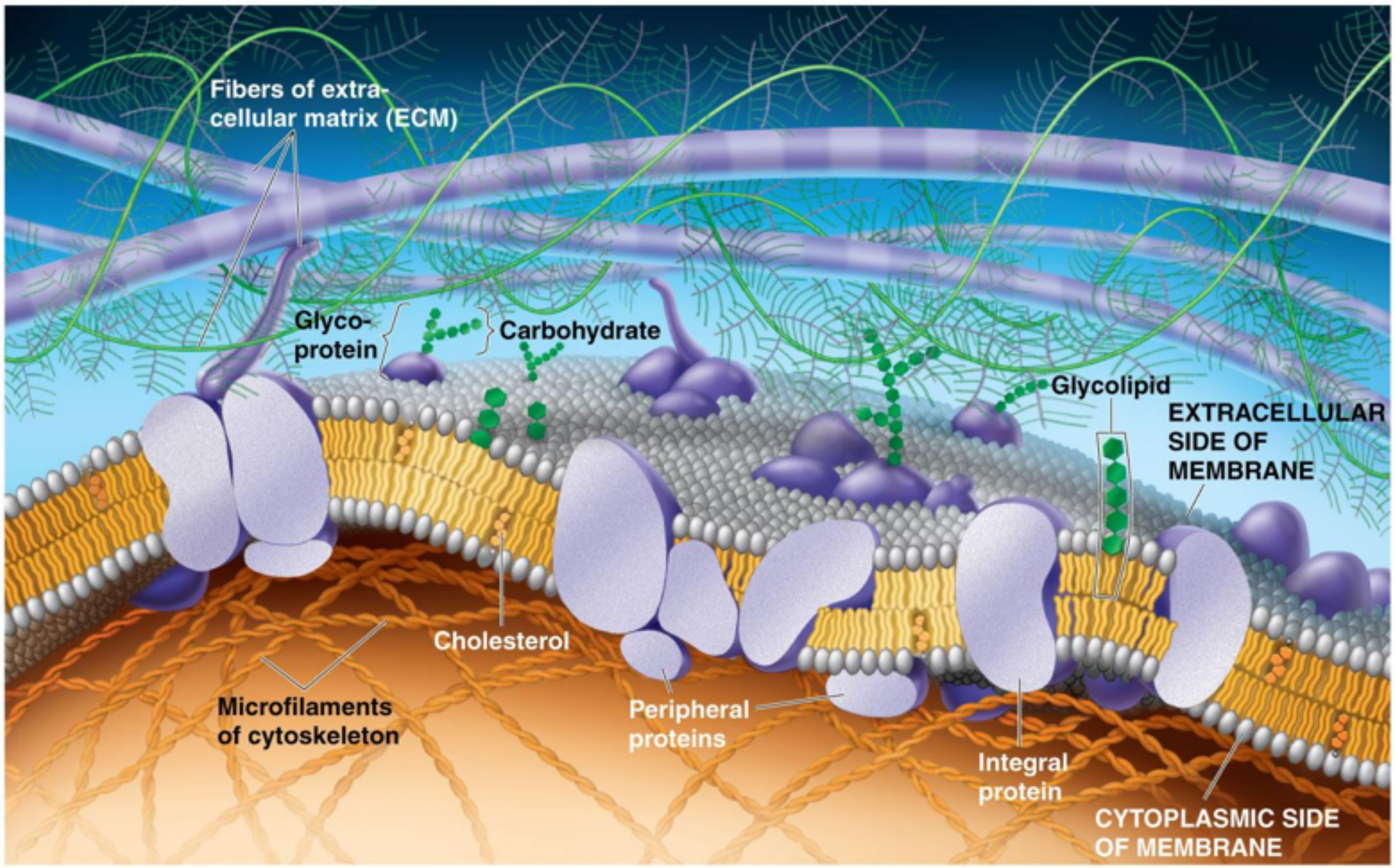
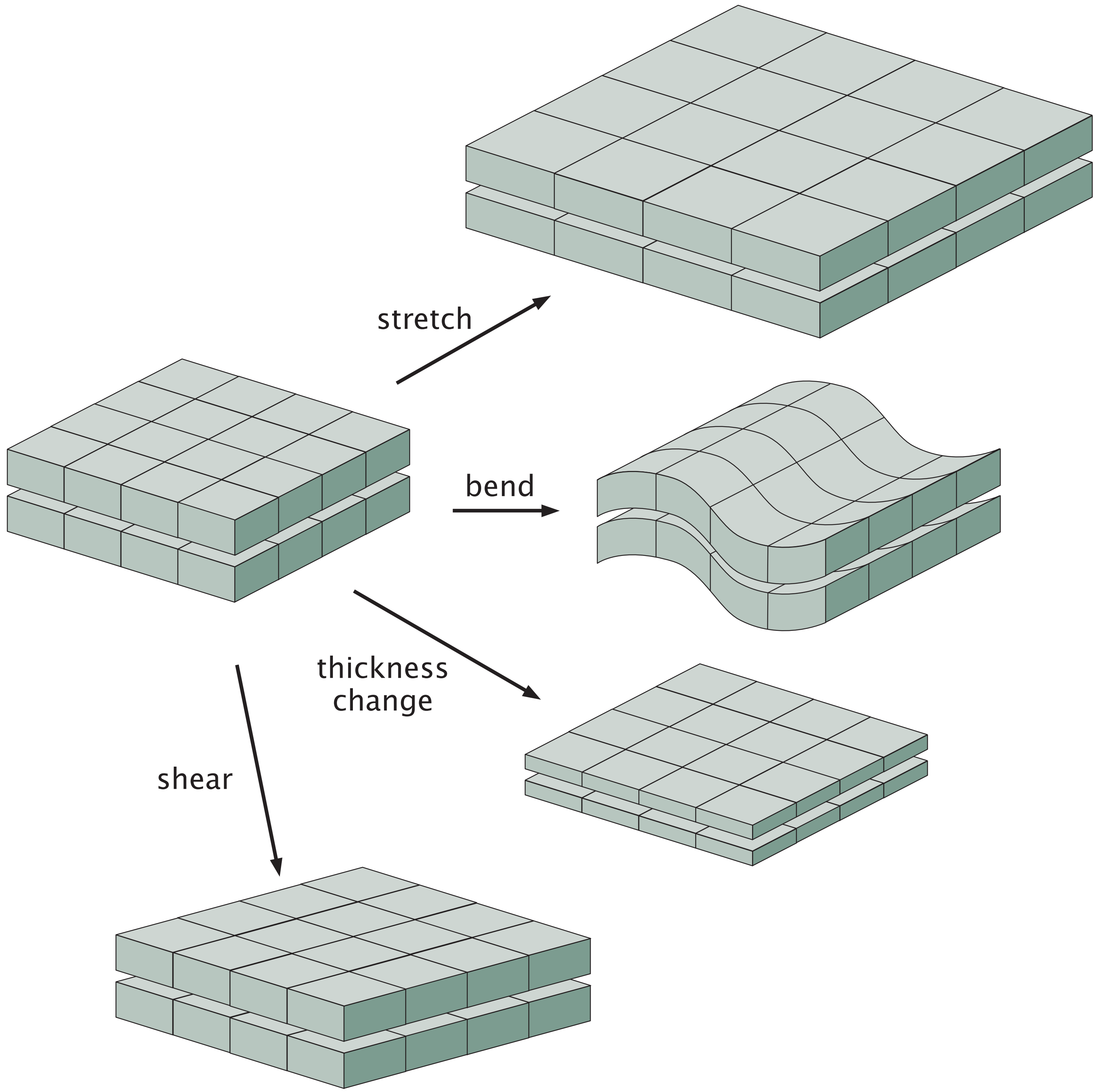
MAE 545: Lecture 16 (11/17)

