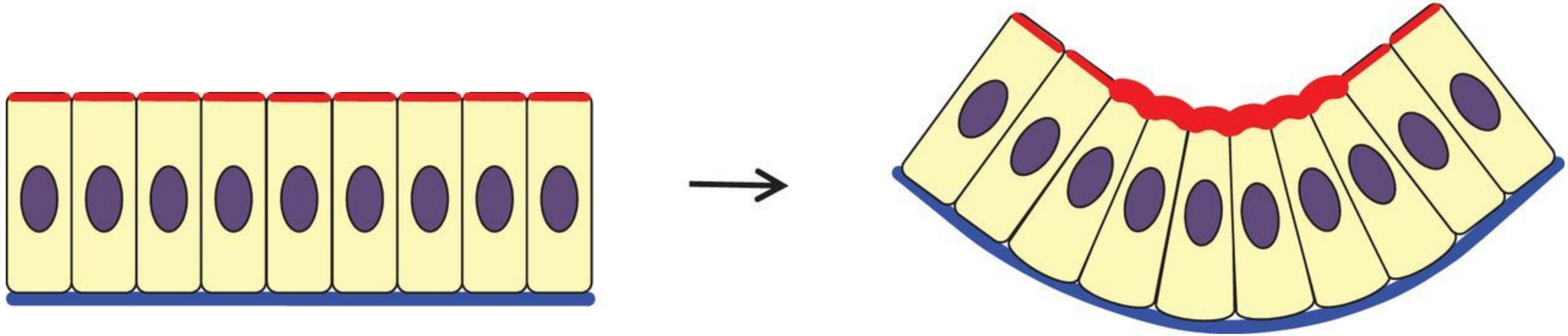
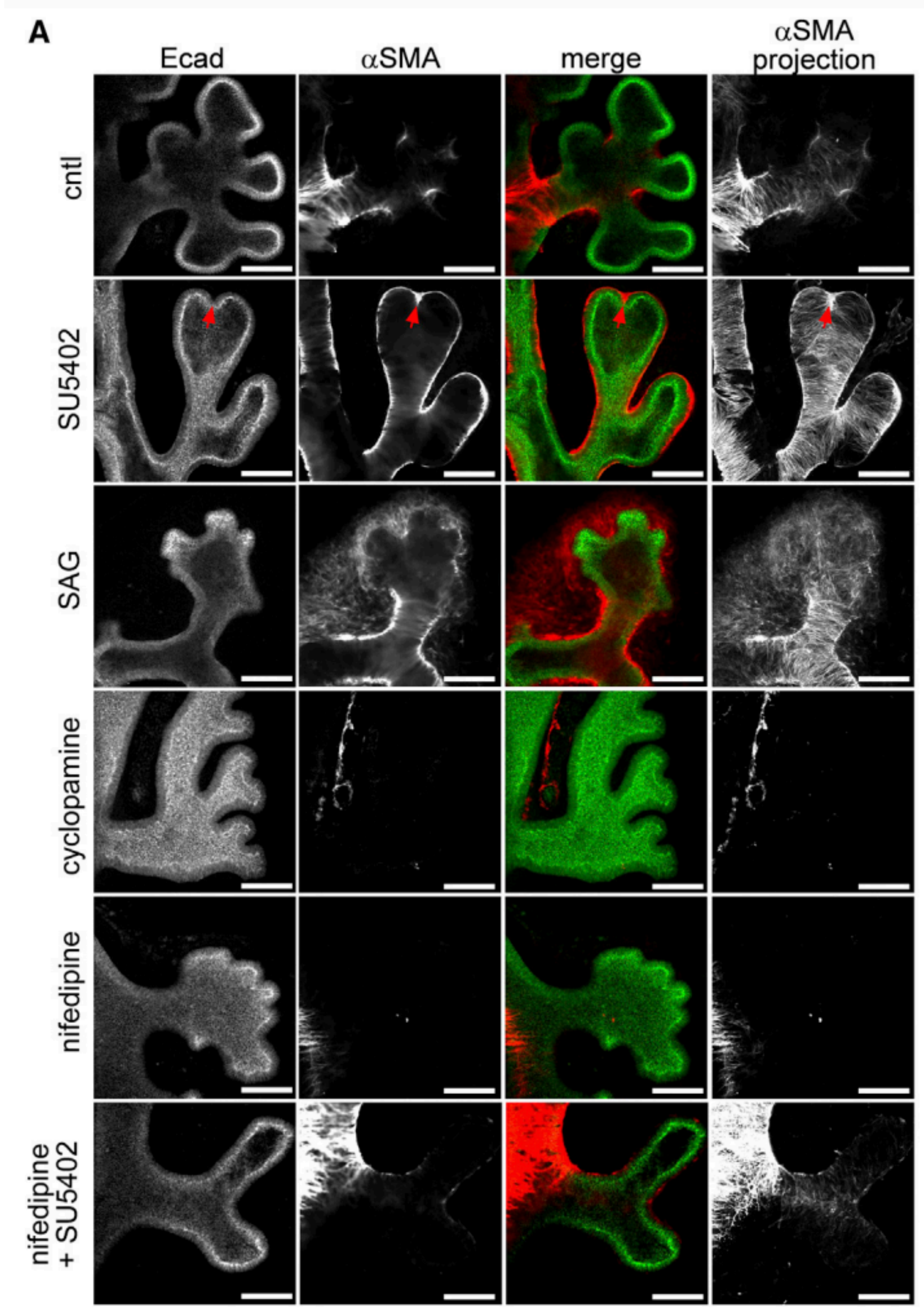


SOME INSTABILITIES IN CONTINUUM MECHANICS OF TISSUES

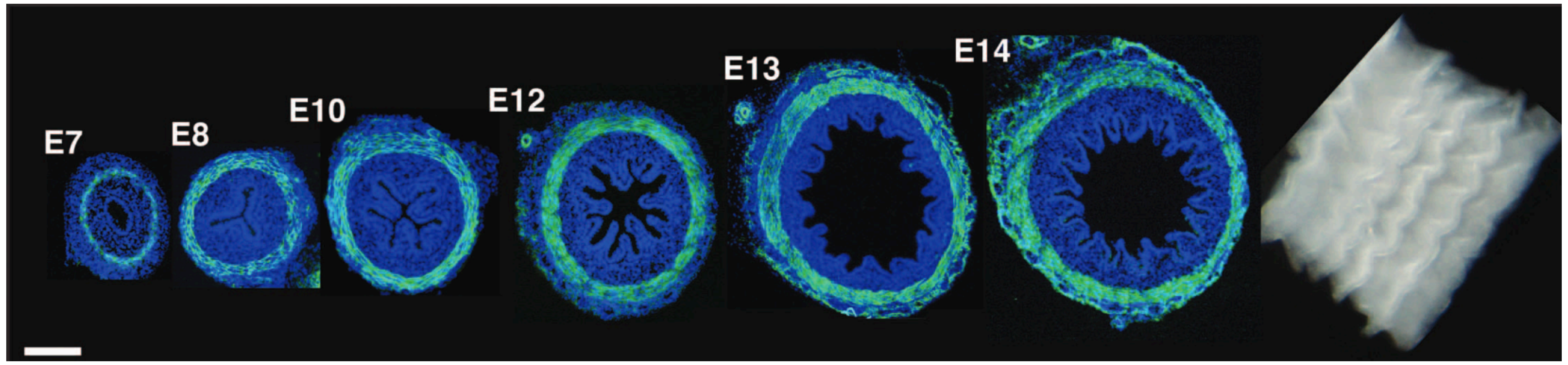
by:
Chandraniva Guha Ray

Supervisor:
Dr. Pierre Haas

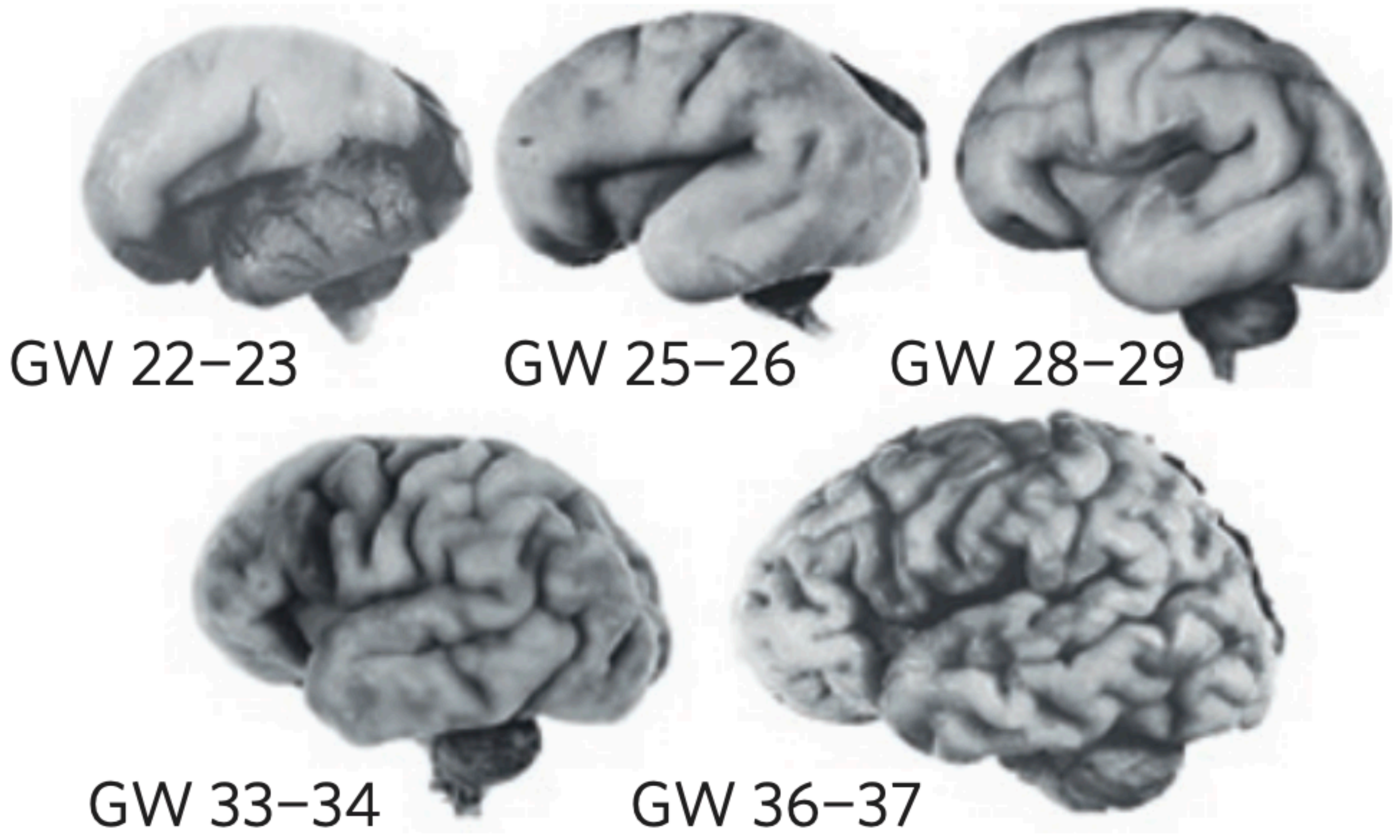
SHAPE DETERMINATION IN BIOLOGY: A FUNDAMENTAL QUESTION



Kim et al., *Localized Smooth Muscle Differentiation Is Essential for Epithelial Bifurcation during Branching Morphogenesis of the Mammalian Lung (2015)*

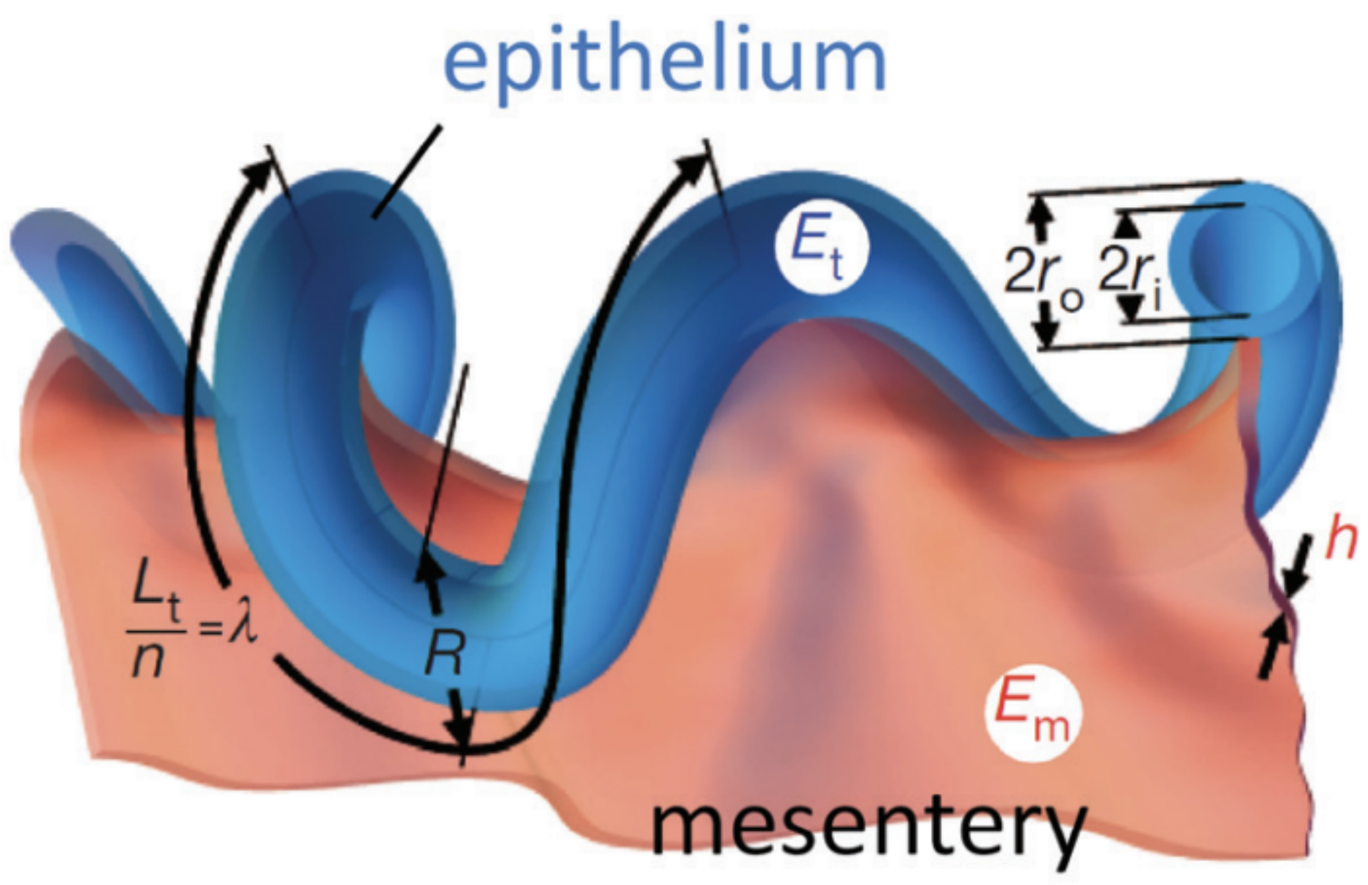


Shyer et al.,Villification: How the Gut Gets Its Villi (2013)



