

MD in Coarse-Graining: an overview

Application for solid ionic-liquid interfaces

Lecture for Themosia Winter School– Lyon, February 22-23, 2026

PAULO C. T. SOUZA



My scientific and professional journey

2000

Chemical technician



2003

Bachelor, Master and PhD in Brazil
Physical-Chemistry
Prof. Munir S. Skaf (IQ-UNICAMP)



2013

Intership and Senior Postdoc
Biophysics
Prof. Siewert J. Marrink (RUG).



university of
groningen



2020

Senior Scientist in PharmCADD



2021

→ Researcher at CNRS/UCBL
Researcher at CNRS/ENS de Lyon



2022



My scientific interest: development of CG approaches for modeling and design



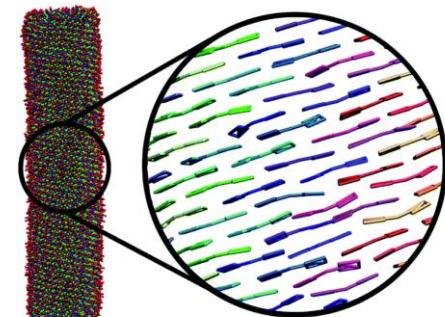
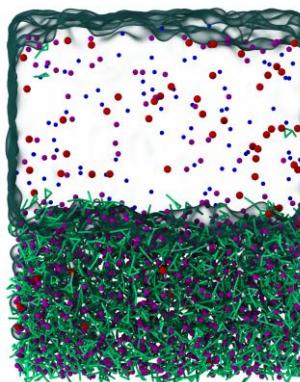
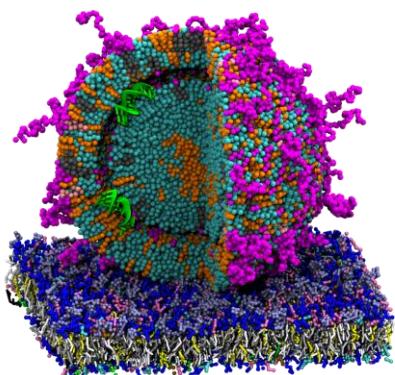
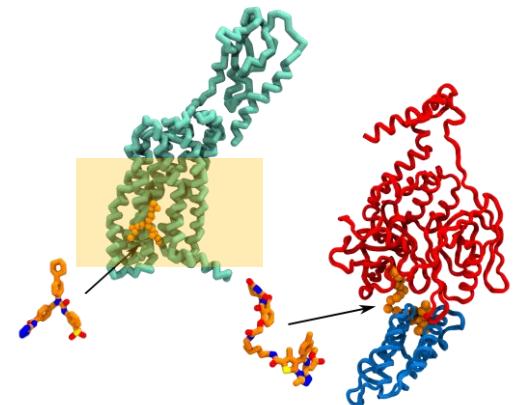
**Method development:
Martini CG Models**

**Finding pockets
in hard targets**

**Delivery
Systems**

**Green solvents
and Extraction**

**Supramolecular
aggregates**

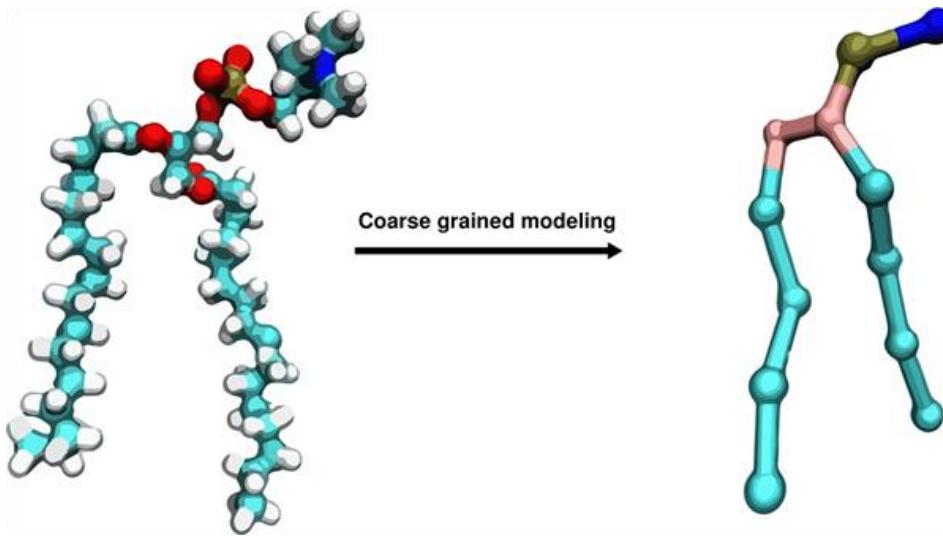


Strategy: Focused on exploring the limitations of other computational approaches.

Outline of the CG Module

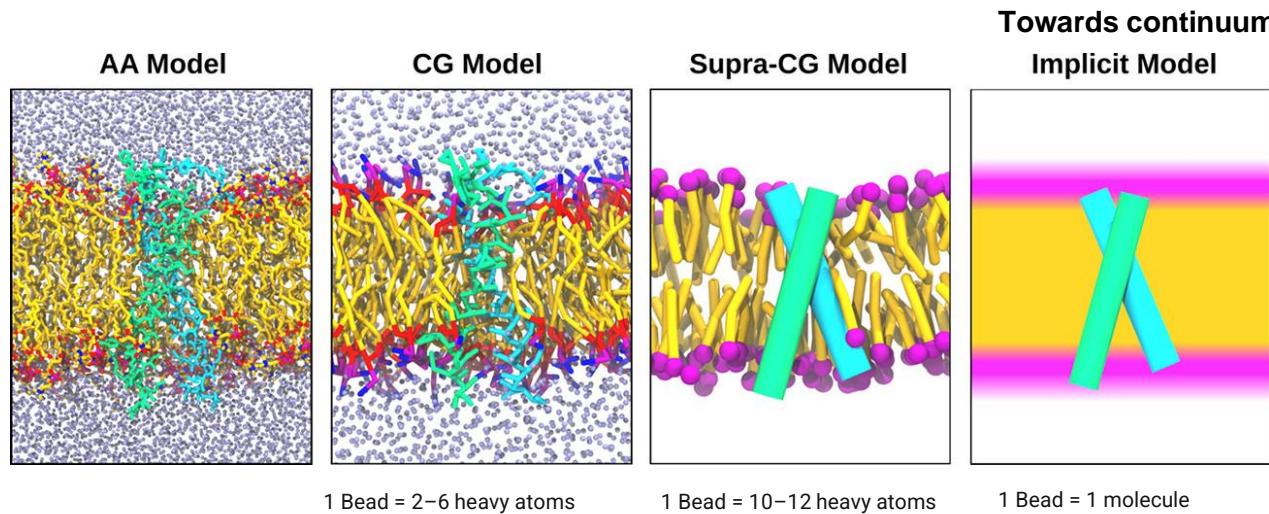
- Lecture on Coarse-graining and Martini Model
- Hands-on 01 – Building Solid surfaces
- Hands-on 02 – Building Solid–Ionic Liquid Interfaces
- Hands-on 03 – Running CG MD and Analysis
- Evaluation for the Master Students

What are Coarse-Grained Models?



