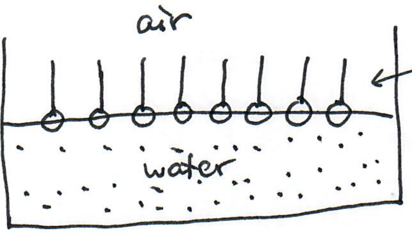
Lecture VI Lipids

1. Why lipids?

Biologically extremely important. form bilayer membranes

2. Self-assembly

Middle-school physics

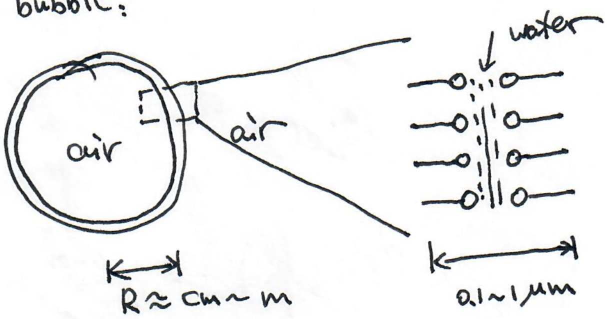


fatty acid ("oil")

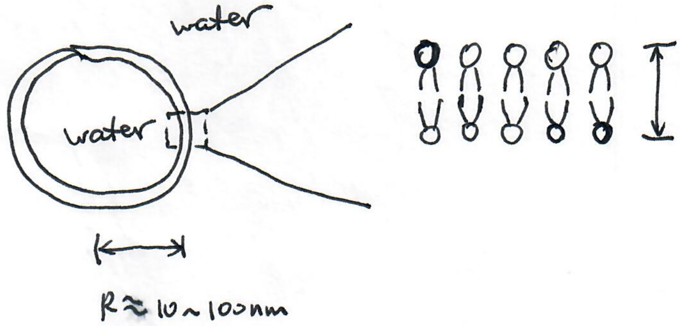
mono layer structure

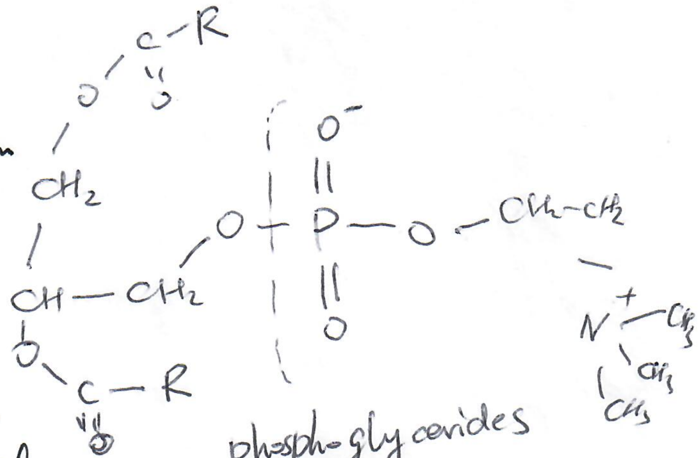
$$l = \frac{m}{\rho A_{int}}$$

soap bubble:



lipid vesicle





lipid → phospholipid  → hydrophilic head → two hydrophobic tails

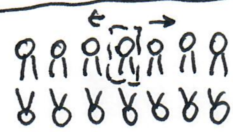
phosphoglycerides
磷酸甘油酯

3. Motions in a lipid bilayer

Question: Which state, fluid or solid, do you expect cell membrane to be?

