MOLECULAR DYNAMICS STUDY OF LIPOSOMES WITH A NEW COARSE-GRAINED MOLECULAR MODEL

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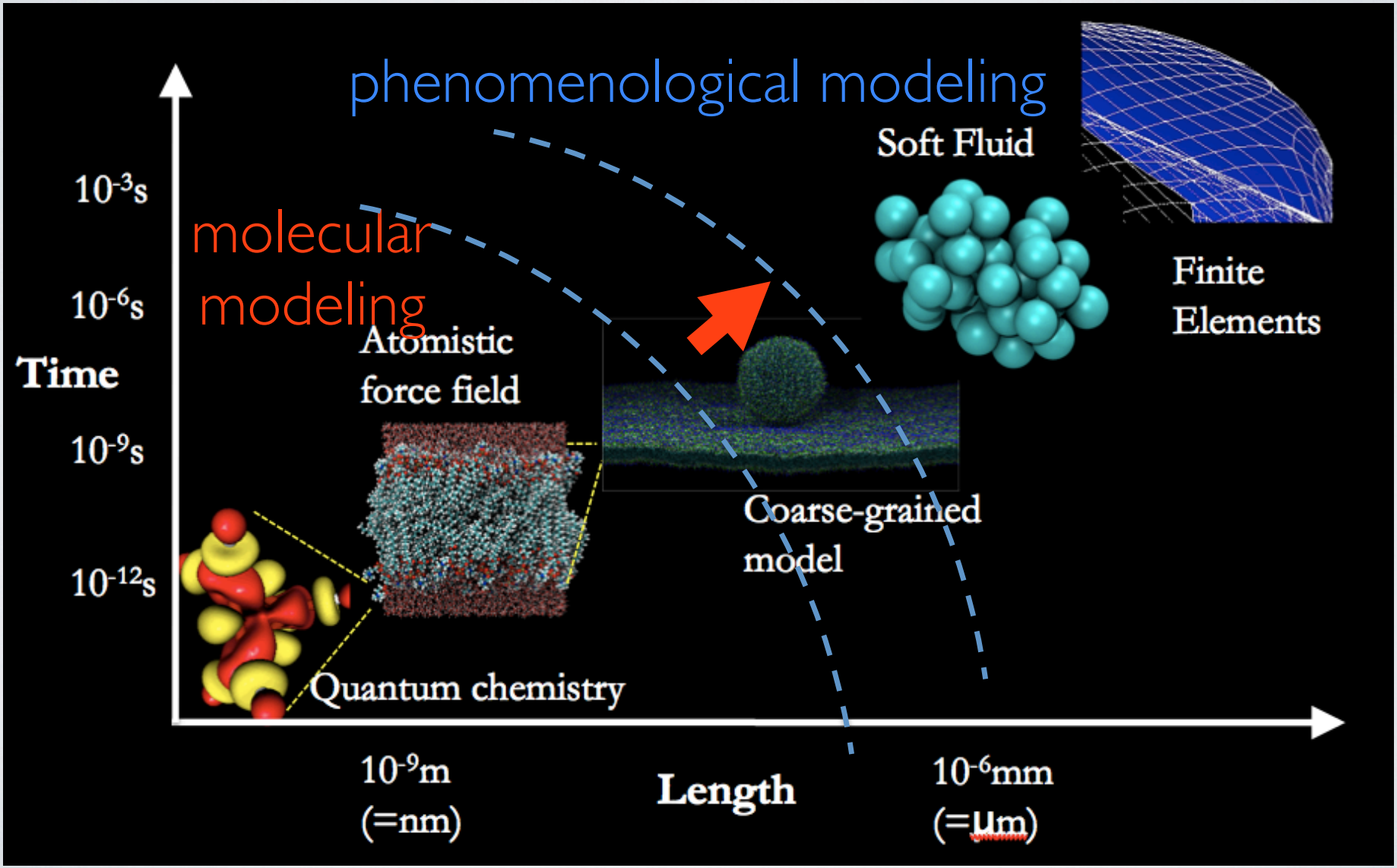
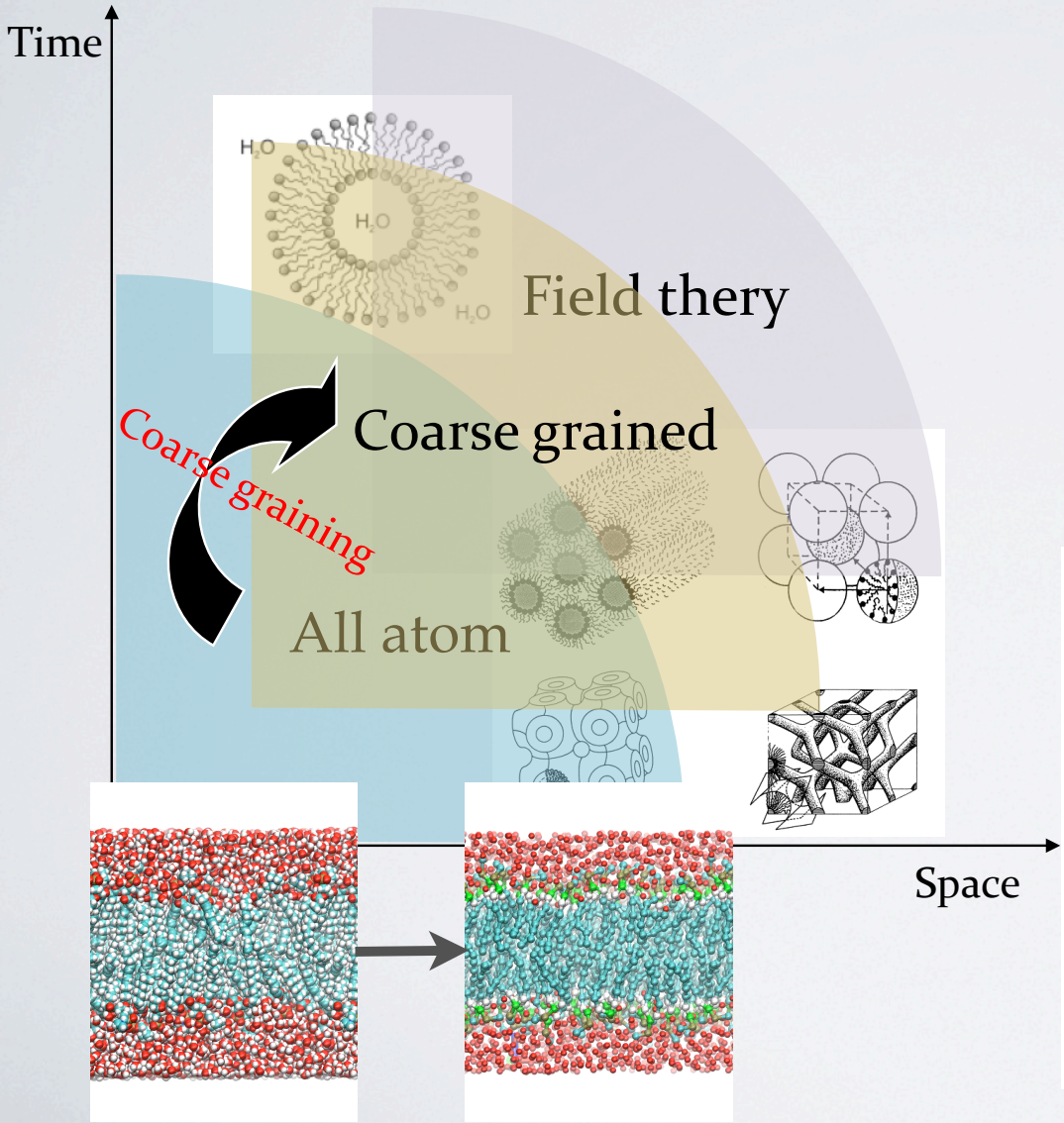
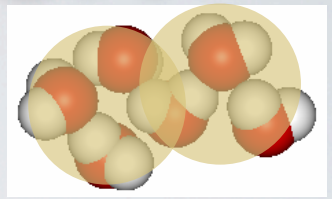
MULTI-SCALE MODELING

