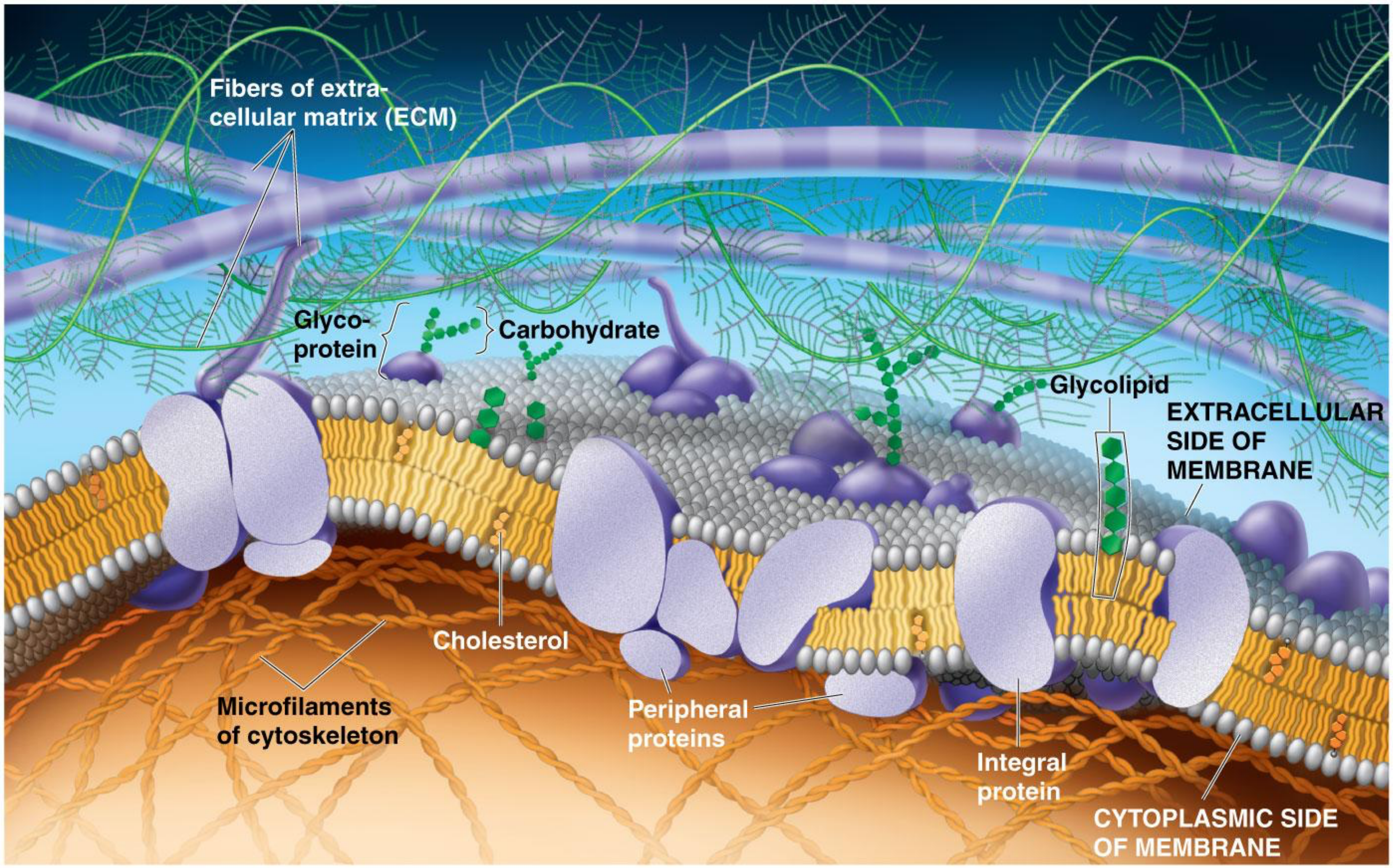
MAE 545: Lectures 12,13 (3/27)

Osmotic pressure and mechanics of cell membranes



Gibbs free energy

$$\boxed{G = E + pV - TS = \sum_i N_i \mu_i}$$

energy — pressure, volume — temperature, entropy — chemical potential of component *i*

Entropy

$$S = k_B \ln \Omega$$

Boltzmann constant — number of configurations

Derivatives of system energy

$$dE = TdS - pdV + \sum_i \mu_i dN_i$$

$$T = \left(\frac{\partial E}{\partial S}\right)_{V,N_i} \qquad p = -\left(\frac{\partial E}{\partial V}\right)_{S,N_i}$$

$$\mu_i = \left(\frac{\partial E}{\partial N_i}\right)_{S,V}$$

Derivatives of Gibbs free energy

$$dG = -SdT + Vdp + \sum_i \mu_i dN_i$$

$$S = -\left(\frac{\partial G}{\partial T}\right)_{p,N_i} \qquad V = \left(\frac{\partial G}{\partial p}\right)_{T,N_i}$$

$$\mu_i = \left(\frac{\partial G}{\partial N_i}\right)_{T,p}$$

In thermodynamic equilibrium system minimizes Gibbs free energy, when temperature *T* and pressure *p* are fixed!

Charge dissociation in solution

example
NaCl salt

binding energy

$$-E_b$$

entropy

$$k_B \ln v_0$$

some characteristic volume

interaction energy

$$\approx 0$$

entropy

$$k_B \ln(V/N)$$

volume of the whole system

number of dissociated pairs

Free energy change for charge dissociation

$$\Delta G = \Delta E - T\Delta S = E_b - k_B T \ln(V/N v_0)$$

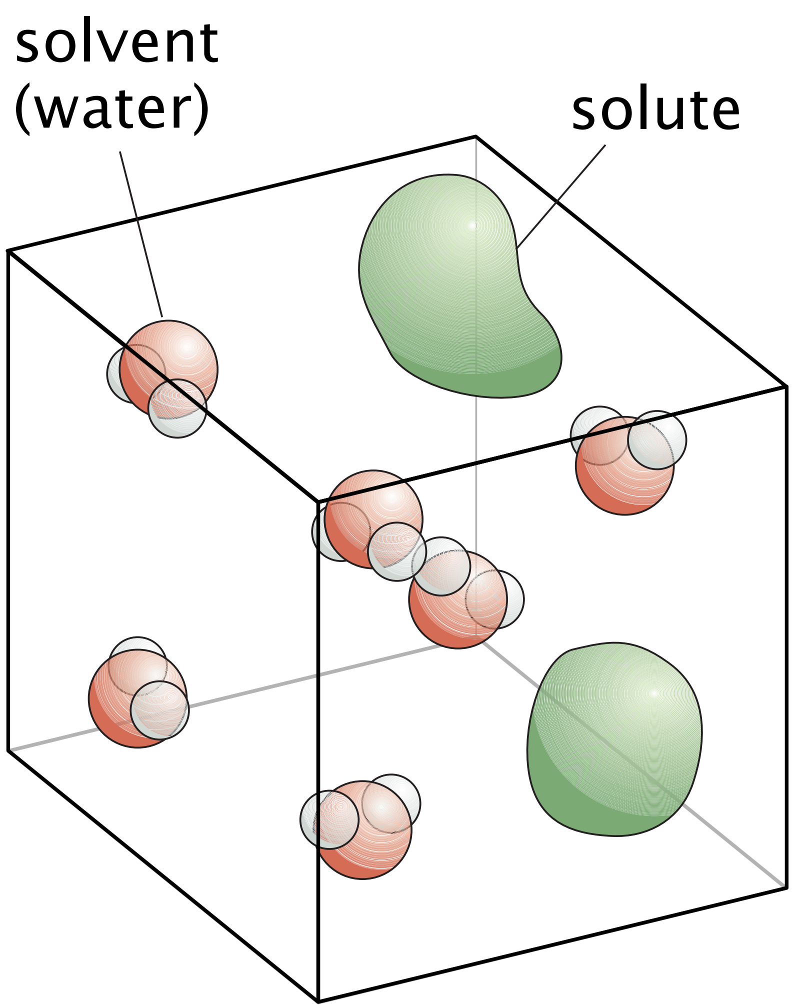
In thermodynamic equilibrium $\Delta G = 0$

$$\boxed{c = \frac{N}{V} = \frac{1}{v_0} e^{-E_b/k_B T}}$$

concentration of dissociated ions

Entropy is the reason why many molecules dissociate and ionize in solution!

Free energy of dilute solutions



Ideal solution: interactions between solute particles are negligible

Gibbs free energy of ideal solution

$$\boxed{G = N_{\mathrm{H_2O}}\mu^0_{\mathrm{H_2O}} + N_s\epsilon_s - TS_{\mathrm{mix}}}$$

water free energy | **solute energy** | **mixing entropy**

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

Mixing entropy of dilute solutions

Let's divide volume in small boxes each containing one water molecule or one solute molecule.

How many different configurations of water and solute molecules are possible?

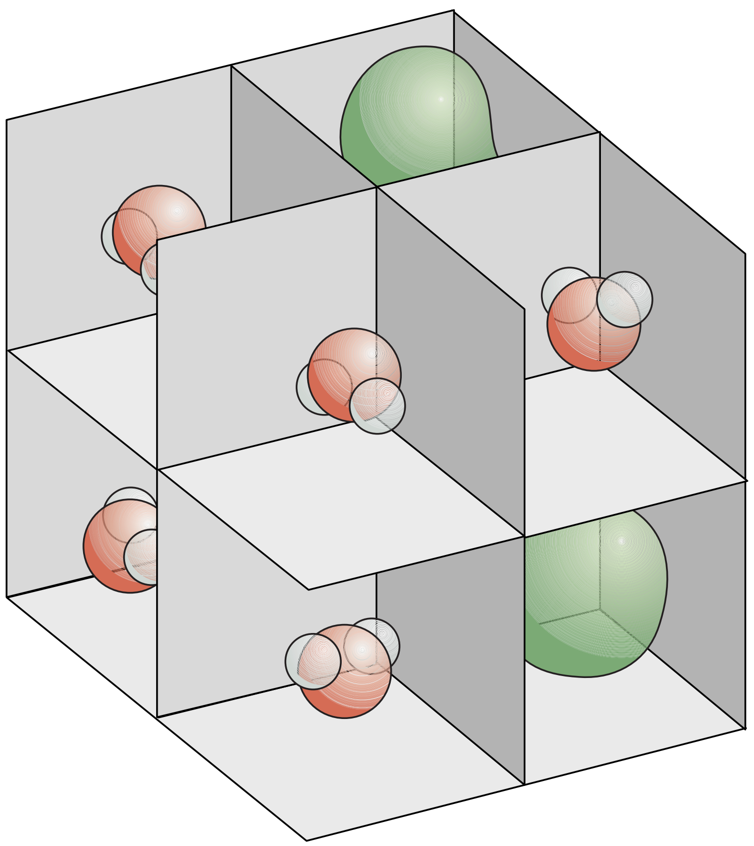


Figure from R. Phillips et al., Physical Biology of the Cell

$$\Omega = \binom{N_{\mathrm{H_2O}} + N_s}{N_s} = \frac{(N_{\mathrm{H_2O}} + N_s)!}{N_{\mathrm{H_2O}}!N_s!}$$

$$S_{\mathrm{mix}} = k_B \ln \Omega$$

Stirling approximation

$\ln N! \approx N \ln N$

$$S_{\mathrm{mix}} \approx k_B \left[N_{\mathrm{H_2O}} \ln \left(\frac{N_{\mathrm{H_2O}} + N_s}{N_{\mathrm{H_2O}}} \right) + N_s \ln \left(\frac{N_{\mathrm{H_2O}} + N_s}{N_s} \right) \right]$$

Small number of solute particles $N_s \ll N_{\mathrm{H_2O}}$

$$S_{\mathrm{mix}} \approx k_B \left[N_s - N_s \ln \left(\frac{N_s}{N_{\mathrm{H_2O}}} \right) \right]$$

Chemical potentials in dilute solution

$$G = N_{\mathrm{H_2O}}\mu^0_{\mathrm{H_2O}} + N_s\epsilon_s - TS_{\mathrm{mix}}$$

$$G \approx N_{\mathrm{H_2O}}\mu^0_{\mathrm{H_2O}} + N_s\epsilon_s + k_BT\left[N_s \ln\left(\frac{N_s}{N_{\mathrm{H_2O}}}\right) - N_s\right]$$

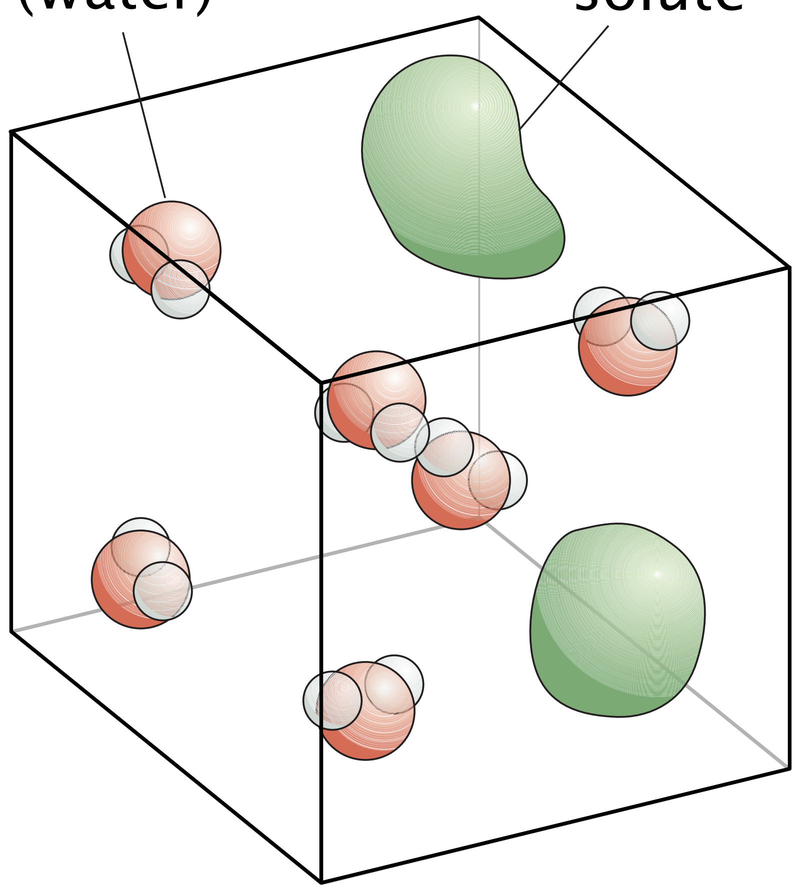


Figure from R. Phillips et al.,
Physical Biology of the Cell

Chemical potential of solute

$$\mu_s = \frac{\partial G}{\partial N_s} = \epsilon_s + k_BT\ln\left(\frac{N_s}{N_{\mathrm{H_2O}}}\right)$$

$$\boxed{\mu_s(T,p,c_s) = \epsilon_s(T,p) + k_BT\ln(c_sv)}$$

solute concentration $c_s = N_s/V$

volume occupied by one water molecule $v = V/N_{\mathrm{H_2O}}$

Chemical potential of water

$$\mu_{\mathrm{H_2O}} = \frac{\partial G}{\partial N_{\mathrm{H_2O}}} = \mu^0_{\mathrm{H_2O}} - k_BT\frac{N_s}{N_{\mathrm{H_2O}}}$$

$$\boxed{\mu_{\mathrm{H_2O}}(T,p,c_s) = \mu^0_{\mathrm{H_2O}}(T,p) - k_BTc_sv}$$

Osmotic pressure

Small water molecules can pass through a semipermeable membrane, which blocks large solute macromolecules.