Mechanics of cell membranes



Membrane deformations



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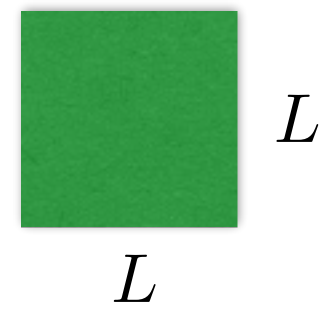
Energy cost for stretching and shearing

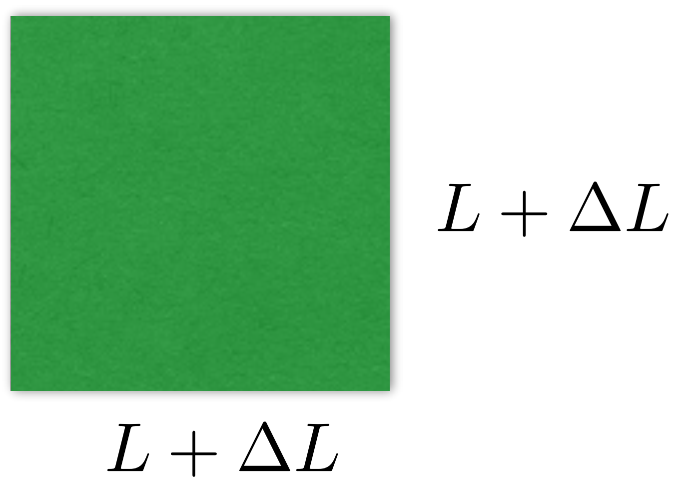
undeformed square patch



patch area

$A = L^2$

isotropic deformation



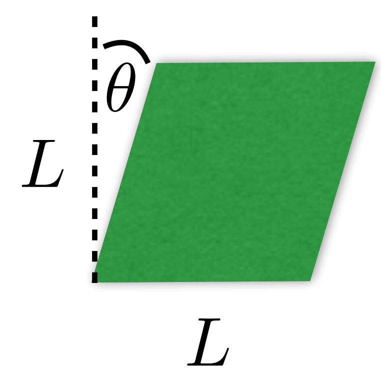
$$\frac{E}{A} = \frac{B}{2}\left(\frac{\Delta A}{A}\right)^2 \approx \frac{B}{2}\left(\frac{2\Delta L}{L}\right)^2$$

bulk modulus

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

(lipid bilayer)

shear deformation



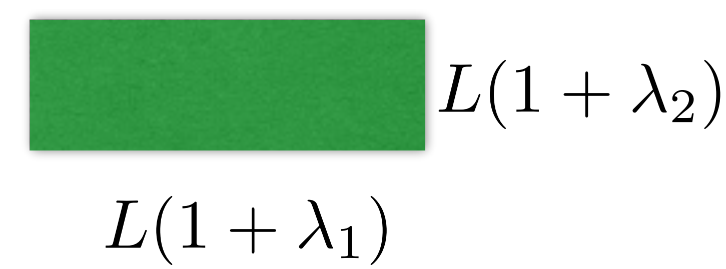
$$\frac{E}{A} = \frac{\mu\theta^2}{2}$$

shear modulus

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

(spectrin network)

anisotropic stretching



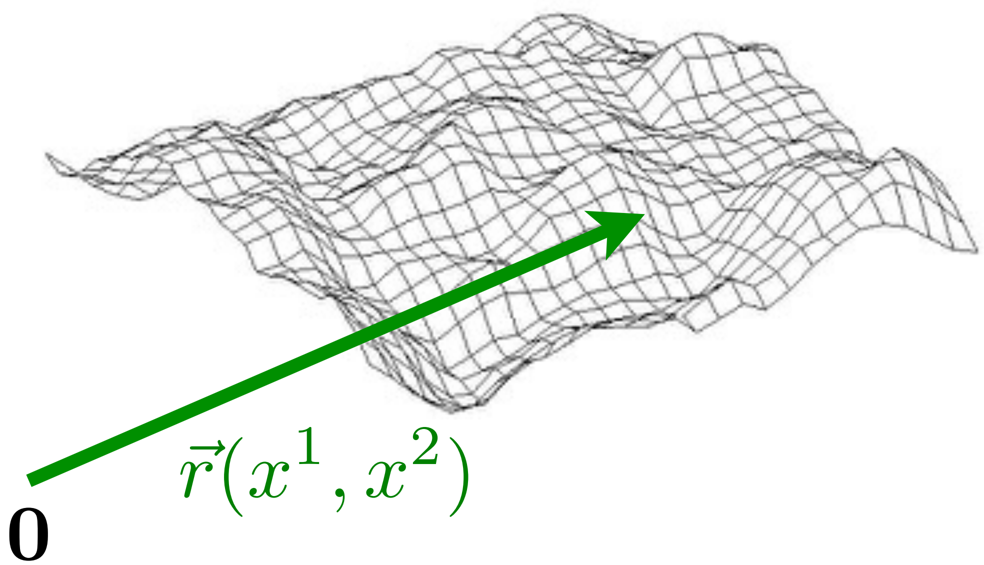
$$\frac{E}{A} \approx \frac{B}{2}(\lambda_1+\lambda_2)^2 + \frac{\mu}{2}(\lambda_1-\lambda_2)^2$$

$\lambda_1, \lambda_2 \ll 1$

(shearing can be interpreted as anisotropic stretching)