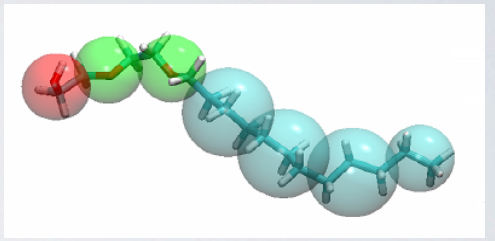


CONTENTS

SCALE ISSUE FOR MOLECULAR SIMULATION

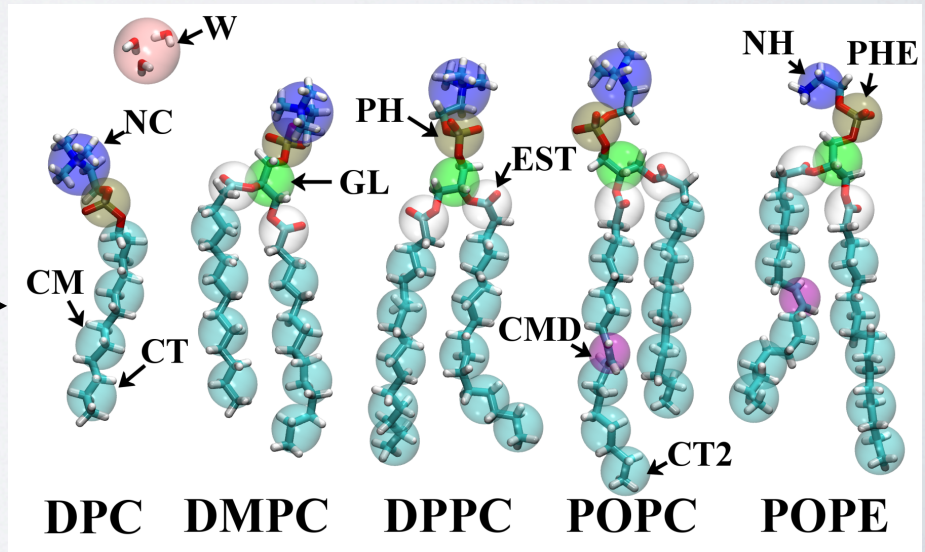






$HOCH_2$-$(CH_2OCH_2)_2$-$(CH_2CH_2CH_2)_3$-CH_2CH_3

OA-$(EO)_2$-$(CM)_3$-CT2



COARSE GRAINING PROCEDURE

MULTI-PROPERTY FITTING

Target properties:

Surface/interfacial tension, density, compressibility,
Solvation free energy, transfer free energy,
Radial distribution functions from all-atomic model

$$U_{\mathrm{bond}}(r) \propto -k_B T \ln\left[P(r)/r^2\right] \qquad U_{\mathrm{angle}}(\theta) \propto -k_B T \ln\left[P(\theta)/\sin\theta\right],$$

Simple potential functions
Intramolecular : harmonic ⟶ Versatility, transferability
Intermolecular : Coulomb + (LJ12-4 or LJ9-6)

$$U_{\mathrm{intra}} = \sum^{Bond} k_b (r - r_0)^2 + \sum^{Angle} k_a (\theta - \theta_0)^2,$$

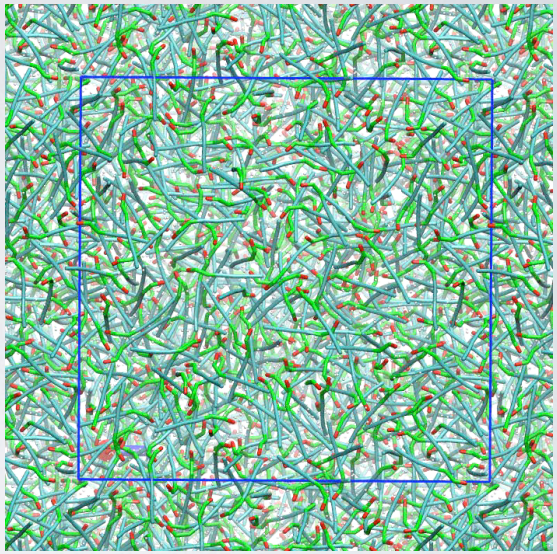
$$U_{\mathrm{LJ9-6}}(r) = \frac{27}{4}\varepsilon\left\{\left(\frac{\sigma}{r}\right)^9 - \left(\frac{\sigma}{r}\right)^6\right\},$$

$$U_{\mathrm{LJ12-4}}(r) = \frac{3\sqrt{3}}{2}\varepsilon\left\{\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^4\right\}.$$

Shinoda et al. *Mol. Simul.* (2007);
Soft Matter (2008); *J. Phys. Chem. B* (2010).

WHAT WE GAIN ... ?

- Mesophase structure
  - Self-assembly
  - Phase transition
  - Correct molecular partition(oil/water)
- Transferability
  - Bulk solution
  - Interfaces (air/water, oil/water, solid/water etc.)
- Systematic parameterization
- Multiscale(AA-CG) / reverse mapping