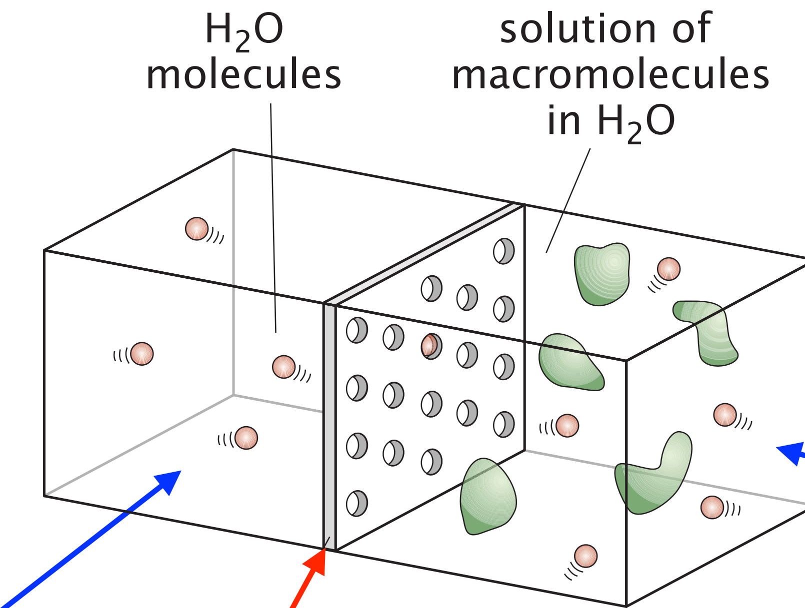


Figure from R. Phillips et al., Physical Biology of the Cell

$$G = N_1 \mu_{\mathrm{H_2O}}(T, p_1, 0) + N_2 \mu_{\mathrm{H_2O}}(T, p_2, c_s) + N_s \mu_s(T, p_2, c_s)$$

In thermodynamic equilibrium the Gibbs free energy *G* is minimized, which means that chemical potentials of water are the same on both sides of the semipermeable membrane!

$$\boxed{\mu_{\mathrm{H_2O}}(T, p_1, 0) = \mu_{\mathrm{H_2O}}(T, p_2, c_s)}$$

Osmotic pressure

Water flows from region of low concentration of macromolecules to region of large concentrations. This additional water increases pressure and the water stops flowing once the osmotic pressure is reached.

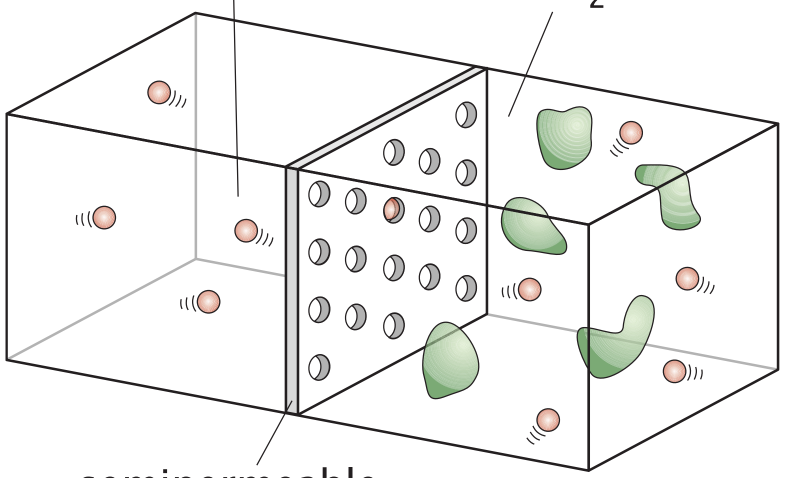


Figure from R. Phillips et al., Physical Biology of the Cell

$$\mu_{\mathrm{H_2O}}(T, p_1, 0) = \mu_{\mathrm{H_2O}}(T, p_2, c_s)$$

$$\mu_{\mathrm{H_2O}}(T, p_2, c_s) = \mu^0_{\mathrm{H_2O}}(T, p_2) - k_B T c_s v$$

$$\mu_{\mathrm{H_2O}}(T, p_2, c_s) \approx \mu^0_{\mathrm{H_2O}}(T, p_1) + \left(\frac{\partial \mu^0_{\mathrm{H_2O}}}{\partial p}\right)(p_2 - p_1) - k_B T c_s v$$

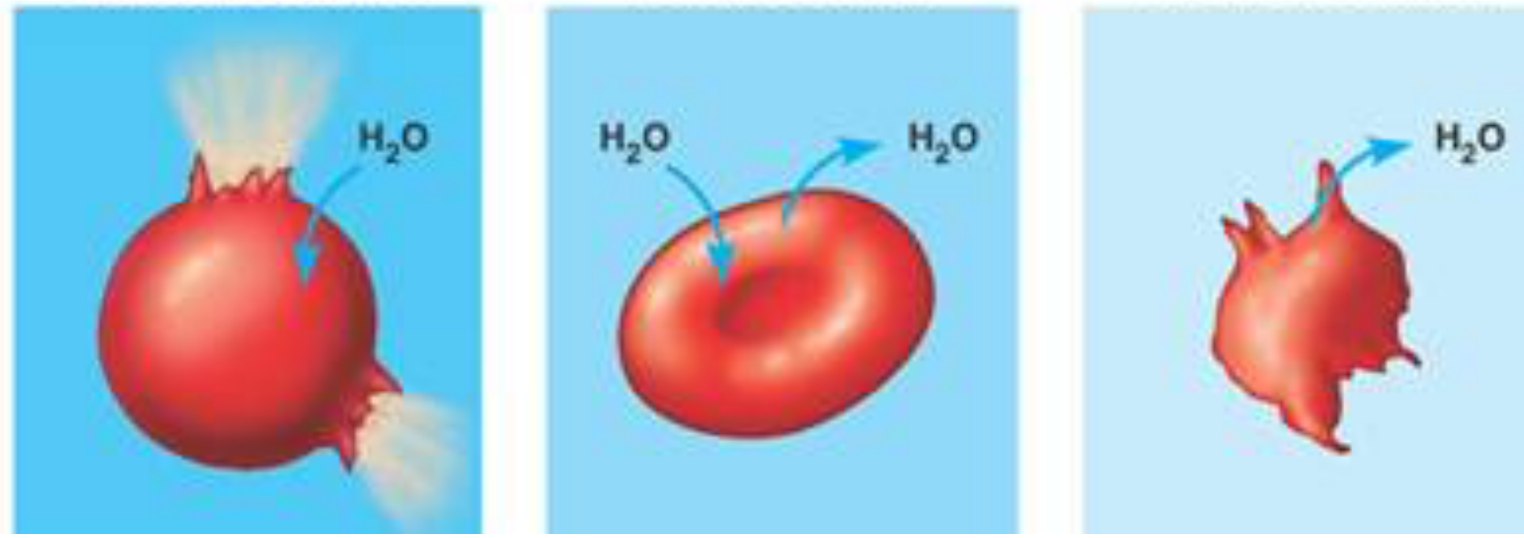
v

$$\boxed{\Pi = p_2 - p_1 = k_B T \Delta c_s}$$

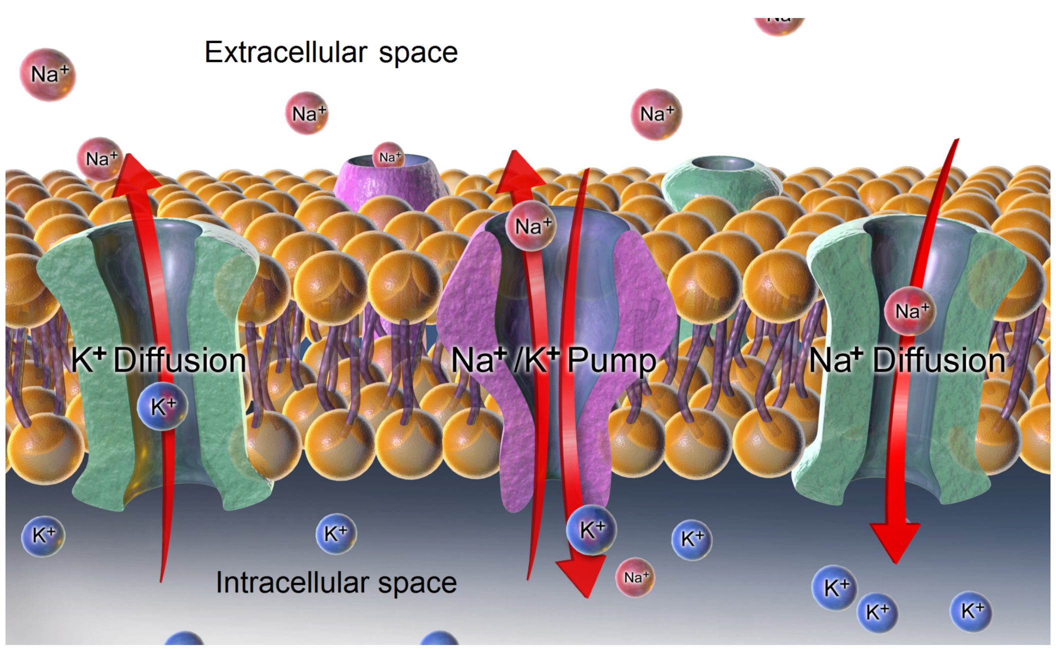
Osmotic pressure depends only on temperature and concentration difference across the membrane!

Osmotic pressure in cells

If extracellular solution has different concentration of ions from the interior of cells, then the resulting flow of water can cause the cell to shrink or swell and even burst.



hypotonic solution	isotonic solution	hypertonic solution
$c_{s,\text{out}} \ll c_{s,\text{in}}$	$c_{s,\text{out}} \sim c_{s,\text{in}}$	$c_{s,\text{out}} \gg c_{s,\text{in}}$

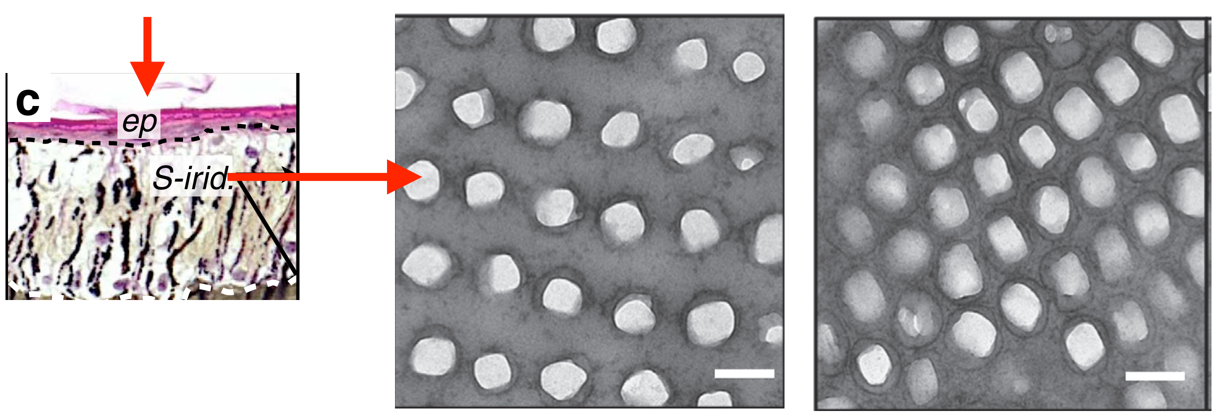


Cells use ion channels and ion pumps to regulate concentration of ions and therefore also the cell volume.

(Note: cell membrane is impermeable for charged particles)

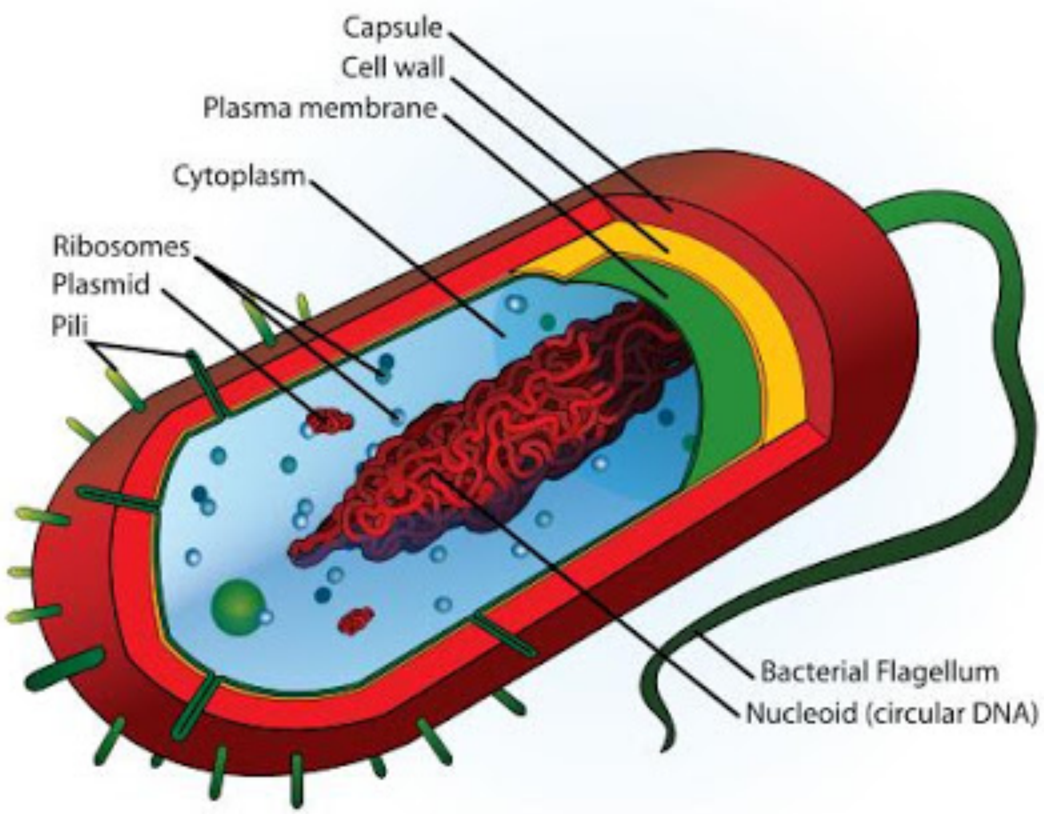
Dynamical structural colors in Chameleon

J. Teyssier et al.,
Nat. Comm. 6, 6368 (2015)



Changes in osmotic concentration lead to the swelling of cells in excited chameleon. This changes the spacing of periodic structure from which the ambient light is reflected.

