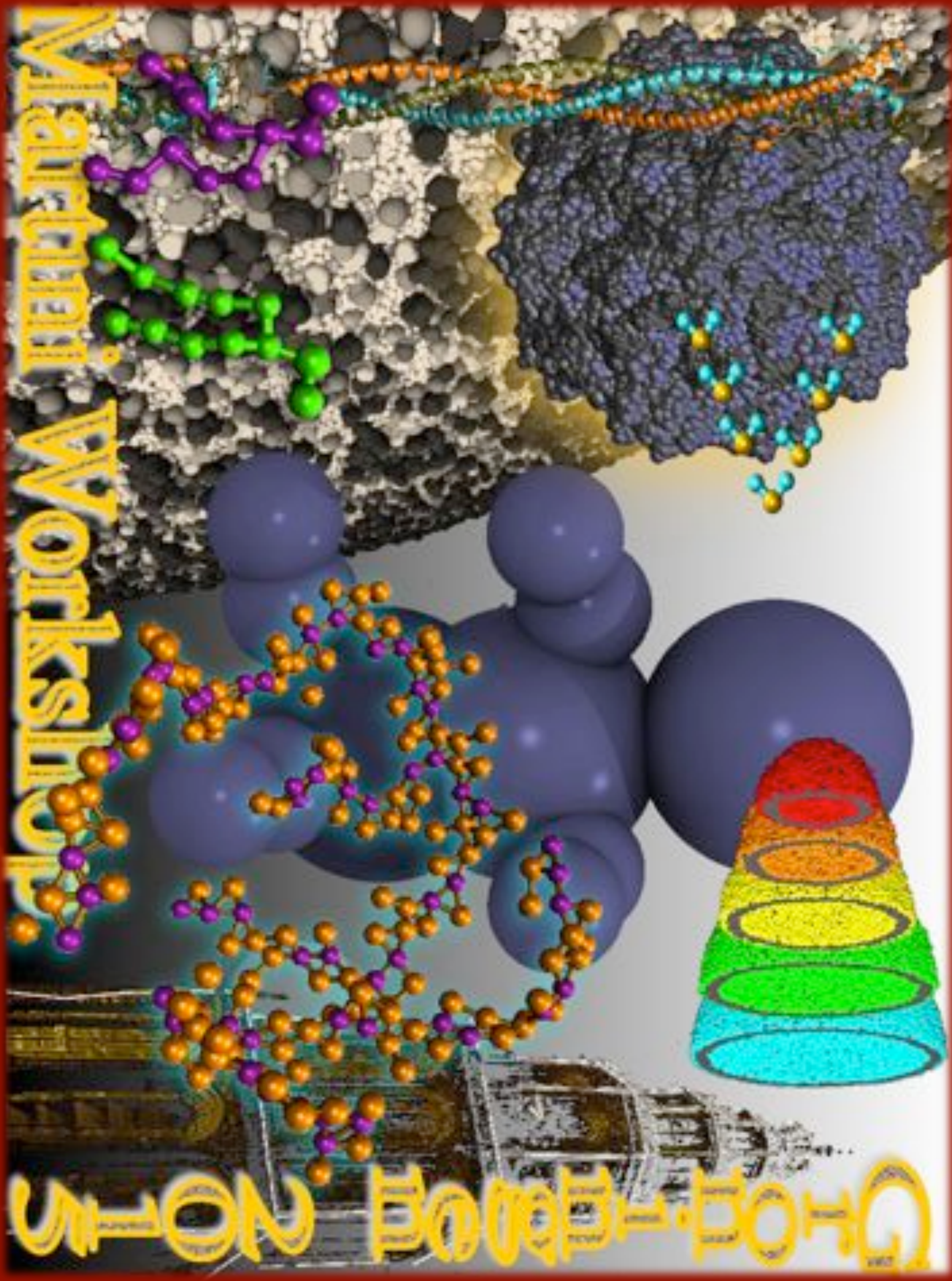
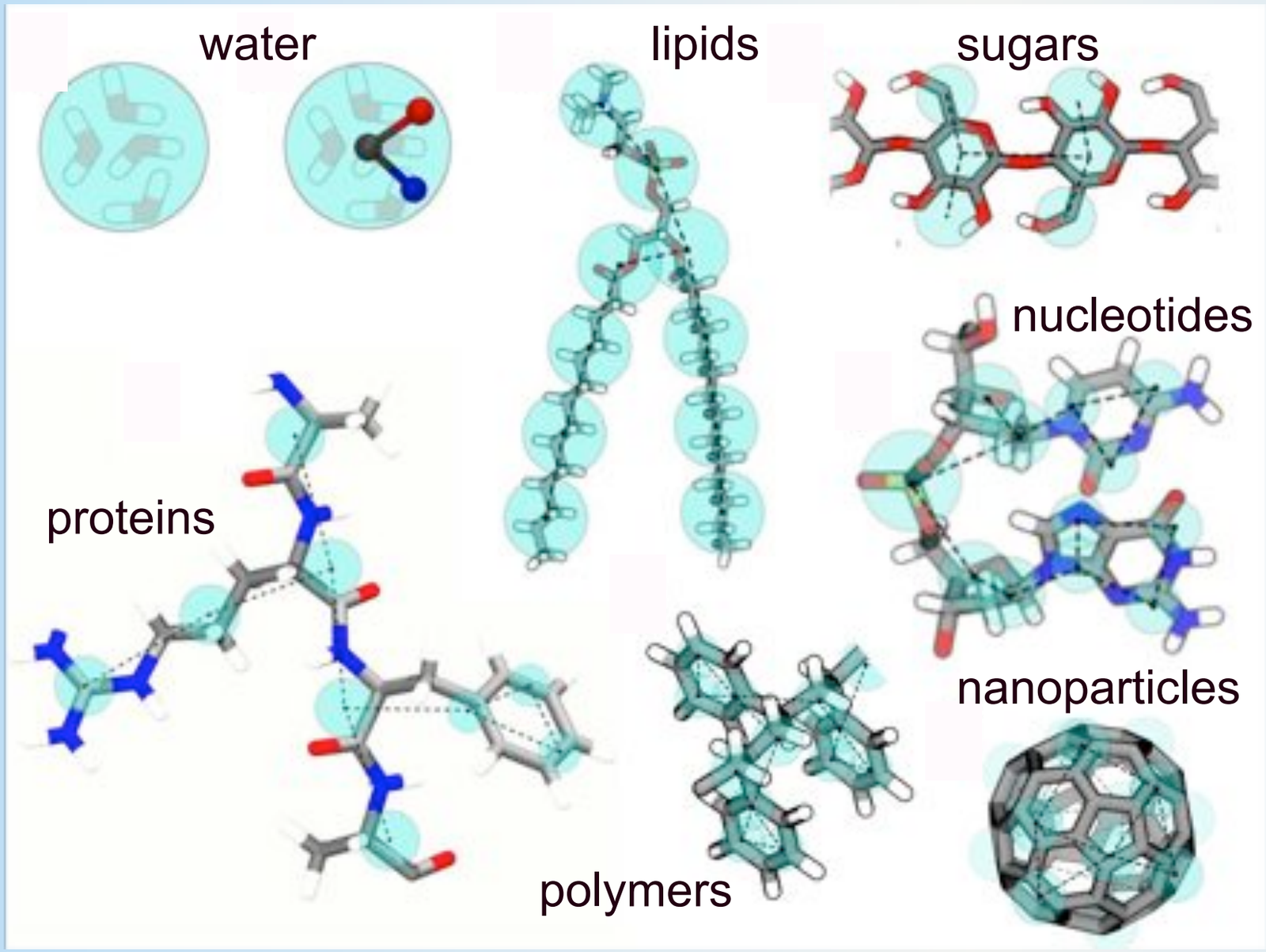

Advanced Topics
Van der Waals Bonding

Looks of the Martini model

Welcome to the Martini zoo!



Key features:

- Chemical specificity
- Fast (10^3 speed-up)
- Compatibility
(building block approach)
- Versatility

Parameterization:

TOP DOWN
Thermodynamic data
BOTTUM UP
Atomistic simulations

SJ Marrink & DP Tieleman, *Chem. Soc. Rev*. (2013)

Overview of this lecture
"Martini Extensions"

- **Sweet Martini**
  Mono-, Di-, and Oligo-saccharides
- **Covering all the bases**
  DNA, RNA
- **Nanoparticle mania**
  Fullerene, CNTs, Graphene, Gold
- **Dry Martini**

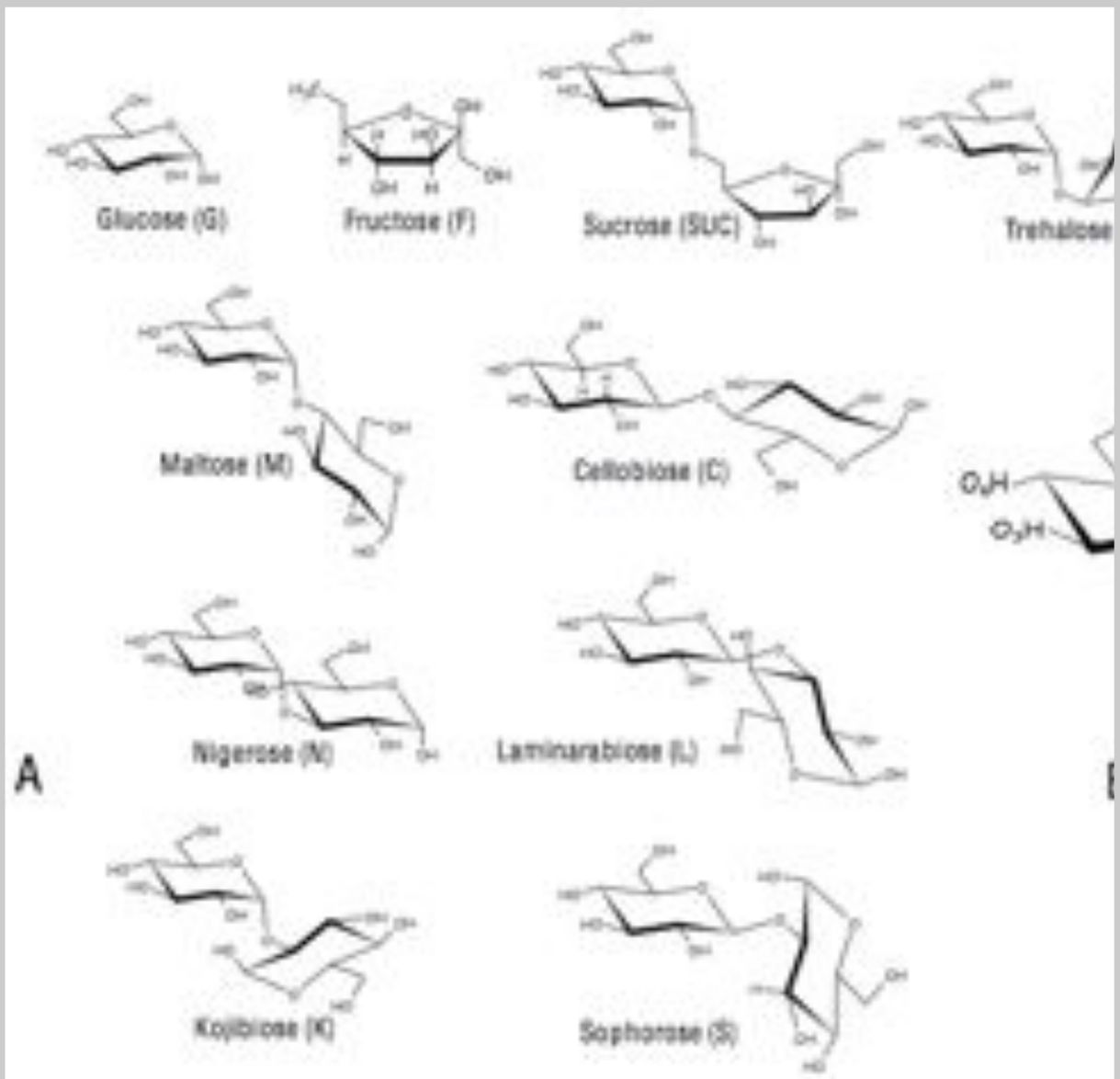
Sweet MARTINI

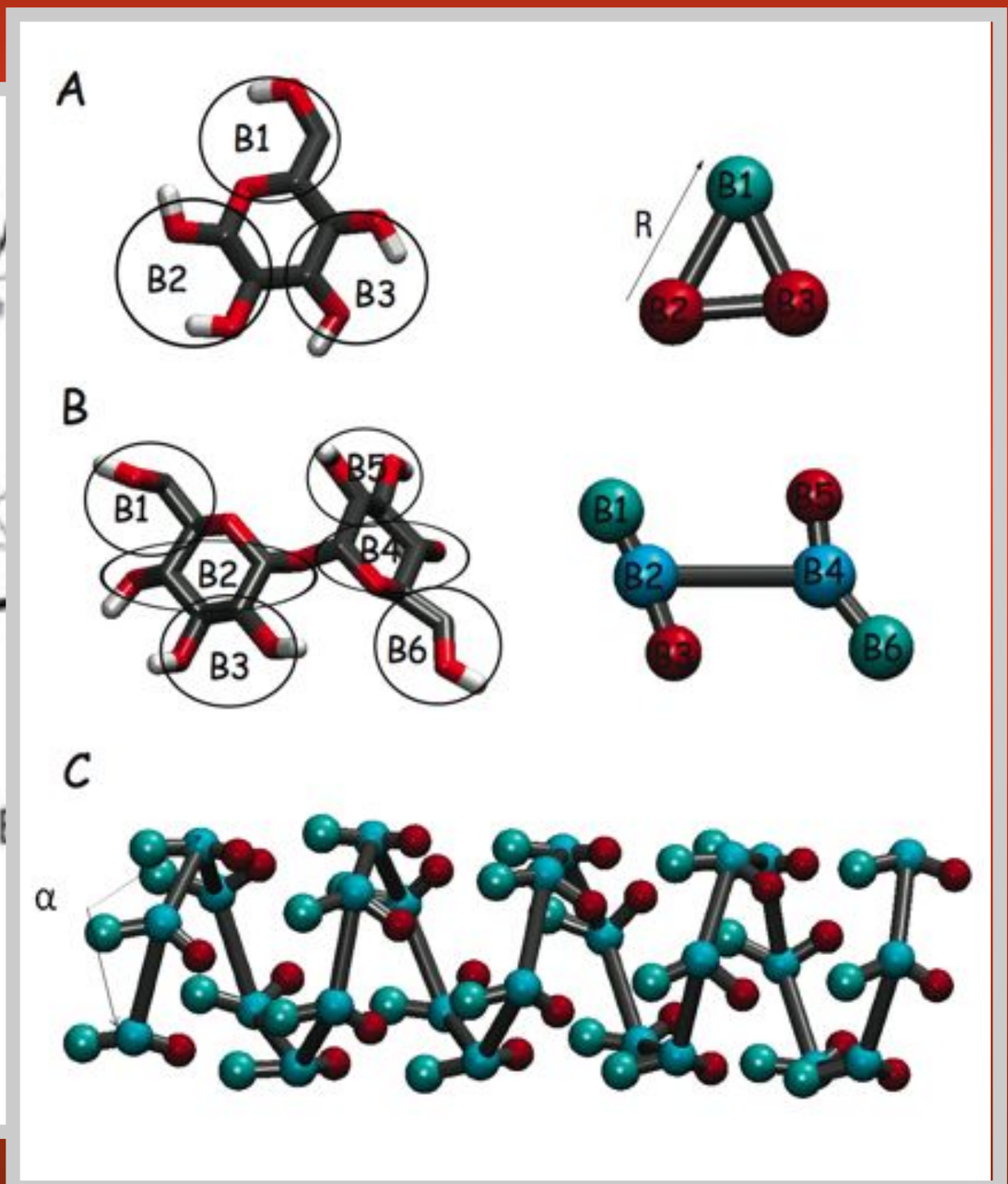
extension of Martini force field to carbohydrates

Lopez et al, JCTC, 2009

Sweet MARTINI

Choosing the mapping





Sweet MARTINI

Parameterization of non-bonded interactions

Type	Building Block	Examples	ΔG^{oct} Exp	CG	ΔG^{hyd} Exp	CG	ΔG^{part}_{HW} Exp	CG	ΔG^{part}_{OW} Exp	CG	ΔG^{part}_{EW} Exp	CG	ΔG^{part}_{OW} Exp	CG
Q_{da}	H_3N^+-C_2-OH	Ethanolamine (protonated)				-25		<-30		-18		-13		-18
Q_d	H_3N^+-C_3	1-Propylamine (protonated)				-25		<-30		-18		-13		-18
	NA^+ OH	Sodium (hydrated)				-25		<-30		-18		-13		-18
Q_a	PO_4^-	Phosphate				-25		<-30		-18		-13		-18
	CL^- HO	Chloride (hydrated)				-25		<-30		-18		-13		-18
Q_0	C_3N^+	Choline				-25		<-30		-18		-13		-18
P_5	H_2N-C_2=O	Acetamide	sol	sol	-40	-25	-27	-28	(-20)	-18	-15	-13	-8	-10
P_4	HOH (×4)	Water	-27	-18	-27	-18	-25	-23		-14	-10	-7	-8	-9
	HO-C_2-OH	Ethanediol	-35	-18	-33	-18	-21	-23		-14		-7	-8	-9
P_3	HO-C_2=O	Aceticacid	-31	-18	-29	-18	-19	-21	-9	-10	-2	-6	-1	-3
	C-NH-C=O	Methylformamide	-35	-18		-18		-21		-10		-6	-5	-7
P_2	C_2-OH	Ethanol	-22	-16	-21	-14	-13	-17	-5	-2	-3	1	-2	-2
P_1	C_3-OH	1-Propanol	-23	-16	-21	-14	-9	-11	-2	-2	0	1	1	-1
		2-Propanol	-22	-16	-20	-14	-10	-11	-2	-2	-1	1	0	-1
N_{da}	C_4-OH													
N_d	H_2N-C_3													
N_a	C_3=O													
	C-NO_2													
	C_3=N													
	C-O-C=O													
	C_2HC=O													
N_0	O-C_2													
C_5														
C_4														
C_3														
C_2	C_3													
C_1	C_4													

P_5	H_2N-C_2=O	Acetamide
P_4	HOH (×4)	Water
	HO-C_2-OH	Ethanediol
P_3	HO-C_2=O	Aceticacid
	C-NH-C=O	Methylformamide
P_2	C_2-OH	Ethanol
P_1	C_3-OH	1-Propanol
		2-Propanol

