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Simulations of lipid dynamics in bilayer mixtures

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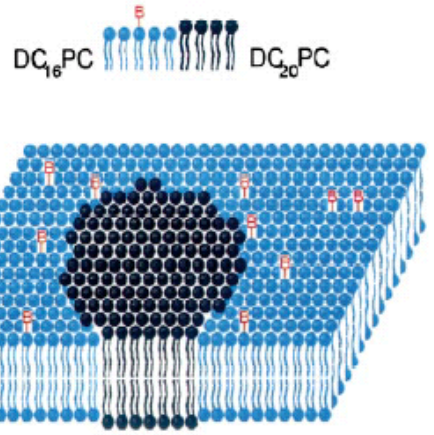
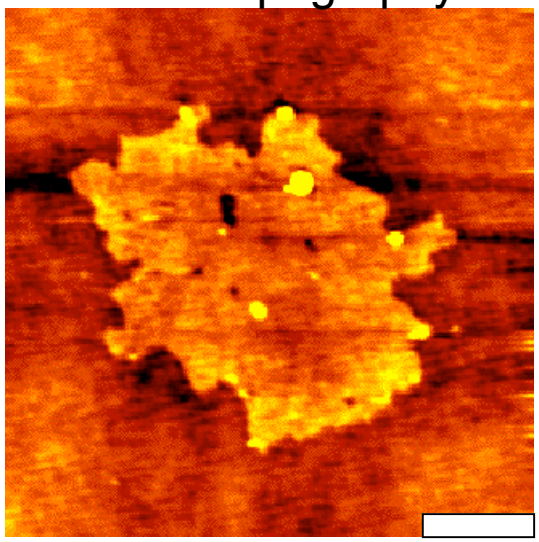
Lipids Domains

- Domains in biomembranes have biological function
  - proteins prefer certain domains
- Coexisting domains form in binary lipid mixtures
  - different chain lengths, saturation levels, ...
  - different phases: e.g. liquid, gel

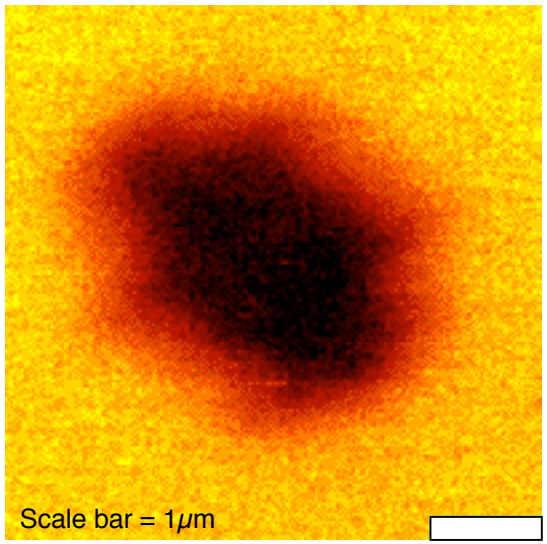


Domain of lipid mixture

AFM Topography



Fluorescence



3:1 DOPC/DPPC with DPPC "rafts"
0.5 % Fluorescent Bodipy-labeled DHPE Alan Burns, SNL