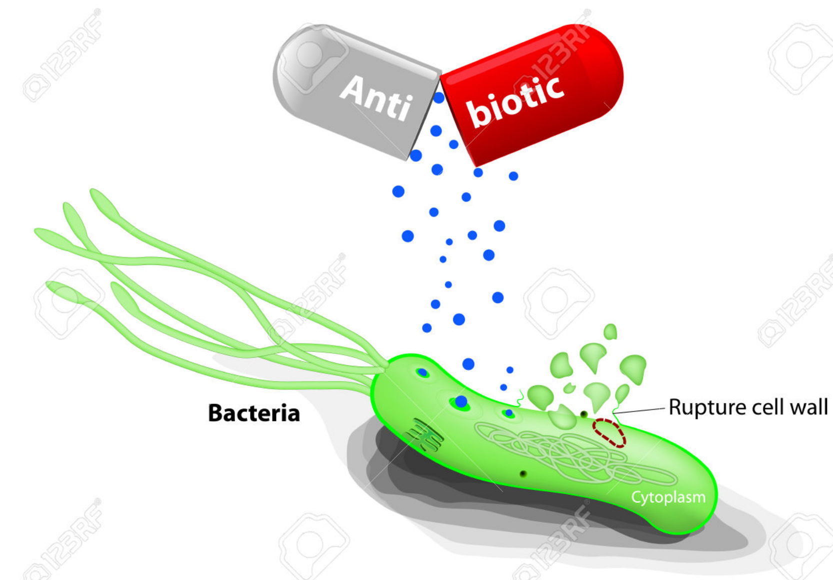
Osmotic pressure in bacteria



Bacteria have strong cell wall that can support large osmotic pressure (Turgor pressure).

$$\Pi \sim 10^5 \mathrm{Pa} \sim 1 \mathrm{bar}$$

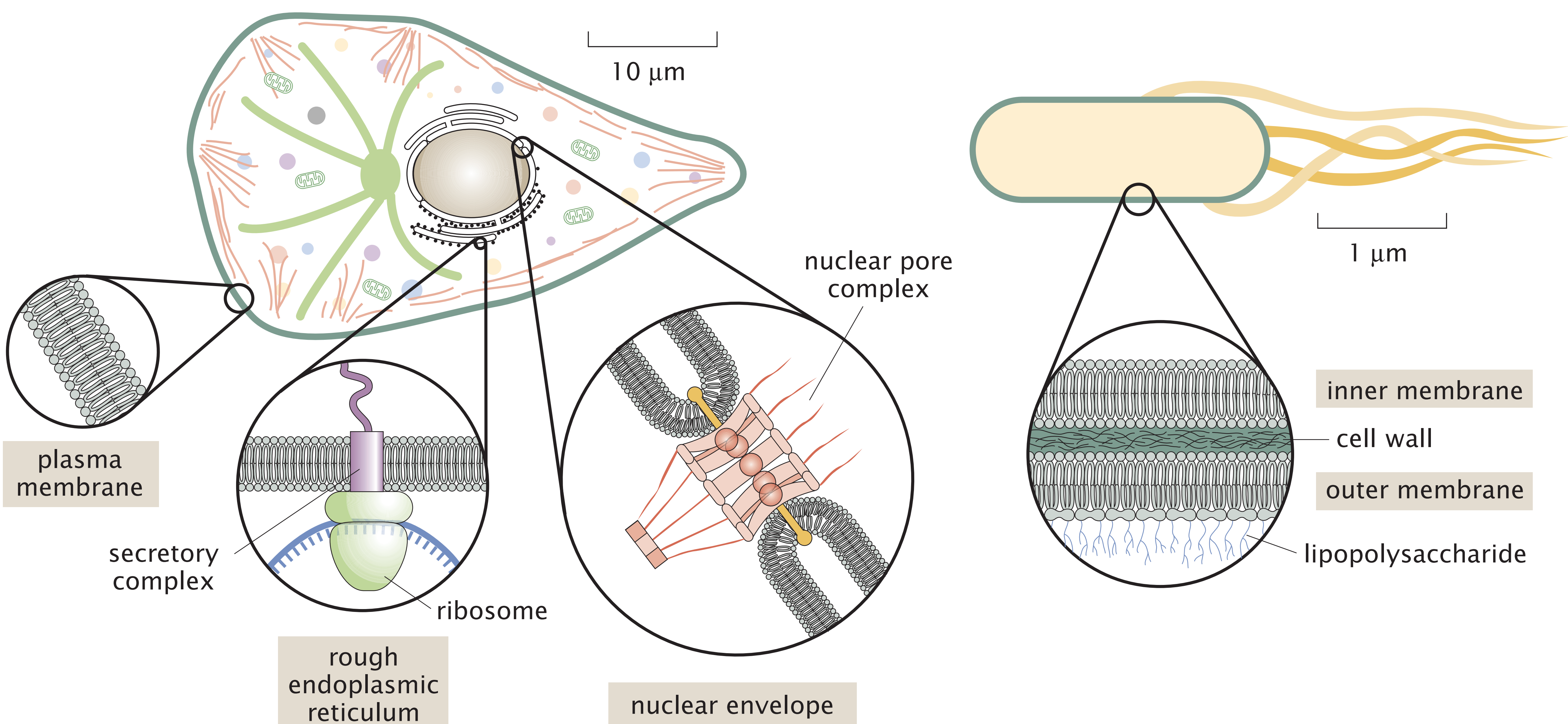
Antibiotics cause damage to cell wall and as a result cells rupture due to large Turgor pressure.