Prayer book of revelations, psalm 69

Sweet MARTINI

Particle types

molecule	B1	B2	B3	B4	B5	B6
glucose (G)	P1	P4	P4			
fructose (F)	P1	P3	P4			
sucrose (SUC)	P1	P2	P4	P1	P1	P4
maltose (M)	P1	P2	P4	P2	P1	P4
cellobiose (C)	P1	P2	P4	P2	P1	P4
kojibiose (K)	P1	P2	P4	P2	P4	P1
sophorose (S)	P1	P2	P4	P2	P4	P1
nigerose (N)	P1	P2	P4	P2	P4	P1
laminarabiose (L)	P1	P2	P4	P2	P4	P1
trehalose (T)	P1	P2	P4	P2	P1	P4

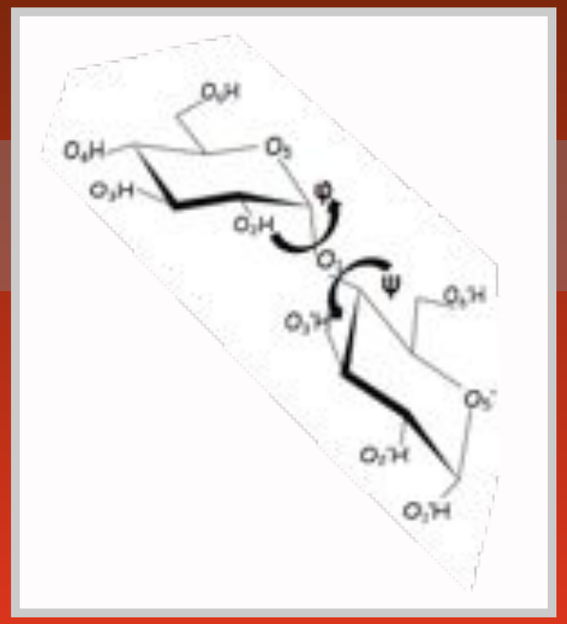
Sweet MARTINI

Testing: partitioning free energy

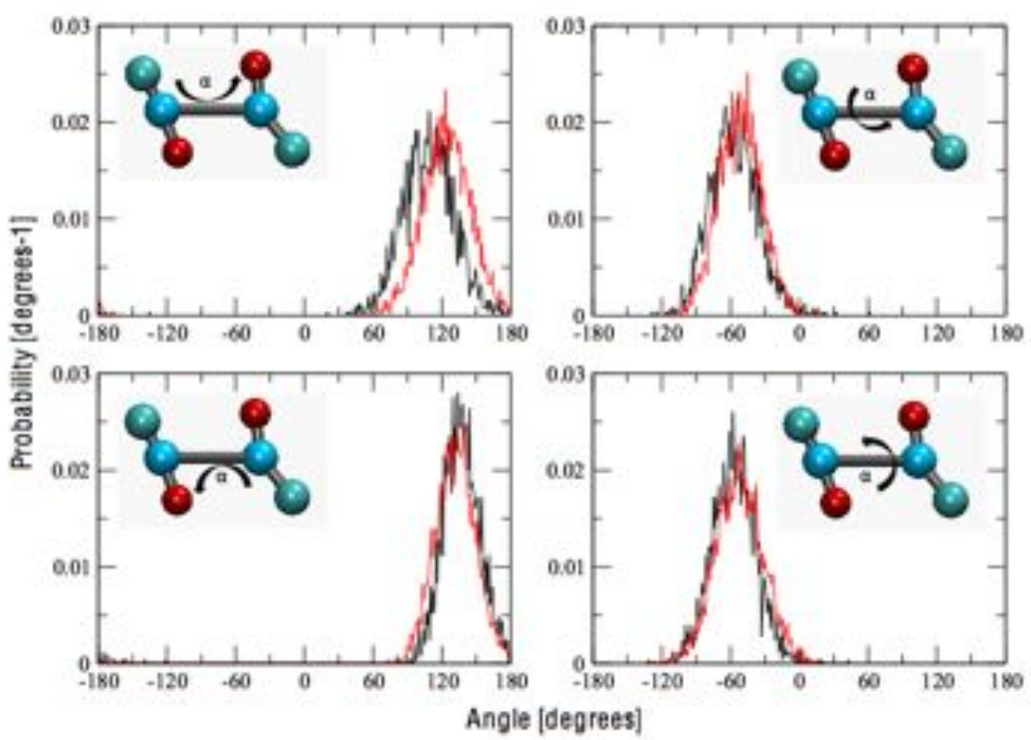
	All-atom (Gromos)				Martini			
molecule	ΔG^{w} (AA) (kJ mol^{-1})	ΔG^{o} (AA) (kJ mol^{-1})	$\Delta\Delta G_{ow}$ (AA) (kJ mol^{-1})	log P_{ow}(AA)	ΔG^{w} (CG) (kJ mol^{-1})	ΔG^{o} (CG) (kJ mol^{-1})	$\Delta\Delta G_{ow}$ (CG) (kJ mol^{-1})	log P_{ow}(CG)	log P_{ow} (exp)
glucose (G)	−89	−74	15	−2.5	−60	−43	17	−2.9	−2.8
fructose (F)	−80	−69	11	−2.0	−60	−44	16	−2.7	
sucrose (SUC)	−107	−89	18	−3.0	−103	−83	20	−3.4	−3.3
maltose (M)	−121	−96	25	−4.2	−120	−96	24	−4.0	
cellobiose (C)	−114	−90	24	−4.0	−120	−96	24	−4.0	
kojibiose (K)	−121	−93	28	−4.7	−120	−96	24	−4.0	
sophorose (S)	−120	−88	32	−5.4	−120	−96	24	−4.0	
nigerose (N)	−119	−89	30	−5.0	−120	−96	24	−4.0	
laminarabiose (L)	−120	−91	29	−5.0	−120	−96	24	−4.0	
trehalose (T)	−120	−92	28	−5.0	−120	−96	24	−4.0	−3.78

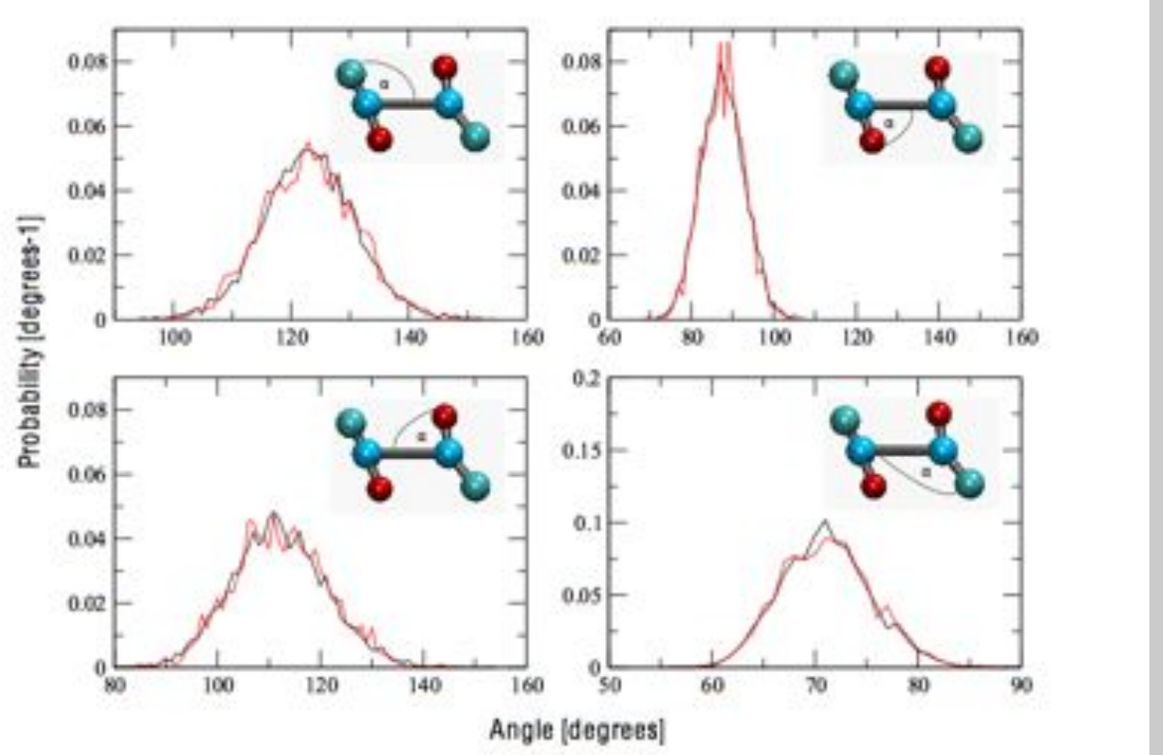
Sweet MARTINI

Parameterization of bonded interactions



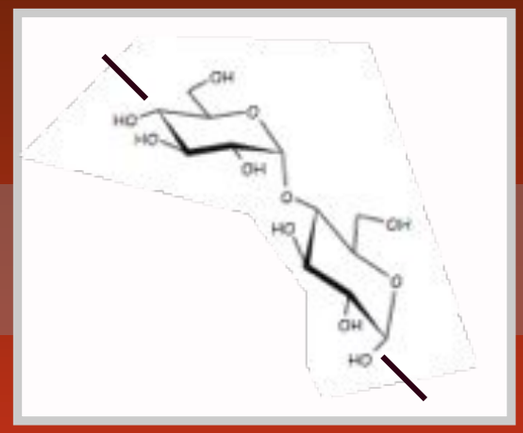
- o Angles and dihedrals should account for rotameric states
- o Bonded parameters fitted to mapped atomistic simulations
- o Most distributions unimodal, except for 1-6 linked sugars



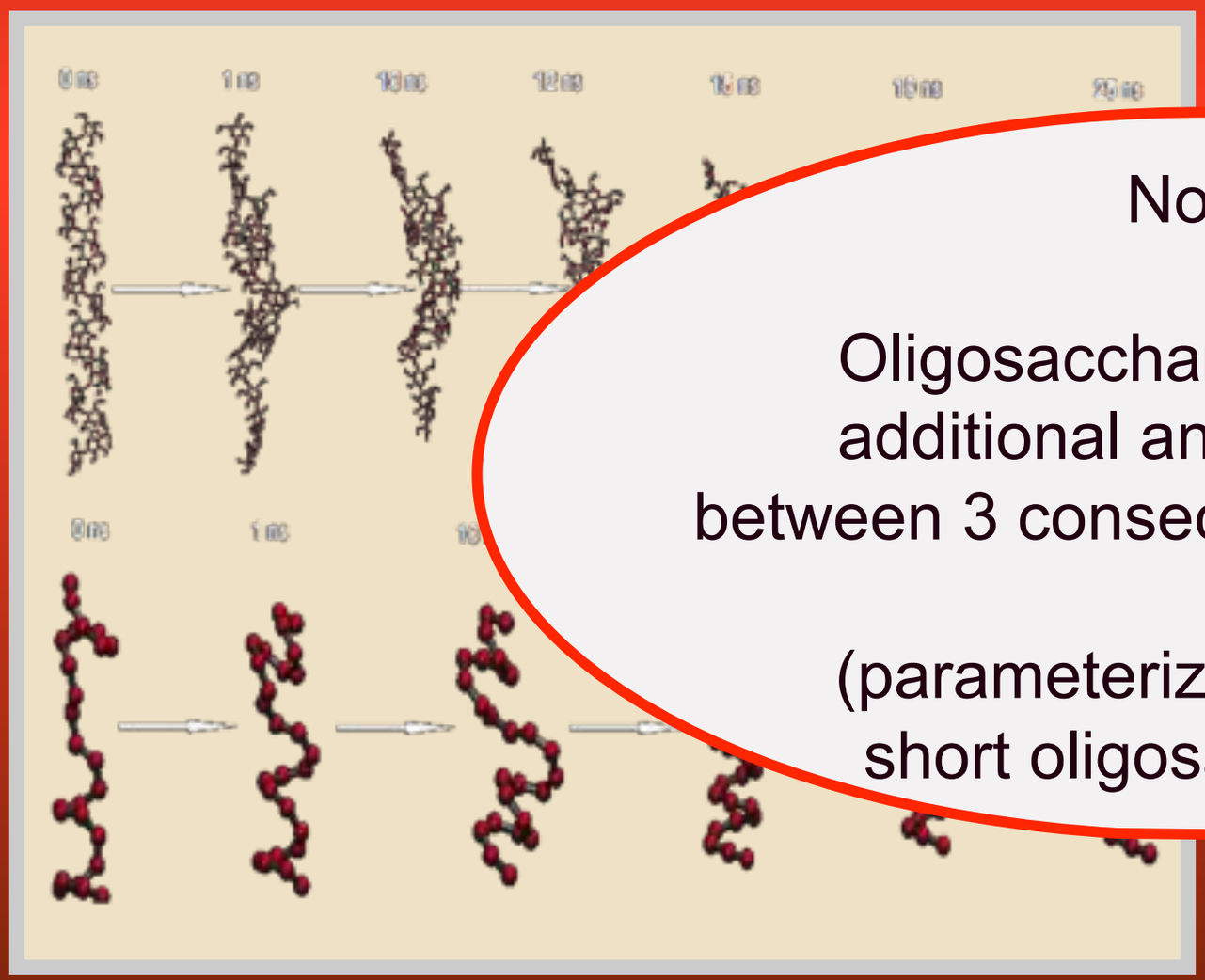


Sweet MARTINI

Testing on oligosaccharides: amylose



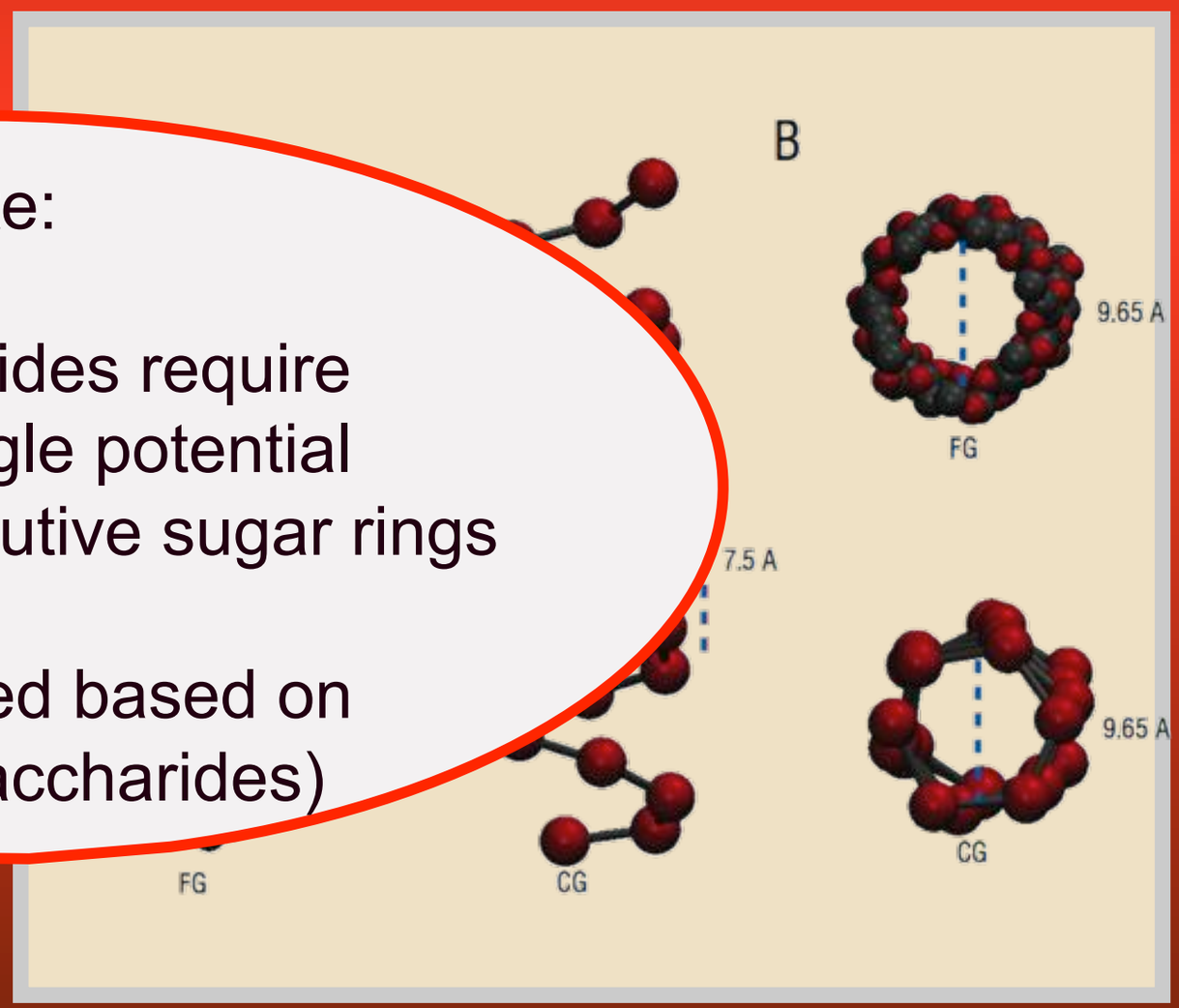
o Amylose is 1-4 linked glucose oligosaccharide (principal component of starch)
o Amylose in apolar solvents forms helical structure (V-amylose)
o Pitch length around 7-8 Angstrom (6-8 sugars)



Note:

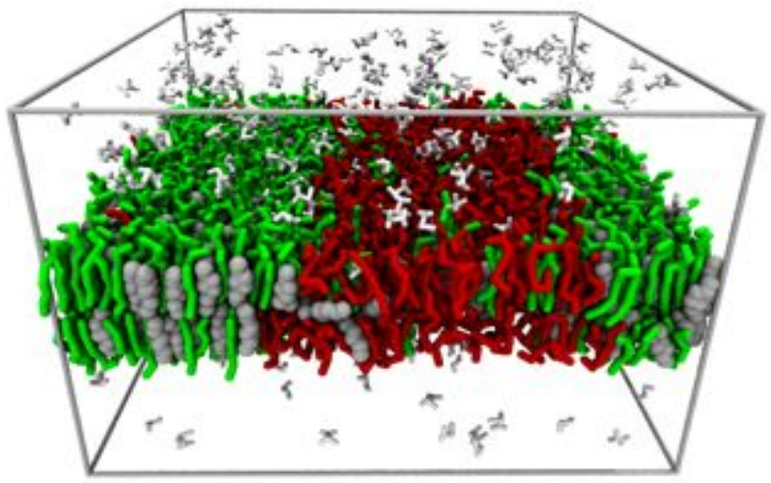
Oligosaccharides require
additional angle potential
between 3 consecutive sugar rings