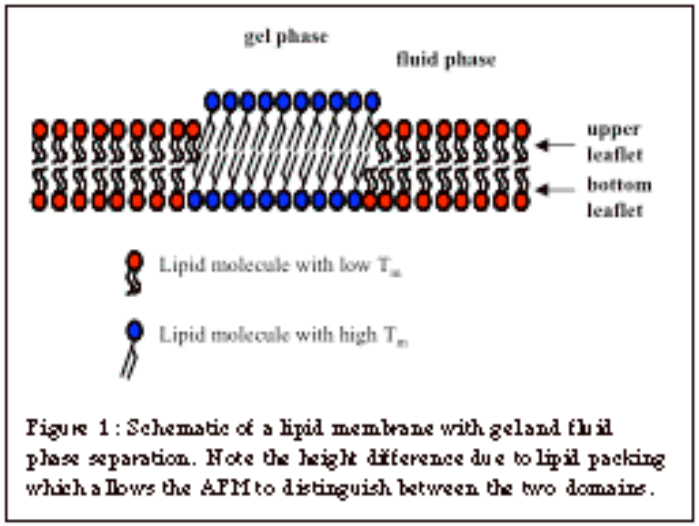


Figure 1: Schematic of a lipid membrane with gel and fluid phase separation. Note the height difference due to lipid packing which allows the AFM to distinguish between the two domains.

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Simulating Biomembranes

We want to simulate lipids *moving!*

However, lipid diffusion is 'slow'

- diffusion constant ~ 10^{-8} cm^2/s
- lipid exchange time ~ 100 ns
- too slow for atomistic simulations

$\Rightarrow$ need to use coarse-grained models

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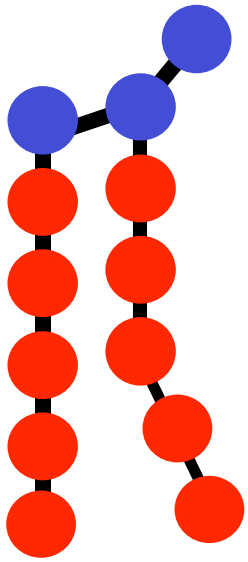
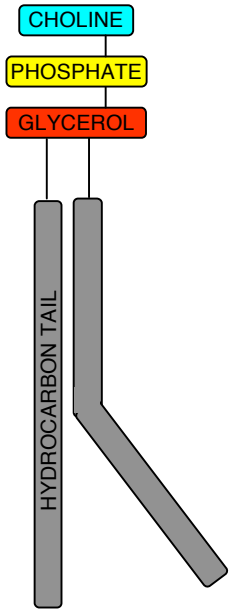
Lipids

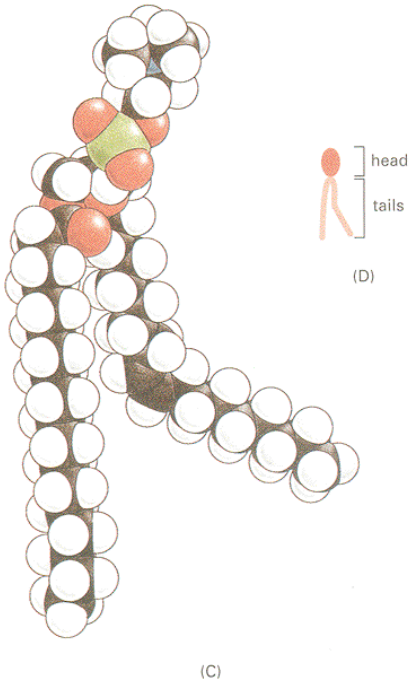
- phosphotidylcholine (PC)



bead-spring model



schematic



van der Waals

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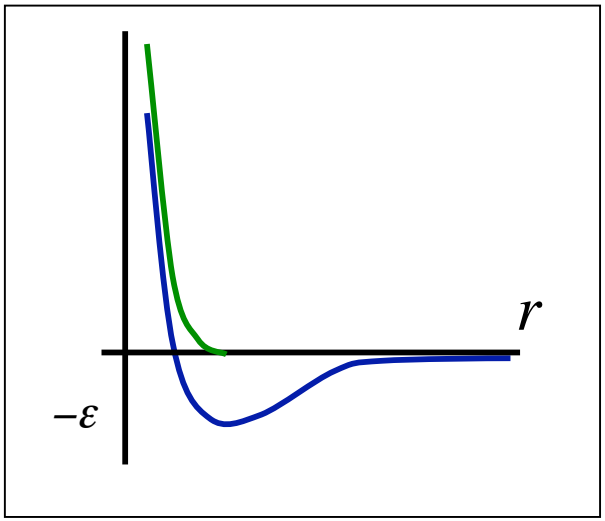
Lipid Model: Interactions

