MAE 545: Lecture 18 (12/1)

Shapes of simple cells

Wrinkled surfaces

Energy cost for stretching and shearing

undeformed square patch

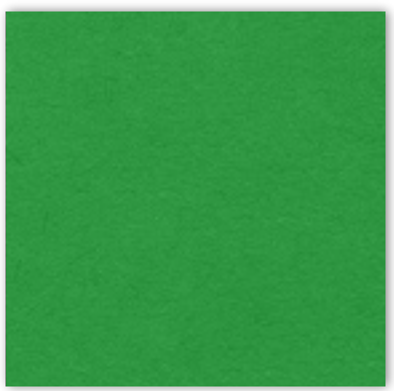
L

L

patch area

$A = L^2$

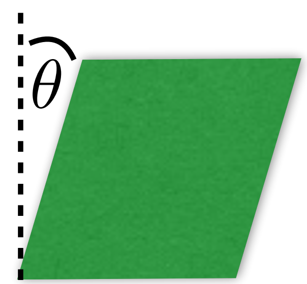
isotropic deformation



$L + \Delta L$

$L + \Delta L$

shear deformation



θ

L

L

$$\frac{E}{A} = \frac{B}{2}\left(\frac{\Delta A}{A}\right)^2 \approx \frac{B}{2}\left(\frac{2\Delta L}{L}\right)^2$$

bulk modulus

$B \sim 0.2\mathrm{N/m}$

(lipid bilayer)

$$\frac{E}{A} = \frac{\mu\theta^2}{2}$$

shear modulus

$\mu \sim 10^{-5}\mathrm{N/m}$

(spectrin network)

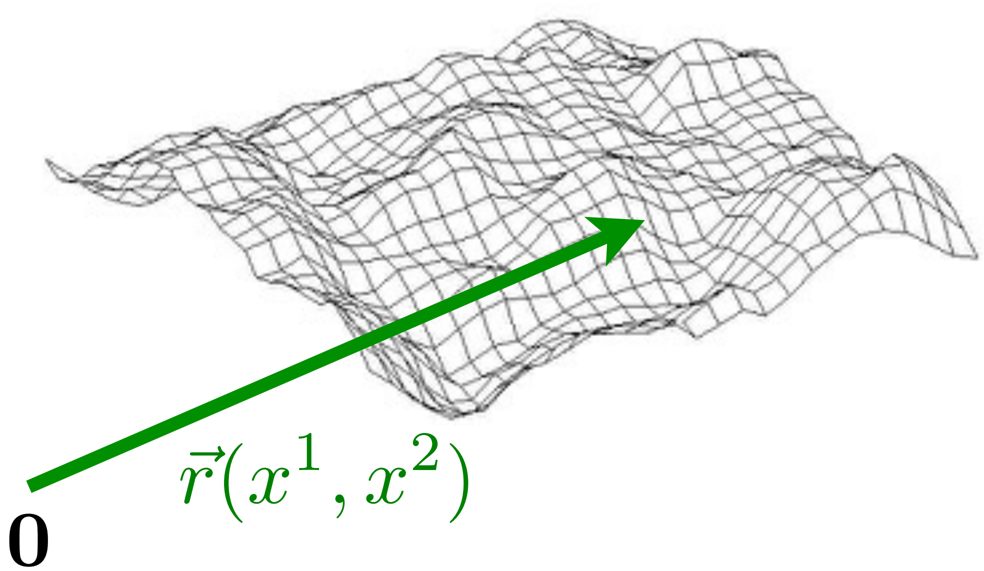
For solid plate of thickness *d*

$$B, \mu \sim E_m d$$

(E_m - 3D Young's modulus)

Strain tensor for deformation of membranes

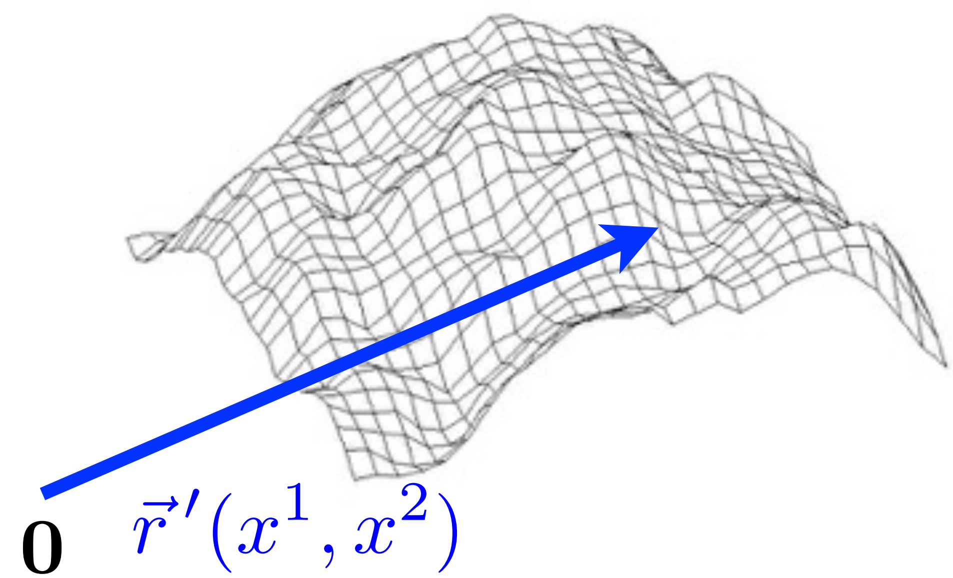
undeformed membrane



$$g_{ij} = \frac{\partial \vec{r}}{\partial x^i} \cdot \frac{\partial \vec{r}}{\partial x^j}$$

$$d\ell^2 = \sum_{i,j} g_{ij} dx^i dx^j$$

deformed membrane



$$g'_{ij} = \frac{\partial \vec{r}\,'}{\partial x^i} \cdot \frac{\partial \vec{r}\,'}{\partial x^j}$$

$$d\ell'^2 = \sum_{i,j} g'_{ij} dx^i dx^j$$

strain tensor

$$u_{ij} = \frac{1}{2} \sum_k (g^{-1})_{ik} \left(g'_{kj} - g_{kj}\right)$$

inverse metric tensor

$$\sum_k (g^{-1})_{ik} g_{kj} = \sum_k g_{ik} (g^{-1})_{kj} = \delta_{ij}$$

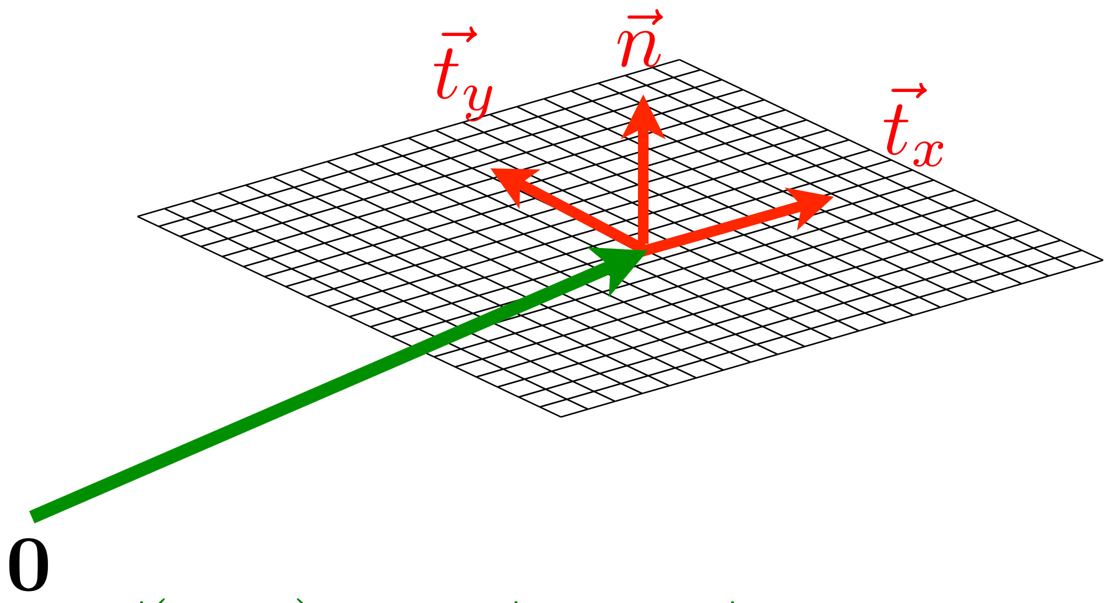
Energy cost for stretching/compressing

$$E = \int \sqrt{g}\, dx^1 dx^2 \, \frac{1}{2} \left[(B-\mu)\Big(\sum_i u_{ii}\Big)^2 + 2\mu \sum_{i,j} u_{ij}^2 \right]$$

$$g = \det(g_{ij}) \qquad \lambda = B - \mu$$

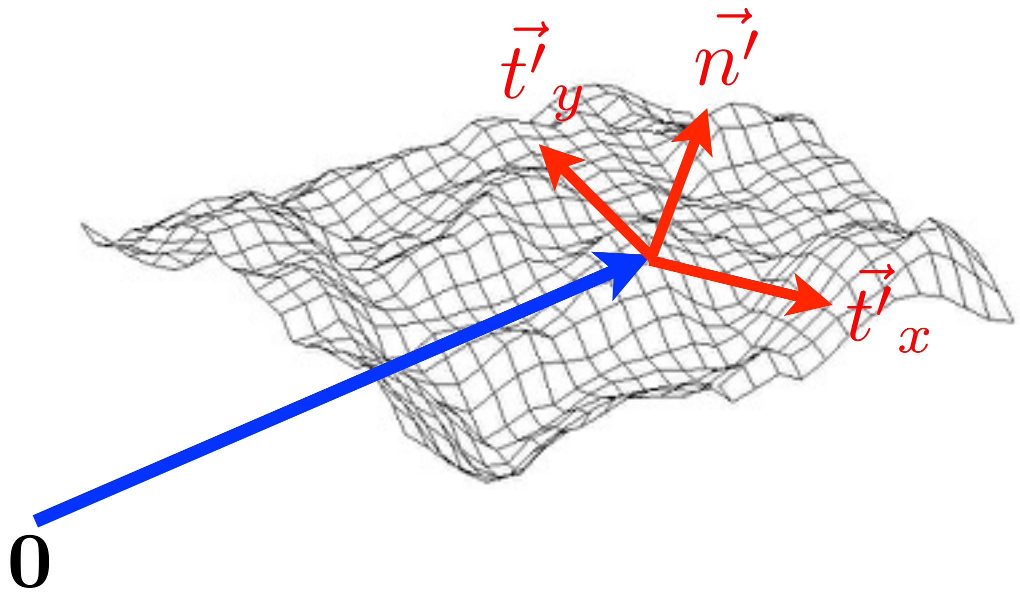
Strain tensor for deformation of flat membranes

undeformed membrane



$$\vec{r}(x,y) = x\vec{e}_x + y\vec{e}_y$$

deformed membrane



$$\vec{r'}(x,y) = \vec{r}(x,y) + u_x(x,y)\vec{e}_x$$
$$+u_y(x,y)\vec{e}_y + h(x,y)\vec{e}_z$$

$i, j, k \in x, y$

local tangents

$$\vec{t}_i = \partial_i \vec{r} \equiv \frac{\partial \vec{r}}{\partial i} = \vec{e}_i$$

local tangents

$$\vec{t'}_i = \partial_i \vec{r'} = \vec{e}_i + \sum_k (\partial_i u_k)\vec{e}_k + (\partial_i h)\vec{e}_z$$

metric tensor

$$g_{ij} = \vec{t}_i \cdot \vec{t}_j = \delta_{ij} \equiv \begin{pmatrix} 1, & 0 \\ 0, & 1 \end{pmatrix}$$