(parameterized based on
short oligosaccharides)

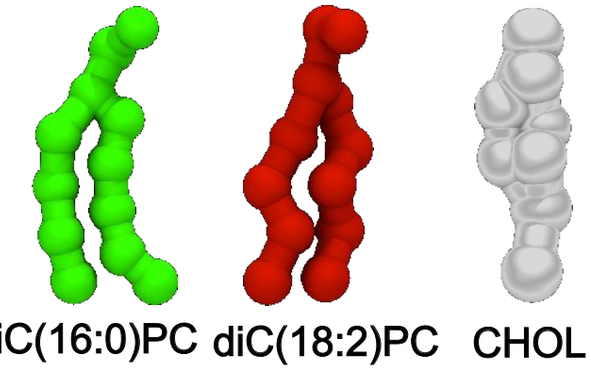


Sweet MARTINI

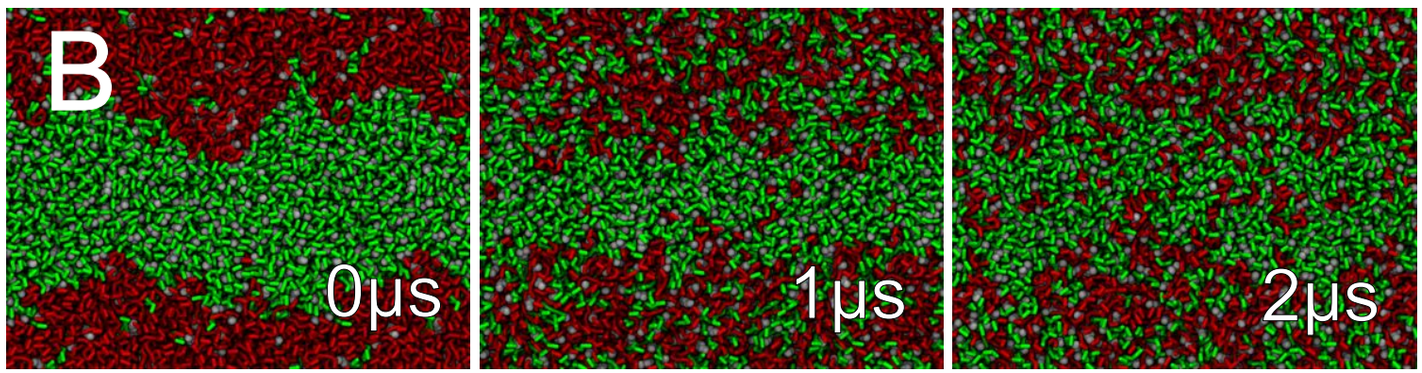
Application: sugar-induced mixing of membrane domains

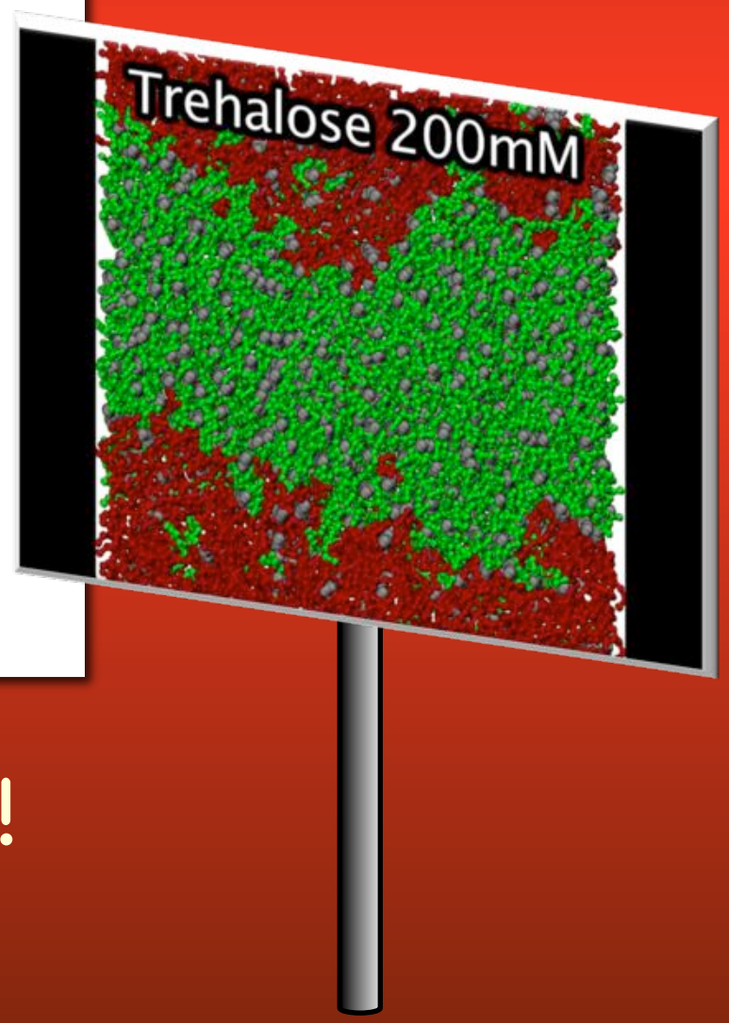


200 mM trehalose



diC(16:0)PC diC(18:2)PC CHOL





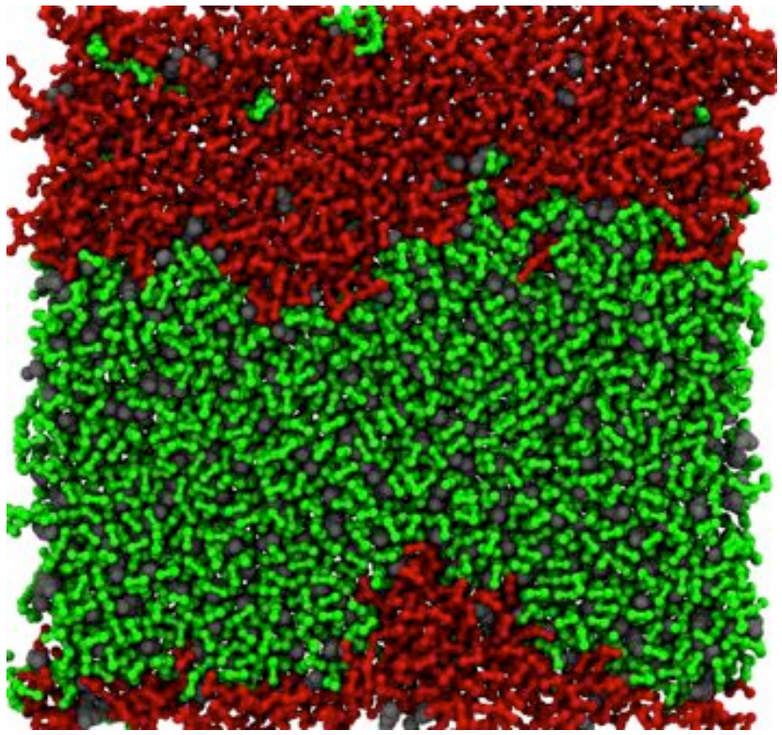
→ Domains destroyed by sugars !!

Moiset et al, JACS, 2014

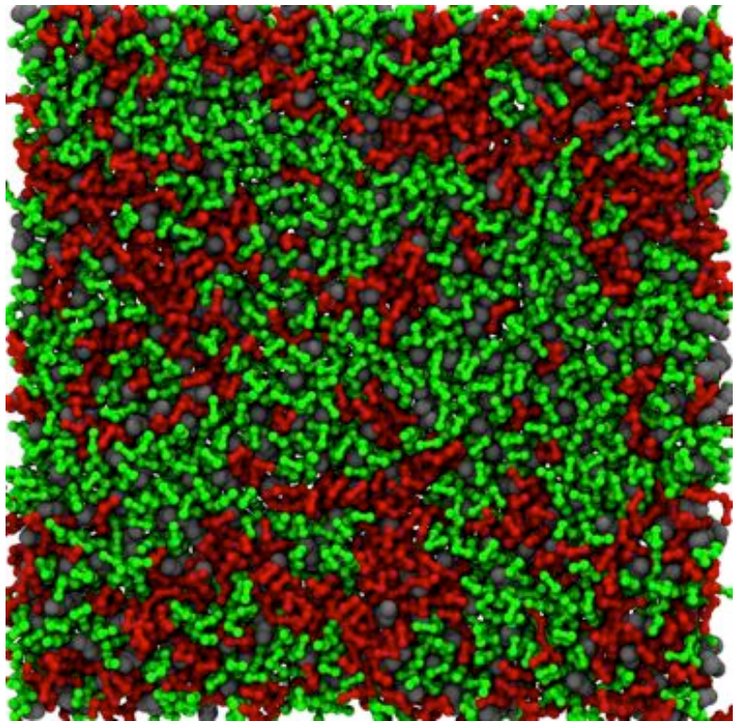
Sweet MARTINI

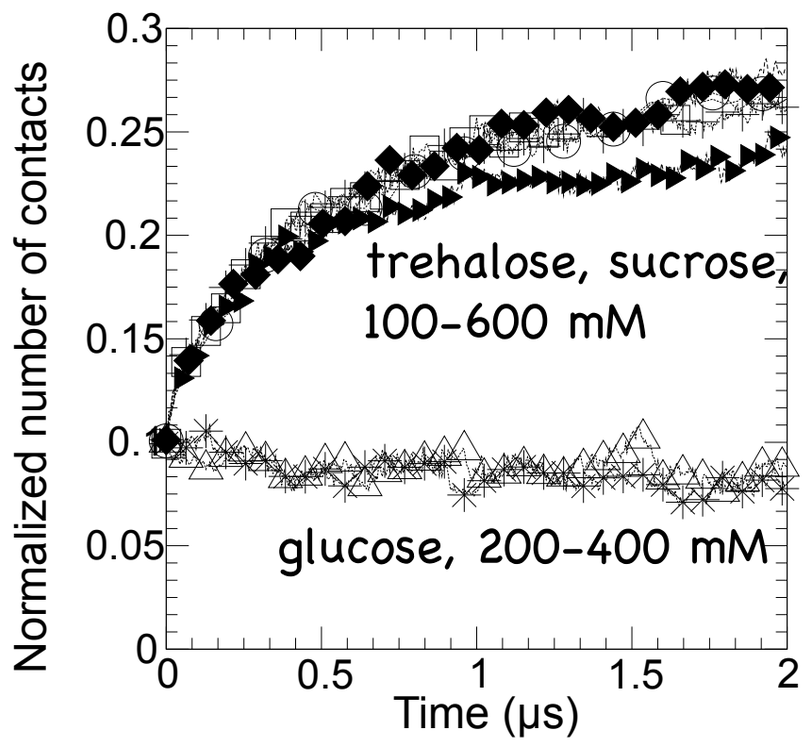
Application: sugar-induced mixing of membrane domains

200 mM glucose



200 mM trehalose



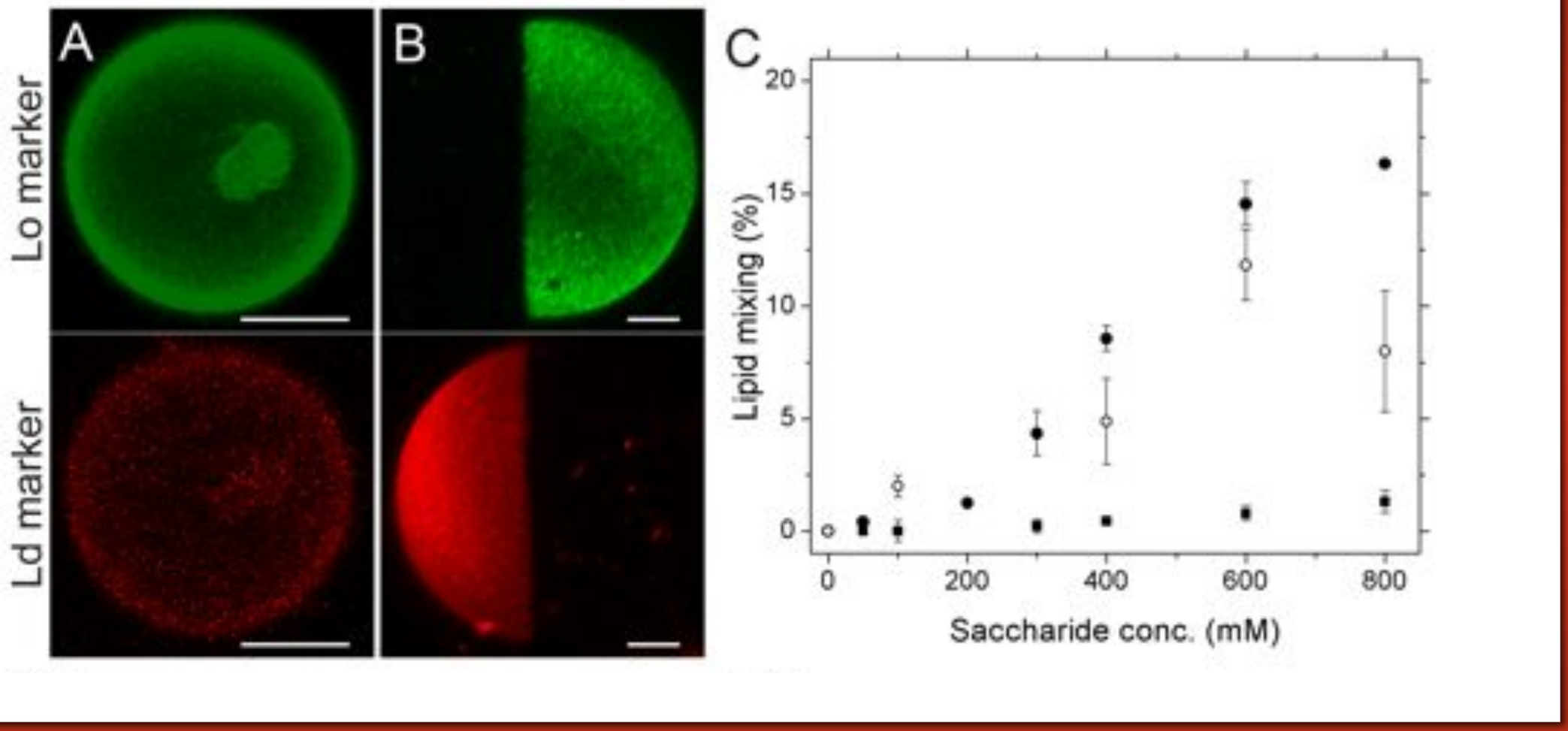


→ Domains destroyed by disaccharides, monosaccharides have no effect

Moiset et al, JACS, 2014

Sweet MARTINI

Application: sugar-induced mixing of membrane domains



→ Experiments confirm in-silico predictions
(or: Experimental set-up validated by computational microscopy)