Strain tensor for deformation of membranes

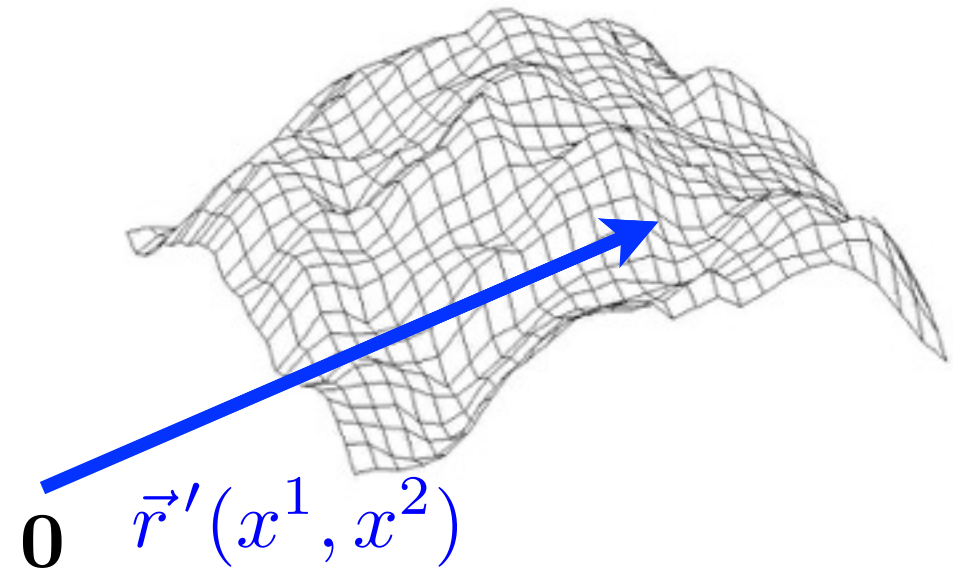
undeformed membrane



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

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

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

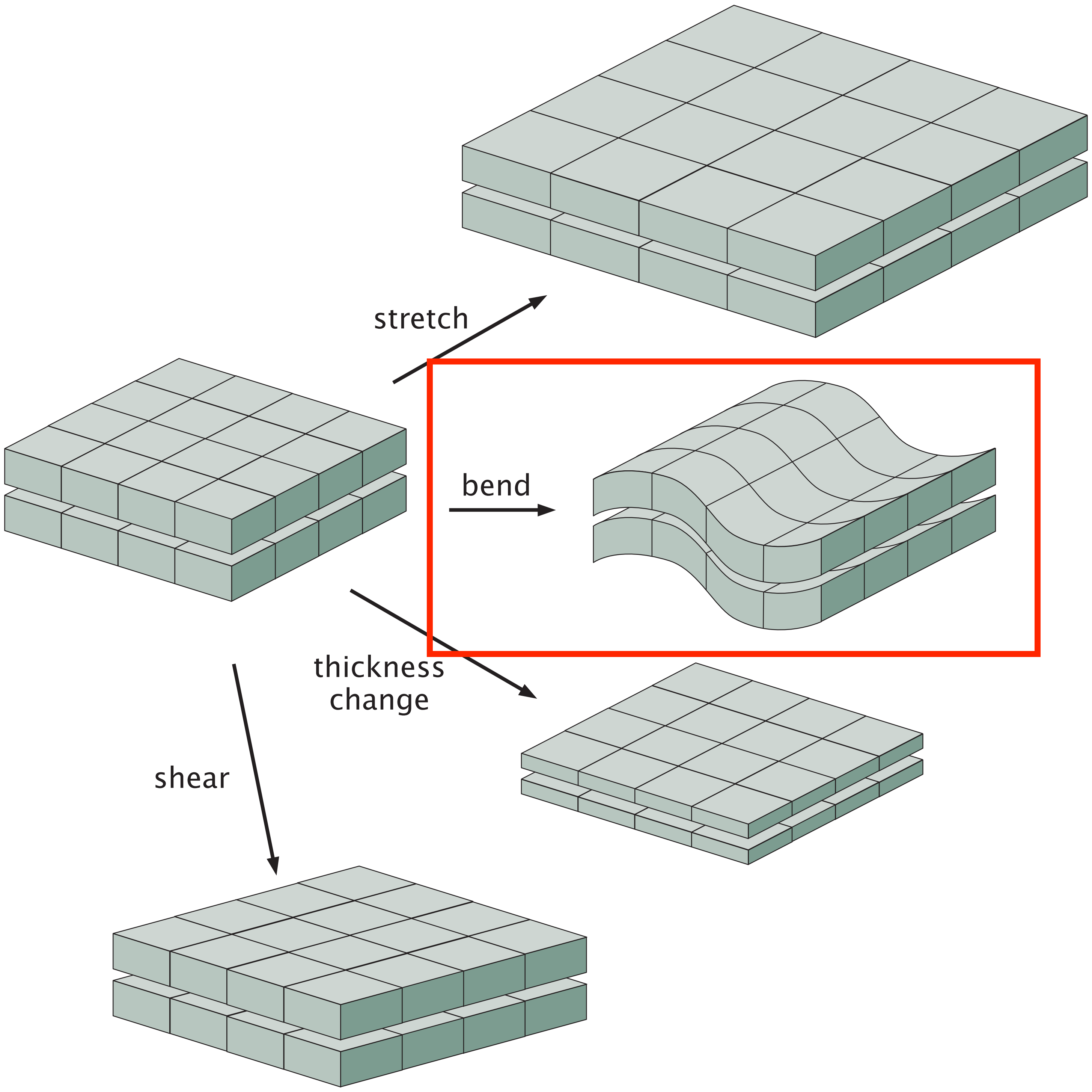
$$\sum_k (g^{-1})_{ik} g_{kj} = \sum_k g_{ik} (g^{-1})_{kj} = \delta_{ij}$$

Energy cost for stretching/compressing

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

$$g = \det(g_{ij})$$

Membrane deformations



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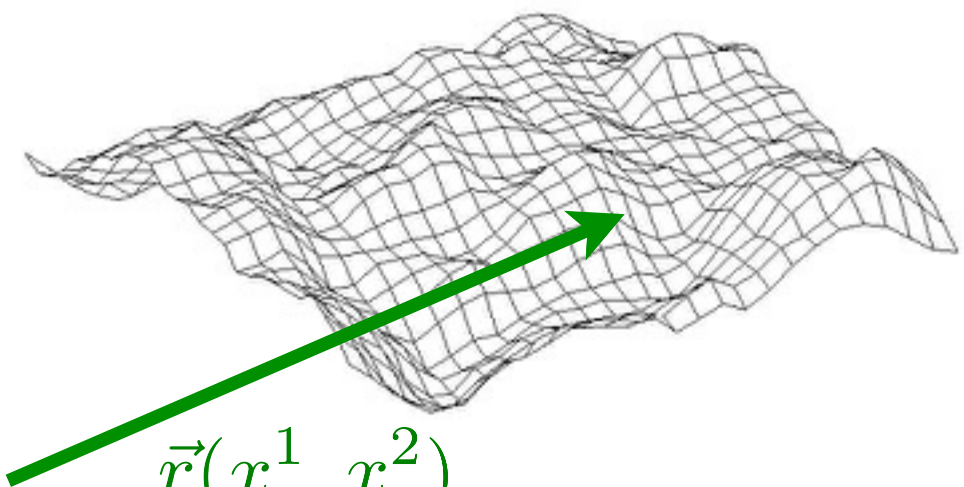
Bending energy for deformation of membranes

undeformed membrane

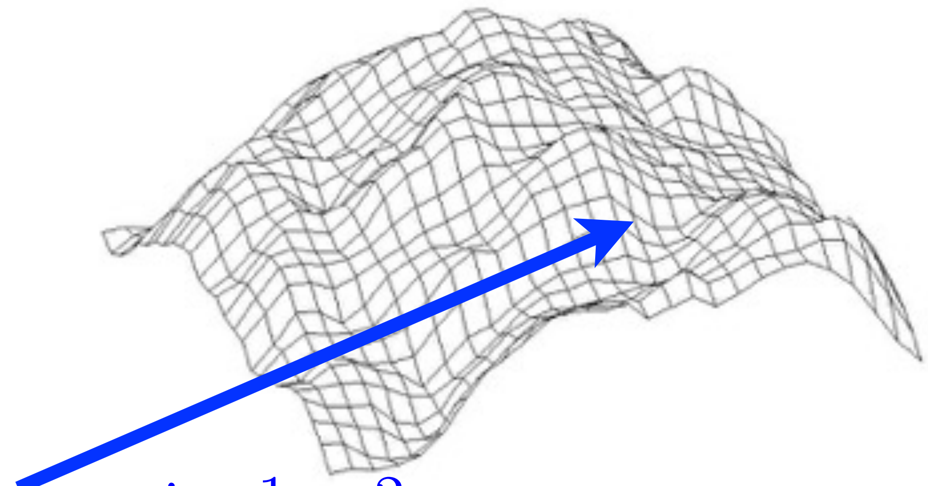


$\vec{r}(x^1, x^2)$

0

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

deformed membrane



0 $\vec{r}\,'(x^1, x^2)$

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

bending strain tensor

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

(local measure of deviation from preferred curvature)