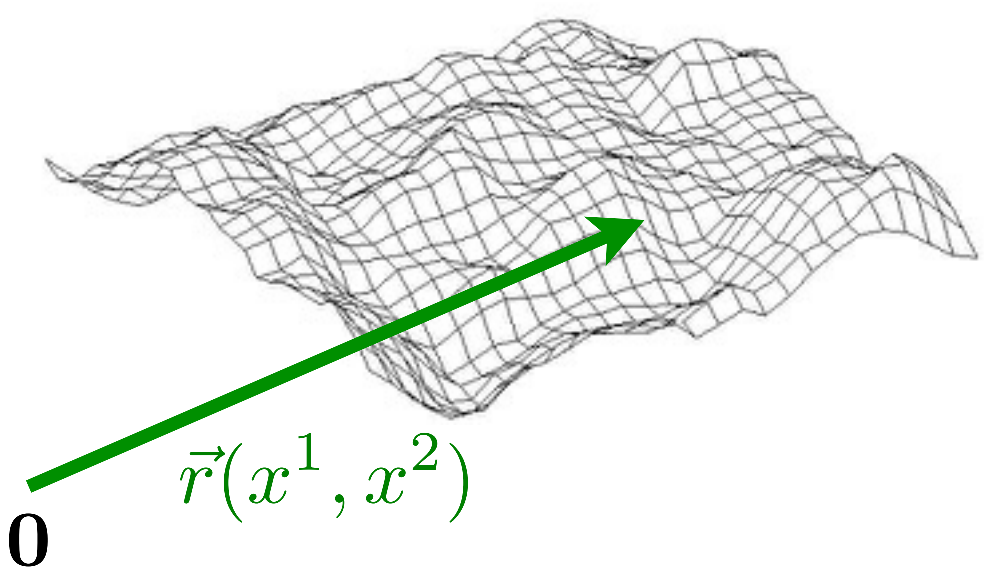
strain tensor

$$u_{ij} = \frac{1}{2}\left(g'_{ij} - \delta_{ij}\right)$$

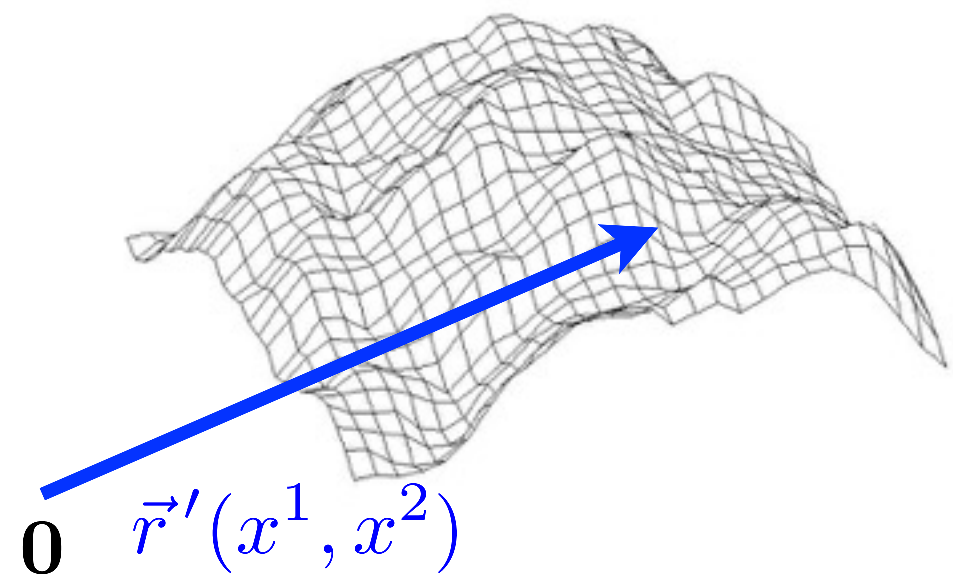
$$2u_{ij} = (\partial_i u_j + \partial_j u_i) + \sum_k \partial_i u_k \partial_j u_k + \partial_i h \partial_j h$$

Bending energy for deformation of membranes

undeformed membrane



deformed membrane



$$K_{ij} = \sum_k \left(g^{-1}\right)_{ik} \left(\vec{n} \cdot \frac{\partial^2 \vec{r}}{\partial x^k \partial x^j}\right)$$

$$K'_{ij} = \sum_k \left(g'^{-1}\right)_{ik} \left(\vec{n}\,' \cdot \frac{\partial^2 \vec{r}\,'}{\partial x^k \partial x^j}\right)$$

bending strain tensor

$$b_{ij} = K'_{ij} - K_{ij}$$

(local measure of deviation from preferred curvature)

Energy cost of bending

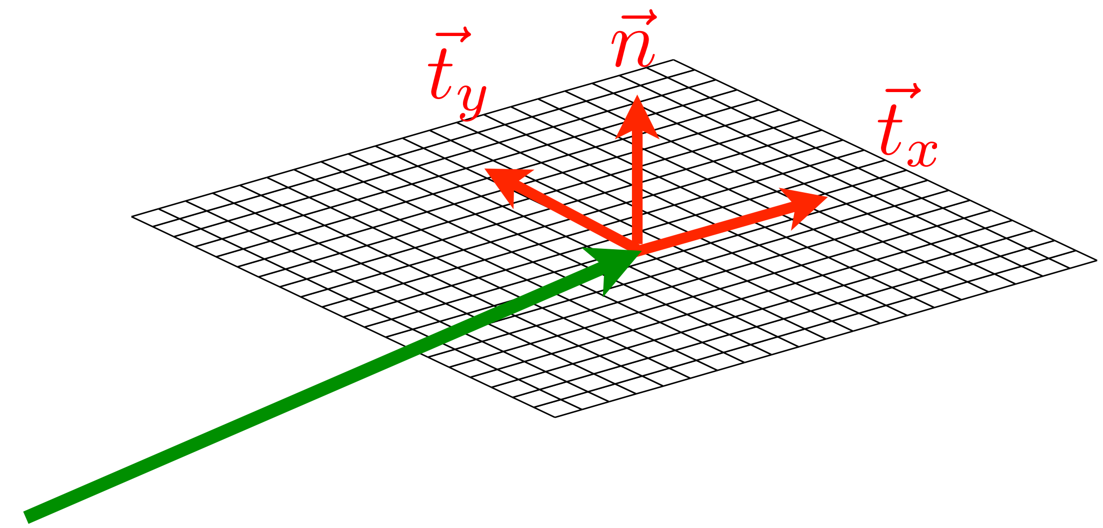
$$E = \int \sqrt{g}\, dx^1 dx^2 \left[\frac{1}{2}\kappa\, \mathrm{tr}(b_{ij})^2 + \kappa_G \det(b_{ij})\right]$$

For solid plate of thickness *d*

$$\kappa, \kappa_G \sim E_m d^3$$

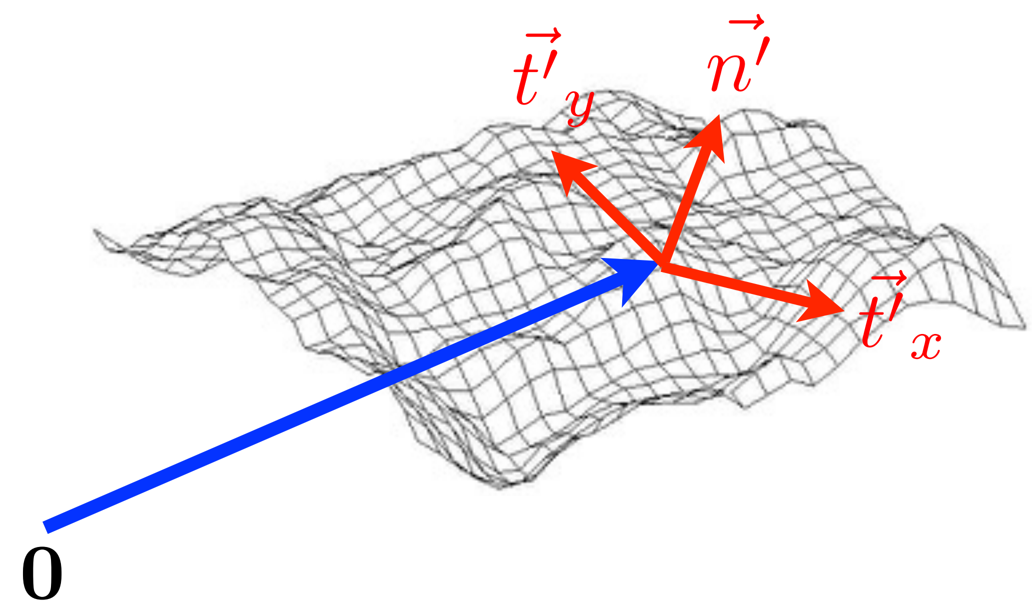
Bending strain for deformation of flat membranes

undeformed membrane



$$\vec{r}(x,y) = x\vec{e}_x + y\vec{e}_y$$

deformed membrane



$$\vec{r'}(x,y) = \vec{r}(x,y) + u_x(x,y)\vec{e}_x + u_y(x,y)\vec{e}_y + h(x,y)\vec{e}_z$$

local normal

$$\vec{n} = \frac{\vec{t}_x \times \vec{t}_y}{|\vec{t}_x \times \vec{t}_y|} = \vec{e}_z$$

local normal (neglecting in-plane deformations)

$$\vec{n'} \approx \frac{\vec{e}_z - (\partial_x h)\,\vec{e}_x - (\partial_y h)\,\vec{e}_y}{\sqrt{1 + (\partial_x h)^2 + (\partial_y h)^2}}$$

reference curvature tensor

$$K_{ij} = \vec{n} \cdot \partial_i \partial_j \vec{r} = 0$$

bending strain tensor

$$b_{ij} = K'_{ij} \approx \partial_i \partial_j h + \cdots$$

Bending energy

$$E = \int dA \left[\frac{\kappa}{2} \left(\frac{1}{R_1} + \frac{1}{R_2} - C_0 \right)^2 + \frac{\kappa_G}{R_1 R_2} \right]$$

Helfrich free energy

bending rigidity $\kappa \sim 20 k_B T$

Gaussian bending rigidity $\kappa_G \sim -0.8\kappa$

mean curvature $H = \frac{1}{2}\left(\frac{1}{R_1} + \frac{1}{R_2} \right)$

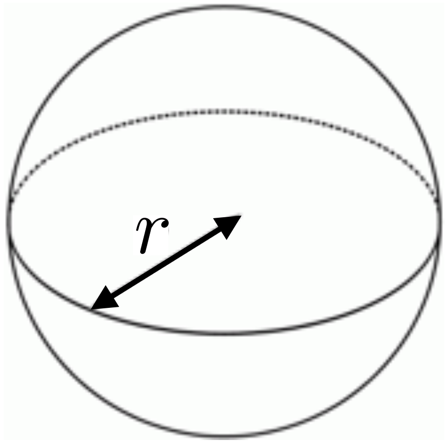
Gaussian curvature $G = \frac{1}{R_1 R_2}$

spontaneous curvature C_0

Example: bending energy for a sphere

$$\frac{1}{R_1} = \frac{1}{R_2} = \frac{1}{r}$$

$$C_0 = 0$$



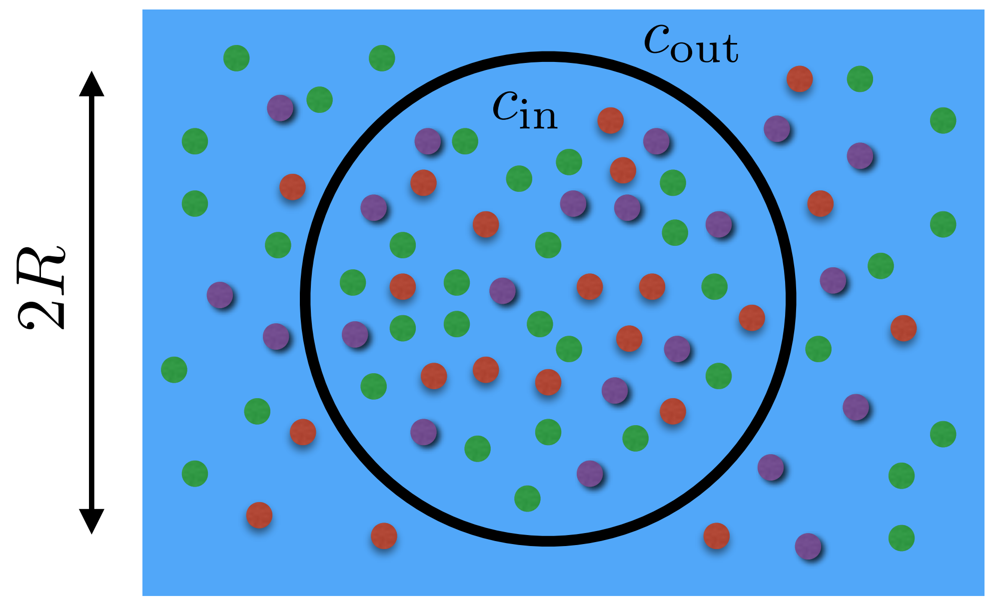
$$E = 4\pi \left(2\kappa + \kappa_G \right) \sim 300 k_B T$$

bending energy is independent of the sphere radius!