Lennard-Jones (LJ) potential

The purely repulsive LJ potential u_{RLJ} is cutoff and shifted at $r_c = 2^{1/6}\sigma$.

$$4\varepsilon_{\alpha\beta}\left[\left(\frac{\sigma_{\alpha\beta}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{\alpha\beta}}{r_{ij}}\right)^{6}\right]$$



Force field parameters

$\varepsilon_{\alpha\beta} = \varepsilon$, and $\sigma_{\alpha\beta} = \sigma$ for all pair types $\alpha\beta$

$r_{c,\alpha\beta}$ $= 2.5\,\sigma$ for $\alpha\beta$ = HH, TT, SS, HS

$= 2^{1/6}\sigma$ for $\alpha\beta$ = HT, TS

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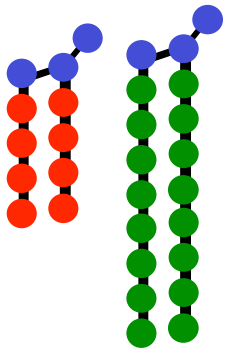
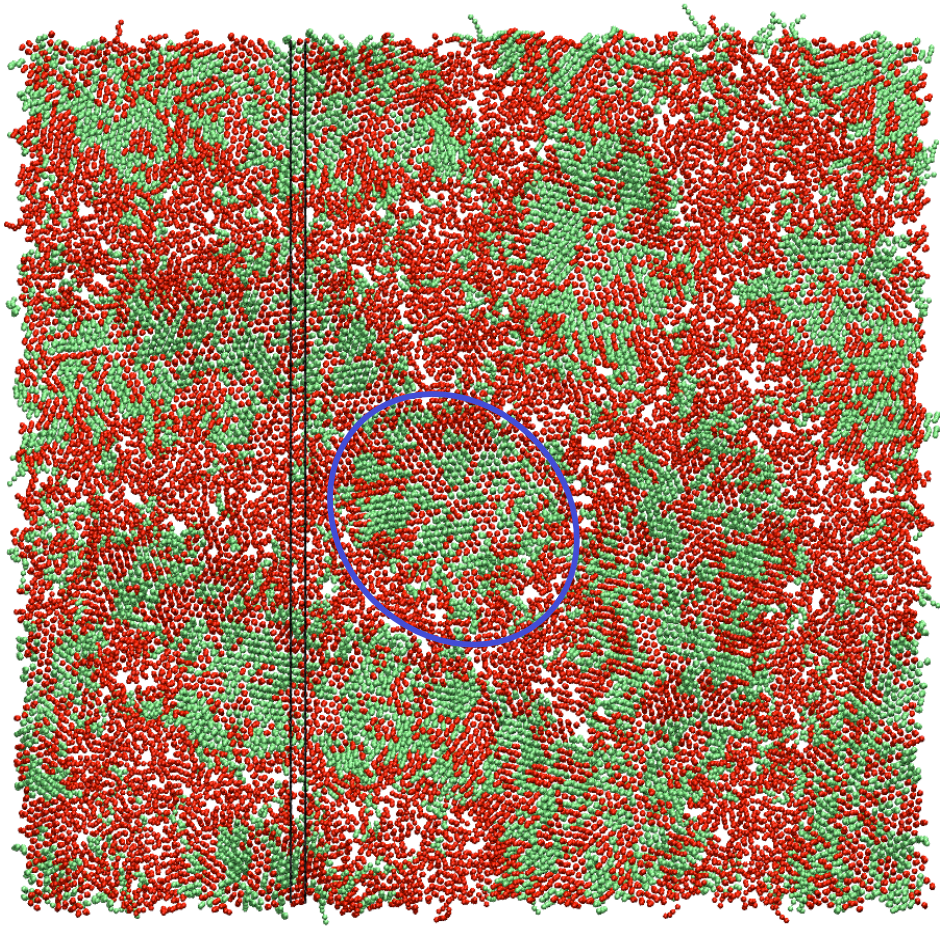
Domain Self-assembly

Start with random configuration of mixed lipids.