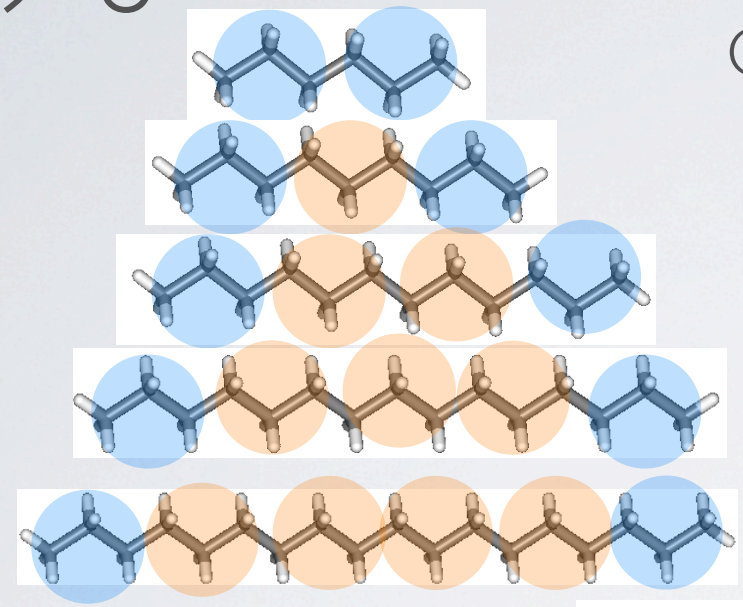
ALKANE MODEL

CT $CH_3CH_2CH_2$-

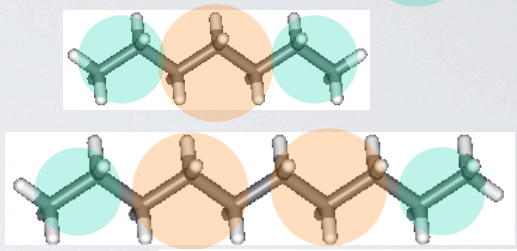
CM -$CH_2CH_2CH_2$-

CT2 CH_3CH_2-

LJ9-6

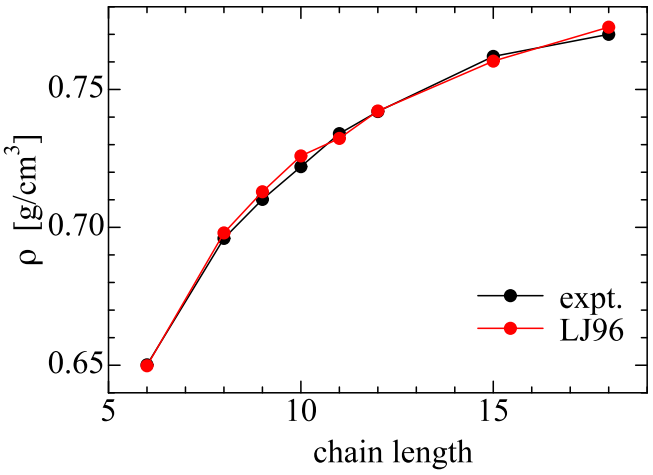


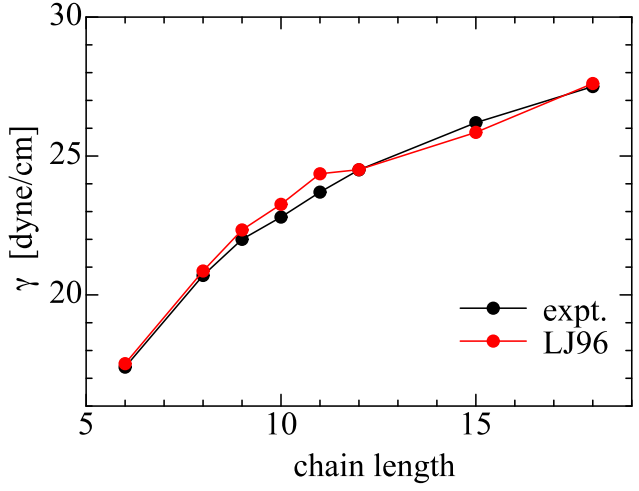
CT-CT

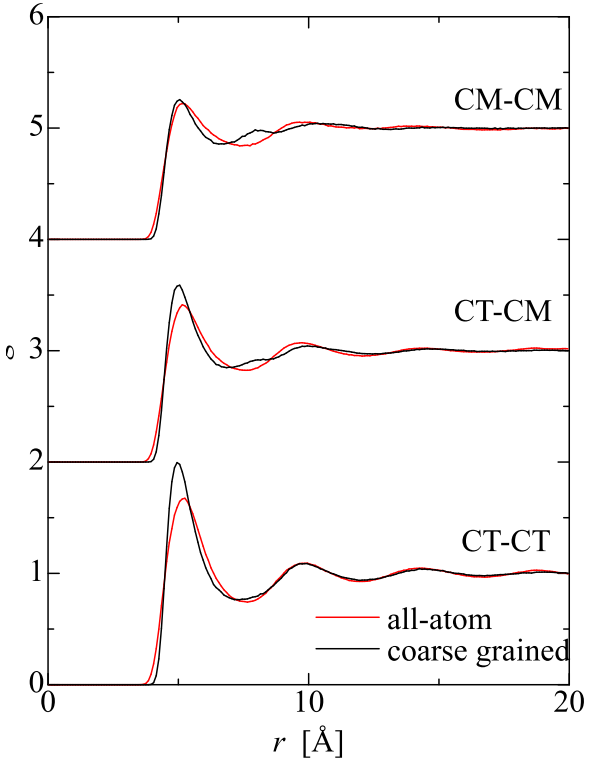


CT2-CM
CT2-CT2

CT-CM
CM-CM



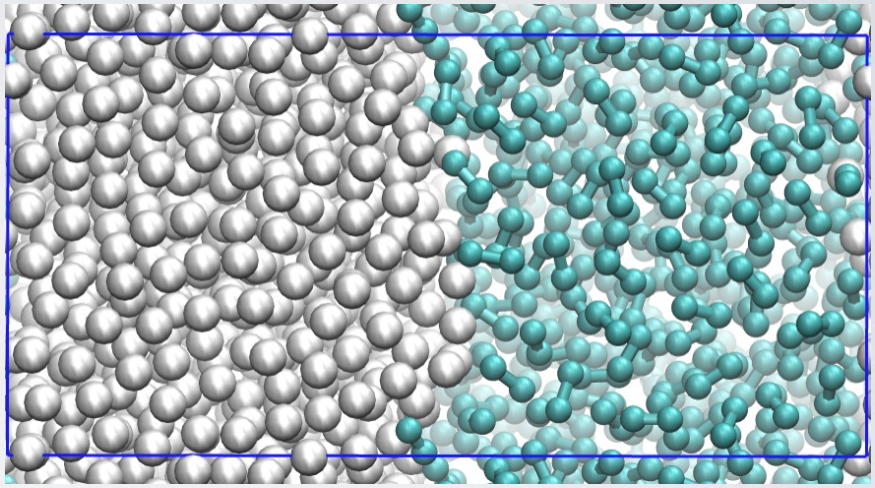




RDF: Dodecane

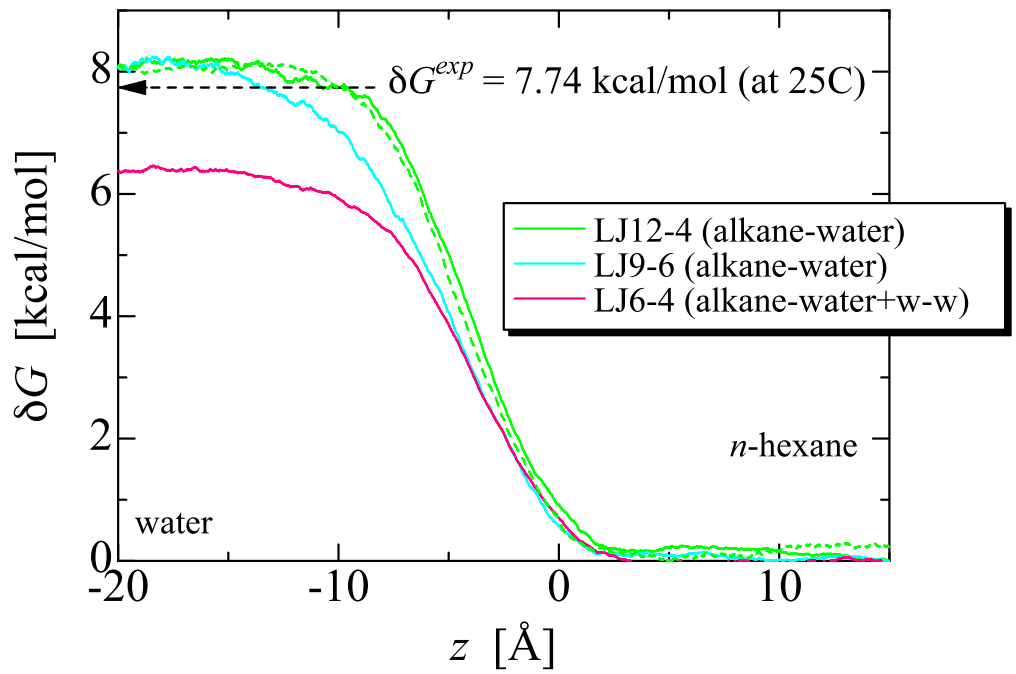
ALKANE-WATER INTERACTION

interface	pair	interfacial tension	
		exp	MD
water/hexane	CT-W	**49.96**	**50.0**
water/nonane	CM-W	**51.21**	**51.9**
water/dodecane		**52.14**	**52.9**
water/pentadecane		**-**	**52.9**
water/heptane	CT2-W	**50.30**	**50.1**