Energy cost of bending

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

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

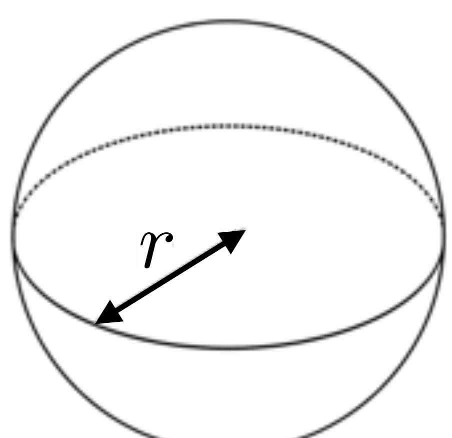
Gaussian curvature $G = \frac{1}{R_1 R_2}$

spontaneous curvature C_0

Example: bending energy for a sphere

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

$$C_0 = 0$$



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

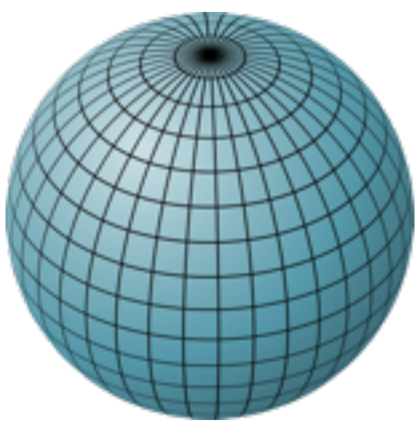
bending energy is independent of the sphere radius!

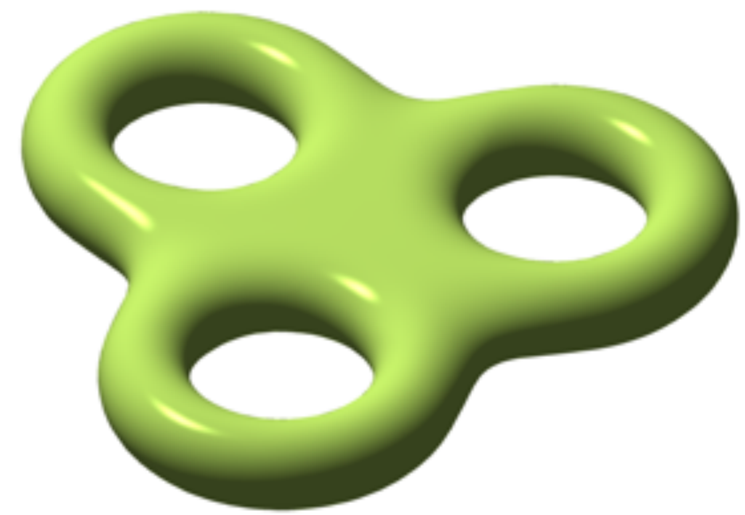
Gauss-Bonet theorem

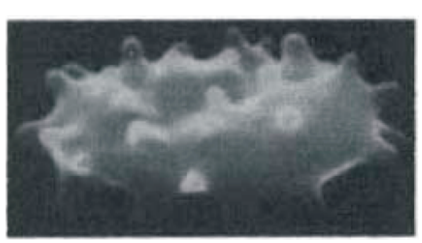
For closed surfaces the integral over Gaussian curvature only depends on the surface topology!