Cell membranes

Eukaryotic cells

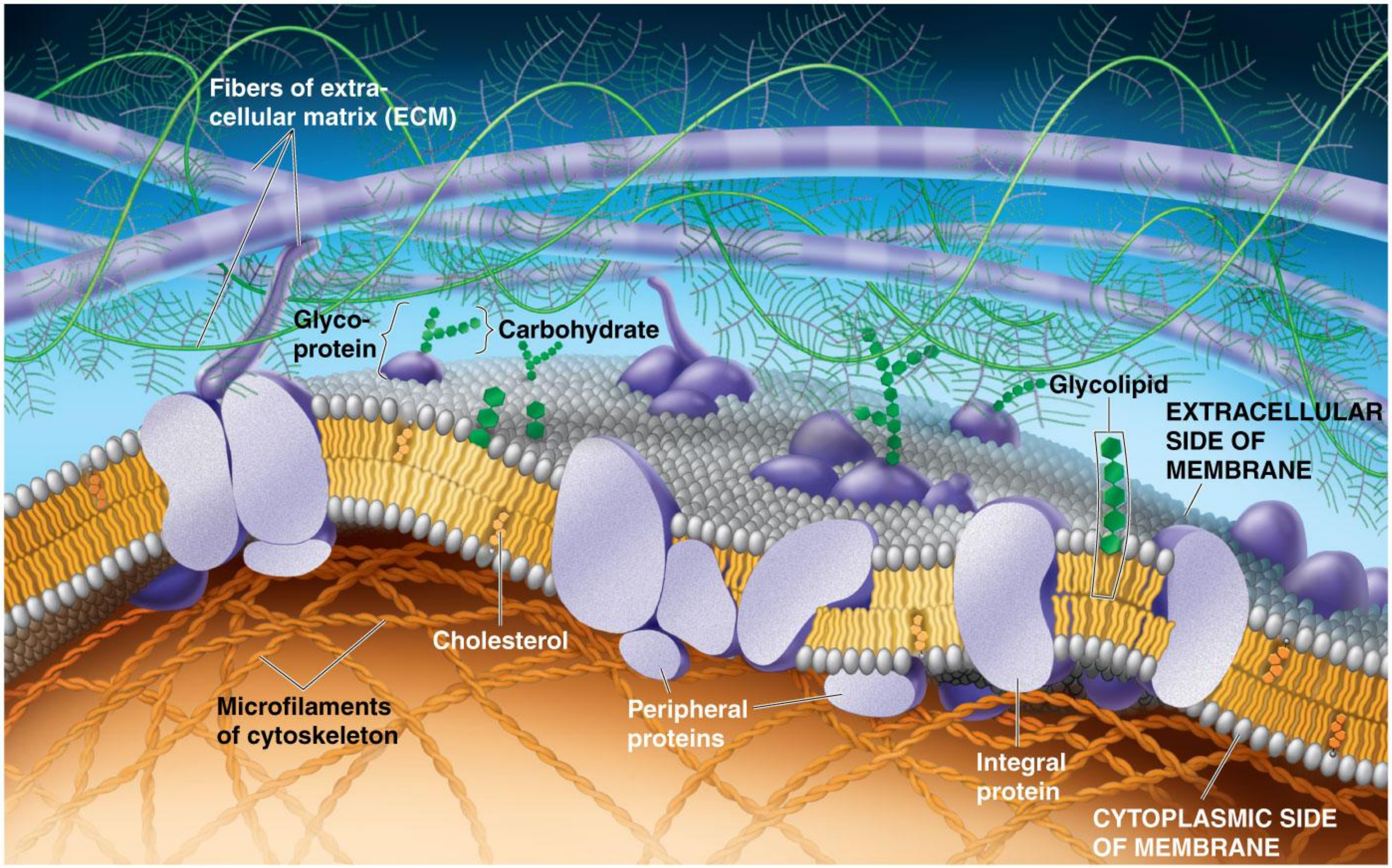
E. Coli



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

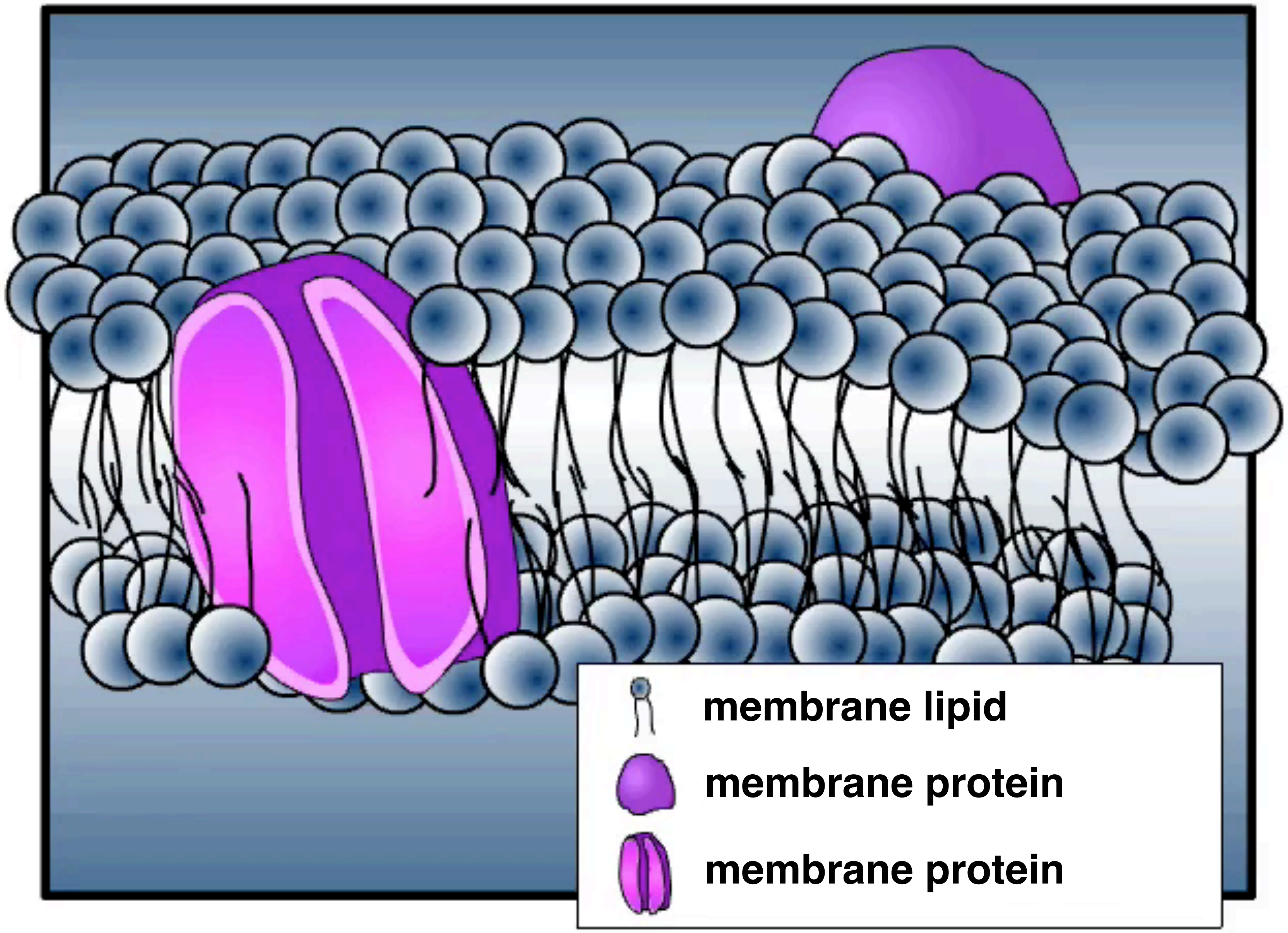
Cell membrane

lipids



5nm

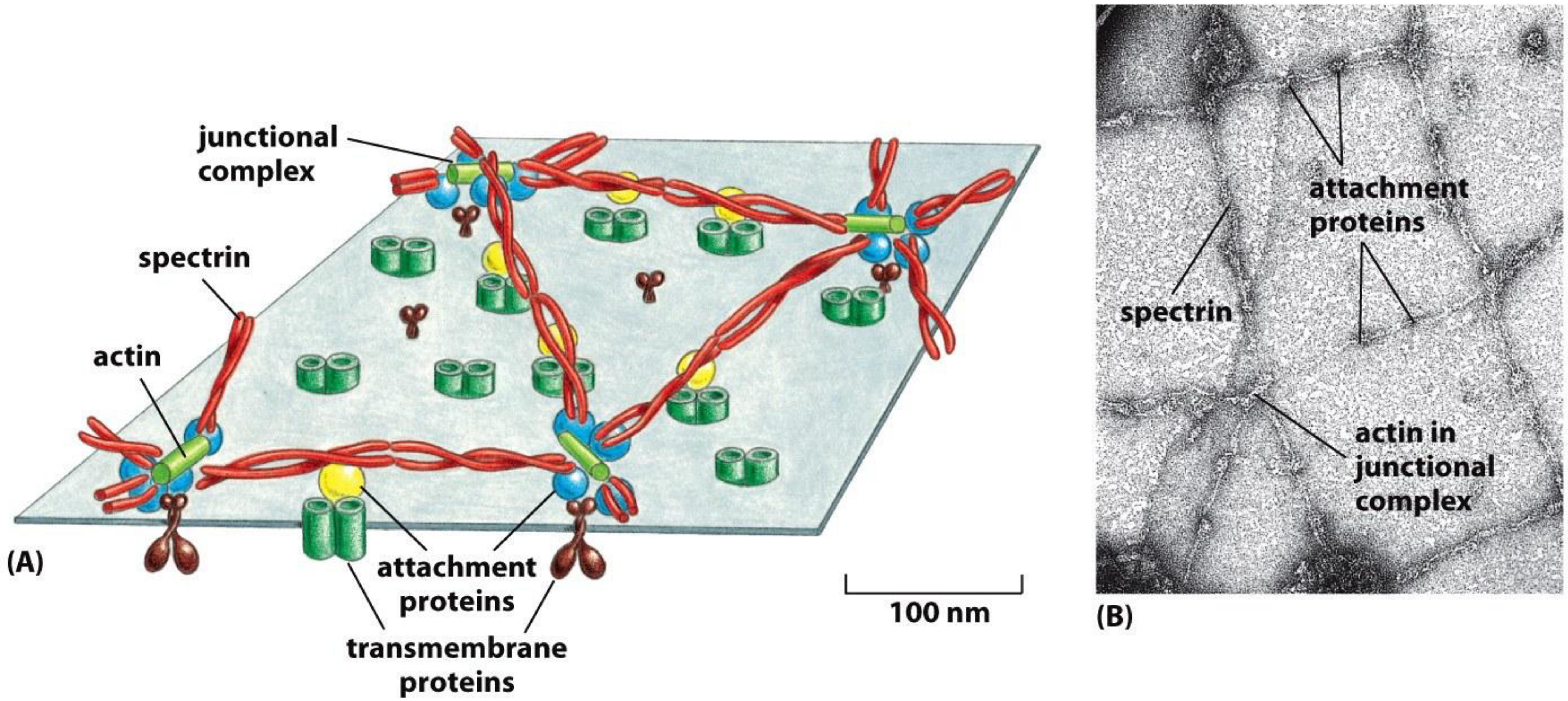
Lipid membrane behaves like fluid



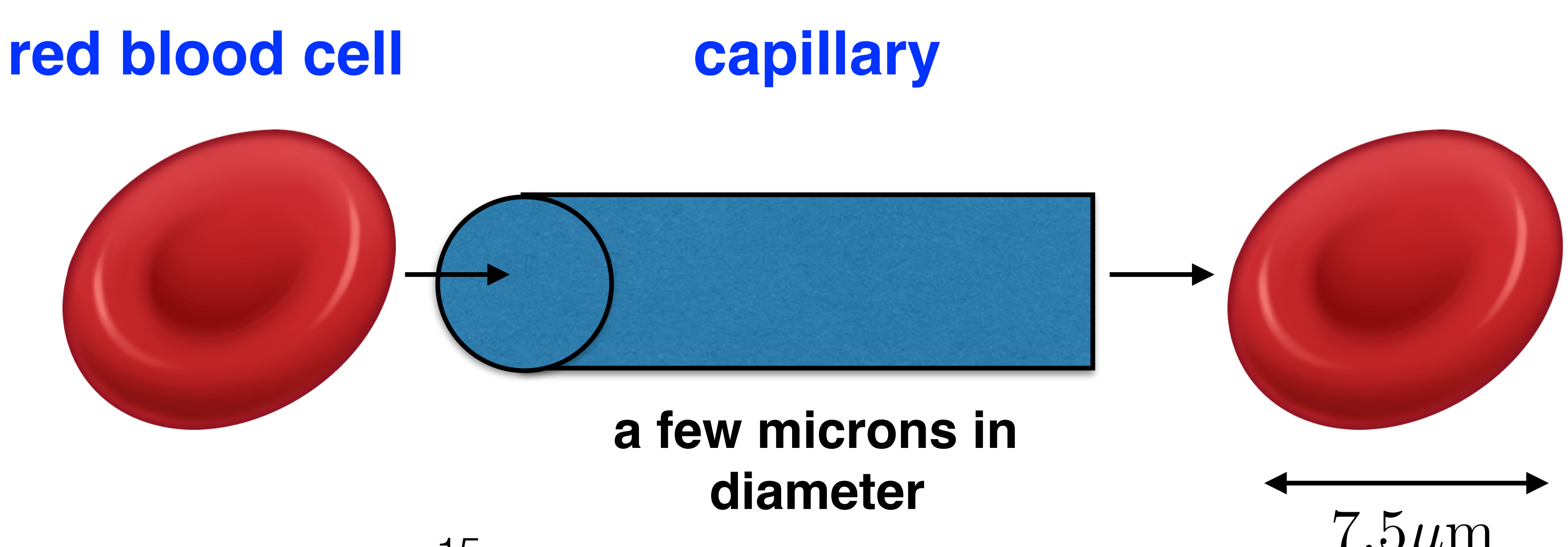
Lipid molecules and proteins can move around!

Flipping of lipid molecules between the layer is unlikely.

Membrane attached spectrin network provides solid-like behavior

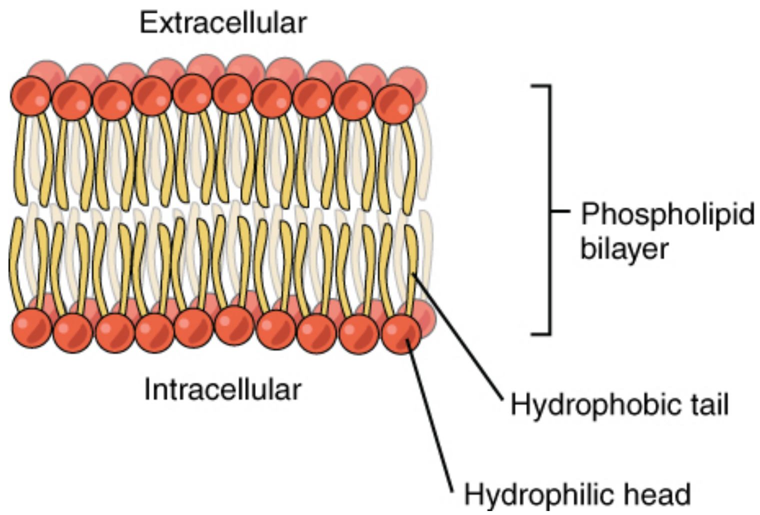


Spectrin network provides structural stability for cells

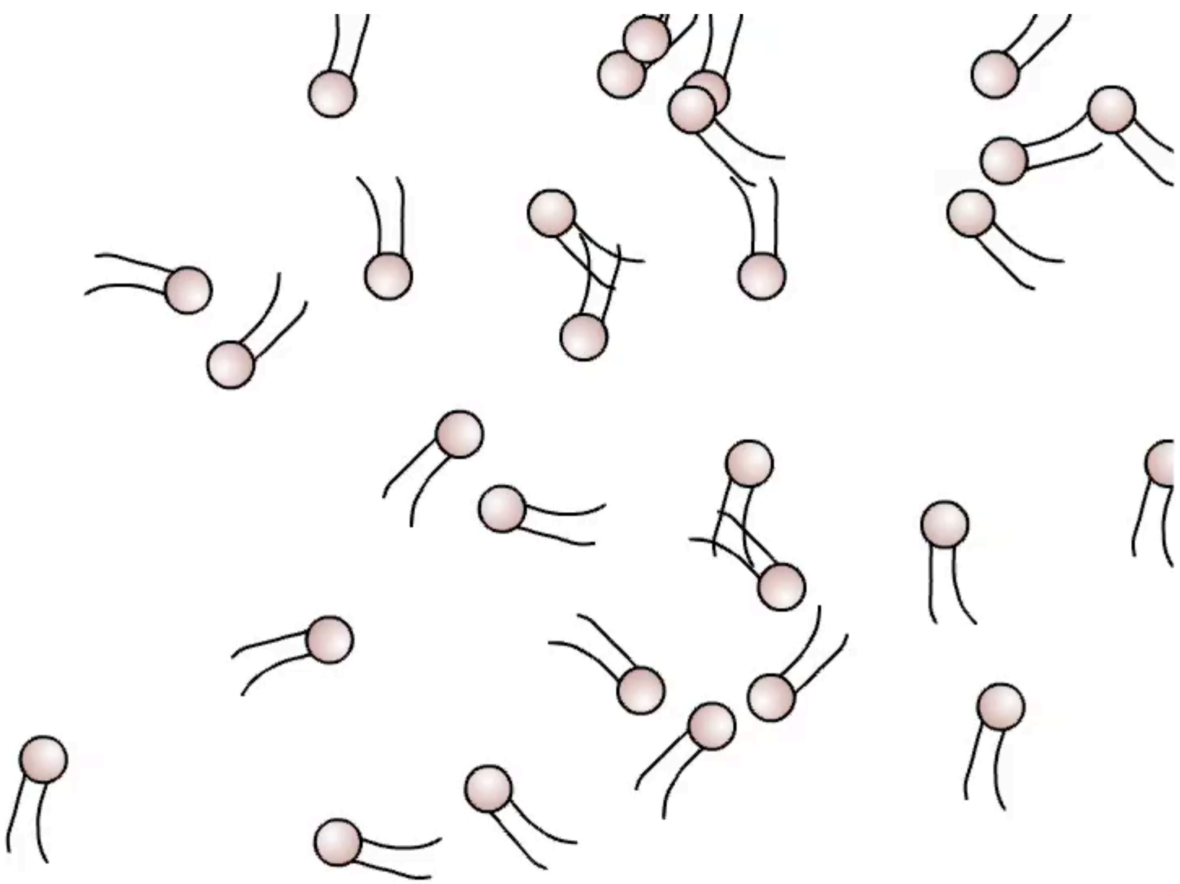


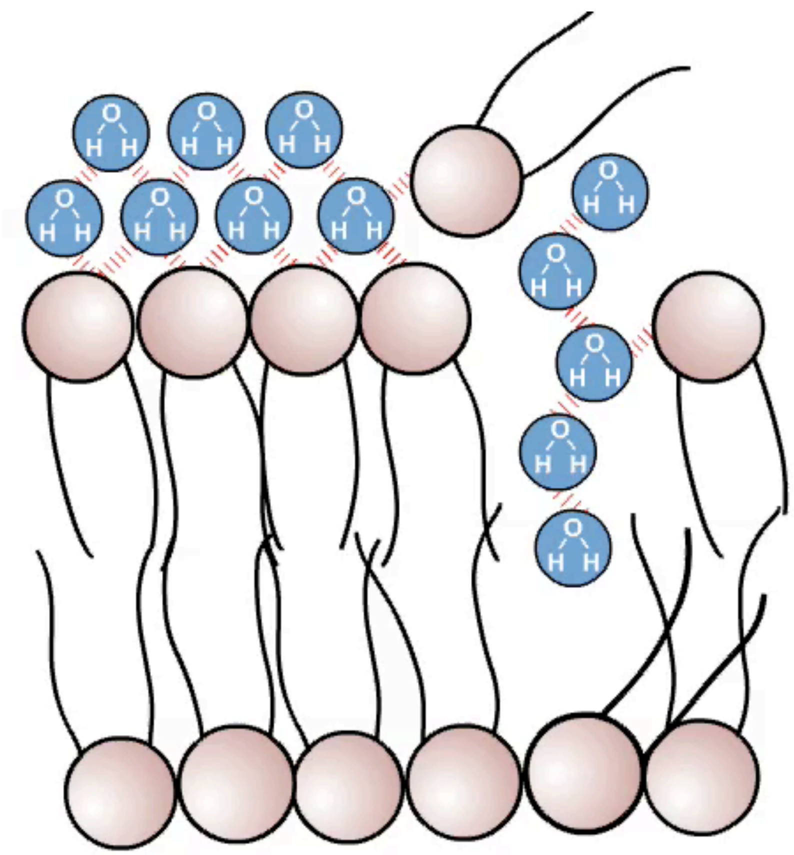
Alberts et al., Molecular Biology of the Cell

Lipid membrane



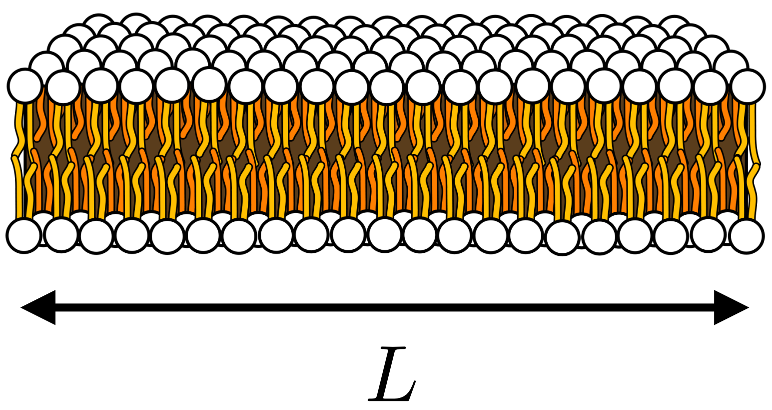
In water solution lipid molecules spontaneously aggregate to prevent undesirable interactions between water and hydrophobic tails.





Flat lipid bilayers vs lipid vesicles

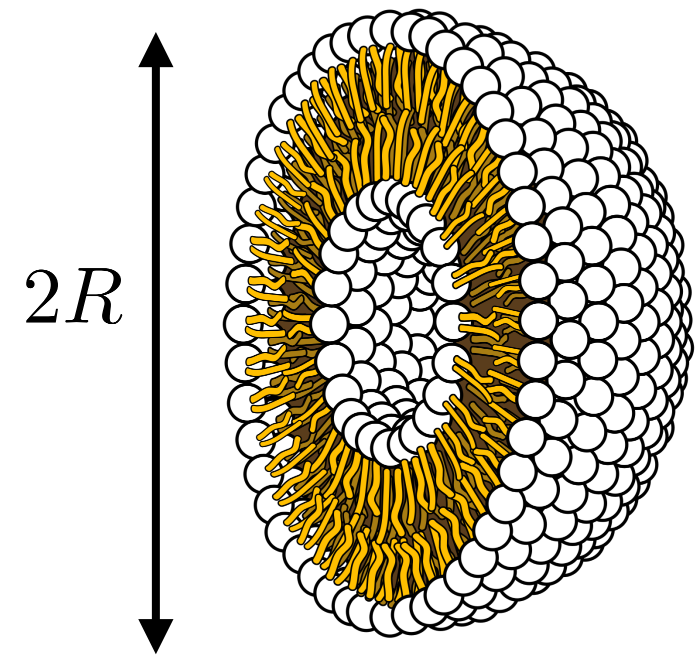
flat bilayer



energy cost on the edge between lipid tails and water molecules

$$\boxed{E \propto L}$$

vesicle

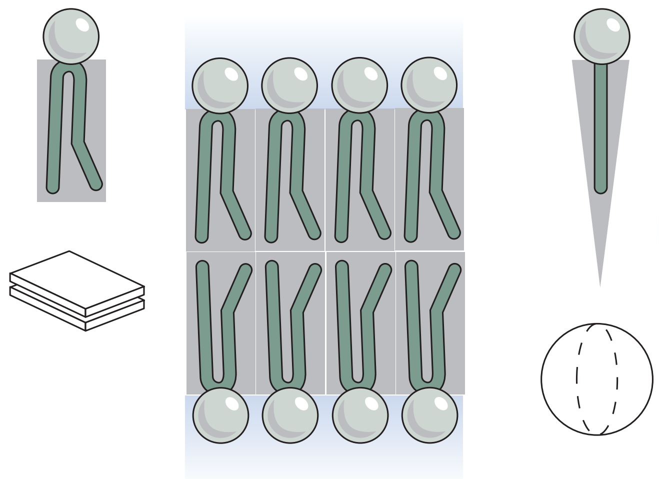


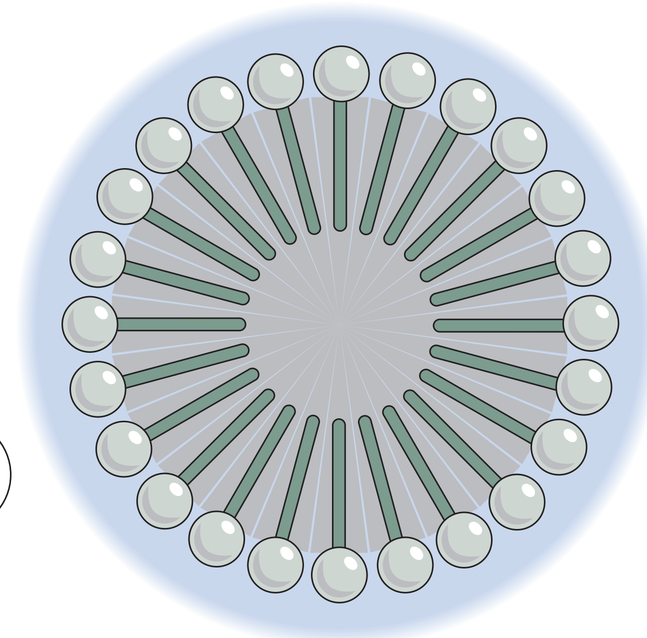
bending energy cost

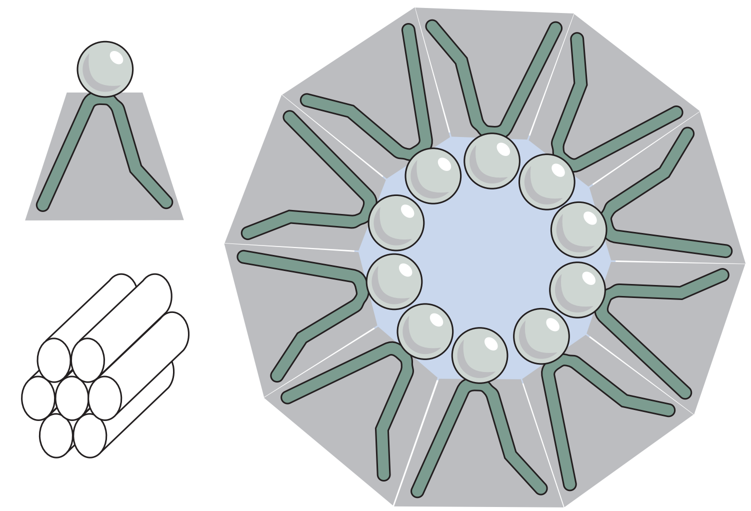
$$\boxed{E \propto \mathrm{const}}$$

Large vesicles have lower energy cost then flat bilayers!