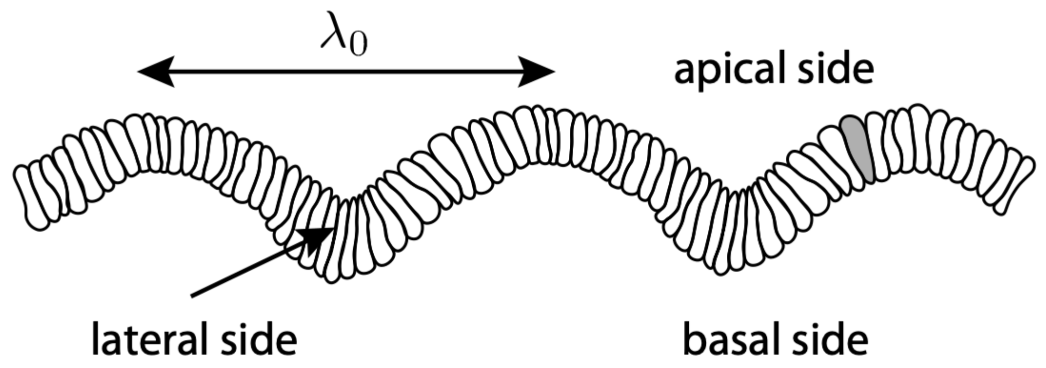
Griffiths et al., Atlas of Fetal and Neonatal Brain MR Imaging (2010)

SHAPES VIA INSTABILITIES

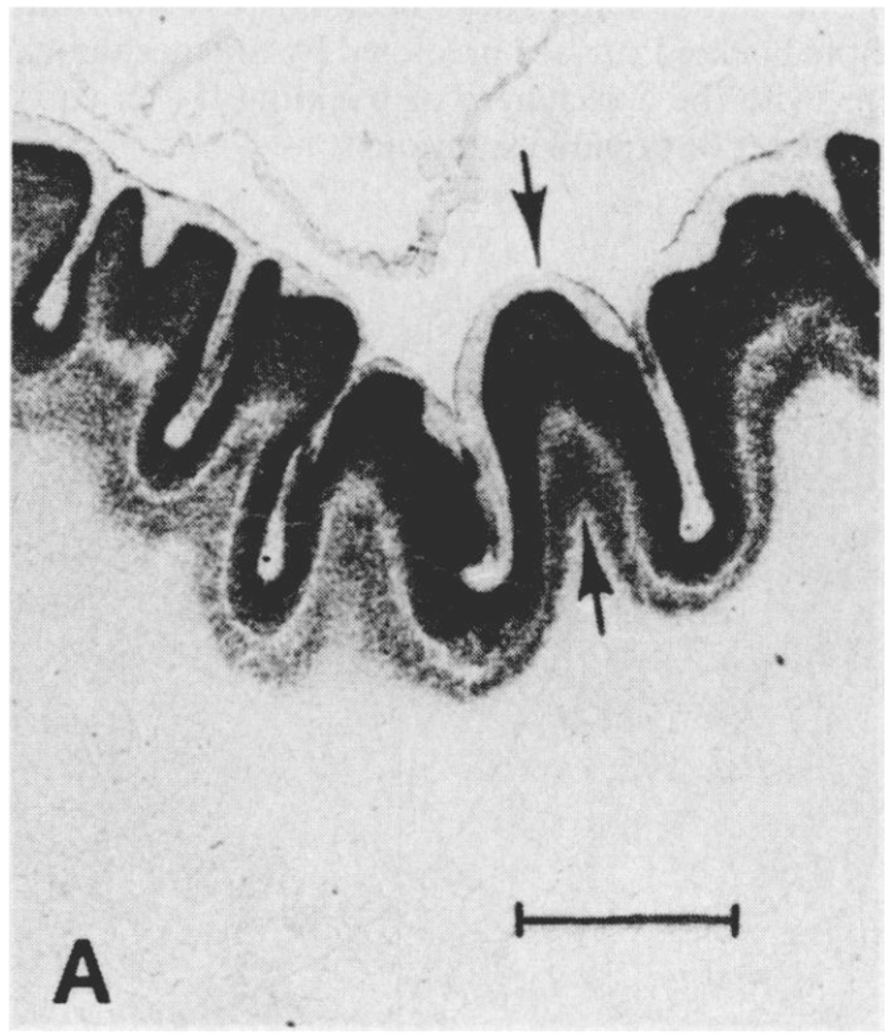


Savin et. al., On the growth and form of the gut (2011)

Wrinkling

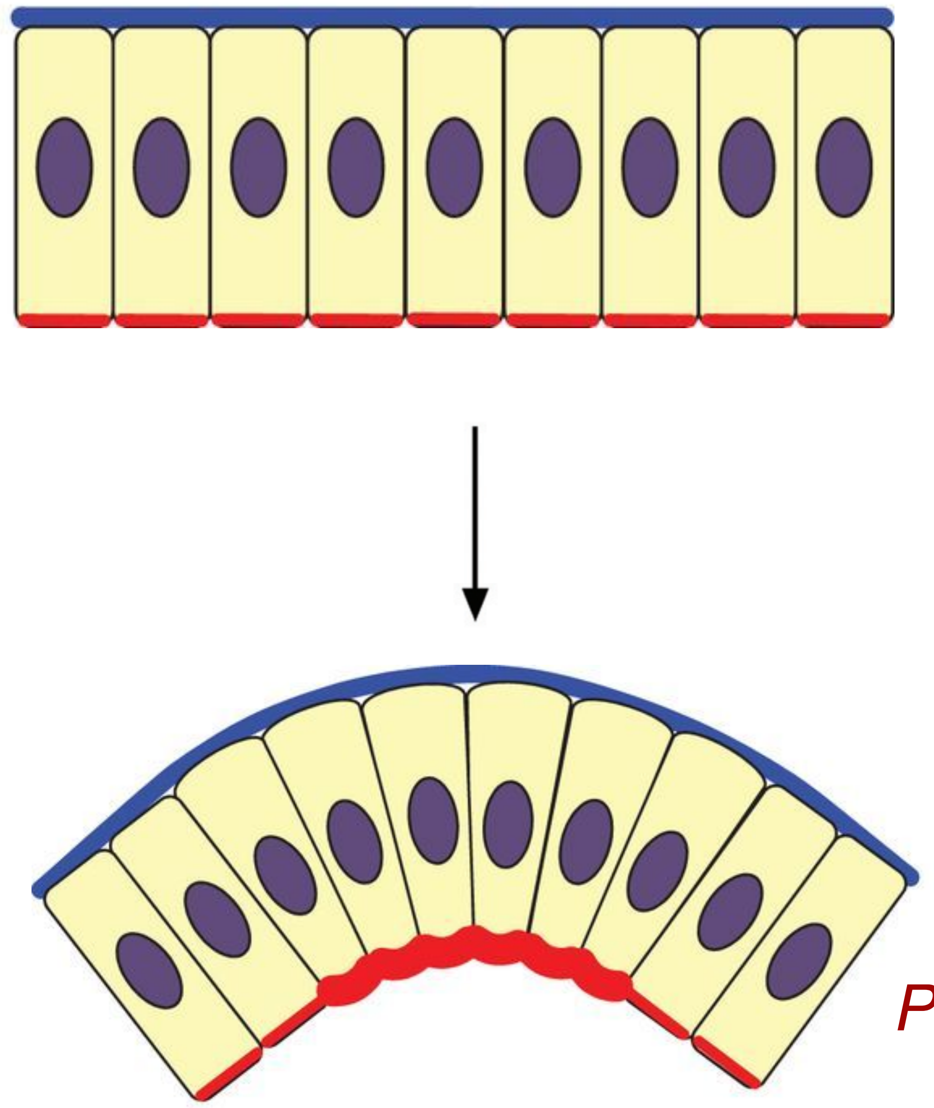


Andrenšek et al., PRL (2023)



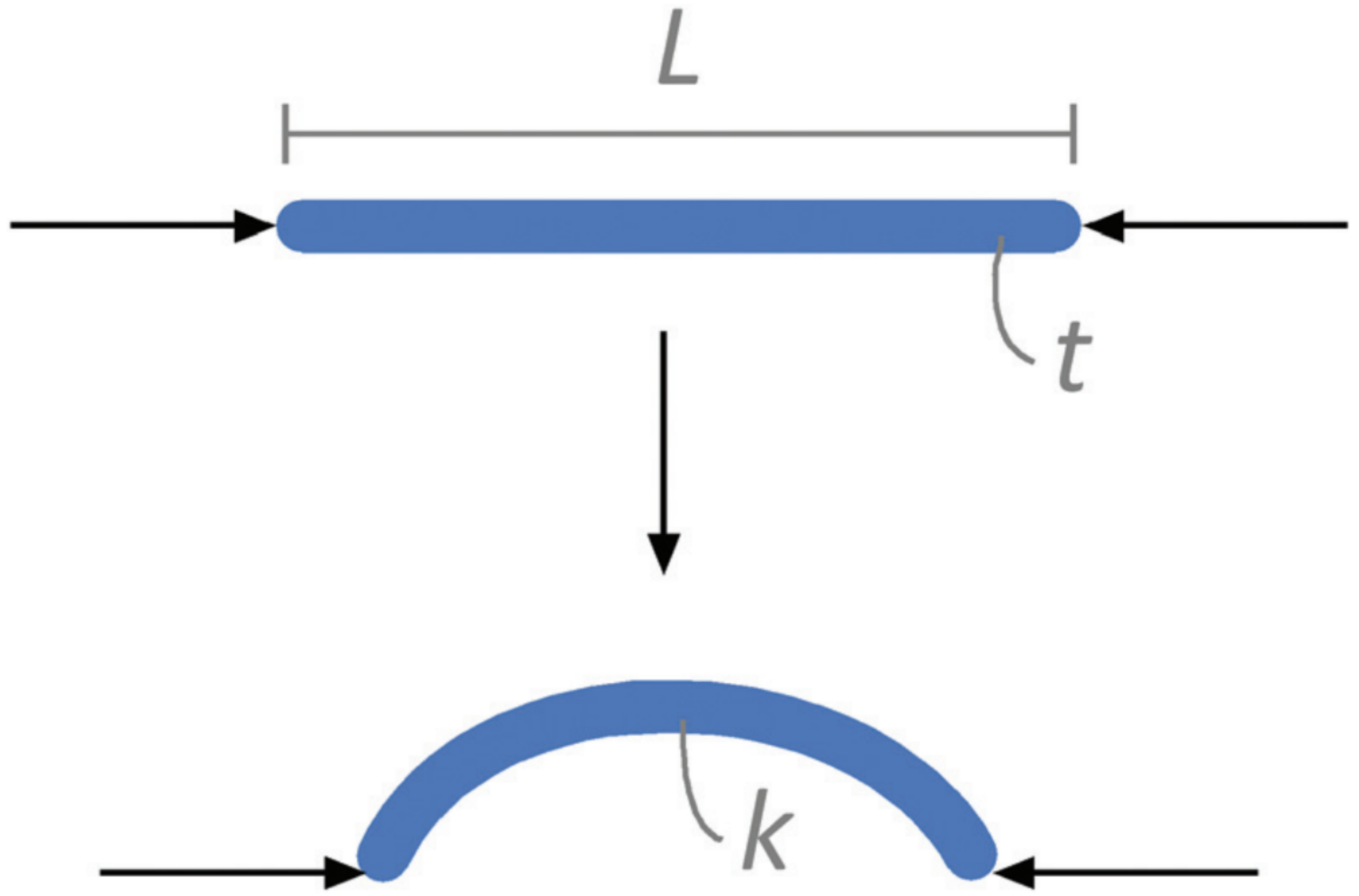
Richmond et al., Mechanical model of brain convolution development (1975)

Buckling



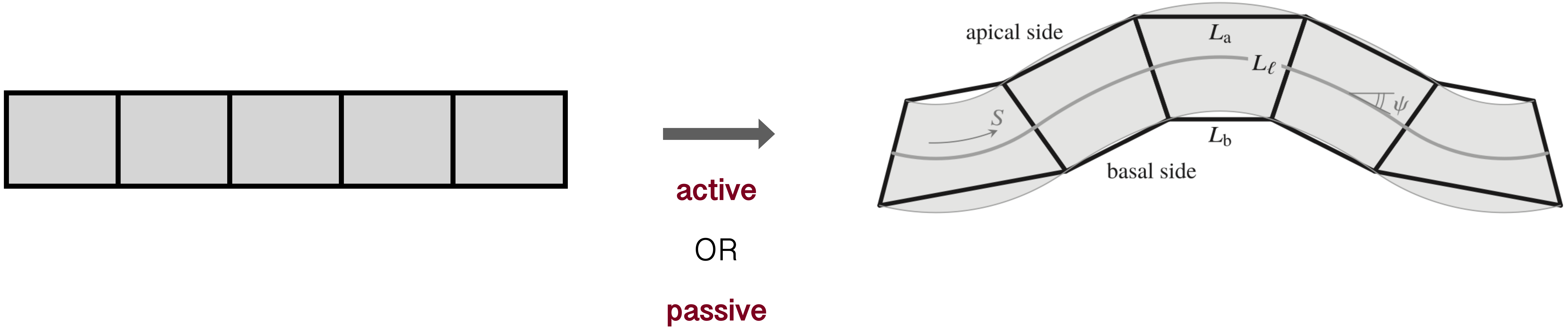
Pearl et. al., Cellular systems for epithelial invagination (2016)

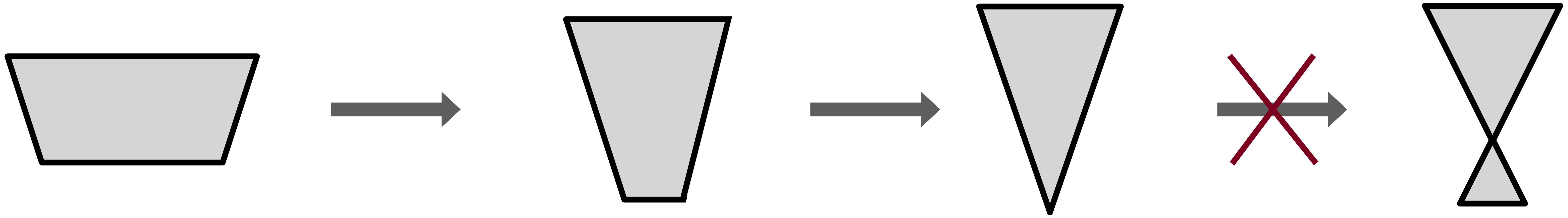
$\overset{?}{=}$



HOW DOES THE DISCRETENESS OF CELLS AFFECT MECHANICAL INSTABILITIES AT THE TISSUE SCALE?