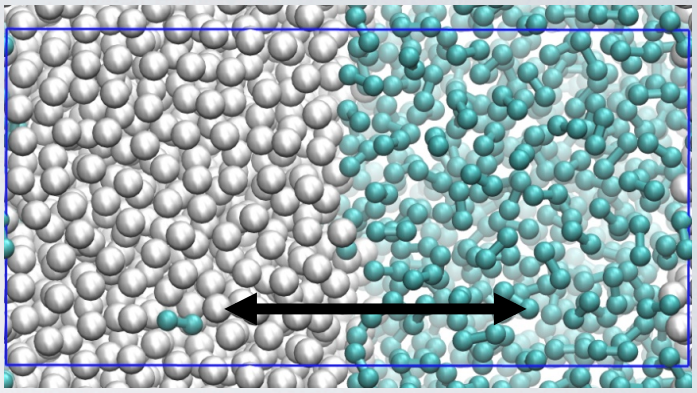


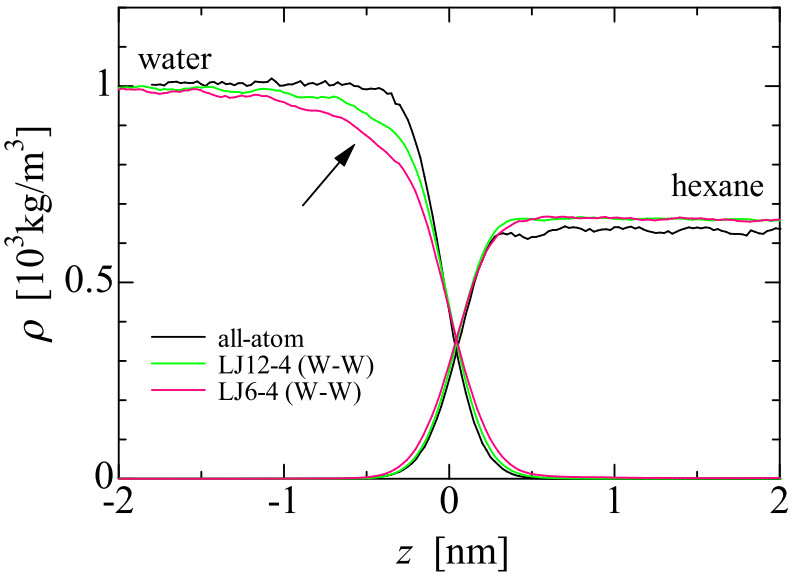
ALKANE-WATER INTERACTION

TRANSFER FREE ENERGY



Transfer free energy :
Tranfer of *n*-hexane from its bulk to water



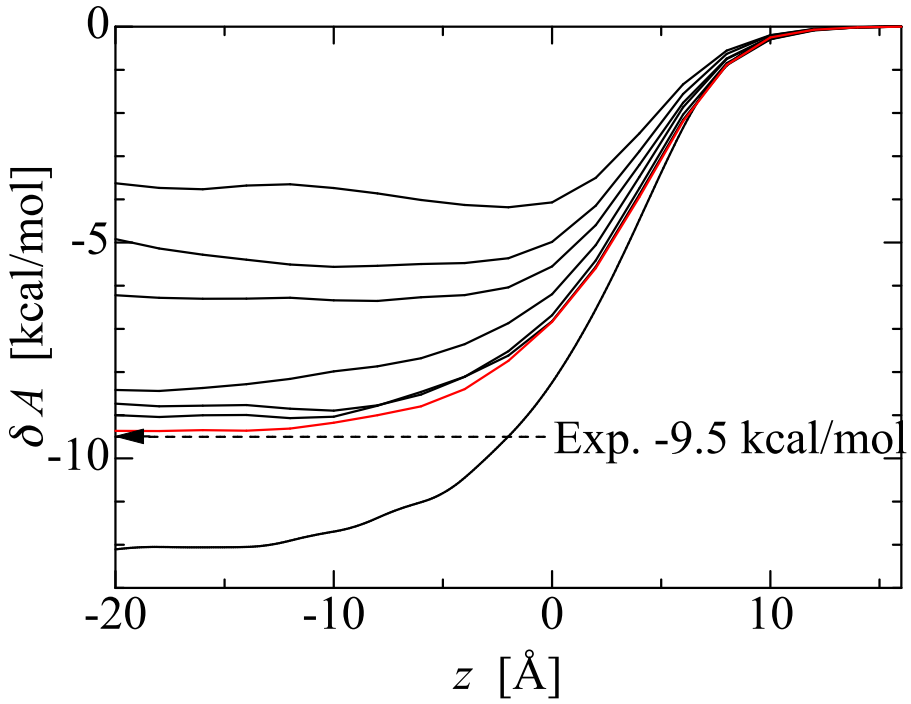


density profile across the hexane/water interface

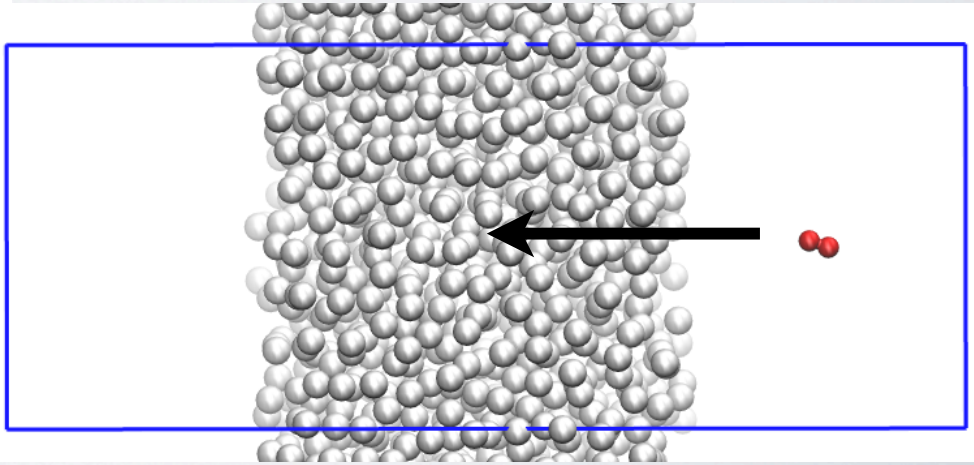
SOLUTE-W INTERFACTION

Hydration free energy → ε

Ex) Ethylene glycol - water



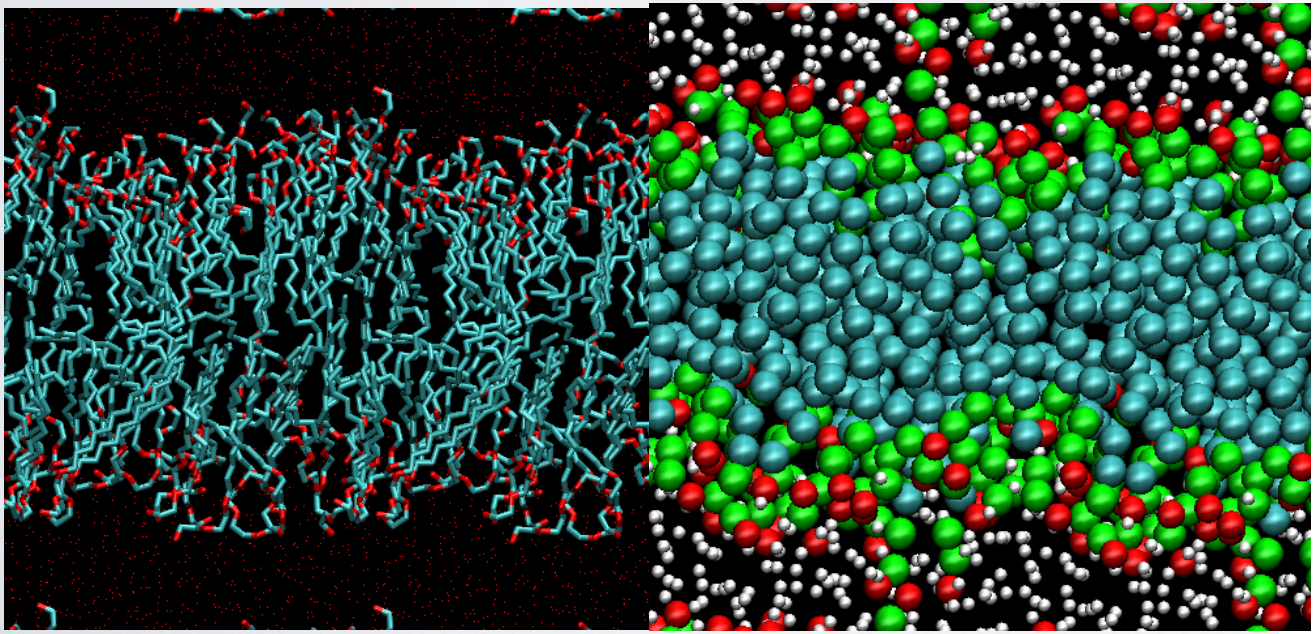
Steered MD / Jarzynski or
Thermodynamic Integration



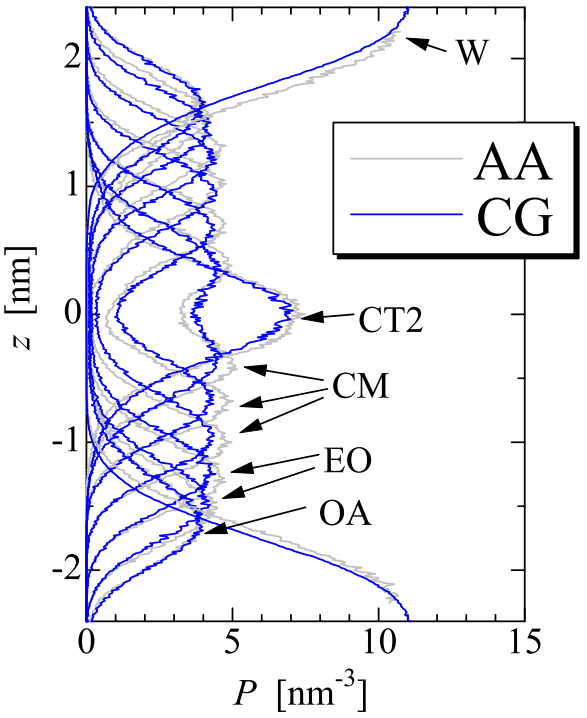
$C_{12}E_2$ LAMELLAR PHASE

Exp: Funari & Rappe, JPCB (1997).
67wt% $C_{12}E_2$, 293.5 K , 1 atm
***A* = 0.30 nm² , *d* = 4.73 nm**

