Coarse-grained simulation studies of mesoscopic membrane phenomena

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with: Ira R. Cooke, Gregoria Illya, Benedict J. Reynwar, Vagelis A. Harmandaris, Kurt Kremer @ MPI-P

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Quick motivation
Membranes

Typical illustration of an animal cell

http://www.animalport.com/img/Animal-Cell.jpg
Quick motivation

Membranes

Almost everything you see here are membranes!

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Quick motivation
Membranes

Almost everything you see here are membranes!

Notice the many changes in morphology!

http://www.animalport.com/img/Animal-Cell.jpg
Quick motivation

Membranes need to be constantly reshaped in order to do their task.

The available energy is (bio)chemical; typically coming from ATP hydrolysis.

\[ E_{\text{available}} \sim 20 \ k_B \ T \quad (\text{physiol. cond.}) \]
Membranes need to be constantly reshaped in order to do their task.

The available energy is (bio)chemical; typically coming from ATP hydrolysis.

\[ E_{\text{available}} \sim 20 \, k_B \, T \quad \text{(physiol. cond.)} \]

The elasticity of membranes needs to match the available deformation energies!
Membrane bending modulus $K$
Membrane bending modulus

\[ \kappa = \frac{1}{12} Y h^3 \]
Membrane bending modulus

\[ \kappa = \frac{1}{12} Y h^3 \]

Young’s modulus

thickness
$20 k_B T \approx \kappa = \frac{1}{12} Y h^3$
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$h \approx 5 \text{ nm}$
\[ 20k_B T \approx \kappa = \frac{1}{12} Y h^3 \]

Energy match

Young’s modulus

thickness

\( h \approx 5 \text{ nm} \)

\( Y \approx 10^7 \text{ Pa} \)
\[ 20k_B T \approx \kappa = \frac{1}{12} Y h^3 \]

Energy match

Young's modulus

thickness

h \approx 5 \text{ nm}

Y \approx 10^7 \text{ Pa}
Let’s hypothesize...

\[ 20k_B T \approx \kappa = \frac{1}{12} Y h^3 \]

Young’s modulus

thickness

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Energy match

\[ Y \approx 10^7 \text{ Pa} \]
Energy match

$20k_B T \approx \kappa = \frac{1}{12} Y h^3$

Young's modulus

thickness

$h \approx 5\text{ nm}$

$Y \approx 10^7\text{ Pa}$

...and insist on metal!
$20k_B T \approx \kappa = \frac{1}{12} Y h^3$

$Y \approx 10^{11} \text{ Pa}$

…and insist on metal!

Young’s modulus

thickness

Energy match

$h \approx 5 \text{ nm}$
20k_B T \approx \kappa = \frac{1}{12} Y h^3

h \approx 2 \text{Å}

Y \approx 10^{11} \text{Pa}

Energy match

Young’s modulus

thickness

...and insist on metal!
\[ 20k_B T \approx \kappa = \frac{1}{12} Y h^3 \]

**Young’s modulus**

**Thickness**

\[ h \approx 2 \text{ Å} \]

\[ Y \approx 10^{11} \text{ Pa} \]

...and insist on metal!
Membranes must be made from soft materials!

We will invariably encounter long time scales!
Quick motivation (II)
Long time scales – How bad is it?
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Long time scales – How bad is it?


All-atom lipid bilayer
20nm × 20nm, 1024 lipids, 10ns
Quick motivation (II)
Long time scales – How bad is it?


All-atom lipid bilayer
20nm×20nm, 1024 lipids, 10ns

What if we want a boxlength of $L=200$nm? How does computing effort scale with $L$?
Quick motivation (II)

Long time scales – How bad is it?


All-atom lipid bilayer
20nm×20nm, 1024 lipids, 10ns

What if we want a boxlength of \( L = 200 \text{nm} \)?
How does computing effort scale with \( L \)?

\[
\text{effort} \sim L^2
\]
Quick motivation (II)

Long time scales – How bad is it?


All-atom lipid bilayer
20nm×20nm, 1024 lipids, 10ns

What if we want a boxlength of $L=200$nm?

How does computing effort scale with $L$?

Effort $\sim L^2 \times L^4$

Amount of material

Equilibration time
Quick motivation (II)

Long time scales – How bad is it?


All-atom lipid bilayer
20nm×20nm, 1024 lipids, 10ns

What if we want a boxlength of $L=200$nm? How does computing effort scale with $L$?

\[
\text{effort} \sim L^2 \times L^4 \sim L^6
\]

Amount of material
Equilibration time
Quick motivation (II)
Long time scales – How bad is it?

20nm  →  200nm

**Million times more computationally expensive!**
Quick motivation (II)
Long time scales – How bad is it?

20nm → 200nm

10^6 ≈ 2^{20}

Million times more computationally expensive!
Quick motivation (II)
Long time scales – How bad is it?