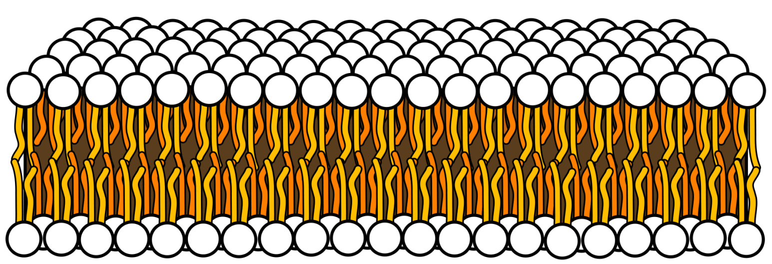
Shape of lipid molecules can induce spontaneous curvature of structures

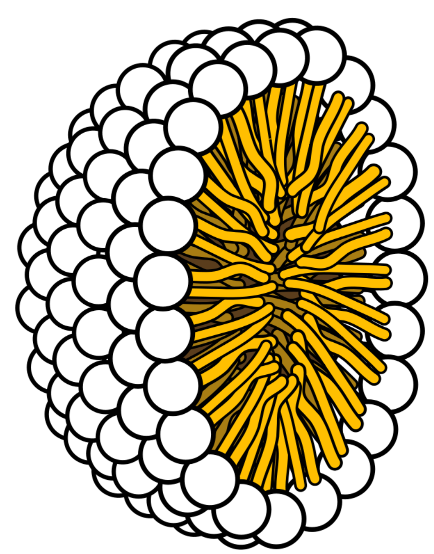


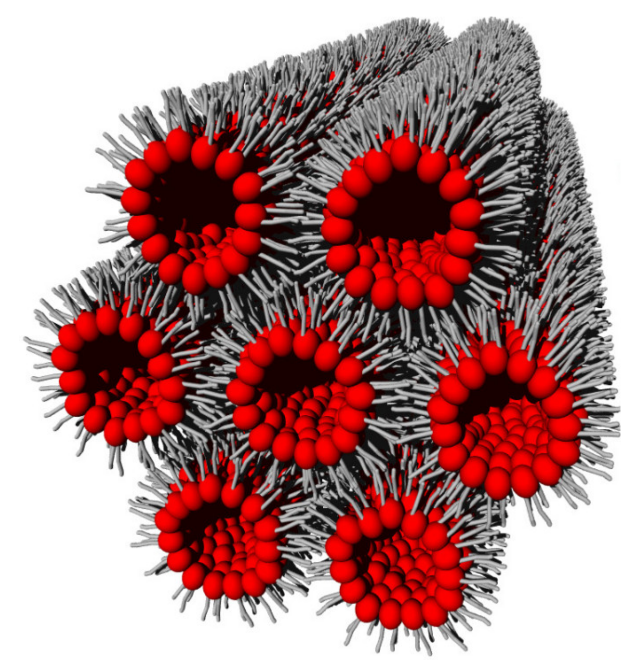




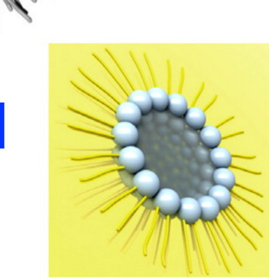
bilayer **micelle** **H-II phase**





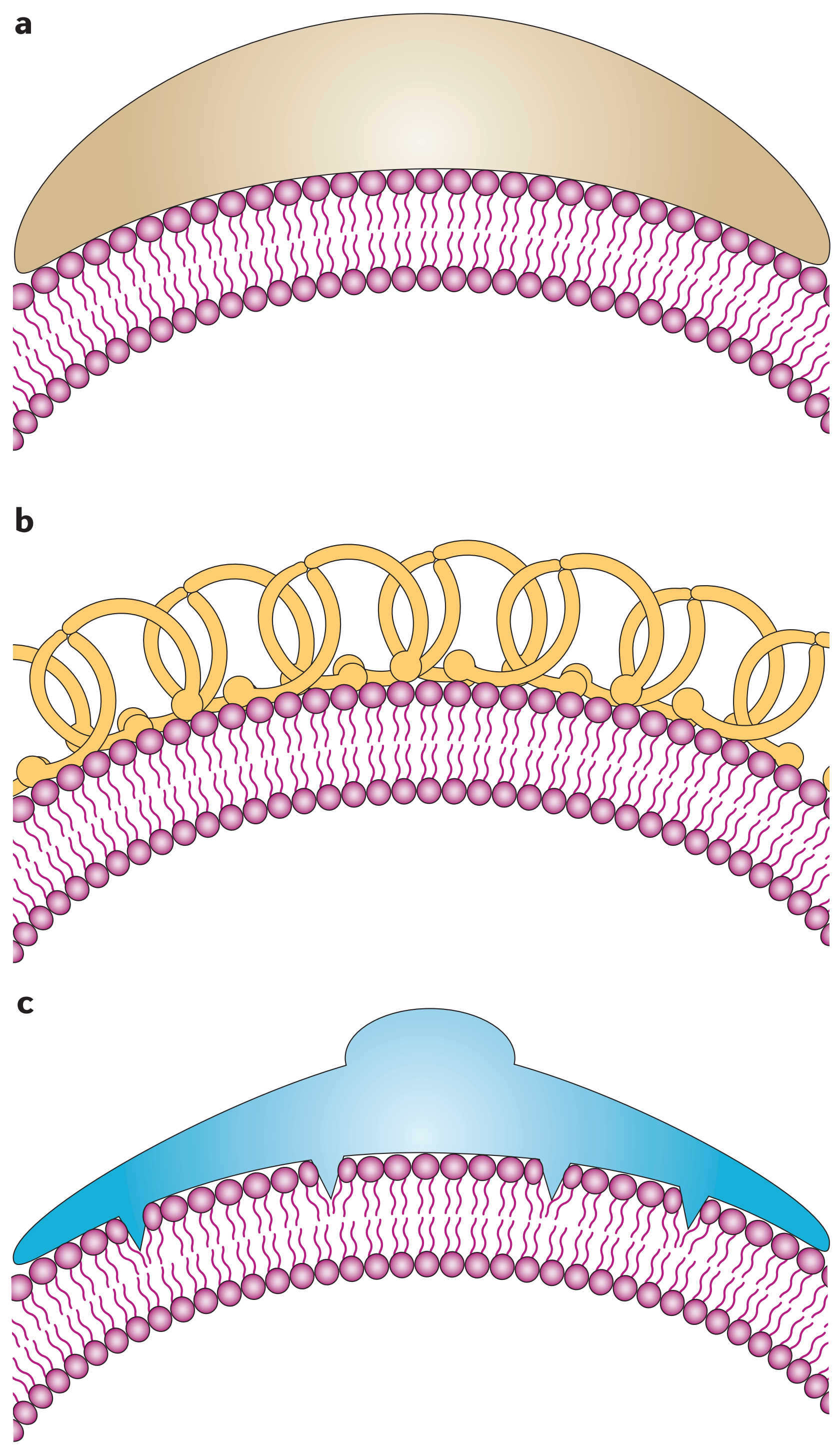


inverted micelle



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

Membrane proteins can induce spontaneous curvature



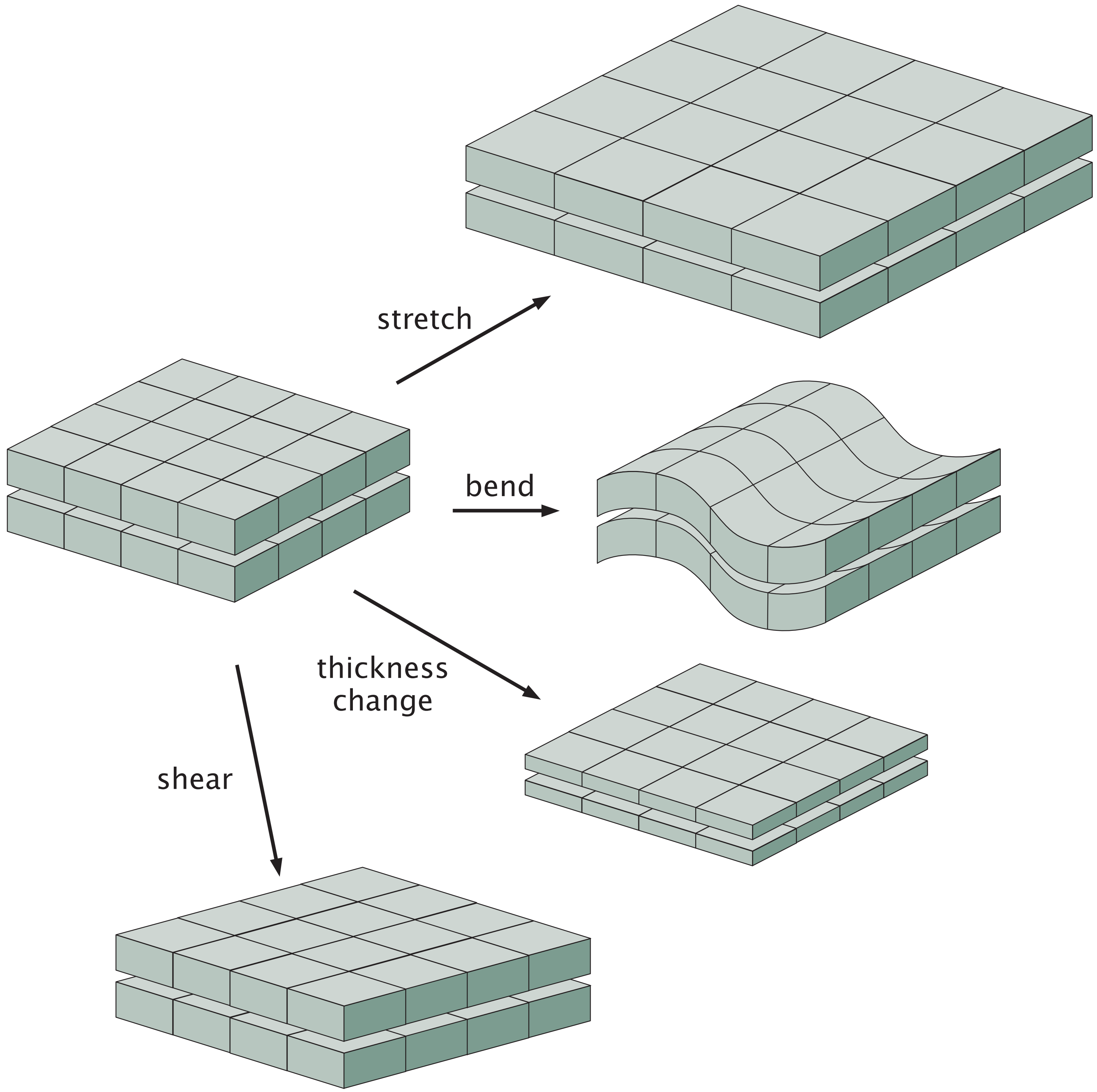
binding of rigid curved proteins

interactions between coat proteins bend the membrane

insertions of protein parts between lipid molecules on one side of the layer

J. Zimmerberg and M.M. Kozlov, Nat. Rev. Mol. Cel. Biol. 7, 9 (2006)

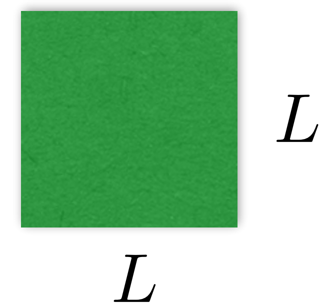
Membrane deformations



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

Energy cost for stretching and shearing

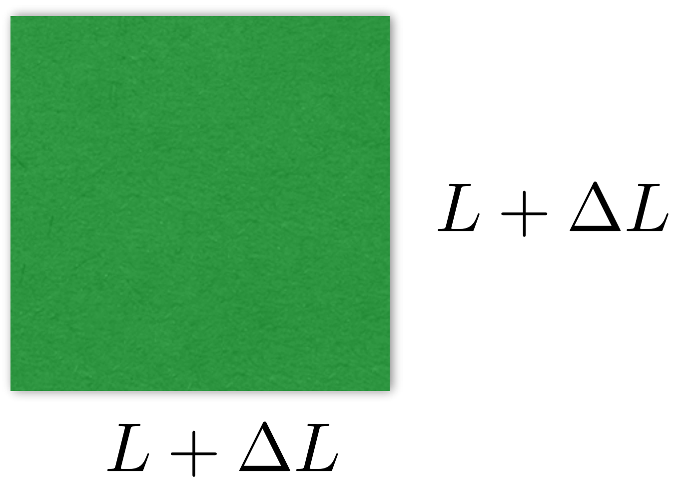
undeformed square patch



patch area

$A = L^2$

isotropic deformation



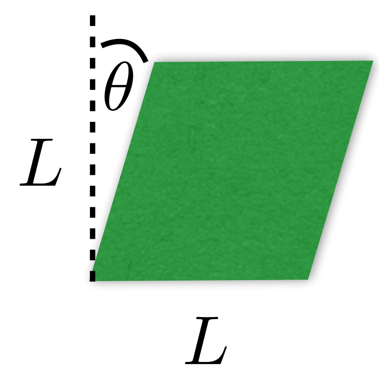
$$\boxed{\frac{E}{A} = \frac{B}{2}\left(\frac{\Delta A}{A}\right)^2 \approx \frac{B}{2}\left(\frac{2\Delta L}{L}\right)^2}$$

bulk modulus

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

(lipid bilayer)

shear deformation



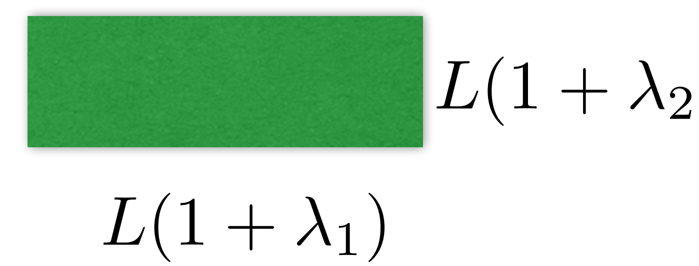
$$\boxed{\frac{E}{A} = \frac{\mu\theta^2}{2}}$$

shear modulus

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

(spectrin network)