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

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



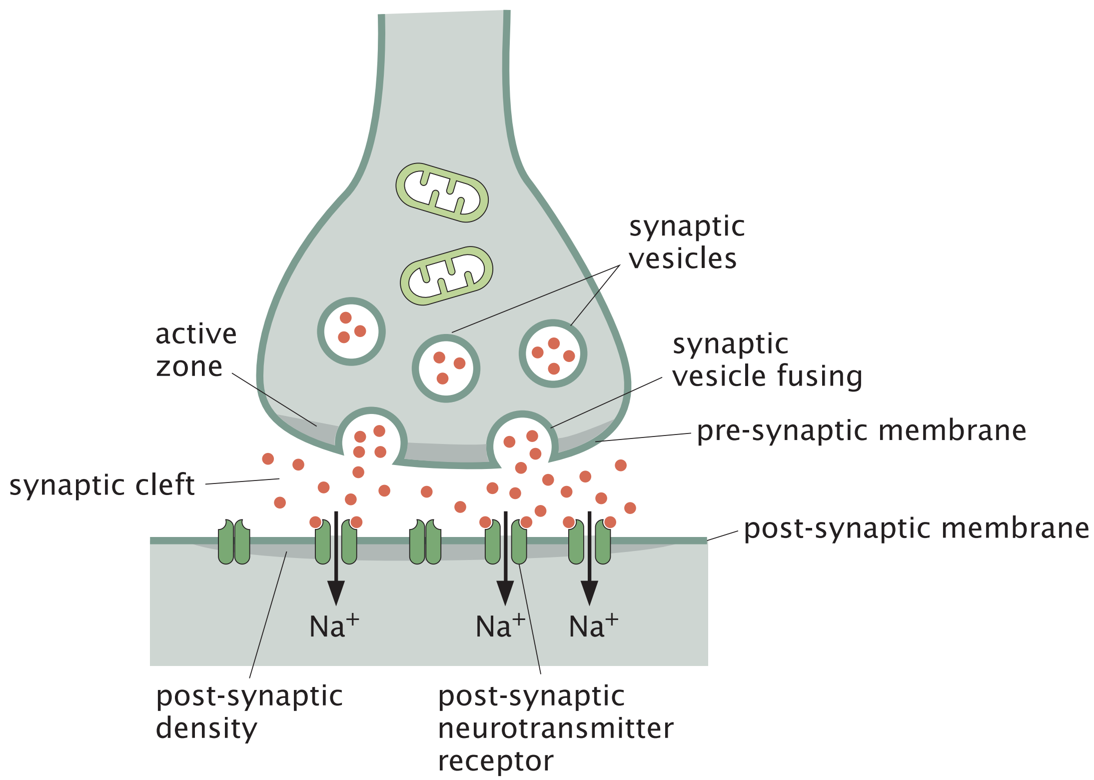


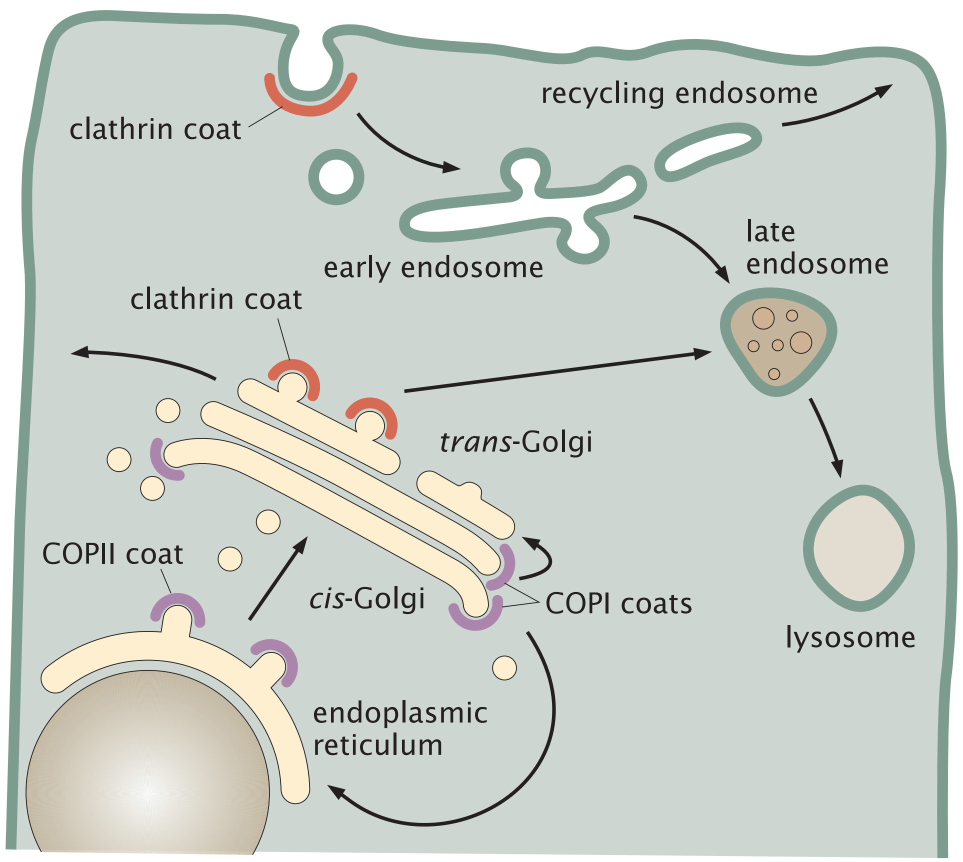


It is hard to experimentally measure the Gaussian bending rigidity for cells, because cell deformations don't change the topology!

Small vesicles are used for cellular transport of molecules

transport of neurotransmitters in neuron cells





Vesicles are changing membrane topology!

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

Membrane fusion

Fusion of small vesicles with the membrane is energetically favorable, but the initial merging provides a large energy barrier!

$E = 4\pi\left(2\kappa + \kappa_G\right)$

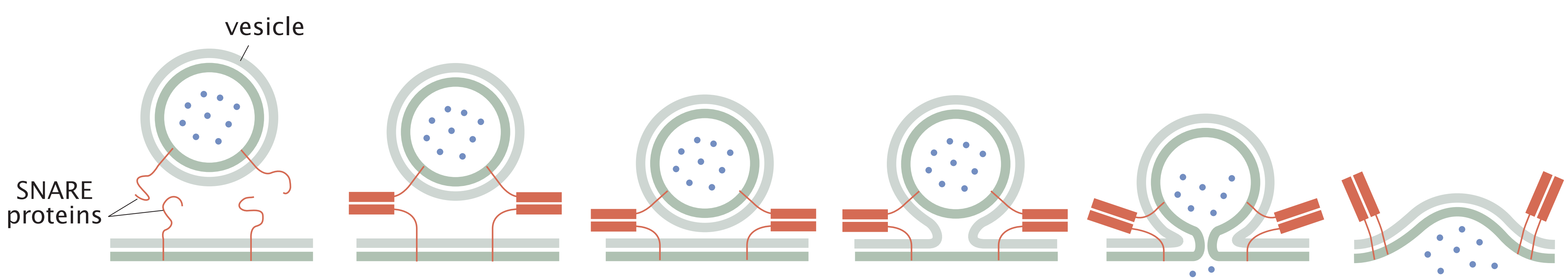
$E \sim +300 k_B T$

$E \approx 8\pi\kappa$

$E \sim +500 k_B T$

$E = 0$

In eukaryotic cells SNARE proteins accelerate membrane fusion by bringing vesicles closer to the membrane!



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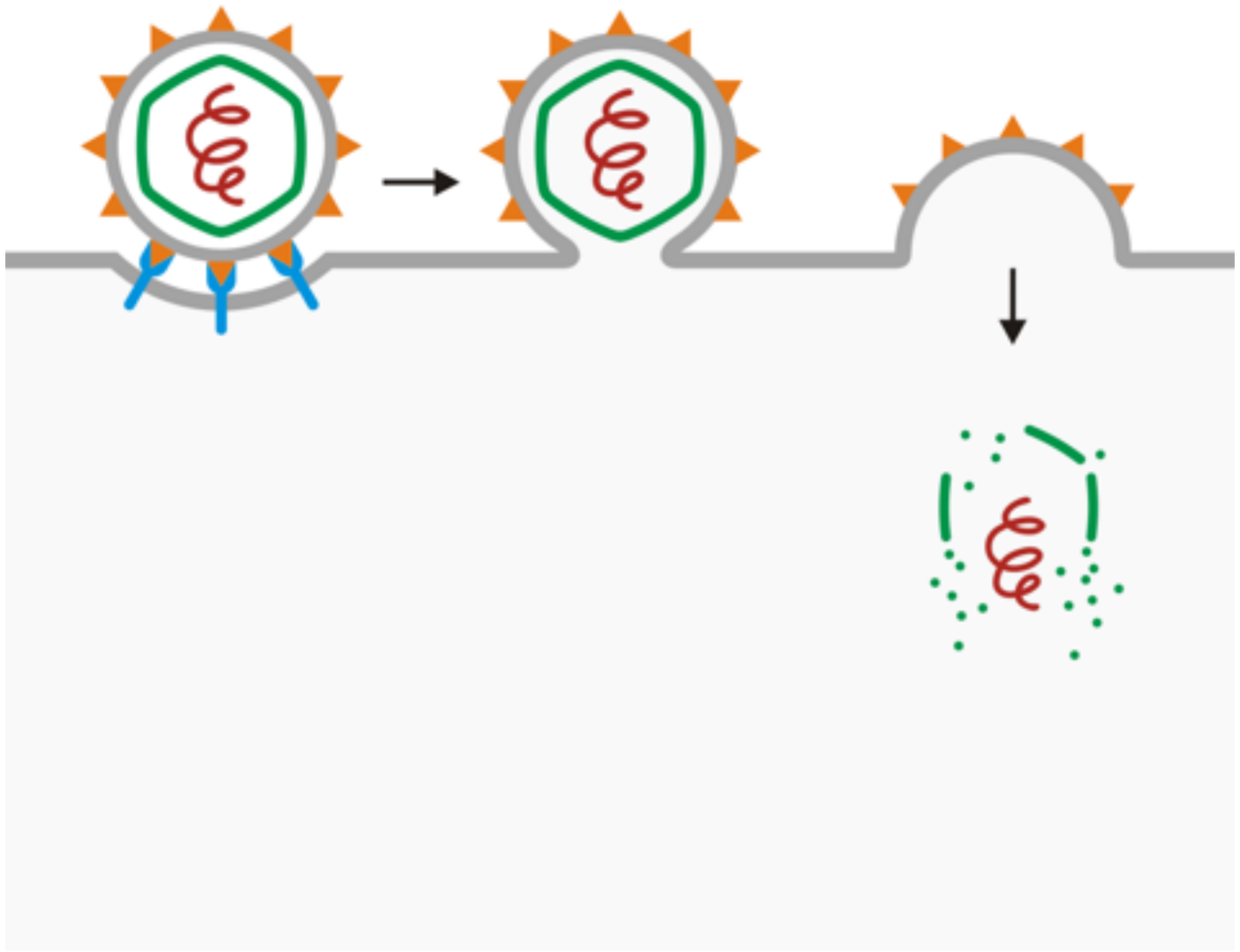
Viral entry to cell via receptor mediated membrane fusion

