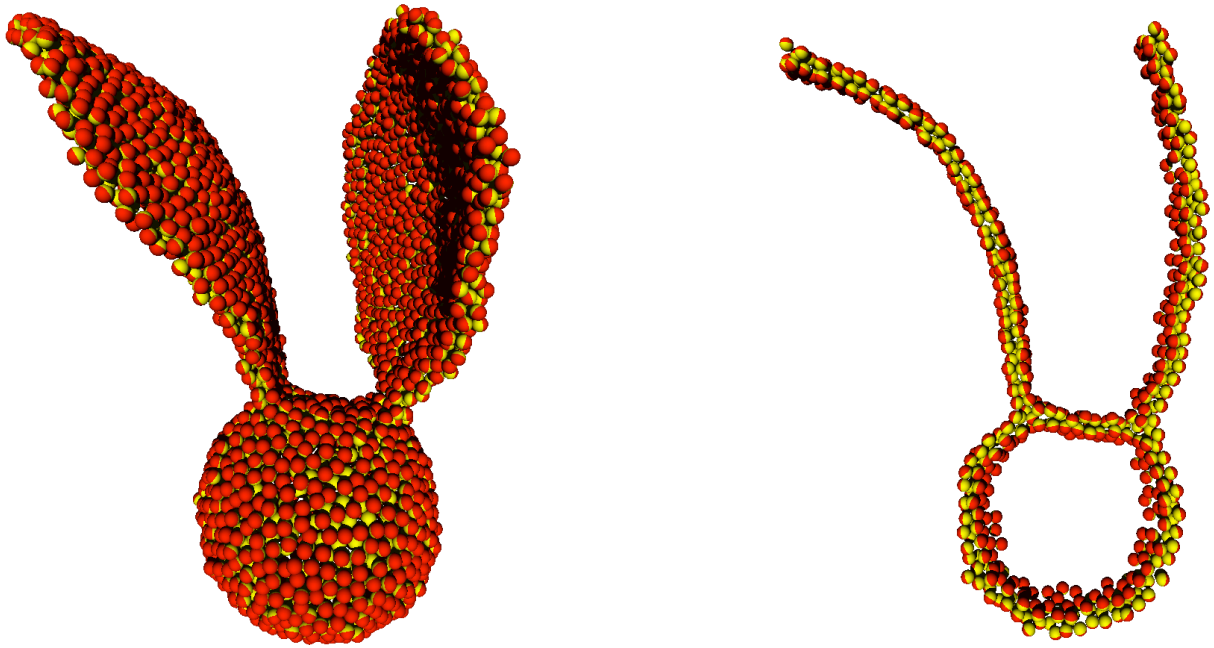
Simple Solvent-Free Molecular Model to Simulate Bilayer Membrane

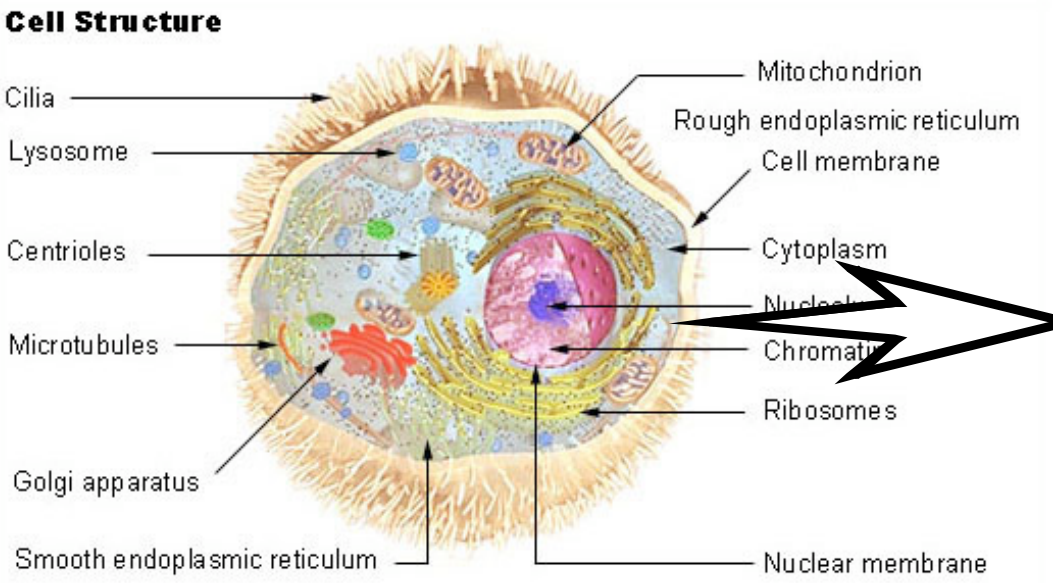


Hiroshi Noguchi

ISSP, University of Tokyo

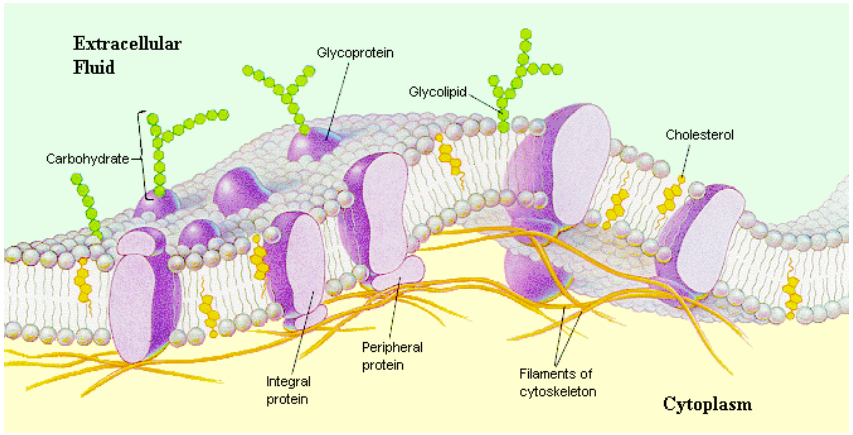
- Biomembrane

Cell



~10μm

Plasma membrane



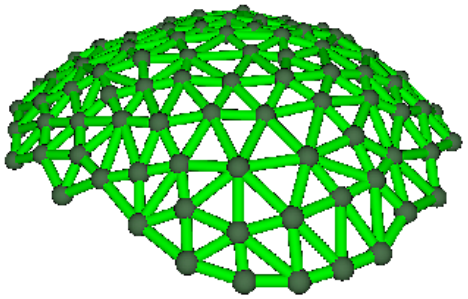
10nm

Large scale gap

http://upload.wikimedia.org/wikipedia/commons/1/10/Illu_cell_structure.jpg

Membrane models

curved surface
(no bilayer structure)

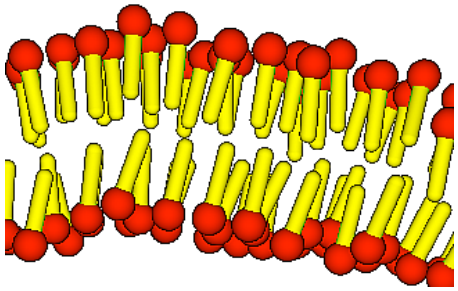


~ μm

Numerically
faster

go down

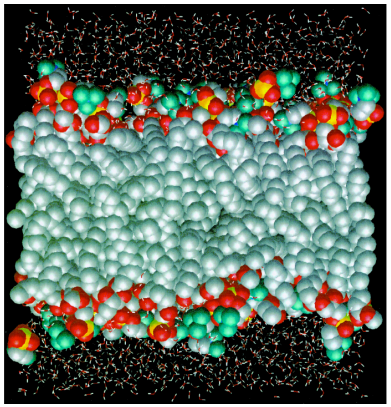
molecular model



coarse grained molecule

length and time scale

atomistic model



More detailed information

bottom up
Shinoda etc.

~ nm

Tieleman, et al. BBA 1331, 225 (1997)

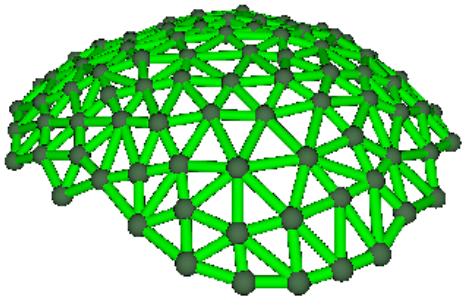
- curved surface
  - theory: continuous surface

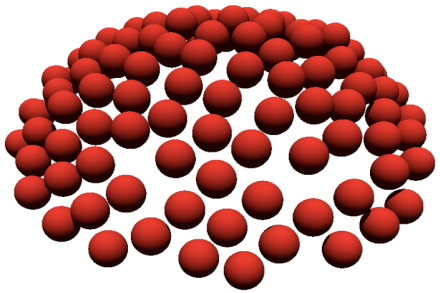
$$F = \int [\gamma + \frac{\kappa}{2}(C_1 + C_2 - C_0)^2 + \bar{\kappa} C_1 C_2] dA$$

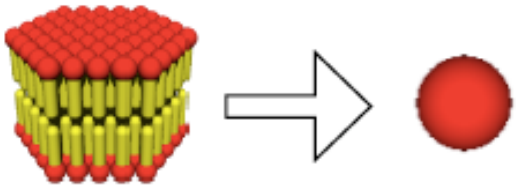
C_1, C_2:principal curvatures、C_0:spontaneous curvature

  - simulation: discretized surface

- mesh methods
- meshless methods



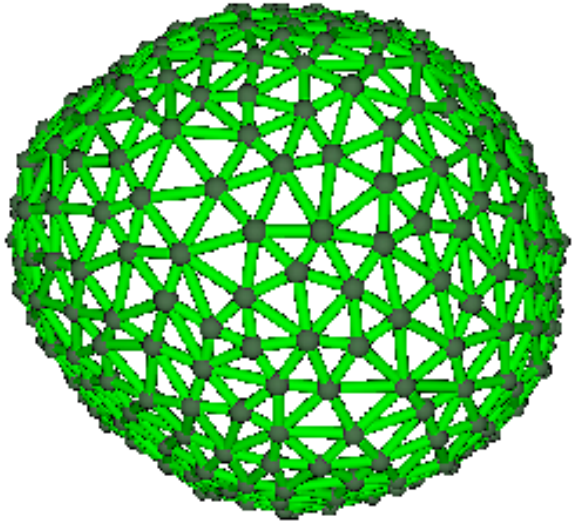




A particle represents
a membrane patch.