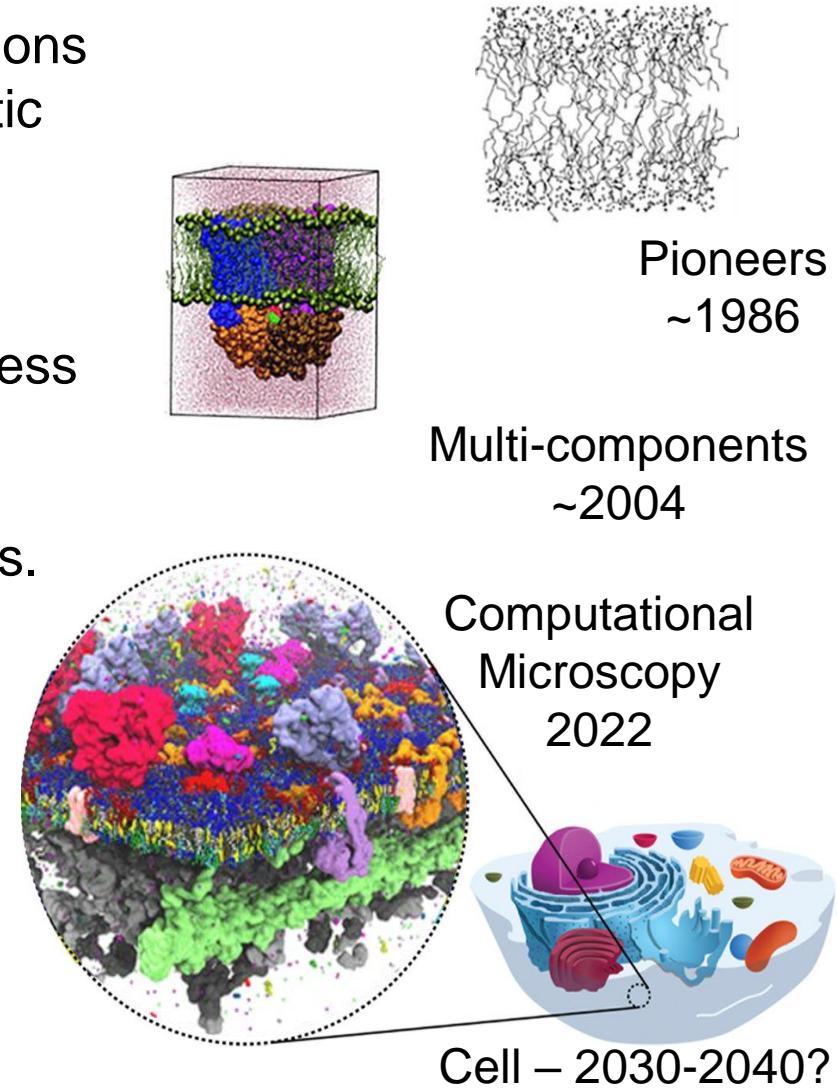
- Simplified models that group atoms into larger units (beads) with the idea of capturing the essential physics/chemistry.

- Can be built at different levels of resolution.
- Best resolution depends on the problem/question you have.

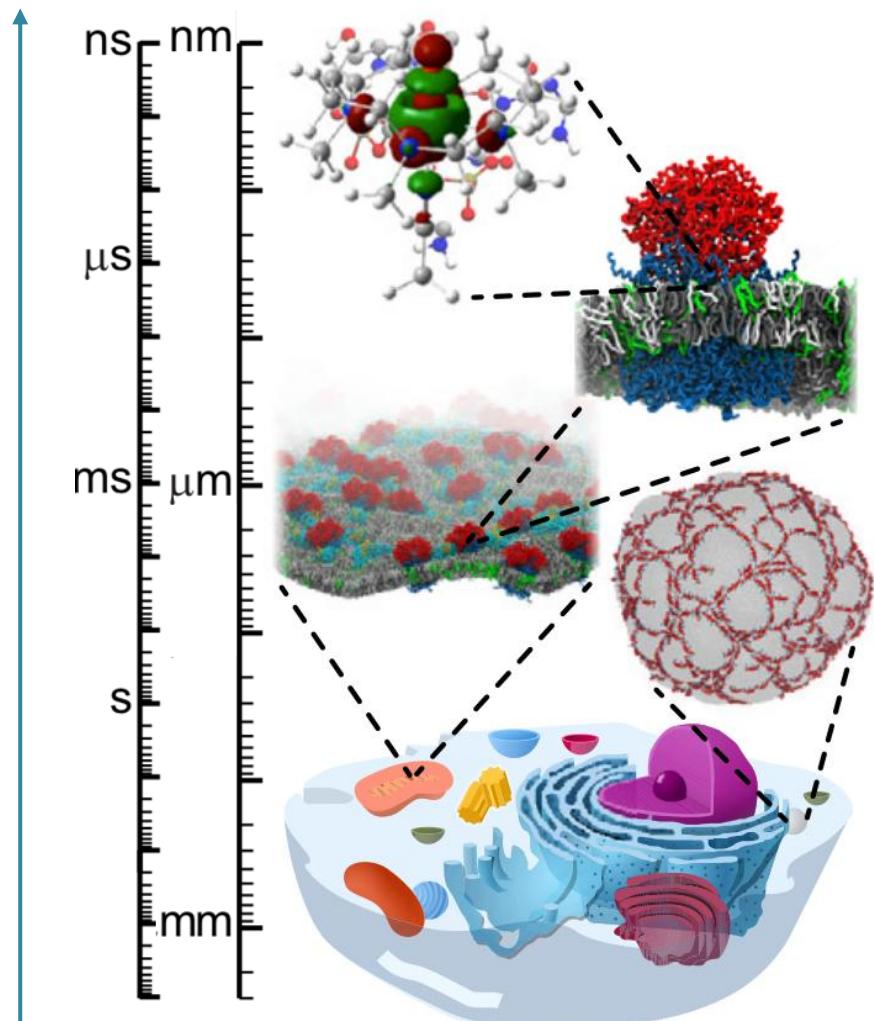


Why use Coarse-Grained models in MD simulations?

- To study process in time-spatial resolutions inaccessible to experiments and atomistic simulations.
- Understand driven-forces behind a process
- As toy models: generate new hypothesis.
- to simulate systems **more realistic in composition and organization.**



What time and spatial scales are coarse-grained models suitable?



Quantum

- atoms, electrons and electron clouds included
- explicit solvent
- quantum mechanics

All-atom

- all or most atoms present
- explicit solvent
- molecular dynamics

CG for
smaller scales?

- “toy model” for ideas
- get more sampling

Coarse-grained

- beads comprising a few atoms
- explicit or implicit solvent
- molecular dynamics

Supra-coarse-grained

- interaction sites comprising many atoms, protein parts or proteins
- implicit solvent
- stochastic dynamics

Continuum

- materials as a continuous mass
- implicit solvent
- continuum mechanics

Connecting all-atom
to continuum scale

HPC + GPUs
are extending
these limits.

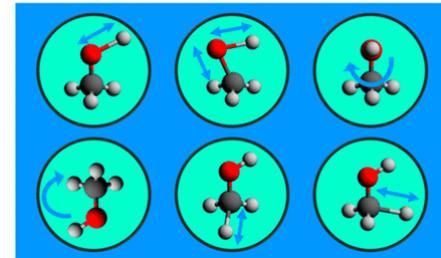


Limitations of coarse-grained models

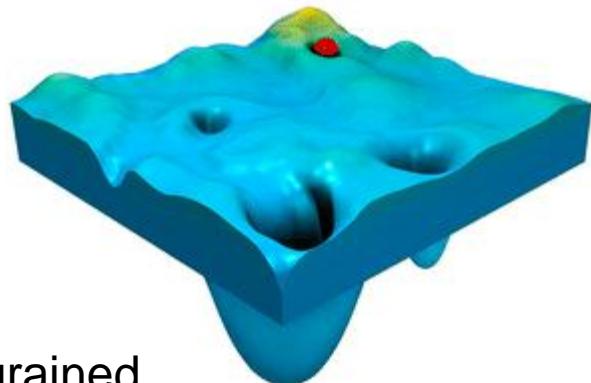
Fundamental problems related with CG approach

- Missing entropy, compensated by reduced enthalpy
- Thermodynamic driving forces may be wrong in some cases.
- Temperature dependence issues.
- Be careful with time scales.

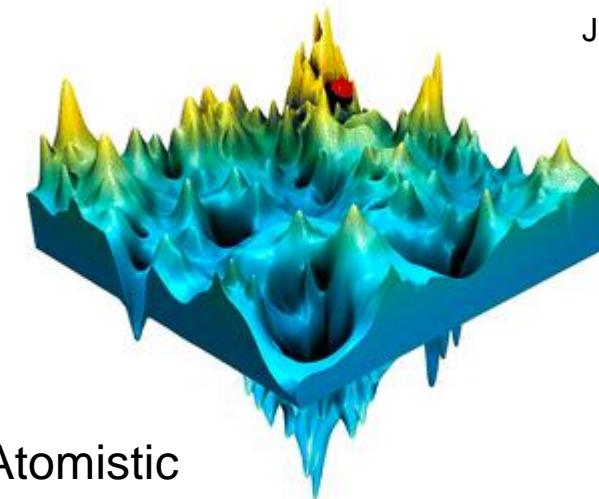
- More specific ones depending on the type CG approach: directionality, electrostatics, etc.