Osmotic pressure

$$\Delta p = p_{\rm in} - p_{\rm out} = k_B T (c_{\rm in} - c_{\rm out})$$

$c_{\rm in} > c_{\rm out}$

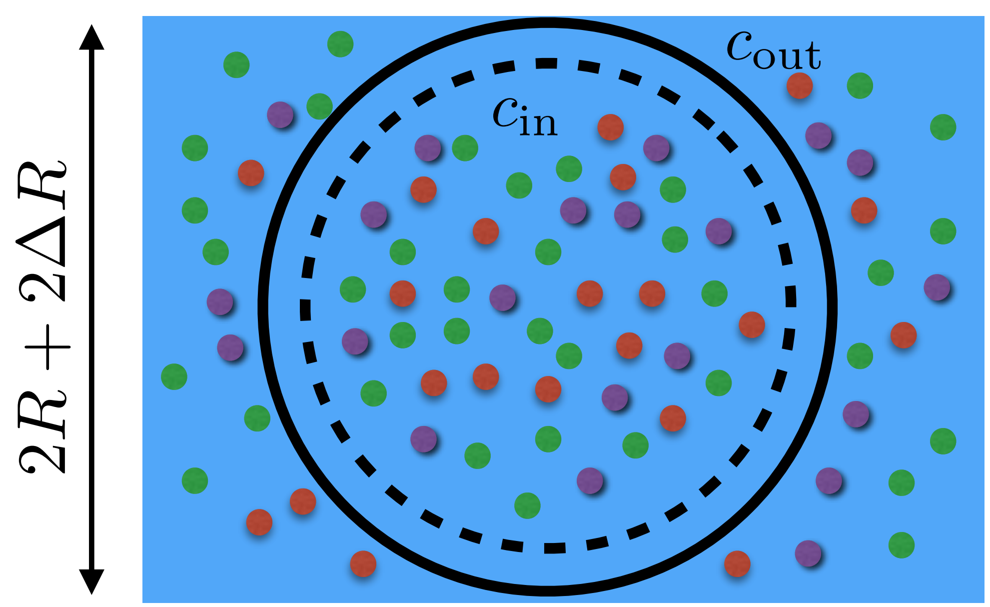


$$A = 4\pi R^2$$

$$V = \frac{4\pi R^3}{3}$$

Water flows in the cell until the mechanical equilibrium is reached.

$c_{\rm in} > c_{\rm out}$



$$\Delta A = 8\pi R \Delta R$$

$$\Delta V = 4\pi R^2 \Delta R$$

The radius of swollen cell can be estimated by minimizing the free energy.

$$E = A\frac{B}{2}\left(\frac{\Delta A}{A}\right)^2 - \Delta p \Delta V$$

$$E = 8\pi B \Delta R^2 - 4\pi R^2 \Delta p \Delta R$$

$$\frac{\Delta R}{R} = \frac{R\Delta p}{4B}$$

Membrane tension

$$\tau = B\frac{\Delta A}{A} = B\frac{2\Delta R}{R} = \frac{R\Delta p}{2}$$

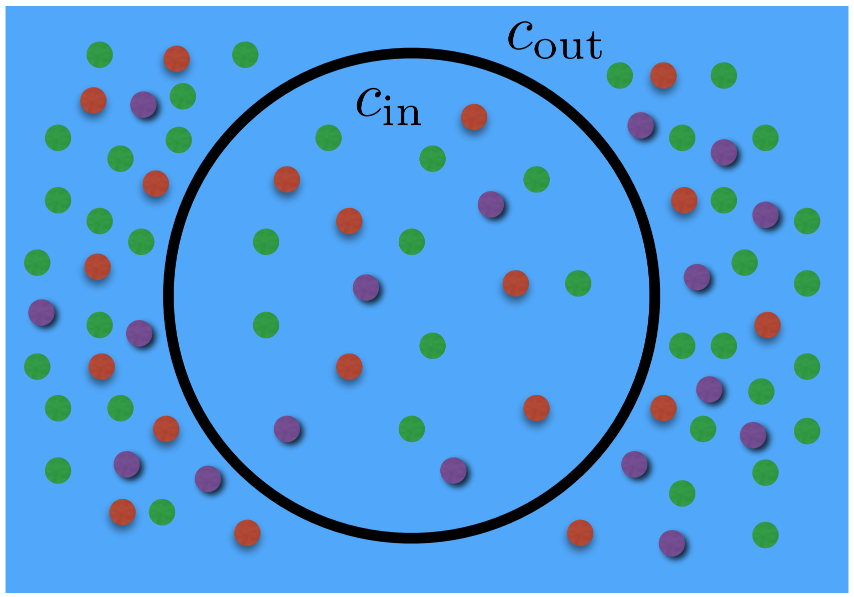
(Young-Laplace equation)

$$\Delta p = \tau\,(1/R_1 + 1/R_2)$$

Osmotic pressure

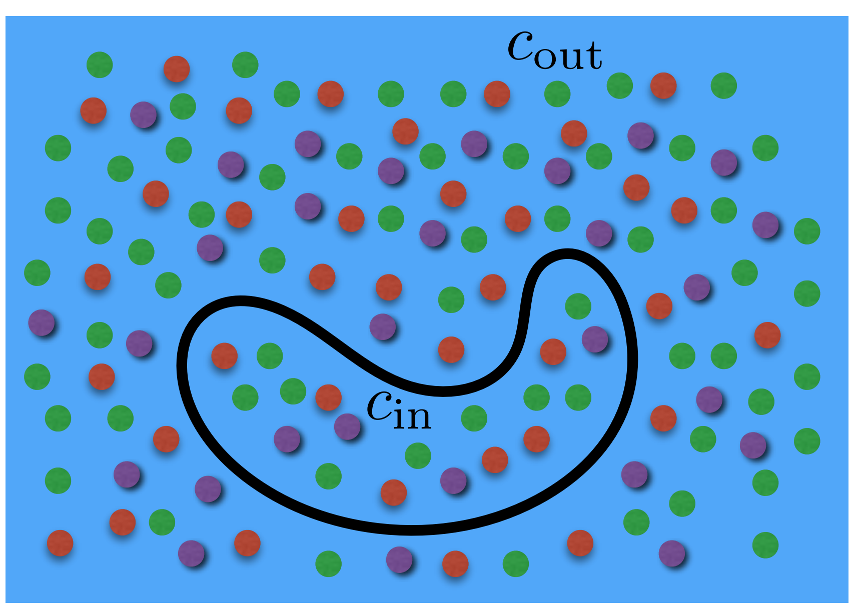
$$\Delta p = p_{\text{in}} - p_{\text{out}} = k_B T (c_{\text{in}} - c_{\text{out}})$$

$c_{\text{in}} < c_{\text{out}}$



Water flows out of the cell until concentrations become equal.

$c_{\text{in}} = c_{\text{out}}$



Total concentration of molecules inside a cell (vesicle)

$$c_{\text{in}} = \frac{N}{V}$$

Preferred cell (vesicle) volume

$$V_0 = \frac{N}{c_{\text{out}}}$$

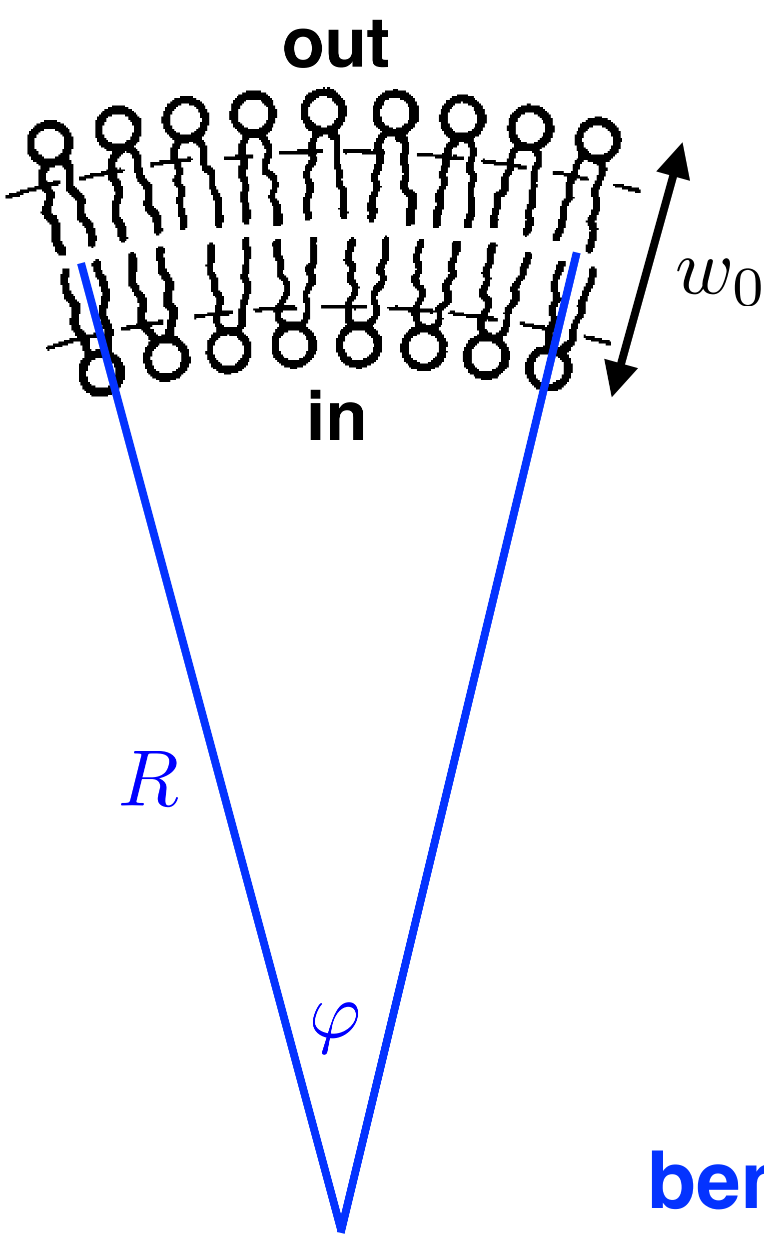
Energy cost for modifying the volume

$$E_v = -\int_{V_0}^{V} \Delta p(V) dV$$

$$E_v = -k_B T \left[N \ln \left(\frac{V}{V_0} \right) - c_{\text{out}} (V - V_0) \right]$$

$$E_v = \frac{1}{2} k_B T c_{\text{out}} V_0 \left(\frac{V - V_0}{V_0} \right)^2$$

Area difference between lipid layers



Length difference for 2D example on the left

$$\Delta\ell = \ell_{\text{out}} - \ell_{\text{in}} = (R + w_0/2)\varphi - (R - w_0/2)\varphi$$

$$\Delta\ell = w_0\varphi = \frac{w_0\ell}{R}$$

Area difference between lipid layers in 3D

$$\Delta A = A_{\text{out}} - A_{\text{in}} = w_0 \int dA \left(\frac{1}{R_1} + \frac{1}{R_2}\right)$$

Lipids can move within a given layer, but flipping between layers is unlikely. This sets a preferred area difference ΔA_0 .