- mesh method

  degrees of freedom: positions and connections of particles



fluid membrane
by bond flip (Monte Carlo)

for fixed topology

works very well

<u>Ochanomizu Lecture (Aug. 23)
by G. Gompper</u>

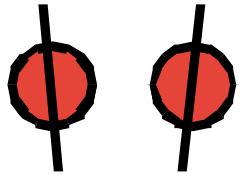
disadvantage

dynamics with topological changes

- meshless methods

1) degrees of freedom: positions and orientation

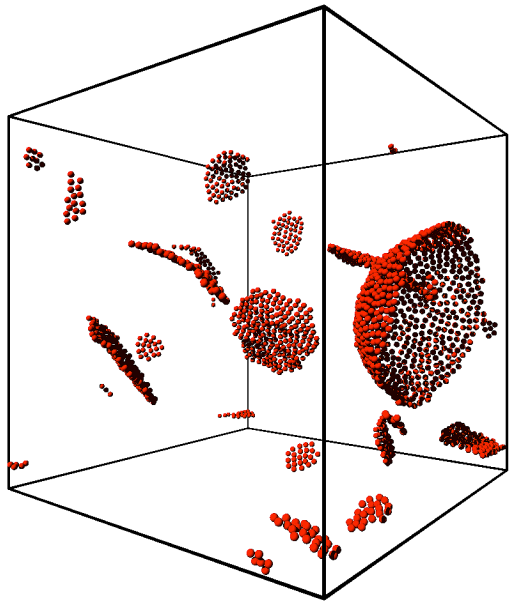
Drouffe, Maggs, S. Leibler Science 254, 1353 (1991).



Del Popolo (2008); T. Kohyama (2009);
P. Liu (2009); H. Yuan (2010).

2) degrees of freedom: only positions

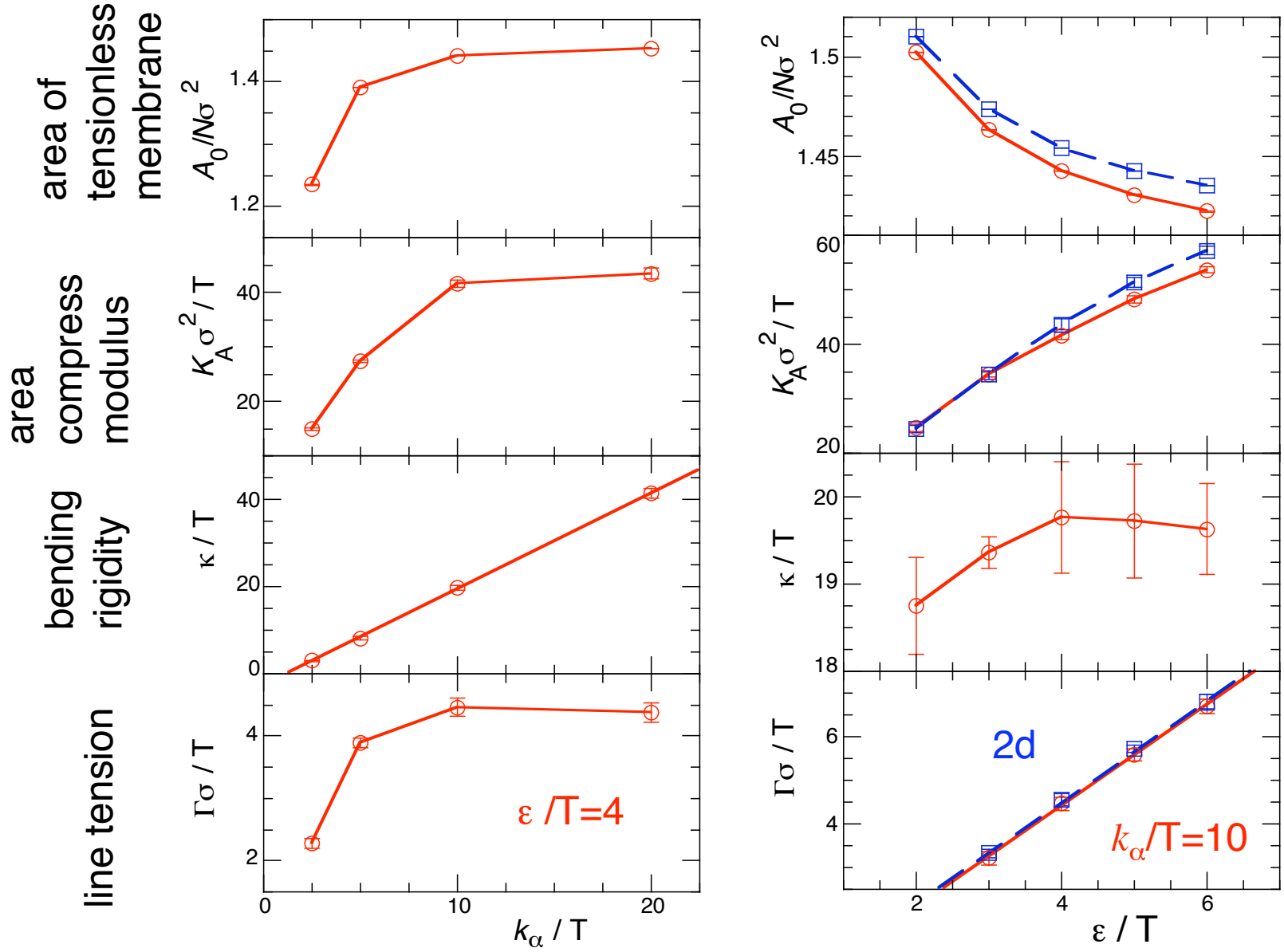
Noguchi and Gompper Phys. Rev. E 73, 021903 (2006).



Advantage:

Naturally applied to the topological changes

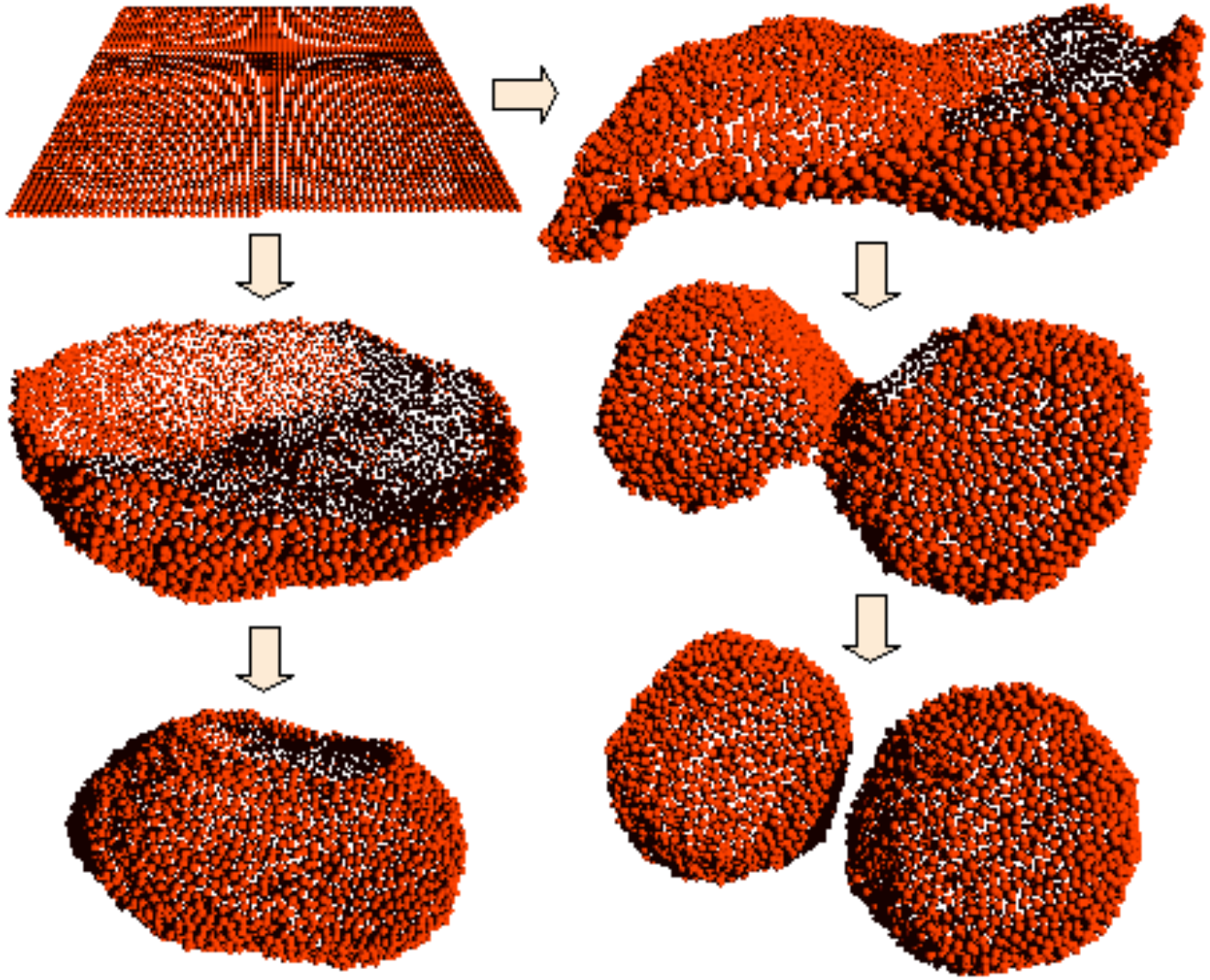
k_α and ε dependence



κ and Γ can be independently varied.