Jin et. al JPCL, 2019.



Coarse-grained



Atomistic

Different ways of coarse-graining

Experimental data

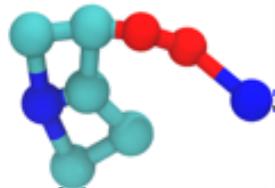


TOP-DOWN

- Phenomenological/Pragmatic approaches
- Reproduce faithfully certain experimental properties
- Developed with certain application area in mind

Examples: MARTINI $\longrightarrow -RT \ln P^{\text{exp}} \approx -RT \ln \left(\frac{p_{\text{CG,water}}}{p_{\text{CG,oil}}} \right)$
SPICA, Gō Models, etc

Coarse-Grained
Models



BOTTOM-UP

- Hierarchical/First principle approaches
- Interactions at CG level from the collective interactions at atomistic level
- General method applicable to any system

Atomistic
Models

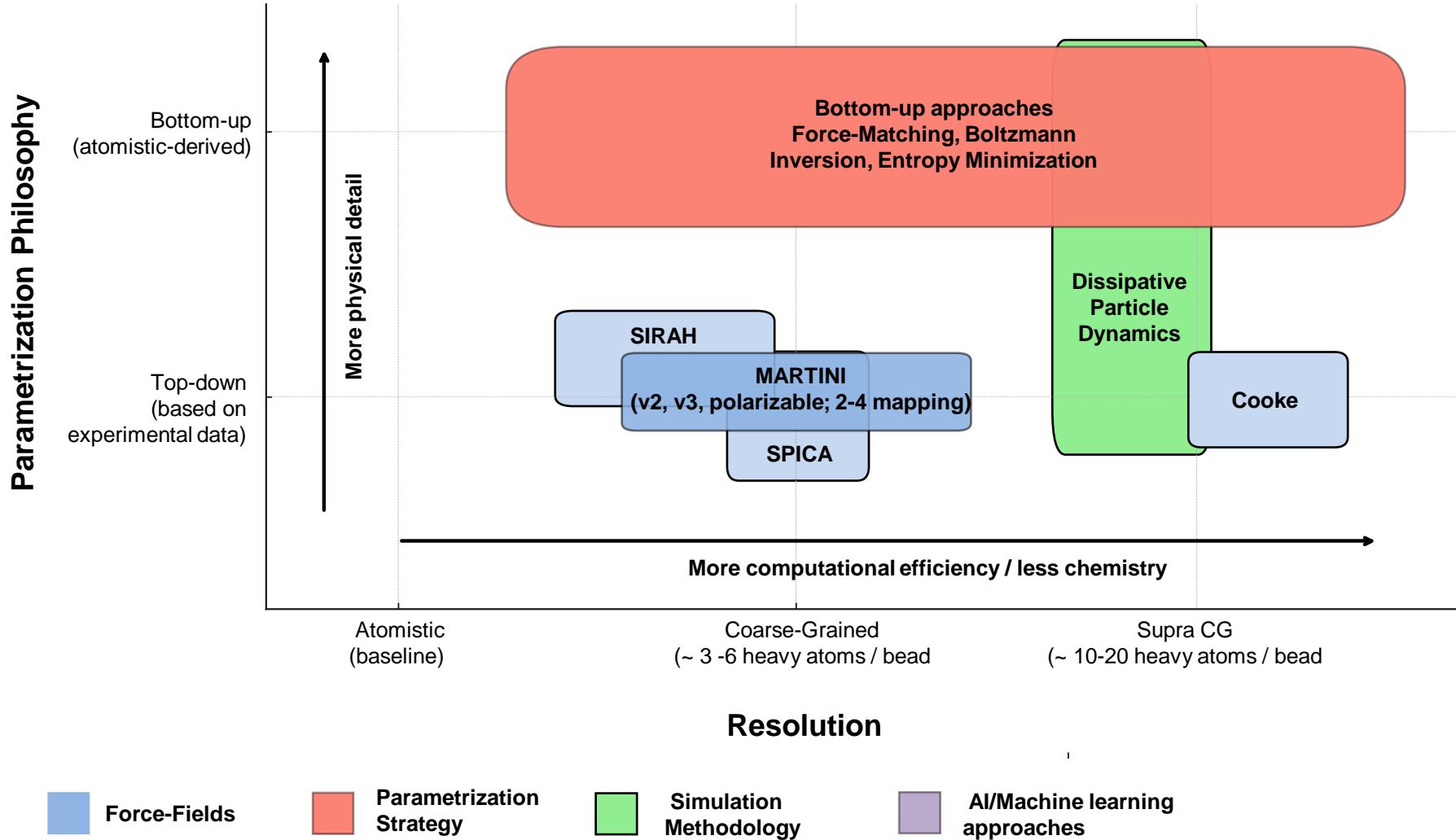


Examples: - Iterative Boltzmann inversion potentials

- Force matching $\longrightarrow F^{\text{CG}}(R) = \langle F^{\text{atom}}(r) | R \rangle$

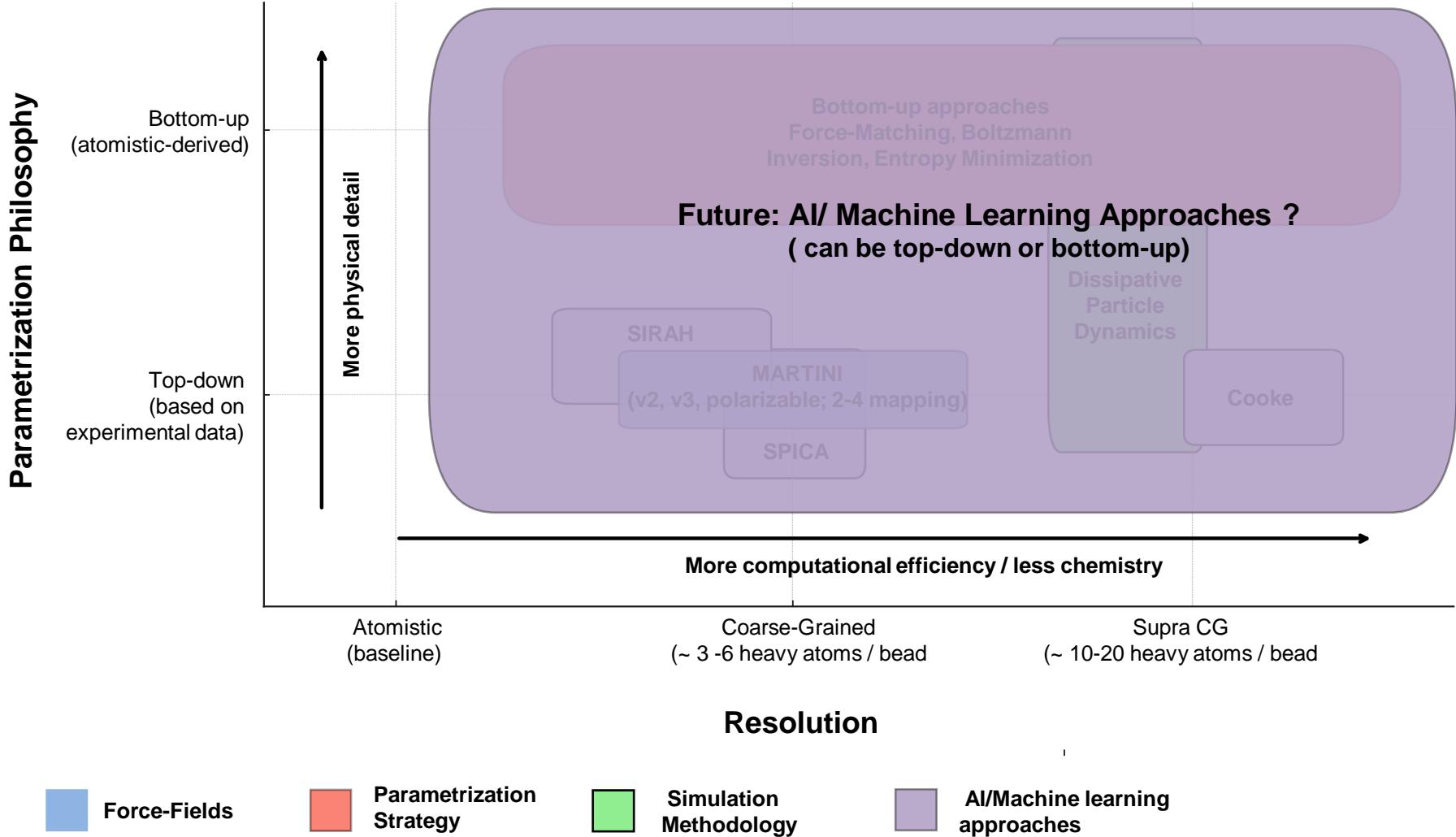
Families of Coarse-Grained Approaches

(non comprehensive summary)