Answer: fluid (flexibility. Material exchange between the inside and the outside of cells)

1) lateral diffusion



Diff. coeff. $D \sim 1\mu m^2/s$ (fluorescent microscope)

water self diff. coeff. : $D \sim 0.1\, cm^2/s$

lipid bilayer is very viscous

2) protrusion (thermal excitation)

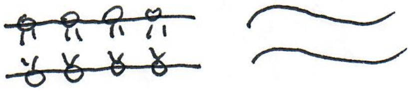
- single molecule or a few molecules relative to the membrane plane
- exposure of hydrophobic cores to water, associated with an energy penalty $\sim \sigma_{pr} A_L$, with σ_{pr} protrusion tension, A_L: area per lipid
- length scales of protrusion, ① amplitude : ~ 0.1 nm
  ② length scale at which the protrusion mode can be seen or measured

3) flip-flop : migration of a lipid molecule from one leaflet to the other.

- involves local rearrangement of neighboring molecules and energetically unfavorable contact of head and tails.
- rare event in real cellular membranes, or synthetic bilayers. rate : ~ 1/hour
- on a not very long time scale the two leaflets are asymmetric
- proteins can catalyze the flip-flop of lipids

4) shape fluctuations (thermal excitation)

"bending"



4. Mechanical deformation of lipid membranes

1) 

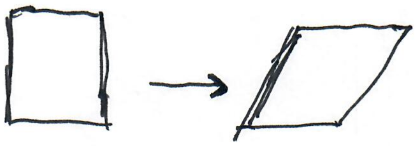
stretching

$$\mathcal{E}_{st} = \frac{1}{2}\frac{K_A}{A_0}(A-A_0)^2$$

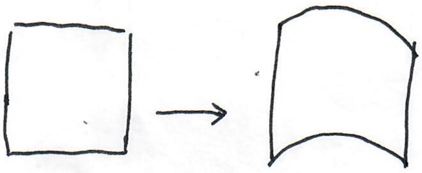
- A close to A_0

A, A_0: area per lipid
K_A: area compressibility modulus. $0.1 \sim 0.2\ J/m^2$
A_0: $\sim 0.5\ nm^2$

- A lipid bilayer ruptures once its area is stretched by 2%–5%.

2) 

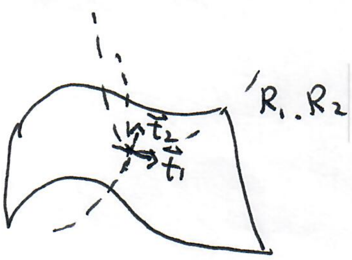
shearing. fluid. no shear resistance

3) 

bending. main contribution

5. Curvature and bending energy

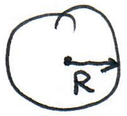
- lateral extension >> membrane thickness (~5 nm). lipid membrane viewed as a thin elastic sheet
- parameterization (differential geometry)



$c_1 = \frac{1}{R_1}$ $c_2 = \frac{1}{R_2}$ curvature

energy density $(\mathcal{E}_{be}/A)$ independent of parameterization. depends on

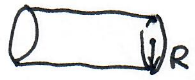
$\bar{c} = \frac{c_1+c_2}{2} \equiv M$ (mean curvature). $c_1 c_2 \equiv G$ (Gaussian curvature)

- 

sphere

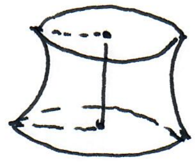
$M = \frac{1}{R}$

$G = \frac{1}{R^2}$



$M = \frac{1}{2R}$

$G = 0$



catenoid
悬链面

$M = 0$

$G = -\frac{1}{R^2}$

- curvature energy

$$\mathcal{E}_{be} = \oint \left(2K_{be}(M-M_0)^2 + K_G G + \underset{\substack{\uparrow \\ \text{tension}}}{\Sigma} \right) dA$$

material parameters:

K_{be}: bending modulus. $\sim 10\, k_BT$

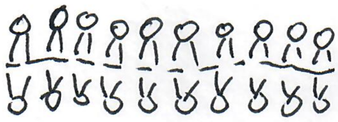
M_0: spontaneous curvature

K_G: Gaussian modulus. for a membrane without topological transformation. $\oint G\, dA = \text{const}$

rather difficult to measure

- How to measure K_{be}?