Non-local bending energy

$$E = \frac{k_r}{2Aw_0^2}\left(\Delta A - \Delta A_0\right)^2$$

$$k_r \approx 3\kappa \approx 60 k_B T$$

Total elastic energy for cells (vesicles)

Shape of cells (vesicles) can be obtained by minimizing the total elastic energy

this term is constant for a given topology

$$E = \int dA \left[\frac{1}{2}(B-\mu)u_{ii}^2 + \mu u_{ij}^2 + \frac{\kappa}{2}\left(\frac{1}{R_1}+\frac{1}{R_2}-C_0\right)^2 + \frac{\kappa_G}{R_1 R_2}\right]$$

$$+ \frac{k_r}{2A_0 w_0^2}(\Delta A - \Delta A_0)^2 + \frac{1}{2}k_B T c_{\mathrm{out}} V_0 \left(\frac{V-V_0}{V_0}\right)^2$$

Energetically it is very costly to change the cell volume V_0 and the membrane area A_0 (large bulk modulus B)!

Introduce dimensionless quantities that would be equal to 1 for sphere

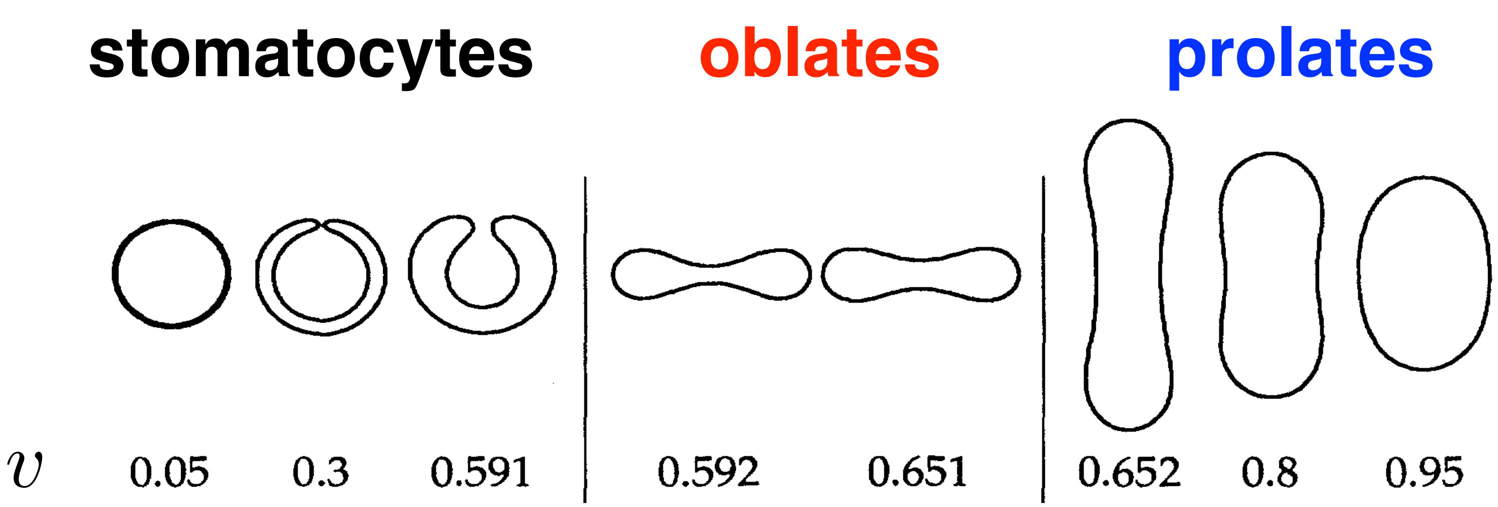
definition for sphere radius	dimensionless area	dimensionless volume	dimensionless curvature	dimensionless area difference between layers	dimensionless energy
$R_0 = \sqrt{\frac{A_0}{4\pi}}$	$a = \frac{A_0}{4\pi R_0^2} = 1$	$v = \frac{V_0}{4\pi R_0^3/3}$	$c_0 = C_0 R_0$	$\Delta a = \frac{\Delta A_0}{8\pi w_0 R_0}$	$e = \frac{E}{8\pi\kappa}$

Minimal model: minimization of bending energy for lipid vesicles

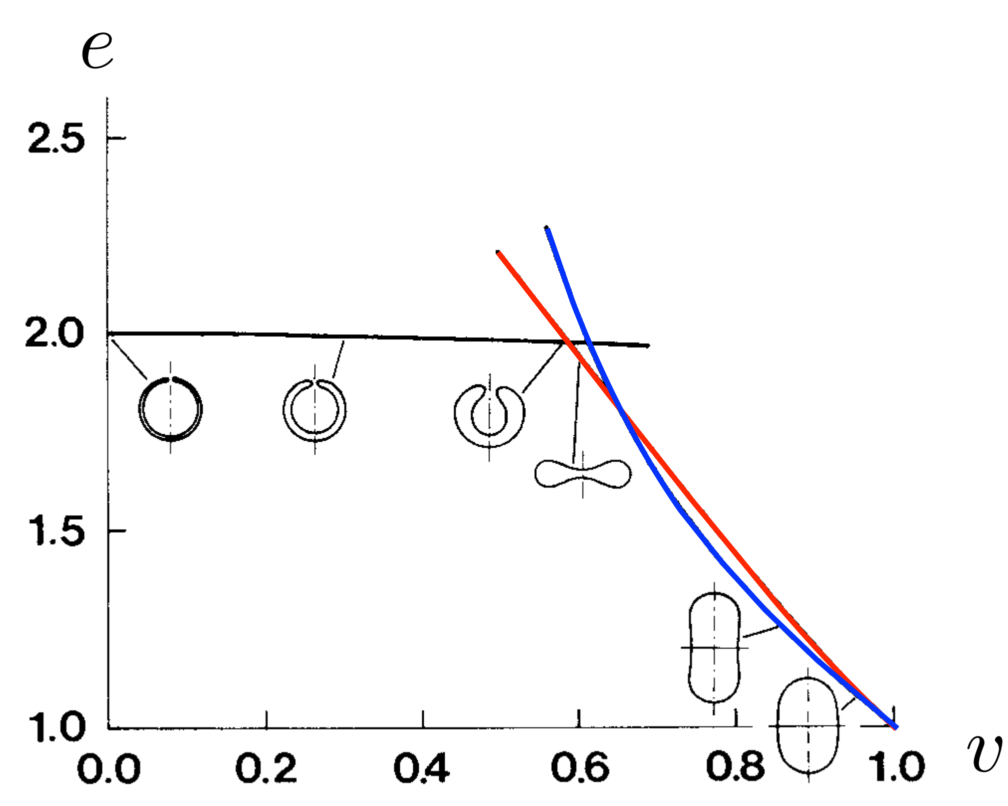
Find the shape of vesicles that minimize bending energy by constraining the volume to *v*<1.

$$e = \int \frac{da}{4} \left(\frac{1}{r_1} + \frac{1}{r_2} \right)^2$$

Minimum energy configurations



U. Seifert *et al.*, PRA 44, 1182 (1991)

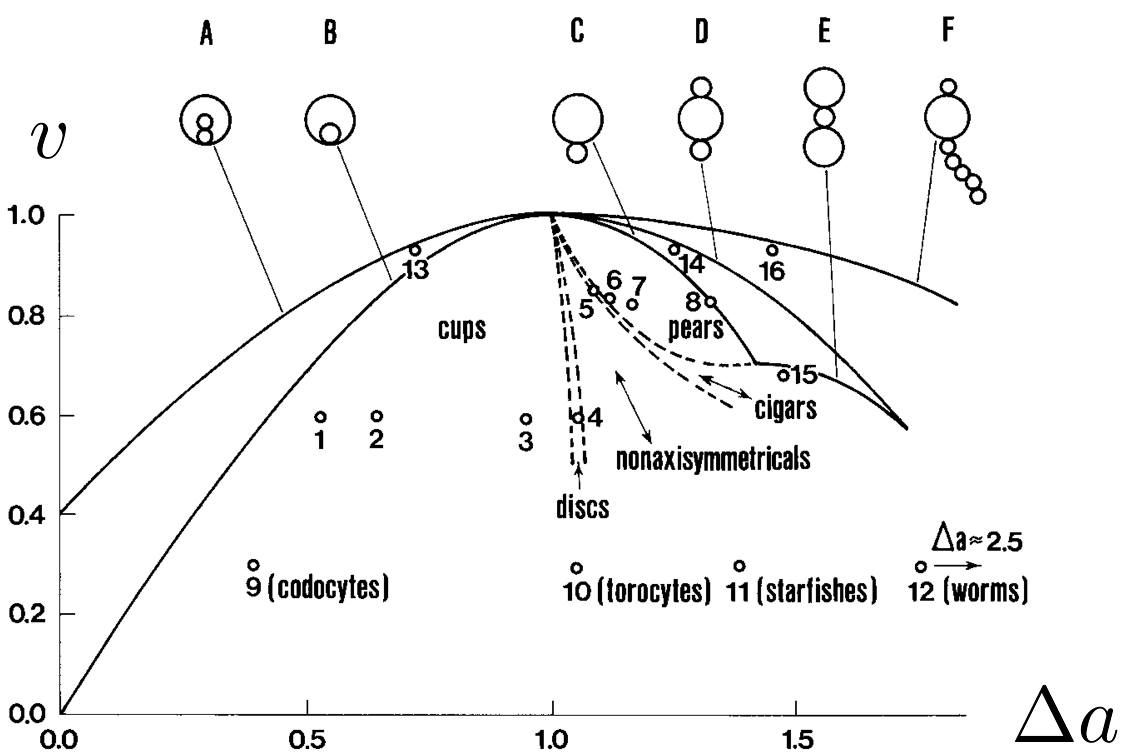


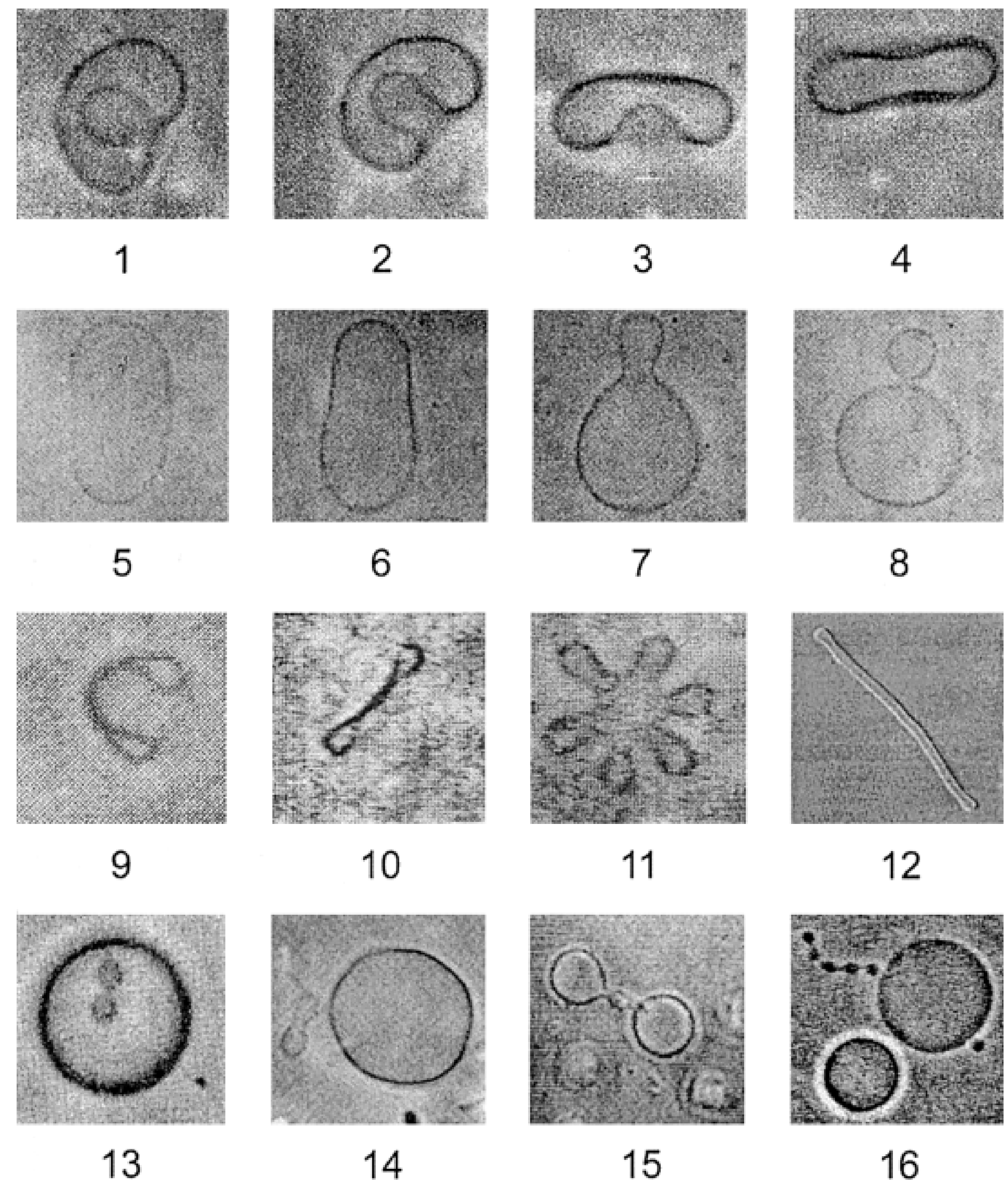
S. Svetina and B. Zeks, Anat. Rec. 268, 215 (2002)

Bilayer couple model of vesicles

$$e = \int \frac{da}{4}\left(\frac{1}{r_1} + \frac{1}{r_2} - c_0\right)^2 + \frac{k_r}{\kappa}\left(\Delta a - \Delta a_0\right)^2$$

Phase diagram of vesicle shapes that minimize the free energy for $c_0 = 0,\ k_r/\kappa \to \infty$.