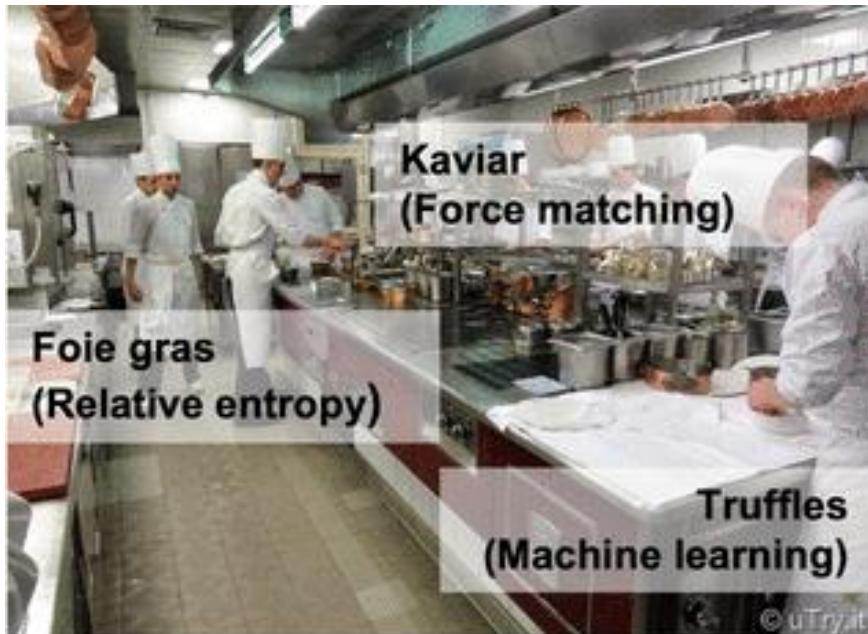
Families of Coarse-Grained Approaches

(non comprehensive summary)



From kaviar to soup: Accessibility of Coarse-Grained Models

BOTTOM-UP/HIERARCHICAL



TOP-DOWN/PRAGMATIC

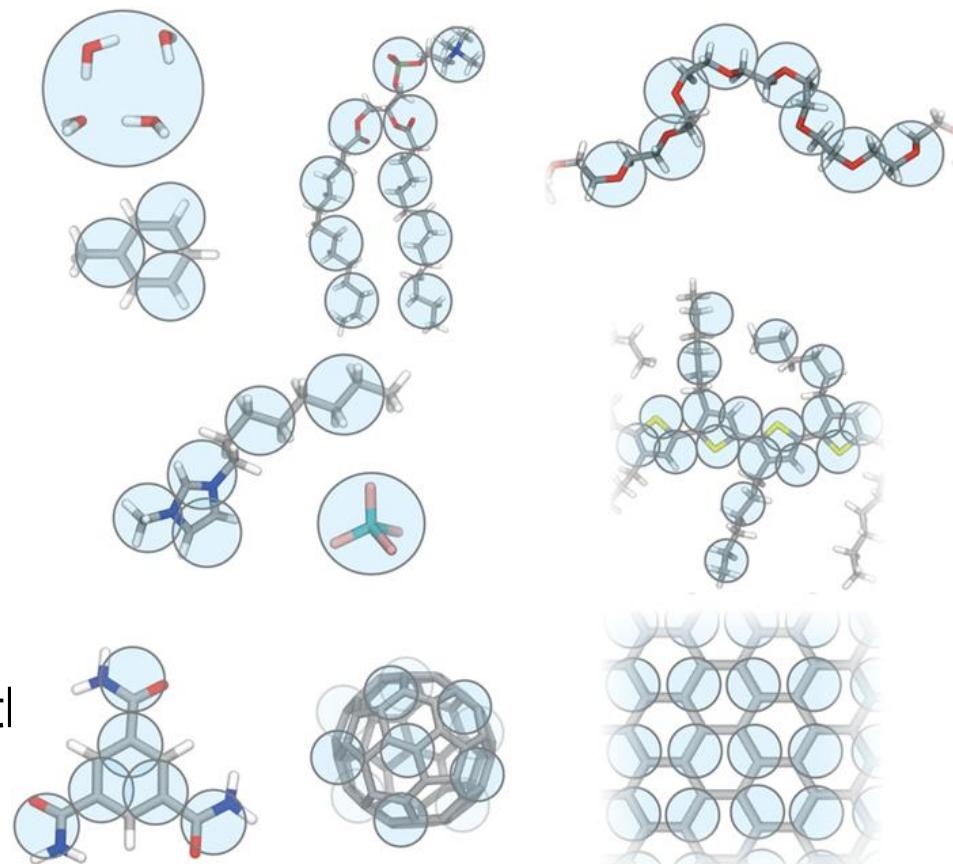


By William Noid (JCTC, 2023) "...while bottom-up approaches promise the caviar of CG models, researchers are often limited in practice to Martini soup"

The Martini Model: Key features

- Build block approach (“Lego”).
- Chemical specificity
- Fast (10^2 - 10^3 speed-up) and Green ($\downarrow \text{CO}_2$ emissions by 99%)
- Implementation in atomistic MD codes.
- Easy-to-use and modify.
- Well-tested, reproducible and with well-known pros/cons.

Approximately 2:1 to 4:1 mapping
of non-hydrogen atoms



Why is it called Martini?

The Martini force field was initially developed in Groningen and named after Saint Martin, patron saint of Groningen.



How the models are calibrated?