virus

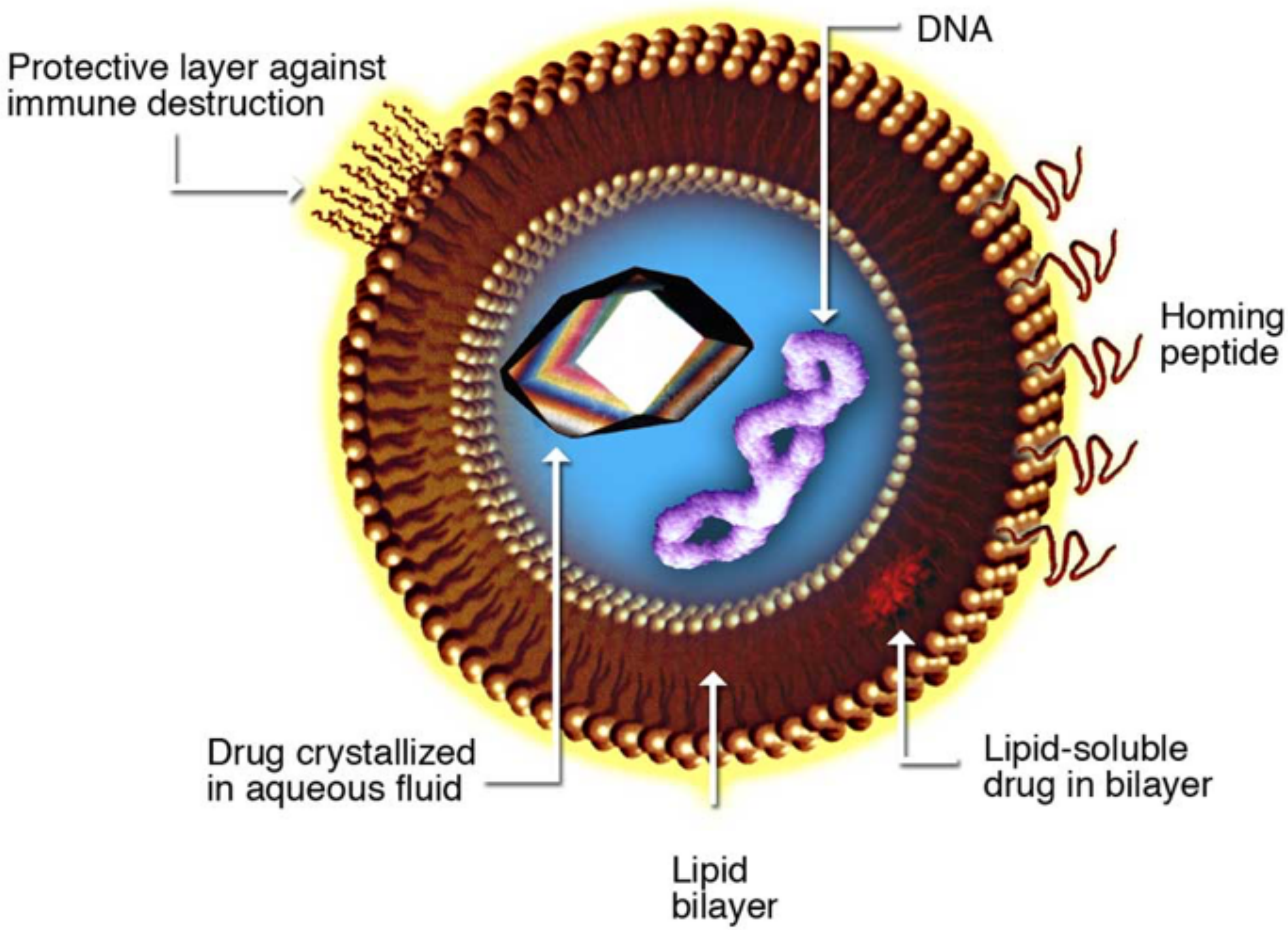
cell



Example of viruses with viral envelope (lipid bilayer): HIV, influenza, hepatitis B virus, herpes viruses, …