See domains form!

- N_T= 4 red
- N_T= 8 green
- 2:1 mixture
- 12096 total lipids
- image shows only tails





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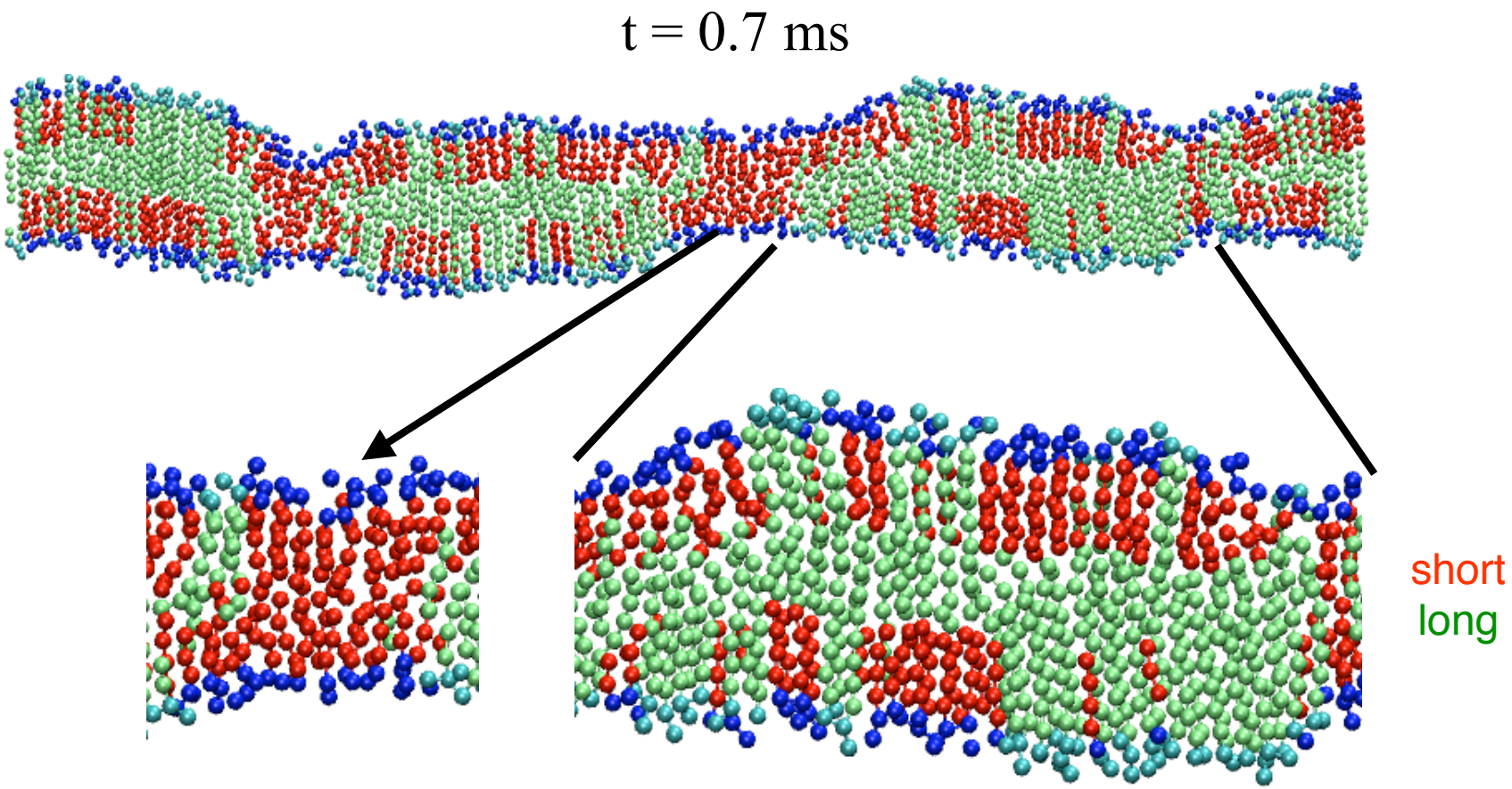
Domain structure: Complementary Matching