Moiset et al, JACS, 2014

Covering all the bases

Coarse-grain Martini model of DNA

Parameters for both single-stranded and double-stranded DNA

Compatible with all other Martini models

Extension to RNA in progress

Uusitalo et al., JCTC, 2015

Covering all the bases: DNA

Mapping of DNA

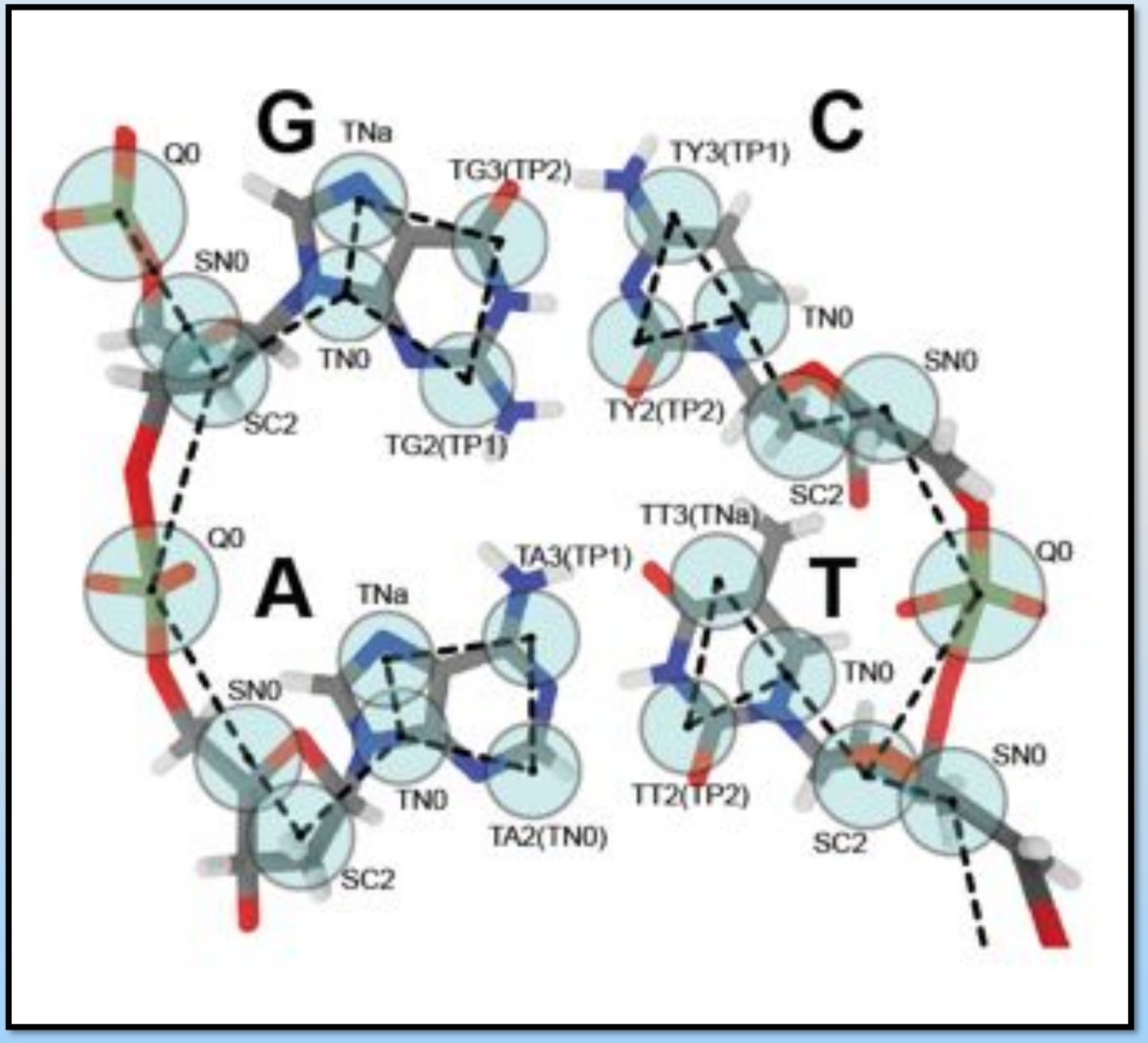
6-7 beads per nucleotide

adenine (A), guanine (G)
4 beads

cytosine (C), thymine (T)
3 beads

phosphate
1 bead

sugar
2 beads



Covering all the bases: DNA

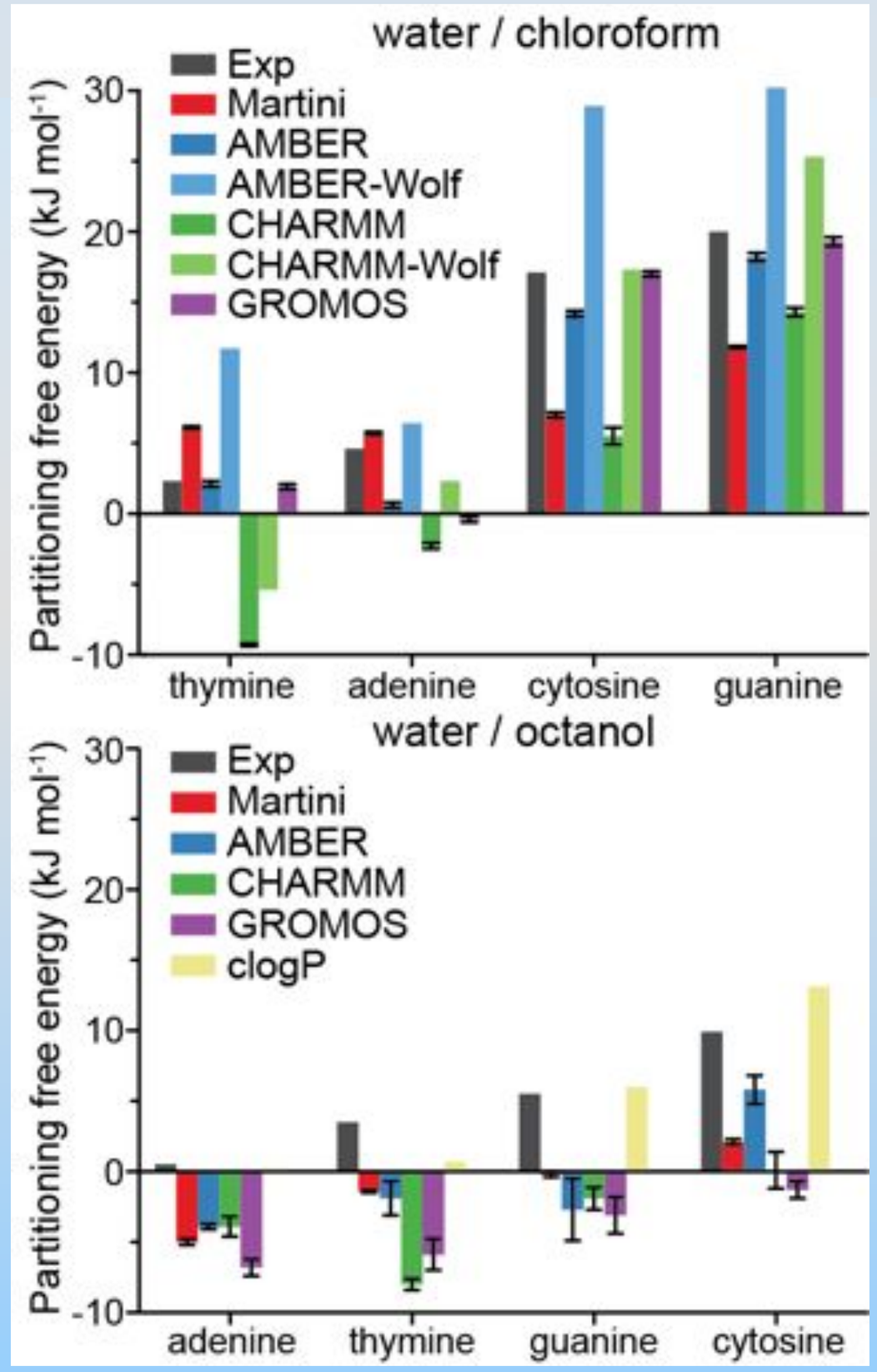
Particle types

Building blocks selected
to match partitioning data

Large spread in
data for all-atom models

Guanine/cytosine
more hydrophilic
than adenine/thymine

Standard particle
types can be used



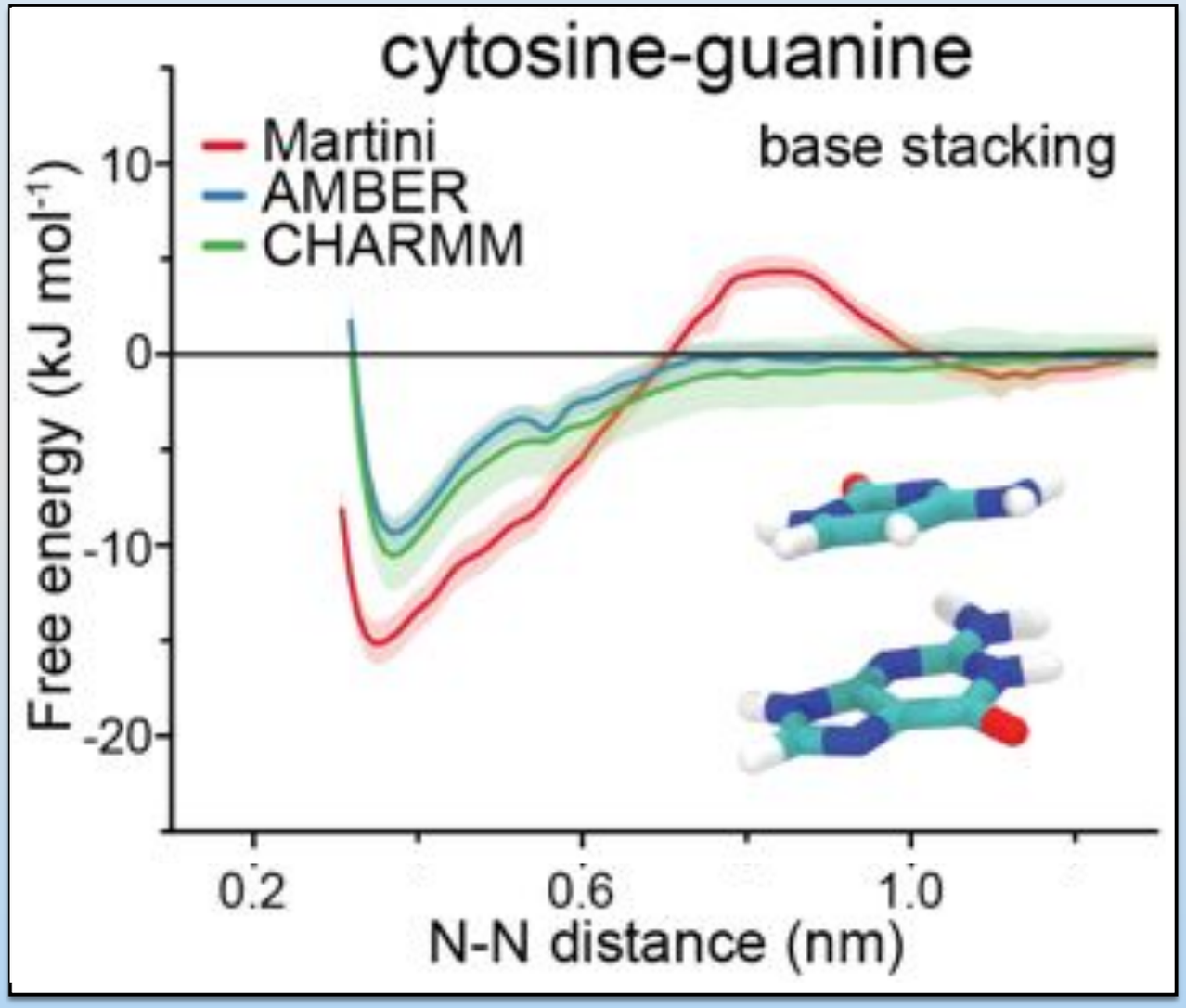
Covering all the bases: DNA

Particle types

<u>Special interactions</u>

Base-base interactions shorter range than rest of Martini

- *"T" particles*



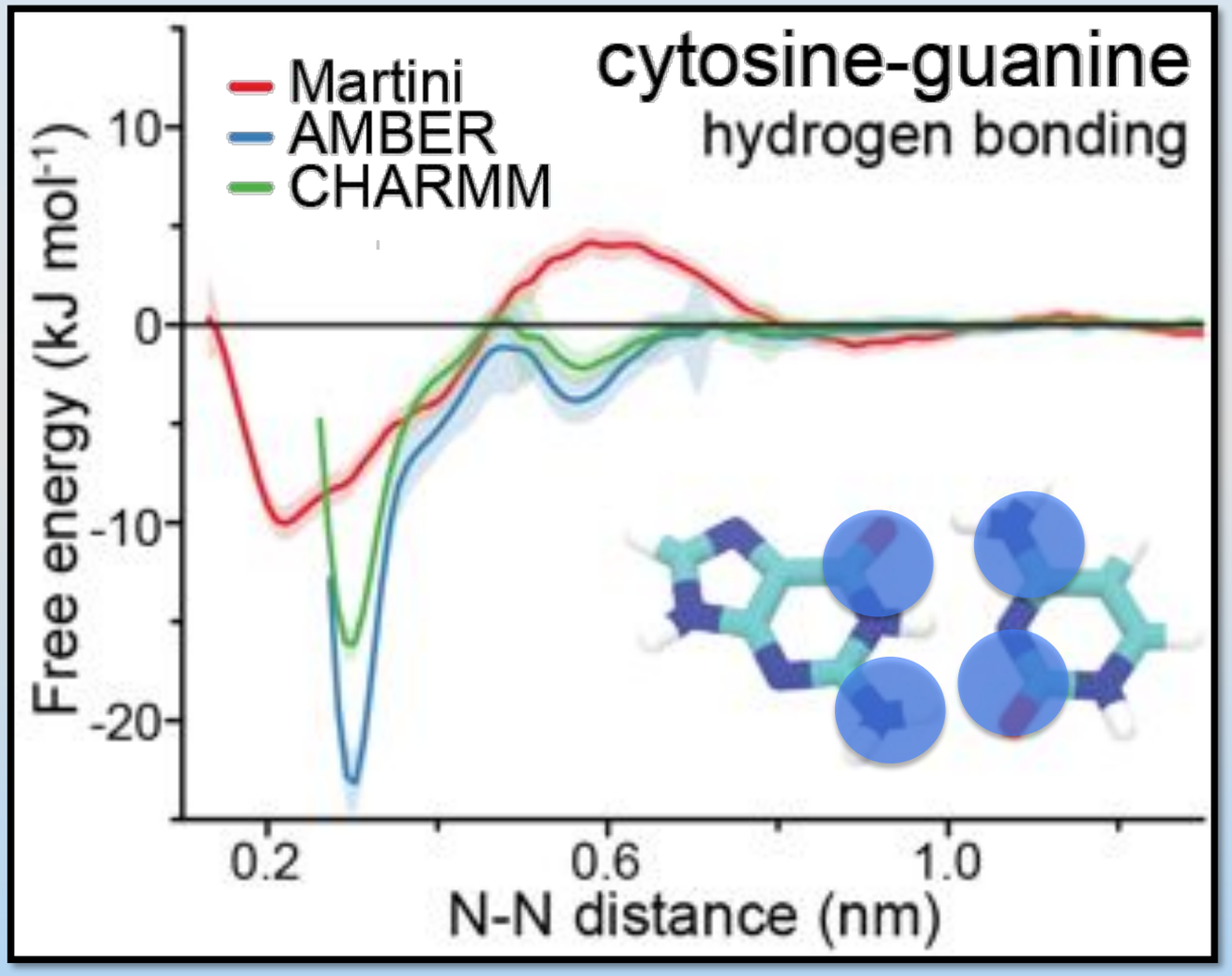
T(iny) particles interact with each other using a reduced σ=0.32 nm but have S type interactions with all other particles

Covering all the bases: DNA

Particle types

<u>Special interactions</u>

Hydrogen bonding mimicked with specific pair interactions



We use special bead types for the hydrogen bonding particles, adding eight special beads that are meant solely for this purpose.
These beads interact with all other bead types based on their underlying chemical group

Covering all the bases: DNA

Particle types

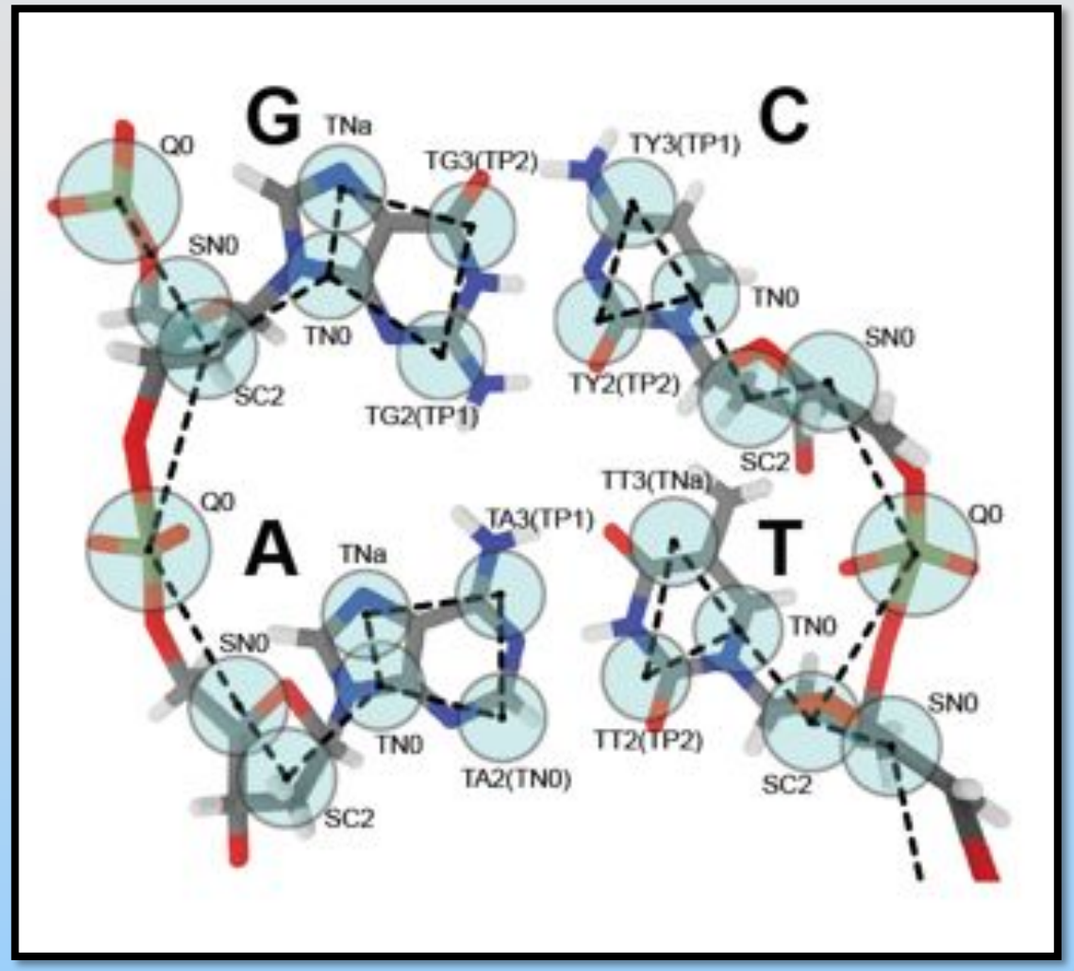
Relative strength of h-bonding between bases reproduced