$$K_A = A_0 \partial\gamma/\partial A|_{A=A_0}$$

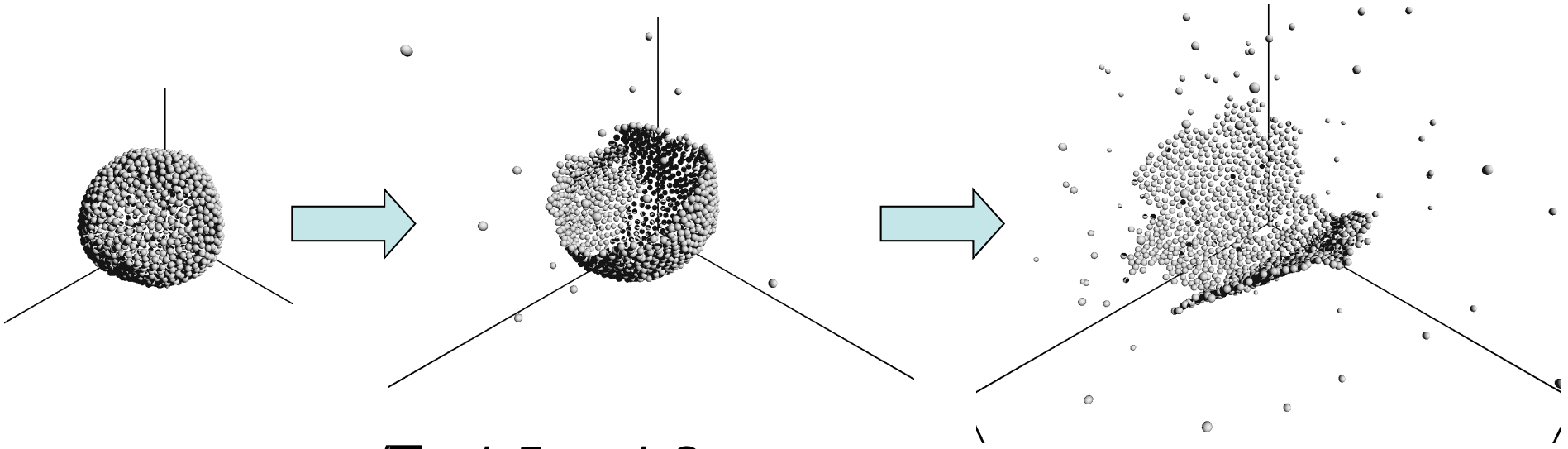
Vesicle formation



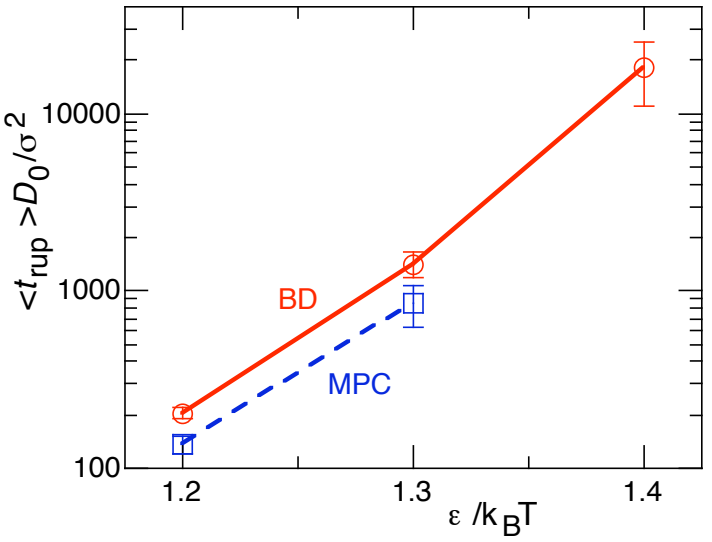
Very large membrane $R_{dis}/\sigma >> 8k_{\alpha}/\varepsilon$

Buckling into two vesicles is also possible.

rupture

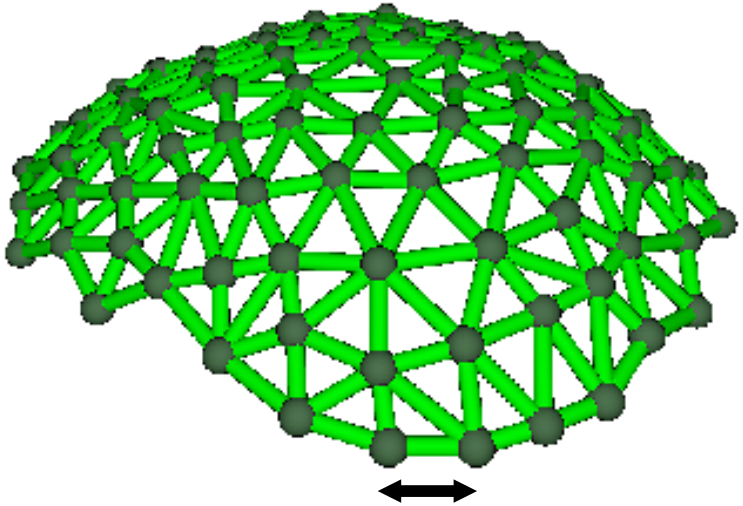


$\varepsilon/T = 1.5 \rightarrow 1.3$



Noguchi and Gompper J. Chem. Phys. 125, 164908 (2006).

curved surface

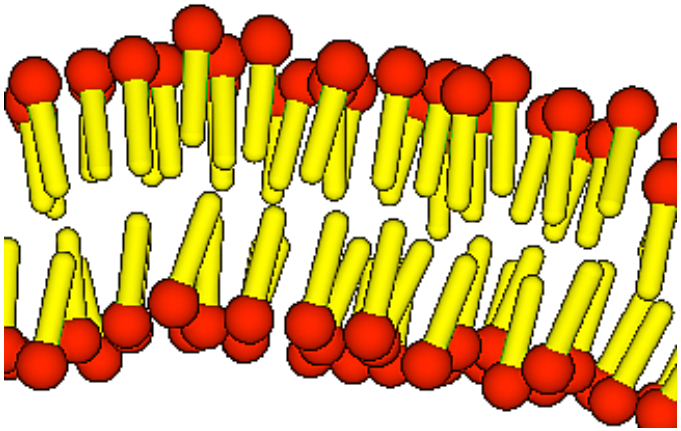


$\sigma \gtrsim$ thickness

1 particle or segment
$\gtrsim$ 100 lipid molecules

length scale $\gtrsim$ 10 times

molecular model



1 coarse-grained molecule
= 1~4 lipid molecules

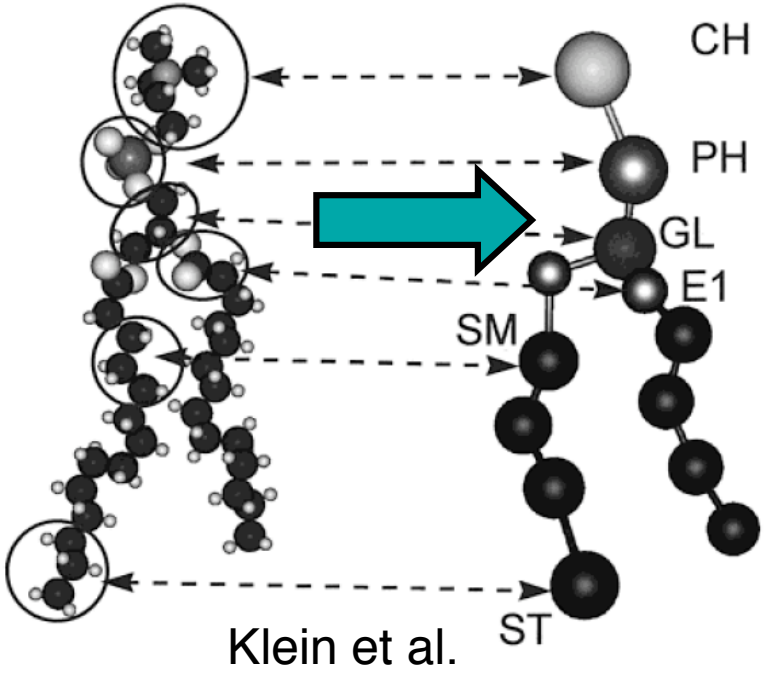
・Coarse-graining of lipids

with explicit solvent

without explicit solvent

atomistic models

coarse-grained models



Klein et al.

?

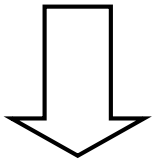
0.1nm

0.4 nm

1nm

solvent-free molecular model for bilayer membrane

H. Noguchi, M. Takasu (2001)



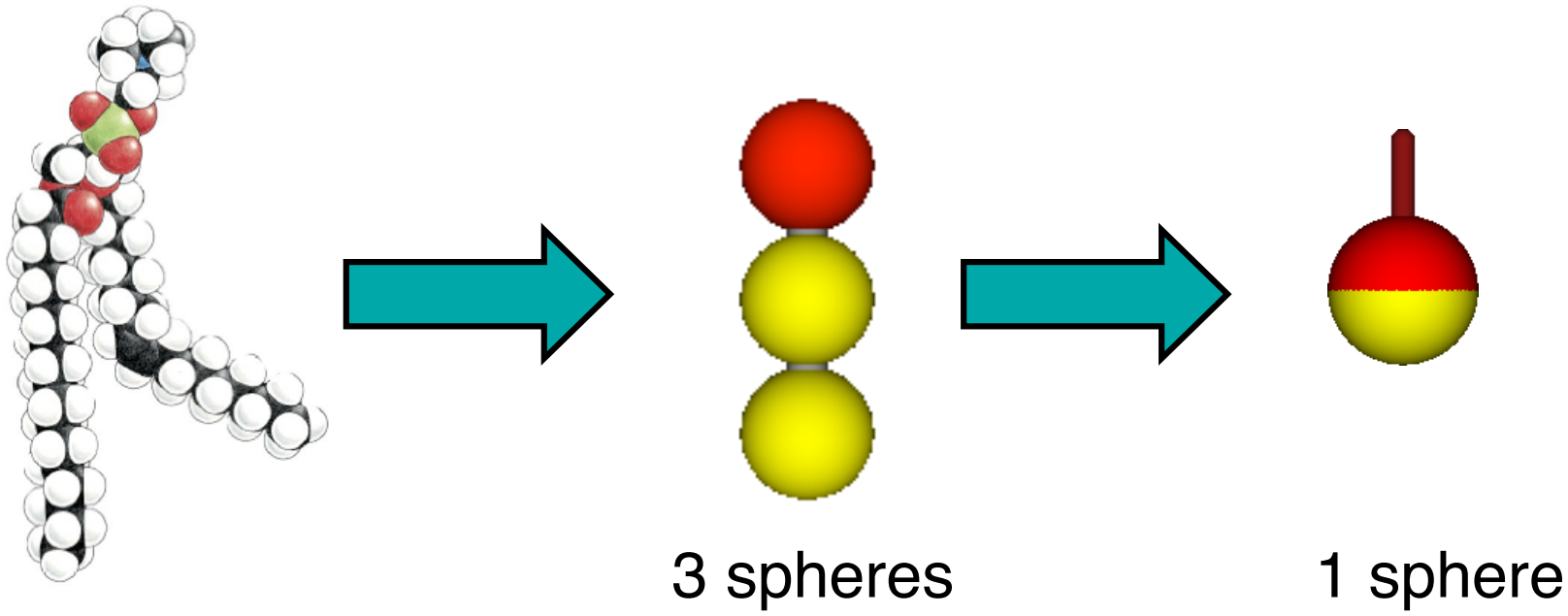
modifications

O. Farago (2003)
G. Brannigan, F.L.H. Brown (2004)
G. Brannigan, P.F. Philips, F.L.H. Brown (2005)
I.R. Cooke, K. Kremer, M. Deserno (2005)
Z.J. Wang, D. Frenkel (2005)
J.D. Revalee, M. Laradji, P.B.S.Kumar (2008).
M. Hoemberg, M. Mueller (2010).