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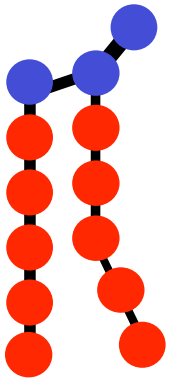
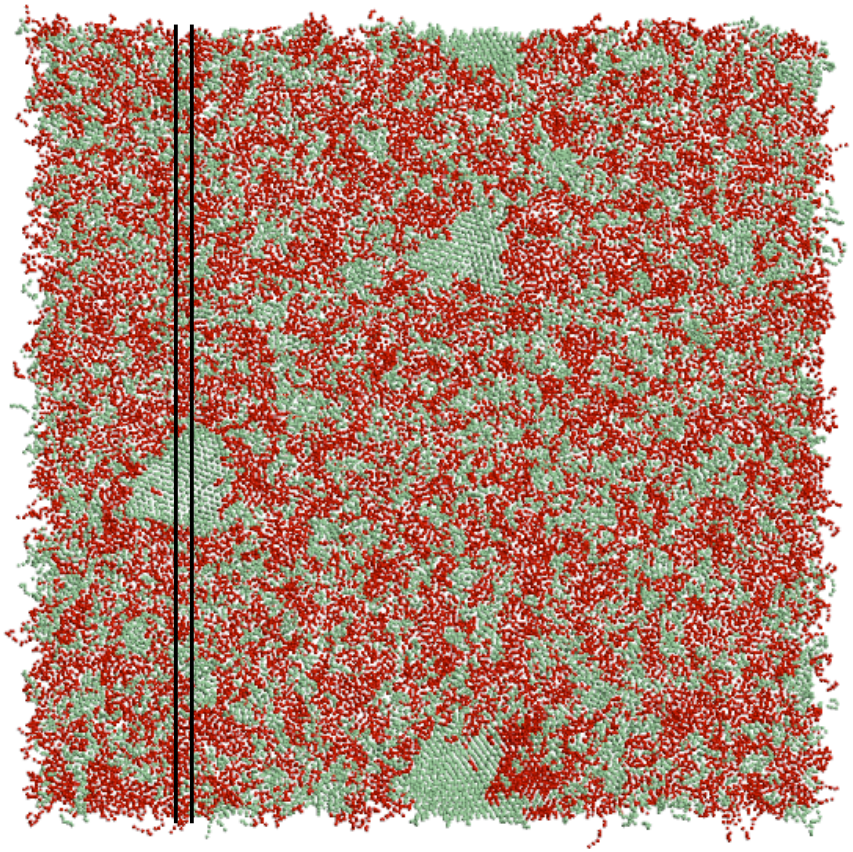
If there is a double bond, then ...

