar{t}^{ij}_e = 2 \frac{\delta F}{\delta g_{ij}} \sim \gamma g_{ij} \qquad \bar{m}^{ij}_e = \frac{\delta F}{\delta C_{ij}} = \kappa ({C_k}^k - C_0) g_{ij}$$

Linear non-equilibrium thermodynamics

Rate of free energy change = -Entropy production:

$$\frac{dF}{dt} = -\sum_i f_i \frac{d\phi_i}{dt}$$

Thermodynamic fields ϕ_i and forces $f_i = -\frac{\delta F}{\delta \phi_i}$

Postulate linear phenomenological relation between fluxes and forces:

$$\frac{d\phi_i}{dt} = \sum_j L_{ij} f_j$$

L_{ij} phenomenological coefficients

[De Groot&Mazur, Non equilibrium thermodynamics, 2013]

Rate of free energy change for an active nematic surface:

$$\frac{dF}{dt} = -\int dS \left[(t^{ij} - t_e^{ij}) v_{ij} + (\bar{m}^{ij} - \bar{m}_e^{ij}) D_t C_{ij} + D_t Q_{ij} H^{ij} + r \Delta\mu \right]$$

Conjugate pairs of fluxes and forces:

Tension tensor (non-equilibrium part)	$\bar{t}^{ij} - \bar{t}_e^{ij}$	Surface shear	$v_{ij} \sim D_t g_{ij}$
Bending moment tensor (non-equilibrium part)	$\bar{m}^{ij} - \bar{m}_e^{ij}$	Rate of change of curvature tensor	$D_t C_{ij}$
Nematodynamics (Corotational time derivative)	$D_t Q_{ij}$	Molecular field	$H^{ij} = \frac{\delta F}{\delta Q_{ij}}$
Rate of ATP consumption	r	Chemical potential of ATP hydrolysis	$\Delta\mu$

[Salbreux&al, PRE, 2017; Salbreux&al, PRR, 2022]

Linear non-equilibrium thermodynamics

Rate of free energy change = -Entropy production:

$$\frac{dF}{dt} = -\sum_i f_i \frac{d\phi_i}{dt}$$

Postulate linear phenomenological relation between fluxes and forces:

$$\frac{d\phi_i}{dt} = \sum_j L_{ij} f_j$$

L_{ij} phenomenological coefficients

Constitutive equations obtained from linear phenomenological relations:

$$\begin{matrix} \bar{t}^{ij} \\ \bar{m}^{ij} \end{matrix} = \boxed{\begin{matrix} \bar{t}_e^{ij} \\ \bar{m}_e^{ij} \end{matrix}} + \boxed{\sim g_{ij}, \sim Q_{ij}} + \boxed{\sim v_{ij}, \sim \frac{DC_{ij}}{Dt}}$$

Helfrich passive terms

Active terms driven by non-equilibrium chemical reactions

Viscous dissipative terms

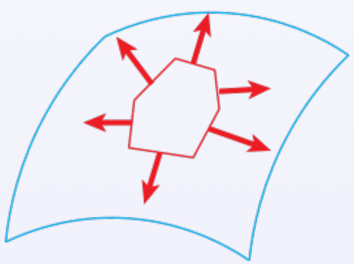
[Salbreux&al, PRE, 2017; Salbreux&al, PRR, 2022]

Active nematic surface theory for tissues

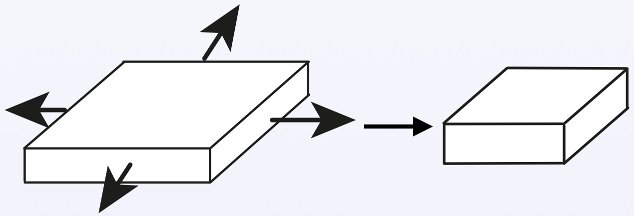
Tension
$$t_{ij} = \underline{2Kug_{ij}} + \underline{\zeta g_{ij}} + \underline{\zeta_n Q_{ij}} + \eta v_{ij}$$

Bending moment
$$\bar{m}_{ij} = \underline{\kappa C_{ij}} + \underline{\zeta_c g_{ij}} + \underline{\zeta_{cn} Q_{ij}} + \eta_c D_t C_{ij}$$

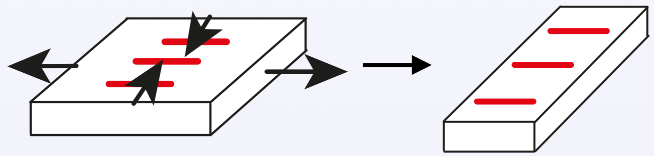
Area elasticity:



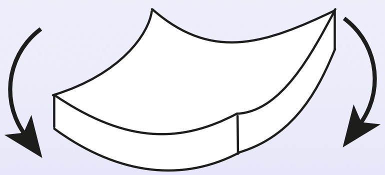
Isotropic tension:



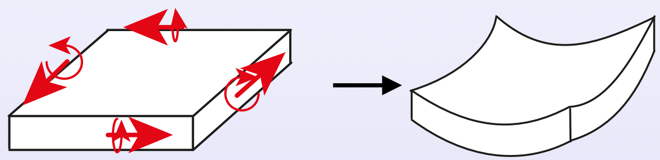
Nematic tension:



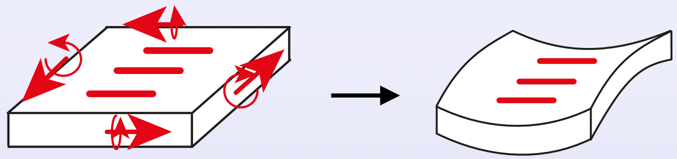
Bending rigidity:



Isotropic bending moment:



Nematic bending moment:

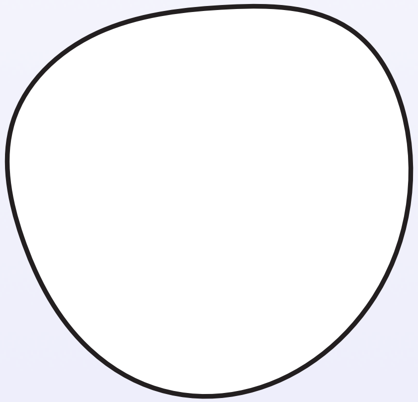


Active nematic surface theory for tissues

Tension $$t_{ij} = 2Kug_{ij} + \zeta g_{ij} + \zeta_n Q_{ij} \; + \eta v_{ij}$$

Bending moment $$\bar{m}_{ij} = \kappa C_{ij} + \zeta_c g_{ij} + \zeta_{cn} Q_{ij} \; + \eta_c D_t C_{ij}$$

<u>Shape at time t</u>



<u>Force balance:</u>

$$\nabla_i t^{ij} + C_i{}^j t^i_n = 0$$

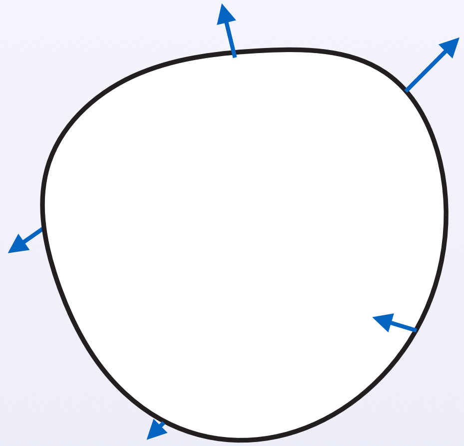
$$\nabla_i t^i_n - C_{ij} t^{ij} = 0$$

<u>Torque balance:</u>

$$t^i_n = \nabla_i \bar{m}^{ij}$$

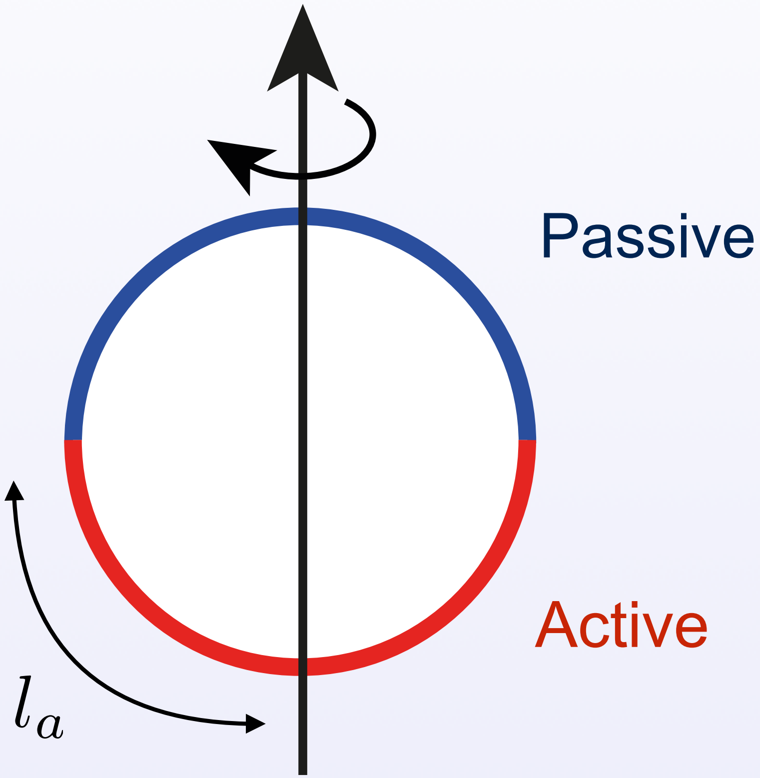
Solve for flow field: →

Update shape according to velocity field:

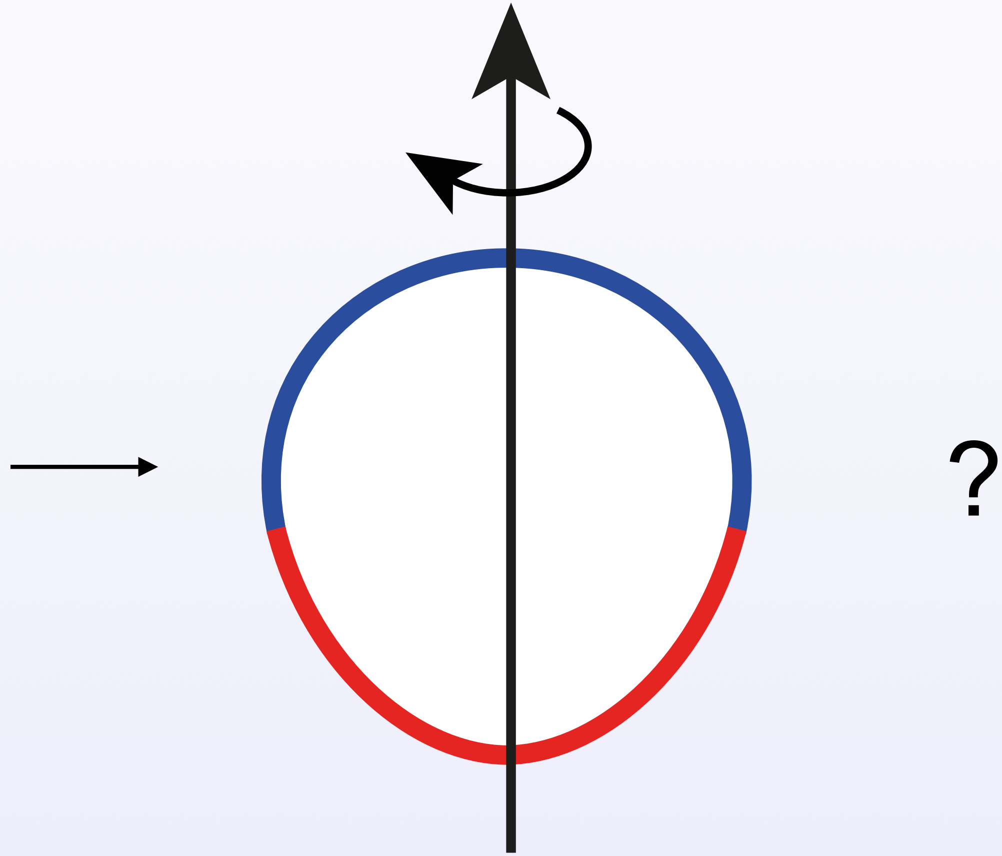


Deformations of mechanically patterned spherical surfaces

Active and passive domains:

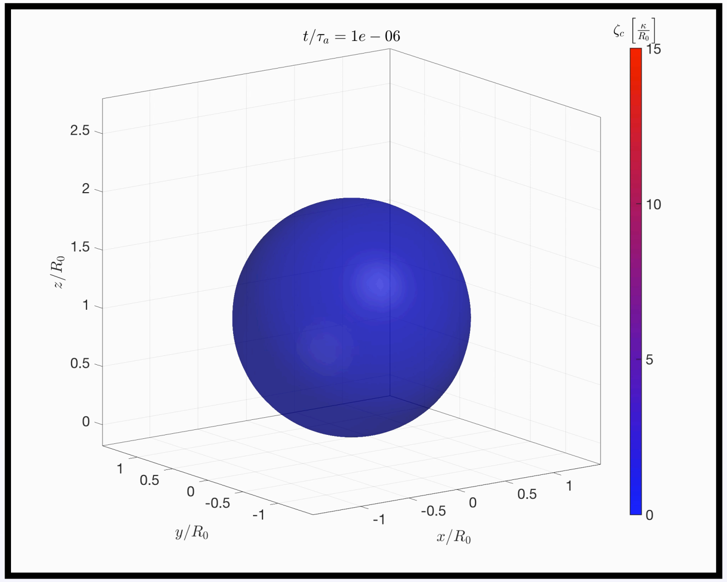


Shape changes?

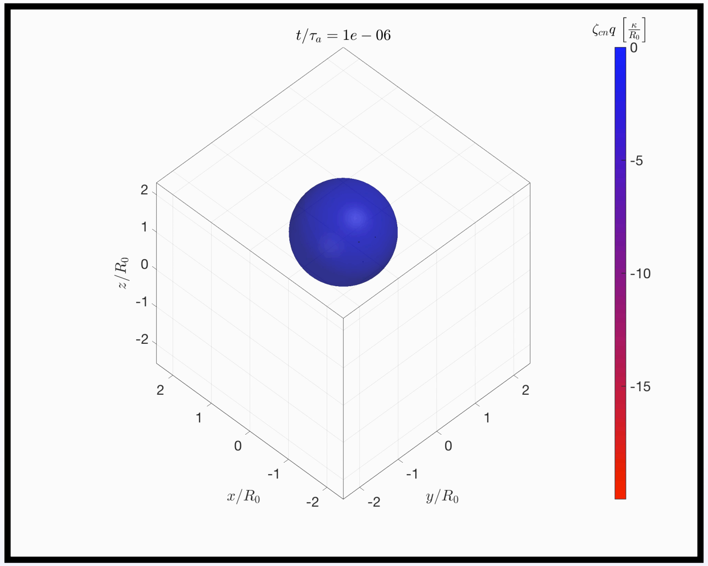


[Khoromskaia&al, eLife, 2023]

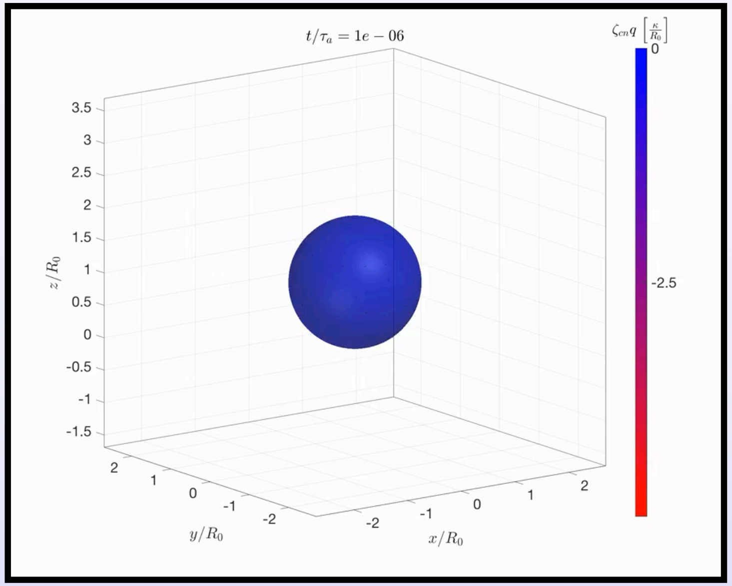
Exploring shape changes of active surfaces



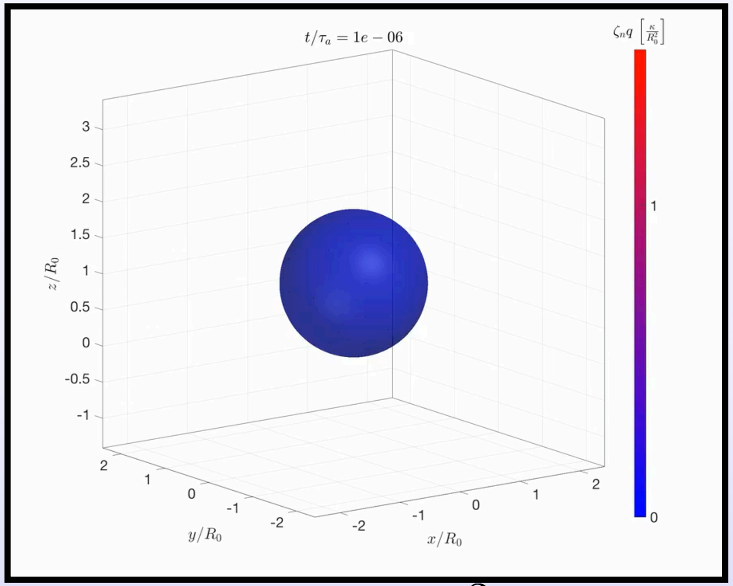
$l_a/L_0 = 0.85 \quad \frac{\zeta_c R_0}{\kappa} = 15$



$l_a/L_0 = 0.3 \quad \frac{\zeta_{cn} R_0}{\kappa} = -20$



$l_a/L_0 = 1 \quad \zeta_{cn} R_0/\kappa = -5$

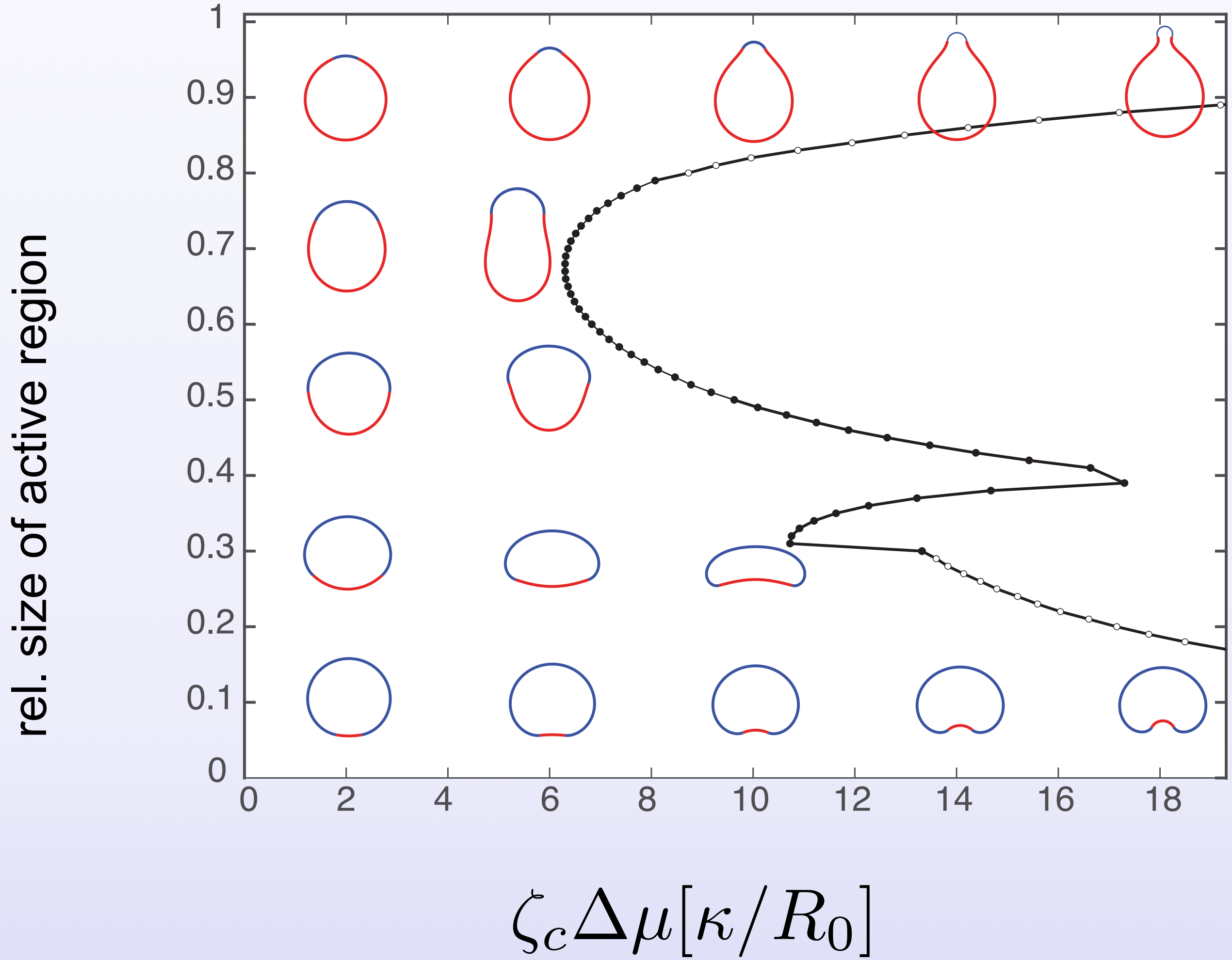


$l_a/L_0 = 1 \quad \zeta_n R_0^2/\kappa = 1.5$

Epithelial shells with isotropic active bending moment

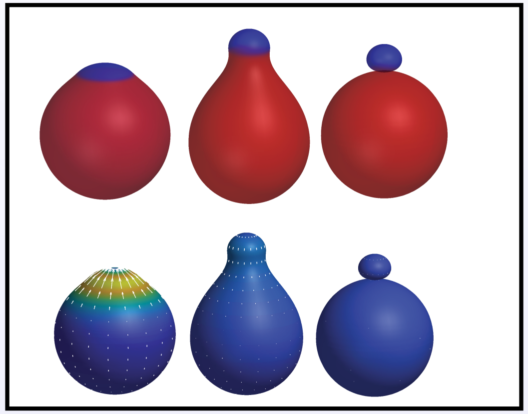
Tension $$t_{ij} = 2Kug_{ij} + \zeta g_{ij} + \zeta_n Q_{ij}$$

Bending moment $$\bar{m}_{ij} = \kappa C_{ij} + \boxed{\zeta_c g_{ij}} + \zeta_{cn} Q_{ij}$$

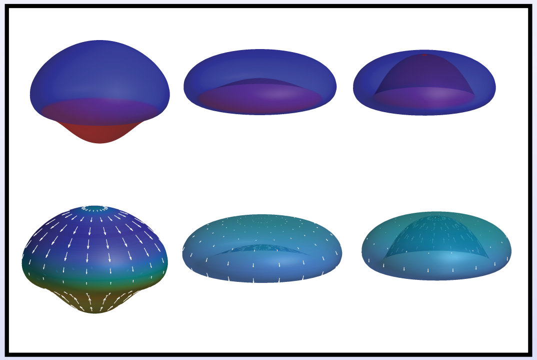


Active bending moment in active region

Neck constriction:



Instability followed by self-intersecting shape:



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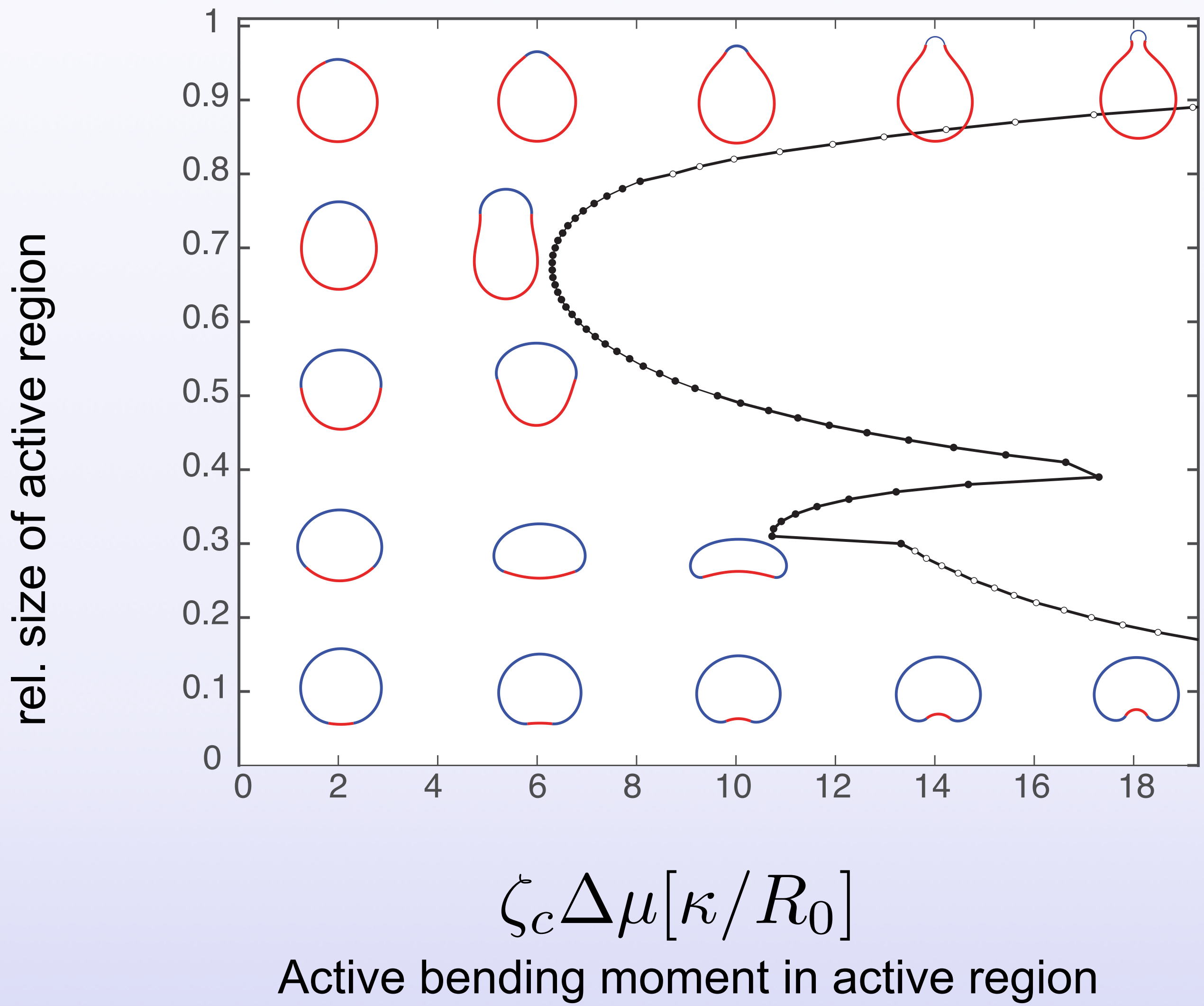
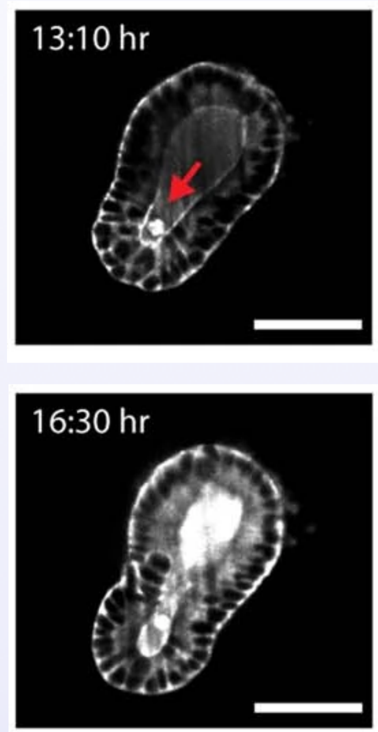


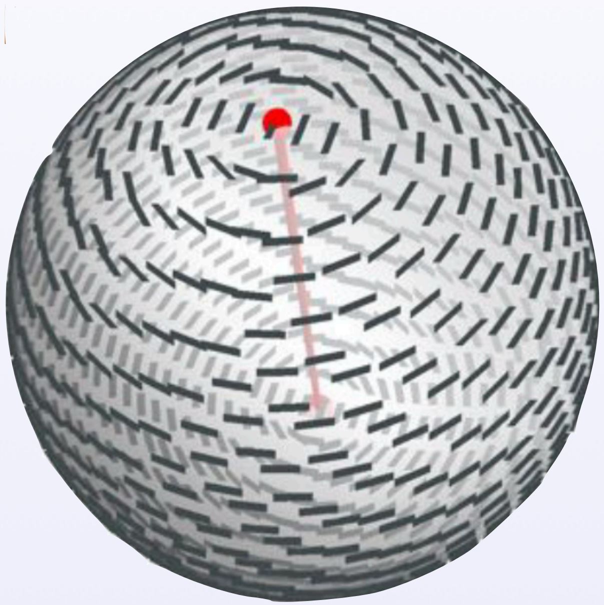
Intestinal organoids:



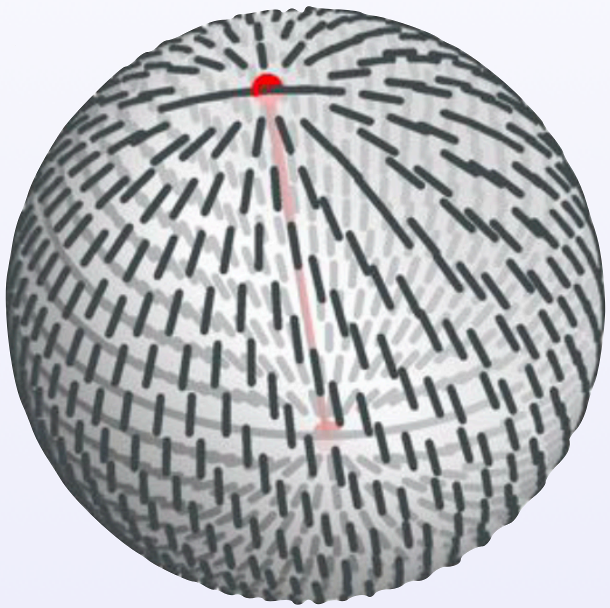
[Yang&al, NCB, 2021]

Deformations of mechanically patterned spherical surfaces

Nematic order: $$F = \int dS \left[\nabla_i Q_{jk} \nabla^i Q^{jk} - \frac{a}{4}\mathbf{Q}^2 + \frac{a}{16}\mathbf{Q}^4 \right]$$



Equatorial

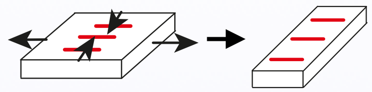


Meridional

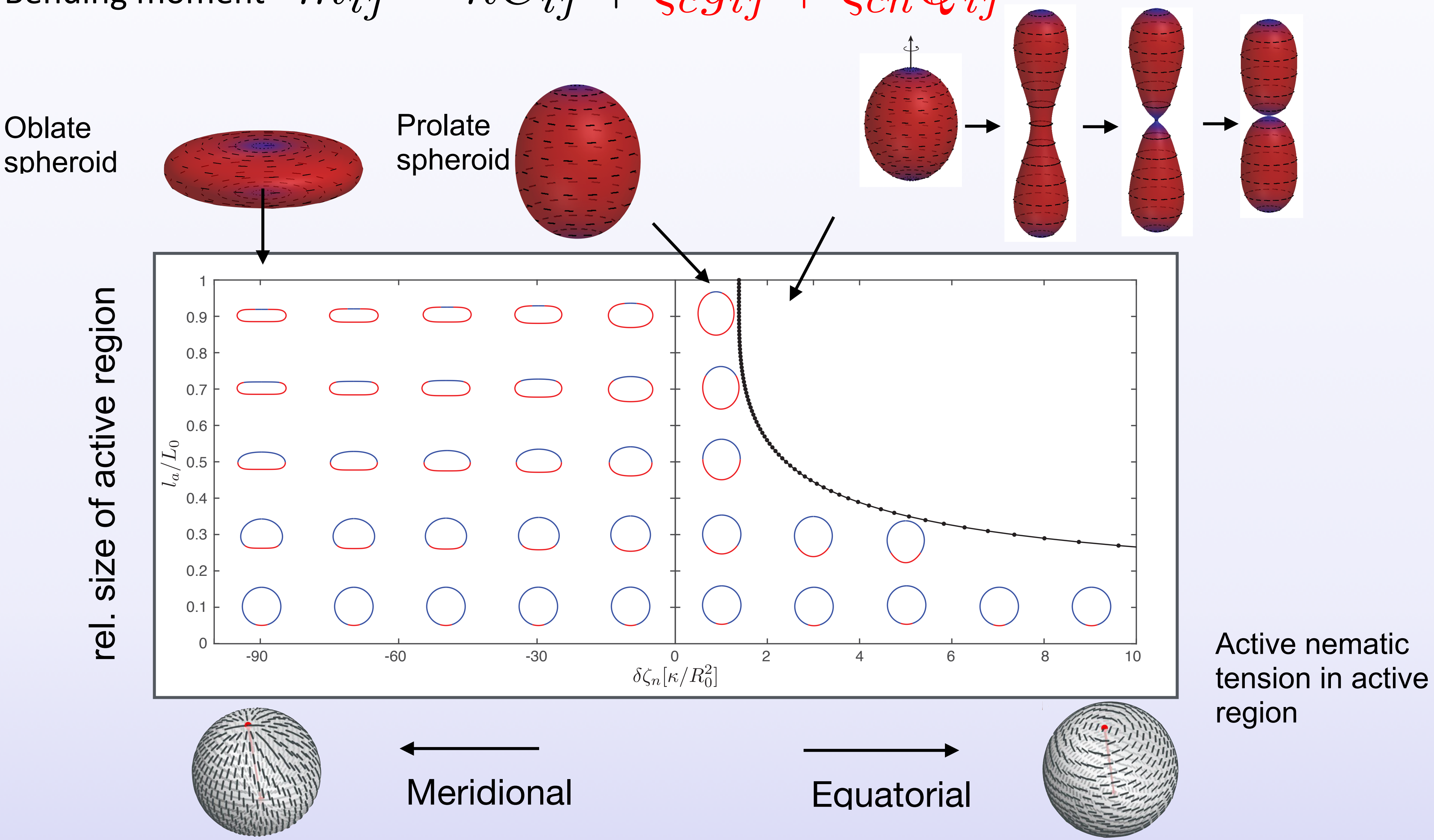
[Khoromskaia&al, eLife, 2023]