20nm → 200nm

$10^6 \approx 2^{20}$

Million times more computationally expensive!

20 doublings of computer power!
Quick motivation (II)

Long time scales – How bad is it?

20nm \rightarrow 200nm

Million times more computationally expensive!

10^6 \approx 2^{20}

20 doublings of computer power!

20 \times 2 \text{ years} \quad \text{(Moore’s law)}
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Long time scales – How bad is it?

20nm → 200nm

Million times more computationally expensive!

\[ 10^6 \approx 2^{20} \]

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20 x 2 years  (Moore’s law)
40 years
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Long time scales – How bad is it?

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Million times more computationally expensive!

$10^6 \approx 2^{20}$

20 doublings of computer power!
20 x 2 years (Moore’s law)
40 years

I’ll be retired by then! (best case scenario)
This is why we all love coarse graining
Today:

I’ll illustrate a way to efficiently treat the ~100nm regime.

- Generic top-down bead-spring
- solvent free
- only pair forces
- robust & physically meaningful

I.R. Cooke, K. Kremer, M. Deserno, Phys. Rev. E 72, 011506 (2005);
Today:

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Long-ranged attractions “save” the system some entropy!

Shape of CG potential is *qualitatively* important!

Illustrations:

- Material properties
- Adsorption to a substrate
- Lipid curvature effects
- Peptide-induced pore formation
- Lipid mixtures
- Protein-induced budding
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Material properties
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Probably most important: bending modulus
Material properties

- Probably most important: bending modulus
- From fluctuations
- From deformations

Can be determined in two very different ways
Material properties

Probably most important: bending modulus

From fluctuations

\[ H \approx \frac{1}{2} \int d^2r \left\{ \kappa (\Delta h)^2 + \sigma (\nabla h)^2 \right\} \]

\[
\langle |h_q|^2 \rangle = \frac{k_B T}{L^2(\kappa q^4 + \sigma q^2)}
\]

\[
\sigma = 0 \quad \Rightarrow \quad \frac{k_B T}{\kappa L^2} q^{-4}
\]
Material properties

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\[ \sigma=0 \quad \frac{k_B T}{\kappa L^2} q^{-4} \]

energy of cylinder

\[ E = \frac{\kappa}{2} \times \frac{1}{R^2} \times A \]

force to hold it

\[ F = \left( \frac{\partial E}{\partial L} \right)_A = \frac{2\pi \kappa}{R} \]

Material properties

Probably most important: bending modulus

From fluctuations

From deformations

Both ways give the same answer

Shows that Helfrich theory works up to extremely large curvature

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Material properties

Probably most important: bending modulus

From fluctuations
From deformations

Both ways give the same answer
Shows that Helfrich theory works up to extremely large curvature

\[ h_q \sim 3 \ldots 30 \ k_B T \]

Other Material properties

Expansion modulus
~ 100 dyn/cm

Line tension
~ 10 pN

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Expansion modulus
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Line tension
~ 10 pN

thermal expansivity
~ $2 \times 10^{-3}$ K$^{-1}$

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Adsorption to a substrate

Adsorption to a substrate

Adsorption to a substrate

Major suppression of perpendicular lipid fluctuations in the proximal leaflet.

Entropy loss, since \( S = -k_B \int dz \, p_i(z) \log p_i(z) \)

Reduction of free energy of binding (here: \(~25\%)\)

Adsorption to a substrate

- “Zero tension case” needs to be precisely defined
- Compressibility increases, since fluctuations are damped

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Lipid curvature effects

The model of Israelachvili, Mitchell and Ninham


\[ P = \frac{V}{LA} \]

\( V \) = lipid volume
\( L \) = lipid length
\( A \) = lipid head area
Lipid curvature effects

The model of Israelachvili, Mitchell and Ninham


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packing parameter
Lipid curvature effects

The model of Israelachvili, Mitchell and Ninham

\[ P = \frac{V}{LA} \]

\( V = \) lipid volume
\( L = \) lipid length
\( A = \) lipid head area

Lipid curvature effects

50:50 mixture

Lipid curvature effects

50:50 mixture

Lipid curvature effects

50:50 mixture

Simple model gives:

\[ E = \frac{1}{2} \mathcal{M} (K - K_\ell)^2 \]

\[ S = \text{ideal gas} \]

Density of big headed lipids in the outer monolayer:

\[ \ln \frac{\phi_{\text{out}}}{\phi_{\text{in}}} = \frac{2\mathcal{M}K_\ell}{k_B T} K \]

Density of big headed lipids in the inner monolayer

Linear in bilayer curvature!