In limiting case of infinite large K_{be}, the lipid membrane prefers a planar shap. This means, the larger K_{be} the less deviation of the membrane from the referen planar shape. By looking at the fluctuations, one can measure K_{be}.


→ midplane $h(\vec{r})$: height field w.r.t. reference state

Fourier transform: $\tilde{h}(\vec{q}) = \int h(\vec{r}) e^{i\vec{q}\cdot\vec{r}} d\vec{r}$.

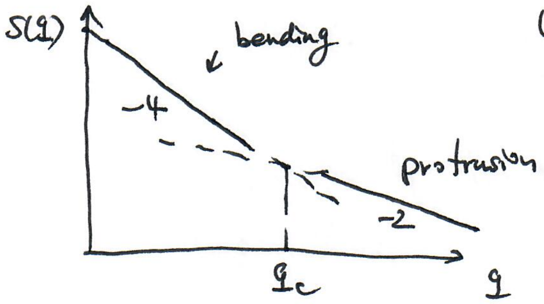
fluctuation spectrum: $S(q) = \langle |\tilde{h}(\vec{q})|^2 \rangle$

- For a tensionless bilayer $(\Sigma = 0)$ $\mathcal{E} = \oint \left[2K_{be}(M-\underset{0}{\underset{\shortparallel}{M_0}})^2 + \sigma_{pr} \right] dA$

$$S(q) \sim \frac{k_BT}{K_{be} q^4} + \frac{k_BT}{\sigma_{pr} q^2}$$

for large q, i.e small length scale. $\frac{k_BT}{\sigma_{pr} q^2}$ dominates. protrusion mode

for small q. i.e. large length scale, k_BT dominates bending mode



log-log plot

$q_c \to L_c \approx$ membrane thickness (5nm)

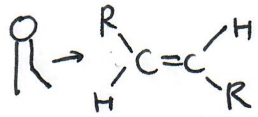
↓

characteristic length scale beyond which bending mode dominates.

6. Multicomponent membranes

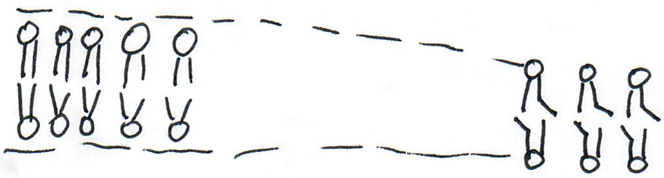
• Two types of phospholipids

 two saturated chains (−C−C−)



cis- C=C bond

unsaturated chain



dense packing

→ high order of the tails

→ Liquid-ordered phase

high K_{be}

loose packing

→ low order of the tails

→ liquid-disordered phase

low K_{be}

• lipid-raft picture of cellular membrane hypothesis

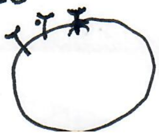
  • separated Lo and Ld domains due to hydrophobic mismatch