Epithelial shells with nematic active tension

Tension $t_{ij} = 2Kug_{ij} + \zeta g_{ij} + \boxed{\zeta_n Q_{ij}}$



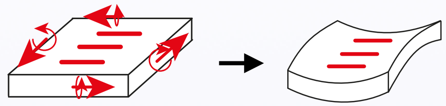
Bending moment $\bar{m}_{ij} = \kappa C_{ij} + \zeta_c g_{ij} + \zeta_{cn} Q_{ij}$

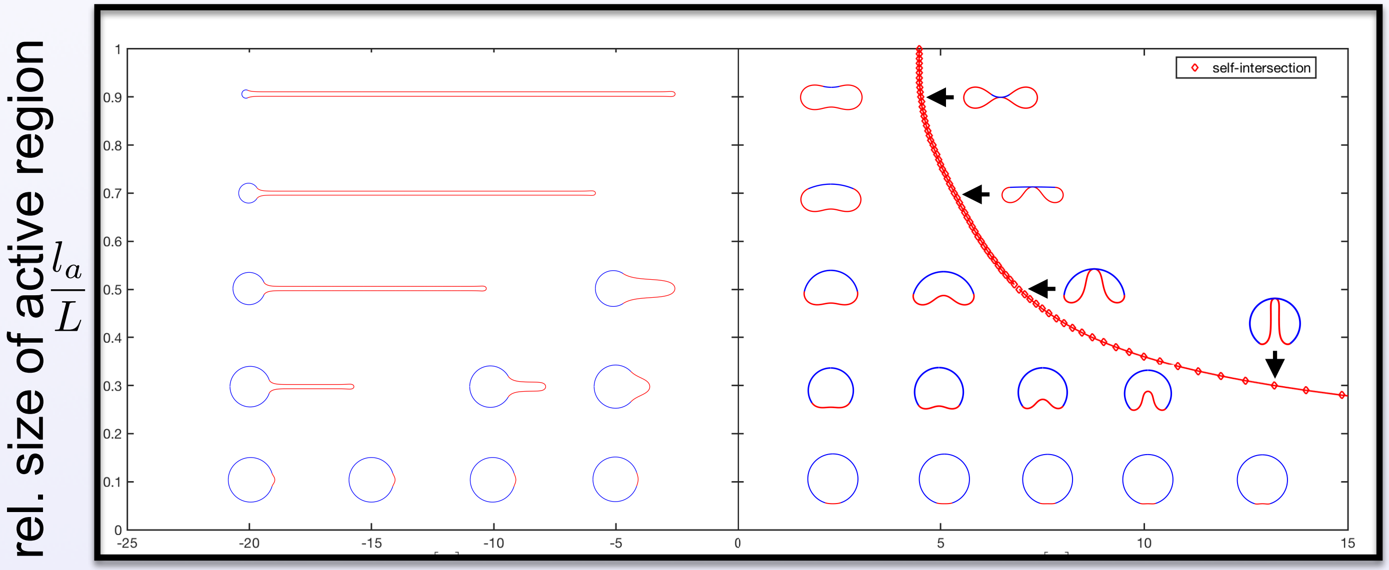


Nematic active bending moment: tubulogenesis

Tension $$t_{ij} = 2Kug_{ij} + \zeta g_{ij} + \zeta_n Q_{ij}$$

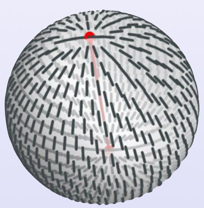
Bending moment $$\bar{m}_{ij} = \kappa C_{ij} + \zeta_c g_{ij} + \boxed{\zeta_{cn} Q_{ij}}$$





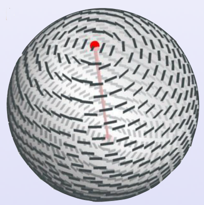
Active nematic torque in active region

$$\zeta_{cn}\Delta\mu[\kappa/R_0]$$

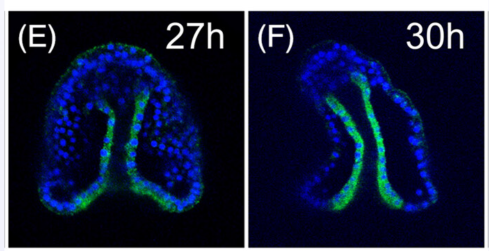


Meridional

Equatorial

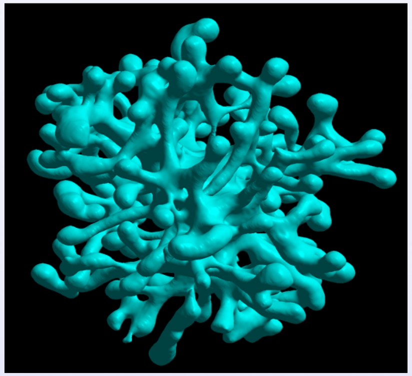


Sea urchin gastrulation:



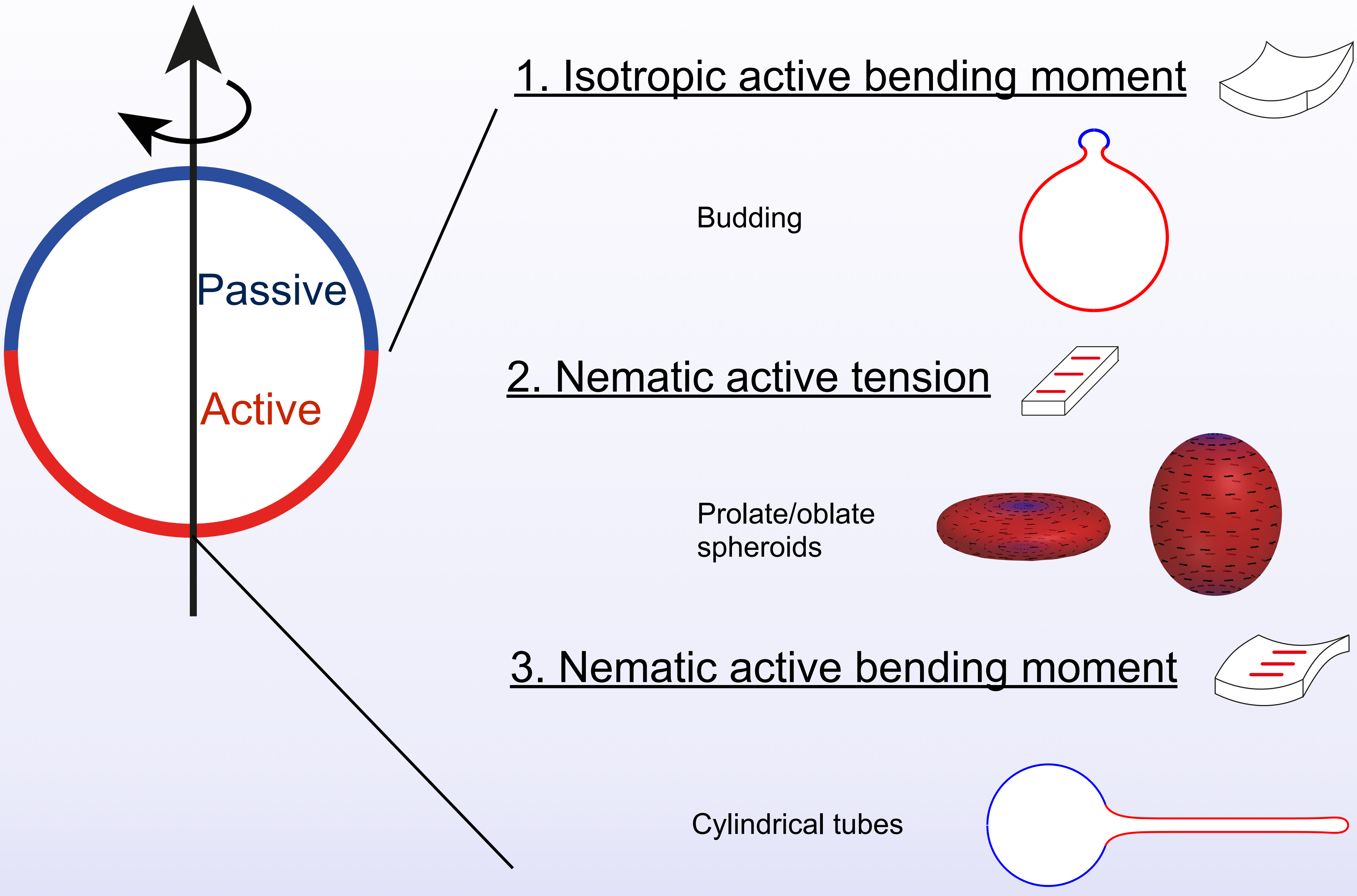
[Kamata&al. 2023]

Mammary gland organoid:



[R. Rollin, B. Canales, A. Elosegui]

Patterned active surface shape zoology:



[Khoromskaia&al, eLife, 2023]

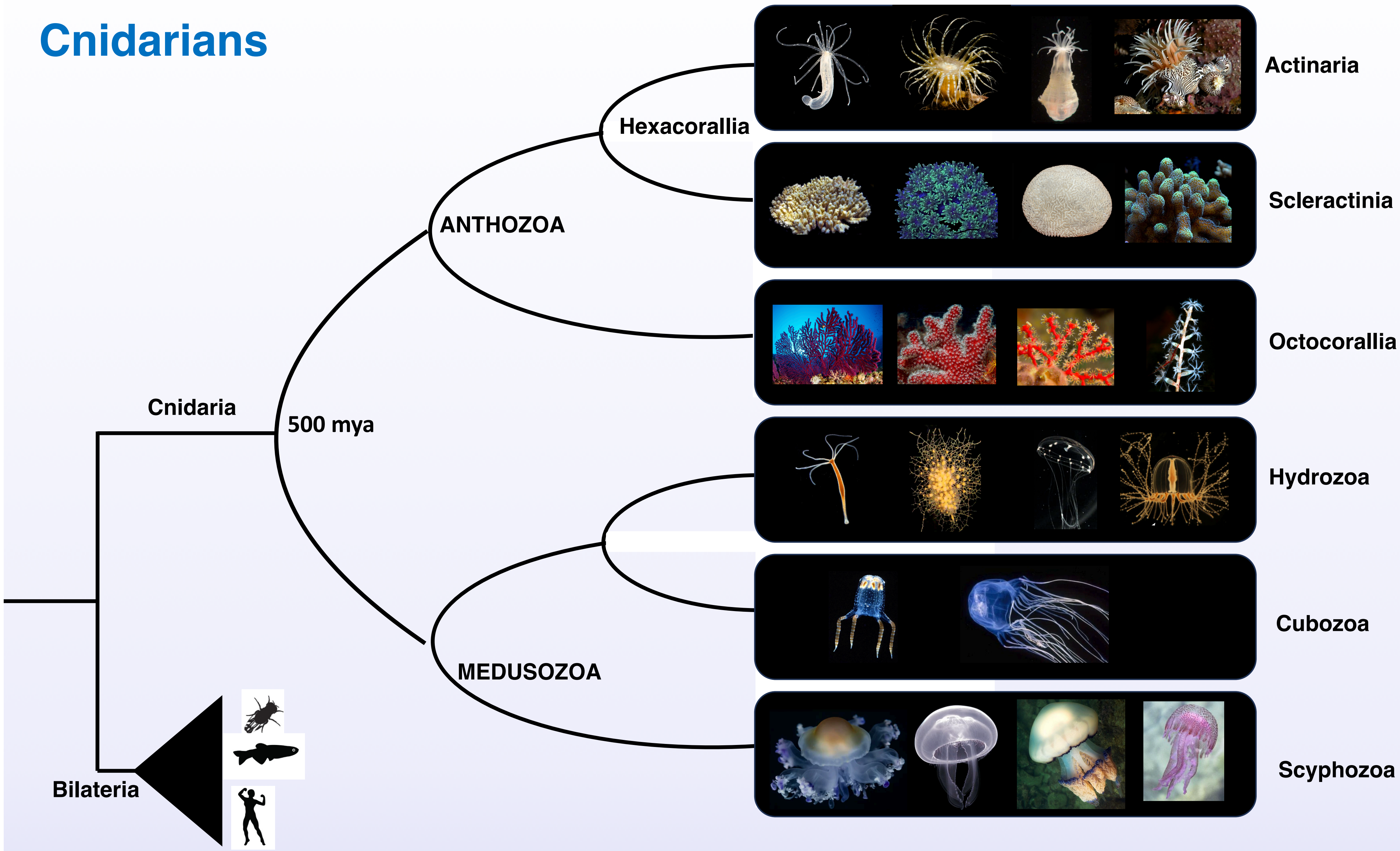
Active surfaces and cnidarian larval shape diversity