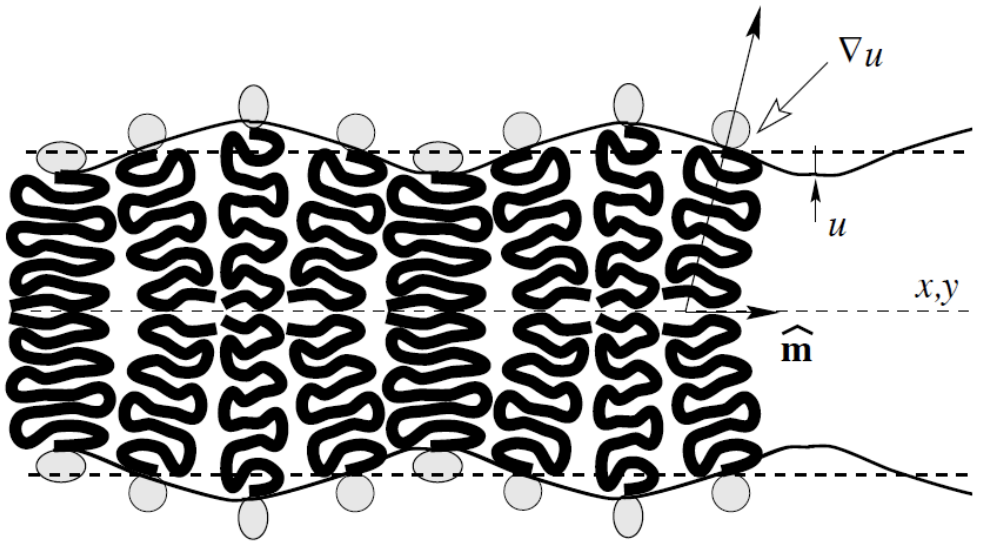
Only narrow parameter range

Aim 1: make a model for wide parameter range

Aim 2: Coarse graining more to simulate larger scale



Continuum theory
for bilayer membrane



$$f = \frac{1}{2} B\, u^2 + \frac{1}{2} \lambda\, (\nabla u)^2 + c\, \hat{\mathbf{m}} \cdot \nabla u$$

$$+ \frac{1}{2} t'\, \hat{\mathbf{m}}^2 + \frac{1}{2} K_1' \, (\nabla \cdot \hat{\mathbf{m}})^2 + \frac{1}{2} K_2' \, (\nabla \times \hat{\mathbf{m}})^2$$

Membrane bending, area dilation,
molecular tilt, chain stretching.

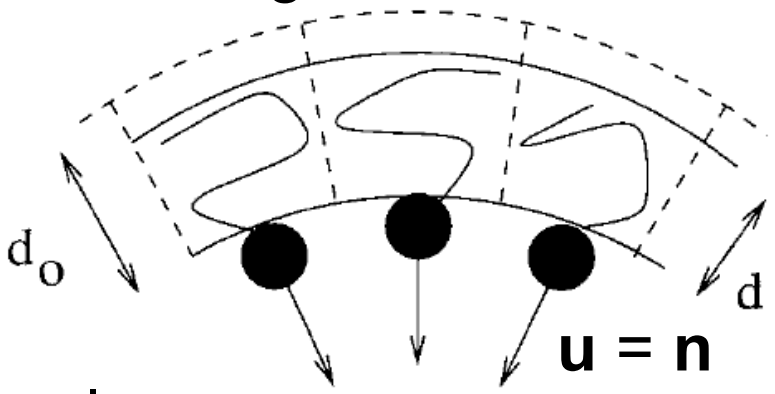
Fournier, EPL 43, 725 (1998).

Tilt + bending of membrane

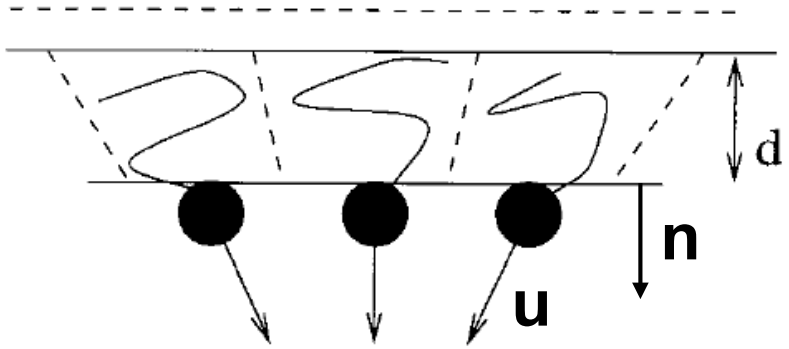
$$F_{\mathrm{cv}} = \frac{\kappa_{\mathrm{cv}}}{2} \int dA \, (\mathrm{div}\ \mathbf{u} - C_0)^2$$

$$F_{\mathrm{tilt}} = \frac{\kappa_{\mathrm{tilt}}}{2} \int dA \, (\frac{\mathbf{u}}{\mathbf{u} \cdot \mathbf{n}} - \mathbf{n})^2$$

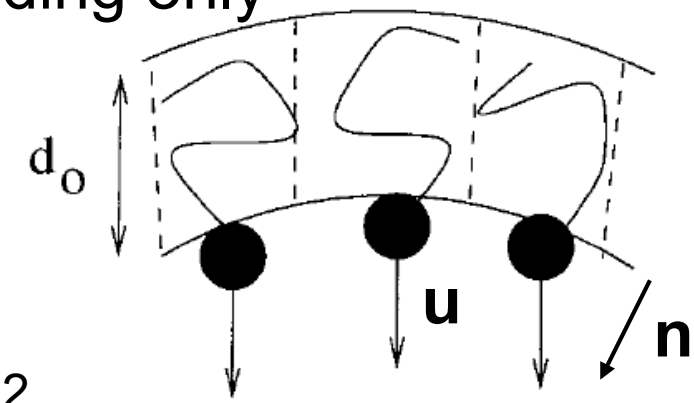
tilt + bending



tilt only



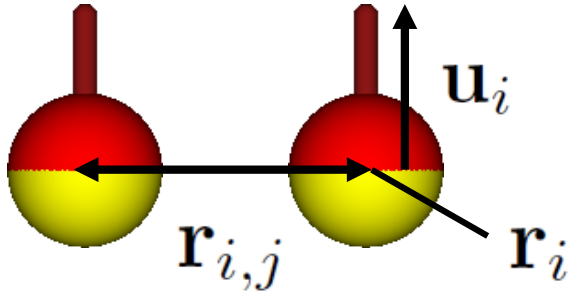
bending only



Kozlovsky and Kozlov, Biophys. J. 2002

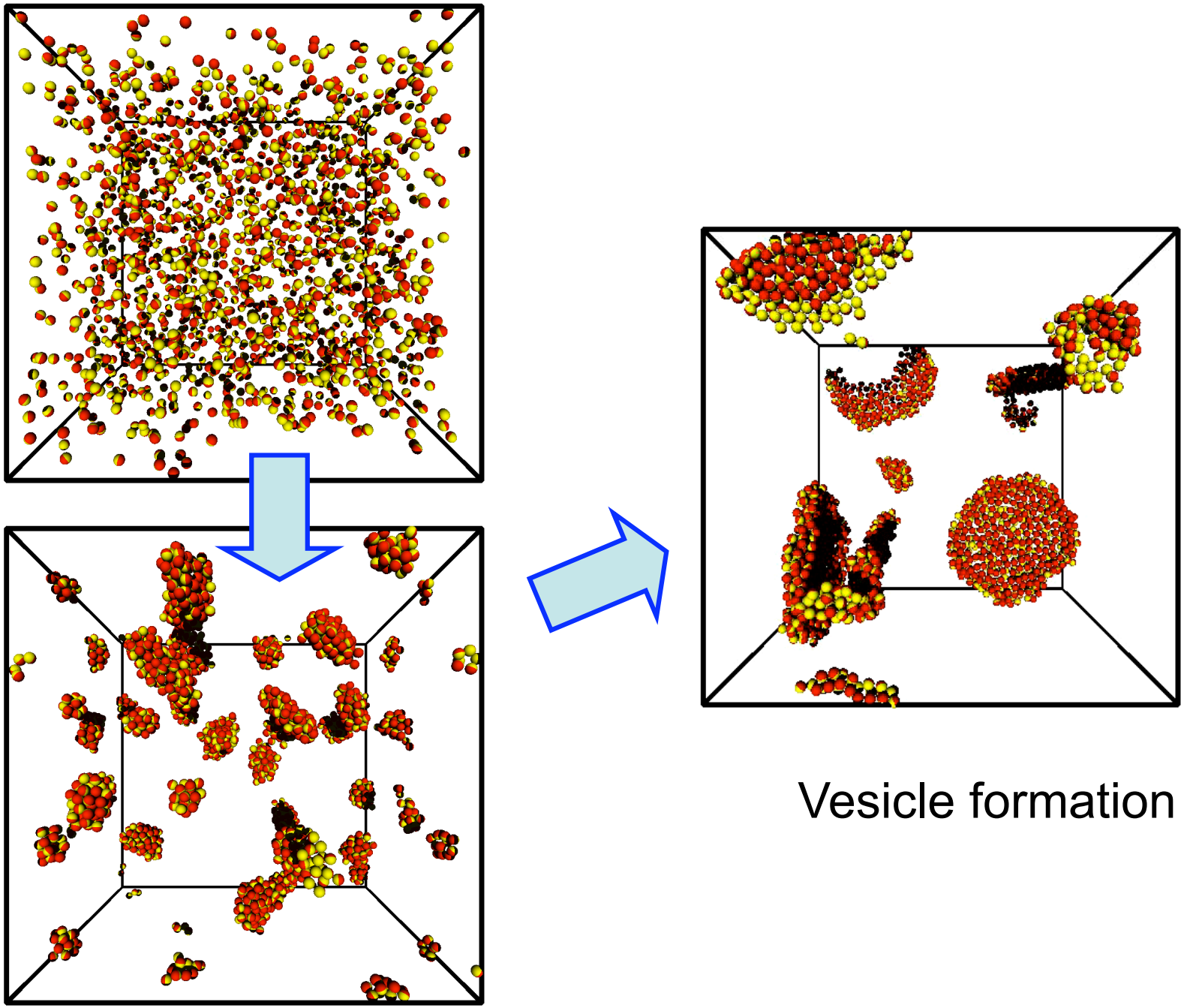
- Our new model

$$\frac{U}{k_{\mathrm{B}}T} = \sum_{i<j} U_{\mathrm{rep}}(r_{i,j}) + \varepsilon \sum_{i} U_{\mathrm{att}}(\rho_i) + \frac{k_{\mathrm{tilt}}}{2} \sum_{i<j} U_{\mathrm{tilt}}(\mathbf{r}_{i,j}, \mathbf{u}_i, \mathbf{u}_j) + \frac{k_{\mathrm{bend}}}{2} \sum_{i<j} U_{\mathrm{bend}}(\mathbf{r}_{i,j}, \mathbf{u}_i, \mathbf{u}_j)$$



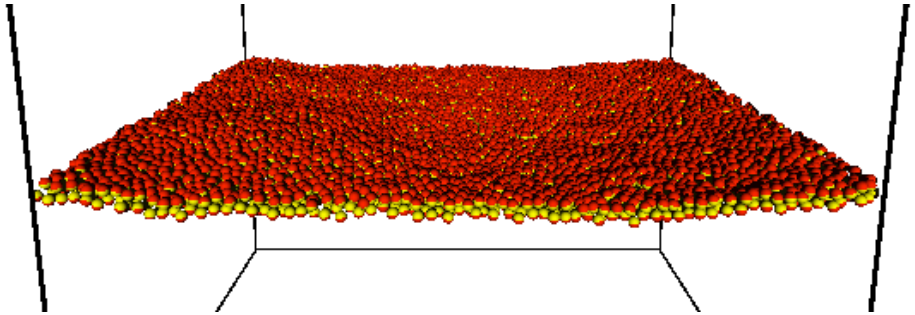
local density $\rho_i = \sum_{j \neq i} f_{\mathrm{cut}}(r_{i,j}/\sigma)$