CELL DISCRETENESS INDUCES MICROSCOPIC CONSTRAINTS

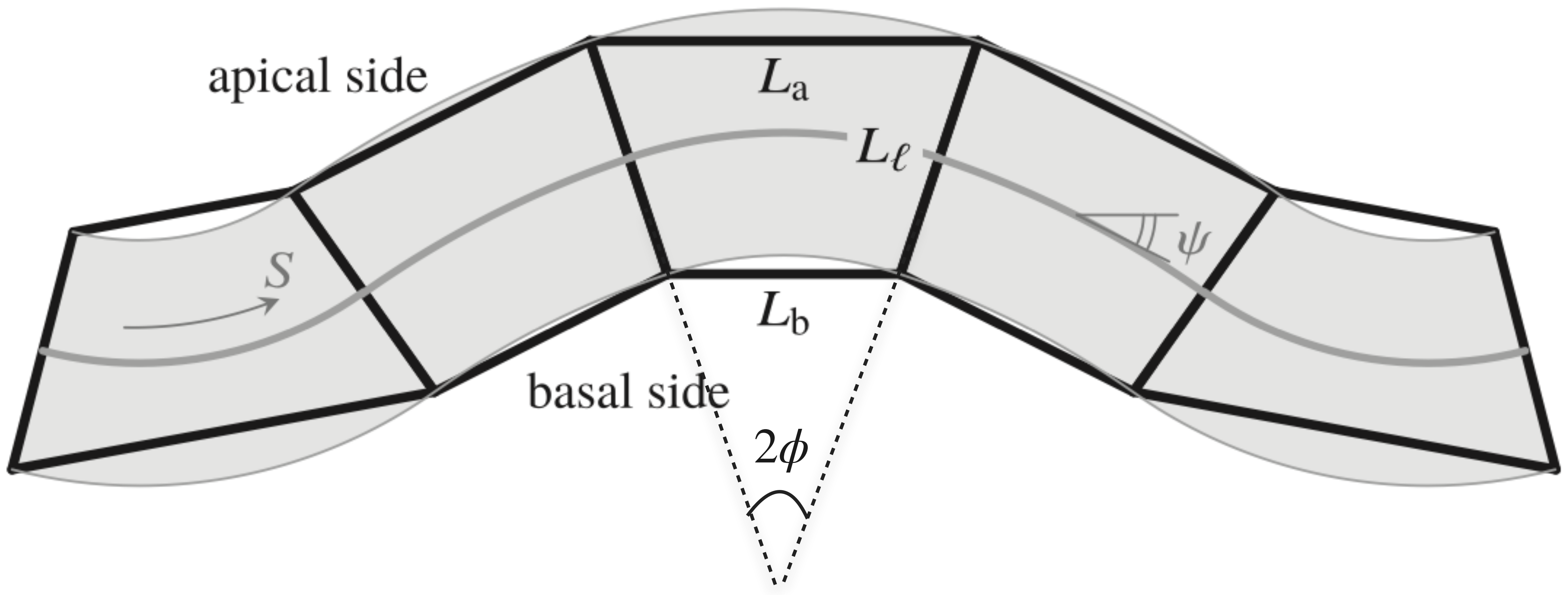




GOAL: UNDERSTANDING THE TISSUE-MECHANICAL CONSEQUENCES OF MICROSCOPIC CONSTRAINTS IN A MINIMAL MODEL

CONTINUUM LIMIT OF A SHEET OF DISCRETE CELLS

Isosceles trapezoids



Differential surface tensions: $\Lambda_a, \Lambda_b, \Lambda_l$

$$E_{\text{cell}} = \Lambda_a L_a + \Lambda_b L_b + \Lambda_l L_l$$

$$K = (L_a + L_b)/2$$

$$L_a = K + L_\ell \sin\phi,$$

$$L_b = K - L_\ell \sin\phi,$$

$$L = L_\ell \cos\phi.$$

+

Impose incompressibility

$$A_c = KL = \text{constant}$$

continuum limit

Total energy of monolayer

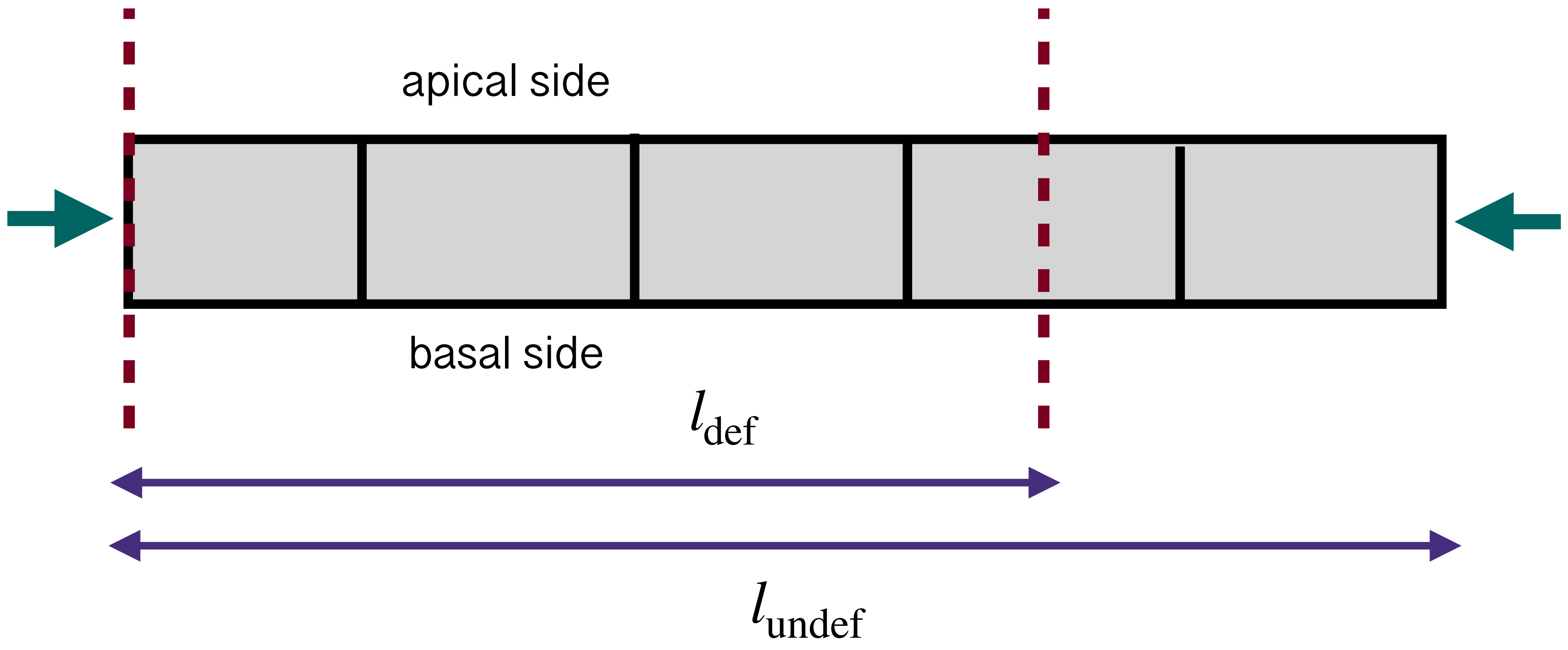
$$\varepsilon = \ell_0^2 \int \left[\frac{\ell_0}{\lambda} \sec\phi + \frac{\lambda}{\ell_0}(1 + \delta \sin\phi) \right] ds,$$

Haas et al., Nonlinear and nonlocal elasticity in coarse-grained differential-tension models of epithelia, PRE (2019)

Energy minimisation problem!

BUCKLING TRANSITION

Impose a relative compression D

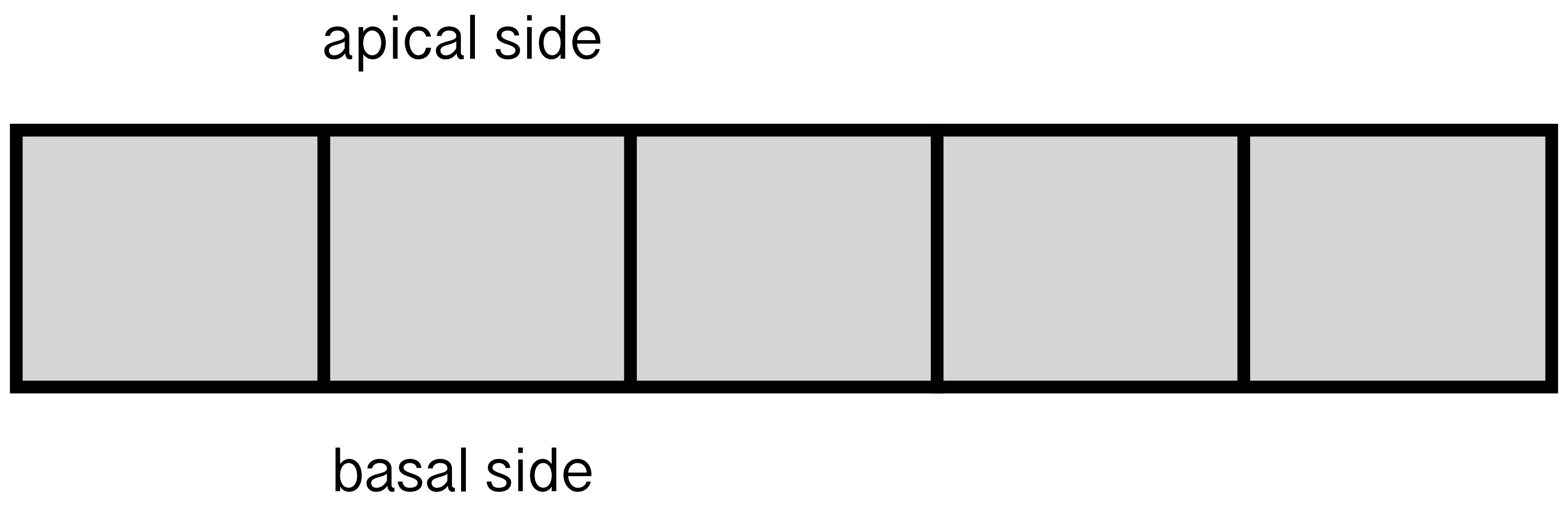


$D = 1 - l_{\mathrm{def}}/l_{\mathrm{undef}}$

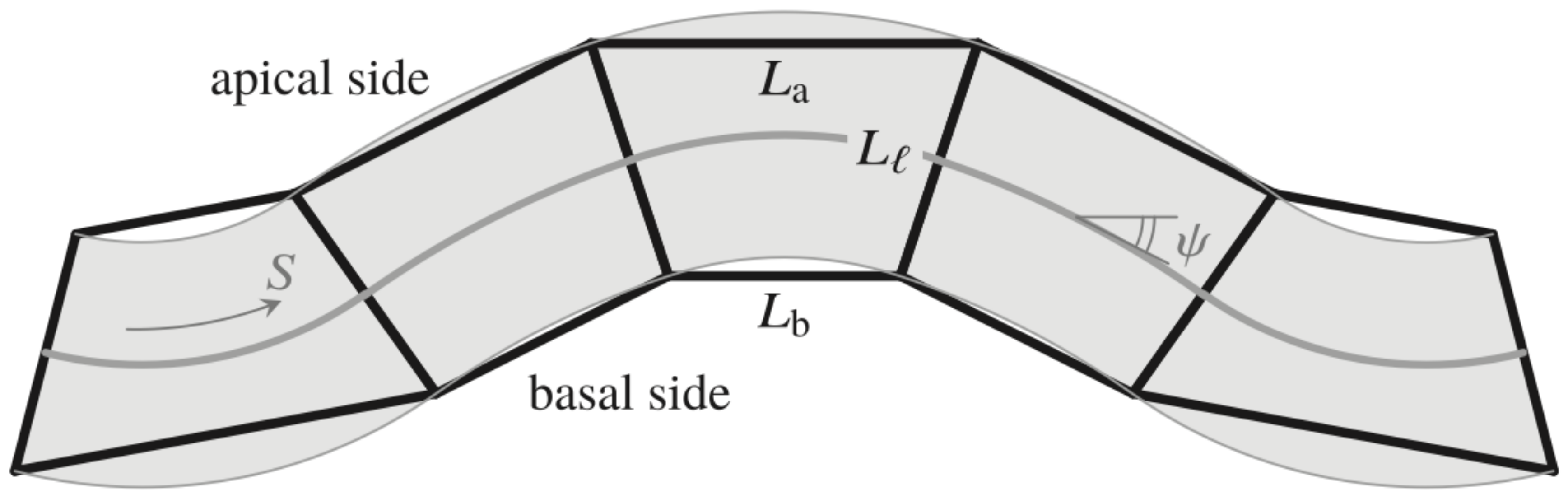
Is $E_{\mathrm{buckled}} < E_{\mathrm{flat}}$?

No

Yes



$D < D_*$: Flat



$D > D_*$: Buckled

VARIATIONAL APPROACH

$$\varepsilon = \ell_0^2 \int \left[\frac{\ell_0}{\lambda} \sec\phi + \frac{\lambda}{\ell_0}(1 + \delta \sin\phi) \right] ds,$$

+

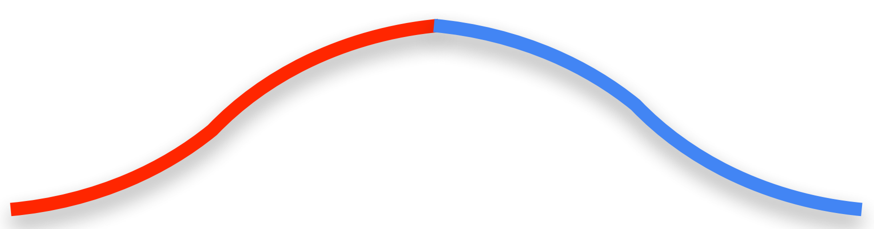
Clamped boundaries:

$$x(2) - x(0) = 2(1 - D)$$

$$y(2) = y(0)$$

$$\psi(0) = \psi(1) = 0$$

Symmetric buckling:



$$\mathcal{L} = \int_0^1 \left[\Lambda + \frac{1}{\Lambda} + \frac{\dot\psi^2}{8\Lambda\Xi^2} - \cancel{\frac{\delta\Lambda\dot\psi^3}{48\Xi^3}} + \cancel{\frac{5\dot\psi^4}{384\Lambda\Xi^4}} + \cancel{\frac{\ddot\psi^2}{48\Lambda\Xi^4}} + \frac{\mu\cos\psi}{\Lambda}\left(1 + \frac{\dot\psi^2}{8\Xi^2} + \cancel{\frac{41\dot\psi^4}{1920\Xi^4}} + \cancel{\frac{\ddot\psi^2}{40\Xi^4}} + \cancel{\frac{\dot\psi\dddot\psi}{240\Xi^4}}\right) + O(\Xi^{-5}) \right] d\sigma.$$

Λ_a

Λ_b

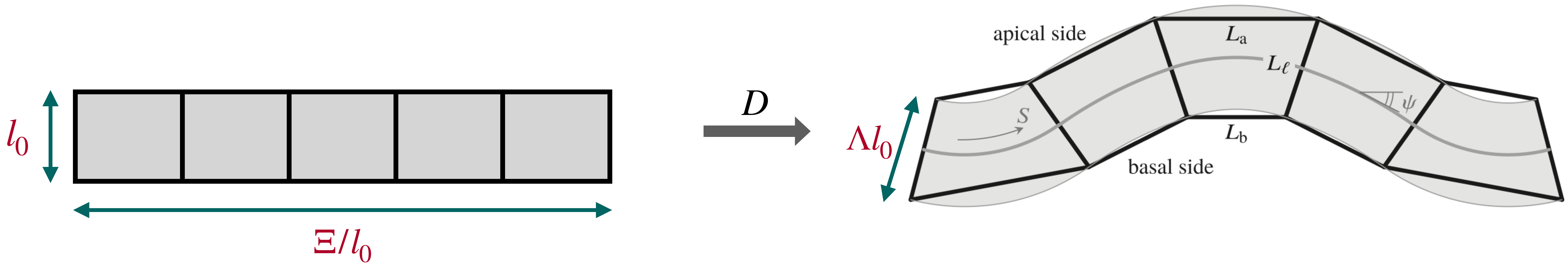
$$\delta \sim |\Lambda_a - \Lambda_b|$$

Horizontal compressive force

$$\delta\mathcal{L} = \delta\mu\frac{d\mathcal{L}}{d\mu} + \delta\Lambda\frac{d\mathcal{L}}{d\Lambda} + \delta\psi\frac{d\mathcal{L}}{d\psi} + \delta\dot\psi\frac{d\mathcal{L}}{d\dot\psi} = 0$$

Haas et al., Nonlinear and nonlocal elasticity in coarse-grained differential-tension models of epithelia, PRE (2019)