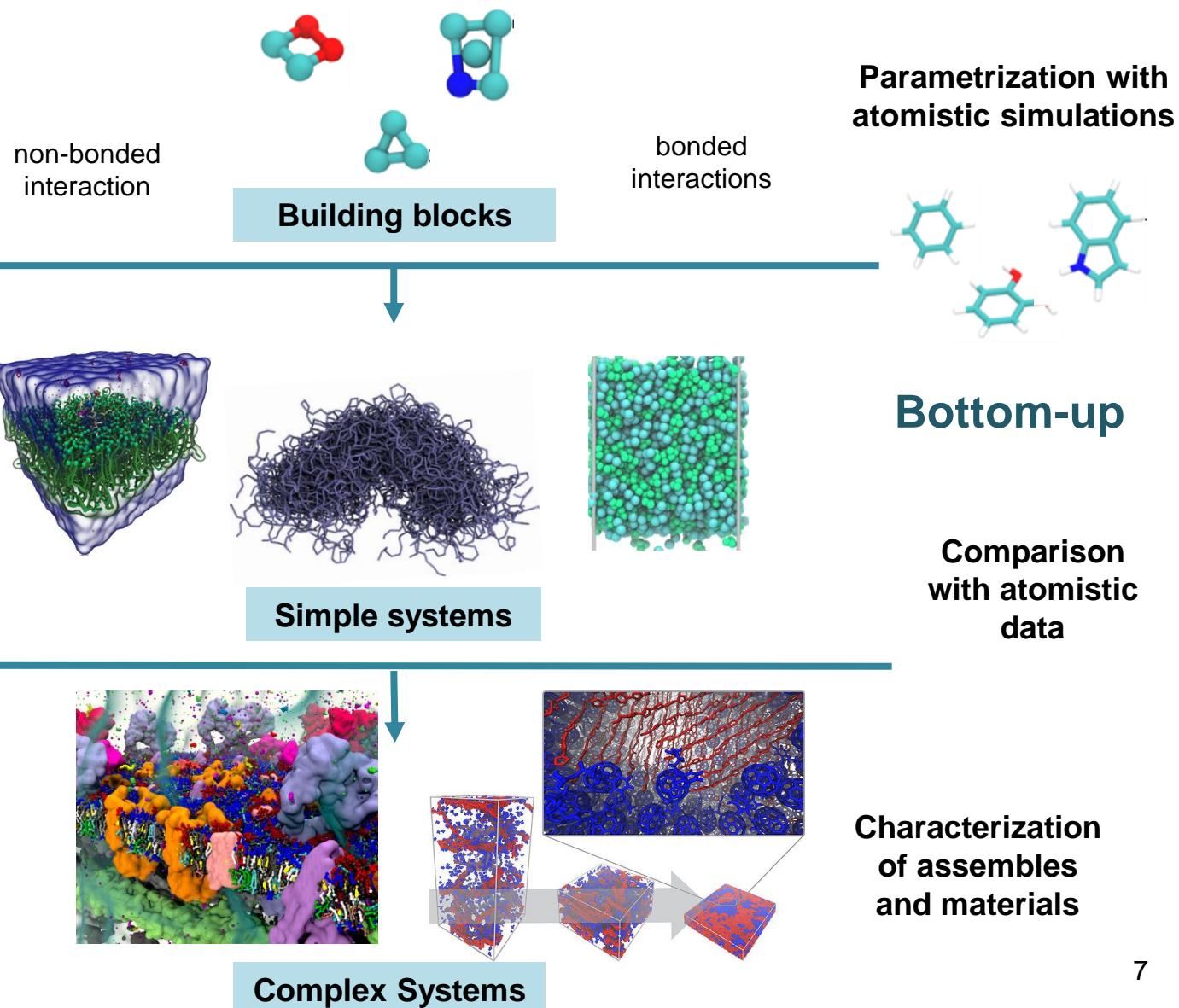
Calibration with thermodynamics data



Top-down

Extensive tests and validation

Insights of collective processes



23 years with Martini model

Martini 1:
for lipids

Marrink et. al JACS,2002
Marrink et. al JPCB,2004.



First Lego ~1949

Martini 2:
for biomolecules

Marrink et. al JPCB,2007.



Lego in ~1980

Martini 3:
for general purpose

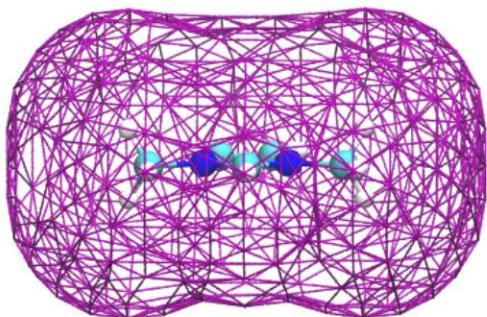
Souza et. al Nature Methods,2021.



Lego today

Easy-to-use versus Accuracy?

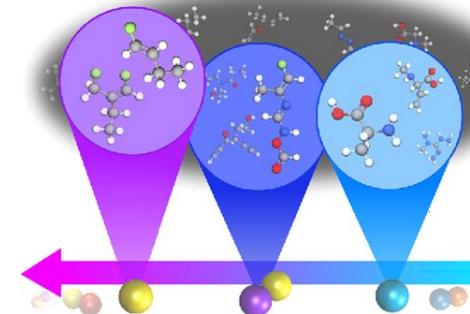
News version is Martini 3 the key improvements of the model



Alessandri,Souza et al, JCTC, 2019

1) Improved interactions and packing

Reparametrized all bead sizes and types, cross interactions and bonds



Kanekal and Bereau , JCP, 2019



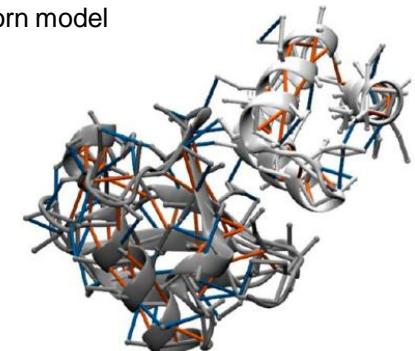
Jungwirth and Cremer, Nature Chemistry, 2014

2) Better Coverage of Chemical Space

New beads and ways to modify them.

3) Reformulation of charged beads

Inspiration from Hofmeister series and trends using Generalized Born model



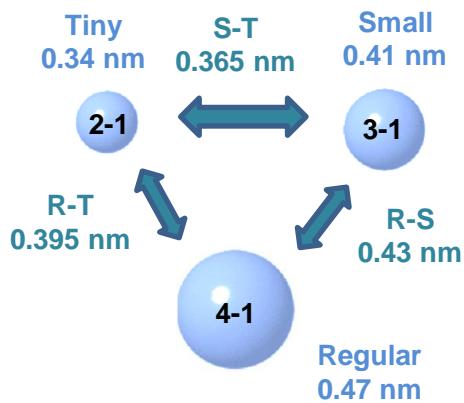
4) Improving bonded terms and flexibility

Improved protein dynamics

Pedersen et al, JCTC, 2024.
Souza et al, Nat. Comm., 2025.

MARTINI 3: THE BEADS TYPES AND SIZES

3 Bead Labels

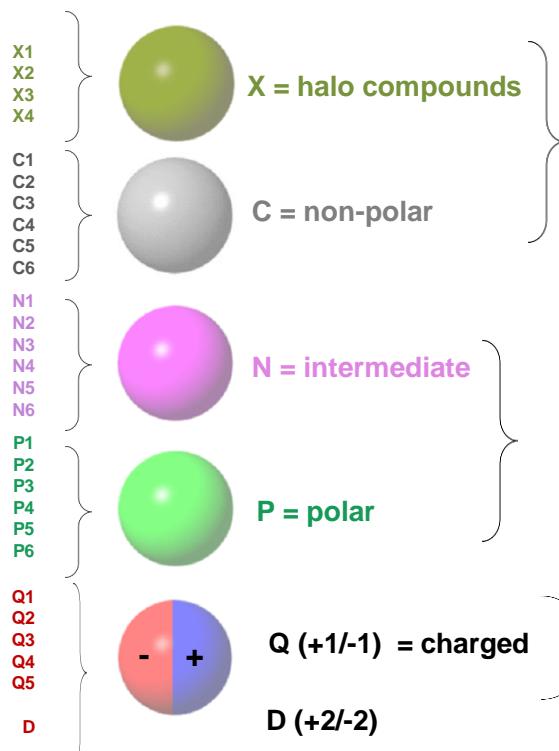


Specific beads for water

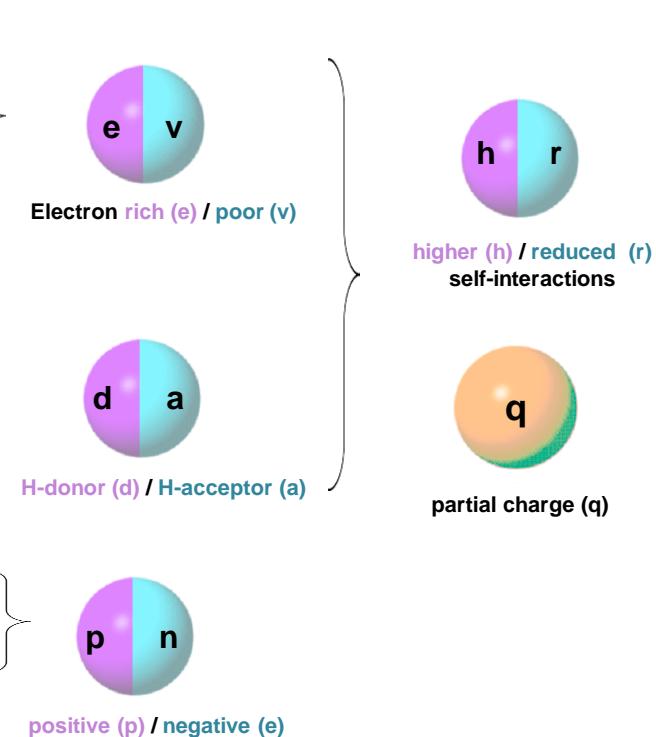


W = water

28 Bead Chemical Types



9 Bead Labels



	Martini 3
Beads	843
Pair interactions	355,746

THE HEART OF MARTINI 3: POTENTIALS AND INTERACTION MATRIX

$$U_{\text{total}} = \sum_{\text{bonds}} U_b + \sum_{\text{angles}} U_\theta + \sum_{\text{dihedrals}} U_\phi + \sum_{\text{impropers}} U_\xi + \sum_{i < j} 4\varepsilon \left[\left(\frac{\sigma}{r_{ij}} \right)^{12} - \left(\frac{\sigma}{r_{ij}} \right)^6 \right] + \sum_{i < j} \frac{1}{4\pi\varepsilon_0\varepsilon_r} \cdot \frac{q_i q_j}{r_{ij}}$$