  • Lo domains: platforms for protein functioning

7. Material exchange (transport) via membranes

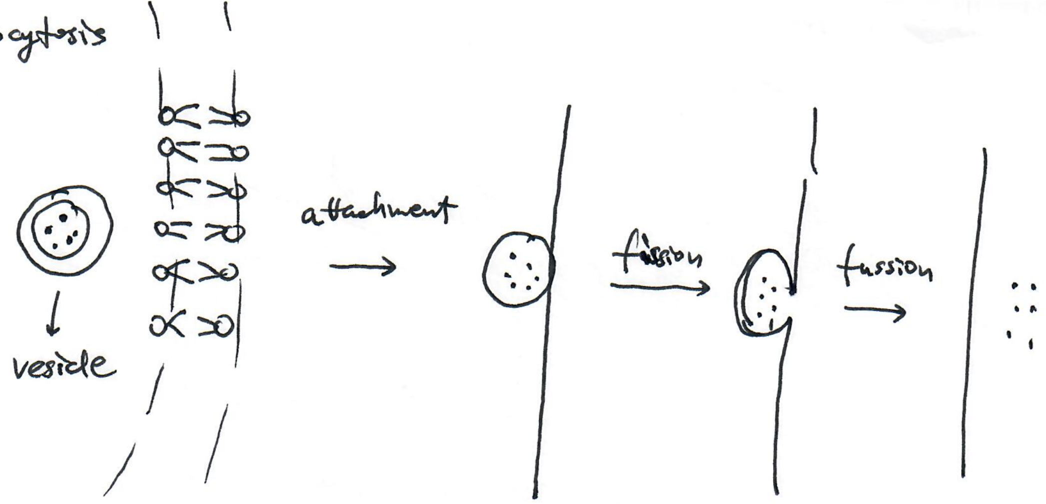
endocytosis, exocytosis

 → nanoparticle (decorated with ligands ↦)

 → cell membranes (with receptors ⊣)

$\xrightarrow[\text{wrapping}]{\text{adhesion}}$

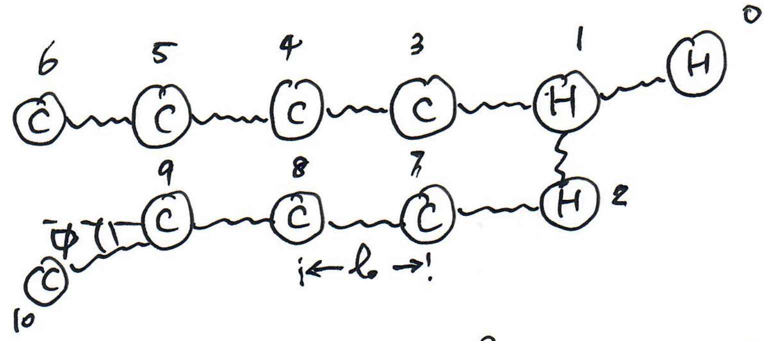
exocytosis

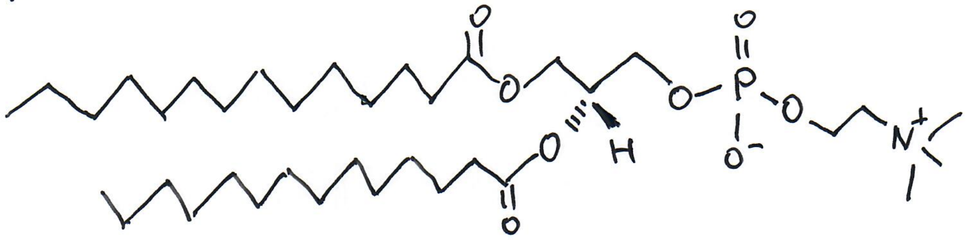


Lecture VI Lipids

Case study:

coarse grained DMPC





1 tail bead $\simeq$ 3.5 $-CH_2-$

bonded interactions

$$U_2 = \frac{1}{2} k_2 (|\vec{r}| - l_0)^2 , \qquad k_2 = \frac{128\, k_BT}{r_0^2}, \quad l_0 = 0.5 r_0$$

$$U_3 = k_3 [1 - \cos(\phi - \phi_0)] ,$$ three consecutive tail beads

$k_3 = 15\, k_BT, \quad \phi_0 = 0$

nonbonded interactions (between any two beads)

conservative force + dissipative (frictional) force + random force

$$\vec{F}_{ij}^C + \vec{F}_{ij}^D + \vec{F}_{ij}^R = \left[a_{ij} \left(1 - \frac{r_{ij}}{r_0}\right) - \gamma_{ij} \left(1 - \frac{r_{ij}}{r_0}\right)^2 (\vec{v}_{ij} \cdot \hat{r}_{ij}) + \sigma_{ij} \left(1 - \frac{r_{ij}}{r_0}\right) \xi_{ij} \delta t^{-1/2} \right] \hat{r}_{ij}$$

$$= \left[a_{ij} \left(\frac{1}{r_{ij}} - \frac{1}{r_0}\right) - \gamma_{ij} \left(\frac{1}{r_{ij}} - \frac{1}{r_0}\right)^2 (\vec{v}_{ij} \cdot \vec{r}_{ij}) + \underbrace{\sigma_{ij}}_{= \sqrt{2\gamma_{ij} k_BT}} \left(\frac{1}{r_{ij}} - \frac{1}{r_0}\right) \delta t^{-1/2} \xi_{ij} \right] \vec{r}_{ij}$$