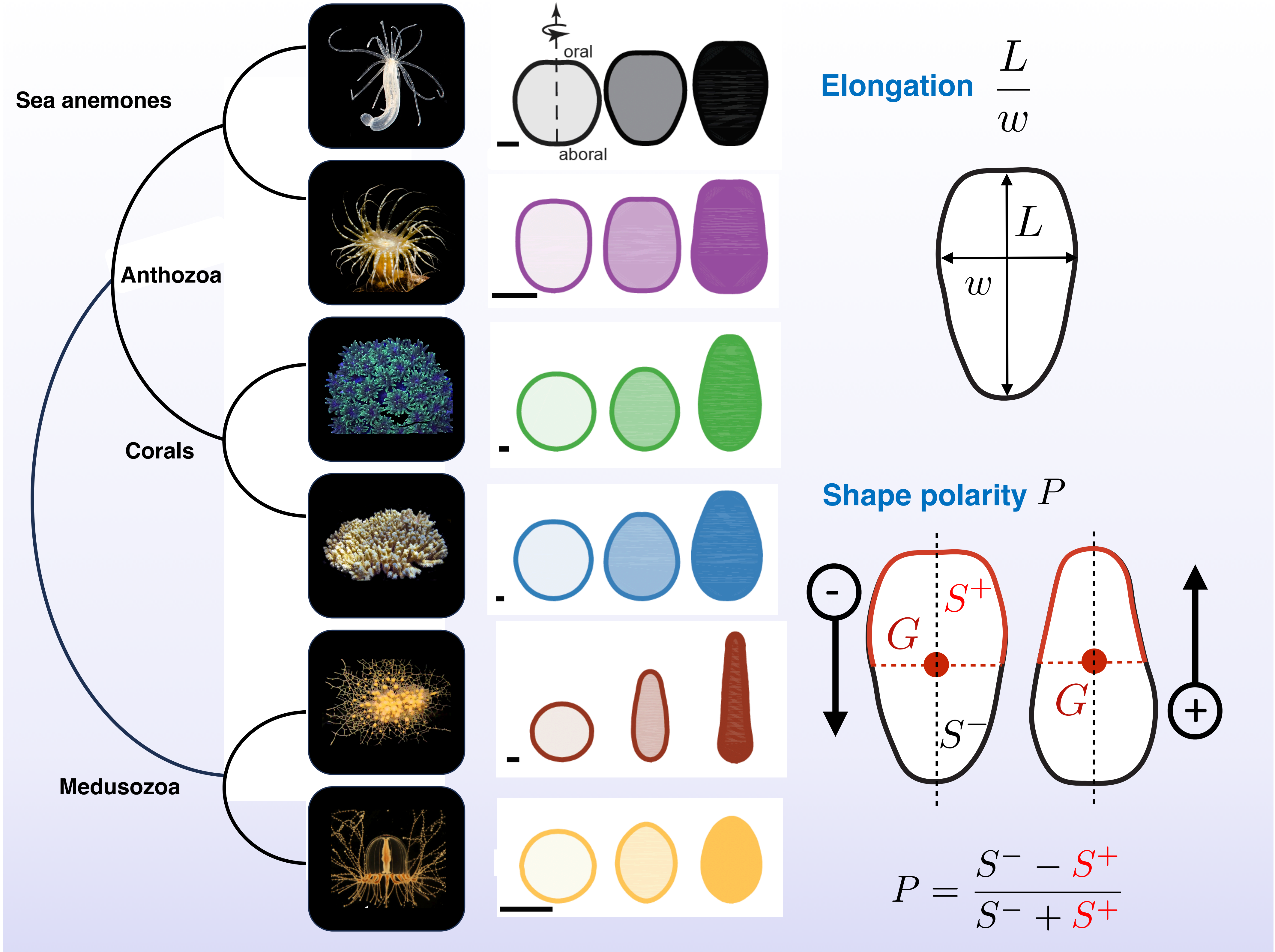
Theory: Nicolas Cuny, Diana Khoromskaia

Experiments: Richard Bailleul, Aissam Ikmi

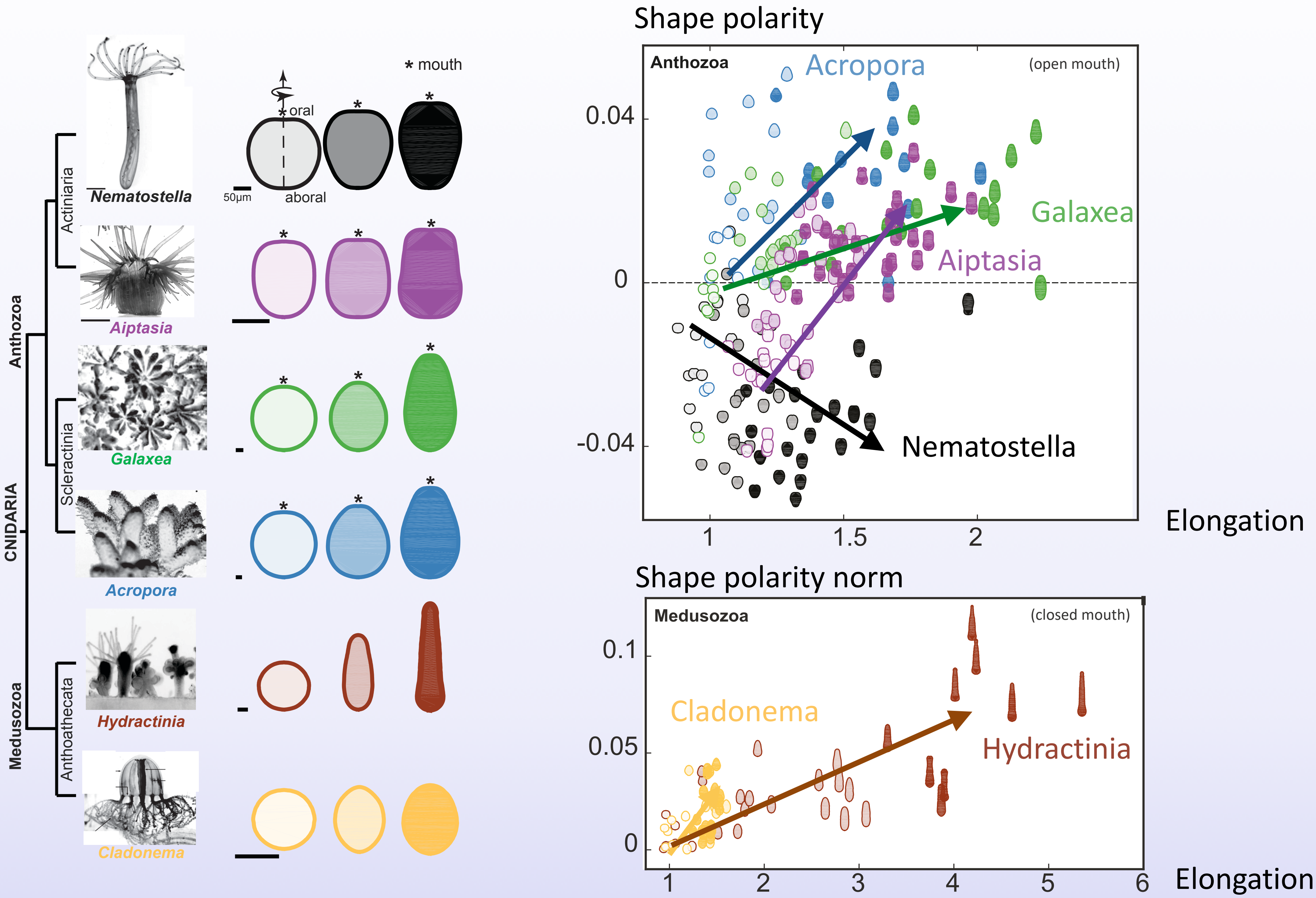



Cnidarians


Actinaria
Hexacorallia
Scleractinia
ANTHOZOA
Octocorallia
Cnidaria
500 mya
Hydrozoa
Cubozoa
MEDUSOZOA
Scyphozoa
Bilateria

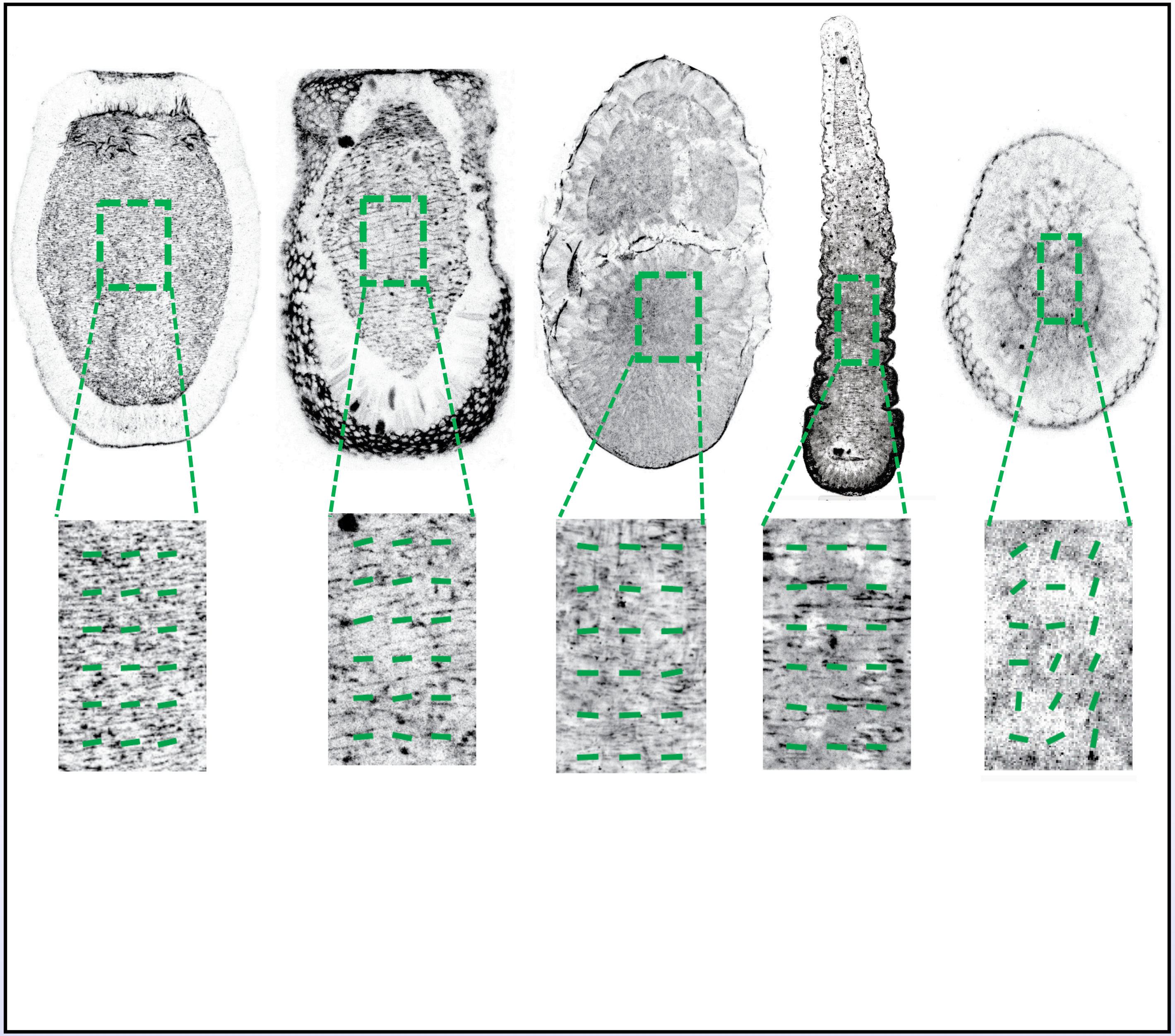

Sea anemones
Anthozoa
Corals
Medusozoa
oral
aboral
Elongation $\frac{L}{w}$
L
w
Shape polarity P
S^+
G
S^-
-
+
$P = \frac{S^- - S^+}{S^- + S^+}$