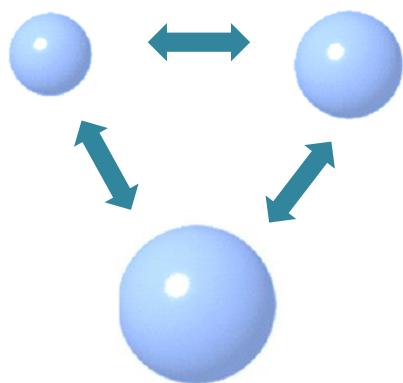
effective potential

D	Q5 Q4 Q3 Q2 Q1	P6 P5 P4 P3 P2 P1 N6 N5 N4 N3 N2 N1 C6 C5 C4 C3 C2 C1	X4 X3 X2 X1	W
D	0	1 2 3 4	15 16 17 18	0
Q5	0	0 1 3 8 11	14 15 16 17	1
Q4	1	1 2 4 8 11	13 14 15 16	2
Q3	2	3 4 4 7 11	12 13 14 15	3
Q2	3	8 8 7 7 10	11 12 13 14	4
Q1	4	11 11 11 10 10	11 11 12 13	5
P6	1	2 3 5 6 7	13 14 15 16 17 18	4
P5	2	3 4 5 5 6	12 13 13 15	4
P4	3	3 4 5 5 6	12 13 13 15	5
P3	3	4 4 5 6 6	12 12 13 14	6
P2	3	4 5 6 6 6	12 12 13 14	6
P1	4	5 6 7 7 6	12 12 13 14	7
N6	4	5 6 7 7 6	11 12 13 13	7
N5	5	6 6 7 7 7	10 11 12 13 13	8
N4	6	6 7 7 7 7	10 11 12 13 14 15	9
N3	6	7 8 8 8 7	9 10 11 12 13 14 15	9
N2	7	7 8 8 8 8	9 10 11 12 13 14 15	10
N1	12	8 8 8 9	8 9 10 11 12 13 14 15	11
C6	16	13 12 12 10 9	8 9 10 11 12 13 14 15	11
C5	18	17 15 13 12 11	12 13 13 14 15	12
C4	19	18 16 14 13 12	12 12 13 14 15	12
C3	20	19 17 15 14 13	12 12 13 14 15	13
C2	21	21 20 19 19 18	12 12 13 14 15	13
C1	21	21 20 19 19 18	12 12 13 14 15	14
X4	15	14 13 12 11 11	11 12 13 14 15	13
X3	16	15 14 13 12 11	11 10 10 10 10	14
X2	17	16 15 14 13 12	10 11 11 11 11	14
X1	18	17 16 15 14 13	10 11 11 11 11	15
W	0	1 2 3 4 5	13 14 14 16	0
D	Q5 Q4 Q3 Q2 Q1	P6 P5 P4 P3 P2 P1 N6 N5 N4 N3 N2 N1 C6 C5 C4 C3 C2 C1	X4 X3 X2 X1	Martini 3
organic		levels	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	Beads
water			hyper attractive super attractive attractive almost attractive semi attractive intermediate almost intermediate semi repulsive repulsive almost repulsive super repulsive	843
ion				Pair interactions
ion-others				355,746

No Lorentz-Berthelot rules !

How did we get the new model/parameters?

Defining your universe



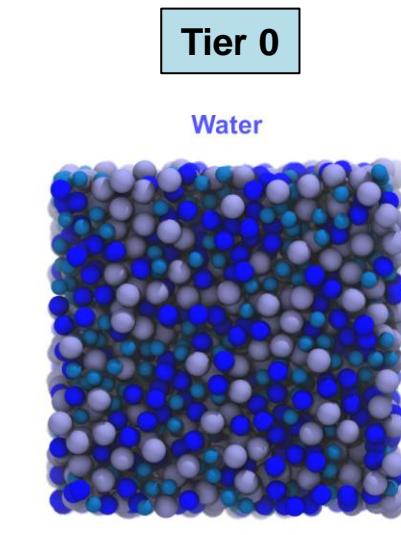
$$V_{\text{non-bonded}} = \sum_{i,j} 4\epsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right] + \sum_{i,j} \frac{q_i q_j}{4\pi\epsilon_0 \epsilon_{rel} r_{ij}}$$

Where V_{IJ} is the Lennard-Jones potential and V_{Coul} is the Coulomb potential.

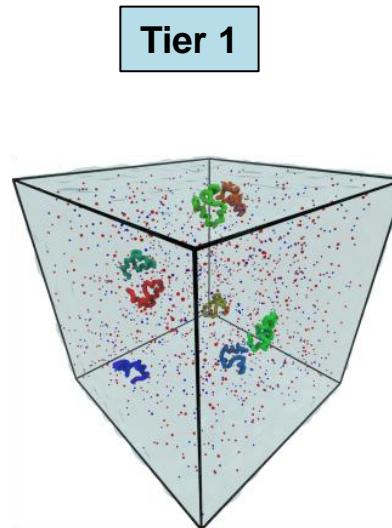
- Choice of Hamiltonian
- # of types and sizes
- # of interaction levels
- Rules for mapping
- Rules for bonds
- Bead assignments
- Interaction matrix

Mainly Calibration

Defining the interaction matrix and interaction levels

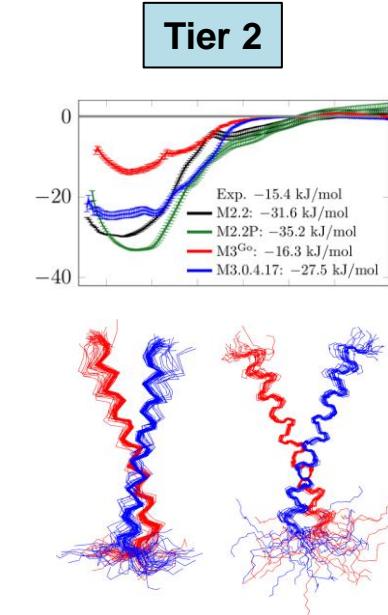


Tier 1



- Quality control**
- quick simulation tests
 - Yes/No answers.
 - avoid parameters with clear problems

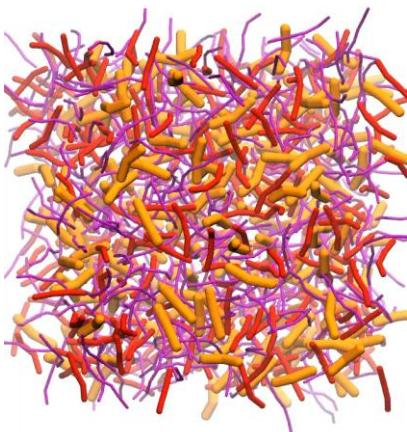
Mainly Validation



- Quantitative tests**
- expensive tests.
 - big/complex systems
 - taskforces and external collaborators