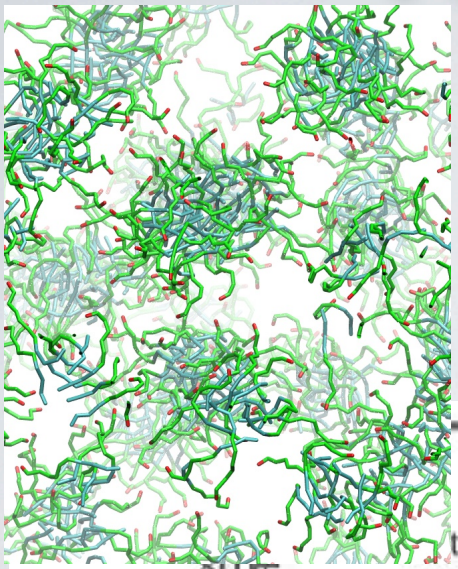
CG:
***A* = 0.30 nm² , *d* = 4.81 nm**

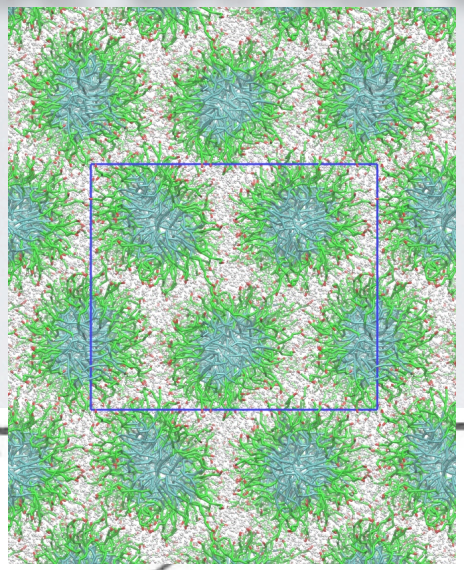


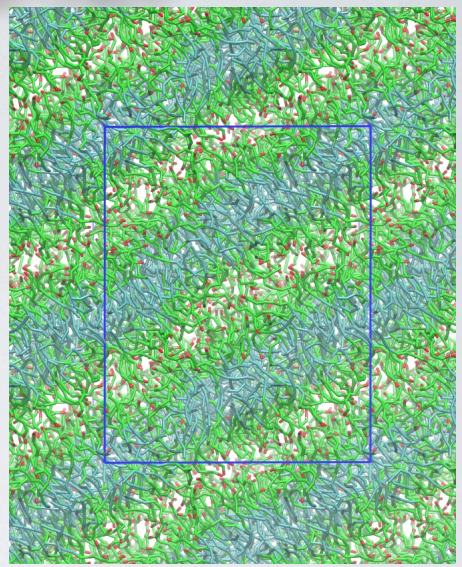
AA CG

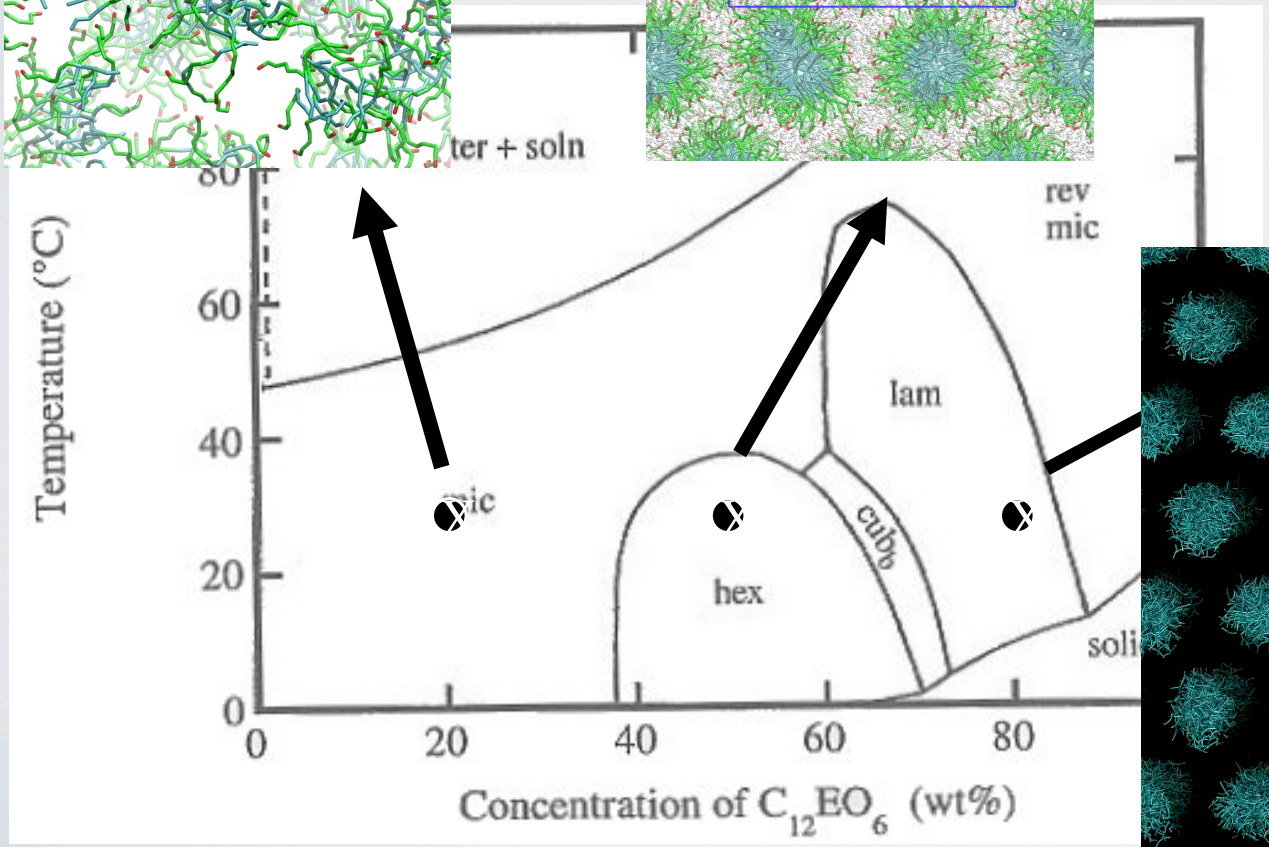


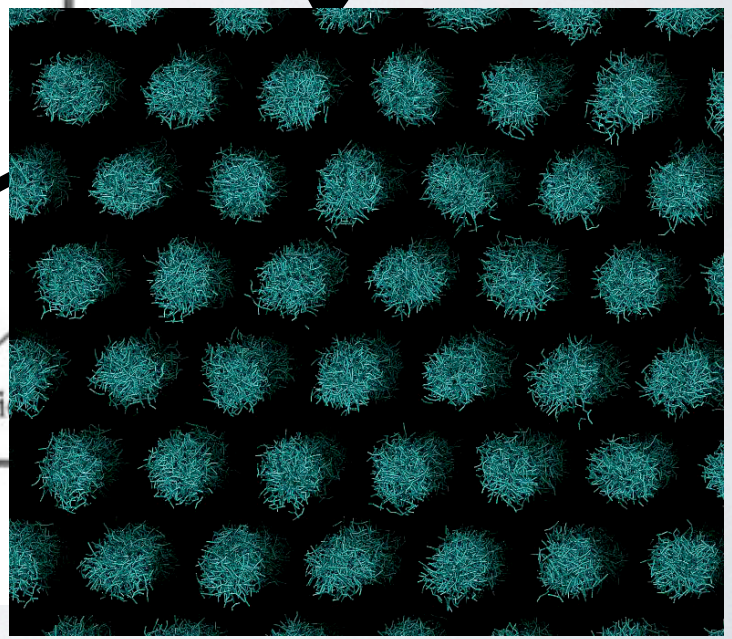
PHASE DIAGRAM $C_{12}E_6$





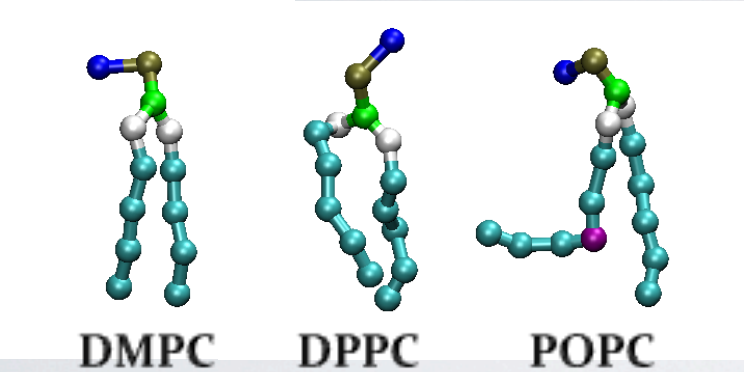






Jonsson et al., 'Surfactants and Polymers in Aqueous Solution'

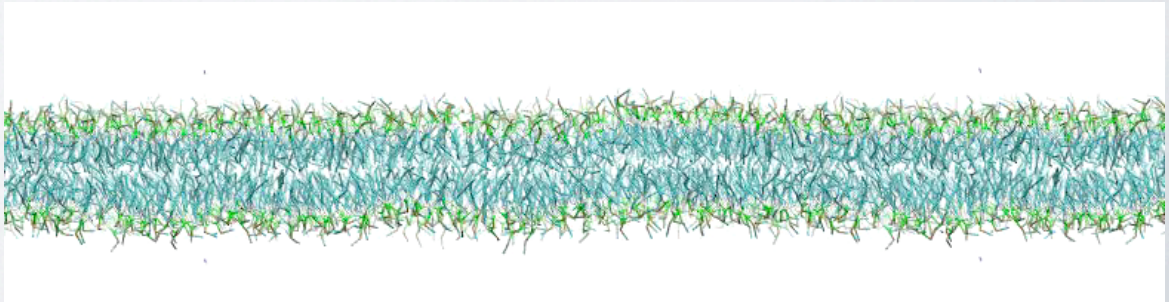
PHOSPHATIDYLCHOLINE(PC): LIPID BILAYER



CG-MD has carried out for 100ns in the NPT ensemble

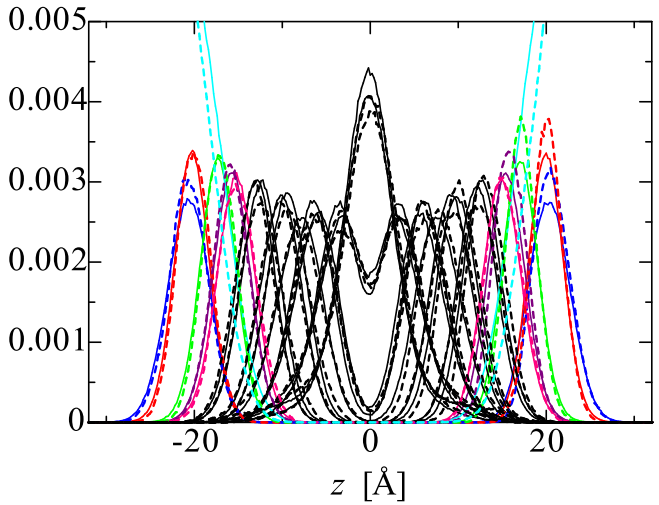
Area per lipid: **A**, repeat spacing: **d**, area expansion modulus: K_A, bending modulus: κ

	T [K]	A [Å^2]		d [Å]		K_A [dyn/cm]		κ [10^{-20} J]	
		MD	Expt.	MD	Expt.	MD	Expt.	MD	Expt.
DMPC	310	62.0	60.6	60.0	—	226	234	6.90	5.6, ~10
DPPC	323	63.8	64	66.9	67	233	—	6.41	~10
POPC	303	64.6	64	66.2	—	296	—	5.68	—