$a_{ij}(\sigma_{ij})$	$i=H$	$i=C$	$i=\text{Water}$
$j=H$	30(4.5)	35(9.0)	30(4.5)
$j=C$	35(9.0)	10(4.5)	75(20.0)
$j=\text{water}$	30(4.5)	75(20.0)	25(4.5)

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bonded forces

if $|\vec{r}|>l_0$, $\vec{F}_i, \vec{r}_{ij}$ opposite sign

if $|\vec{r}|<l_0$ $\vec{F}_i, \vec{F}_{ij}$ same sign

$$U_2(\vec{r}) = \frac{1}{2}k_2(|\vec{r}|-l_0)^2$$

$$\vec{r} \equiv \vec{r}_i - \vec{r}_j, \quad |\vec{r}| = |\vec{r}_i - \vec{r}_j|$$

$$\vec{F}_i = -\frac{\partial U_2(\vec{r})}{\partial \vec{r}_i} = -\frac{\partial U_2(\vec{r})}{\partial \vec{r}}\frac{\partial \vec{r}}{\partial \vec{r}_i} = -\frac{\partial U_2(\vec{r})}{\partial \vec{r}}, \quad \vec{F}_j = -\vec{F}_i$$

$$-\frac{\partial U(\vec{r})}{\partial \vec{r}} = -\nabla_{\vec{r}} U(\vec{r}) = -\frac{\partial U}{\partial |\vec{r}|}\frac{\partial |\vec{r}|}{\partial \vec{r}} = -k_2(|\vec{r}|-l_0)\frac{\partial |\vec{r}|}{\partial \vec{r}}$$

$$= -k_2(|\vec{r}|-l_0)\frac{\vec{r}}{|\vec{r}|}$$

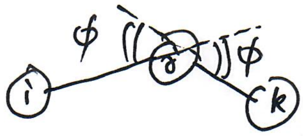
$$= -k_2\left(1-\frac{l_0}{|\vec{r}|}\right)\vec{r}$$

$$\boxed{\frac{\partial |\vec{r}|}{\partial \vec{r}} \equiv \frac{\partial\left[(\vec{r}\cdot\vec{r})^{\frac{1}{2}}\right]}{\partial \vec{r}} = \frac{\partial (\vec{r}\cdot\vec{r})^{\frac{1}{2}}}{\partial (\vec{r}\cdot\vec{r})} \cdot \frac{\partial (\vec{r}\cdot\vec{r})}{\partial \vec{r}} = \frac{1}{2}(\vec{r}\cdot\vec{r})^{-\frac{1}{2}} 2\vec{r}} = \frac{\vec{r}}{|\vec{r}|}$$

$$\vec{F}_i = -k_2\left(1-\frac{l_0}{|\vec{r}|}\right)\vec{r}$$

$$\vec{F}_j = k_2\left(1-\frac{l_0}{|\vec{r}|}\right)\vec{r}$$

$$\frac{\partial |\vec{r}|}{\partial \vec{r}} = \hat{r}$$



$$U_3(\vec{r}_i, \vec{r}_j, \vec{r}_k) = k_3\left[1-\cos(\phi-\phi_0)\right] \overset{\phi_0=0}{=\!=} k_3(1-\cos\phi)$$

$$\cos\phi = \frac{\vec{r}_{ji}\cdot\vec{r}_{kj}}{|\vec{r}_{ji}||\vec{r}_{kj}|}$$