Basic behaviour of the Martini Model

- Well-balanced sizes



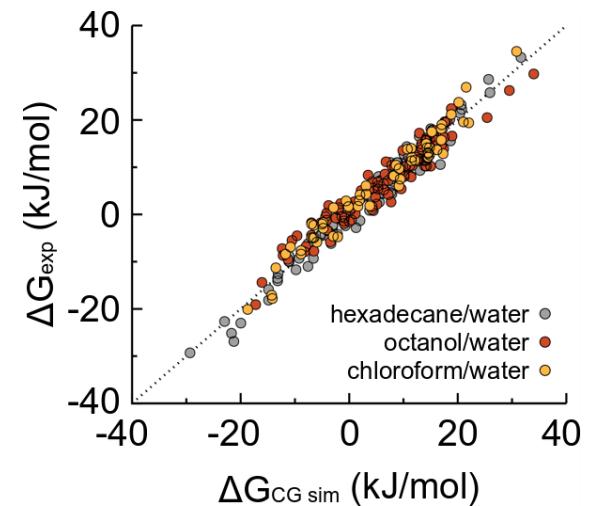
4-1 3-1 2-1

Kirkwood–Buff (KB) integrals

$$G_{ij}(R) = \frac{4\pi}{n_R} \int_0^R [g_{ij}(r) - 1] r^2 dr$$

$$\Delta G_{ij} = G_{ii} + G_{jj} - 2G_{ij} \approx 0$$

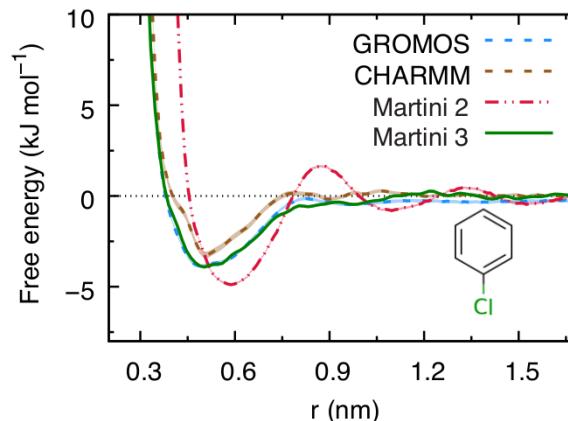
- Improved water/oil partitioning



Souza et. al / Nature Methods, 2021.

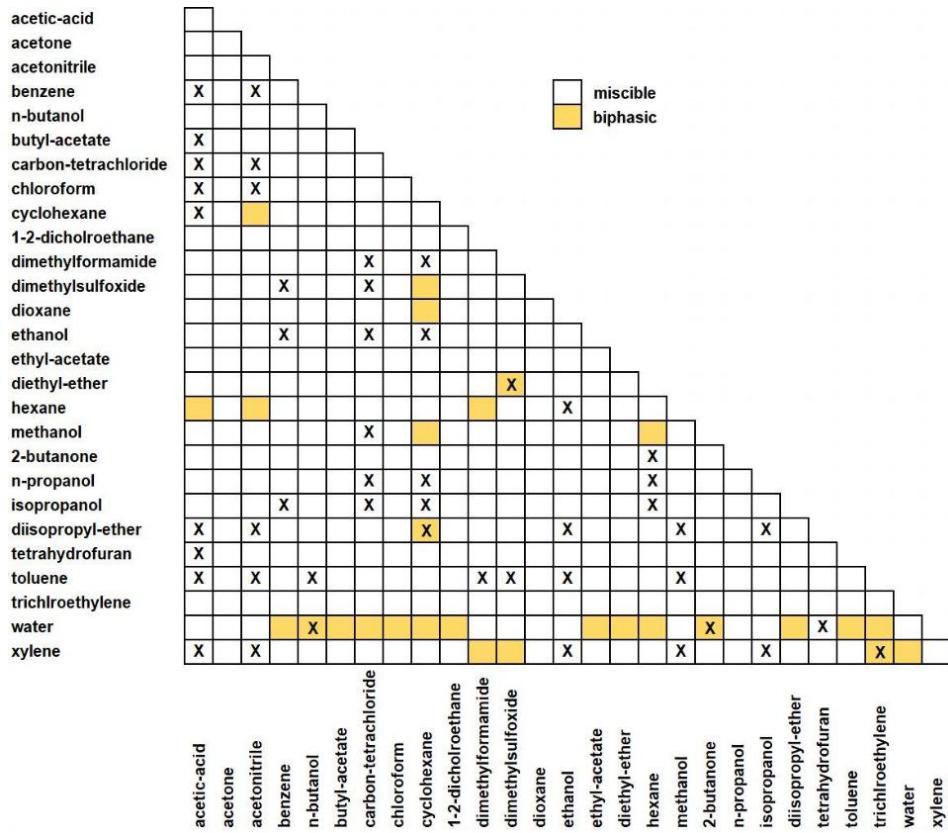
- Improved barriers for dissociation

Alessandri et. al / Adv. Theory Simul. 2022



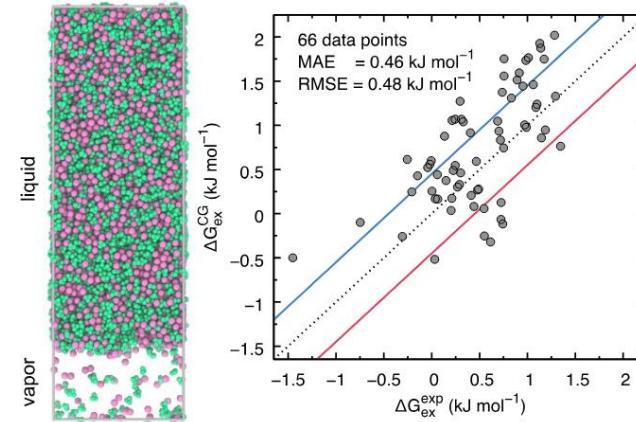
Miscibility and interfacial tension

Martini Miscibility table

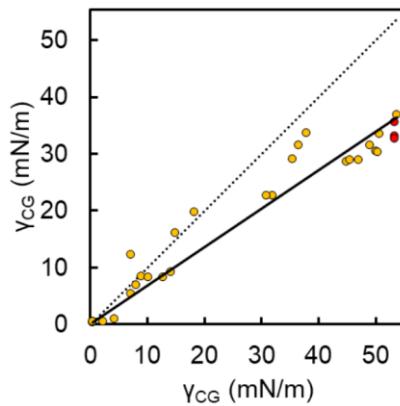


Souza et. al / Nature Methods, 2021.

Miscible binary mixture: Excess free energy of mixing

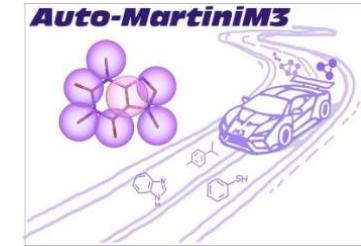
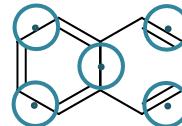


Biphasic binary mixture: Interfacial Tensio



Now that you know the beads and how they interact, so how you create new Martini CG models?

Step 1) Atoms-to-bead mapping:

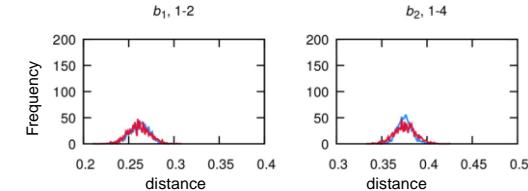


Szczuka et. al JCTC, 2026.

Step 2) Assignment of the Bead chemical type



Step 3) Bonded parameters refinement and numerical stability

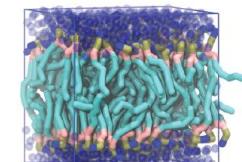
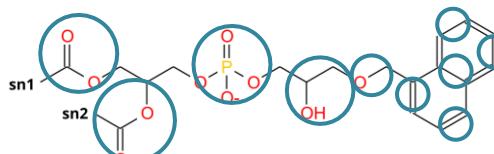


Pereira et. al JCTC, 2025.