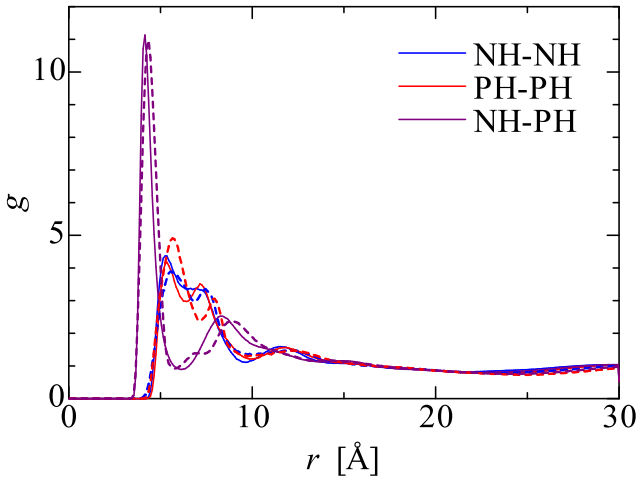


PHOSPHATIDYLETHANOLAMINE(PE) POPE BILAYER

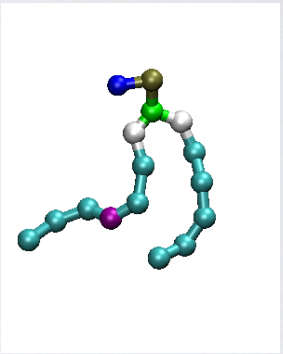
	T [K]	A [Å^2]		d [Å]		K_A [dyn/cm]		$\varkappa$ [10^{-20} J]	
		MD	Expt.	MD	Expt.	MD	Expt.	MD	Expt.
POPE	308	60.3	60	67.7	—	296	—	6.45	—



Probability density of CG segments along the bilayer normal

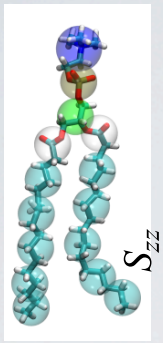


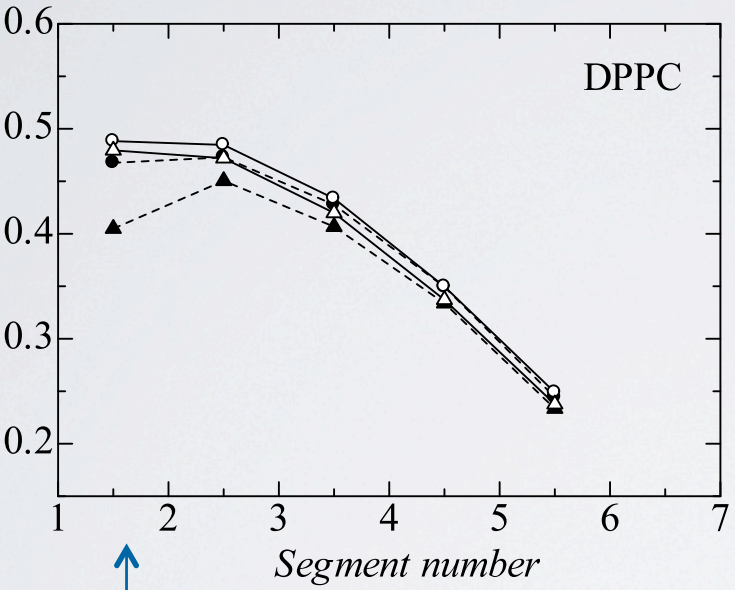
Radial distribution function among headgroup segments

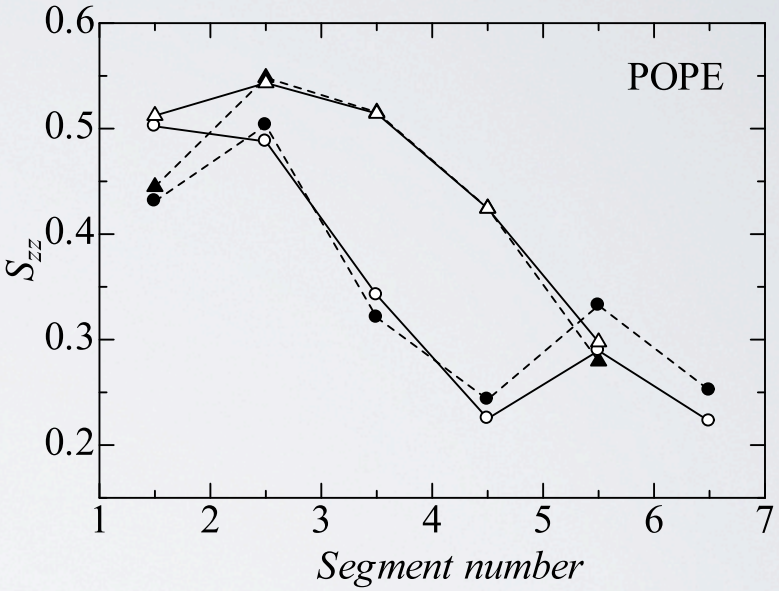


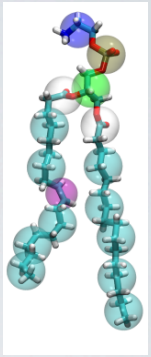
Solid lines: CG-MD
Dashed lines: AA-MD

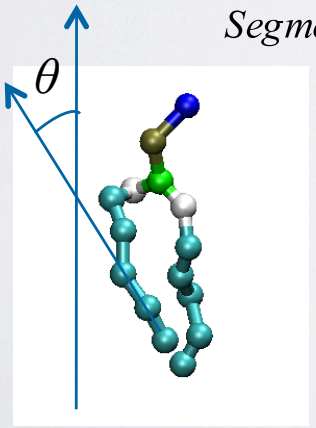
ORDER PARAMETER PROFILES







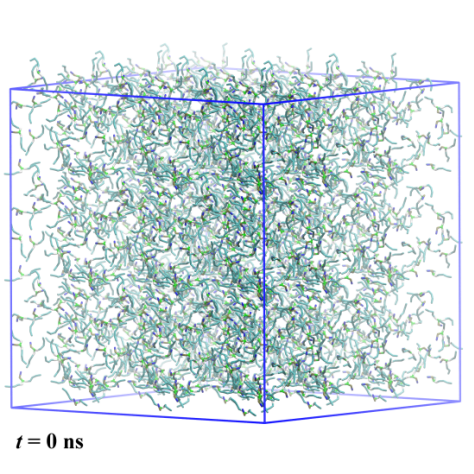


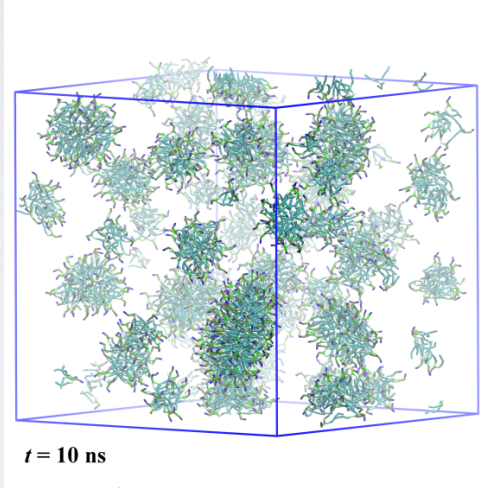


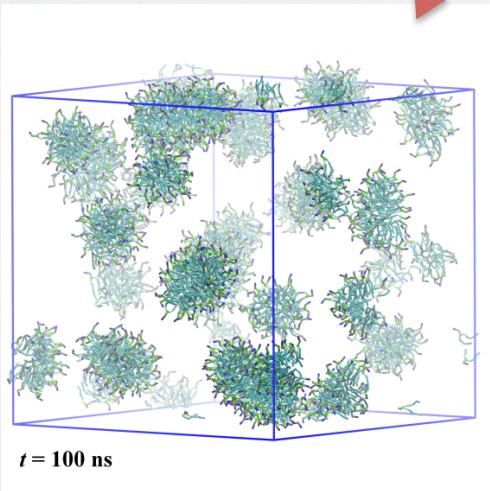
$$S_{ZZ} = \frac{1}{2}\left\langle 3\cos^2\theta - 1 \right\rangle$$

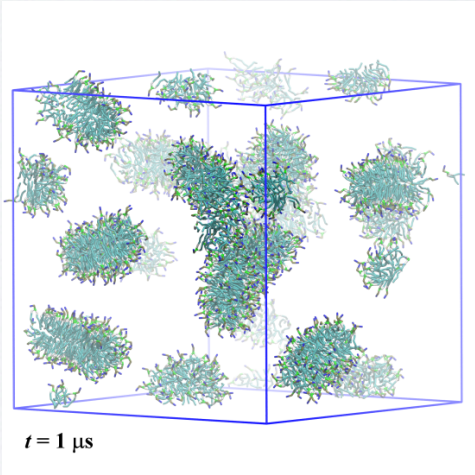
Doted line: all-atomic MD
Solid line: coarse-grained MD