- Self-assembly



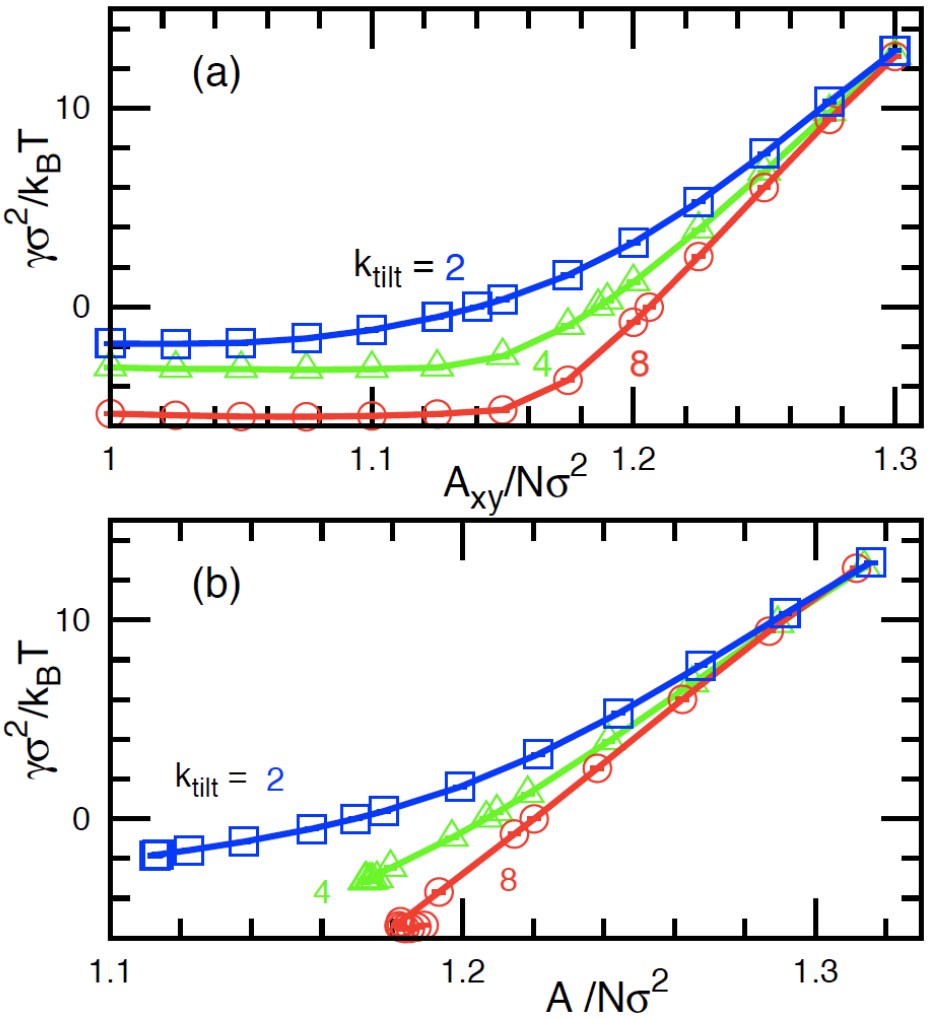
Vesicle formation

tensionless membrane



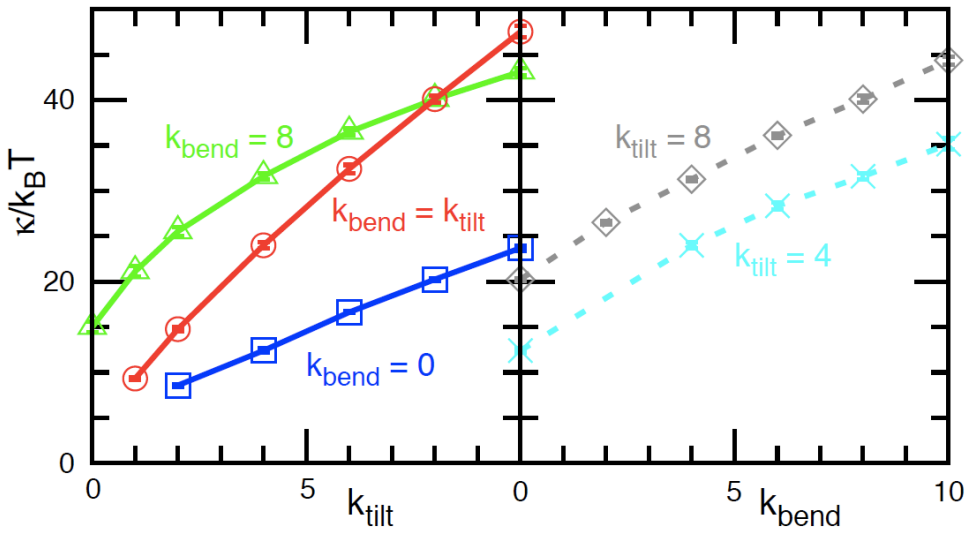
bilayer structure

surface tension

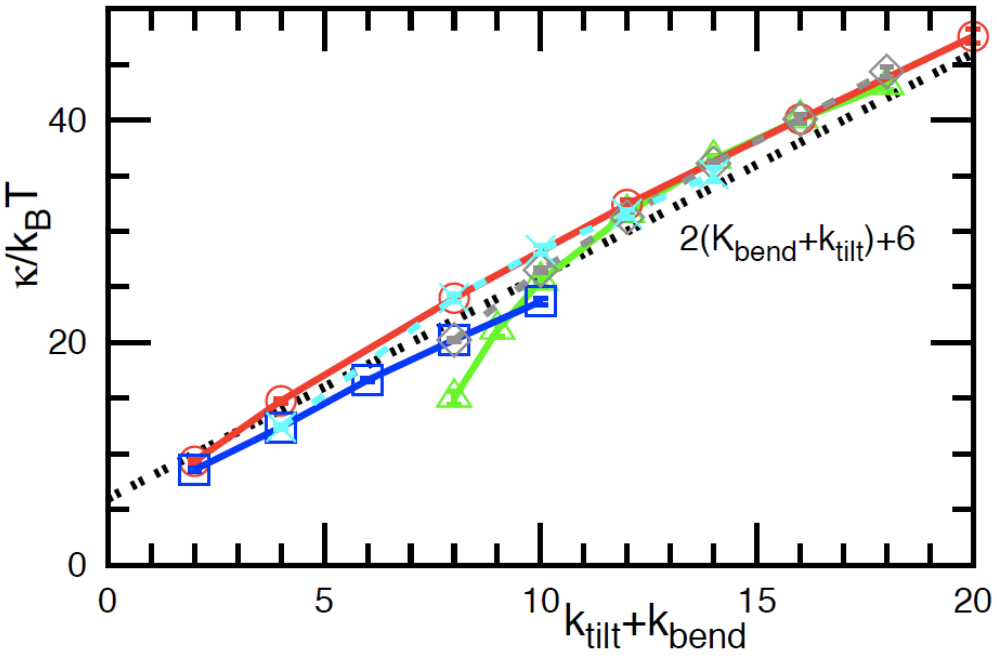


bending rigidity κ

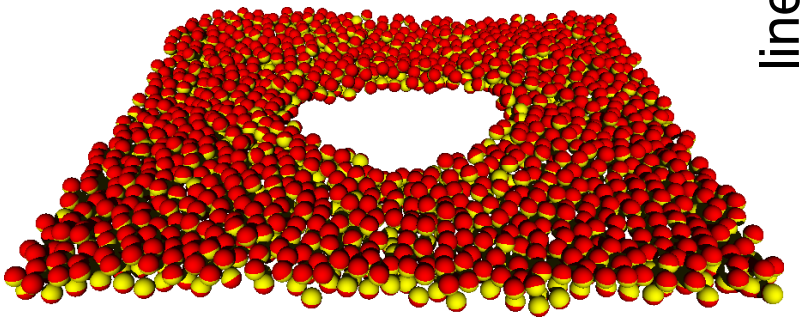
$$\langle h(q)^2 \rangle = \frac{T}{\gamma q^2 + \kappa q^4}$$