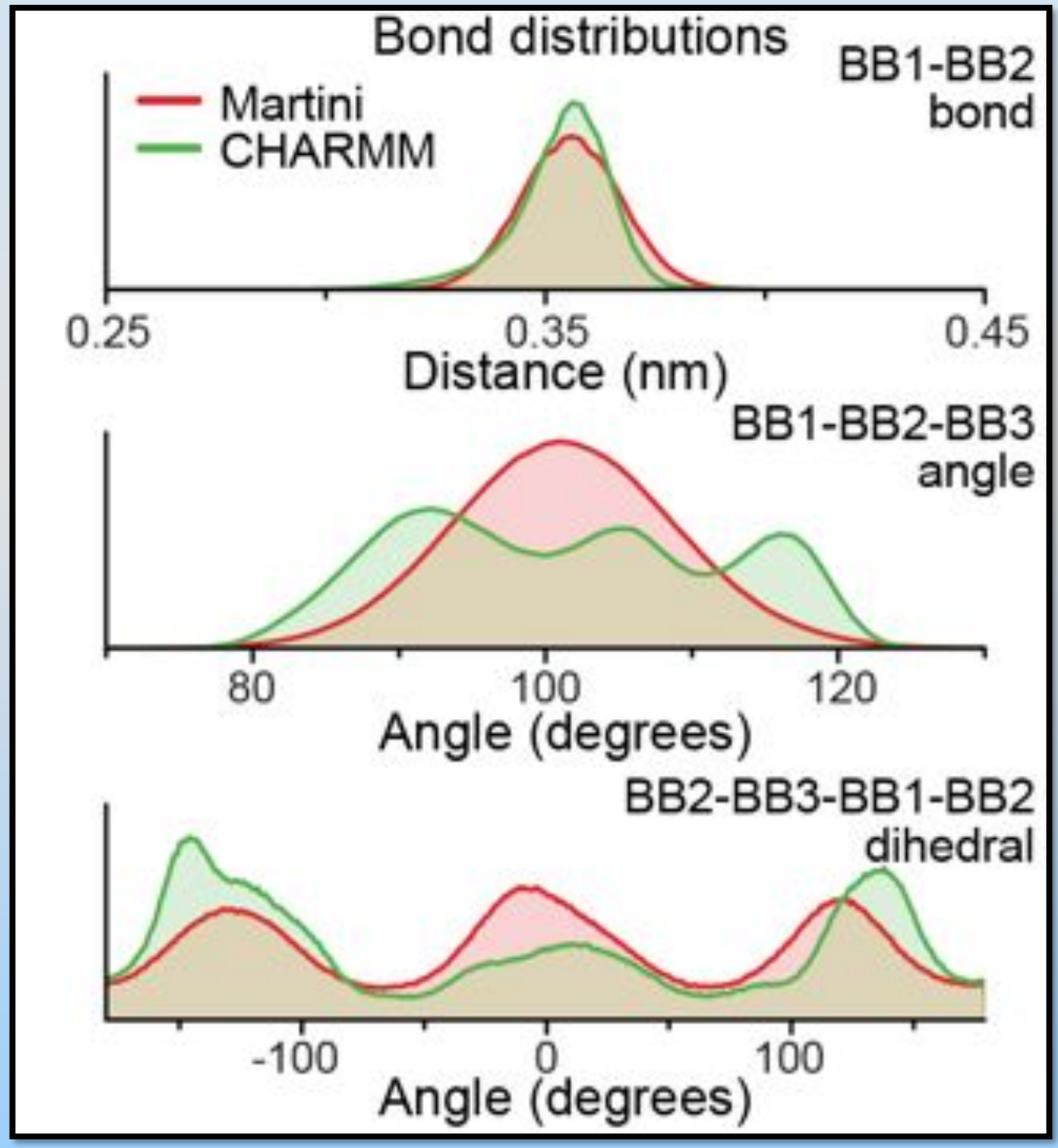
	AMBER	CHARMM	Martini
base pair	ΔG (kJ mol^{-1})	ΔG (kJ mol^{-1})	ΔG (kJ mol^{-1})
C-G	-22.6 ± 1.6	-16.5 ± 1.3	-10.0 ± 1.0
A-T	-15.8 ± 0.8	-13.6 ± 0.2	-9.8 ± 1.5
C-T	-11.3 ± 1.2	-11.8 ± 0.3	-9.2 ± 0.8
T-T	-9.4 ± 0.6	-6.5 ± 0.2	-8.7 ± 1.0
A-G	-8.8 ± 1.0	-9.6 ± 0.7	-8.3 ± 0.8
G-T	-7.8 ± 1.0	-5.2 ± 0.2	-6.2 ± 1.0
A-A	-4.6 ± 0.6	-5.8 ± 0.7	-5.6 ± 1.0
A-C	-3.2 ± 0.8	-2.6 ± 0.8	-5.1 ± 1.0
C-C	-1.6 ± 1.5	-1.0 ± 1.2	-5.0 ± 1.0
G-G	3.7 ± 1.7	5.4 ± 0.3	-4.8 ± 0.5

Covering all the bases: DNA

Bonded interactions

<u>All-atom simulations of short ssDNAs used as target</u>

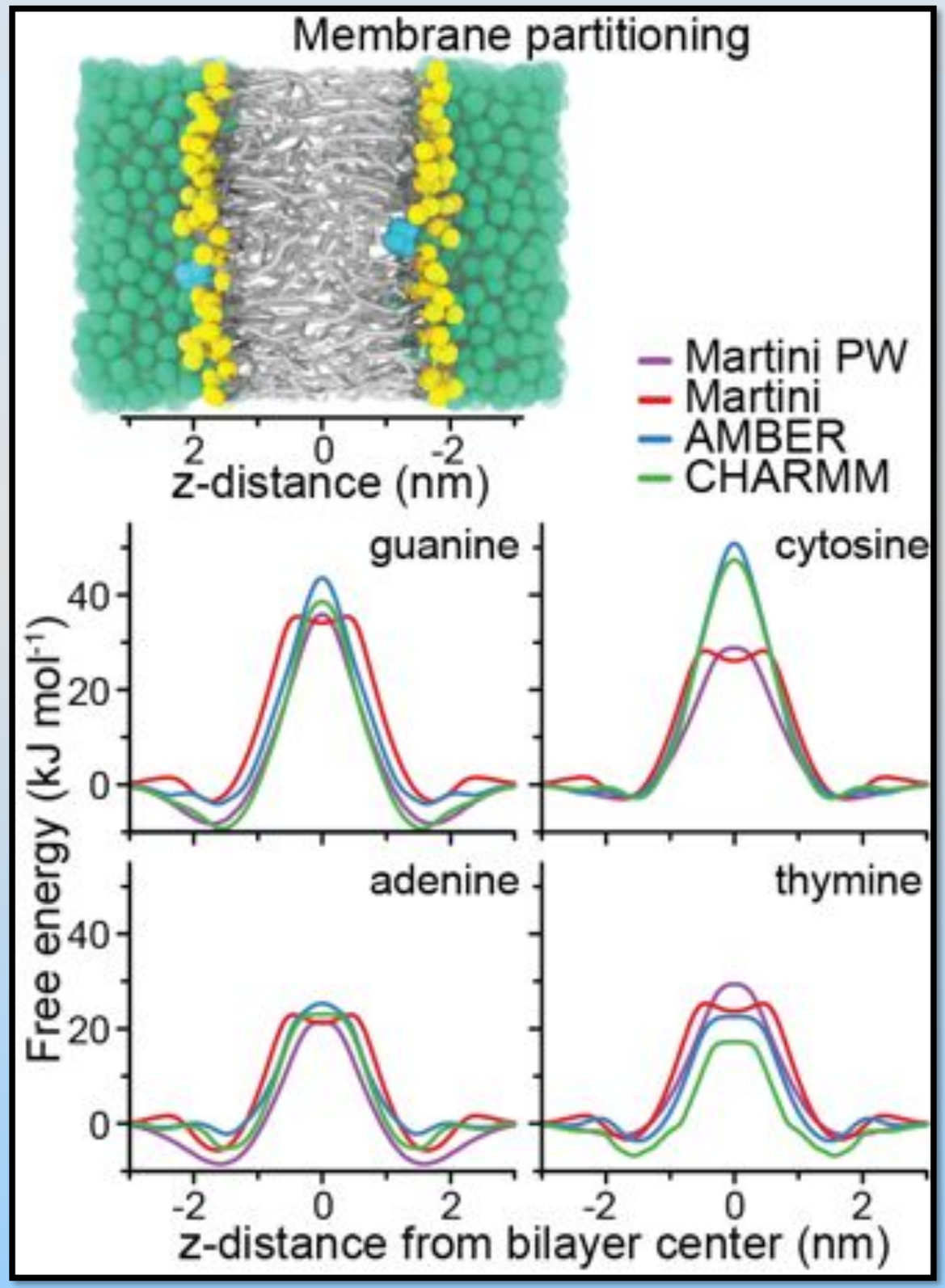




Covering all the bases: DNA

Validation of the basic DNA model

Partitioning of bases across membrane well reproduced

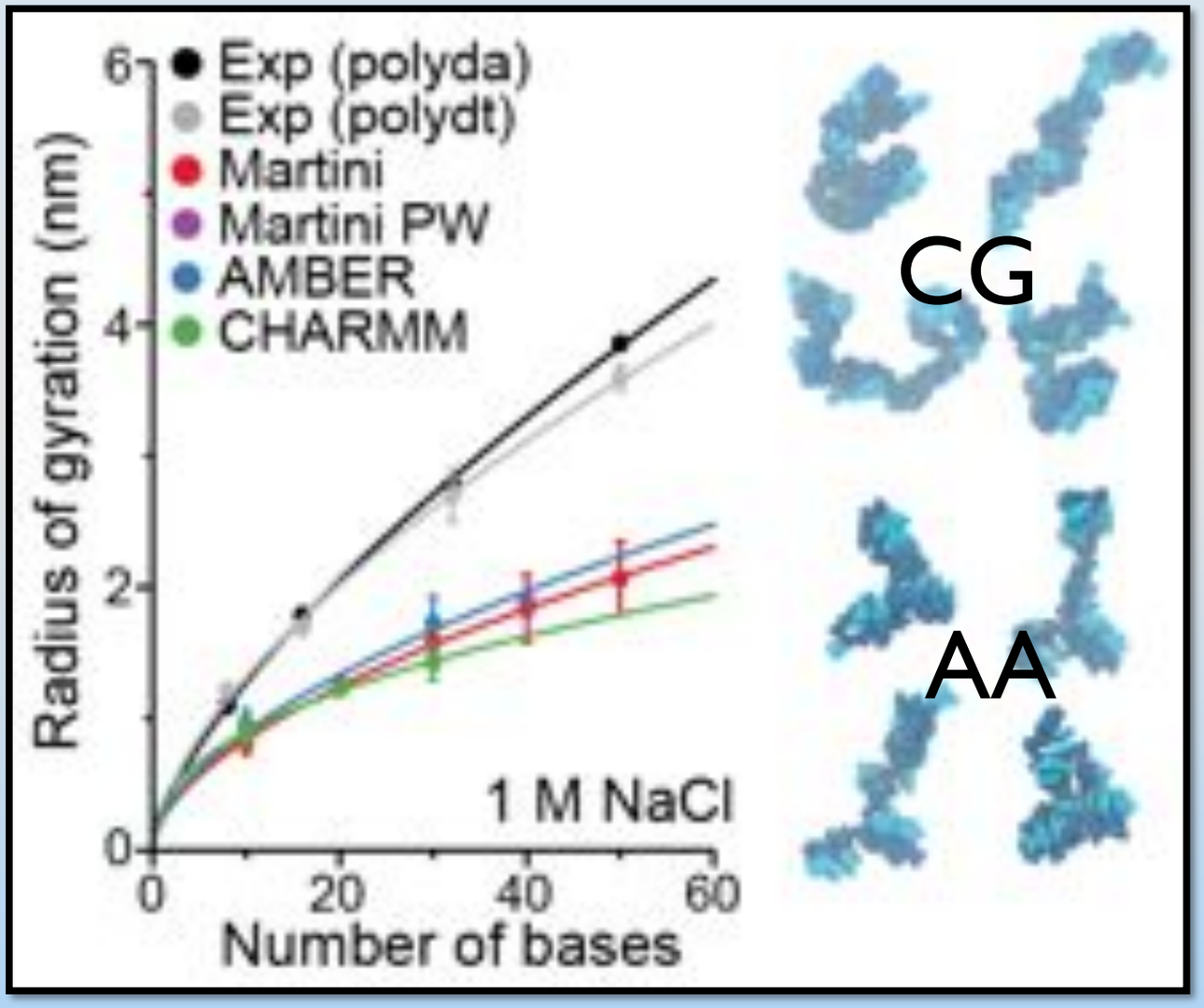


Covering all the bases: DNA

Validation of the basic DNA model

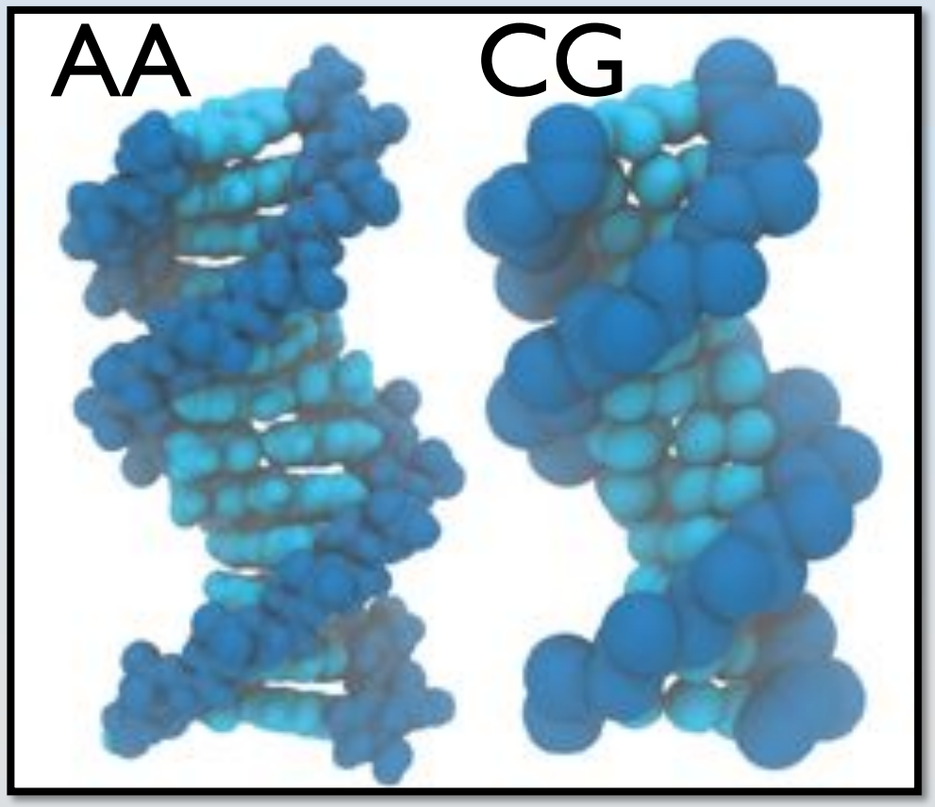
<u>Realistic radius of gyration for ssDNA</u>

(at least compared to all-atom models)



Covering all the bases: DNA

Double stranded DNA (dsDNA)

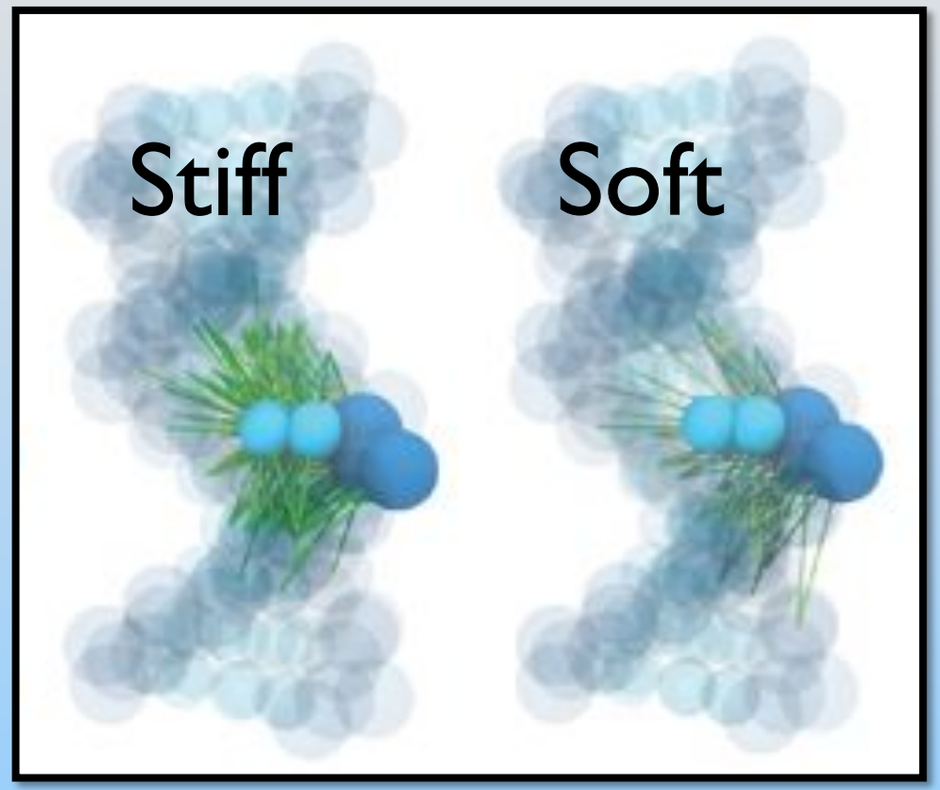


<u>dsDNA structurally similar to all-atom models</u>

<u>Stability, however, requires an elastic network</u>

Stiff:
For rigid DNA structures and short double strands, runs with larger time step

Soft:
More flexible strand and more freedom in movements of nucleobases, requires shorter time step

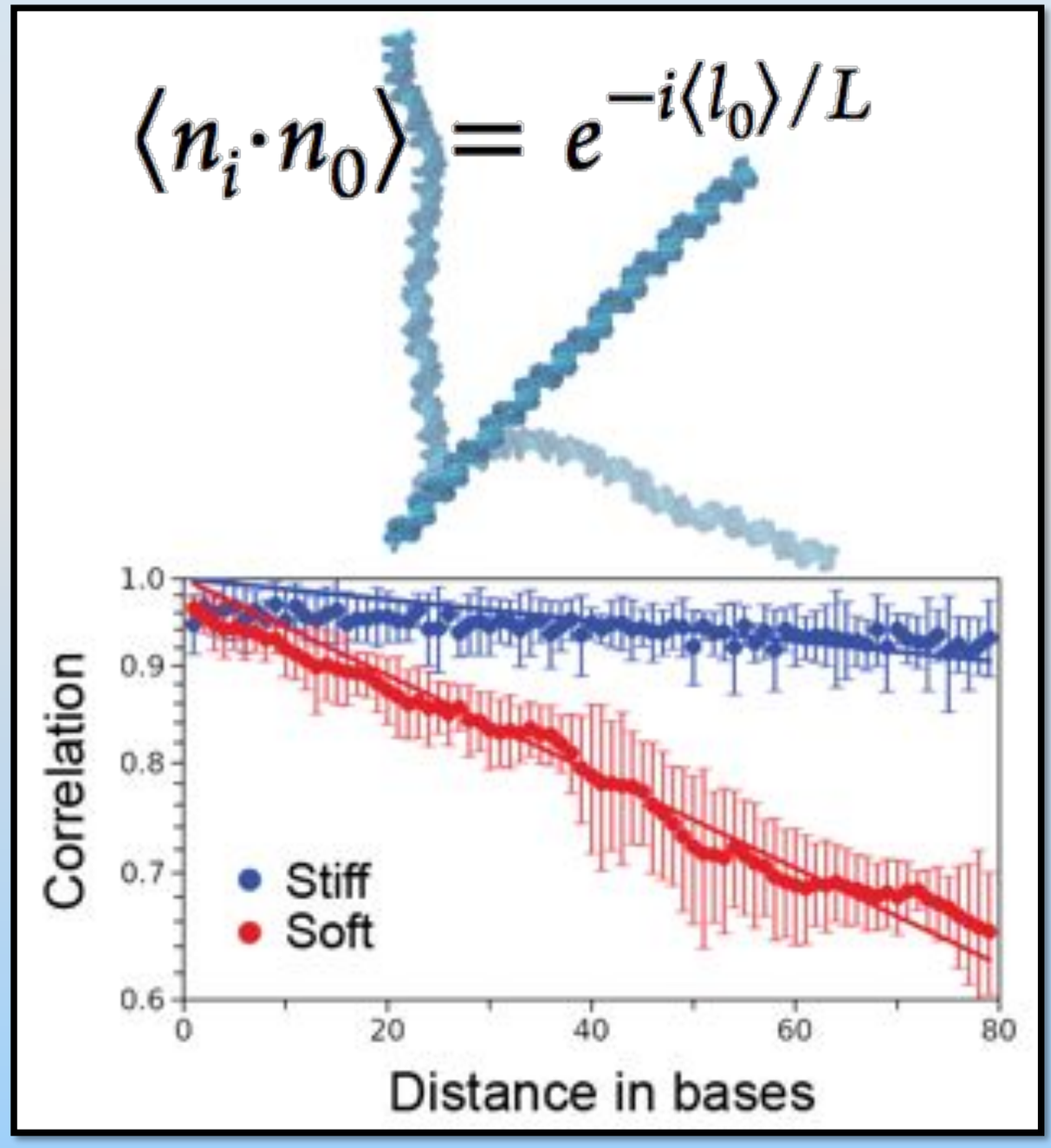


Covering all the bases: DNA

Validation of double stranded DNA

<u>Soft model has a realistic persistence length</u>

about L=60 nm in 100 mM salt (experimentally about L=50 nm)