$$\frac{\partial U_3}{\partial \cos\phi} = -k_3,$$

$$\vec{F}_i = -\frac{\partial U_3}{\partial \vec{r}_i} = -\frac{\partial U_3}{\partial \cos\phi}\frac{\partial \cos\phi}{\partial \vec{r}_i} = k_3\frac{\partial \cos\phi}{\partial \vec{r}_i}.$$

$$\frac{\partial \cos\phi}{\partial \vec r_i} = \underbrace{\frac{\partial \cos\phi}{\partial \vec r_{ji}}}_{\text{vector}} \underbrace{\frac{\partial \vec r_{ji}}{\partial \vec r_i}}_{3\times 3\ \text{Identity matrix}} = -\frac{\partial \cos\phi}{\partial \vec r_{ji}} = -\frac{\vec r_{kj}}{|\vec r_{ji}||\vec r_{kj}|} - \frac{\vec r_{ji}\cdot\vec r_{kj}}{|\vec r_{kj}|}\frac{\partial \frac{1}{|\vec r_{ji}|}}{\partial \vec r_{ji}}$$

$$\frac{\partial |\vec r_{ji}|^{-1}}{\partial \vec r_{ji}} = \frac{\partial |\vec r_{ji}|^{-1}}{\partial |\vec r_{ji}|}\frac{\partial |\vec r_{ji}|}{\partial \vec r_{ji}} = -|\vec r_{ji}|^{-2}\frac{\vec r_{ji}}{|\vec r_{ji}|} = -\frac{\vec r_{ji}}{|\vec r_{ji}|^3}$$

$$\frac{\partial \cos\phi}{\partial \vec r_i} = -\frac{\vec r_{kj}}{|\vec r_{ji}||\vec r_{kj}|} + \frac{(\vec r_{kj}\cdot\vec r_{ji})\,\vec r_{ji}}{|\vec r_{ji}|^3|\vec r_{kj}|} = \frac{(\vec r_{kj}\cdot\hat r_{ji})\,\hat r_{ji} - \vec r_{kj}}{|\vec r_{ji}||\vec r_{kj}|}$$

$$F_i = k_3\frac{(\vec r_{kj}\cdot\hat r_{ji})\,\hat r_{ji} - \vec r_{kj}}{|\vec r_{ji}||\vec r_{kj}|} = k_3\frac{\cos\phi\,\hat r_{ji} - \hat r_{kj}}{|\vec r_{ji}|\,|\vec r_{kj}|^2}$$

Rewrite $\cos\phi = -\frac{\vec r_{ij}\cdot\vec r_{kj}}{|\vec r_{ij}||\vec r_{kj}|}$, i, k are exchangable

$$F_k = k_3\frac{(\vec r_{ij}\cdot\hat r_{jk})\,\hat r_{jk} - \vec r_{ij}}{|\vec r_{ji}||\vec r_{kj}|} = k_3\frac{\vec r_{ji} - (\vec r_{ji}\cdot\hat r_{kj})\,\hat r_{kj}}{|\vec r_{ji}||\vec r_{kj}|}$$

$$= \frac{\hat r_{ji} - \cos\phi\,\hat r_{kj}}{|\vec r_{ji}|^2|\vec r_{kj}|}$$

$$F_j = -(F_i + F_k)$$

Simulation setup

system II

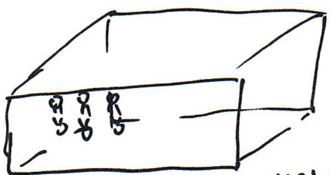
L_x L_y L_z

$20\times 20\times 10\ r_0^3$ box

$N_{Lipid} = 320\cdot 2 = 640$ $\bar A_L = 1.25\ r_0^2$

$\rho = 3/r_0^3$

$N_{Lipid}\cdot 11 + N_{water} = \rho V = 12000$



system I

$L_x = 10$

$L_y = 10$

$L_z = 10$

$N_{Lipid} = 80\cdot 2 = 160$ $\bar A_L = 1.25\ r_0^2$

$\rho V = 3000$