GOVERNING EQUATIONS



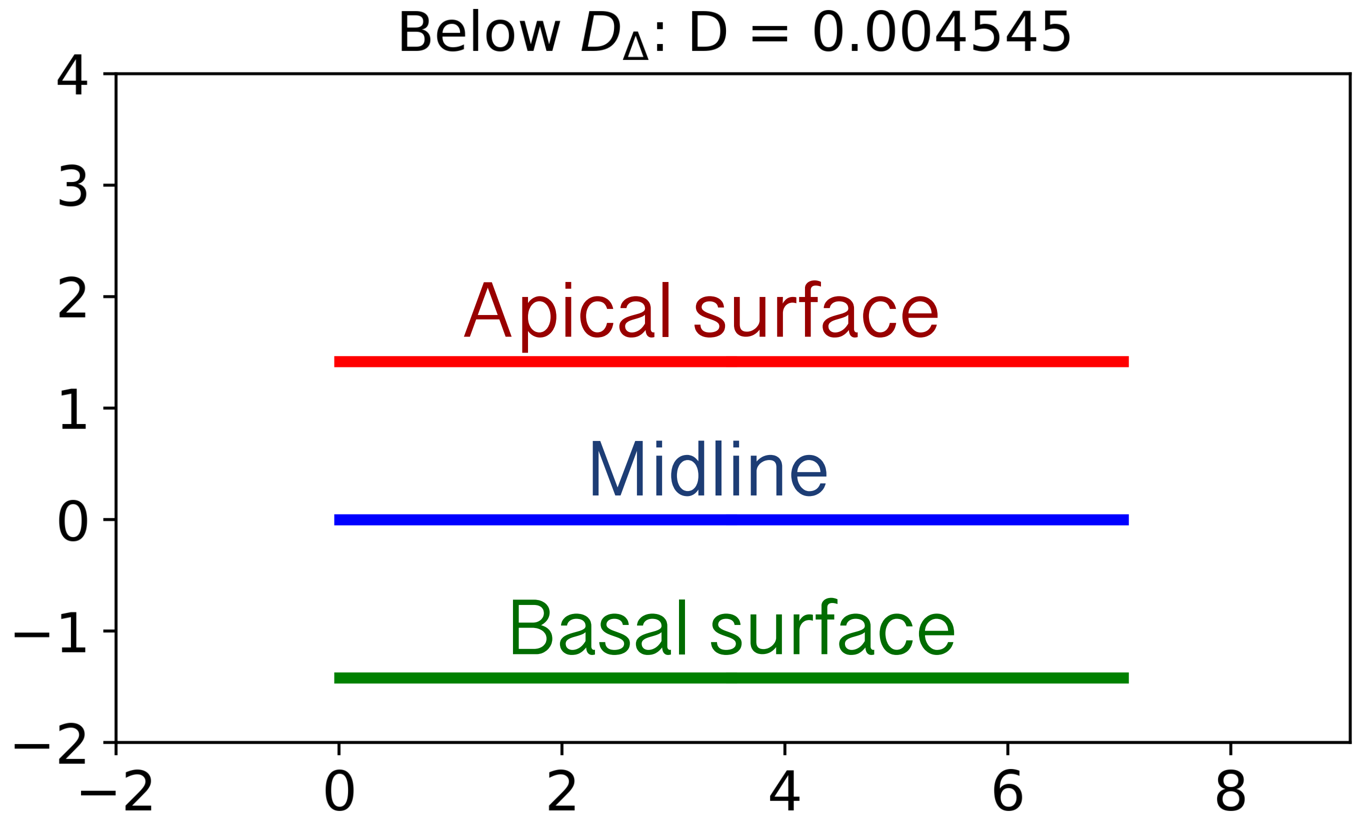
Exact shape is determined for any D

$$\frac{d\psi}{d\sigma} = \dot{\psi} \qquad \frac{d\dot{\psi}}{d\sigma} = \frac{4\mu\Xi^2 \sin\psi}{1+\mu\cos\psi}\left(\frac{\dot{\psi}^2}{8\Xi^2} - 1\right) \qquad \frac{dI}{d\sigma} = \cos\psi\left(1 + \frac{\dot{\psi}^2}{8\Xi^2}\right) \qquad \frac{dJ}{d\sigma} = \frac{\dot{\psi}^2}{8\Xi^2} \qquad \frac{d\Lambda}{d\sigma} = 0 \qquad \frac{d\mu}{d\sigma} = 0$$

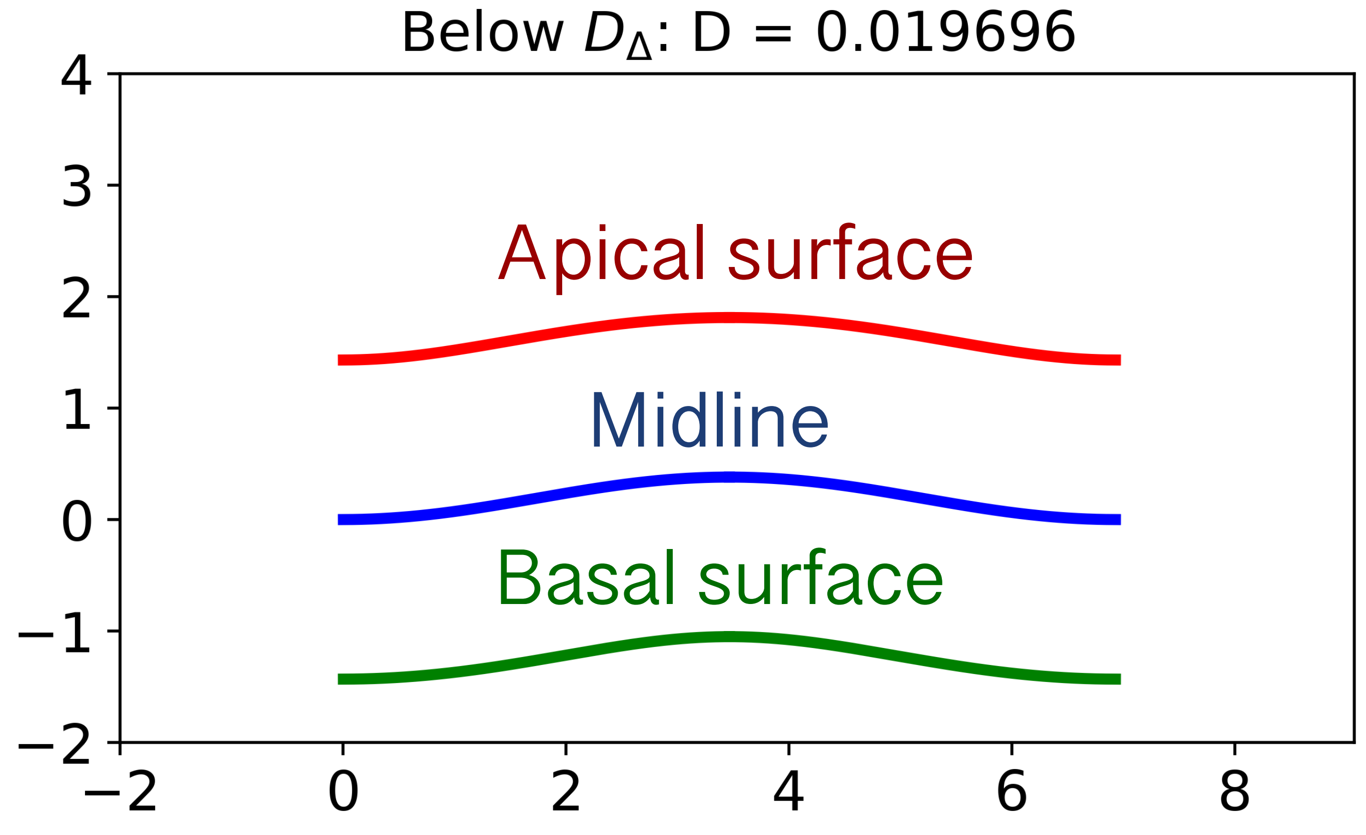
$$\psi(0) = 0 \qquad \psi(1) = 0 \qquad I(0) = 0 \qquad I(1) = \Lambda(1-D) \qquad J(0) = 0 \qquad J(1) = \Lambda^2 - 1 - \mu\Lambda(1-D)$$

Boundary value problem!