Covering all the bases: DNA

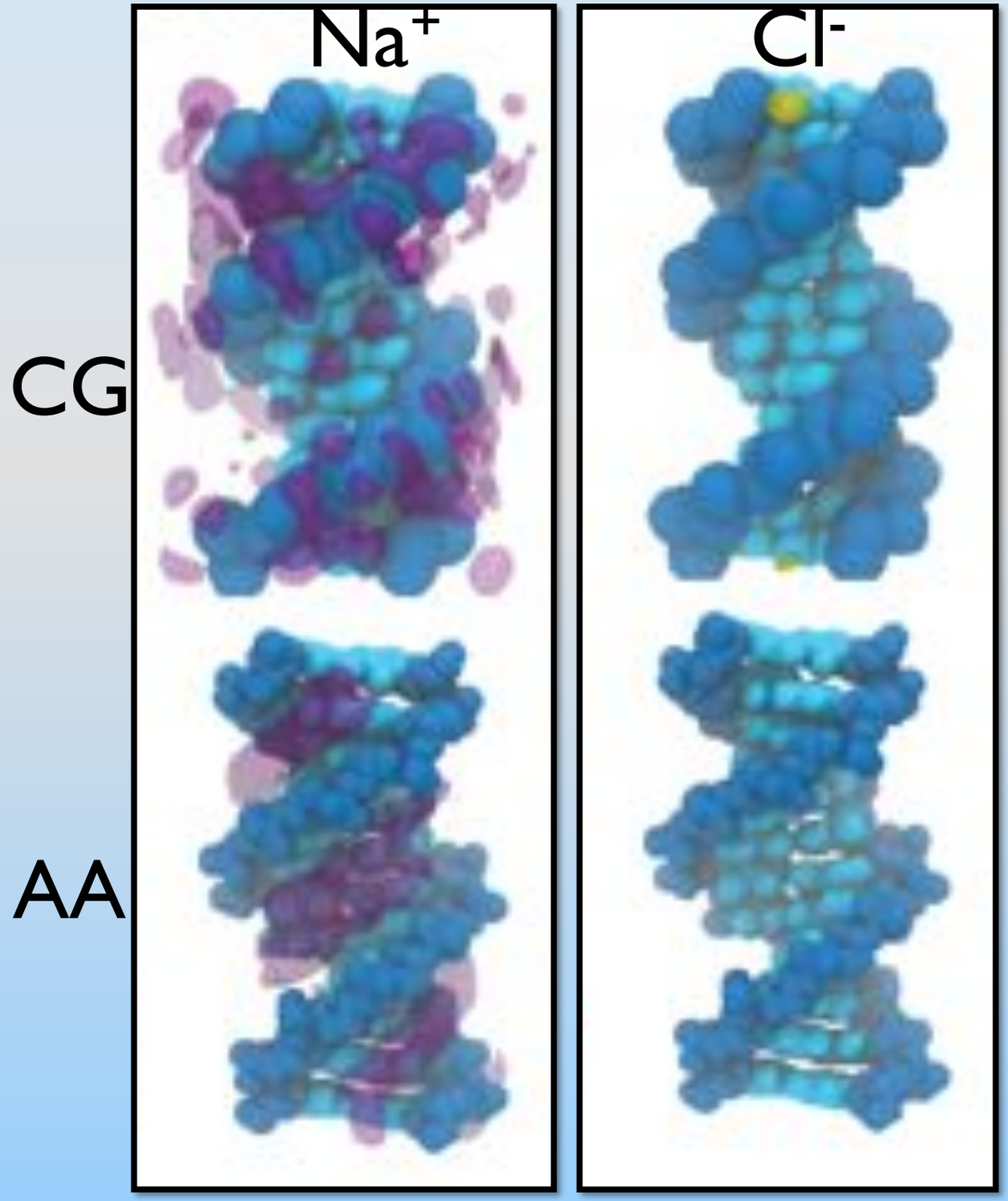
Validation of double stranded DNA

<u>Counterion condensation on dsDNA reproduced</u>

(at a qualitative level)

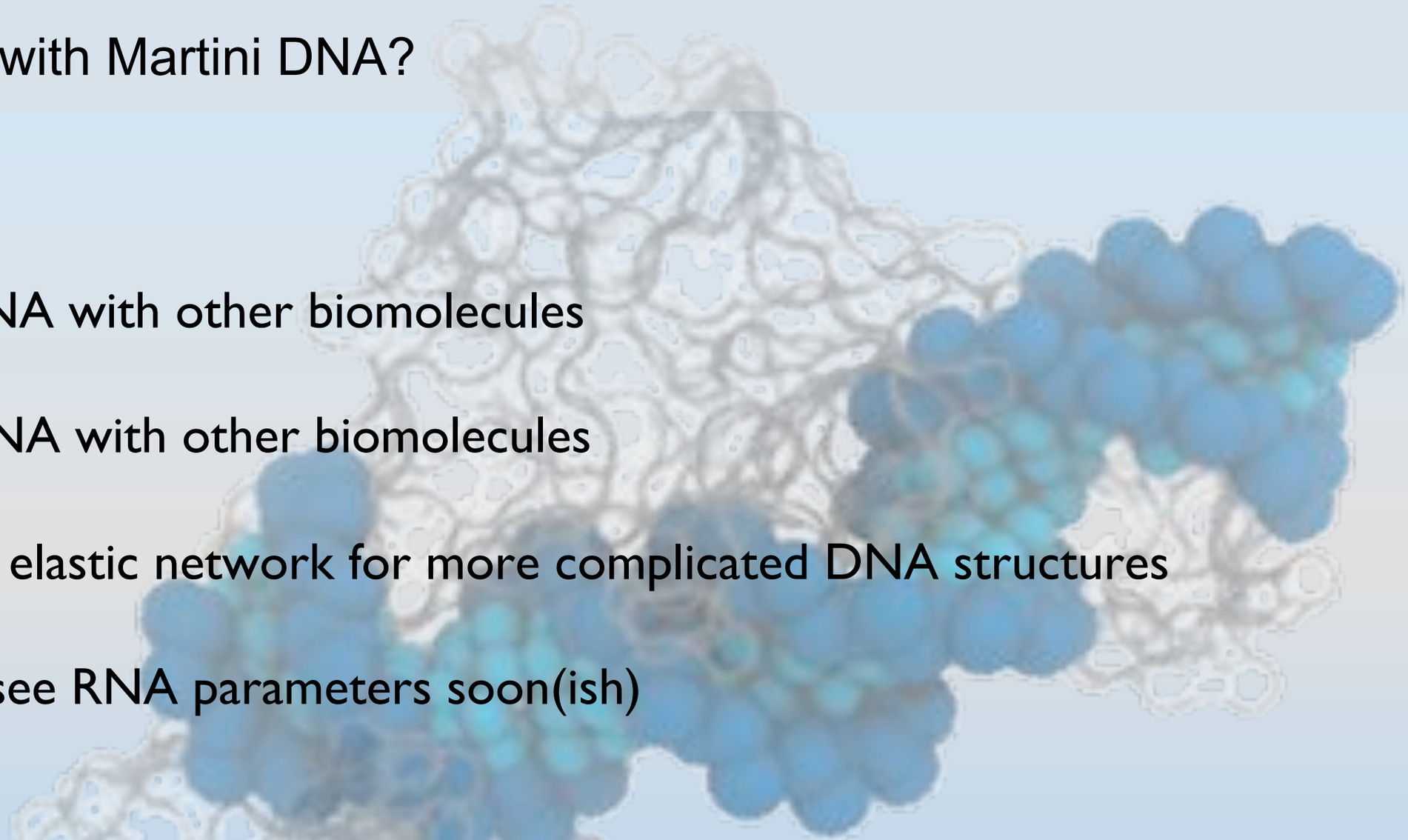
sodium localises further away from DNA than in AA, due to CG bead size

chloride not completely excluded from DNA due to implicit screening in Martini



Covering all the bases: DNA

What can we do with Martini DNA?



Do

- Study ssDNA with other biomolecules
- Study dsDNA with other biomolecules
- Modify the elastic network for more complicated DNA structures
- Expect to see RNA parameters soon(ish)

Don’t

- Try to hybridise ssDNAs to dsDNA
- Expect DNA to drastically change conformation

Nanoparticle mania

Nanograins

Fullerene

Graphene

Polymers

Dendrimers

Gold

Carbon Nanotubes

Nanoparticle mania: Fullerene

Mapping of fullerene

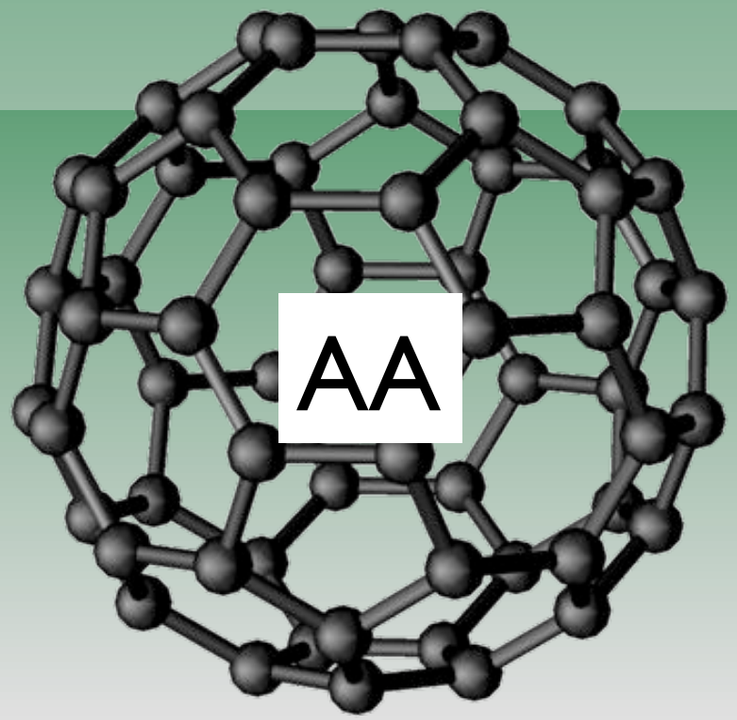
Two models tested

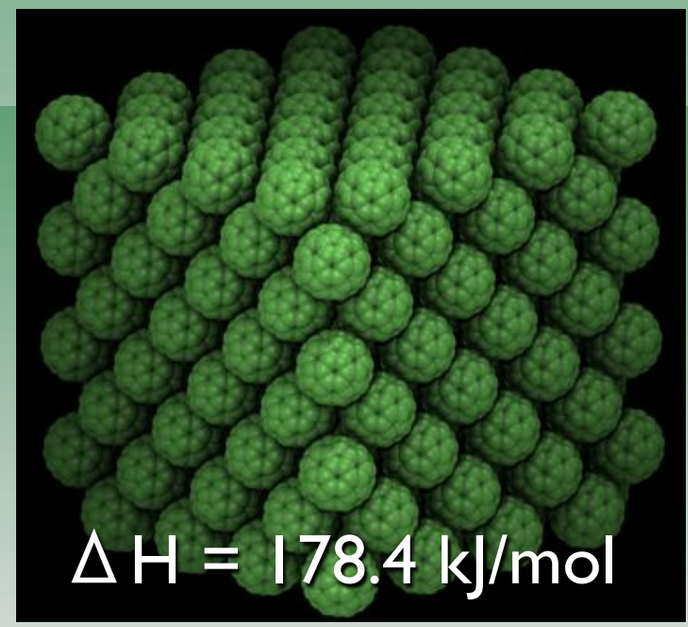
- 16 bead model (4-to-1)
- 20 bead model (3-to-1)

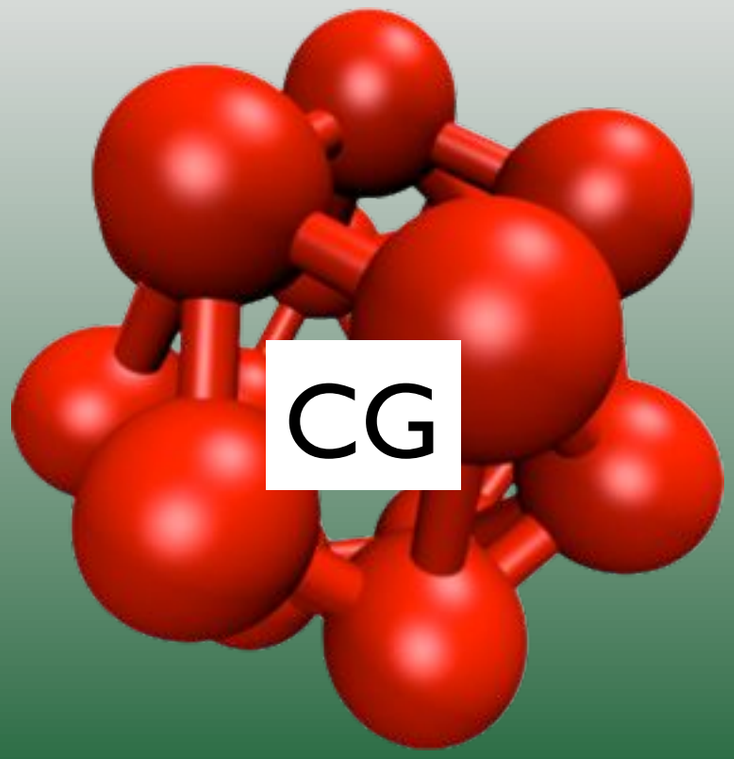
16-bead model more closely reproduces sublimation enthalpy due to less optimal packing

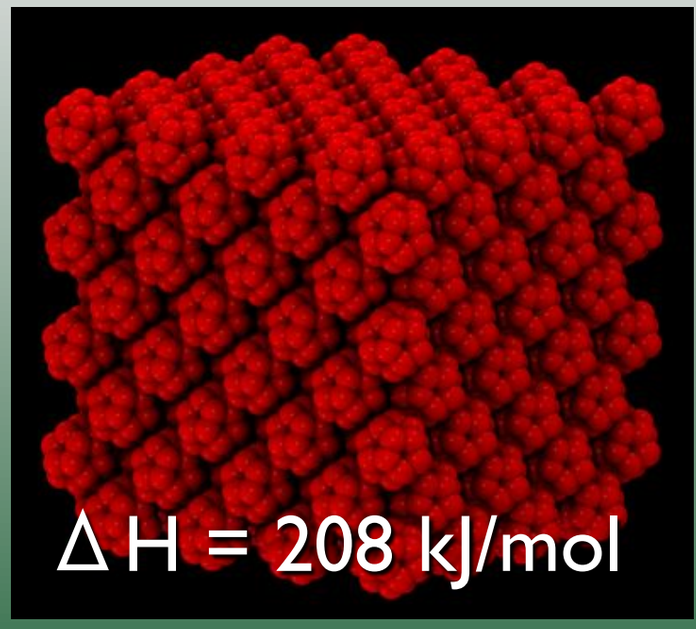
Elastic network to keep overall geometry

Monticelli, JCTC, 2012

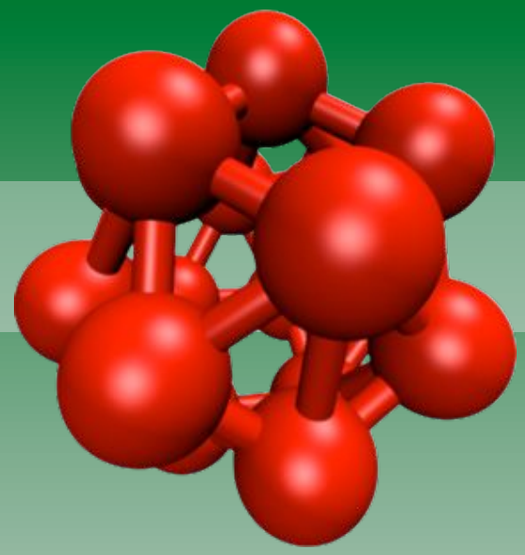








Nanoparticle mania: Fullerene



Finetuning of non-bonded interactions

Fullerene-solvent interactions

Based on SC4 type (benzene), but slightly modified to reproduce partitioning

Experiments

ΔG_transfer	benzene	octane	cyclohexane	acetone	1-butanol	ethanol
benzene						
octane	8.6					
chyclohexane	12.1	3.5				
acetone	15.2	6.6	3.1			
1-butanol	15.9	7.3	3.8	0.7		
ethanol	22.5	13.9	10.4	7.4	6.7	
water	105.3	96.7	93.2	90.1	89.4	82.7