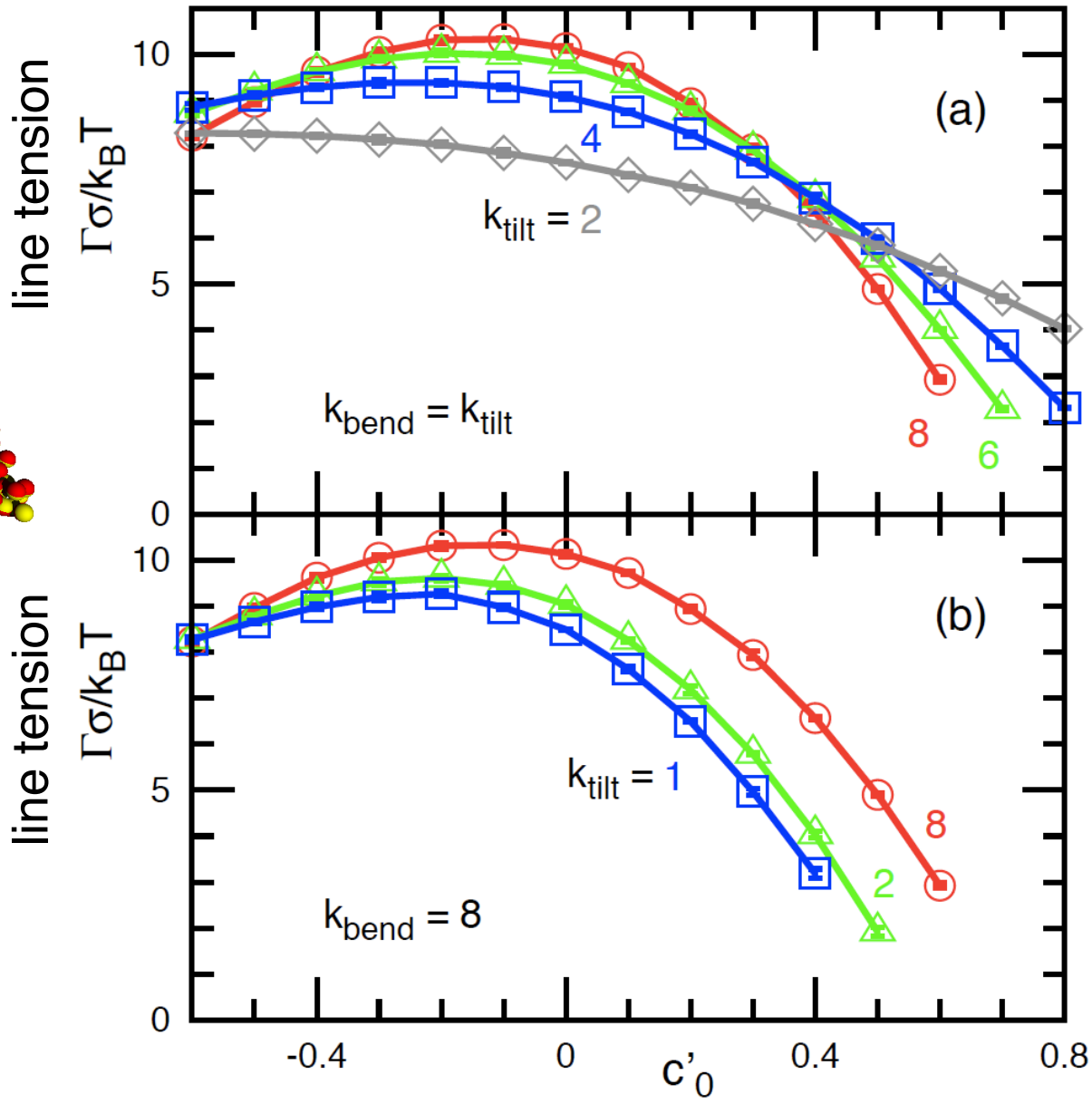


linear dependence on k_{tilt} and k_{bend}

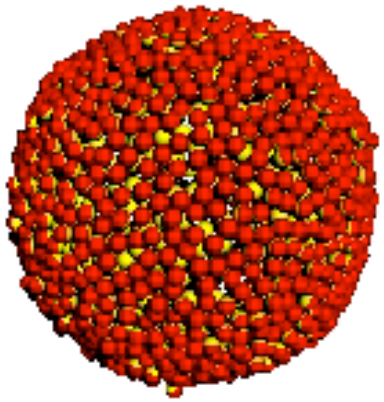


line tension of
membrane edge



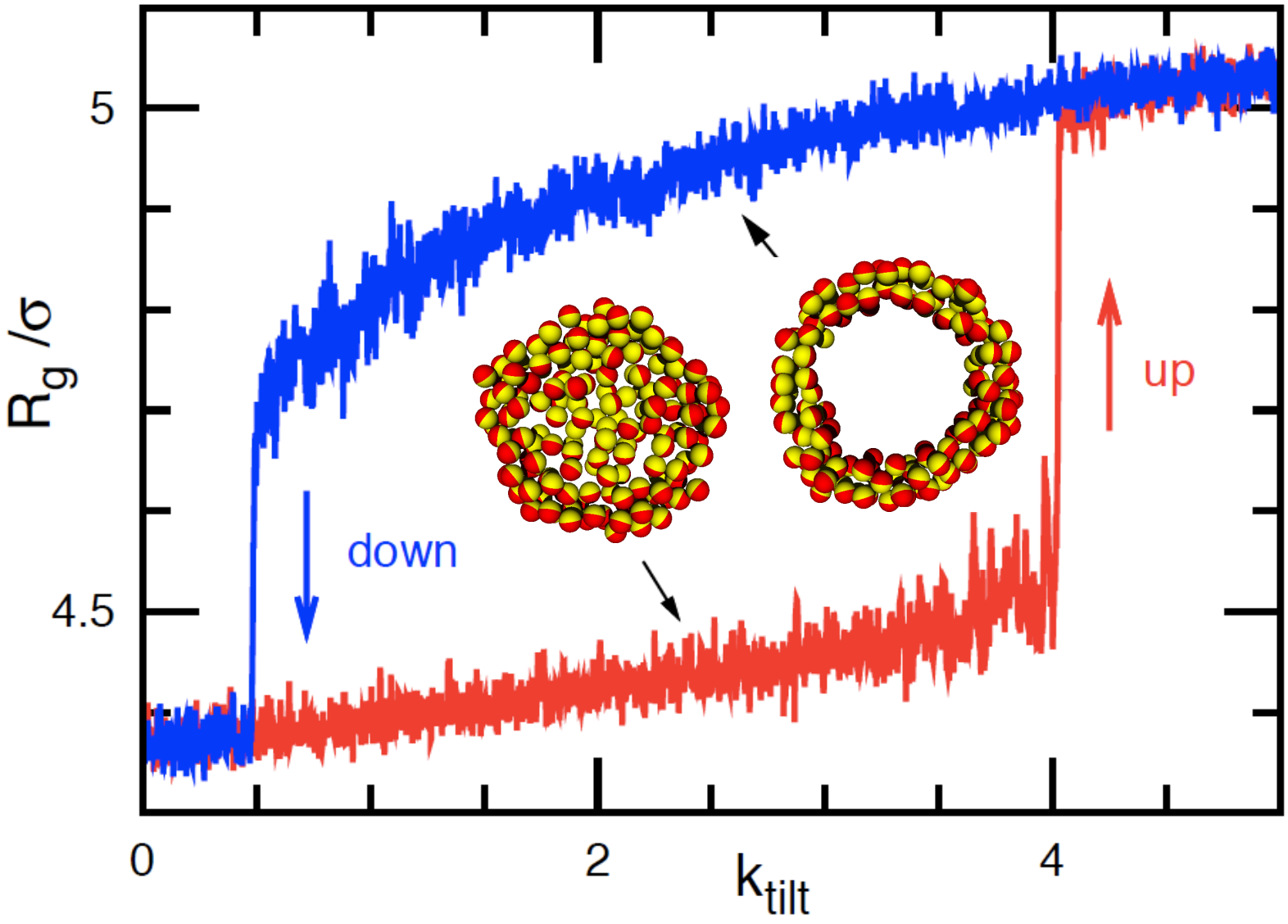


rupture



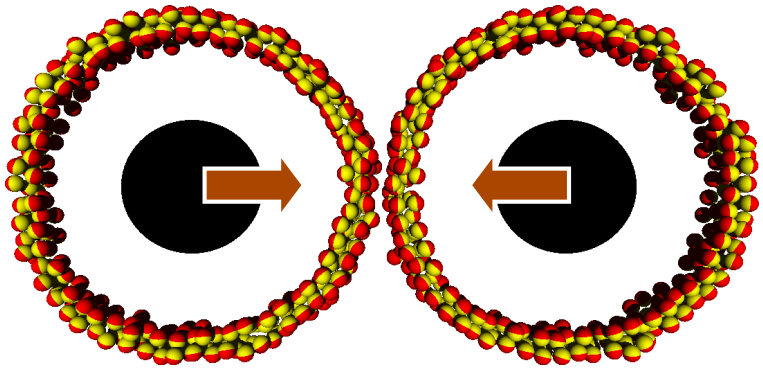
$C'_0 = 0 \rightarrow 0.85$

- droplet-vesicle transition

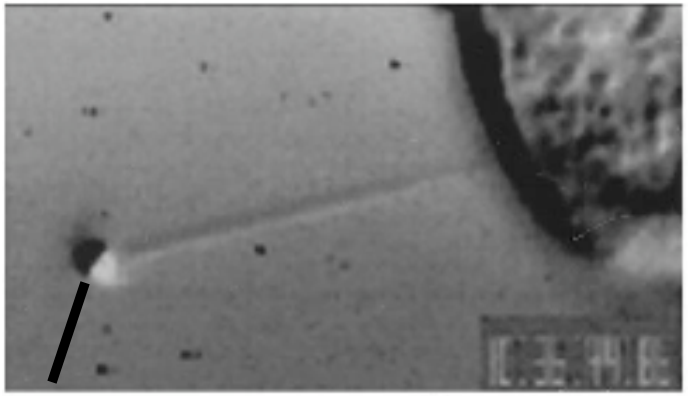


Bilayer is metastable at $k_{tilt} = 0$.

Preliminary simulation: Membrane fusion



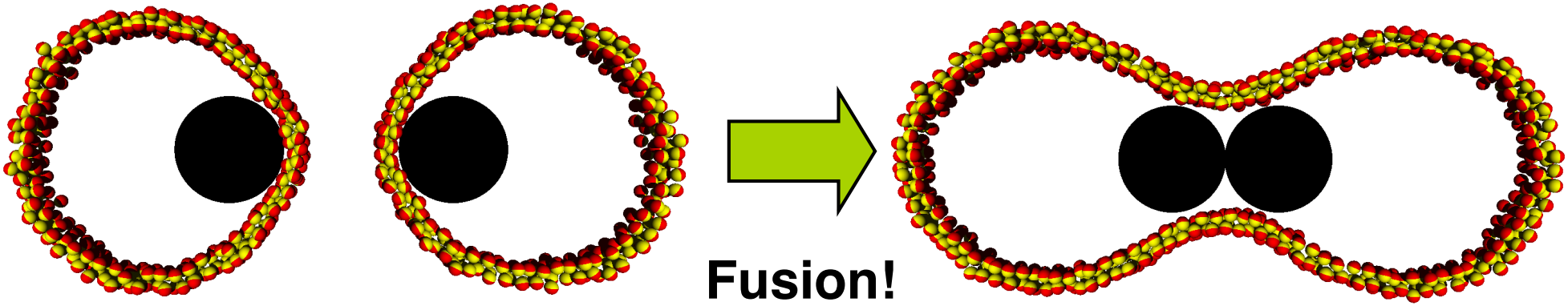
External force



Optical tweezers

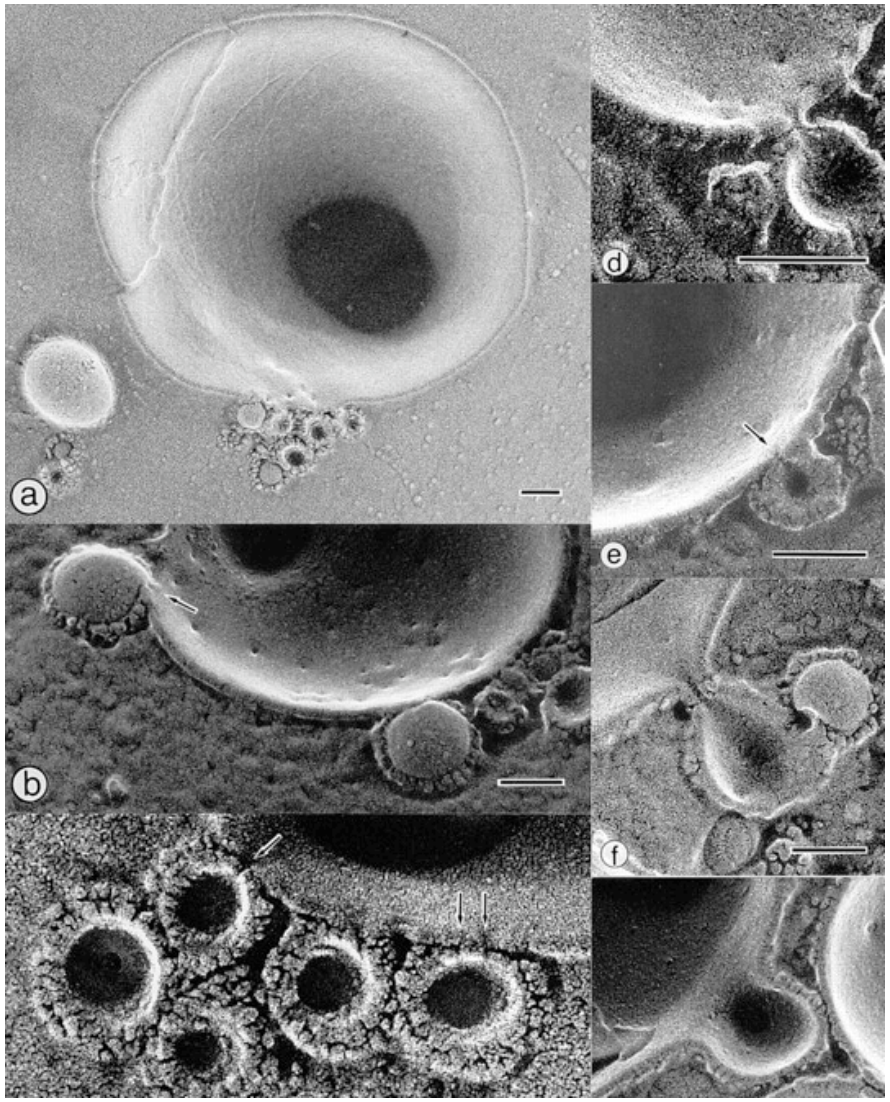
2.5mm

Dai et al., J. Neurosci. 18, 6681 (1998).