Wikipedia

Lipid vesicles can be used for administration of drugs and nutrients

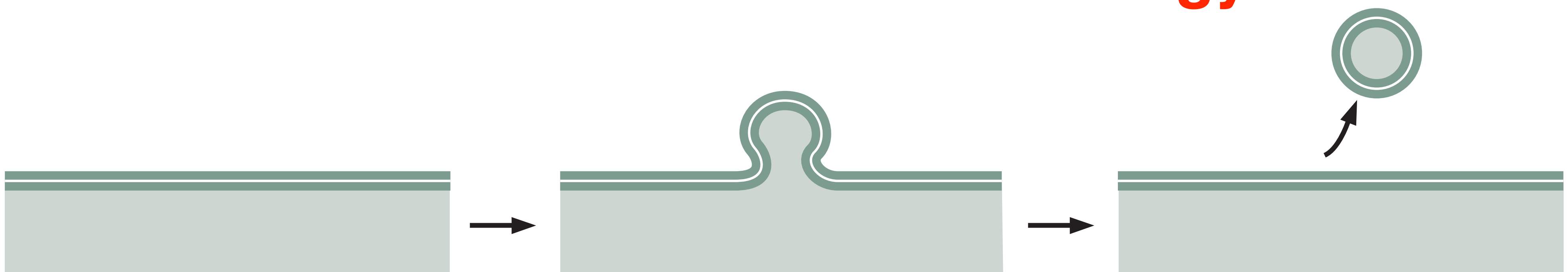


peptides bind to receptors expressed on the surface of target cells

Wikipedia

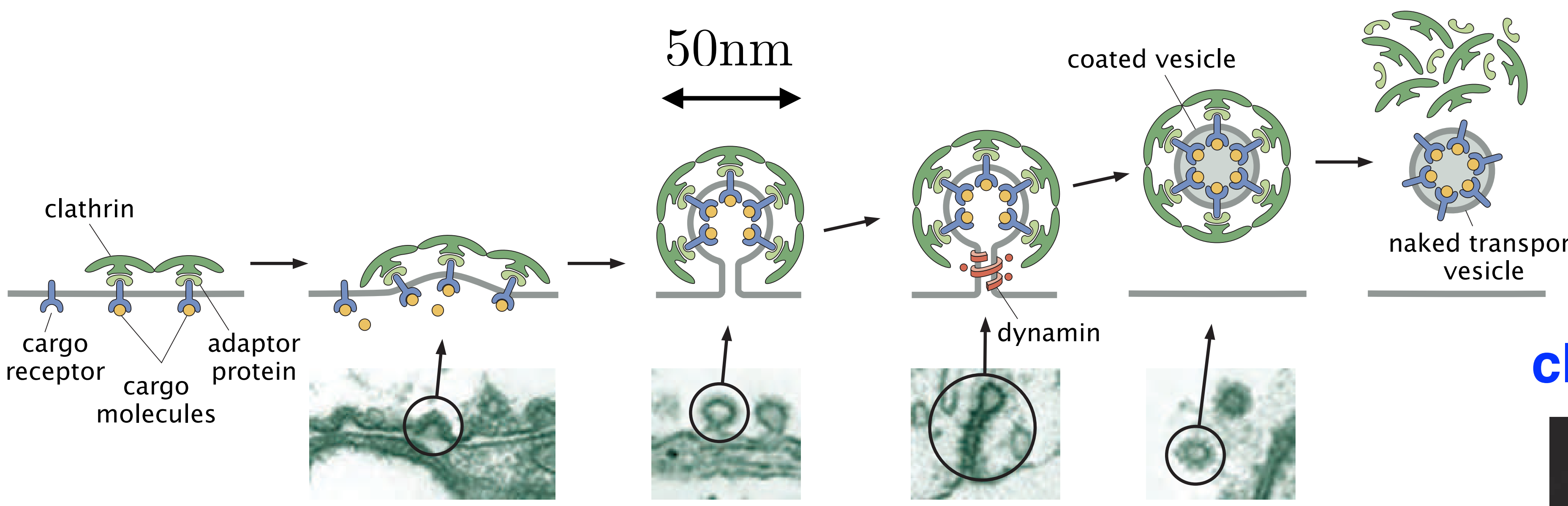
Membrane budding

Creation of new vesicles costs energy!

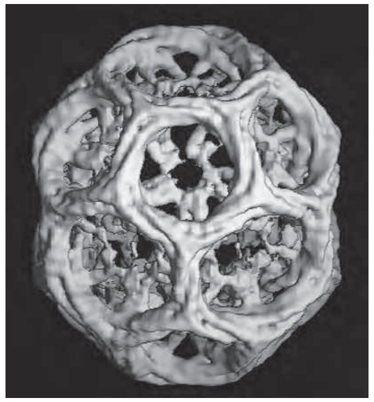


$E = 0$ $\rightarrow$ $E \approx 8\pi\kappa$, $E \sim +500 k_B T$ $\rightarrow$ $E = 4\pi\left(2\kappa + \kappa_G\right)$, $E \sim +300 k_B T$

Creation of new cargo vesicles is assisted with receptor mediated coating of proteins (clathrin, COPI)



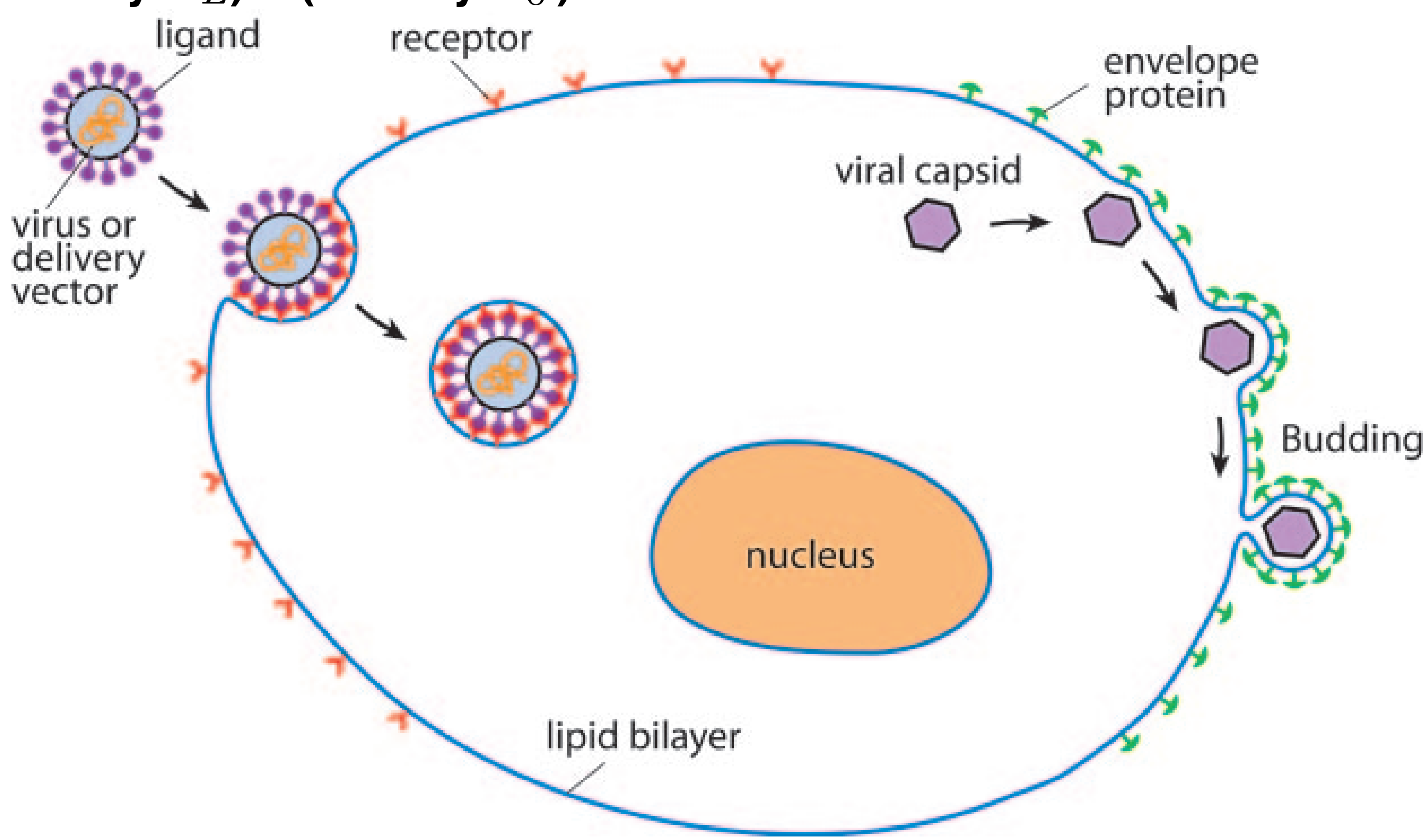
clathrin cage



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

Viral entry to cell via receptor mediated endocytosis

(density n_L) (density n_0)



(similar process may help during budding of enveloped viruses)

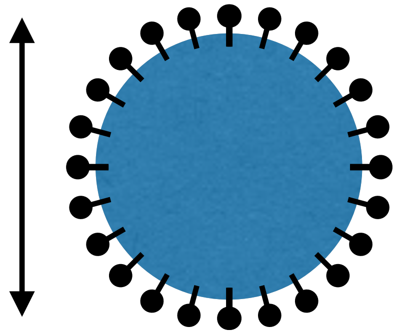
Bending energy cost and loss of entropy for receptors is compensated by the binding energy between cell receptors and ligands on the surface of viral capsid.