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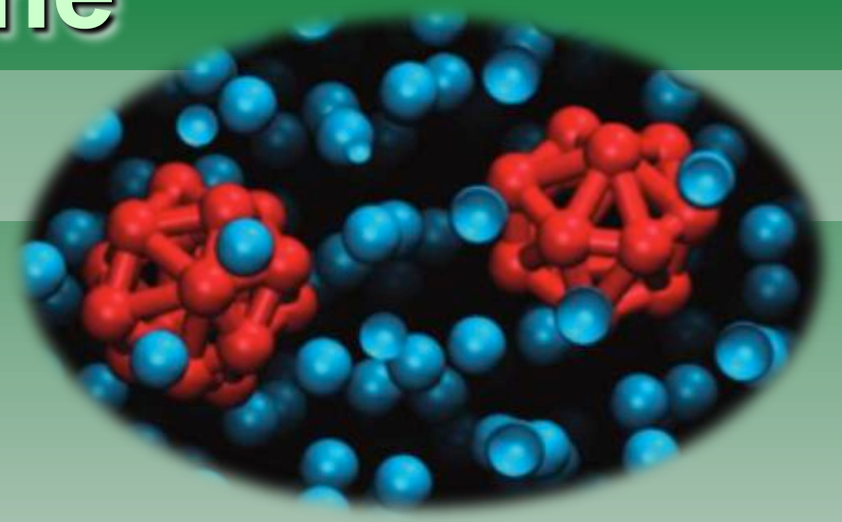
ΔG_transfer	benzene	octane	cyclohexane	acetone	1-butanol	ethanol
benzene						
octane	10.1					
chyclohexane	12.9	2.7				
acetone	14.5	4.4	1.7			
1-butanol	18.4	8.2	5.5	3.8		
ethanol	23.1	12.9	10.2	8.5	4.7	
water	85.5	75.3	72.6	70.9	67.1	62.4
average unsigned error (excluding water)	1.4					

Monticelli, JCTC, 2012

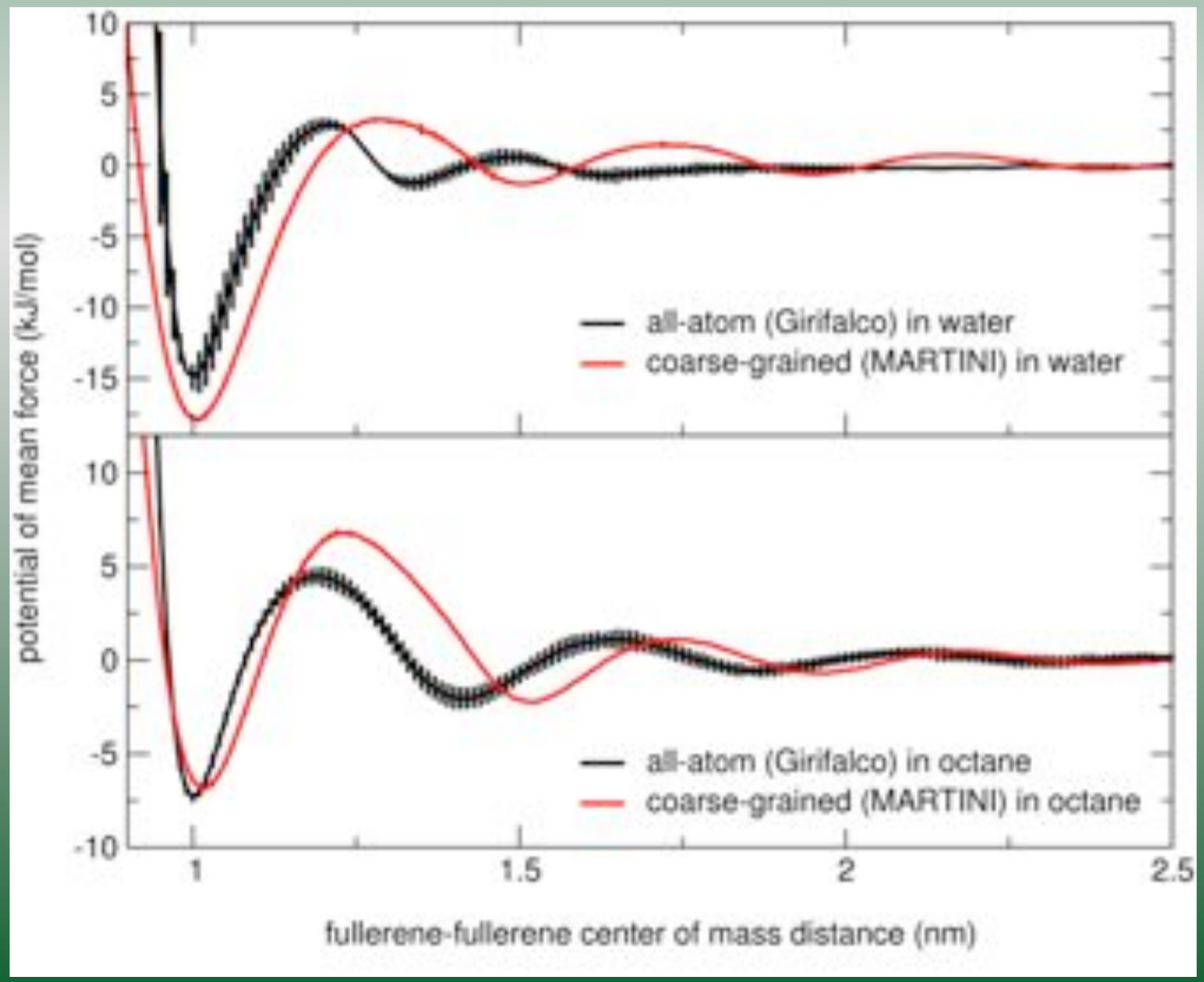
Nanoparticle mania: Fullerene

Finetuning of non-bonded interactions



Self interactions

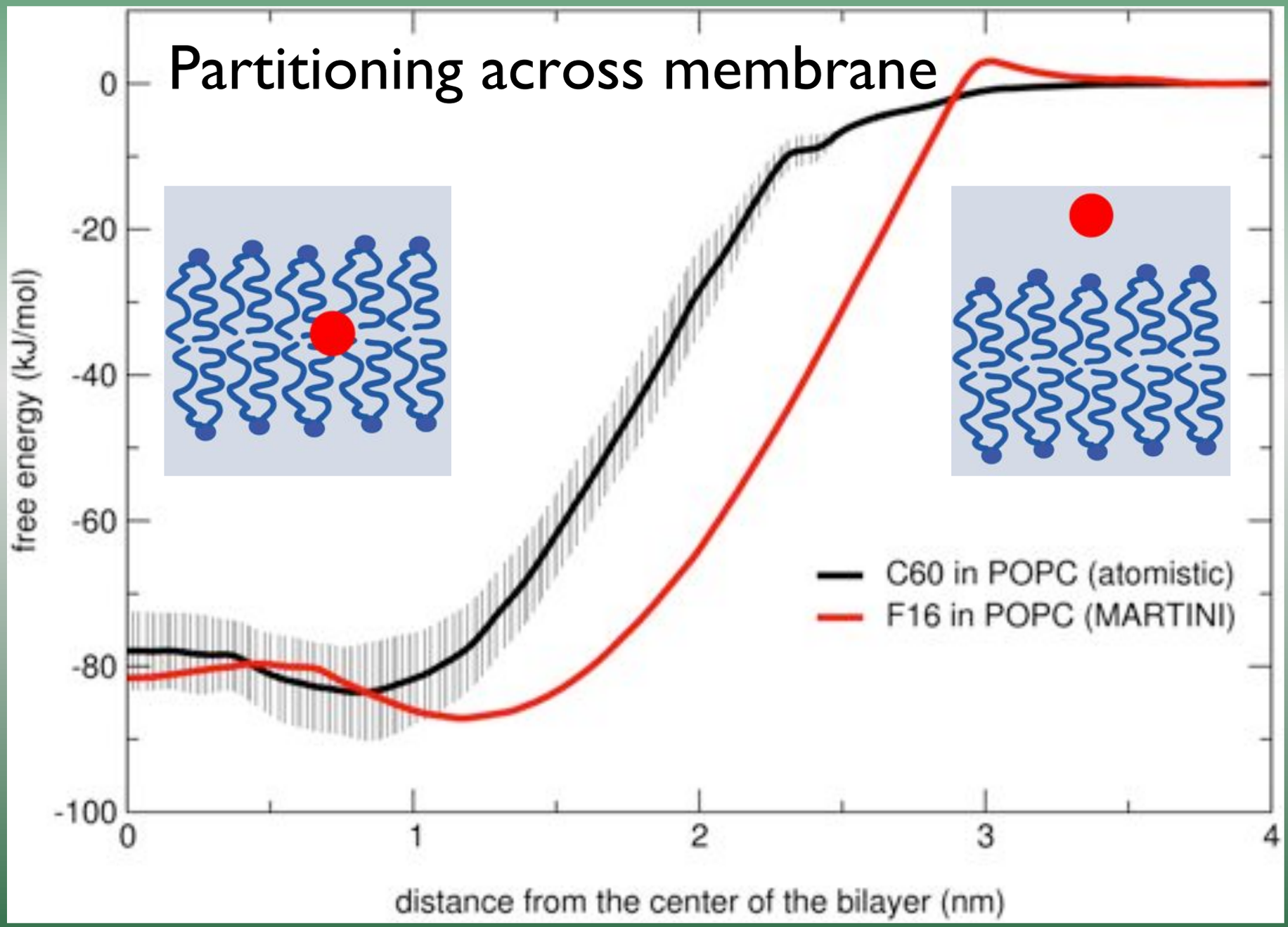
Reproducing fullerene-fullerene PMFs in different solvents