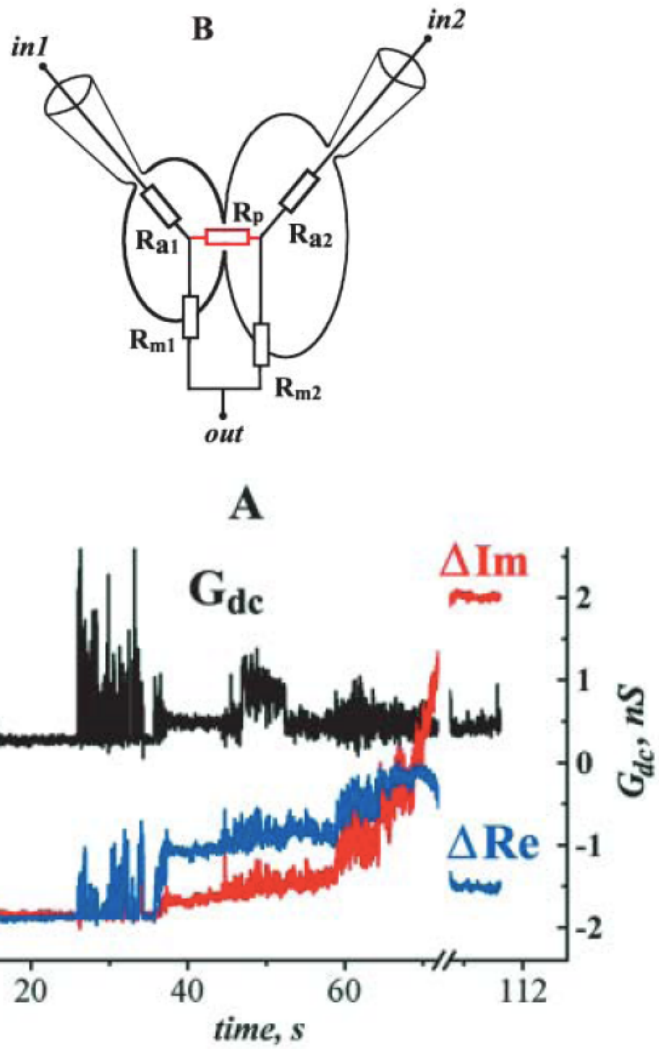


Fusion!

Experimental studies



Quick-freezing Electron microscopy images Bars, 100 nm.
Kanaseki et al. *J. Cell Biol*. 137, 1041 (1997).



Electric resistance measurement
V.A. Frolov et al. *Biophys*. J. 85, 1725 (2003).

fusion pathways found by simulations

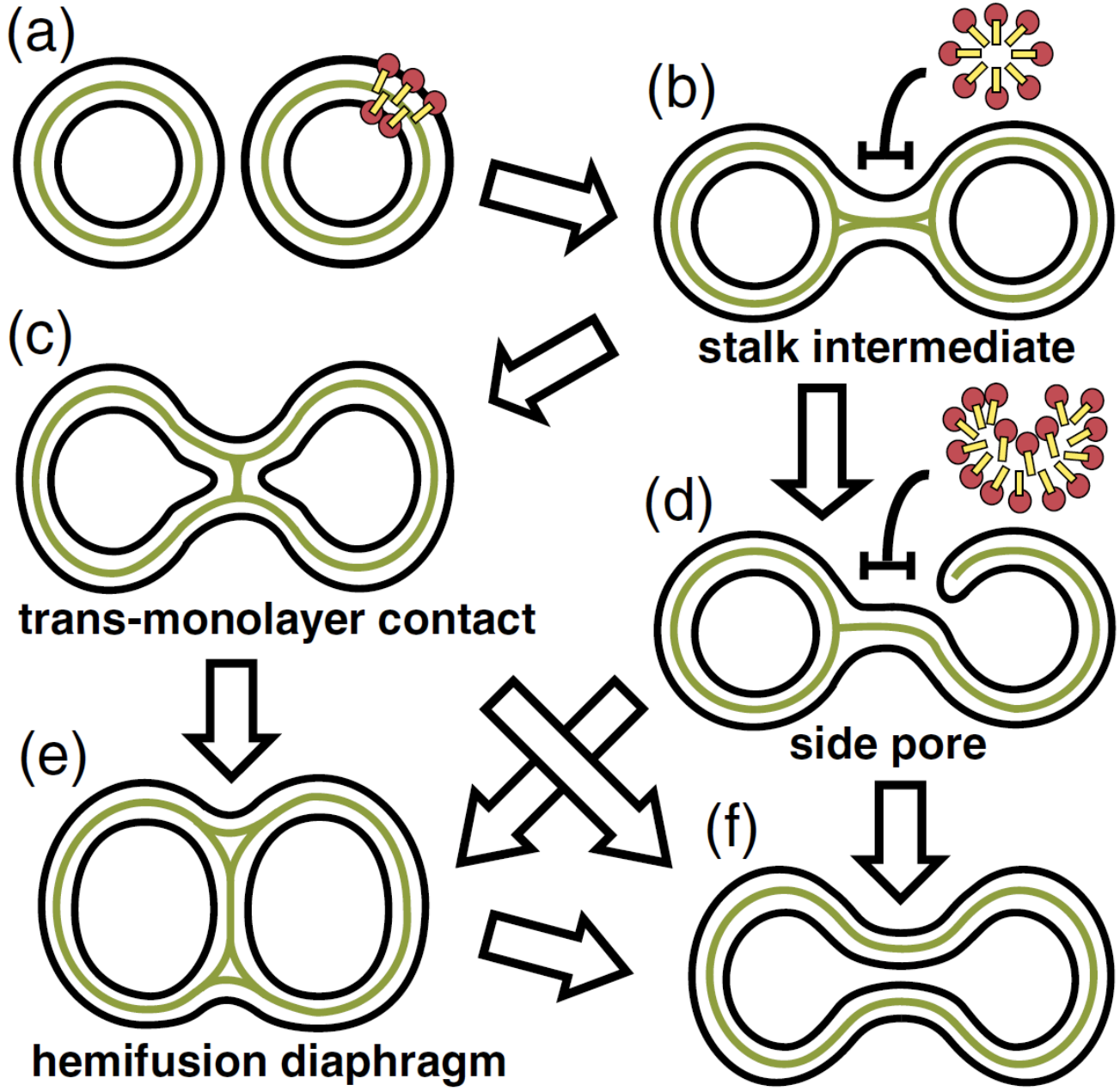
Solvent-free models
Noguchi et al. 2001

Lattice MC
Mueller, et al. 2002

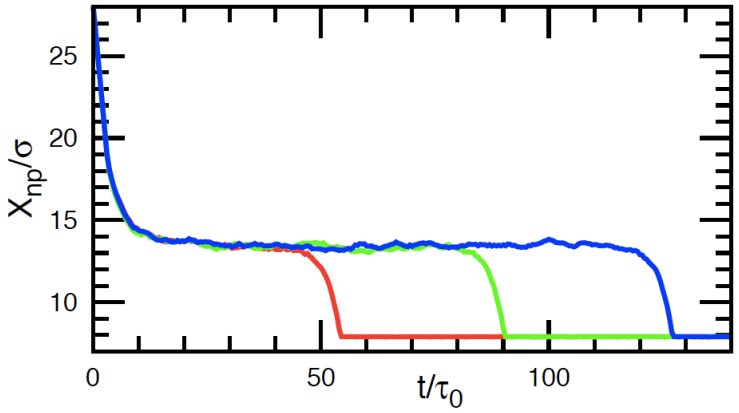
LJ model
Marrink et al. 2003
Stevens et al. 2003
Smeijers, et al. 2006
Kasson et al. 2007