AT BUCKLING TRANSITION: RELEASE OF STIFFNESS

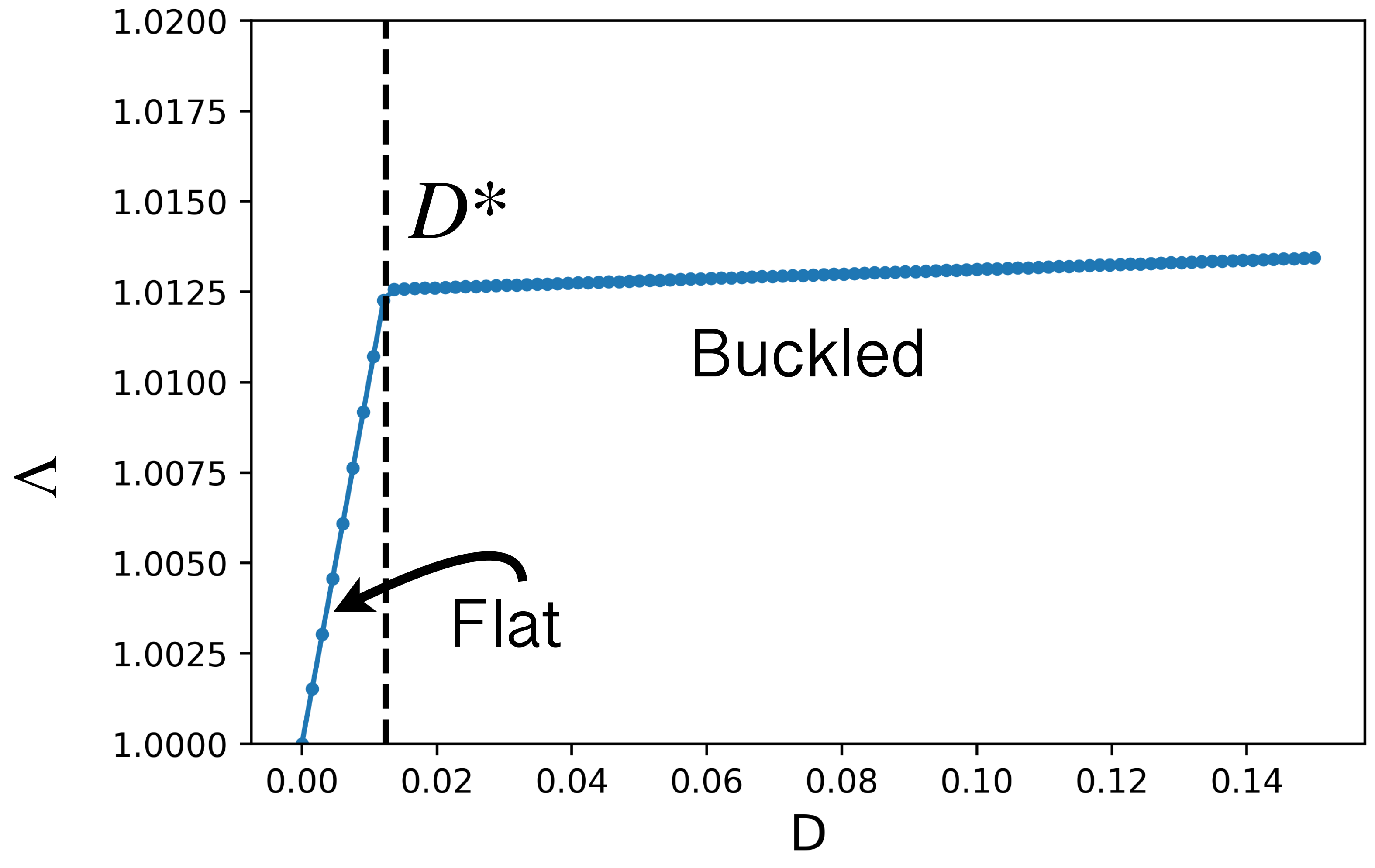


$D < D^*$

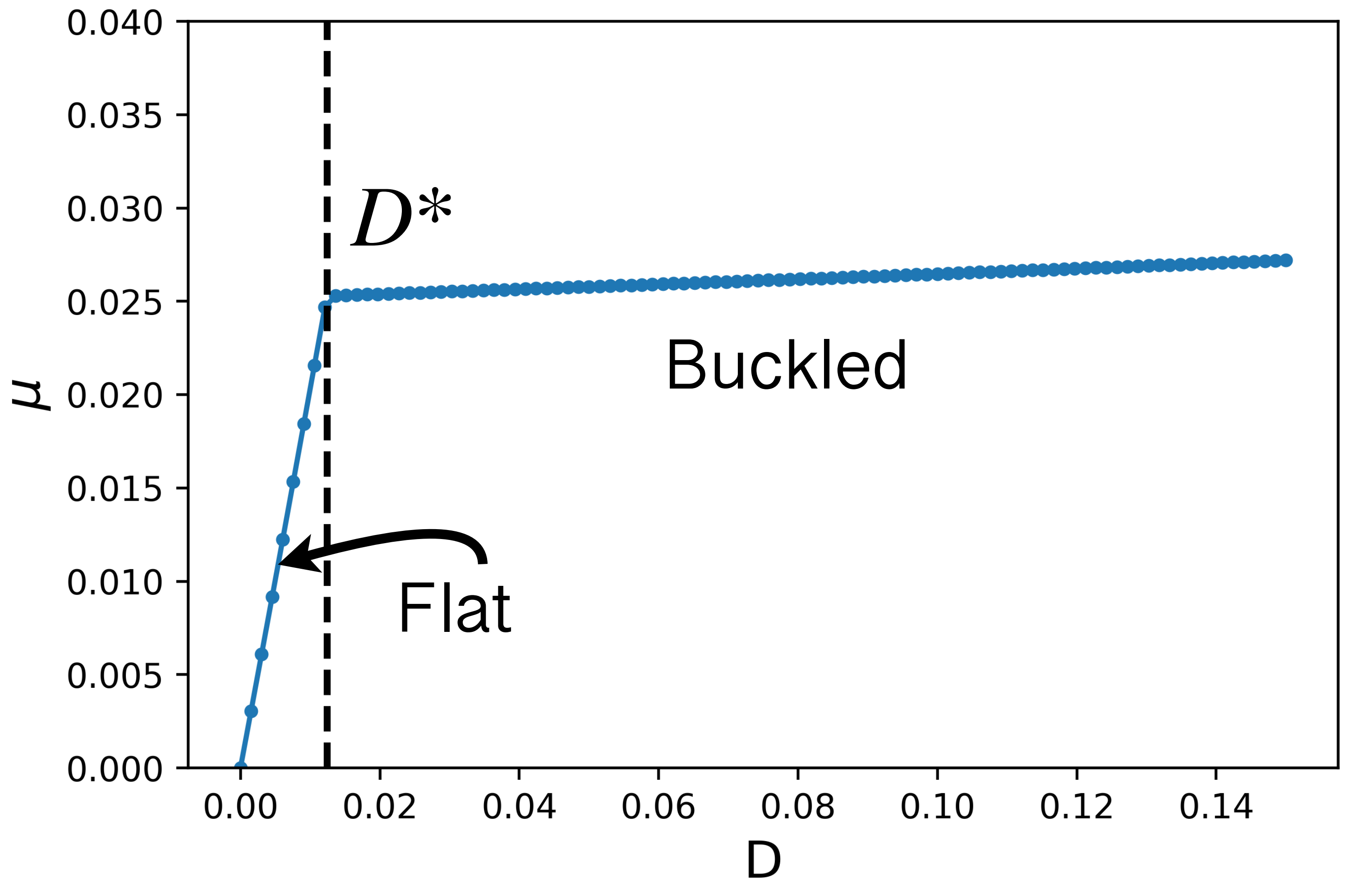


$D > D^*$

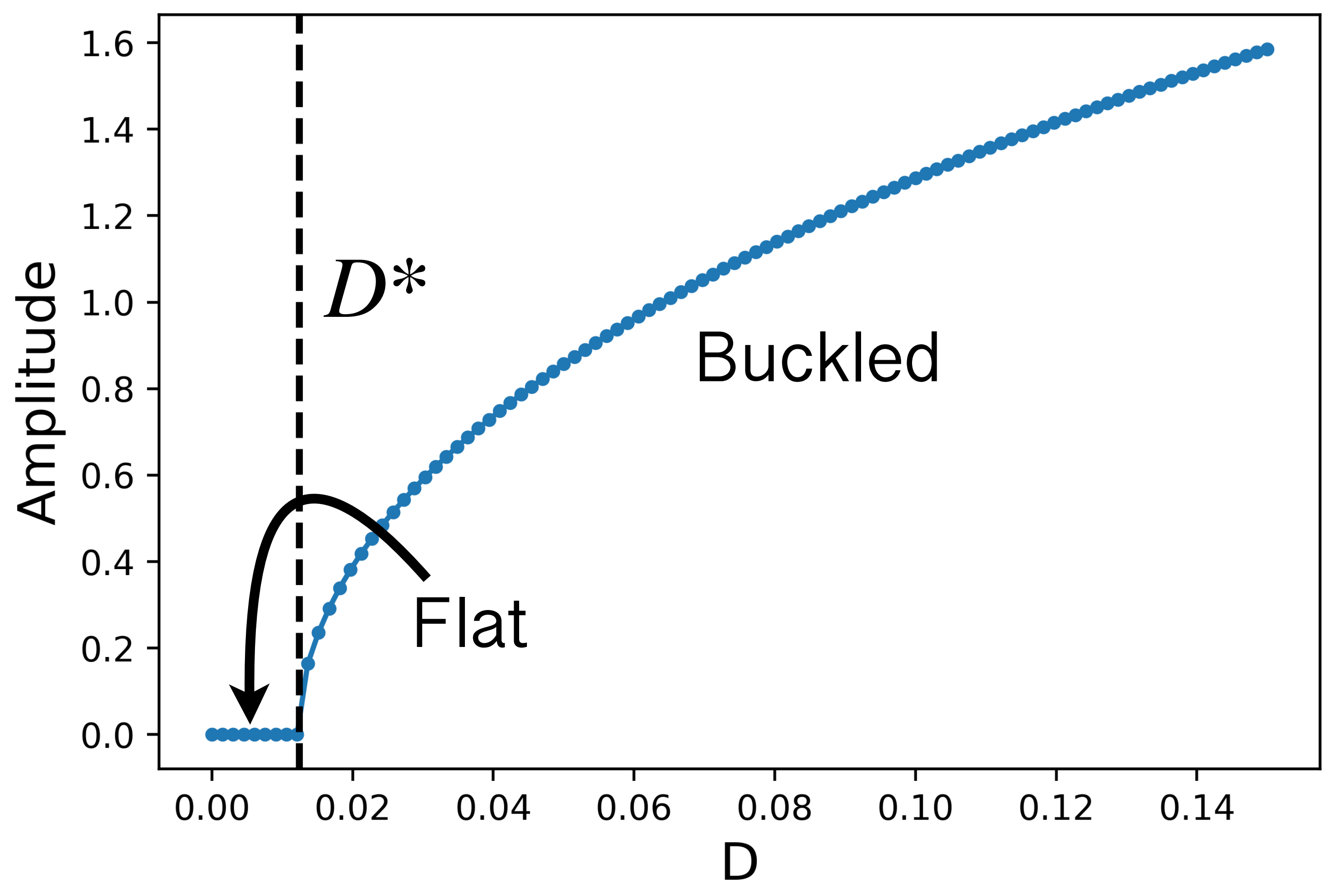
Λ = Deformed relative thickness



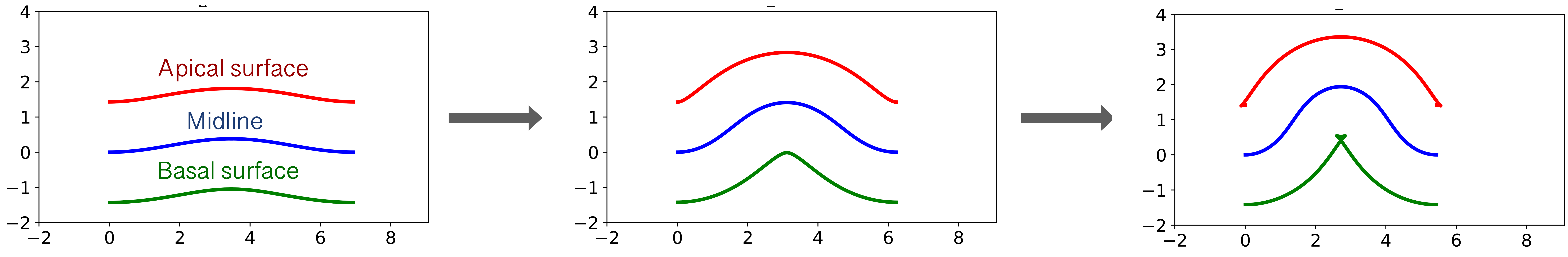
μ = Compressive force



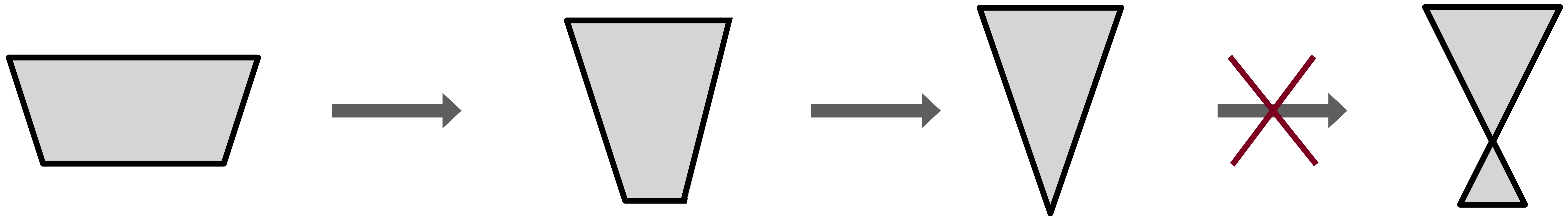
Amplitude = Maximum vertical displacement of midline



WHAT HAPPENS UNDER FURTHER COMPRESSION?

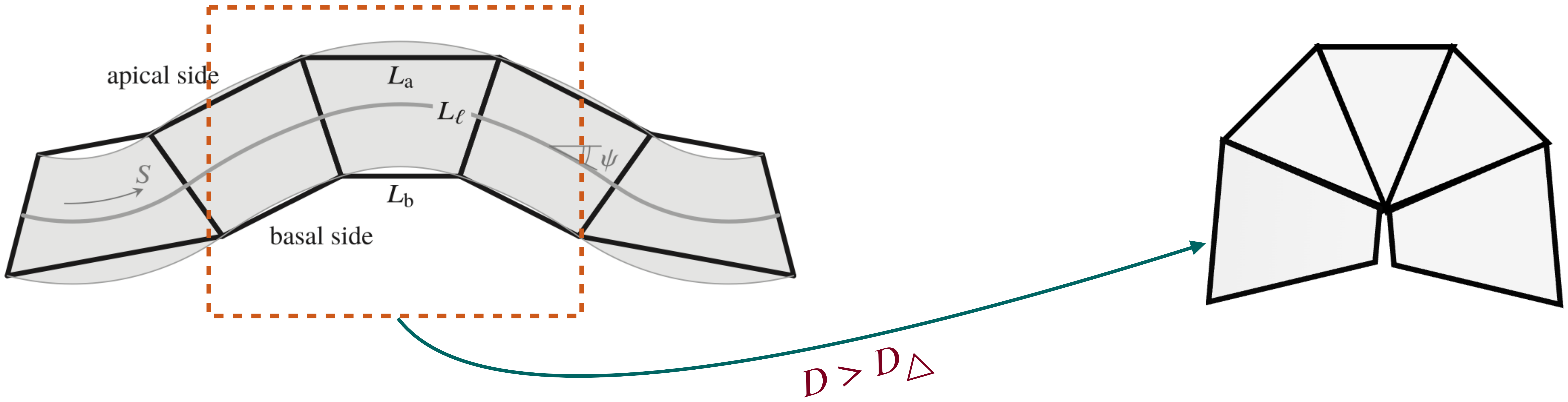


Model breaks down!



Cells self-intersect

NEW GOVERNING EQUATIONS



Introduce S_* ~ Fraction of △ cells

$\sigma \in [0, s_*]$ ⟹ △ cells that cannot fold further

$\sigma \in \left[s_*, \frac{1}{2}\right]$ ⟹ Cells that can still fold

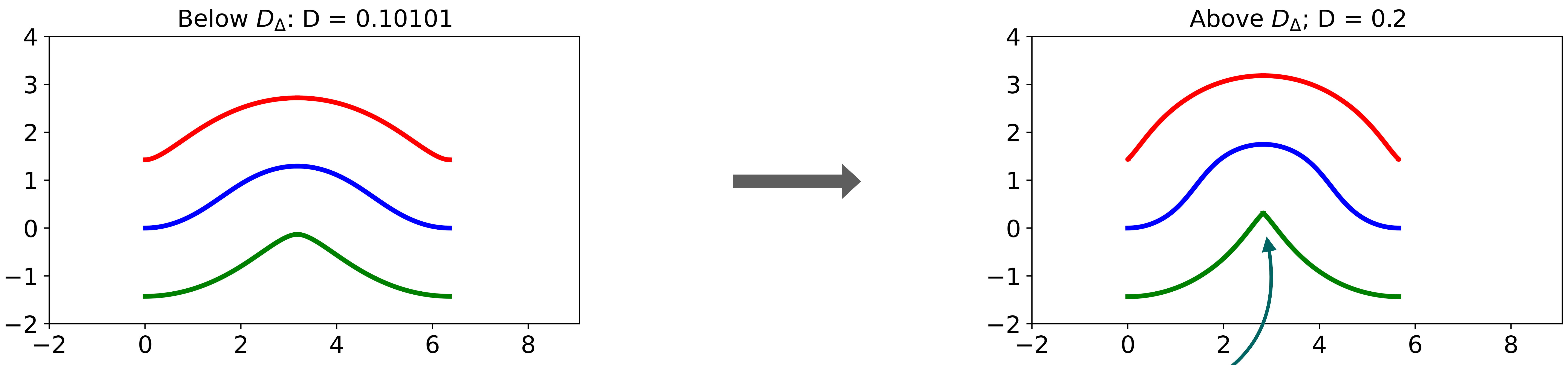
$$\sigma = s_* + (1 - 2s_*)\sigma'$$

$$\frac{d\psi}{d\sigma'} = \dot{\psi} \qquad \frac{dJ}{d\sigma'} = \frac{\dot{\psi}^2}{8\Xi^2}(1 - 2s_*) \qquad \frac{d\mu}{d\sigma'} = 0$$

$$\frac{d\dot{\psi}}{d\sigma'} = \frac{4\mu\Xi^2 \sin\psi}{1 + \mu\cos\psi}\left(\frac{\dot{\psi}^2}{8\Xi^2(1 - 2s_*)^2} - 1\right)(1 - 2s_*) \qquad \frac{d\Lambda}{d\sigma'} = 0$$

$$\frac{dI}{d\sigma'} = \cos\psi\left(1 + \frac{\dot{\psi}^2}{8\Xi^2(1 - 2s_*)^2}\right) \qquad \frac{ds_*}{d\sigma'} = 0$$