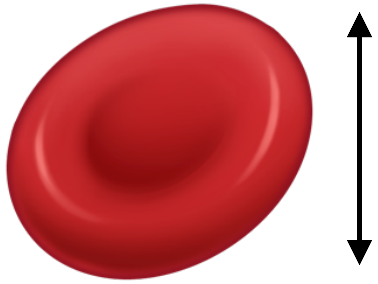




S. Svetina and B. Zeks,
Anat. Rec. 268, 215 (2002)

Shape of red blood cells

In the usual environment red blood cells have discocyte shape. Modifying cell environment can induce different shapes.

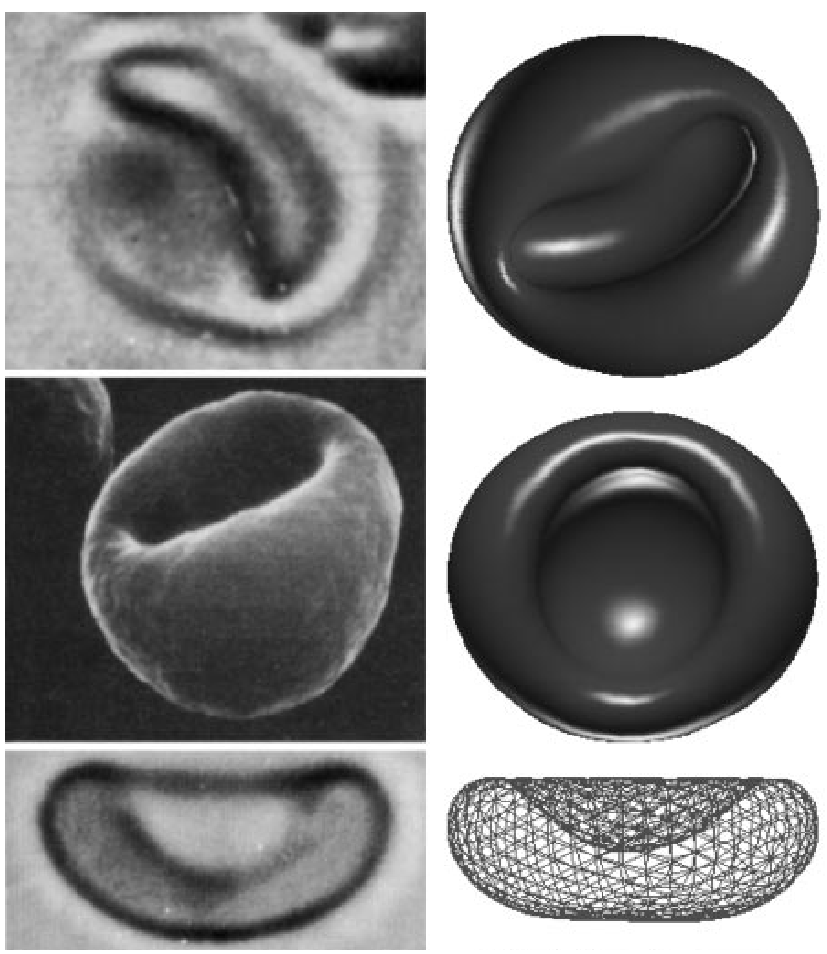


$\sim 7\mu\text{m}$

stomatocytes

cationic amphipaths, low salt, low pH, cholesterol depletion

experiments **simulations** $v = 0.950$



$\Delta a_0 = -0.858$

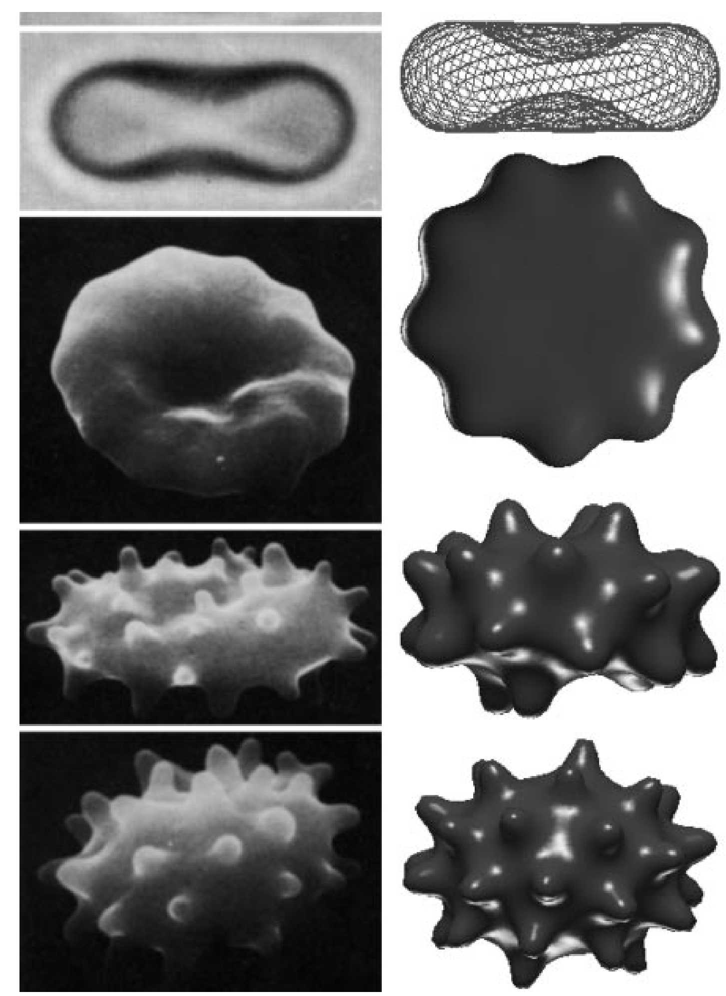
$\Delta a_0 = -0.358$

$\Delta a_0 = 0.072$

echinocytes

anionic amphipaths, high salt, high pH, cholesterol enrichment

experiments **simulations** $v = 0.950$



$\Delta a_0 = 0.143$

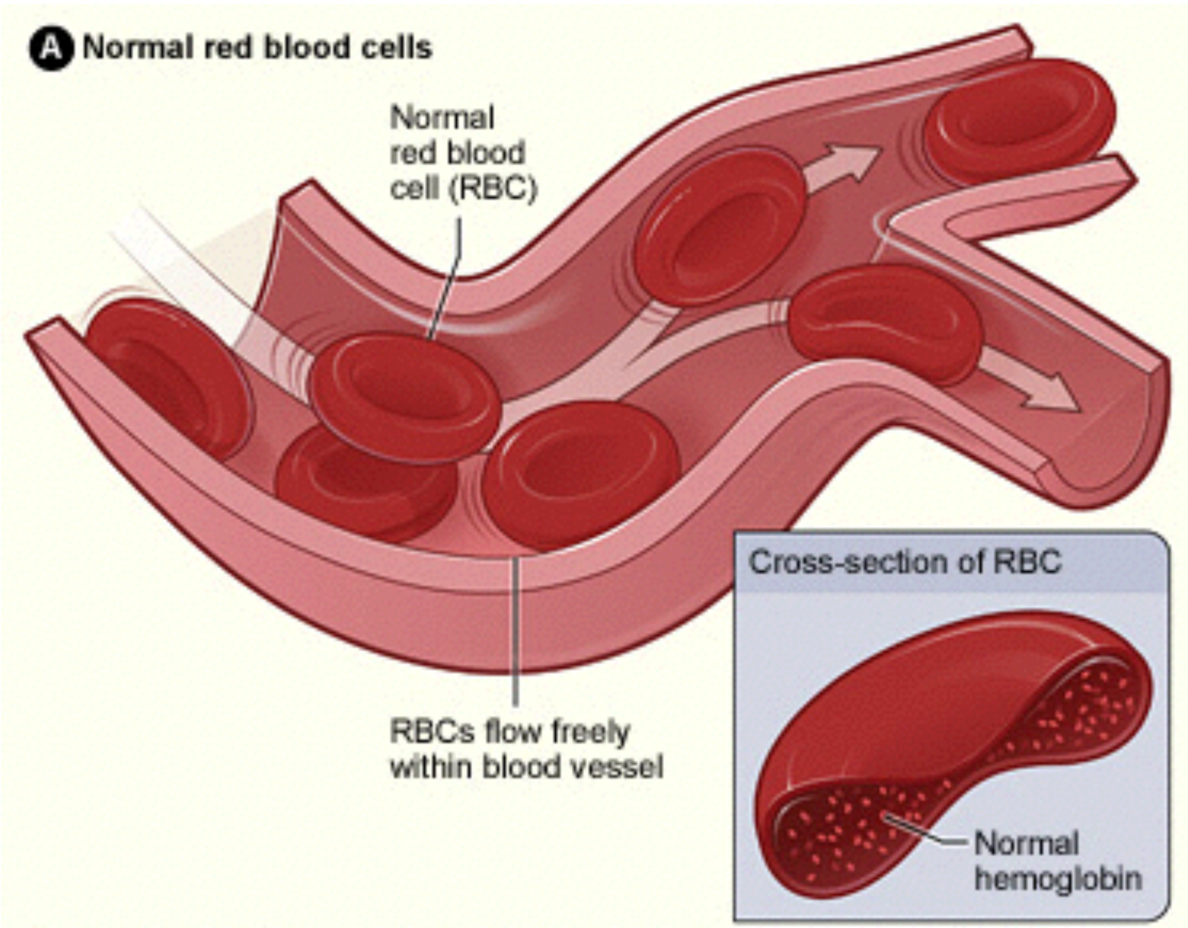
$\Delta a_0 = 1.717$

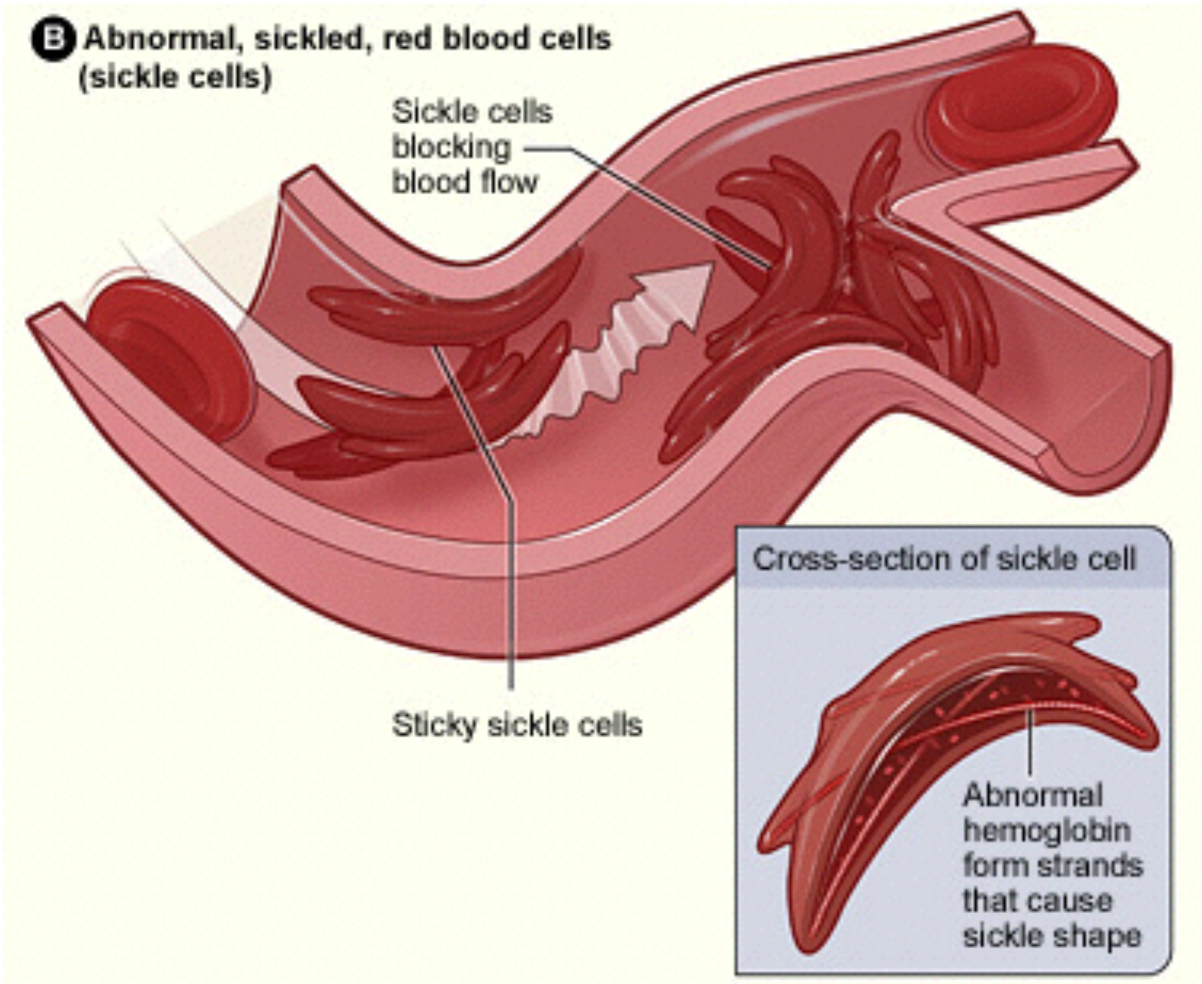
$\Delta a_0 = 1.788$

$\Delta a_0 = 2.003$

G. Lim *et al.*, PNAS 99, 16766 (2002)

Sickle-cell disease (anaemia)





In low oxygen environment hemoglobin proteins inside sickle cells polymerize and form long strands.

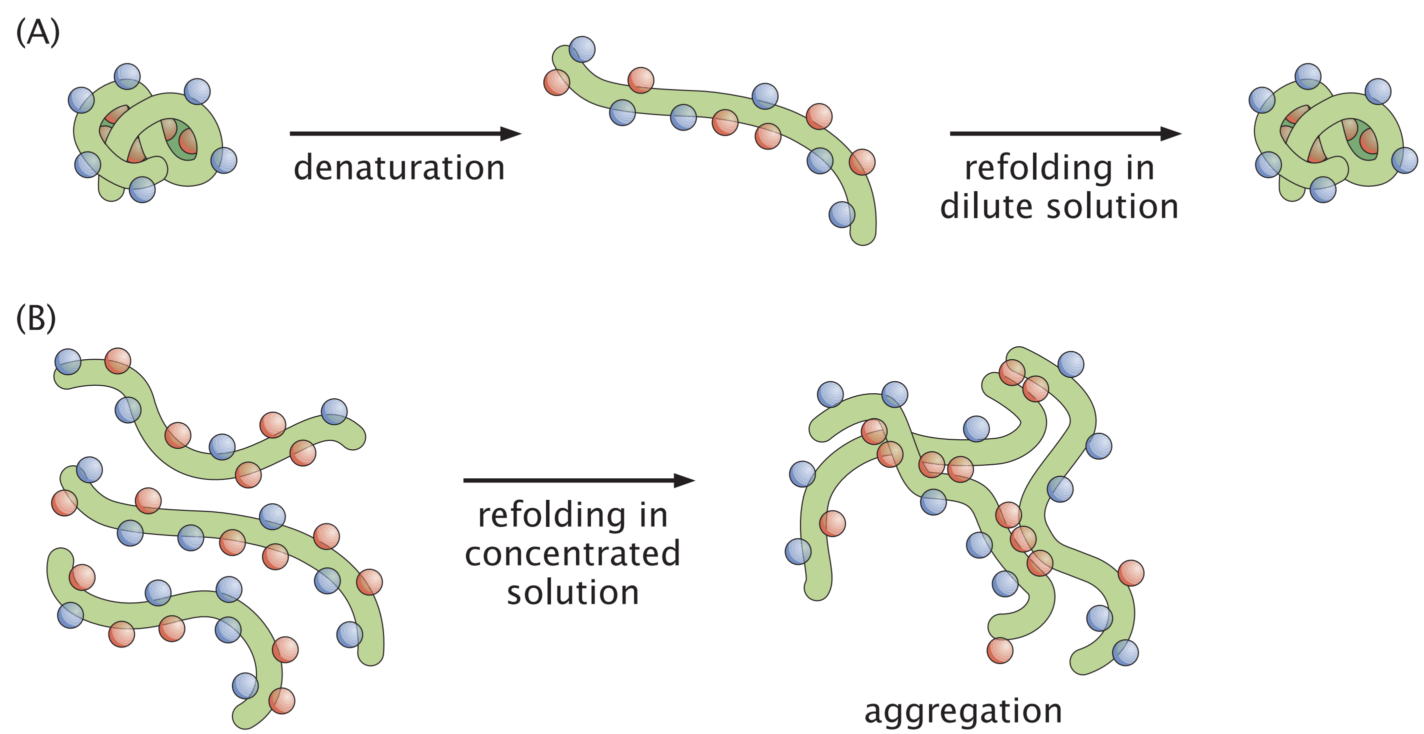
Sickle cells are much stiffer and cannot deform in order to pass through small capillaries.

Wikipedia

Protein aggregation and diseases

(A) In dilute solution misfolded proteins refold back into their native state.

R. Phillips et al., Physical Biology of the Cell