DPD model
Li and Liu 2005
Shillcock et al. 2005

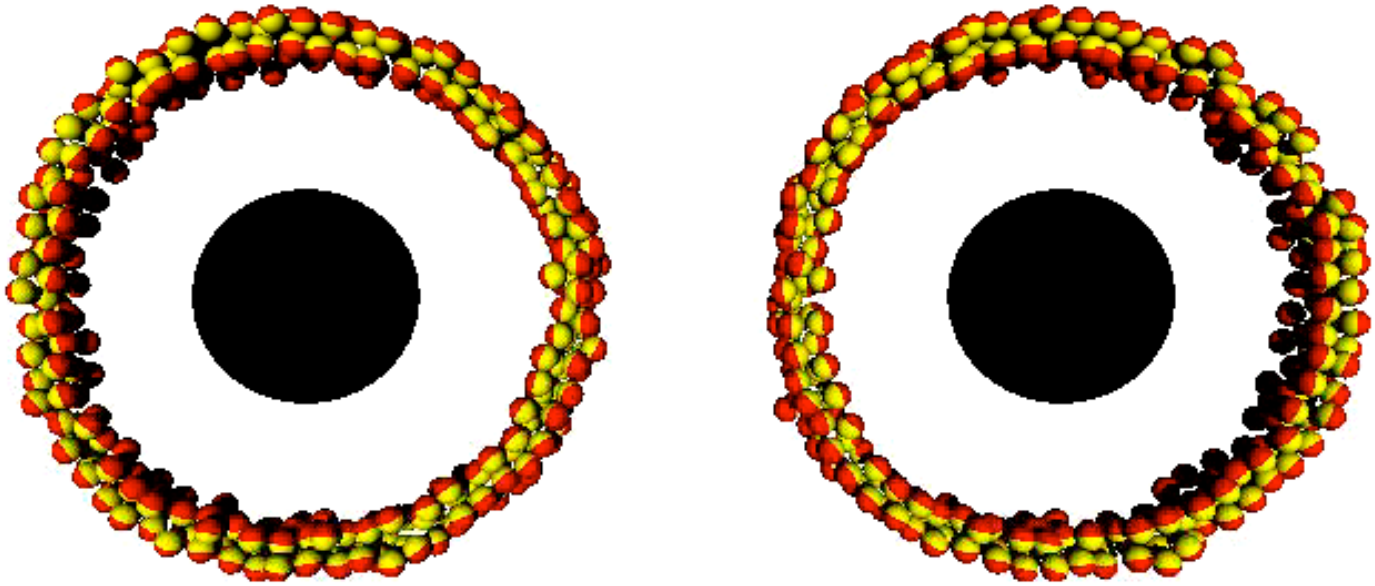
Atomistic model
Knecht and Marrink 2007



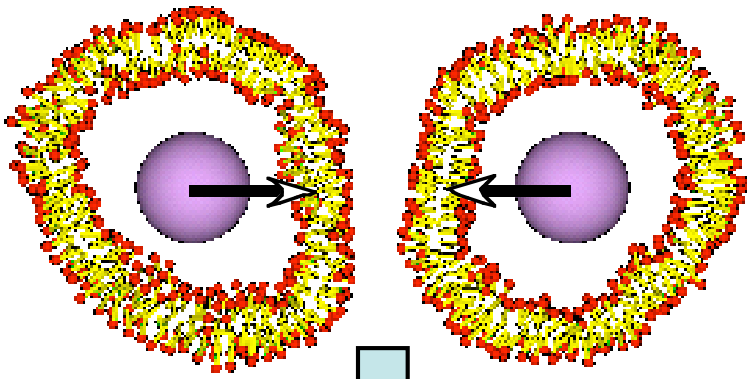
Membrane fusion by mechanical force

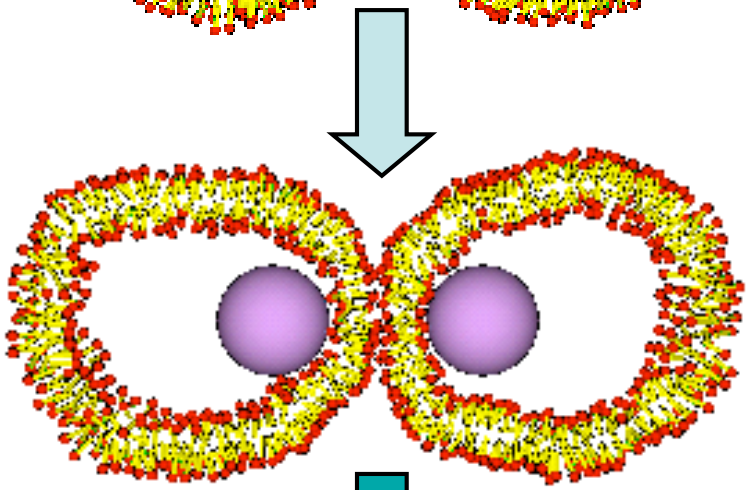


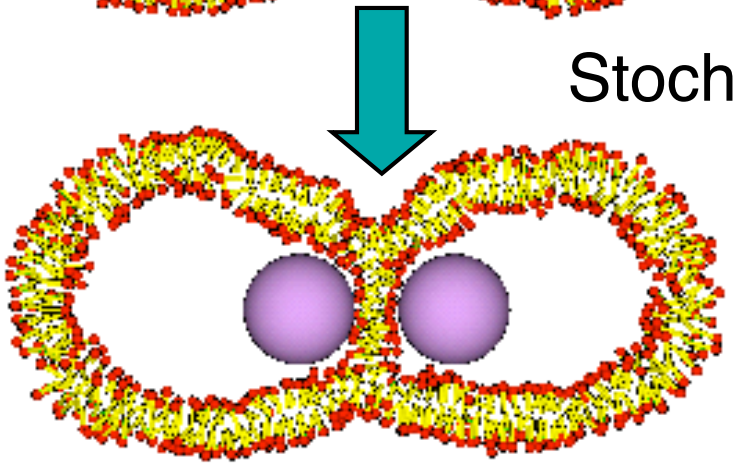
Pathway of modified stalk model



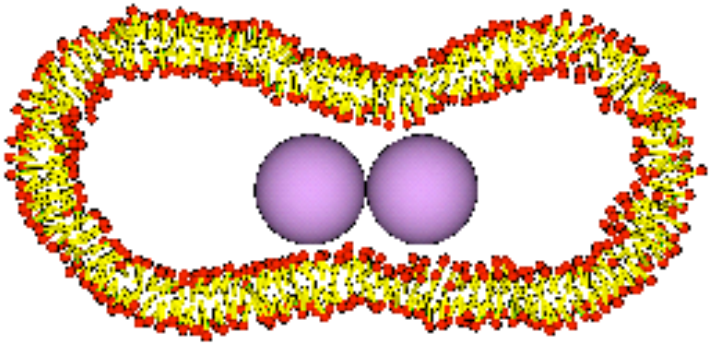
My previous simulation

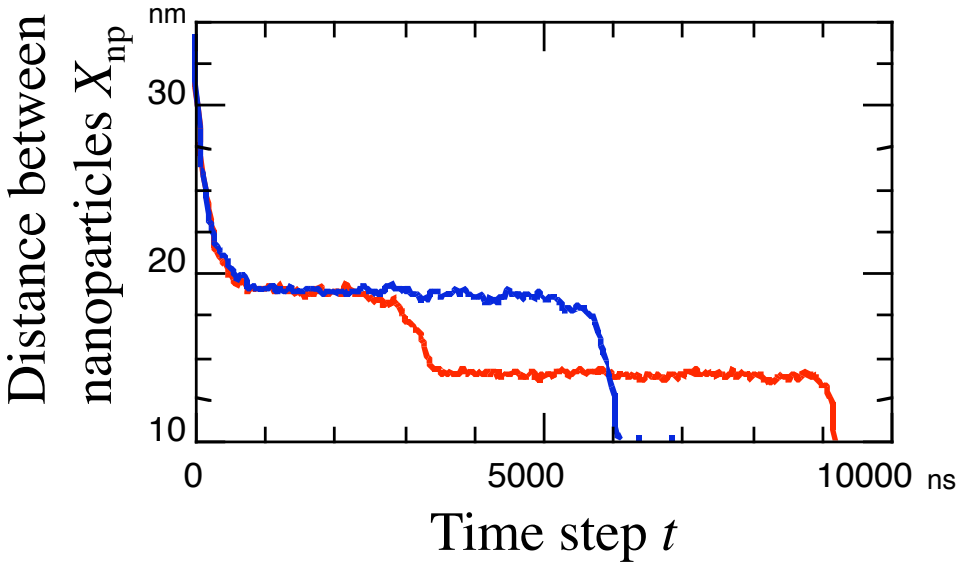






Stochastically





Noguchi J. Chem. Phys. 117, 8130 (2002).

Summary

○ A new CG model is proposed.

- Minimum molecular size: a sphere and orientation
- Membrane properties can be varied in wide range
  (including metastable bilayer).
- Application:
  membrane fusion etc.

Thank you for your attention!

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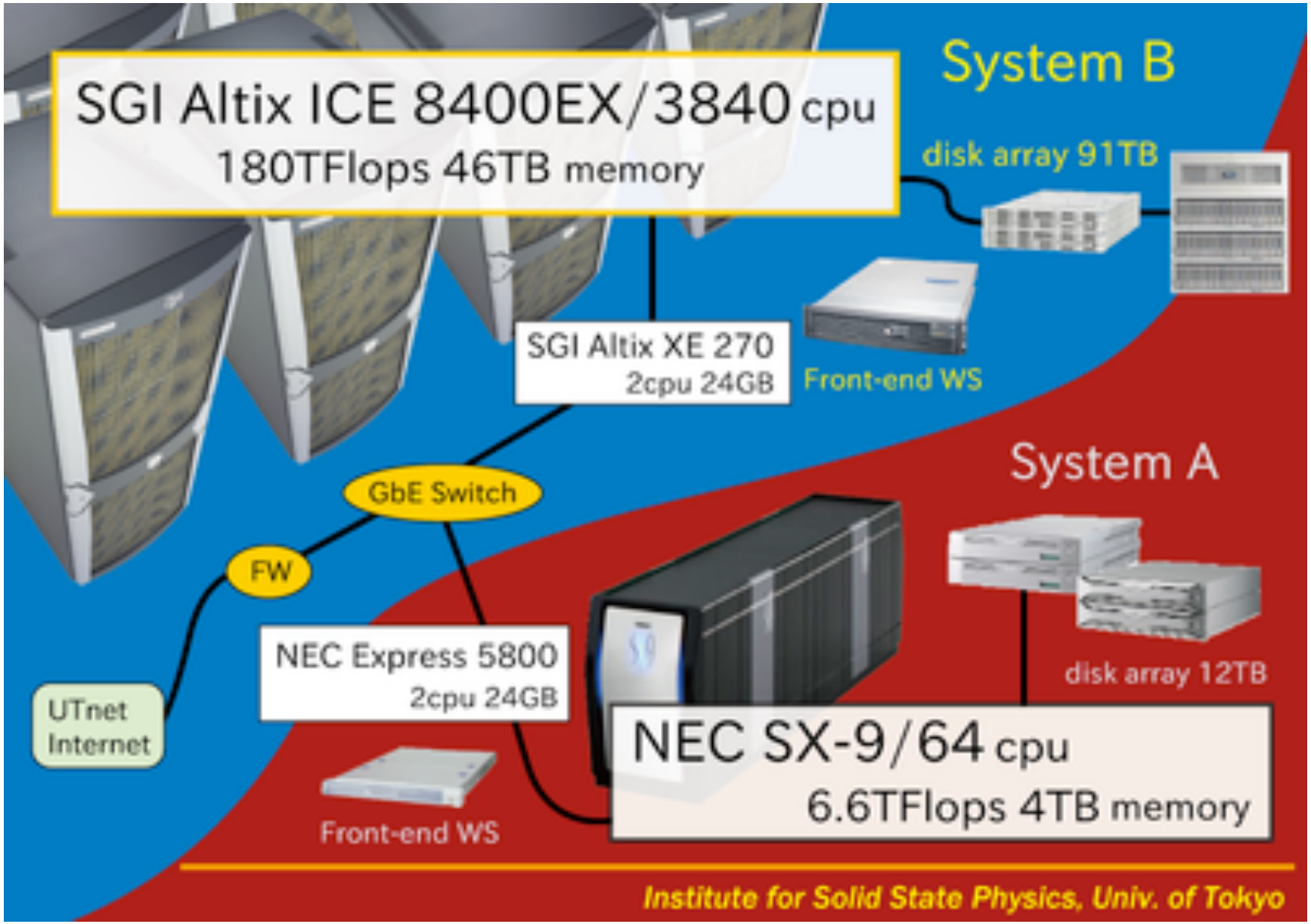
ISSP Supercomputer



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