- Unsaturated (U):Saturated (S) mixture
- N_T= 6uu & 6 (U:S)
- 3:2 mixture





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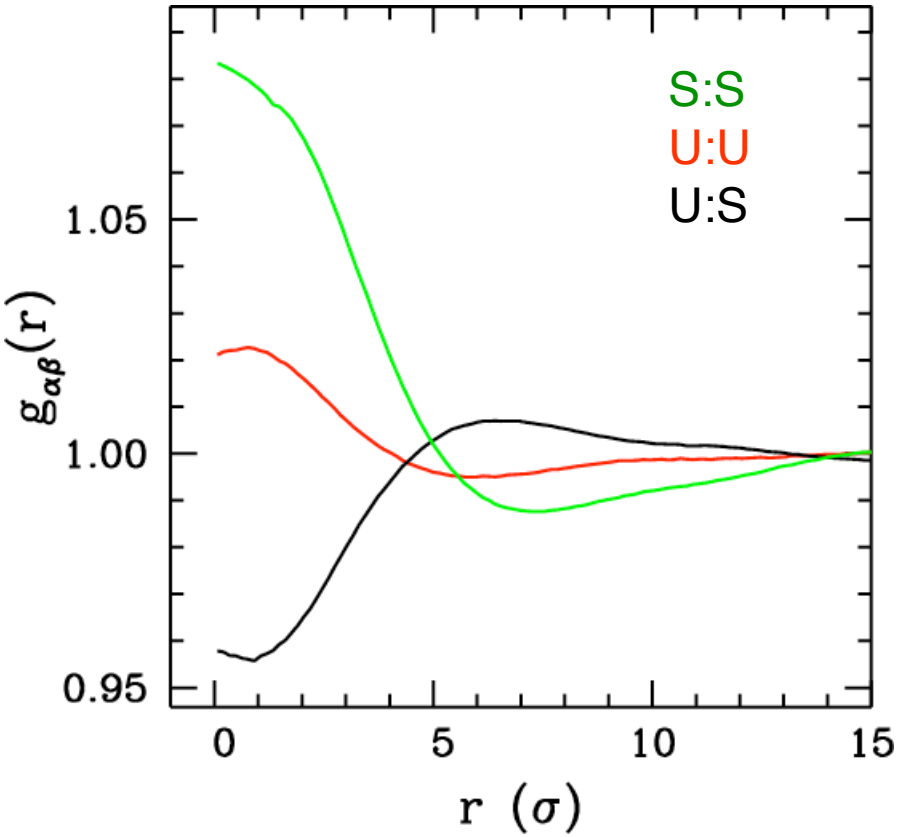
Gel domains



Now find gel domains composed of single lipid type.

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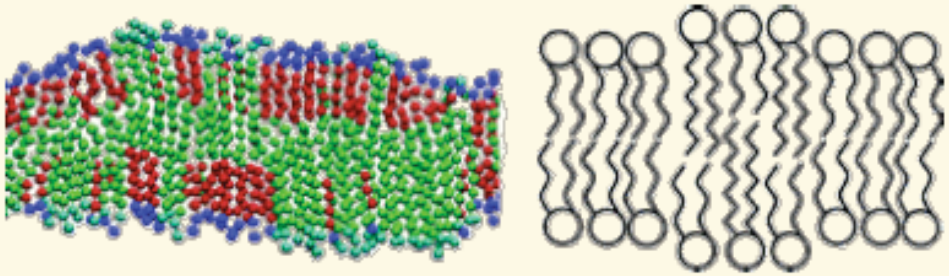
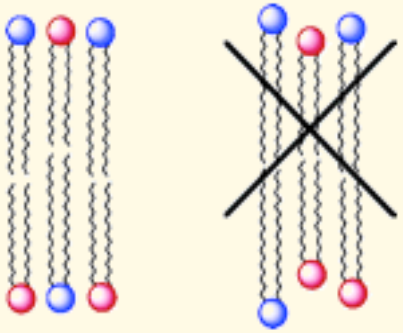
Summary

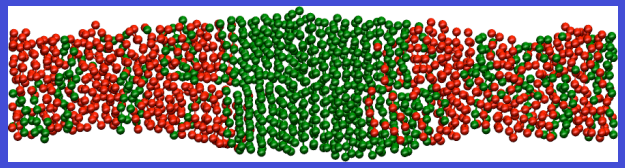
Complementary Matching in Domain Formation within Lipid Bilayers
Mark J. Stevens
J. Am. Chem. Soc.; **2005**; *127*(44) pp 15330 - 15331; **(Communication)** DOI: 10.1021/ja043611q