MAKING A VESICLE



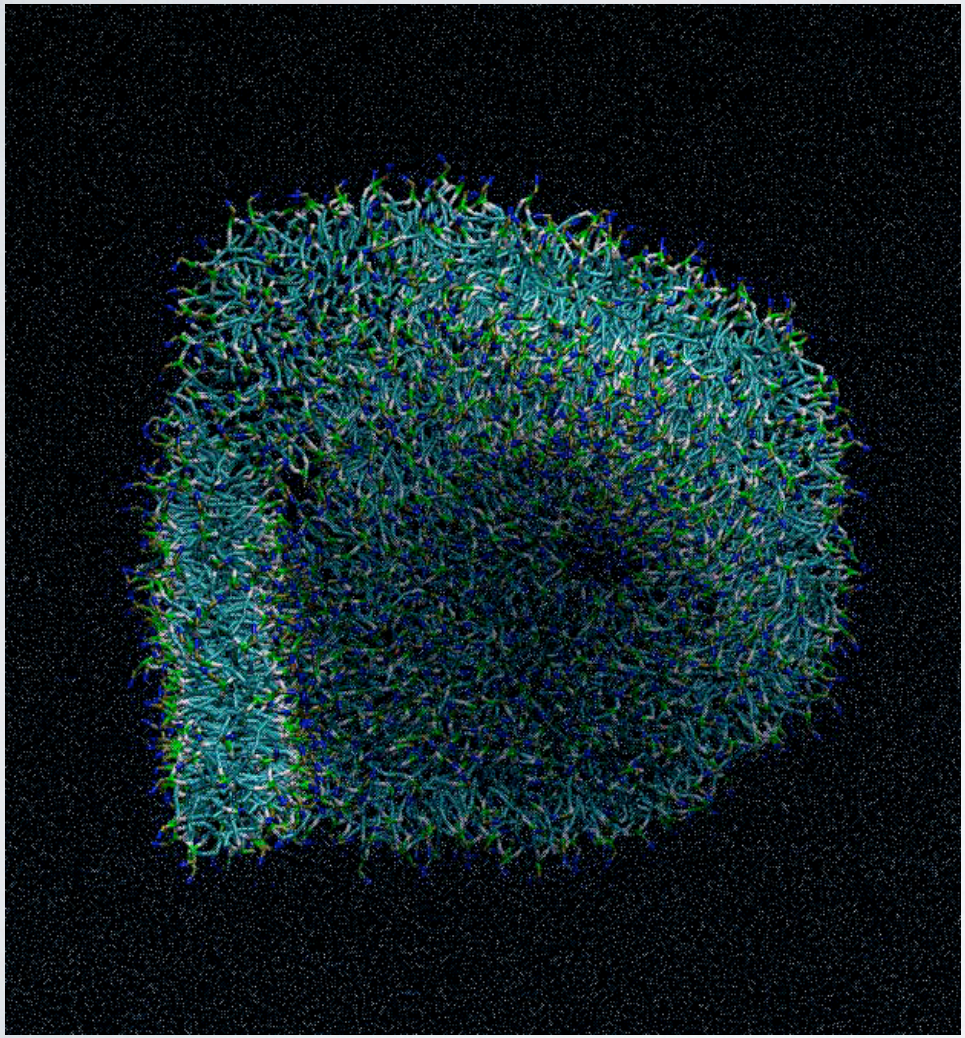




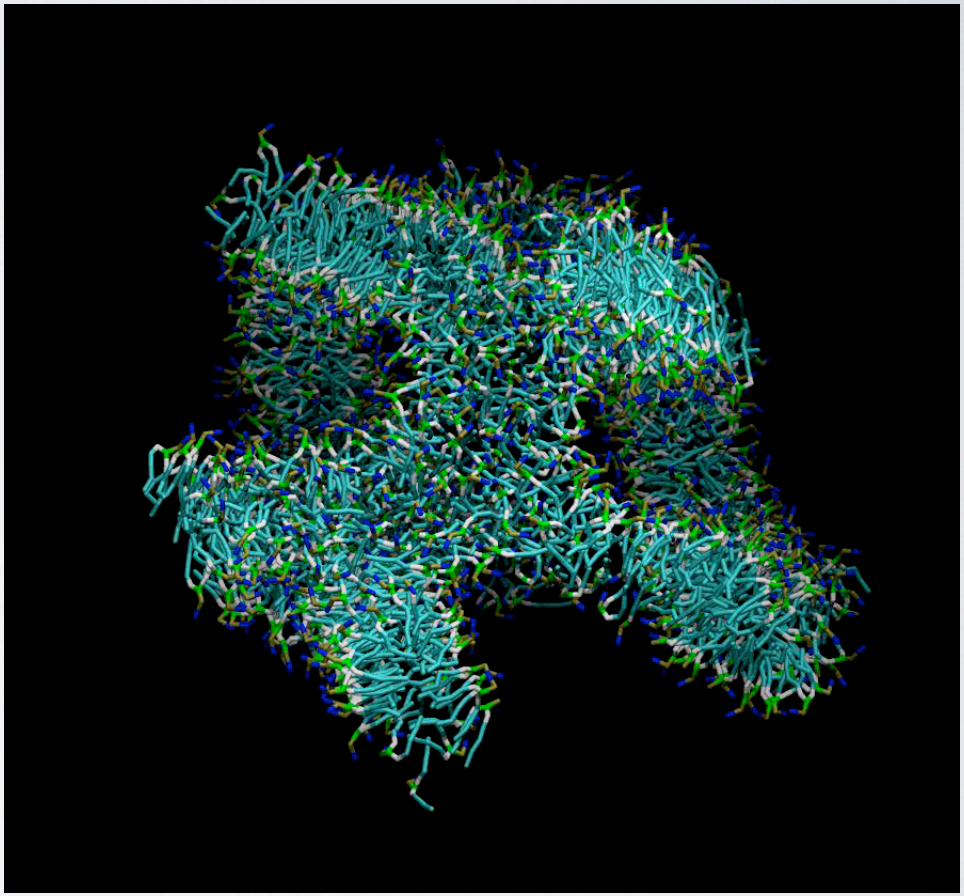


long time.....

MORPHOLOGY OF LIPID AGGREGATE (VESICLE, BICELLE)