Monticelli, JCTC, 2012

Nanoparticle mania: Fullerene

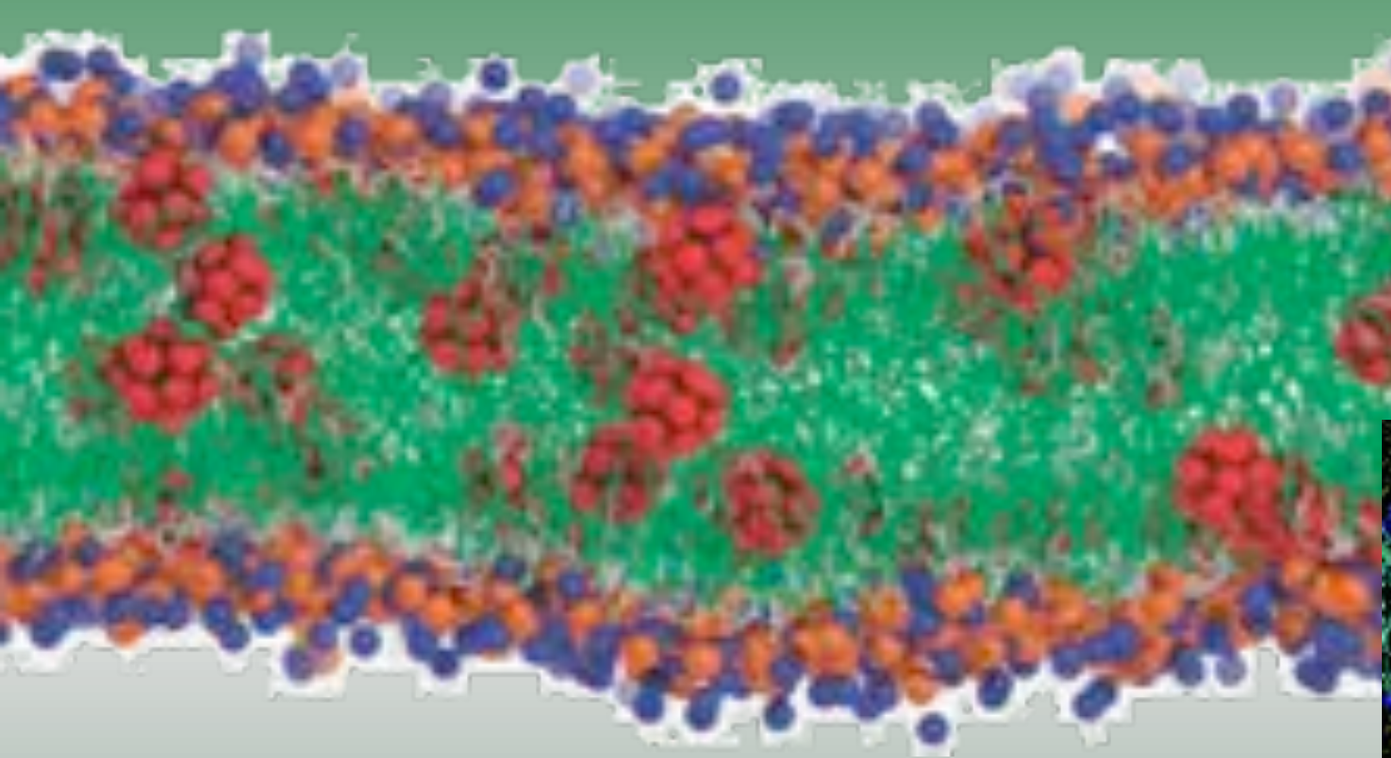
Validation example of fullerene model

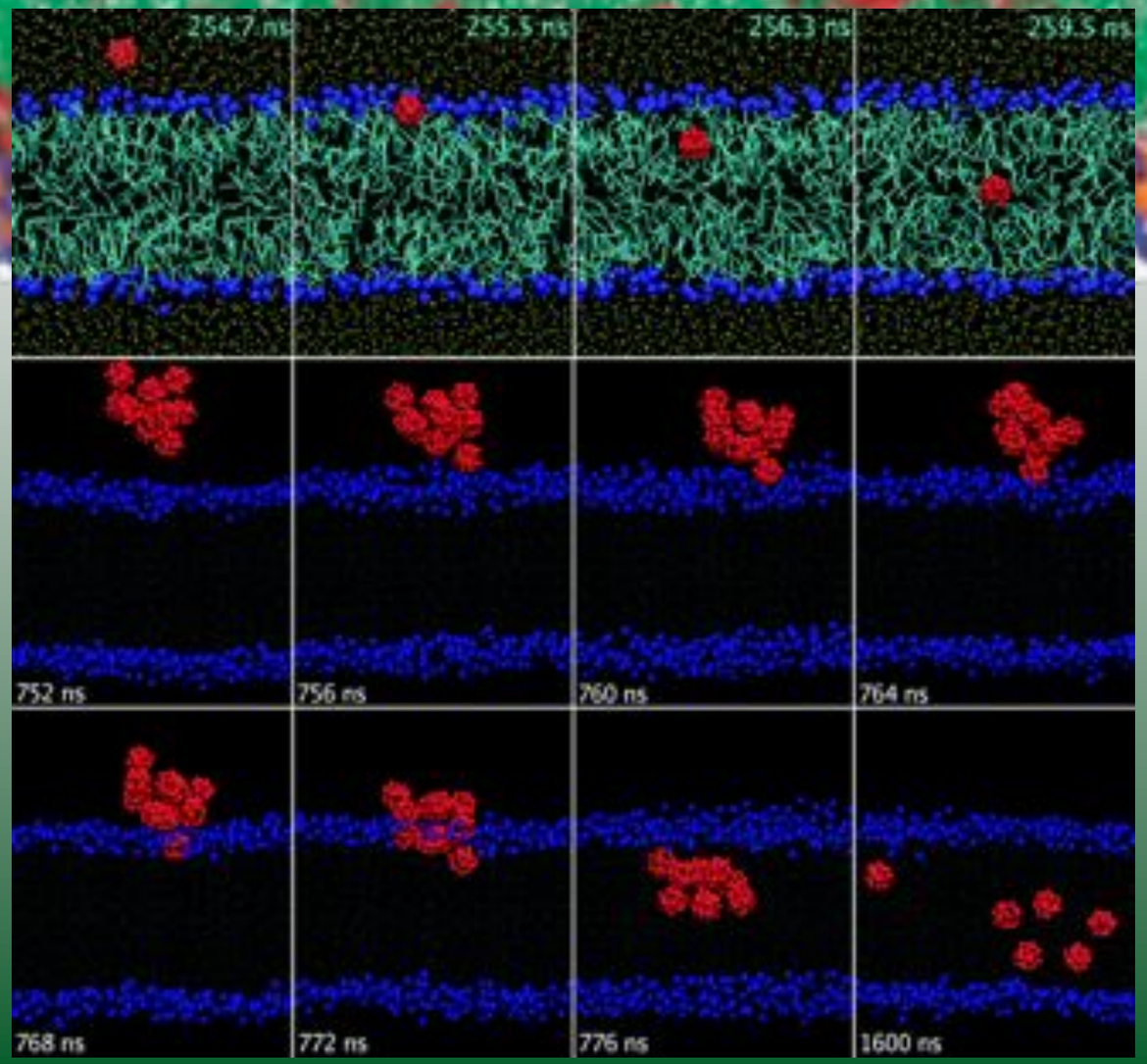


Monticelli, JCTC, 2012

Nanoparticle mania: Fullerene

Application example of fullerene model



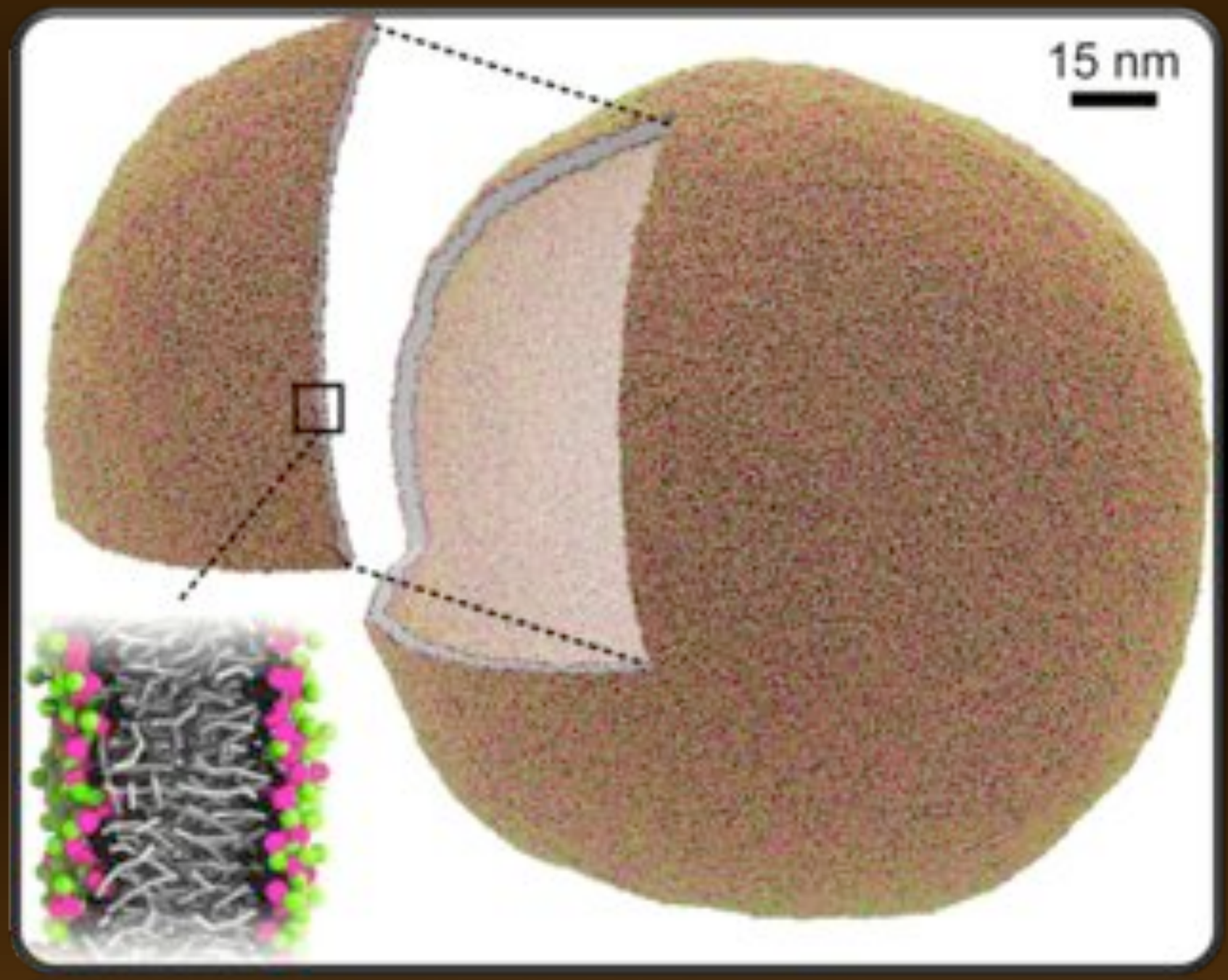


Lipid bilayer:
a perfect solvent for fullerene

Wong-Ekkabut et al, Nat. Nanotech., 2008

Dry Martini

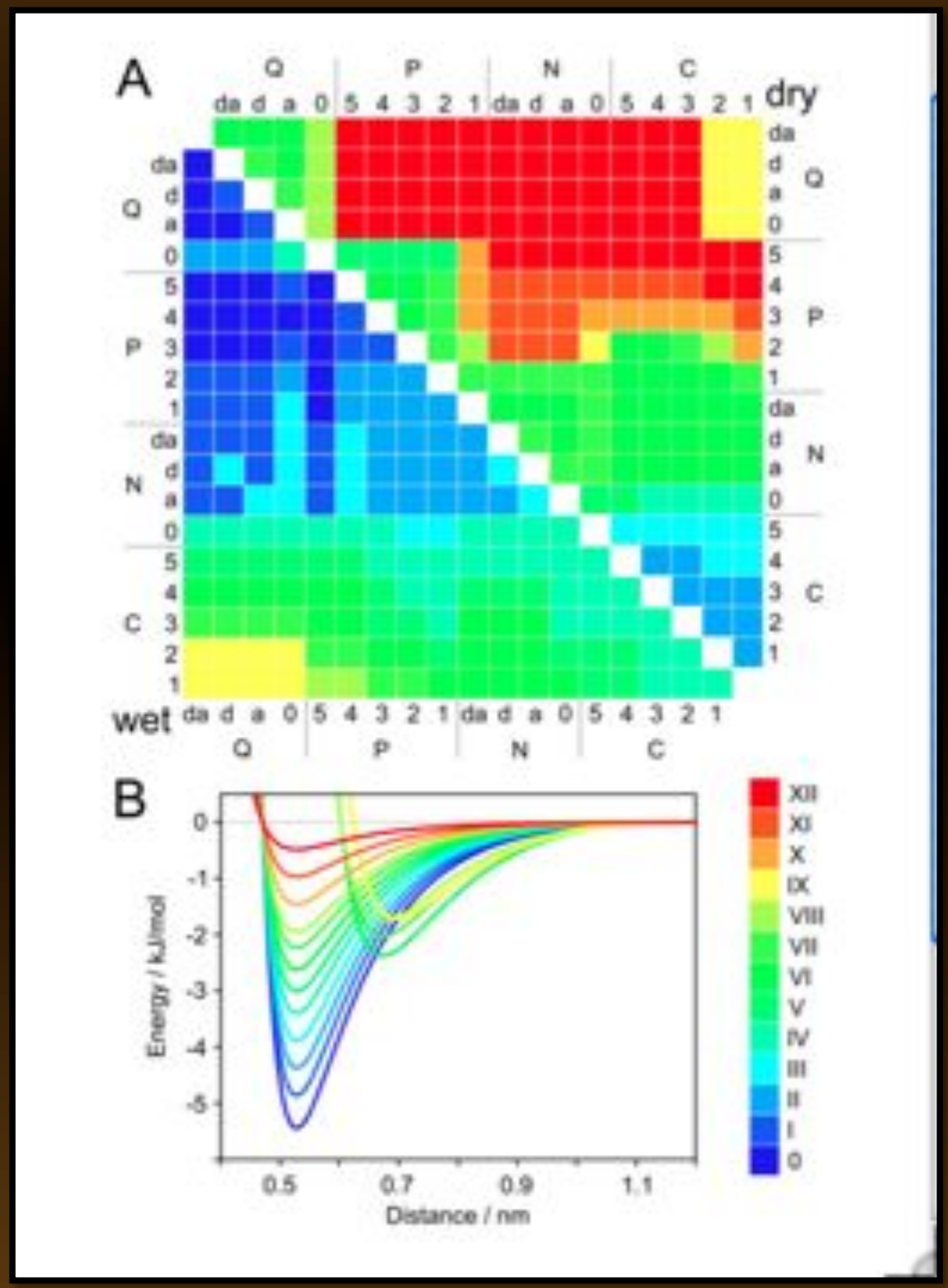
coarse-grained force field for lipid membrane simulations with implicit solvent



C. Arnarez et al, JCTC, 11:260–275, 2015

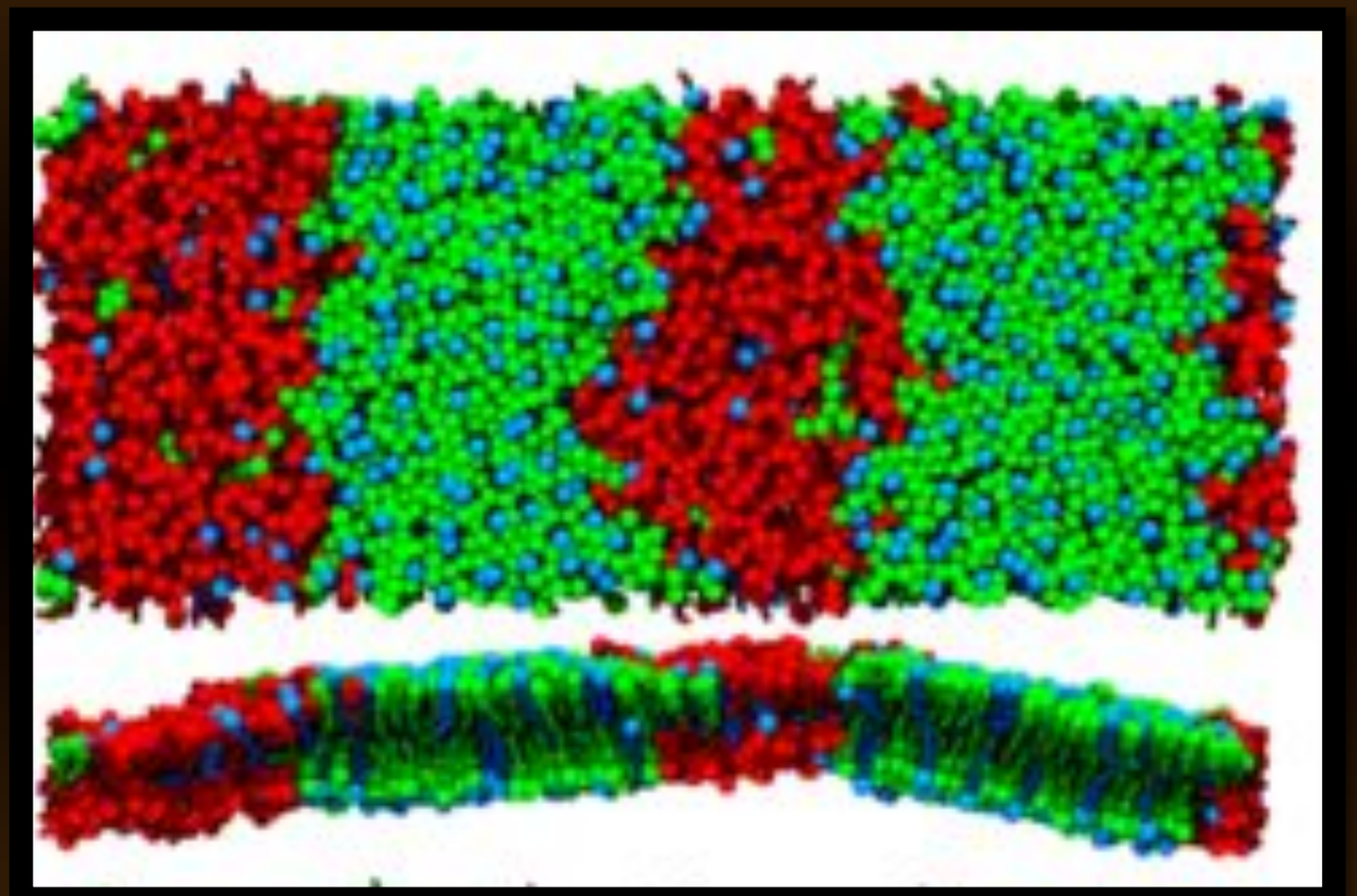
Dry Martini

Reshuffling non-bonded interactions

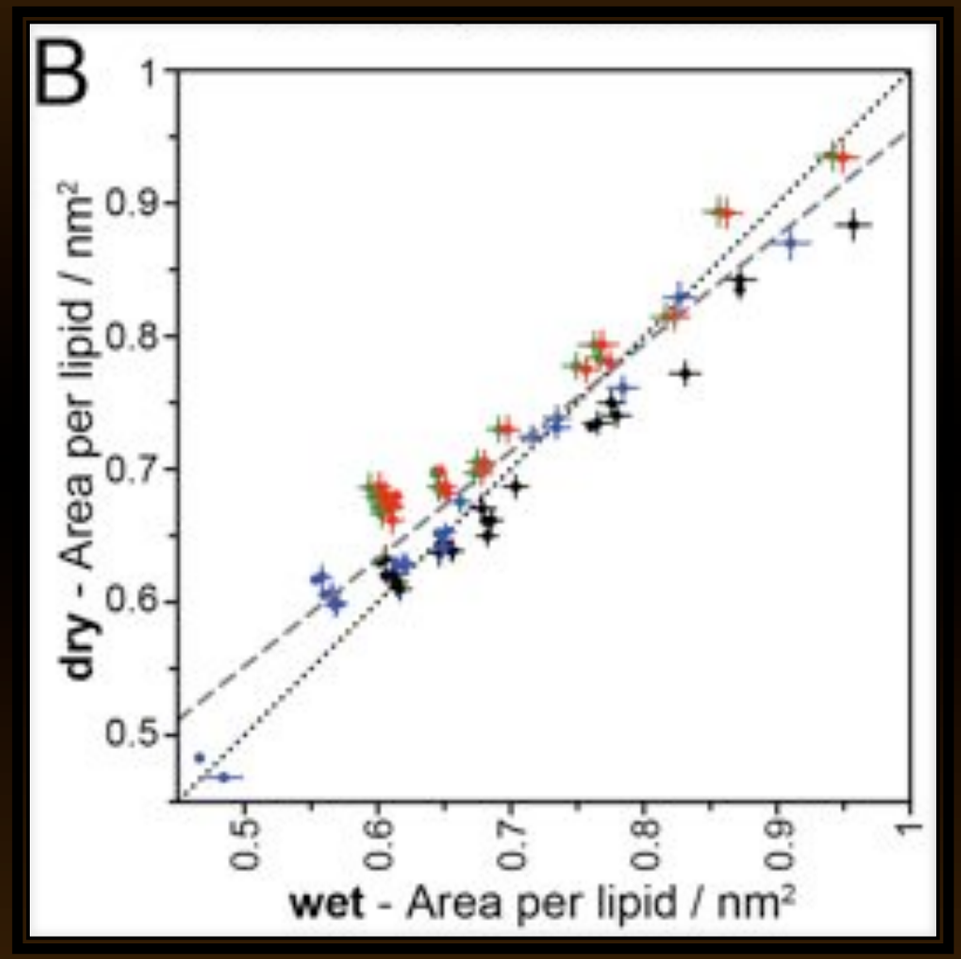


Dry Martini

Validation examples



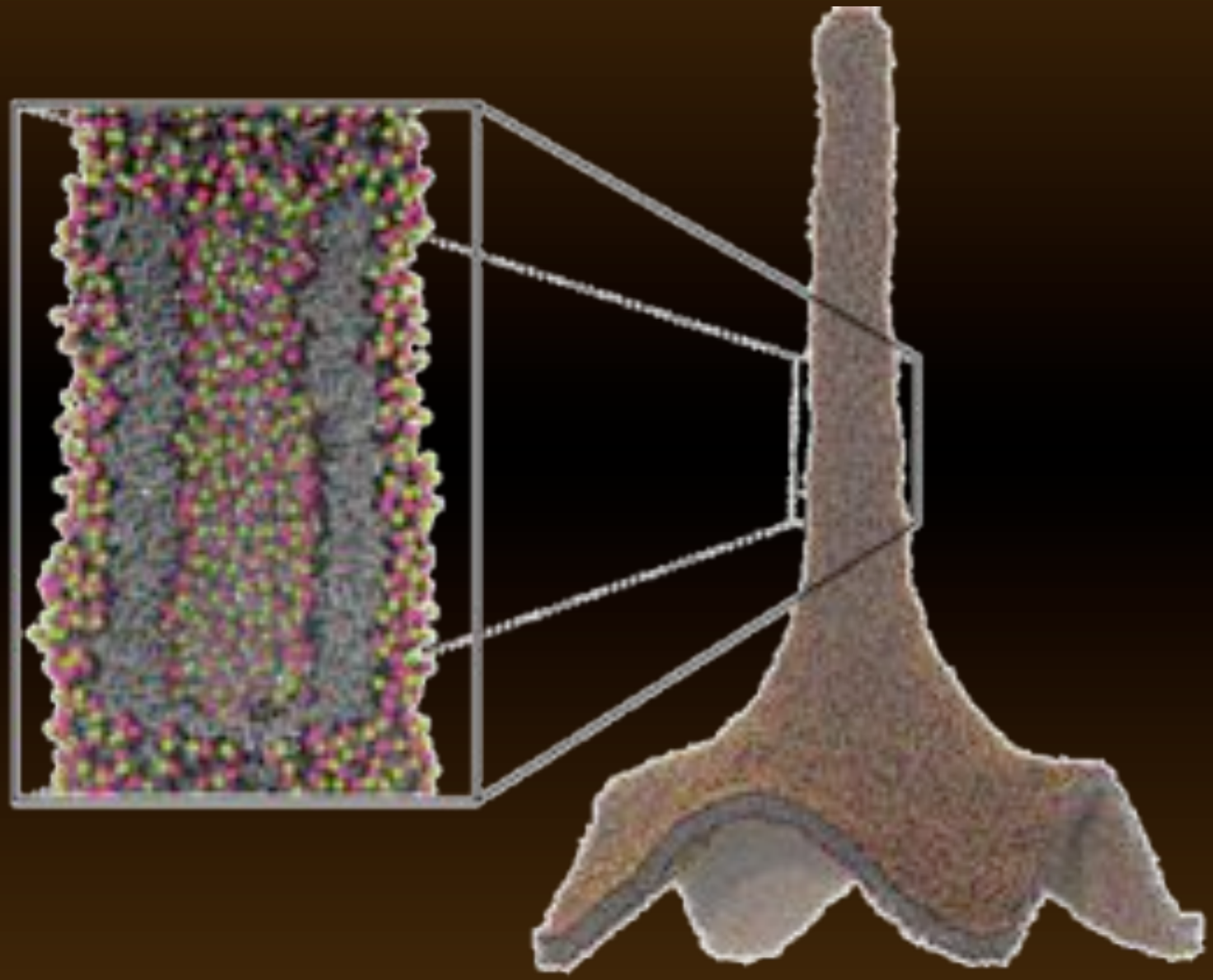
Lipid phase behaviour



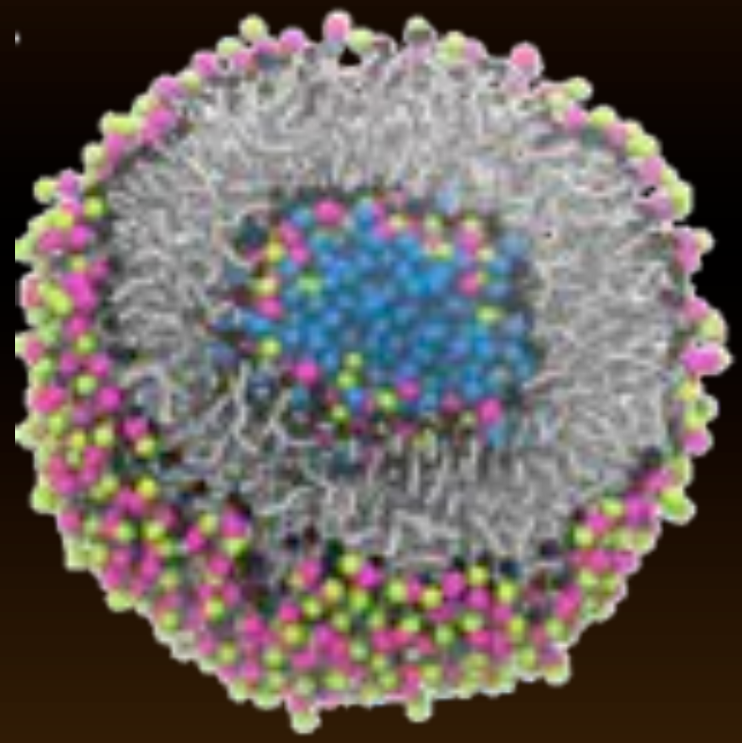
Structural membrane properties

Dry Martini

Potential application areas



Large scale membrane deformations



Combining with wet Martini

Enjoy Sampling Martinis !!