G. Bao and X.R. Bao, PNAS 102, 9997 (2005)

Viral entry to cell via receptor mediated endocytosis

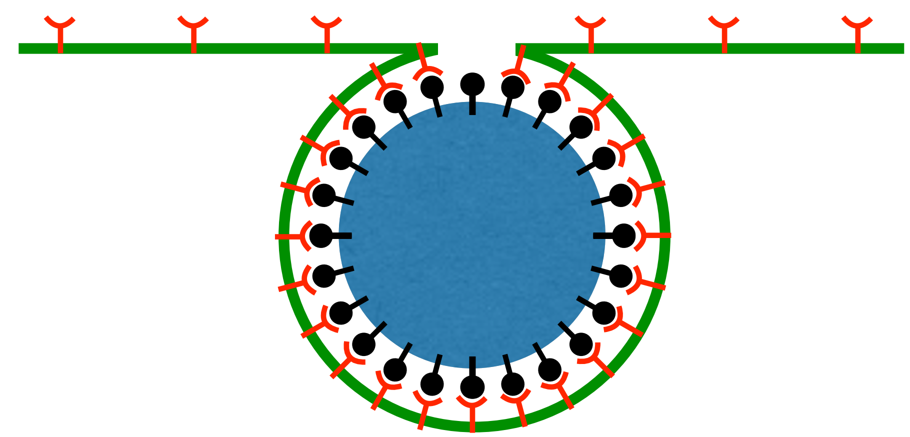
H. Gao *et al.*, PNAS 102, 9469 (2005)

$2R$



$n_L \sim 5000 \mu\text{m}^{-2}$
density of ligands

$n_0 \sim 50\text{-}500 \mu\text{m}^{-2}$
density of receptors



receptor-ligand binding energy
$U_b \sim 15 k_B T$

bending rigidity
$\kappa \sim 20 k_B T$

total number of ligands
$N_L = 4\pi R^2 n_L$

$$\Delta E \approx 8\pi\kappa - 4\pi R^2 n_L U_B + 4\pi R^2 k_B T n_L \ln(n_L/n_0)$$

membrane bending energy — **binding energy of receptors** — **loss of entropy for receptors**

Endocytosis occurs when $\Delta E < 0$:

$$R > \sqrt{\frac{2\kappa}{n_L\left(U_B - k_B T \ln(n_L/n_0)\right)}} \sim 30\text{nm}$$

How fast is this process?

Viral entry to cell via receptor mediated endocytosis

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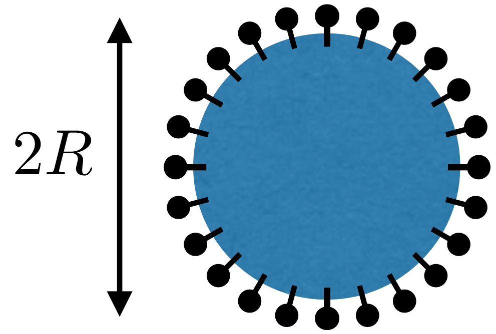
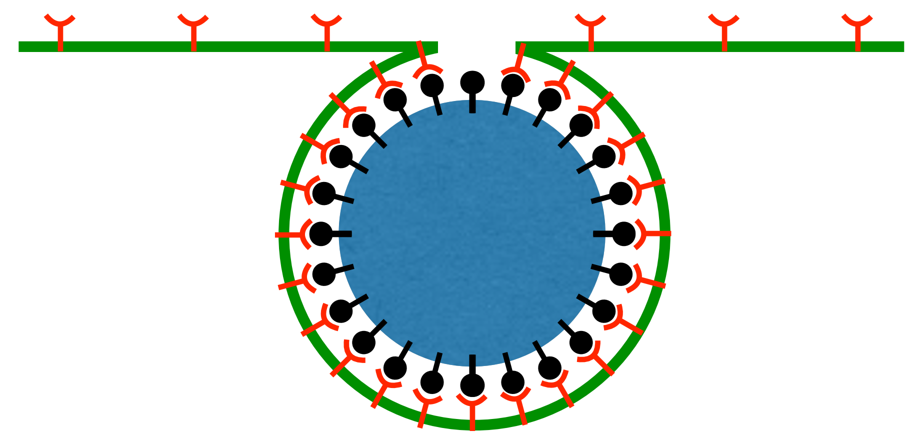


$n_L \sim 5000\mu\text{m}^{-2}$

density of ligands

$n_0 \sim 50\text{-}500\mu\text{m}^{-2}$

density of receptors



receptor-ligand binding energy

$U_b \sim 15k_BT$

bending rigidity

$\kappa \sim 20k_BT$

total number of ligands

$N_L = 4\pi R^2 n_L$

diffusion of receptors

$D \sim 10^4\text{nm}^2/\text{s}$

$$R > \sqrt{\frac{2\kappa}{n_L\left(U_B - k_BT\ln(n_L/n_0)\right)}} \sim 30\text{nm}$$

Need to recruit N_L receptors from circular region of radius L via diffusion

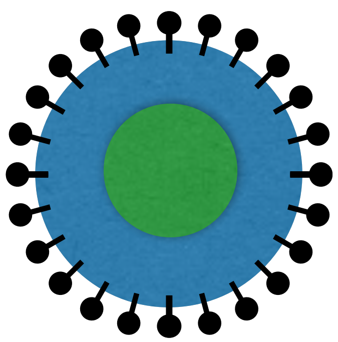
$$N_L = \pi L^2 n_0 = 4\pi R^2 n_L$$

→

$$t \sim \frac{L^2}{D} \sim \frac{R^2 n_L}{D n_0} \gtrsim 10\text{s}$$

Use of magnetic nanoparticles for diagnostic and treatment of tumors

Receptors for LHRH hormone are over-expressed in breast, ovarian, and prostate cancer cells



LHRH hormone

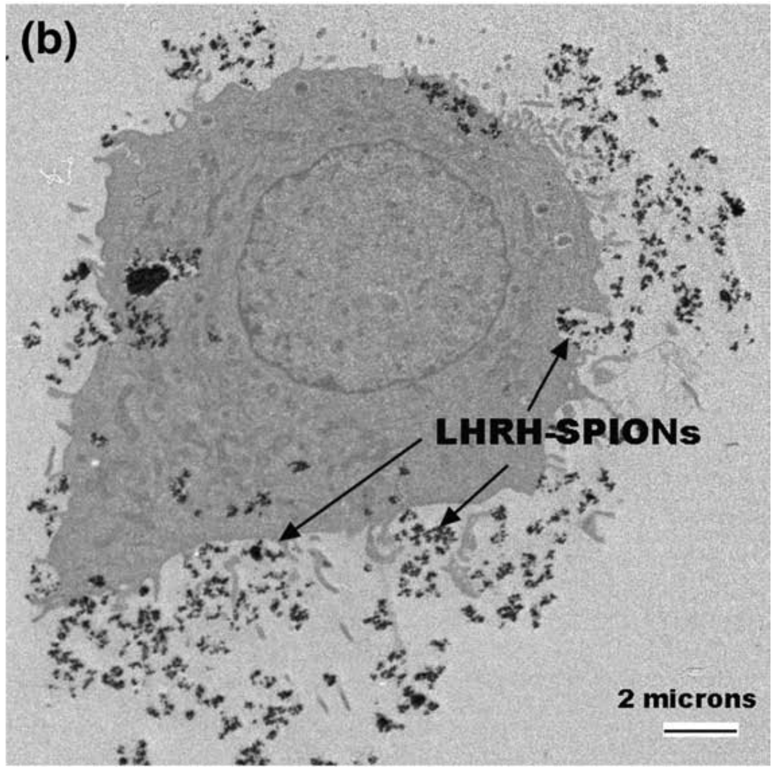
PEG coating

magnetic core

Magnetic particles enter only cancer cells via LHRH-receptor mediated endocytosis

PEG coating shields nanoparticles from immune system and prevents macro-clustering of nanoparticles.

Cancer cells containing magnetic nanoparticles can be detected with MRI (magnetic resonance imaging). Then magnetic particles can be heated via magnetic field to destroys cancer cells.



W. Soboyejo *et al.*