hydrophilic amino acids

hydrophobic amino acids

(B) In concentrated solution misfolded proteins tend to form aggregates.

Cells have special proteins called chaperons, which assist proteins folding into their native state and thus prevent aggregation.

Protein aggregation is a cause of many diseases (Alzheimer's, Parkinson's, …)

What happens in the presence of thermal fluctuations?

flat phase

low temperature phase

$$k_B T \lesssim \kappa$$

crumpled phase

high temperature phase

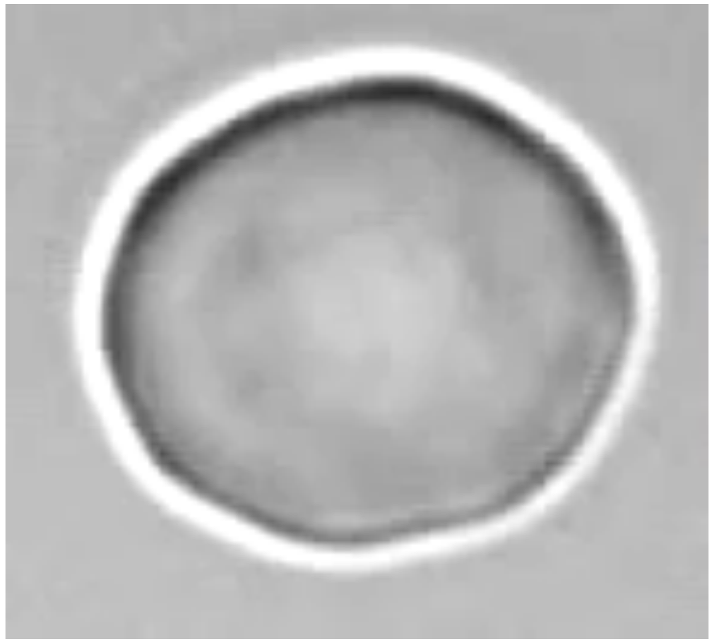
$$k_B T \gtrsim \kappa$$

$$T^* \sim \kappa/k_B \sim 6000\text{K}$$

This phase hasn't been observed experimentally, because membranes melt before reaching this temperature!

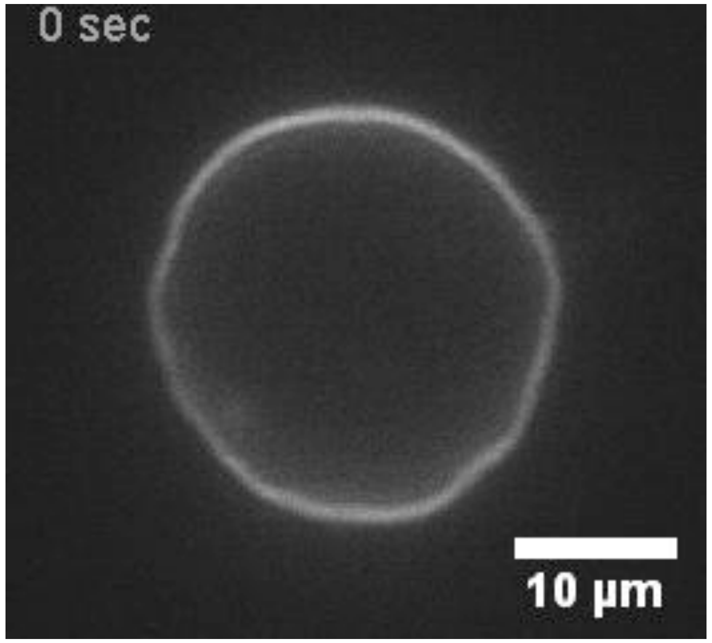
Flickering of cells

red blood cells



https://www.youtube.com/watch?v=VwhNLaRCD-4

giant lipid vesicles



A. F. Loftus et al., Langmuir 29, 14588 (2013)

For flat membranes

amplitude of height fluctuations at low temperatures

$$\left\langle |\tilde{h}(\vec{q})|^2 \right\rangle \approx \frac{k_B T}{A(\kappa|\vec{q}|^4 + \tau|\vec{q}|^2)}$$

frequency of oscillations

$$\omega(\vec{q}) \approx \sqrt{\frac{(\kappa|\vec{q}|^4 + \tau|\vec{q}|^2)}{\rho}}$$

In bacteria thermal fluctuations are suppressed due to the surface tension generated by large internal pressure!