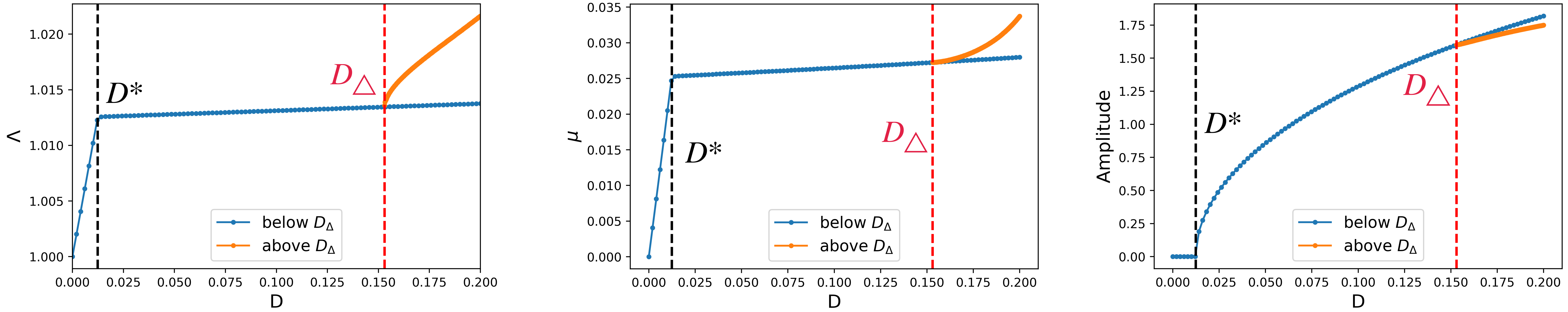
△ CELLS STIFFEN THE MONOLAYER



$D^* < D < D_\triangle$

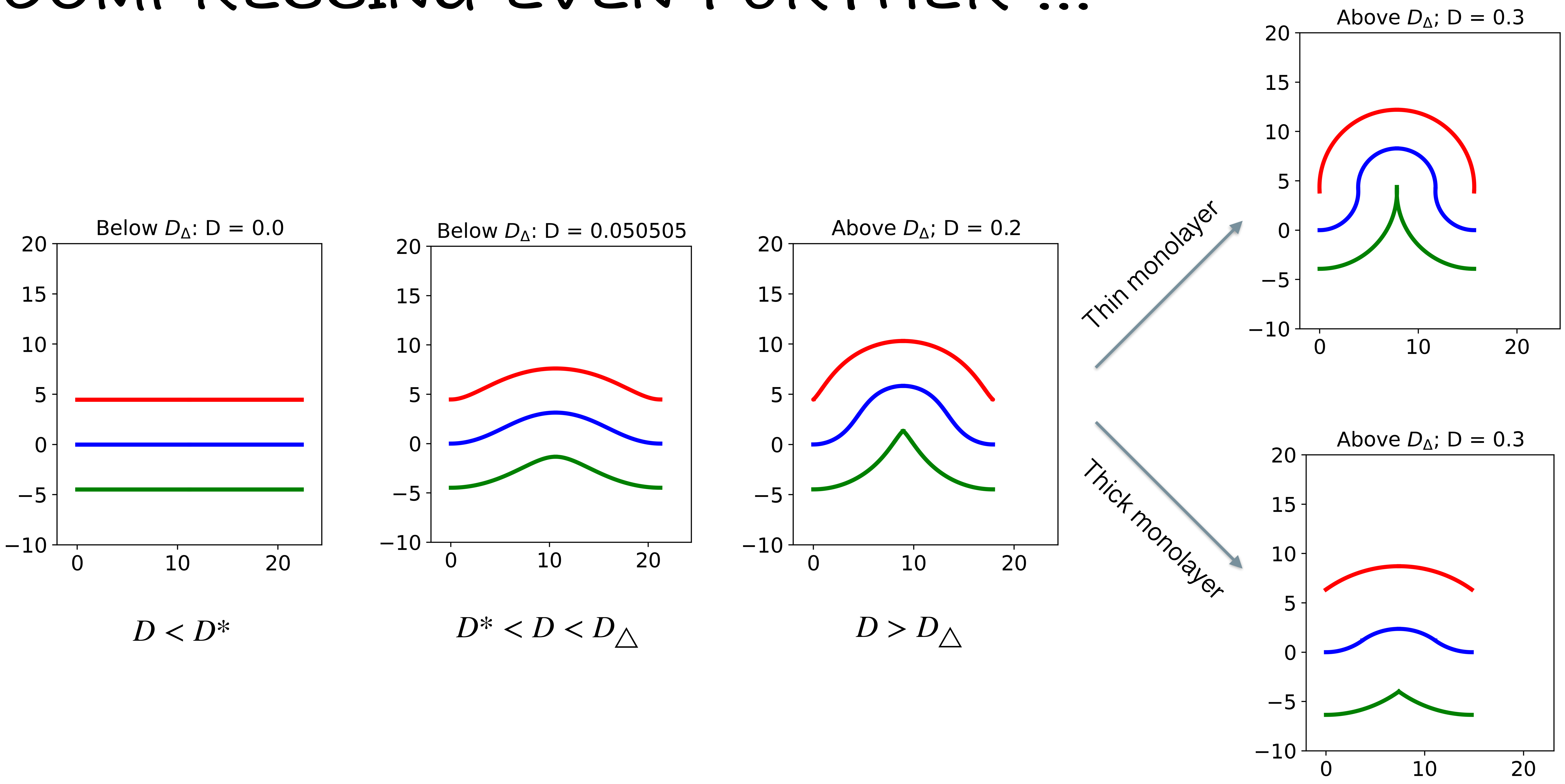
Kink due to △ cells

$D > D_\triangle$



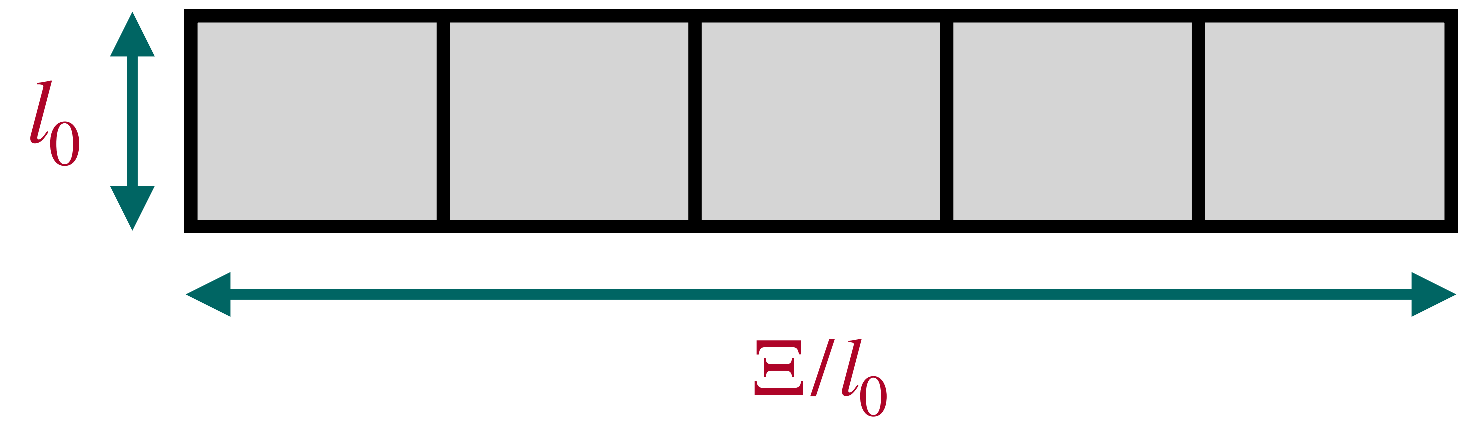
Monolayer stiffens once again!

COMPRESSING EVEN FURTHER …

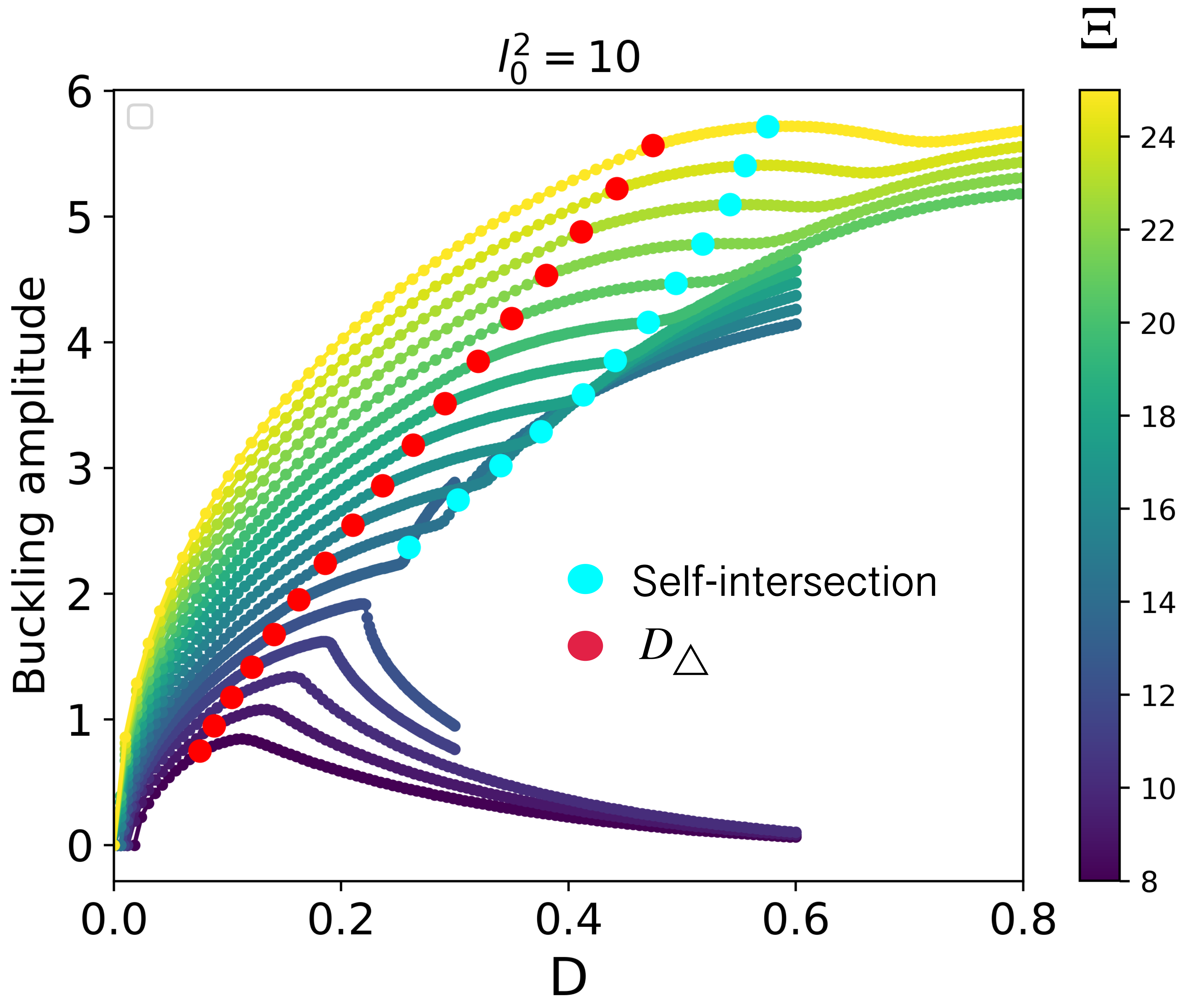


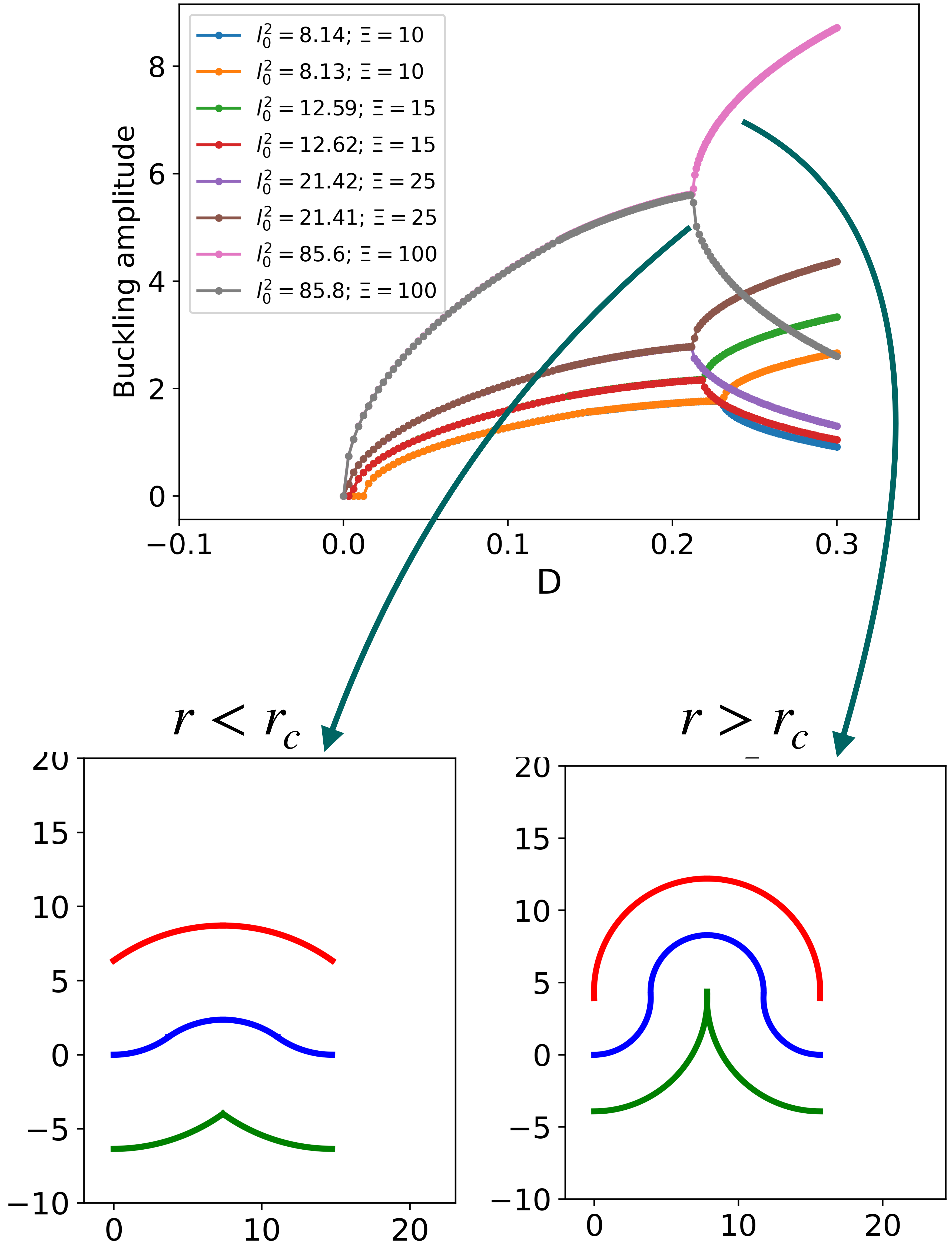
Two different behaviours emerge!