The cnidarian larvae morphospace



Nematic order in cnidarian larvae

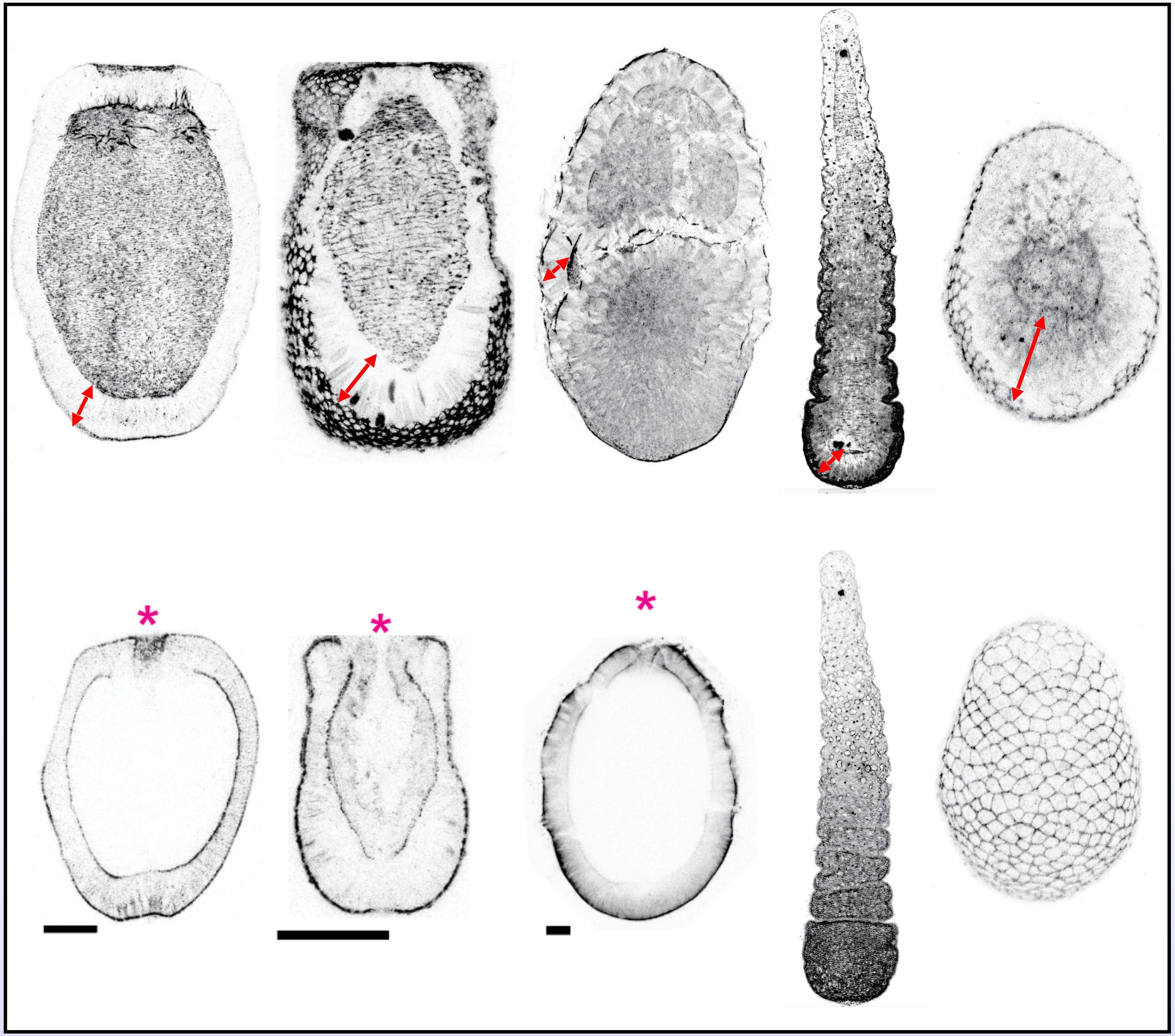
Nematostella *Aiptasia* *Galaxea* *Hydractinia* *Cladonema*



- **Uniform circumferential order of stress fibres on the basal surface of the endoderm/ ectoderm**

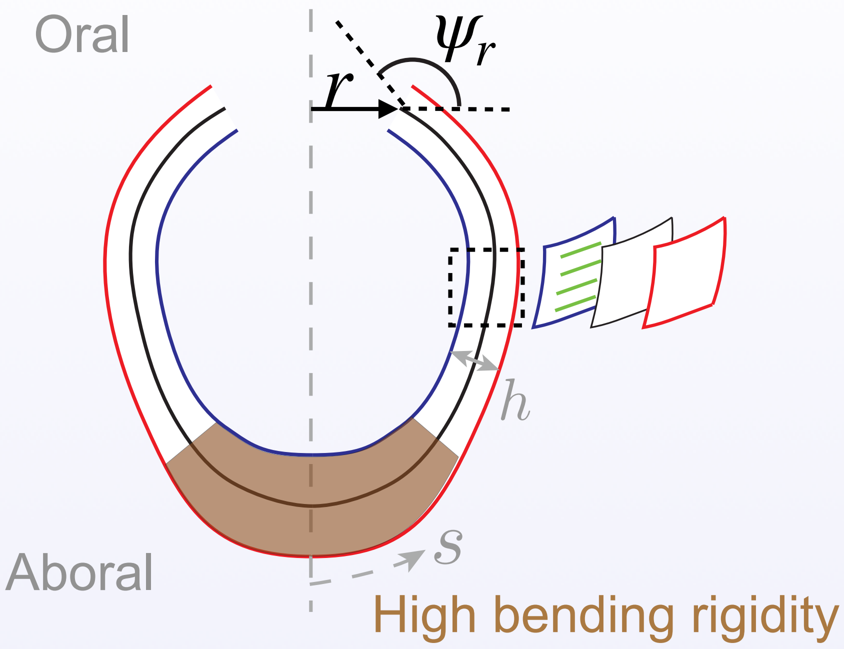
Comparing cnidarian larvae

Nematostella *Aiptasia* *Galaxea* *Hydractinia* *Cladonema*



- Species-specific variations in thickness profiles of the ectoderm
- Variable oral opening geometry

Active surface theory for cnidarian larvae

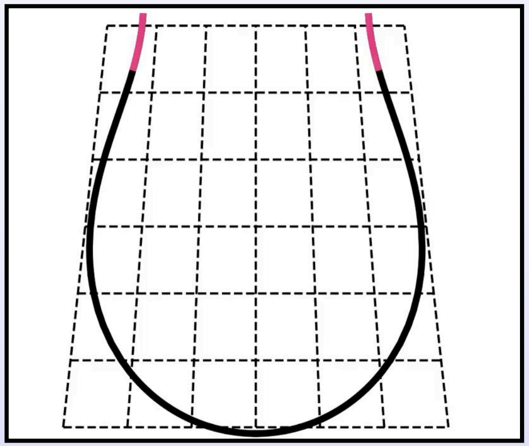


Constitutive equations for tensions and bending moments:

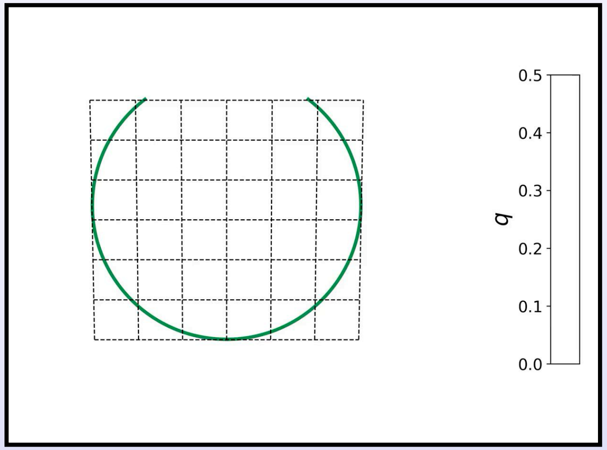
$$t_{ij} = 2Kug_{ij} + \zeta_n Q_{ij}$$

$$\bar{m}_{ij} = 2\kappa(s) C_k{}^k g_{ij} - \frac{h}{2}\zeta_n Q_{ij}$$

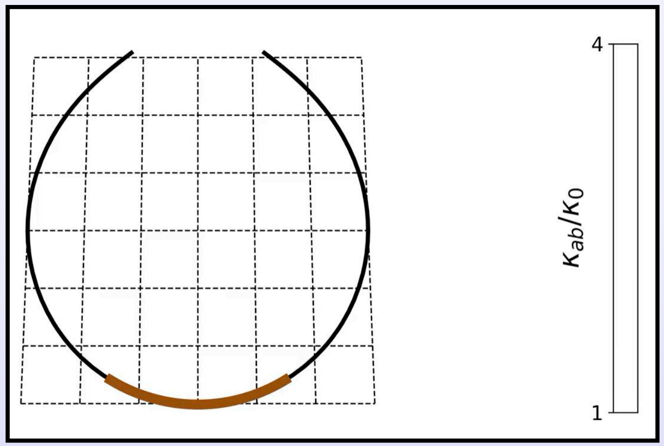
Boundary conditions r, ψ_r :



Active nematic stresses ζ_n:

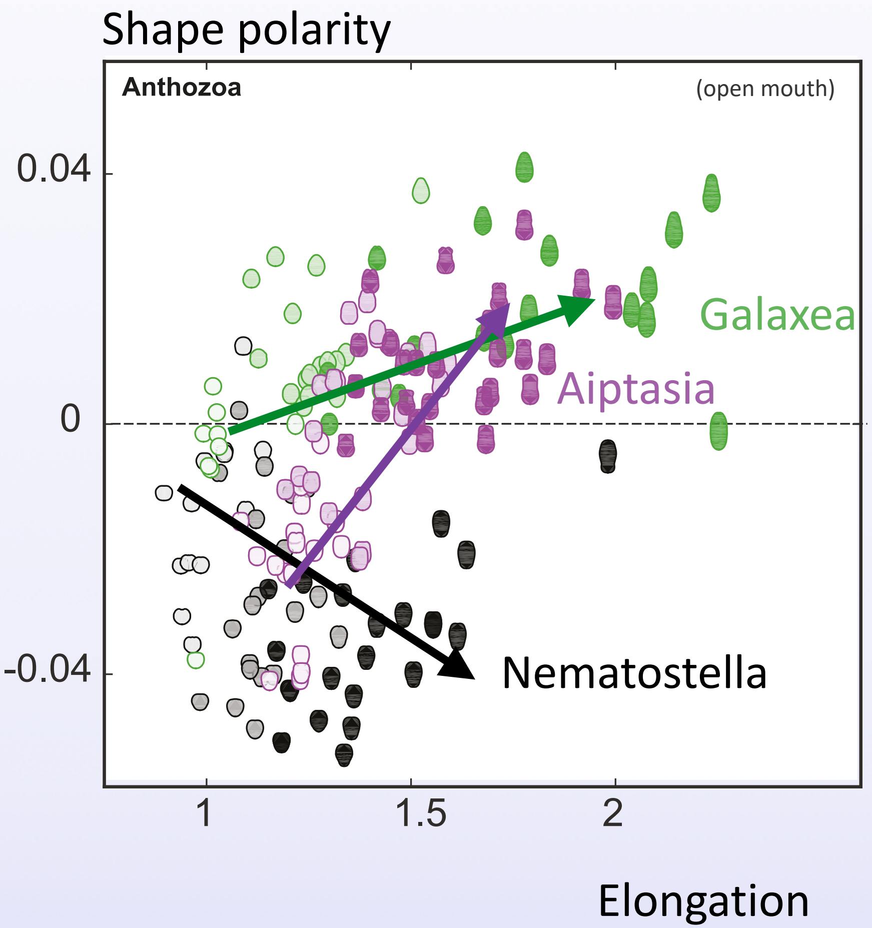


Gradient of bending rigidity $\kappa(s)$:

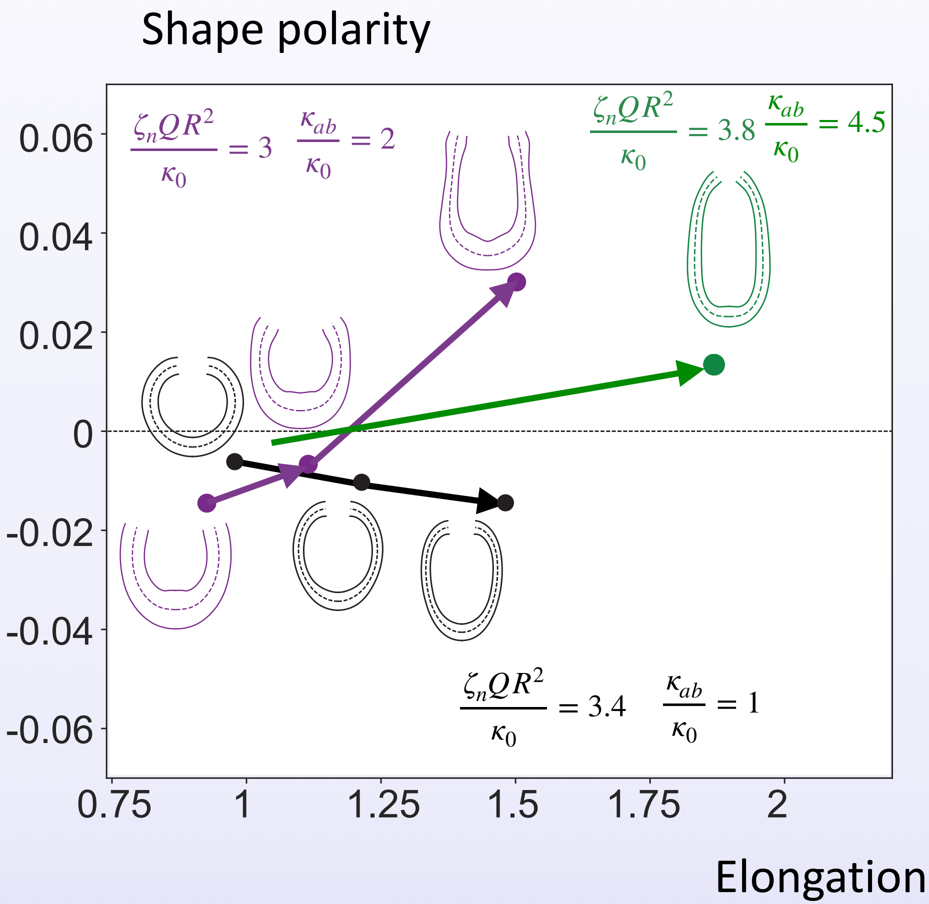


From active surface theory to morphospace

<u>Morphospace (experiment)</u>



<u>Morphospace (theory, aboral increased bending rigidity)</u>



Varying two free parameters per species

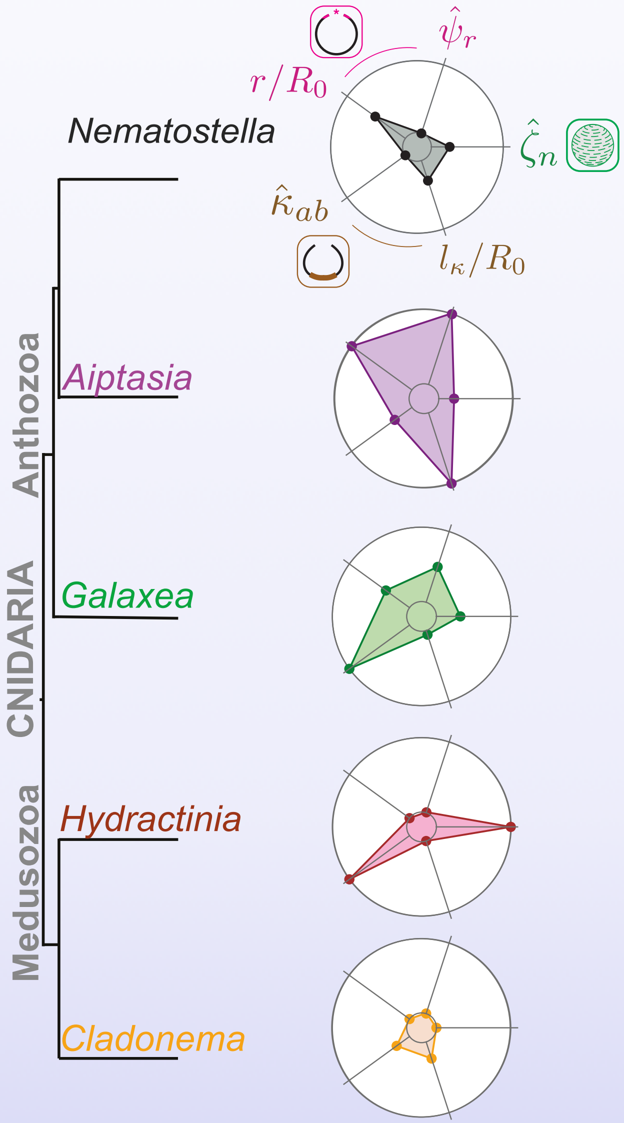
From “mechanotype” to phenotype

Nematic active surface theory

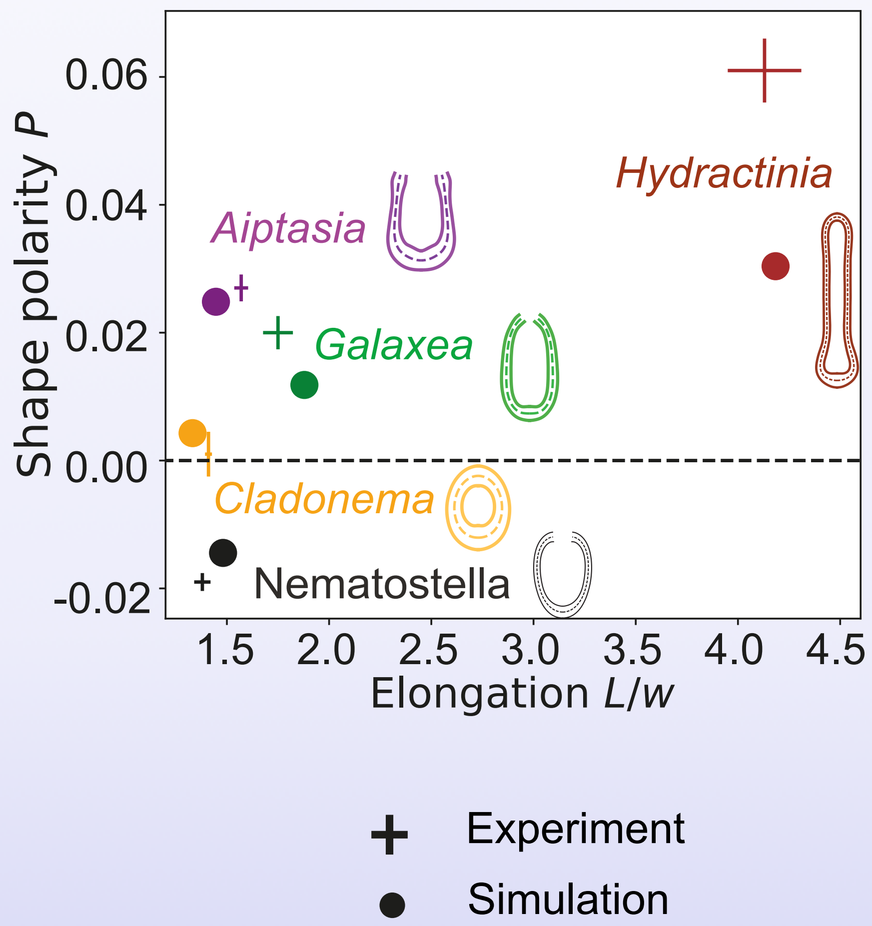
$$t_{ij} = 2Kug_{ij} + \zeta_n Q_{ij}$$

+B.C. r, ψ_r

$$\bar{m}_{ij} = 2\kappa(s) C_k{}^k g_{ij} - \frac{h}{2}\zeta_n Q_{ij}$$

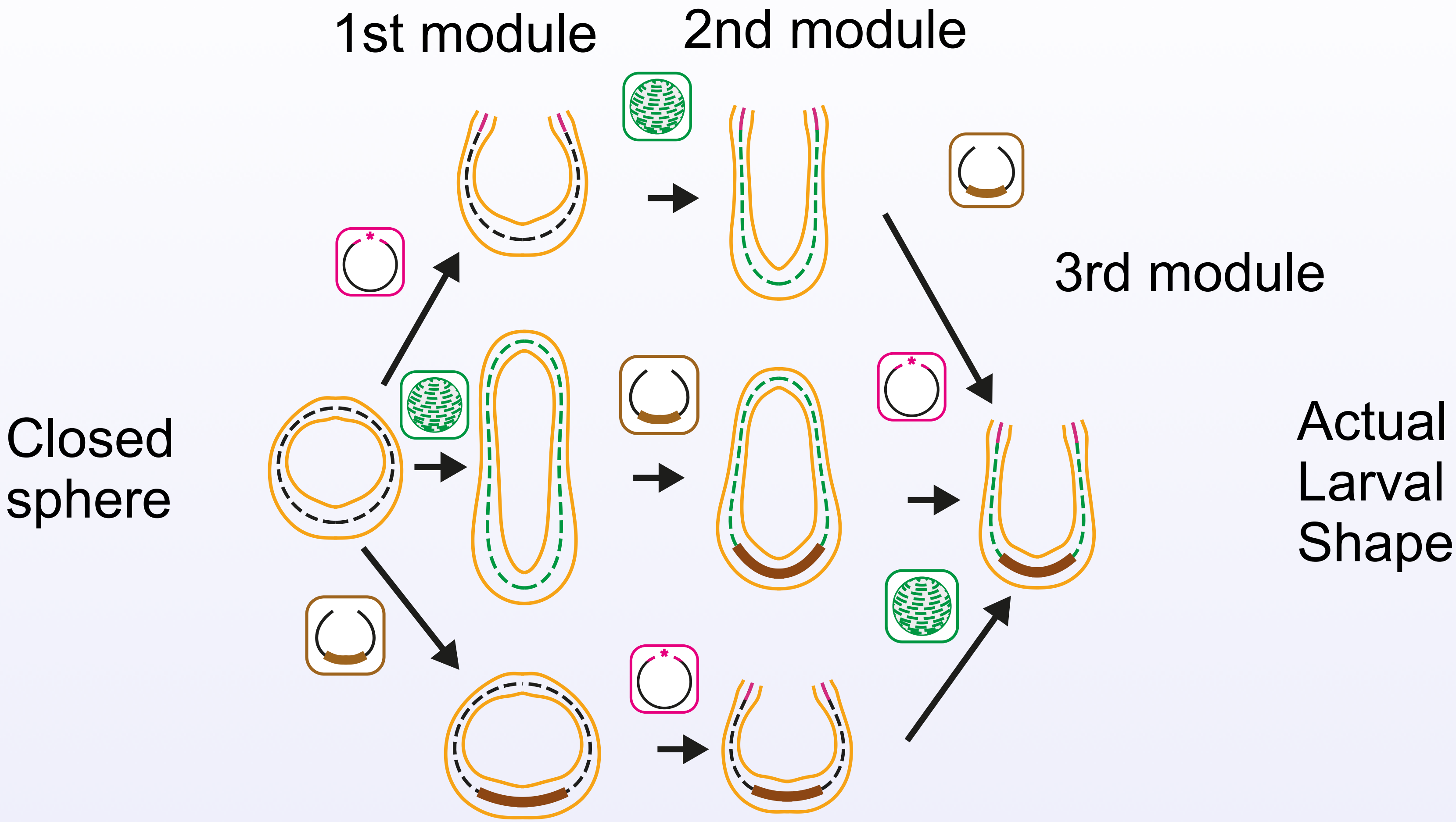


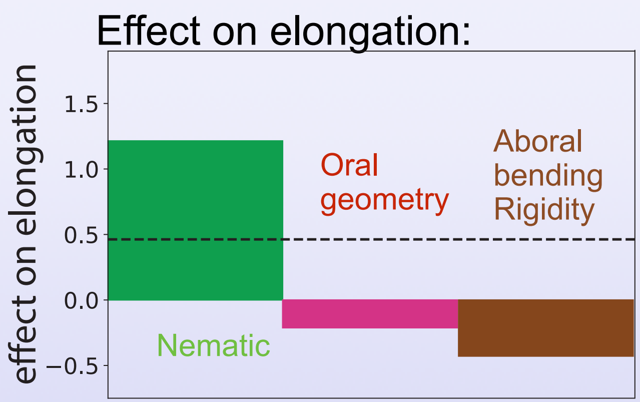
Shape (morphospace)

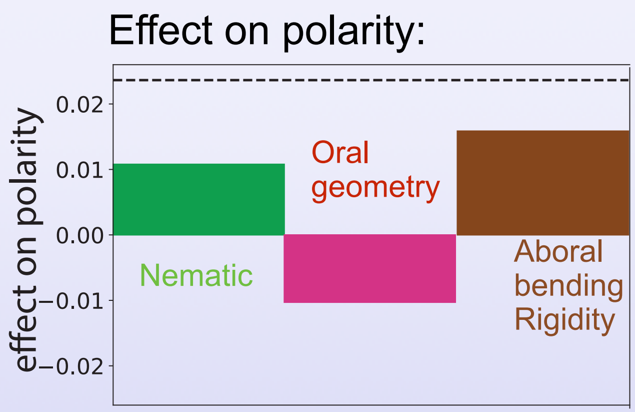


Dissociating modules

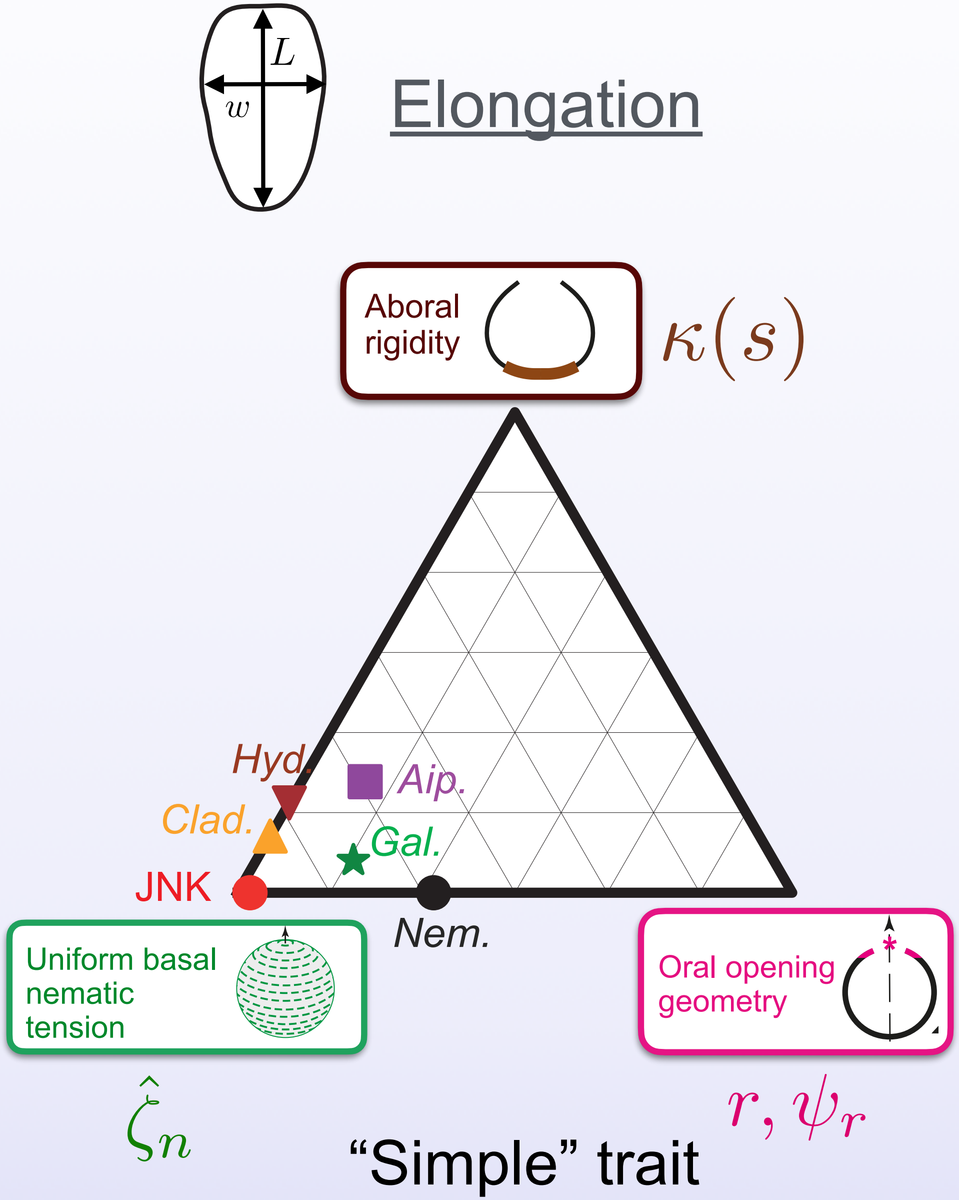
Aiptasia

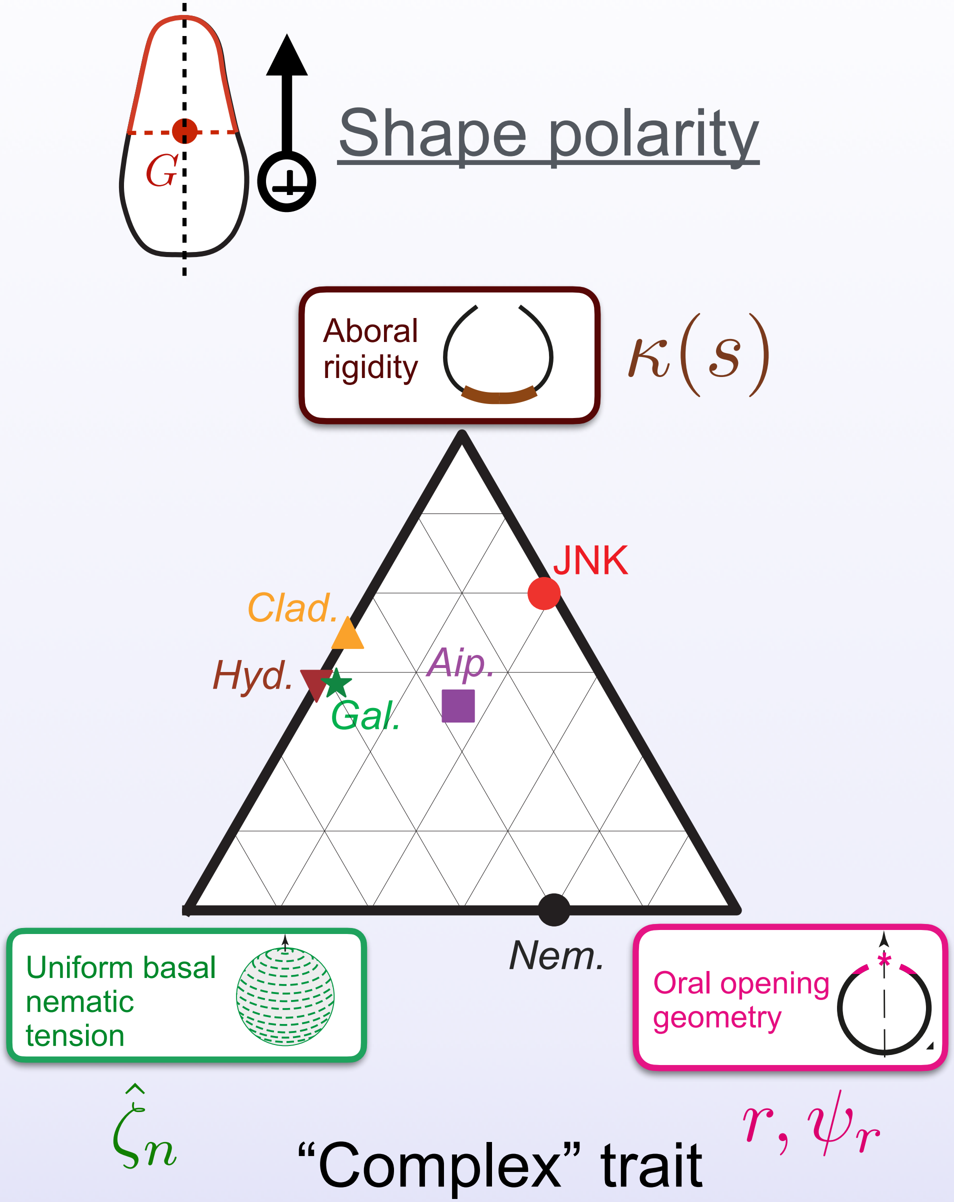