Fourier modes $h(\vec{x}) = \sum_{\vec{q}} e^{i\vec{q}\cdot\vec{x}} \tilde{h}(\vec{q})$

membrane area A

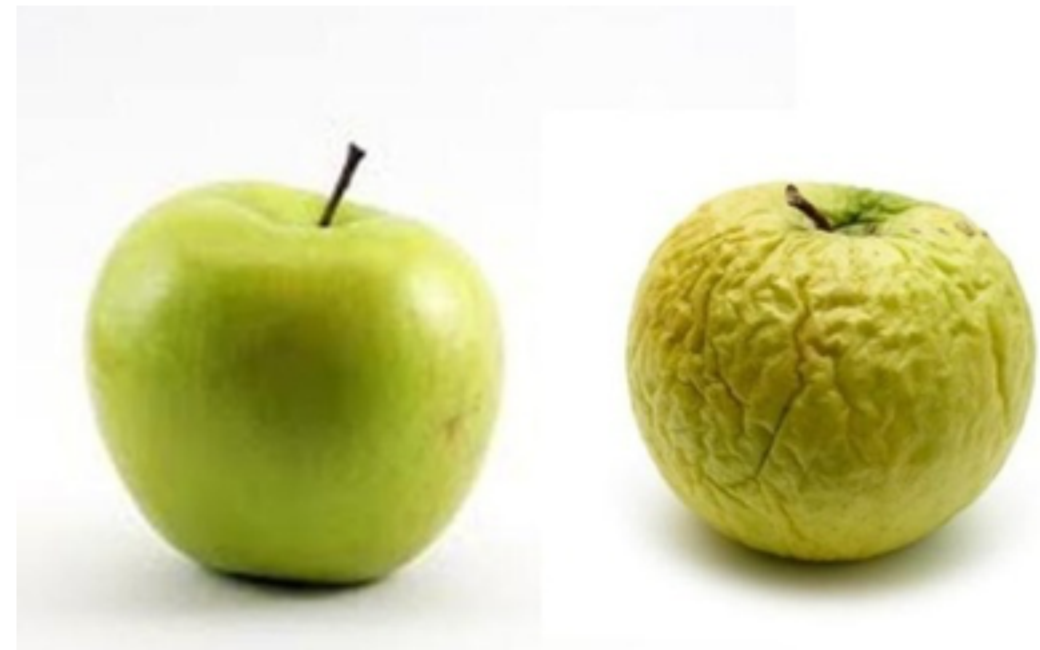
mass density per unit area ρ

surface tension τ

Why do we get wrinkled surfaces?

Fingers after being exposed to water for some time

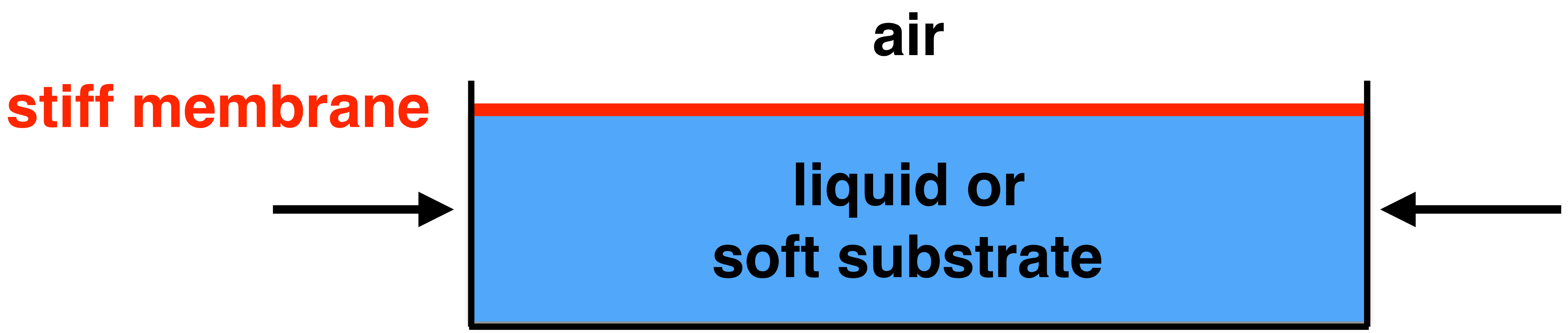
Old apple



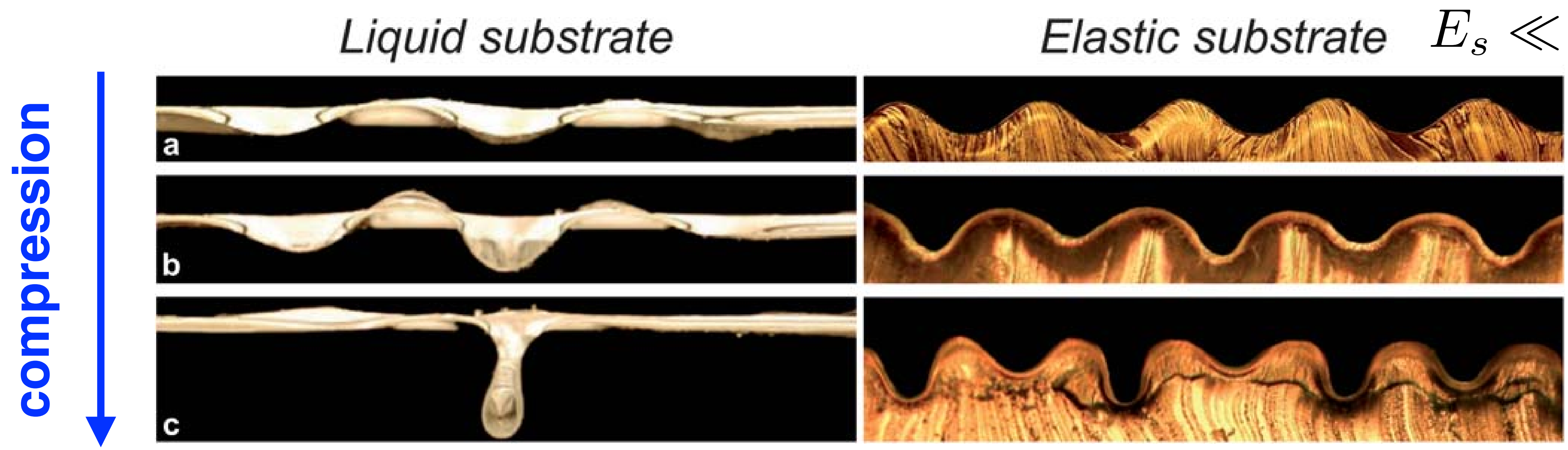
Brain

Rising dough

Compression of stiff thin membranes on liquid and soft elastic substrates



$E_s \ll E_m$



10 μm thin sheet of polyester on water

$$\lambda_0 \sim 1.6\text{cm}$$

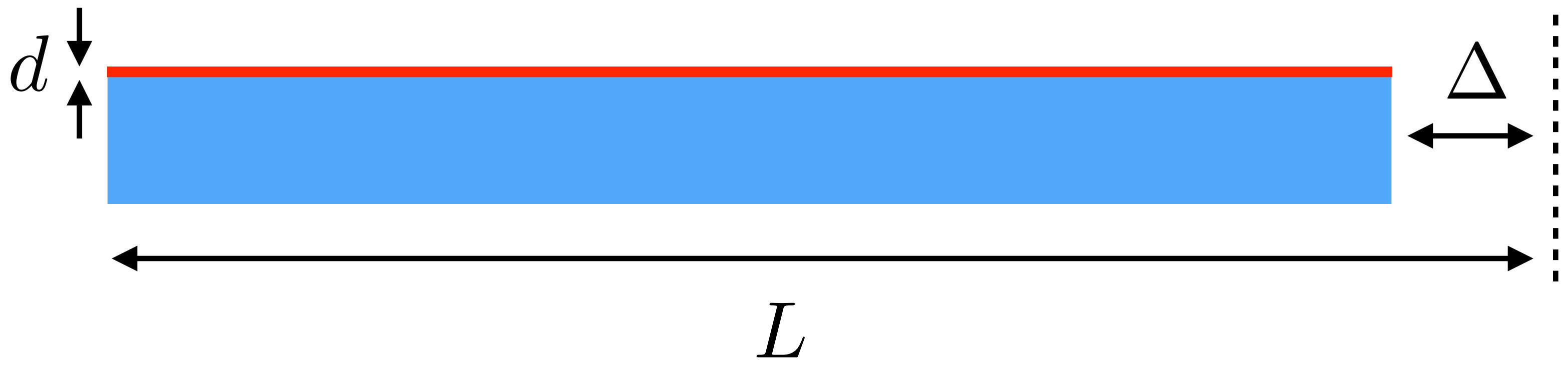
~10 μm thin PDMS (stiffer) sheet on PDMS (softer) substrate

$$\lambda_0 \sim 70\mu\text{m}$$

L. Pocivavsek et al., Science 320, 912 (2008)

F. Brau et al., Soft Matter 9, 8177 (2013)

Compression of stiff thin membranes on liquid substrates



compression energy of thin membrane

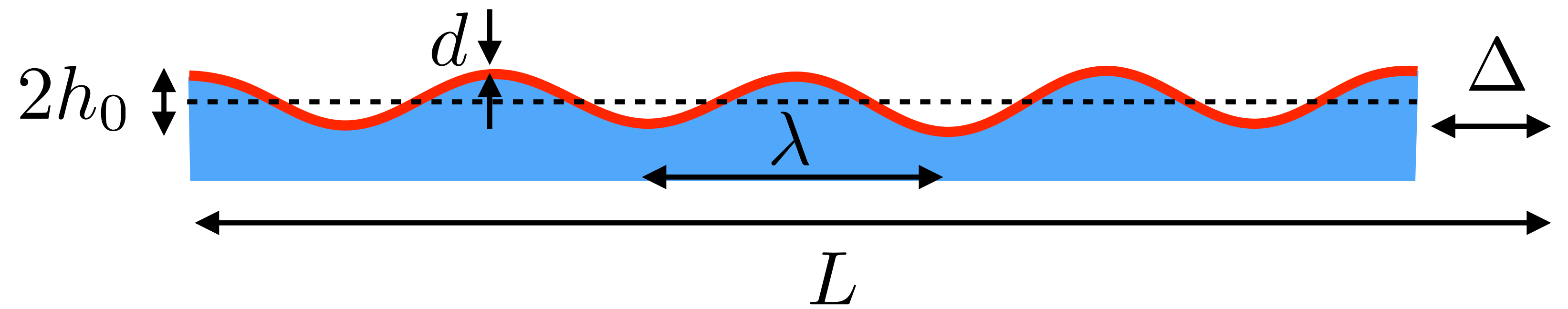
$$U_c \sim A \times E_m d \times \epsilon^2$$

membrane area	membrane 3D Young's modulus	strain	liquid density
$A = WL$	E_m	$\epsilon = \frac{\Delta}{L}$	ρ

Compression of stiff thin membranes on liquid substrates

assumed profile

$$h(s) = h_0 \cos(2\pi s/\lambda)$$



projected length assuming that membrane doesn't stretch

$$L - \Delta = \int_0^L ds \sqrt{1 - h'(s)^2} \approx \int_0^L ds \left(1 - h'(s)^2/2\right) \approx L\left(1 - \frac{\pi^2 h_0^2}{\lambda^2}\right)$$

amplitude of wrinkles

$$h_0 = \frac{\lambda}{\pi}\sqrt{\frac{\Delta}{L}} = \frac{\lambda\sqrt{\epsilon}}{\pi}$$

bending energy of stiff membrane

$$U_b \sim A \times \kappa \times \frac{1}{R^2} \sim A \times E_m d^3 \times \frac{h_0^2}{\lambda^4} \sim \frac{A E_m d^3 \epsilon}{\lambda^2}$$

potential energy of liquid

$$U_p \sim m \times g \times \Delta h \sim \rho \times A h_0 \times g \times h_0 \sim A \rho g \lambda^2 \epsilon$$