anisotropic stretching

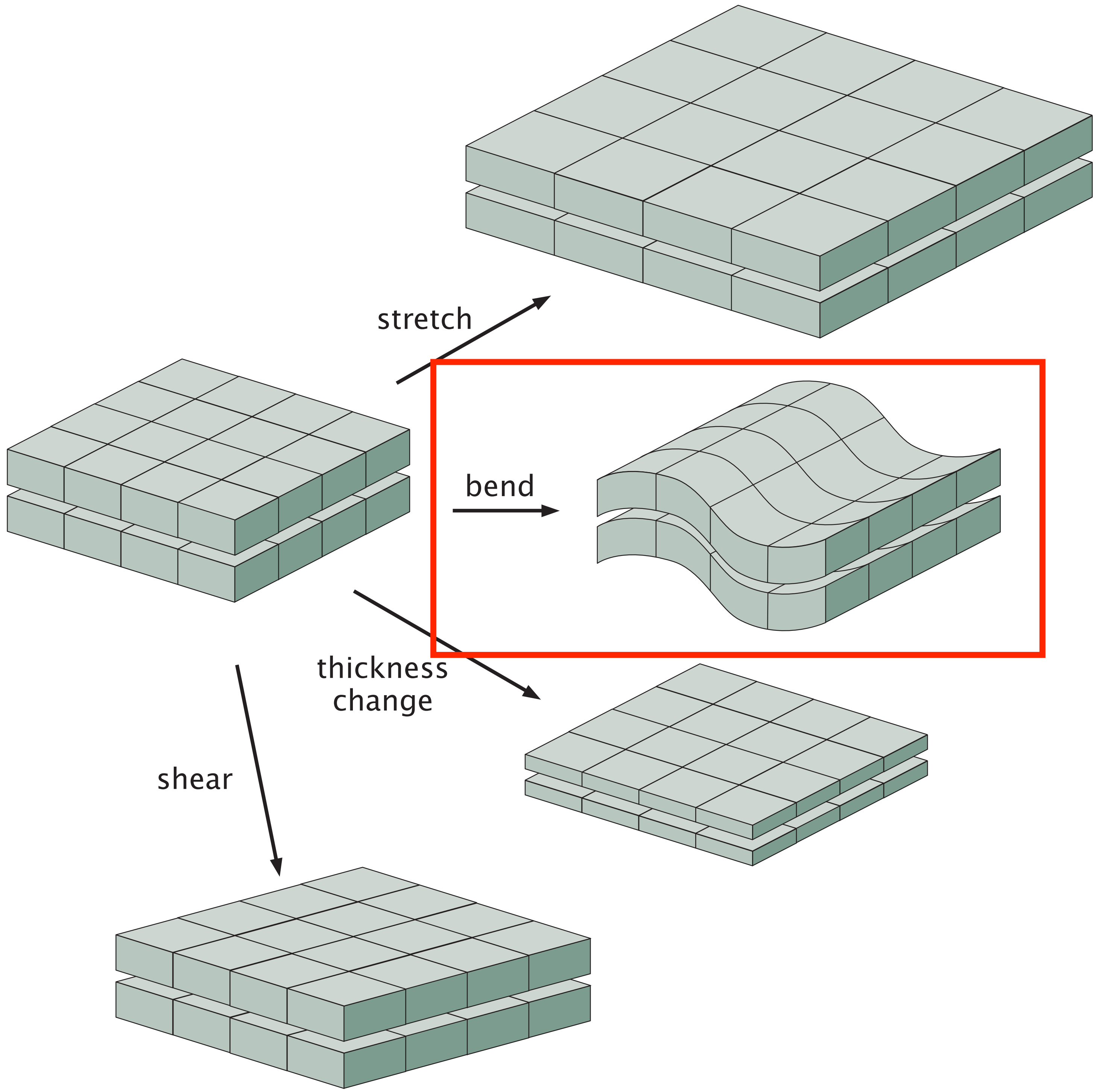


$$\boxed{\frac{E}{A} \approx \frac{B}{2}(\lambda_1 + \lambda_2)^2 + \frac{\mu}{2}(\lambda_1 - \lambda_2)^2}$$

$\lambda_1, \lambda_2 \ll 1$

(shearing can be interpreted as anisotropic stretching)

Membrane deformations



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

Bending energy

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

Helfrich free energy

bending rigidity $\kappa \sim 20 k_B T$

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

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

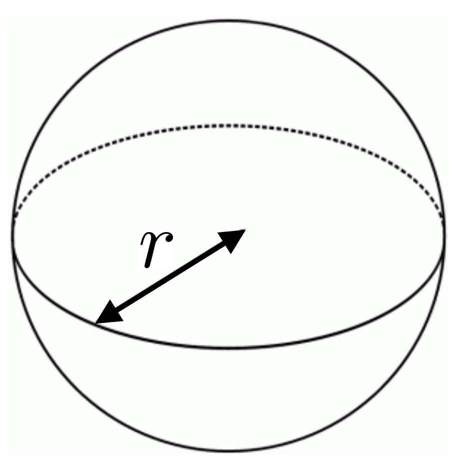
Gaussian curvature $G = \frac{1}{R_1 R_2}$

spontaneous curvature C_0

Example: bending energy for a sphere

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

$$C_0 = 0$$



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

bending energy is independent of the sphere radius!

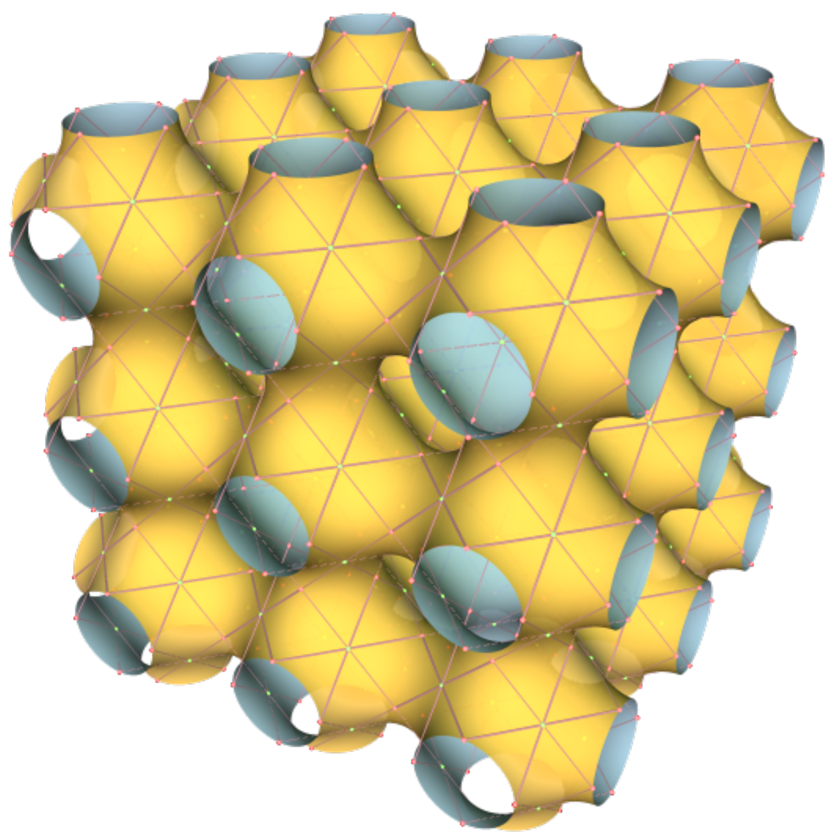
Bending energy

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

Gaussian bending rigidity κ_G has to be negative for stability of membranes

Schwarz minimal surface

Such surfaces would be preferred for positive Gaussian bending rigidity, when C_0=0.



$$\frac{1}{R_1} + \frac{1}{R_2} = 0$$

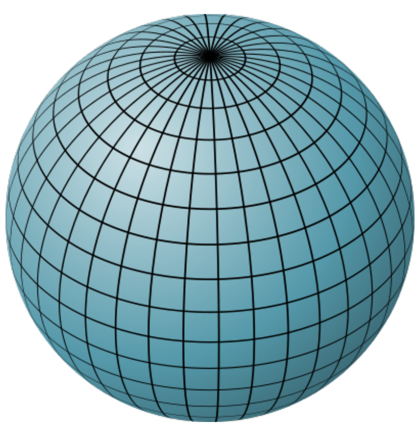
$$\frac{1}{R_1 R_2} < 0$$

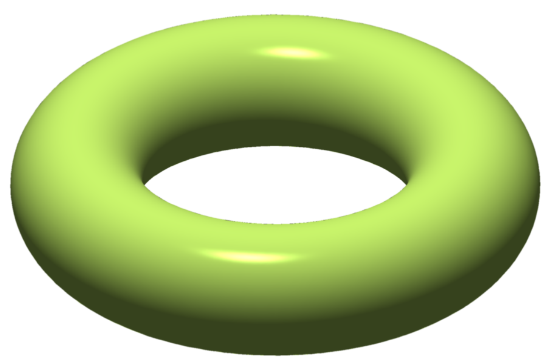
Gauss-Bonet theorem

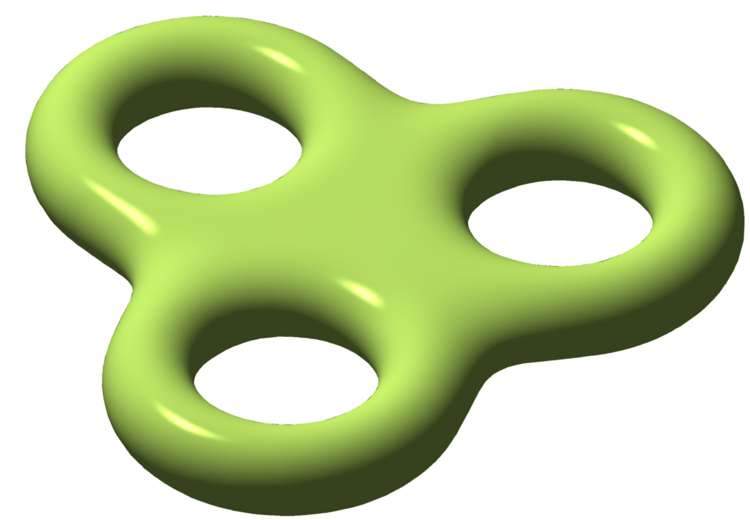
For closed surfaces the integral over Gaussian curvature only depends on the surface topology!

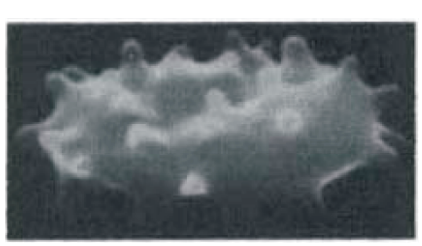
$$\boxed{\int \frac{dA}{R_1 R_2} = 4\pi\,(1 - g)}$$

$g = 0$ $\quad$ $g = 1$ $\quad$ $g = 2$ $\quad$ $g = 3$



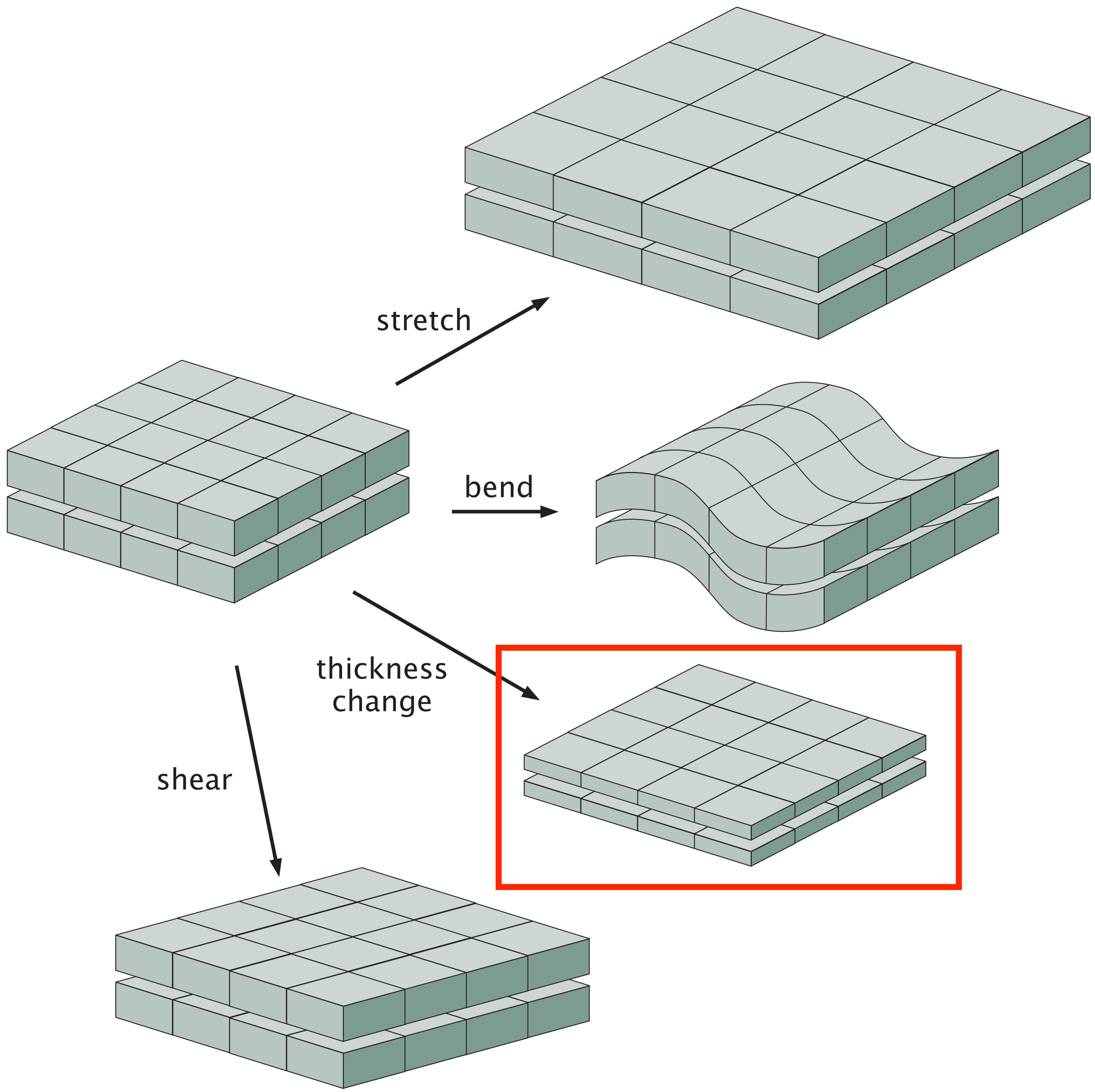






It is hard to experimentally measure the Gaussian bending rigidity for cells, because cell deformations don't change the topology!