Relative role of mechanical modules in setting elongation and shape polarity



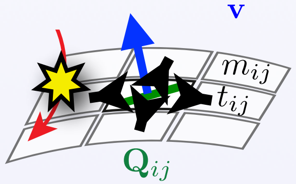


[Bailleul, Cuny &al, 2026]

The rich physics of active nematic surfaces

- Nematic order dynamics is key to biological tissues

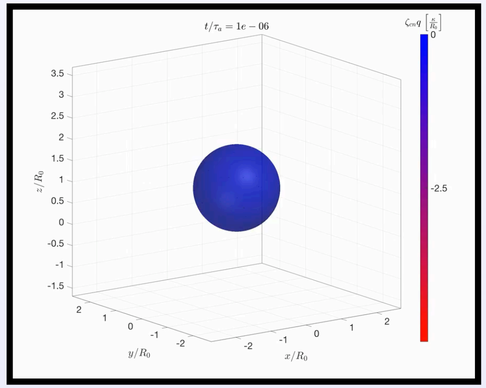
- Hydrodynamic theory of active surfaces with tensions and bending moments



$$t_{ij} = 2Kug_{ij} + \zeta g_{ij} + \zeta_n Q_{ij} \; + \eta v_{ij}$$

$$\bar{m}_{ij} = \kappa C_{ij} + \zeta_c g_{ij} + \zeta_{cn} Q_{ij} \; + \eta_c D_t C_{ij}$$

- Conditions for spontaneous tubulogenesis in active nematic surfaces



- Mechanical origin of shape diversity in evolution

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K. Marx (De Simone lab)
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Tasmin Sarkany (Paluch lab)