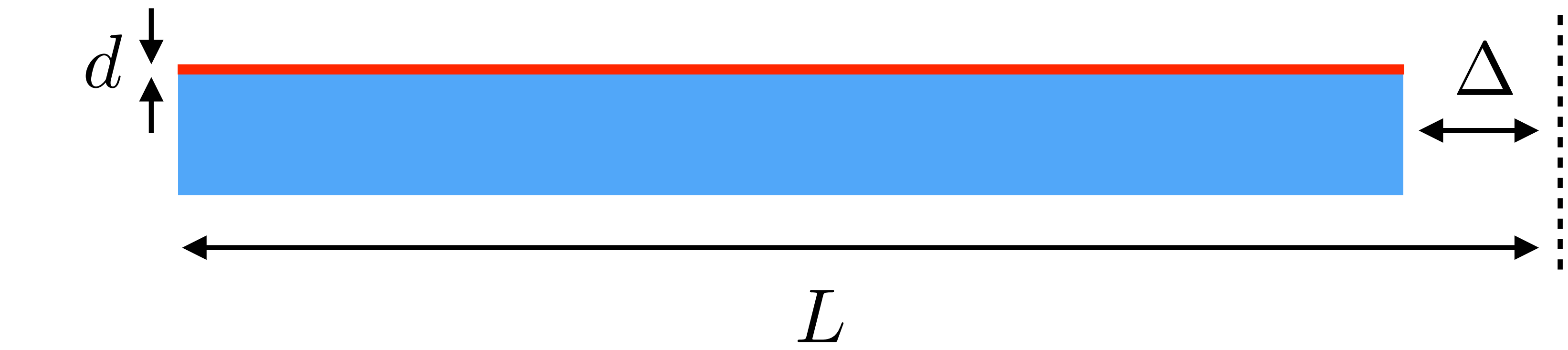
minimize total energy (U_b+U_p) with respect to λ →

$$\lambda \sim \left(\frac{E_m d^3}{\rho g}\right)^{1/4}$$

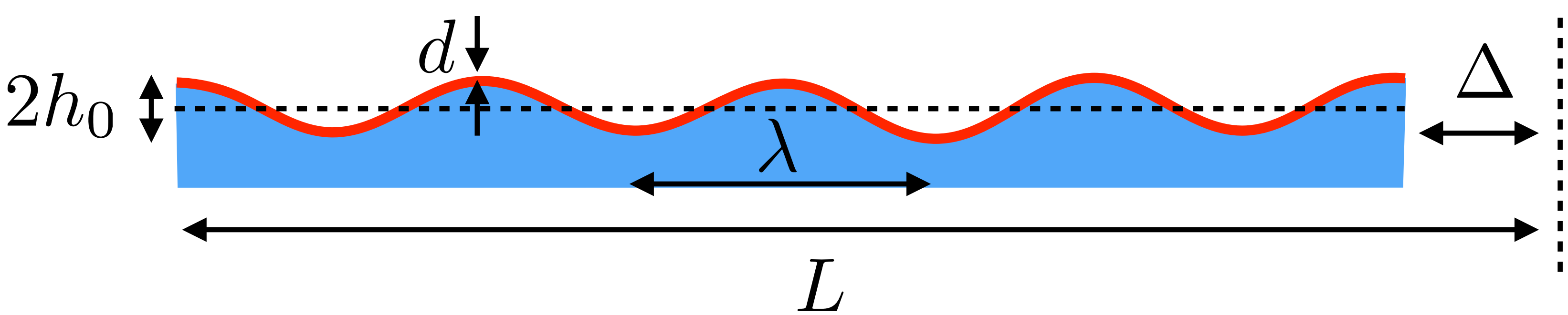
→

$$U_b, U_p \sim A\epsilon\sqrt{E_m d^3 \rho g}$$

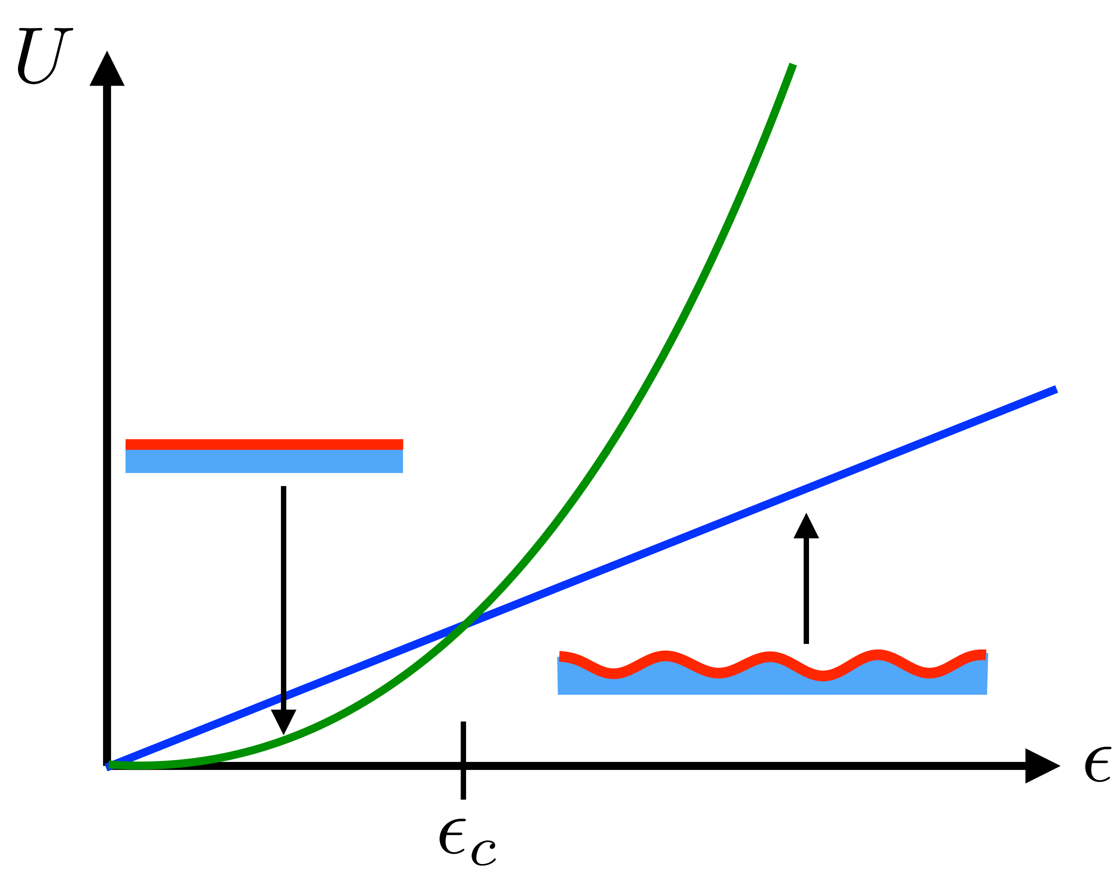
Compression of stiff thin membranes on liquid substrates



$$U_c \sim A \times E_m d \times \epsilon^2$$



$$U_b, U_p \sim A\epsilon\sqrt{E_m d^3 \rho g}$$



wrinkles are stable above the critical strain

$$\epsilon > \epsilon_c \sim \sqrt{\frac{\rho g d}{E_m}}$$

wavelength of wrinkles

$$\lambda \sim \left(\frac{E_m d^3}{\rho g}\right)^{1/4}$$

amplitude of wrinkles at the critical strain

$$h_0^* \sim \lambda\sqrt{\epsilon_c} \sim d$$

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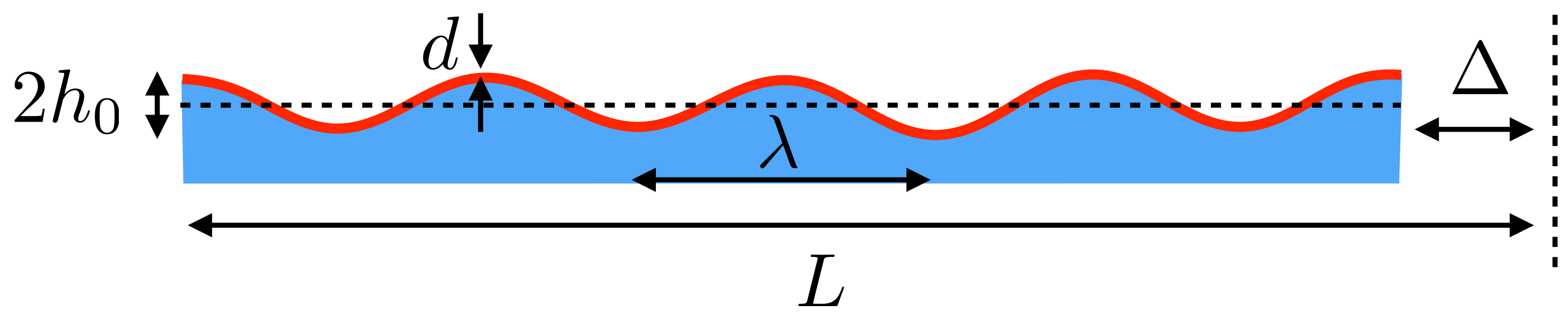
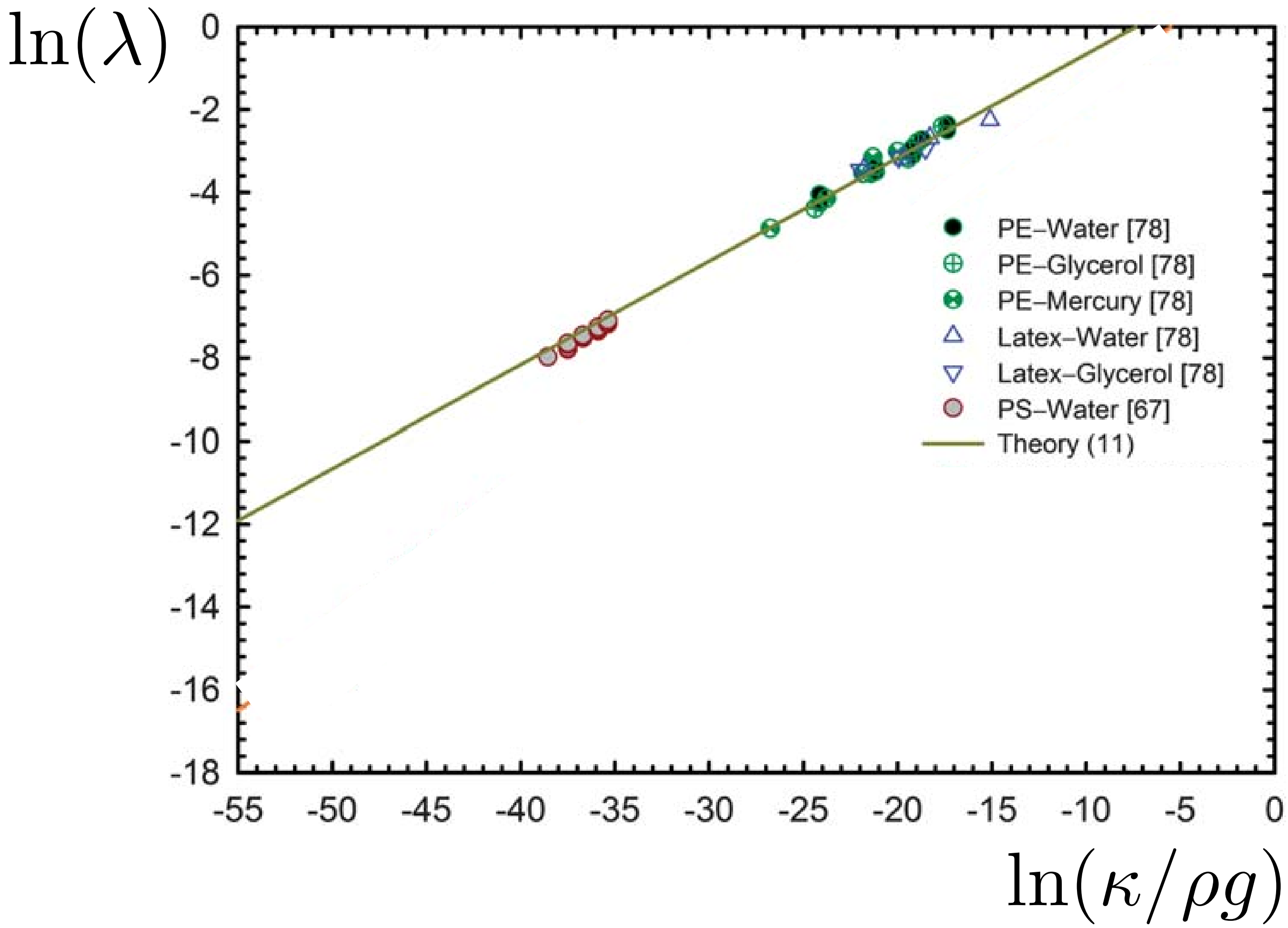


scaling analysis

$$\lambda \sim \left(\frac{E_m d^3}{\rho g} \right)^{1/4}$$

exact result

$$\lambda = 2\pi \left(\frac{\kappa}{\rho g} \right)^{1/4}$$



F. Brau et al., Soft Matter 9, 8177 (2013)