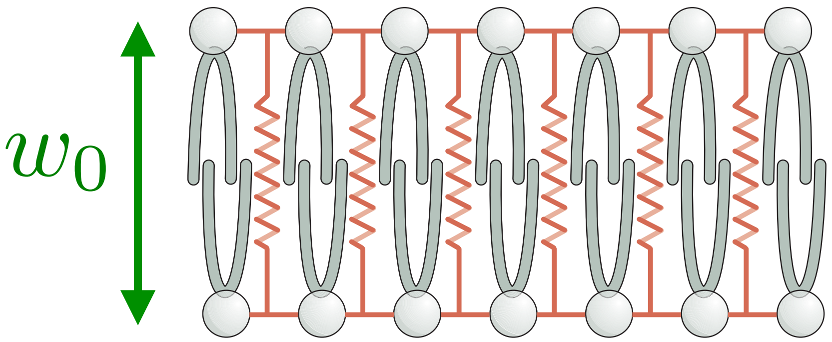
Membrane deformations



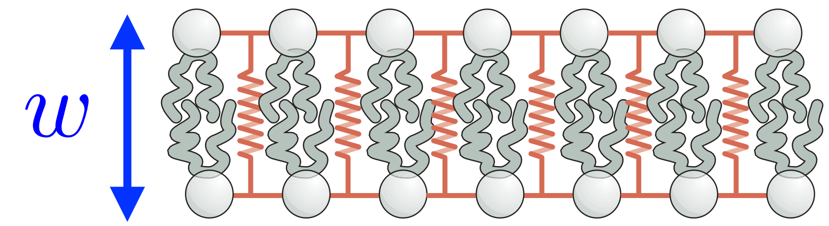
R. Phillips et al., Physical Biology of the Cell

Membrane thickness deformation

undeformed bilayer

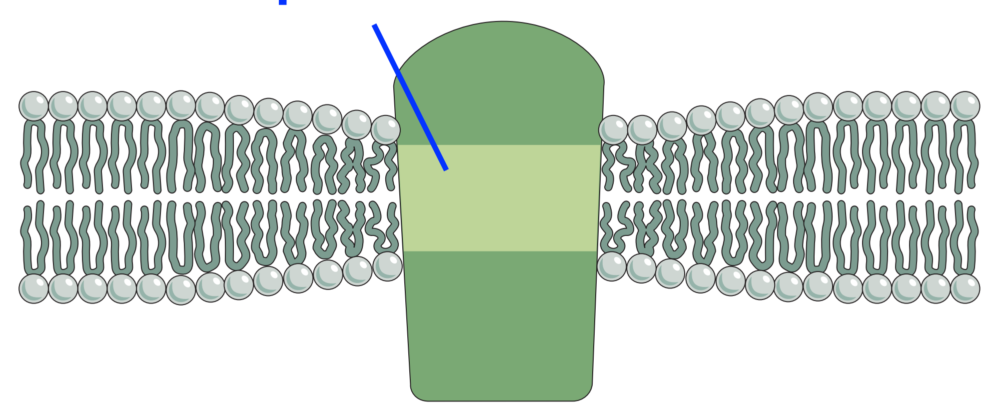


deformed bilayer



$$\boxed{E_t = \frac{K_t}{2}\int dA \left(\frac{w - w_0}{w_0}\right)^2}$$

$$K_t \approx 60 k_B T/\mathrm{nm}^2$$

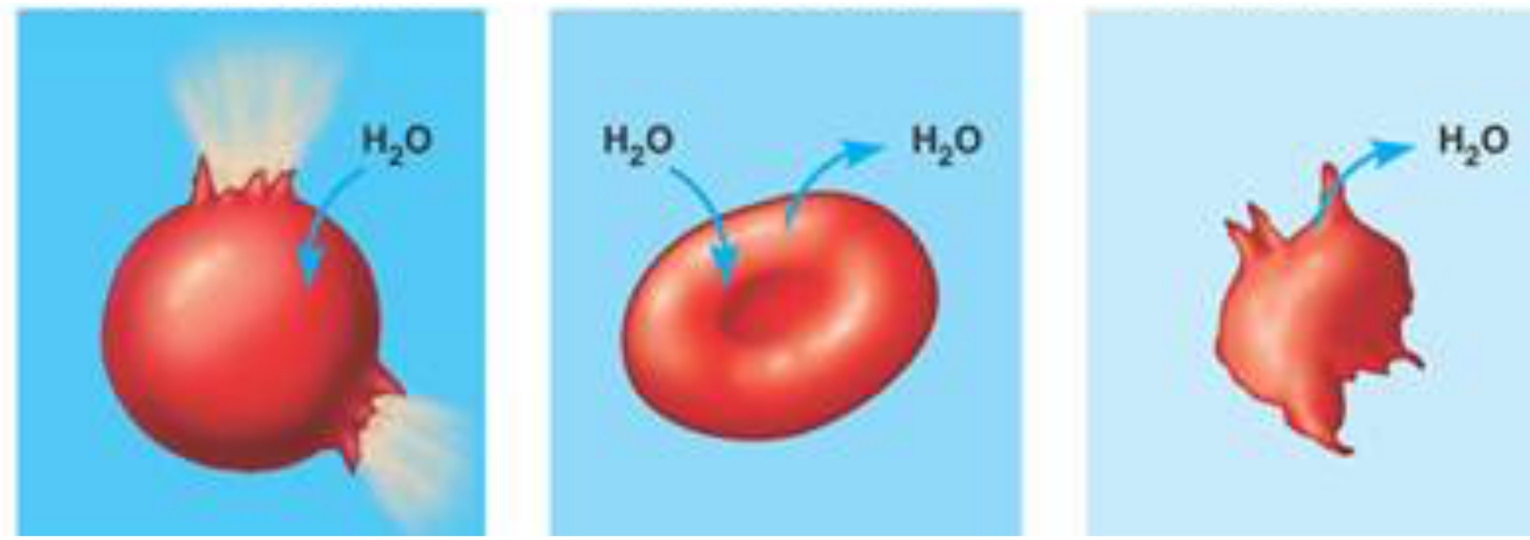


Membrane proteins can locally deform the thickness of lipid bilayer

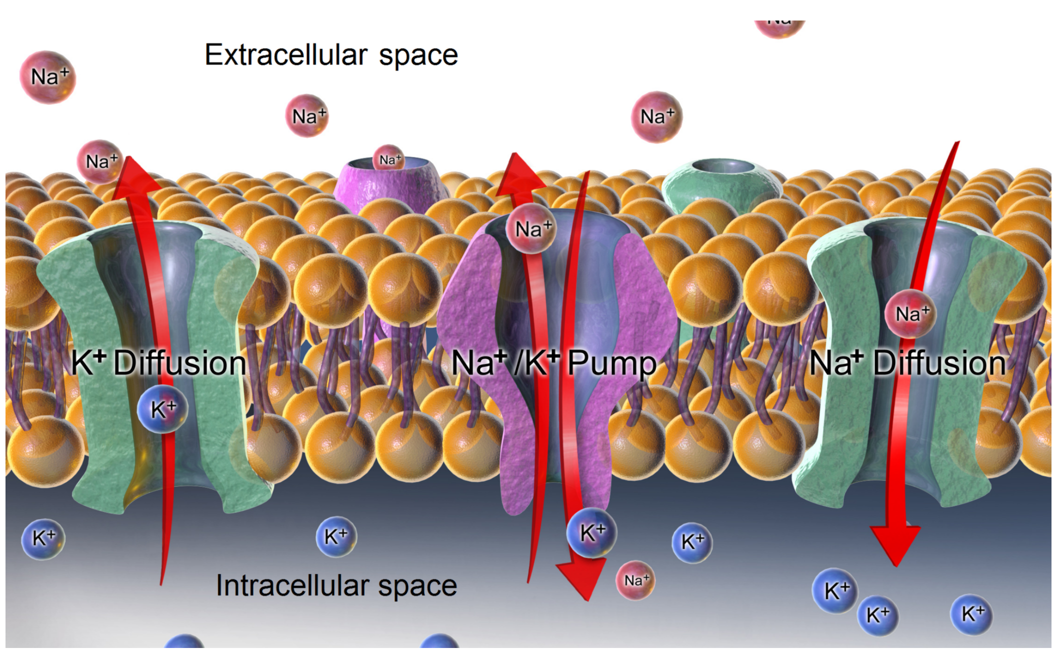
R. Phillips et al., Physical Biology of the Cell

Osmotic pressure in cells

If extracellular solution has different concentration of ions from the interior of cells, then the resulting flow of water can cause the cell to shrink or swell and even burst.



hypotonic solution	isotonic solution	hypertonic solution
$c_{s,\mathrm{out}} \ll c_{s,\mathrm{in}}$	$c_{s,\mathrm{out}} \sim c_{s,\mathrm{in}}$	$c_{s,\mathrm{out}} \gg c_{s,\mathrm{in}}$



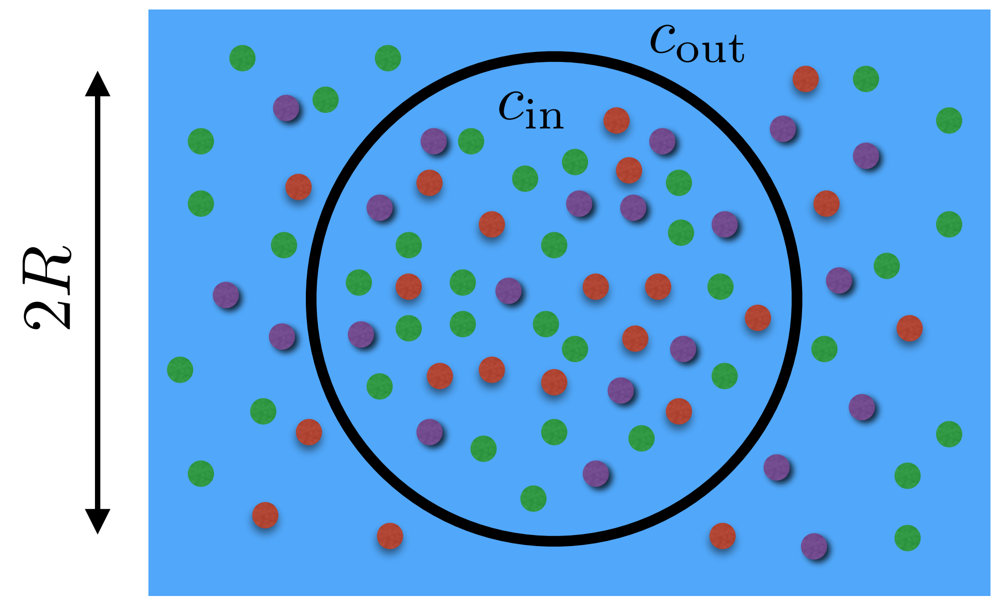
Cells use ion channels and ion pumps to regulate concentration of ions and therefore also the cell volume.

(Note: cell membrane is impermeable for charged particles)

Osmotic pressure

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

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



$A = 4\pi R^2$

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

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

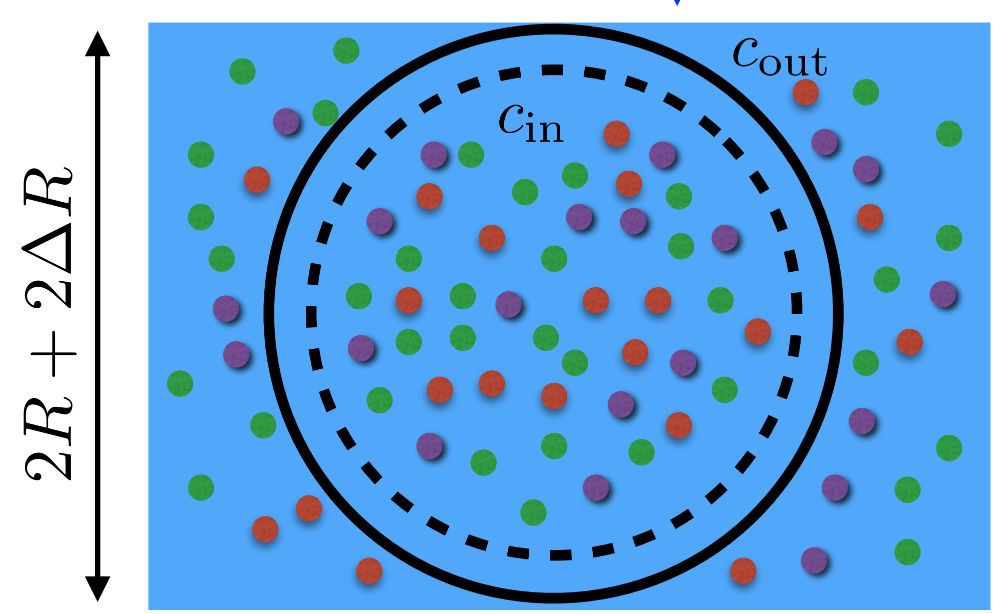
$$E = A\frac{B}{2}\left(\frac{\Delta A}{A}\right)^2 - \Delta p \Delta V$$

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

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

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

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



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

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

Membrane tension

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

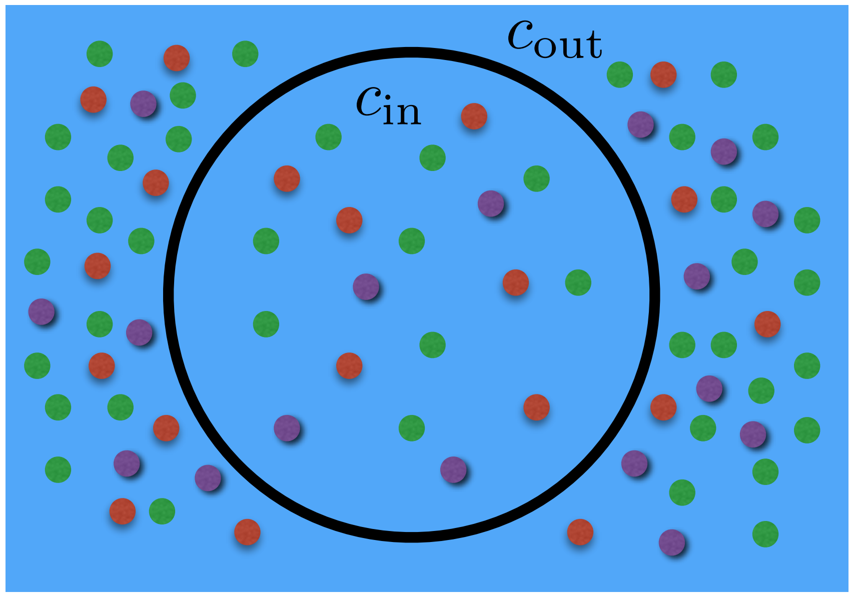
(Young-Laplace equation)

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

Osmotic pressure

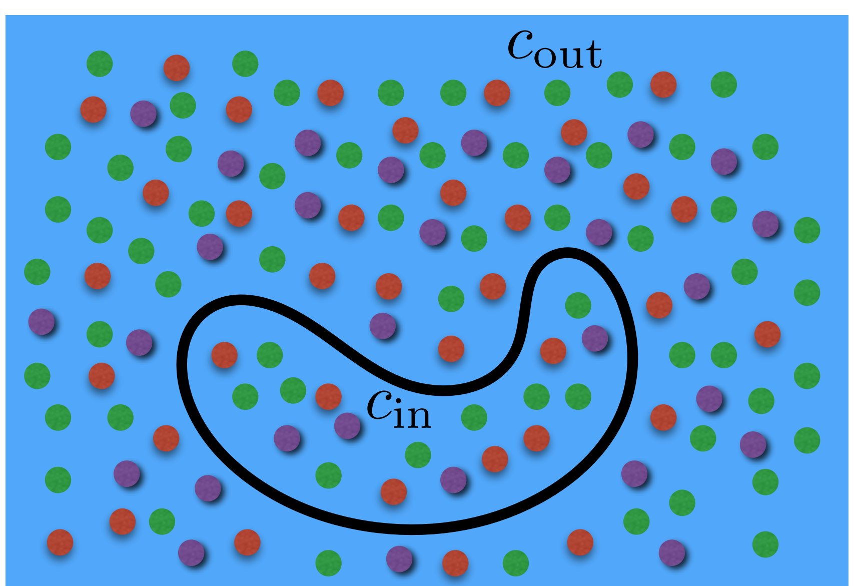
$$\boxed{\Delta p = p_{\rm in} - p_{\rm out} = k_B T (c_{\rm in} - c_{\rm out})}$$

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



Water flows out of the cell until concentrations become equal.

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



How can we estimate the shape of "deflated" cells?