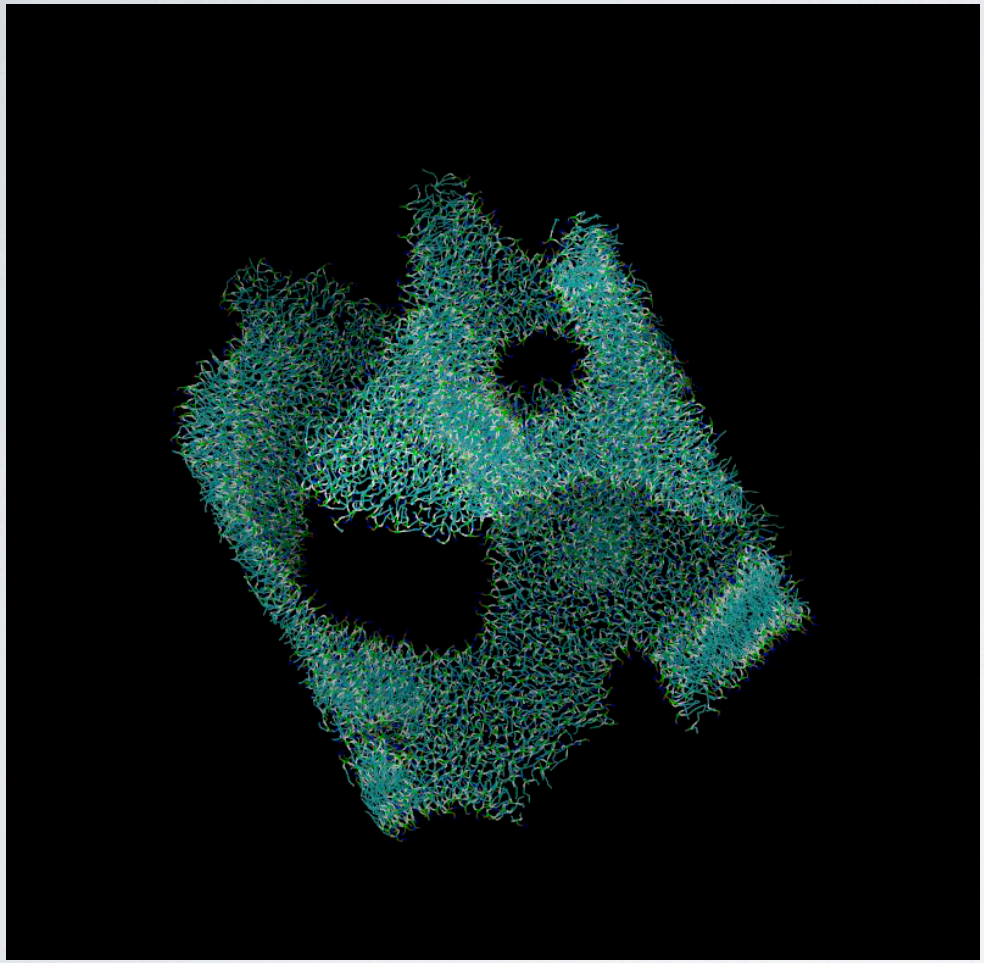


DMPC 1512

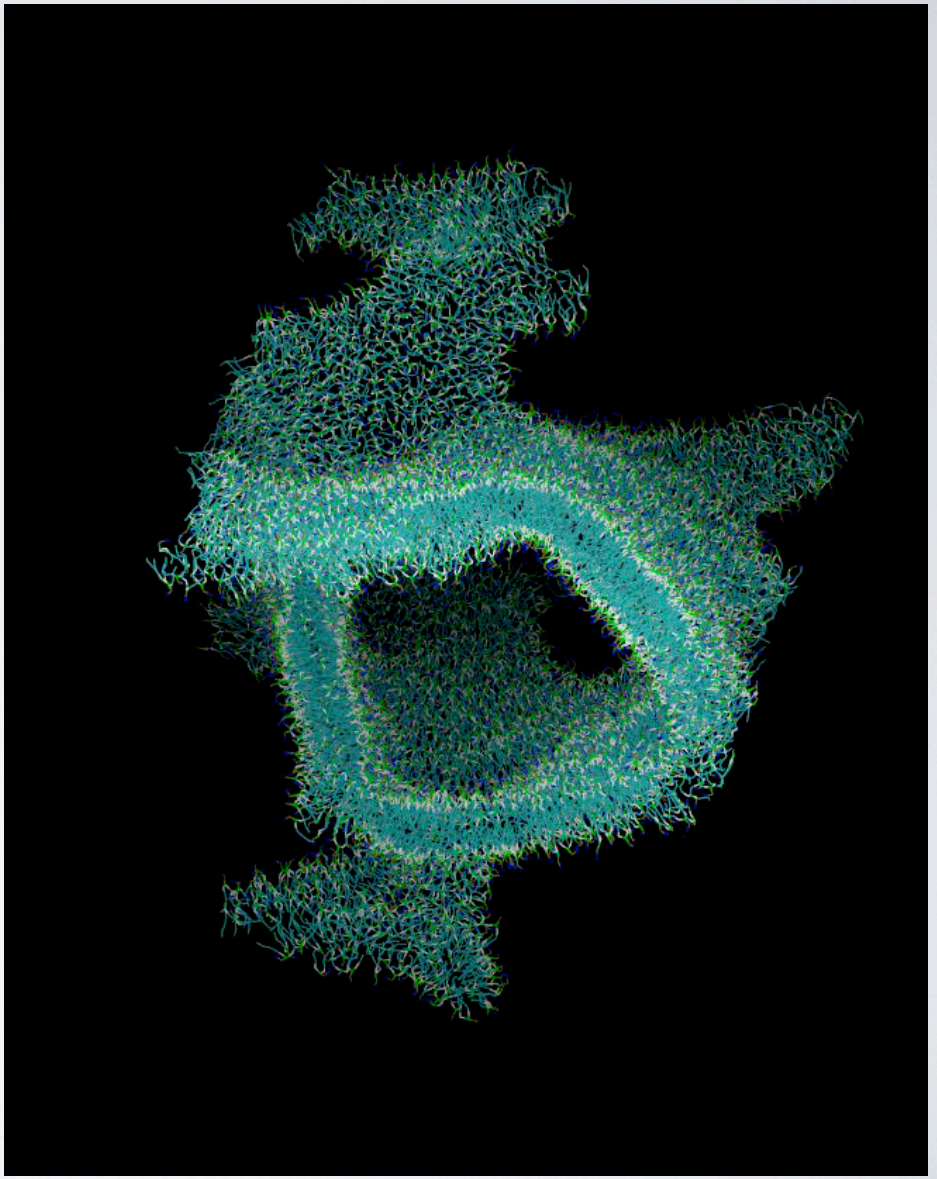


DMPC 1000

VESICLE FORMATION (LARGER SYSTEMS)



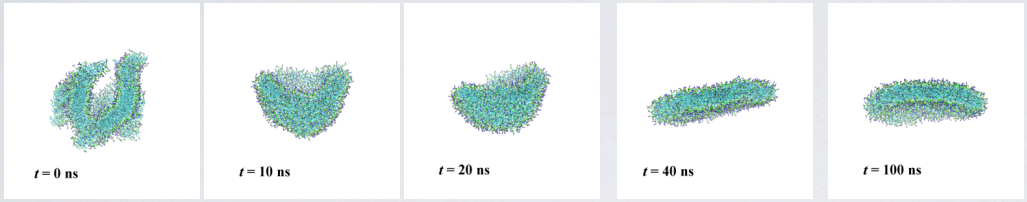
DMPC 3500



DMPC 5000

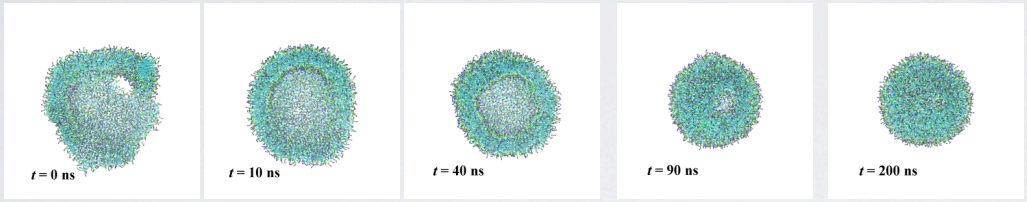
MORPHOLOGY CHANGE (DMPC)

DMPC1000

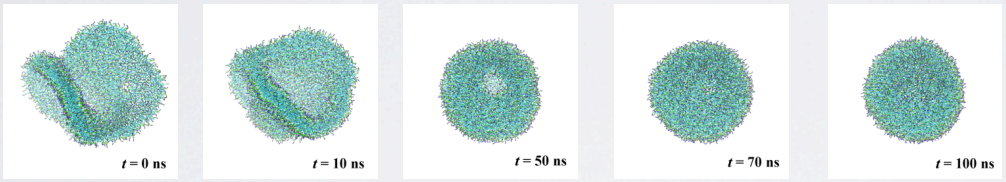


Bicelle (disk)

DMPC1512



DMPC2500



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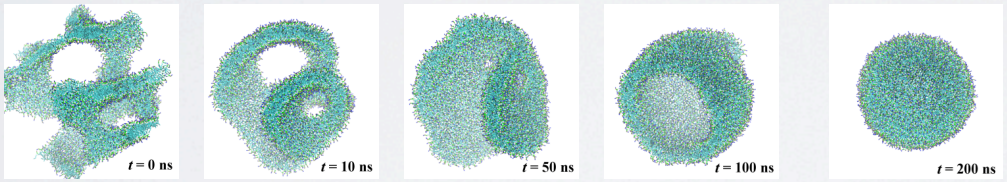
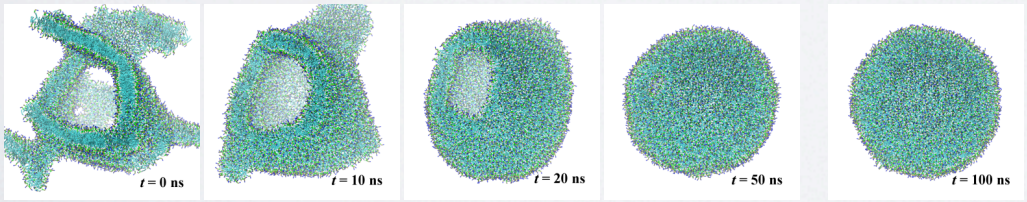


Closed vesicle

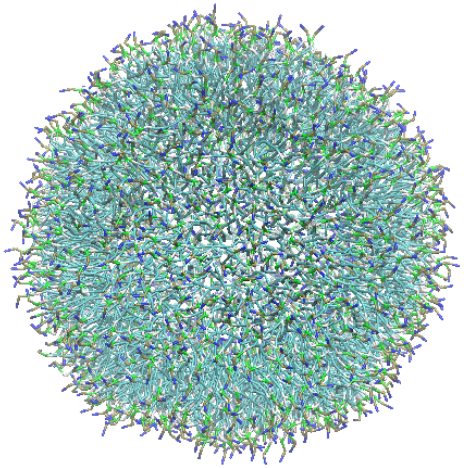
DMPC5000



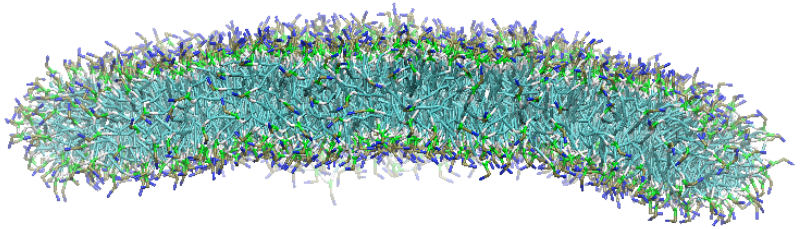
Energy cost at the bilayer edge vs Bending free energy

BISTABILITY OF AGGREGATE

DMPC 1512



Closed Vesicle



Bicelle

Microsec. MD

ACKNOWLEDGMENTS

- CG modeling
  - Prof. Michael L Klein (Temple Univ.)
  - Prof. Russell DeVane (Temple Univ.)
- Implementation of CG model to LAMMPS
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- Free energy analysis
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CREST-JST