PITCHFORK BIFURCATION

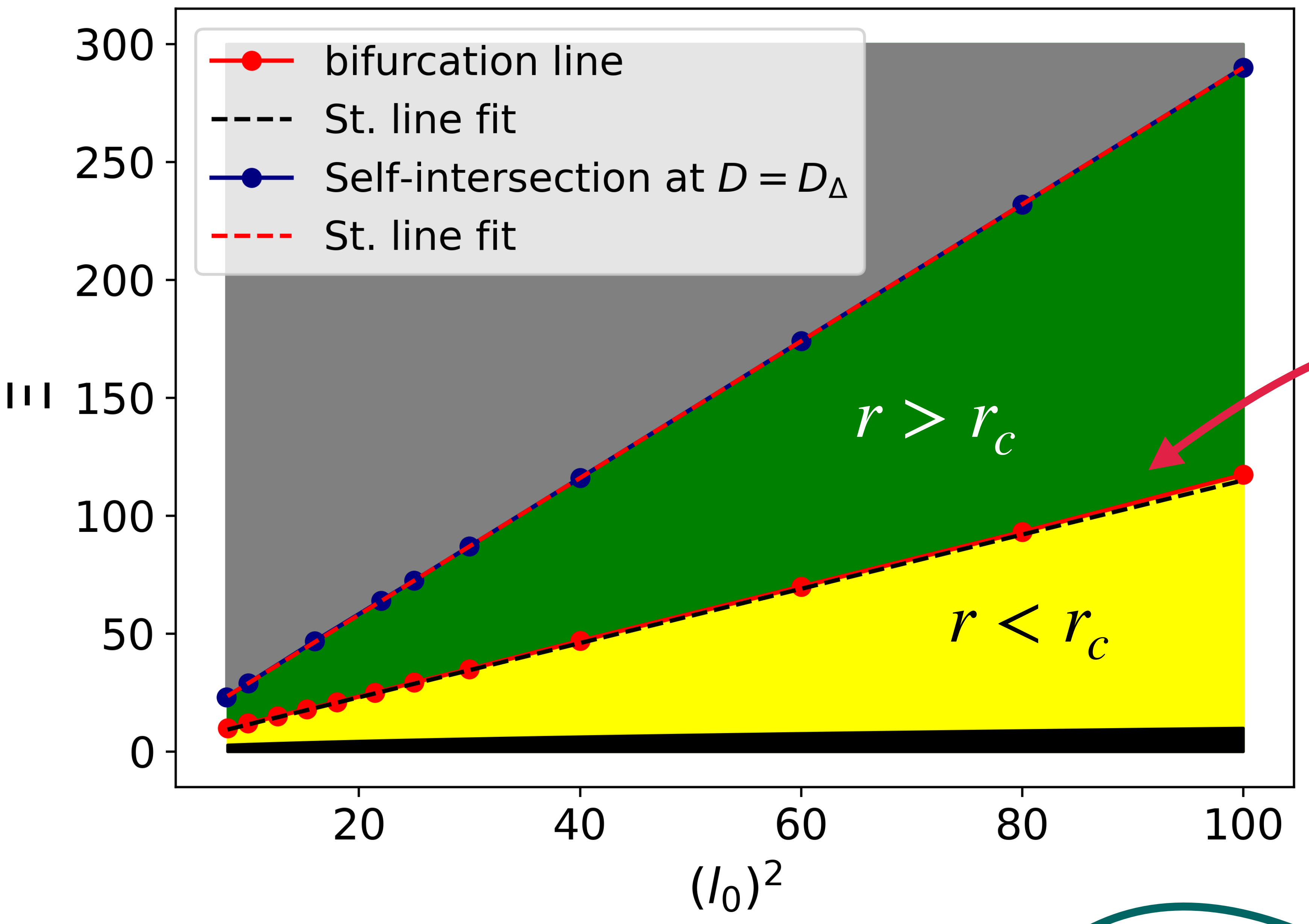


Define $r = \Xi/l_0^2$

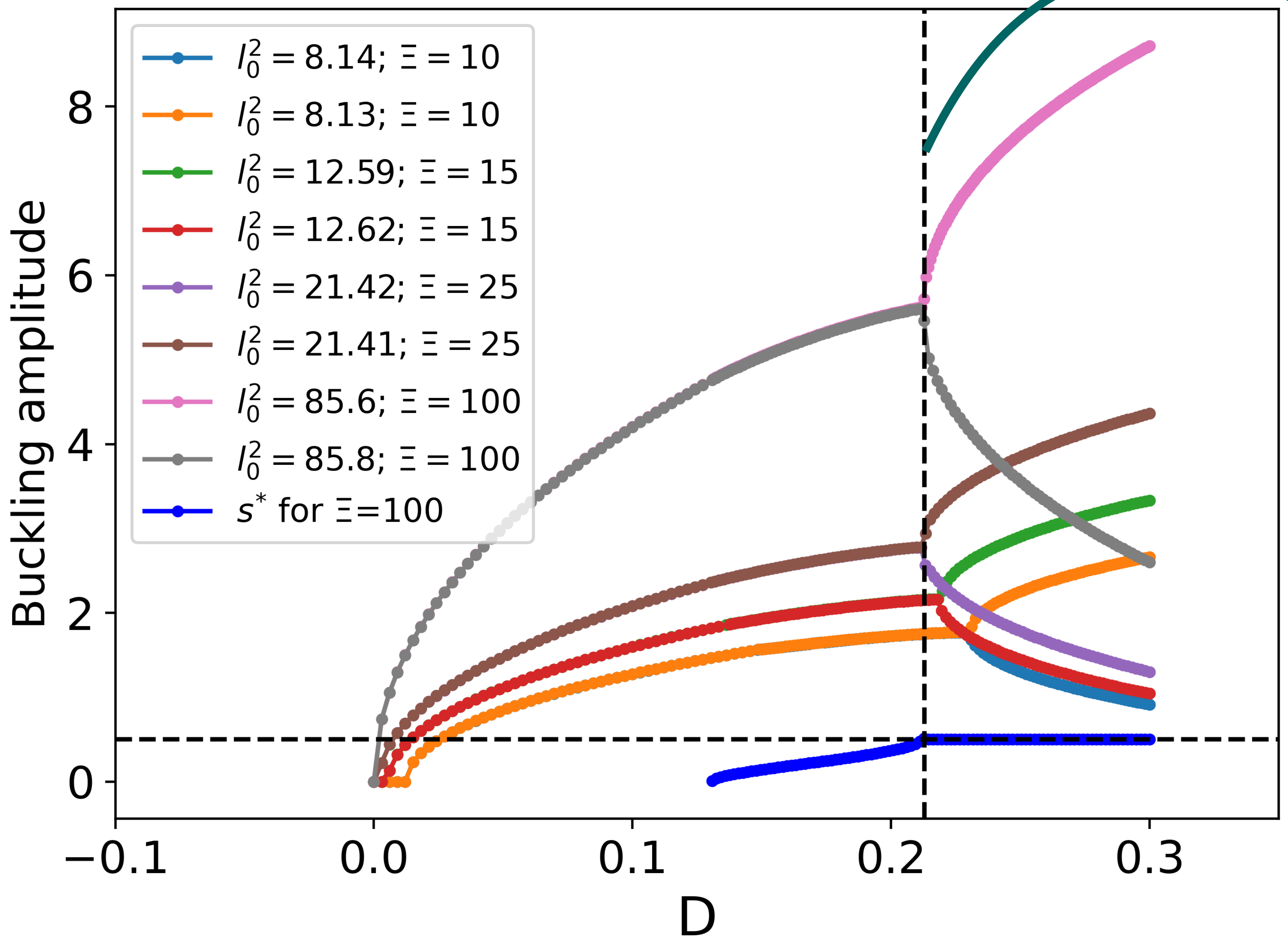




NUMERICS MATCH PRELIMINARY ANALYTICS (?)

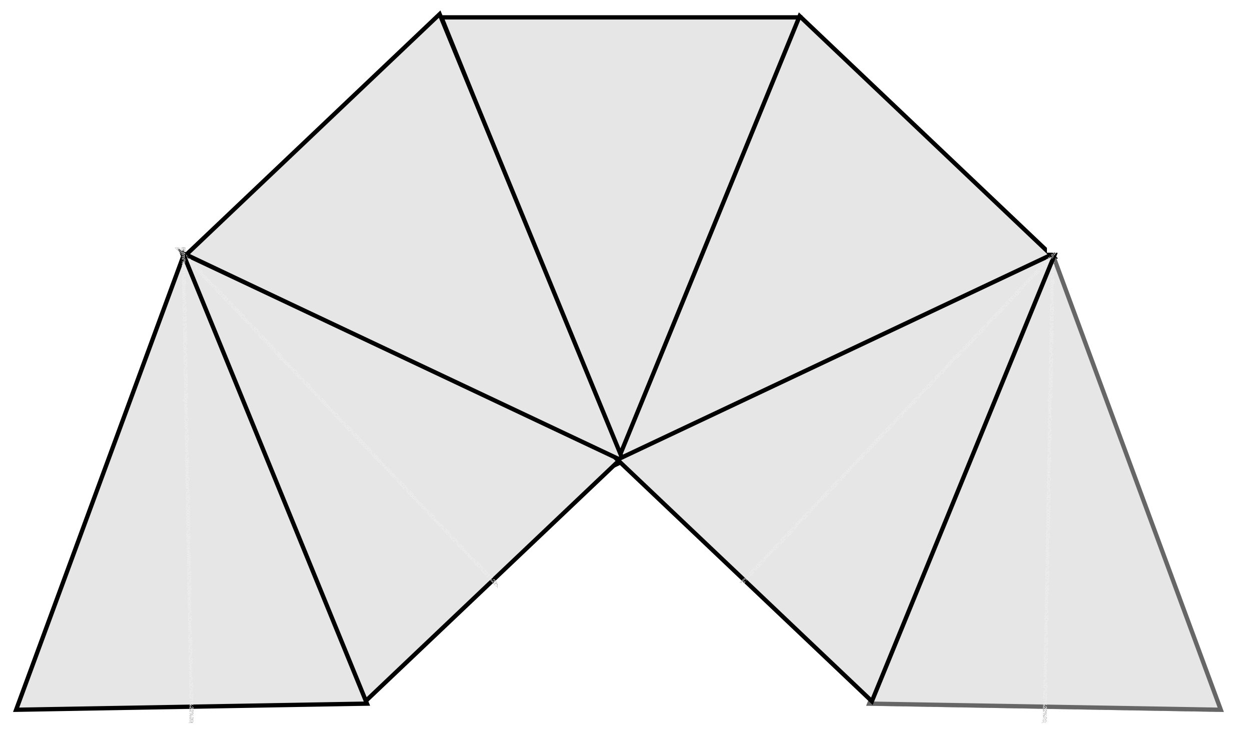


$r_c = 1.16$



$D_{\text{bif}} = 0.21$

Bifurcation due to geometric singularity!



All cells are $\triangle$ ($s_* = 1/2$)

Preliminary Analytics

$\tan r_c = 2 r_c$ **?** $\quad D_{\text{bif}} = 1 - \dfrac{\sin r_c}{r_c}$

$r_c \approx 1.165 \quad D_{\text{bif}} \approx 0.211$

FUTURE DIRECTIONS

Project 1

- Bifurcation analysis
- Consequences on tissue mechanics (eg., monolayer stiffening)

Project 2 : More realistic model

Relaxation of assumptions like "isosceles trapezoids"

—> δ in lowest order —> "wrinkles"

Project 3 : Introduce fluctuations

Fluctuations ⇔ Biology

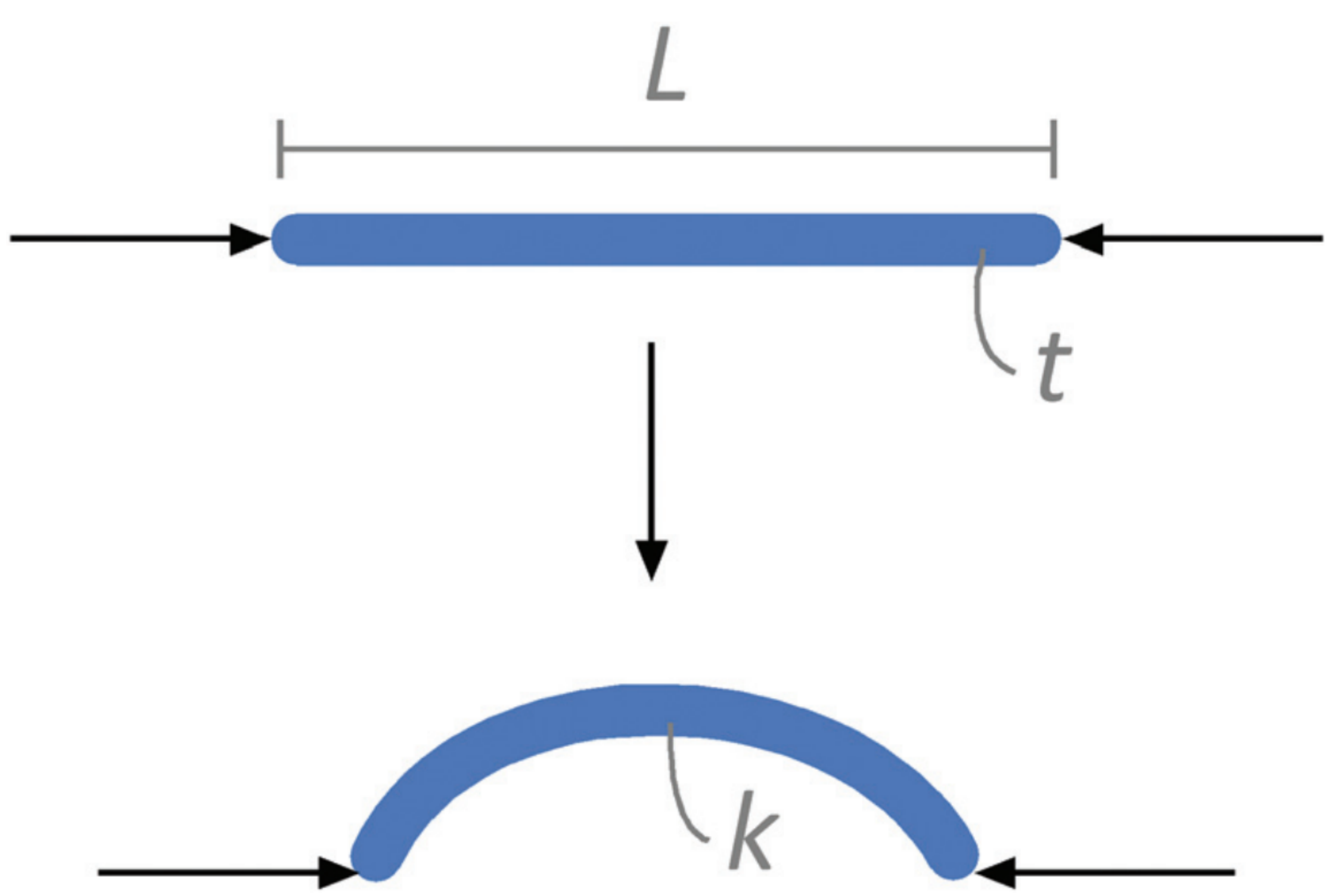
Static noise, i.e., variability

THANK YOU!

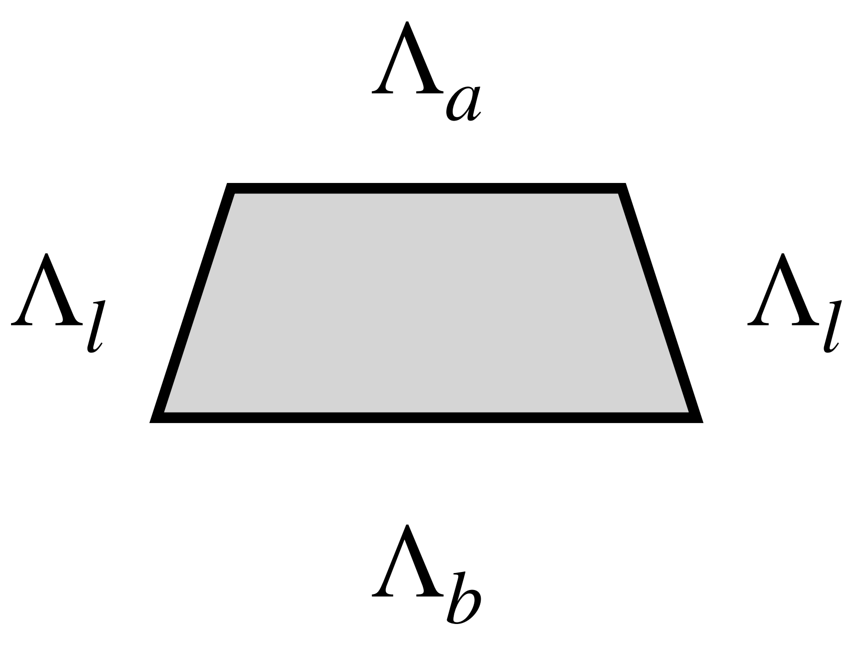
MECHANICAL PROPAGATIO OF GEOMETRIC

Tend to be **thin**

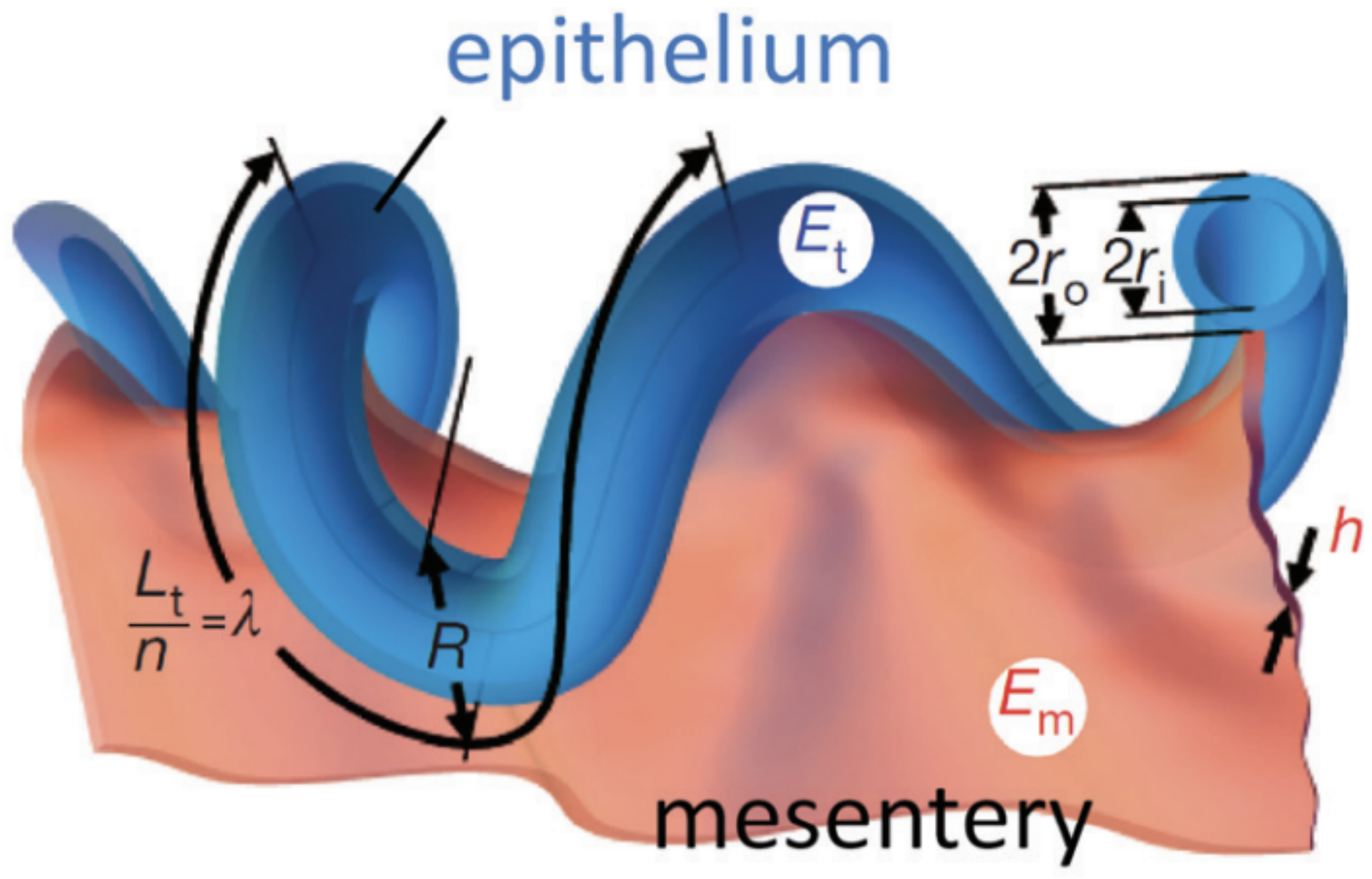
L >> t: more susceptible to instabilities