Total concentration of molecules inside a cell (vesicle)

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

Preferred cell (vesicle) volume

$$\boxed{V_0 = \frac{N}{c_{\rm out}}}$$

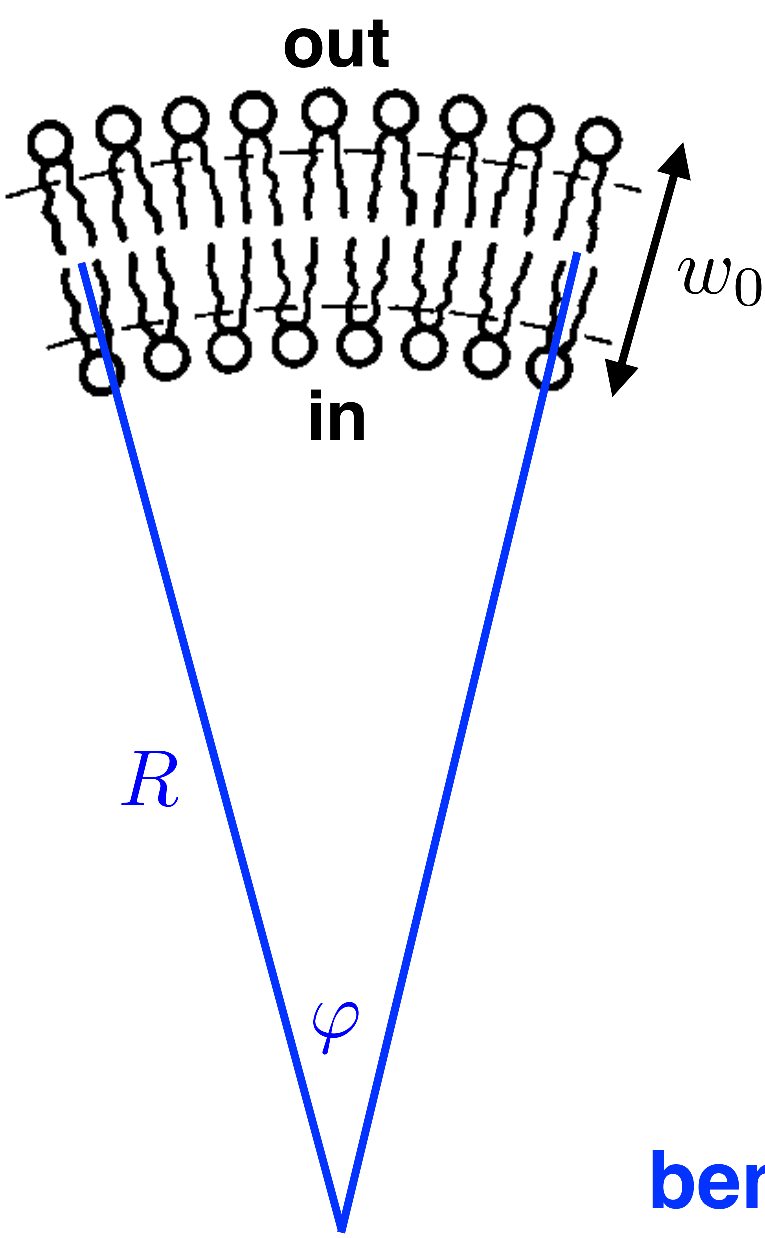
Energy cost for modifying the volume

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

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

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

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

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

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

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

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

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

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
$R_0 = \sqrt{\frac{A_0}{4\pi}}$	$a = \frac{A_0}{4\pi R_0^2} = 1$	$v = \frac{V_0}{4\pi R_0^3/3}$	$c_0 = C_0 R_0$	$\Delta a = \frac{\Delta A_0}{8\pi w_0 R_0}$	$e = \frac{E}{8\pi\kappa}$

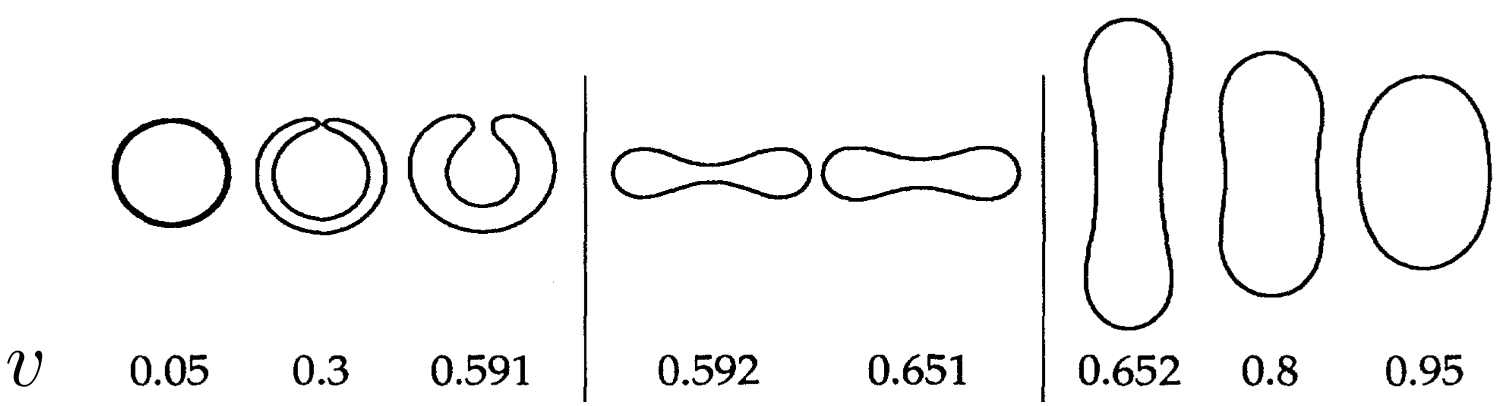
Minimal model: minimization of bending energy for lipid vesicles

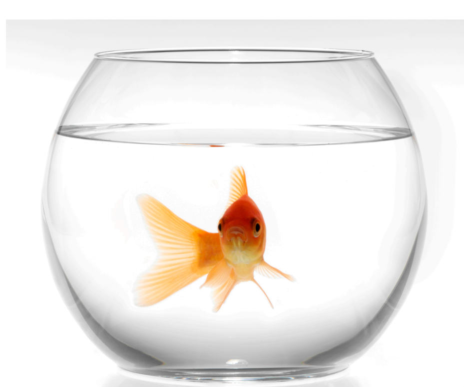
Find the shape of vesicles that minimize bending energy by constraining the volume to *v*<1.

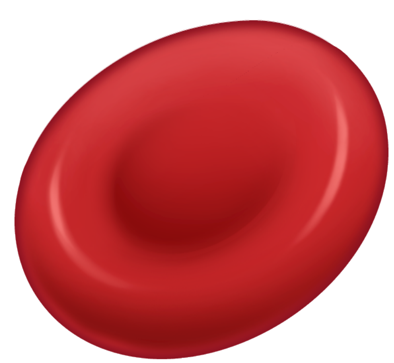
$$e = \int \frac{da}{4} \left(\frac{1}{r_1} + \frac{1}{r_2} \right)^2$$

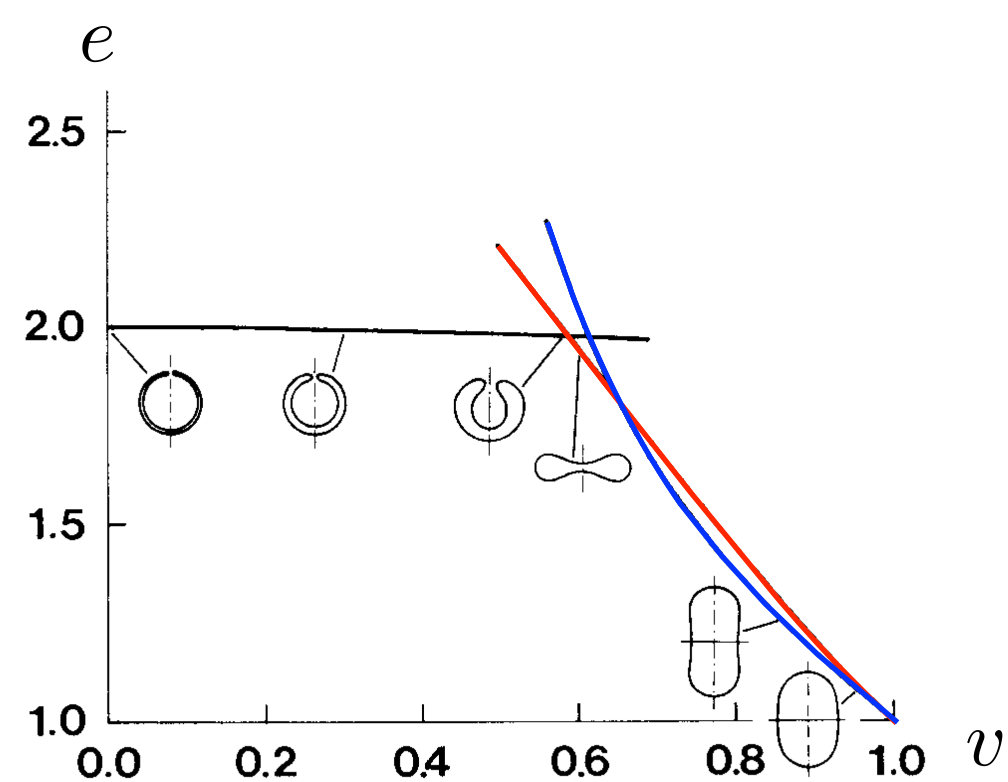
Minimum energy configurations

stomatocytes **oblates** **prolates**









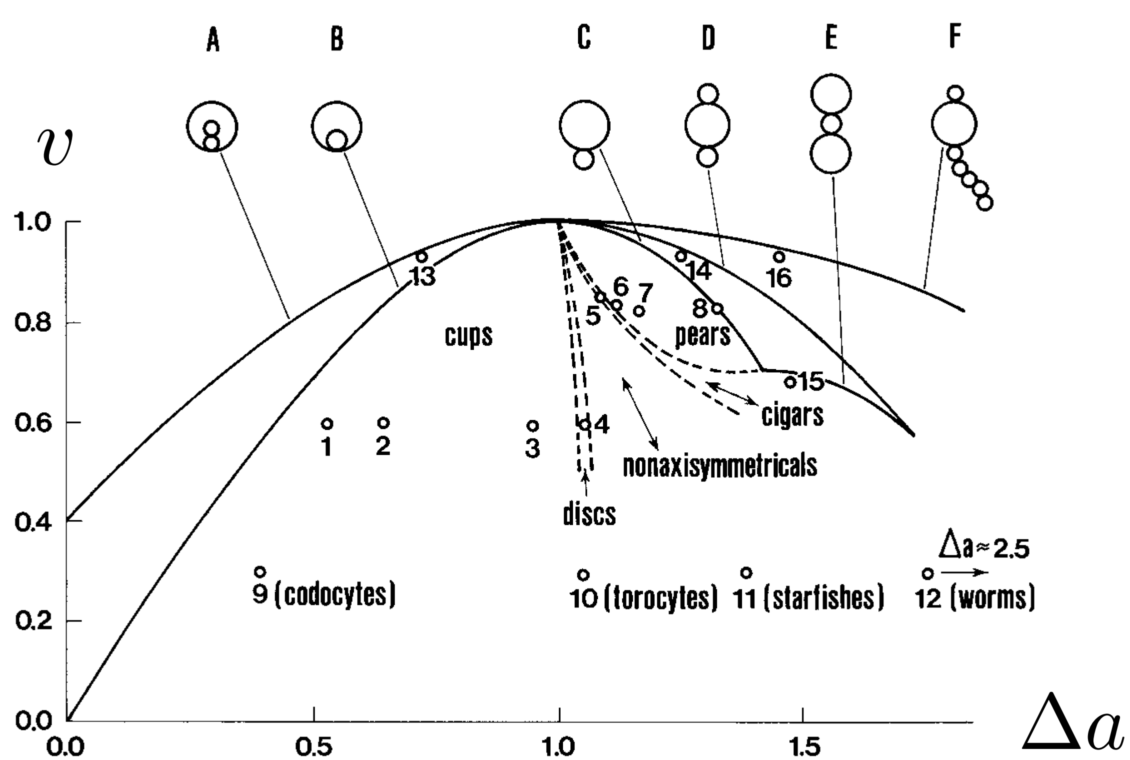
U. Seifert *et al.*, PRA 44, 1182 (1991)

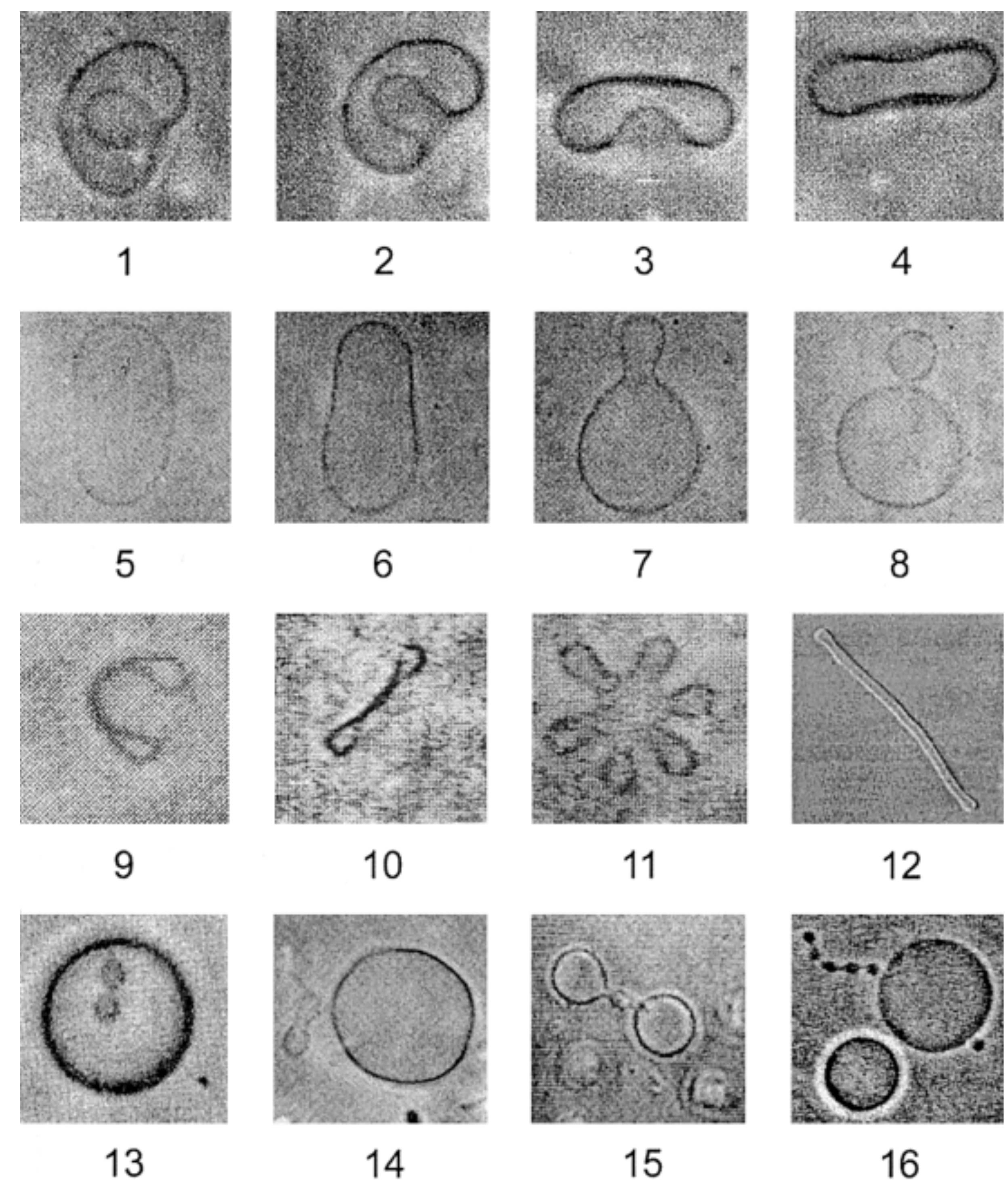
S. Svetina and B. Zeks, Anat. Rec. 268, 215 (2002)

Bilayer couple model of vesicles

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

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)