Lipid curvature effects

50:50 mixture

Density of big headed lipids in the outer monolayer

Simple model gives:

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Density of big headed lipids in the inner monolayer

Linear in bilayer curvature!

Lipid curvature effects

50:50 mixture

\[ \ln \frac{\phi_{\text{out}}}{\phi_{\text{in}}} \]

...for realistic membrane curvatures the effect is **not** enough to drive sorting!

\[ R \approx 50\text{nm} \]
\[ \delta\phi \approx 0.03 \]

Lipid curvature effects

50:50 mixture

\[ \ln \frac{\phi_{\text{out}}}{\phi_{\text{in}}} \]

...for realistic membrane curvatures the effect is not enough to drive sorting!

Tian & Baumgart, preprint

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Peptide-induced pore formation

Antimicrobial Peptide “magainin”

Peptide-induced pore formation

Example above:

\[ P_n^m \] – peptide

\[ P_8^2 \]

Peptide-induced pore formation

Example above:

Peptides:

\[ P_{n}^{m} \] – peptide

Example above: \( P_{8}^{2} \)

Peptide-induced pore formation

a) Surface adsorbed

b) Monolayer contact

c) Sliding in

Peptide-induced pore formation

## Peptide-induced pore formation

<table>
<thead>
<tr>
<th>Binding strength</th>
<th>$k_B T = 1.7$</th>
<th>$k_B T = 1.9$</th>
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<tbody>
<tr>
<td>$P^2_6$</td>
<td></td>
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<tr>
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<td>stray</td>
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</tr>
<tr>
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<td>bound</td>
<td>bound/inserted</td>
</tr>
<tr>
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<td>inserted</td>
<td>inserted</td>
</tr>
<tr>
<td>1.8</td>
<td>inserted</td>
<td>inserted</td>
</tr>
<tr>
<td>$P^2_8$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.4</td>
<td>stray</td>
<td>stray</td>
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<td>bound</td>
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Let us now look at this system consisting of many of these peptides.

Peptide-induced pore formation

...of a peptide which *alone* does *not* insert within $25000\tau$

- Stronger joint perturbation
- Sliding in very efficient

Peptide-induced pore formation

$w_c = 1.5$

$P_8^0, P_8^1, P_8^2, P_8^3$

Peptide-induced pore formation

$w_c = 1.5$

$P_8^0 \rightarrow P_8^1 \rightarrow P_8^2 \rightarrow P_8^3$

No peptide attraction

Some peptide attraction

$P_6^2 \quad w_c = 1.6$

Peptide-induced pore formation

$w_c = 1.5$

$P_8^0$  $P_8^1$  $P_8^2$  $P_8^3$

No peptide attraction

Some peptide attraction

$P_6^2$  $w_c = 1.6$

Illustrations:

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Lipid A-B–mixtures

B.J. Reynwar & M. Deserno, Biointerphases (accepted)
Lipid A-B–mixtures

\[ \mathcal{W}_{AB} < \mathcal{W}_{AA} = \mathcal{W}_{BB} \]

B.J. Reynwar & M. Deserno, Biointerphases (accepted)
Lipid A-B–mixtures

\[ w_{AB} < w_{AA} = w_{BB} \]

B.J. Reynwar & M. Deserno, Biointerphases (accepted)
Lipid A-B–mixtures + proteins

Composition-induced protein aggregation

B.J. Reynwar & M. Deserno, Biointerphases (accepted)
Lipid A-B–mixtures +proteins

Pair potentials can be fitted by simple ground state theory.

B.J. Reynwar & M. Deserno, Biointerphases (accepted)
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Protein-induced budding

Protein-induced budding

Membrane-curving proteins can attract and drive membrane vesiculation

Protein-induced budding

Membrane-curving proteins can attract and drive membrane vesiculation


Intuitive, but no physical justification!
Protein-induced budding

many caps
("contact lens")

36 curved caps, ~50000 lipids, 160nm side-length, total time ~1ms
no lateral tension
no explicit interaction between caps

Protein-induced budding

Protein-induced budding

Some observations:

• Caps attract collectively
• Attractive pair-forces exist
• No crystalline structure
• Cooperative vesiculation
• No “scaffolding”
• 50-100nm length scales
• several milliseconds

Protein-induced budding

Blood and Voth, PNAS 103, 15068 (2006)
Protein-induced budding


Blood and Voth, PNAS 103, 15068 (2006)
Protein-induced budding


Blood and Voth, PNAS 103, 15068 (2006)
Summary

CG membrane model can efficiently treat many mesoscopic membrane processes.

Link to continuum elastic level works

Physical properties turn out reasonable

Link to finer scale ought to be possible!

(under way)
Acknowledgements

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Ira

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Tristan Bereau, Zunjing Wang
...and many more

powered by
ESPResSo
Material properties