Cell polarity: Spatial difference leads to differential material properties



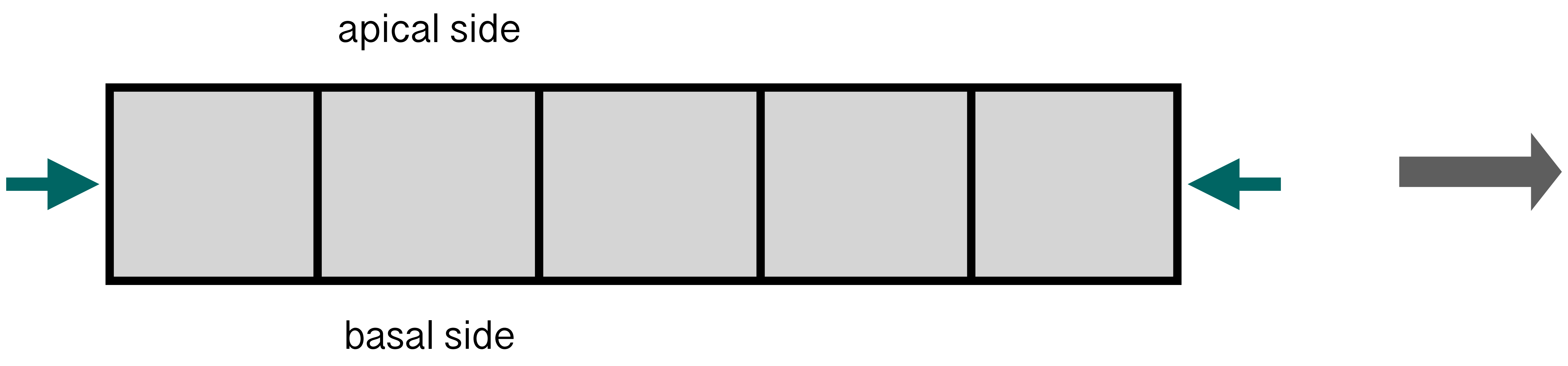
Effective **compression** due to differential growth rates of epithelium and foundation

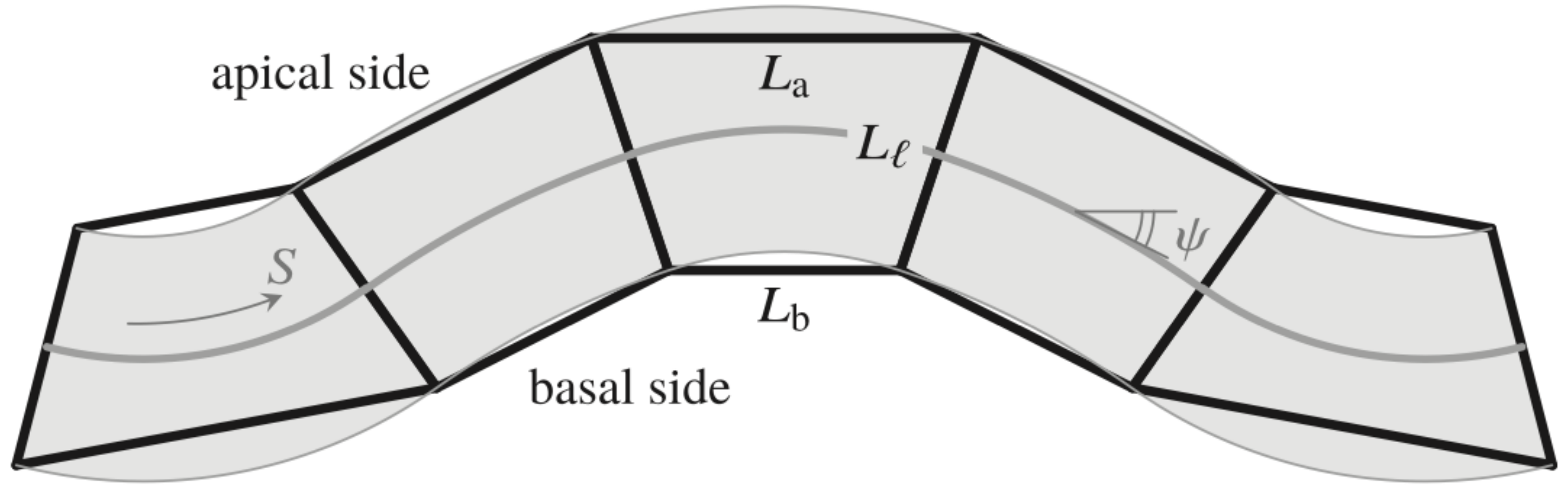


Nelson, On Buckling Morphogenesis (2016)

MECHANICAL INSTABILTIES

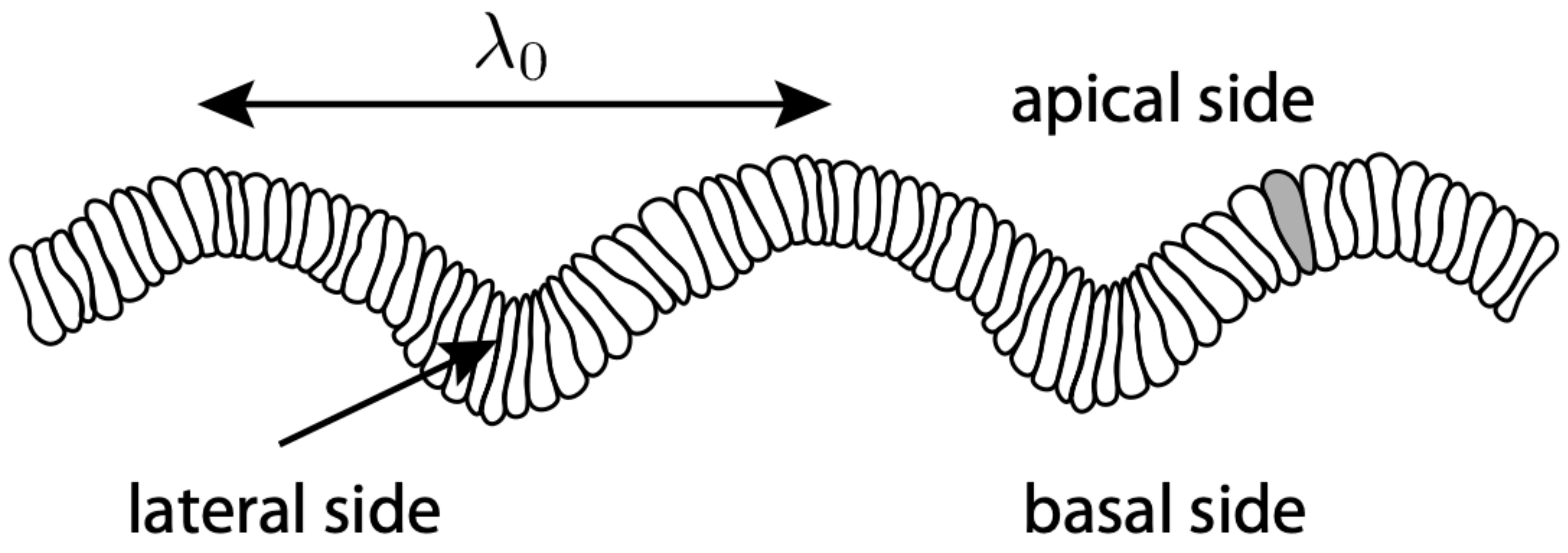
Buckling:





Haas et al., Nonlinear and nonlocal elasticity in coarse-grained differential-tension models of epithelia, PRE (2019)

Wrinkling:



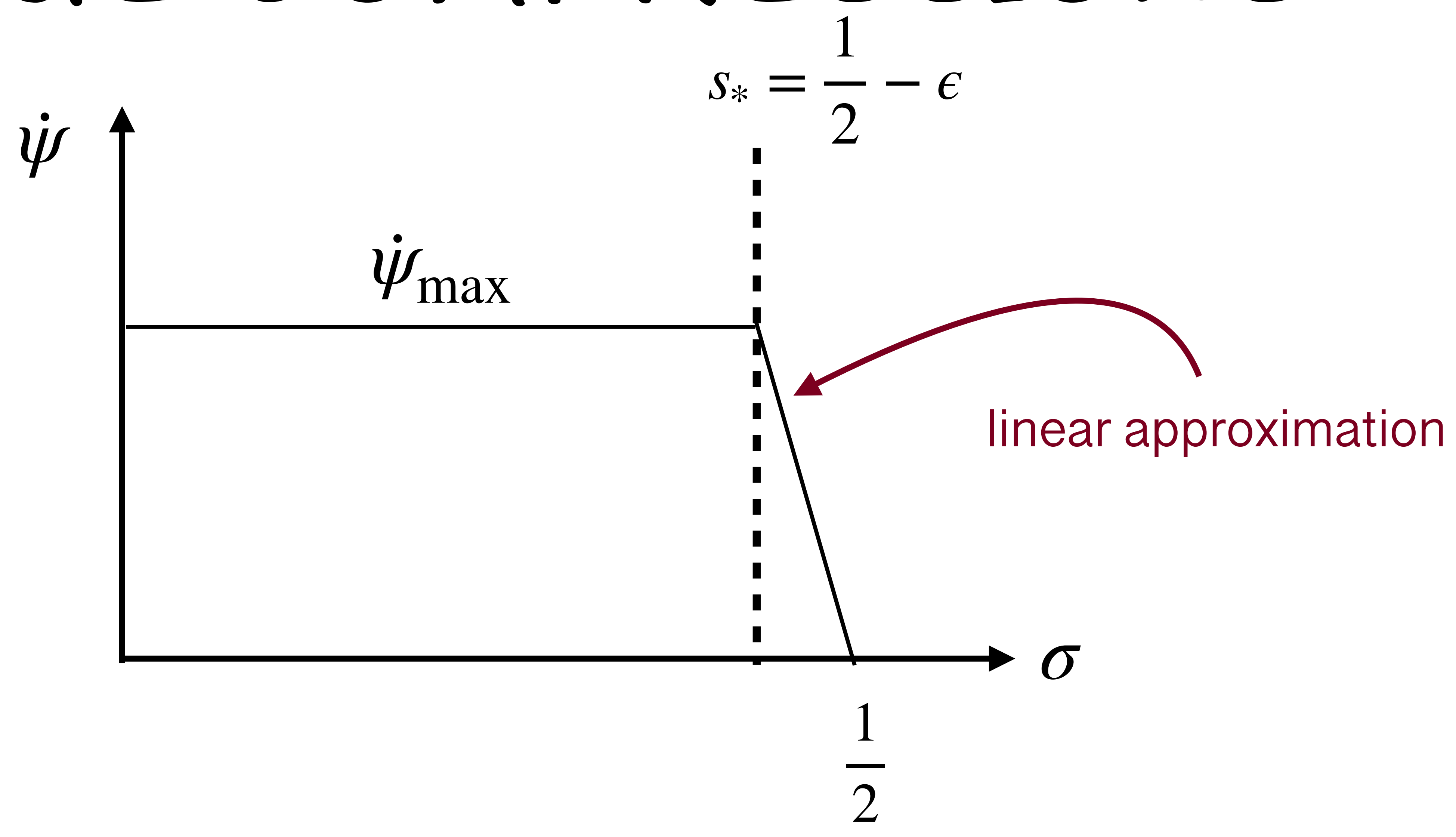
Andrenšek et al., Wrinkling Instability in Unsupported Epithelial Sheets, PRL (2023)

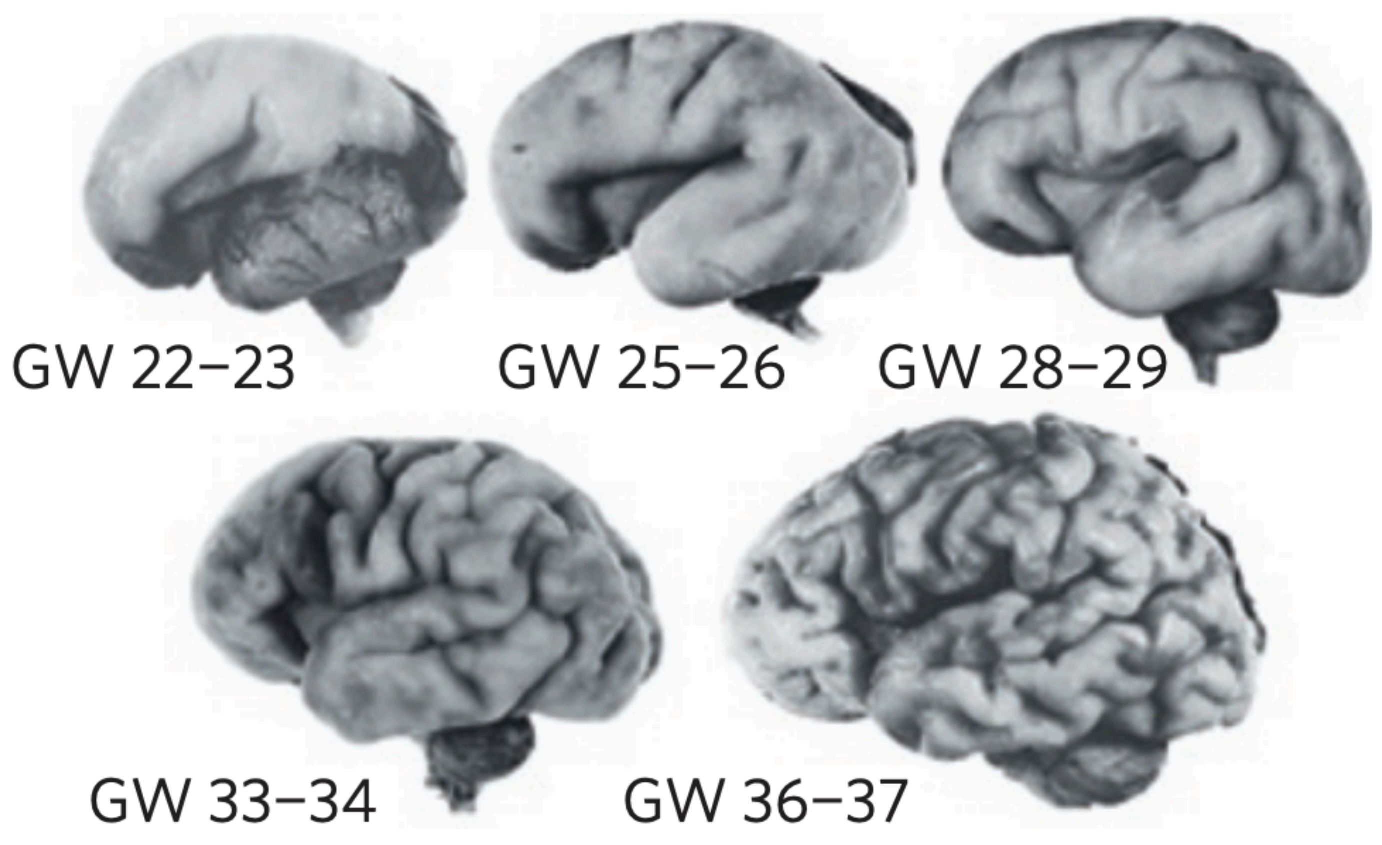
GOAL: INVESTIGATE LARGE COMPRESSIONS

Why?

- Large compressions in biology

- Interesting for continuum mechanics





How?

- write governing ems
- Solve for shapes
- Modification required for large compressions