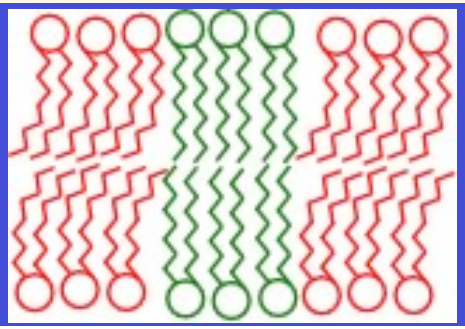


Transbilayer Complementarity of Phospholipids. A Look beyond the Fluid Mosaic Model
Jianbing Zhang, Bingwen Jing, Nobuya Tokutake, and Steven L. Regen
pp 10856 - 10857; **(Communication)** DOI: 10.1021/ja046892a
J. Am. Chem. Soc. 2004



Saturated:Unsaturated mixture





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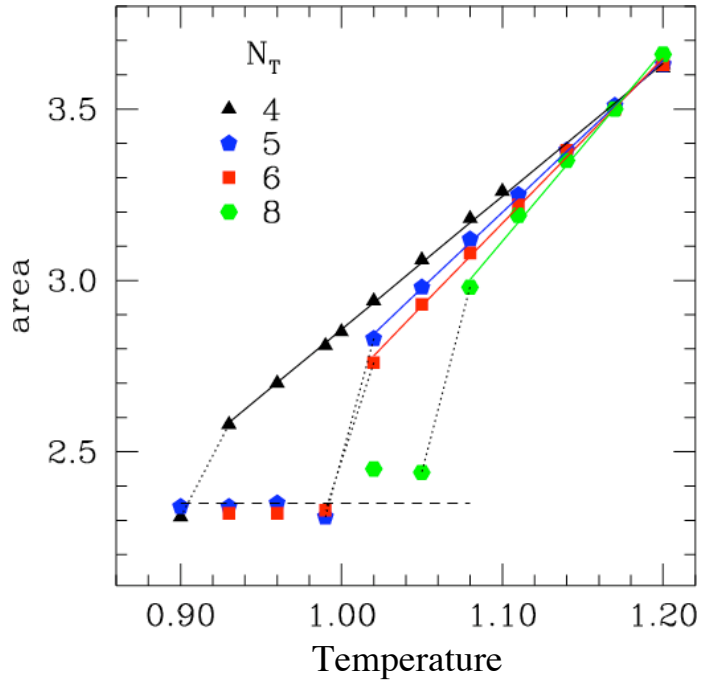
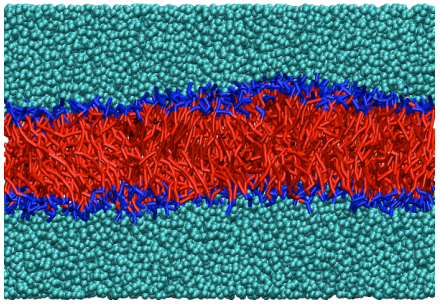
Area per Lipid

Area per lipid A

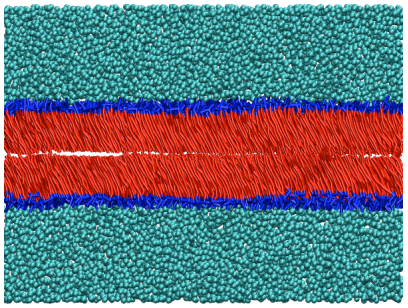
- decreases with temperature T
- has discontinuity at liquid→gel transition
- Phase transition temperature decreases for larger N_T



At T = 0.95, 4 bead lipids are in liquid state, and 8 bead lipids are in the gel state.



liquid



gel

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