Step 4) Model validation and refinement

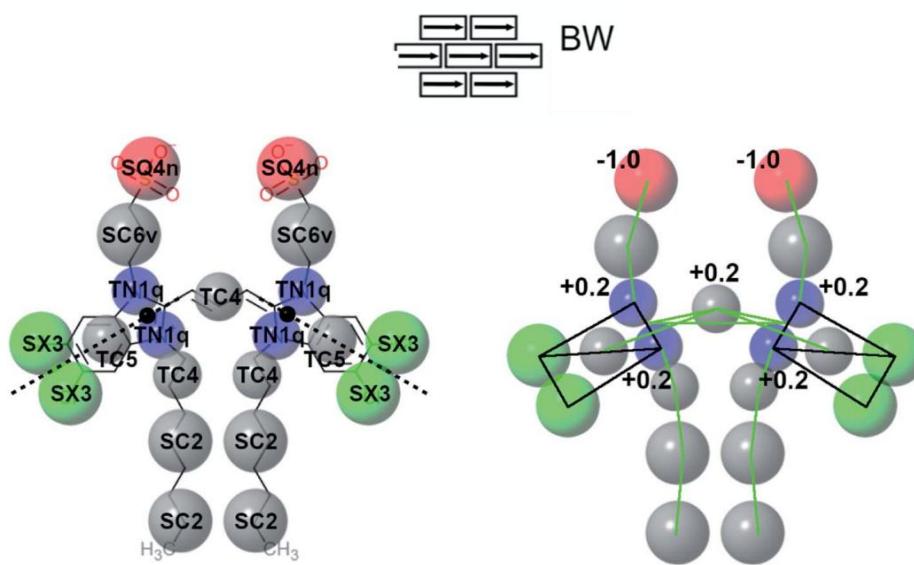
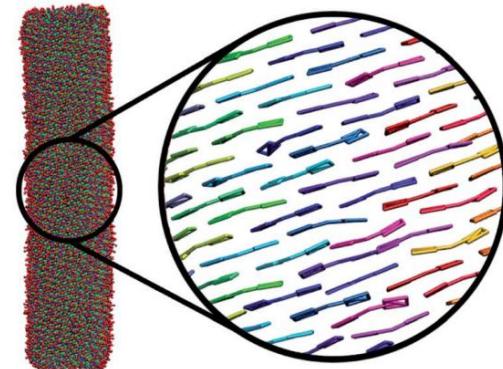


Step 5) Building blocks for more complex molecules and additional validations.

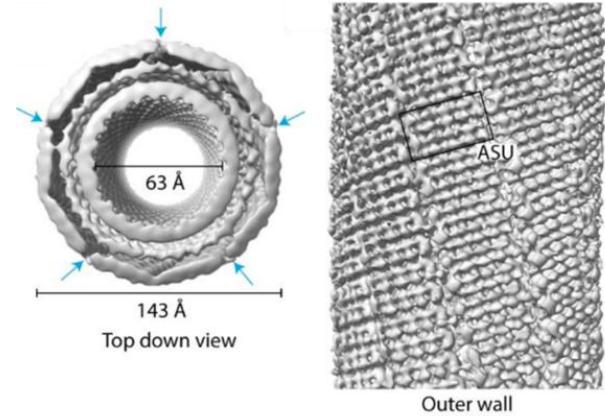
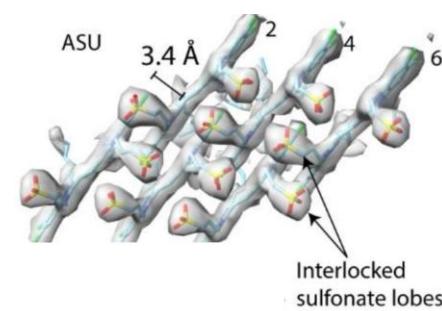


More advanced parametrization strategies can generate very predictive models

- Cyanine dye molecules in a complex double-walled tubular aggregate.
- light-harvesting and energy transport
- What is the organization of this nanotubes?

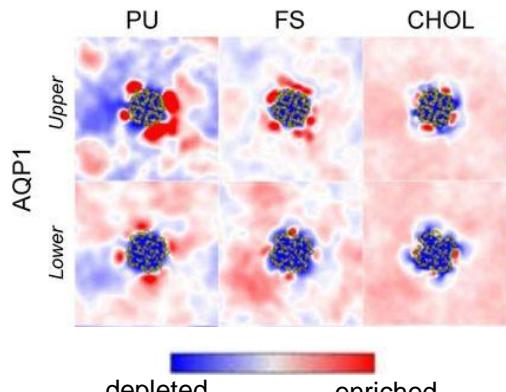


Cryo-EM data show now that the organization is actually brickwall!

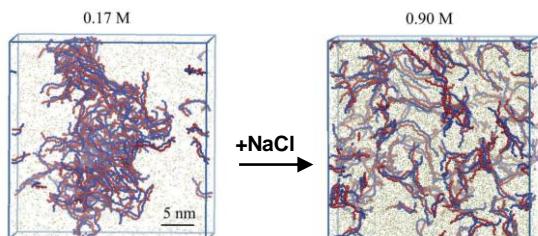


Many successful studies for biological systems

Protein-lipid interactions

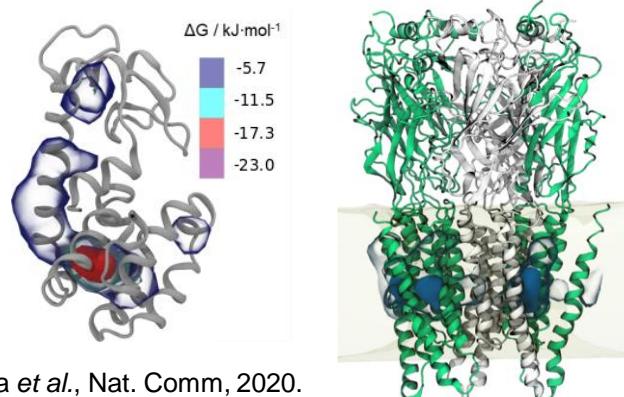


IDPs and biomolecular condensates



Tsanai et al., Chemical Science, 2021.

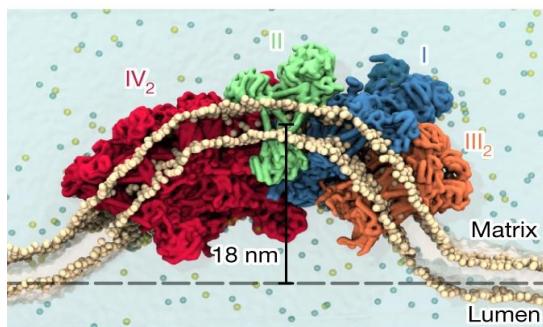
Small-molecule binding to proteins



Souza et al., Nat. Comm, 2020.

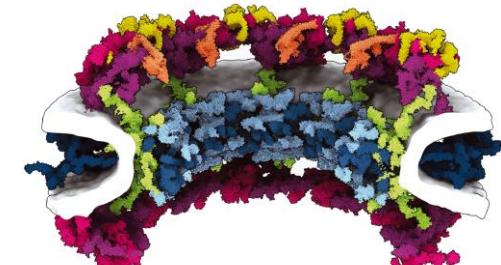
Bartocci et al., Nat. Comm, 2024.

Membrane curvature induced by proteins



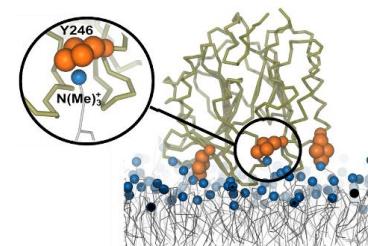
Mühleip et al., Nature, 2023.

Protein nanopores



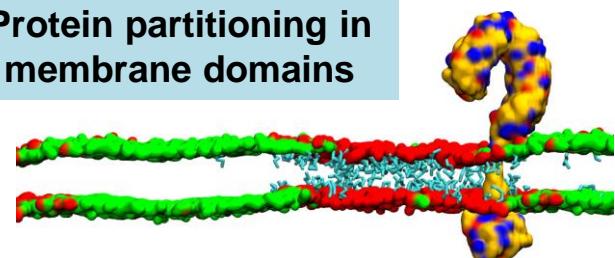
Mosalaganti et al., Science, 2022.

Peripheral membrane proteins



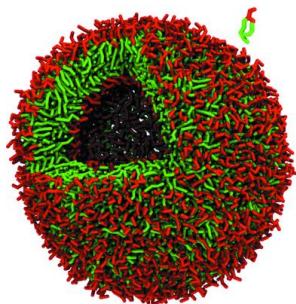
Khan et al., JCTC, 2020.

Protein partitioning in membrane domains

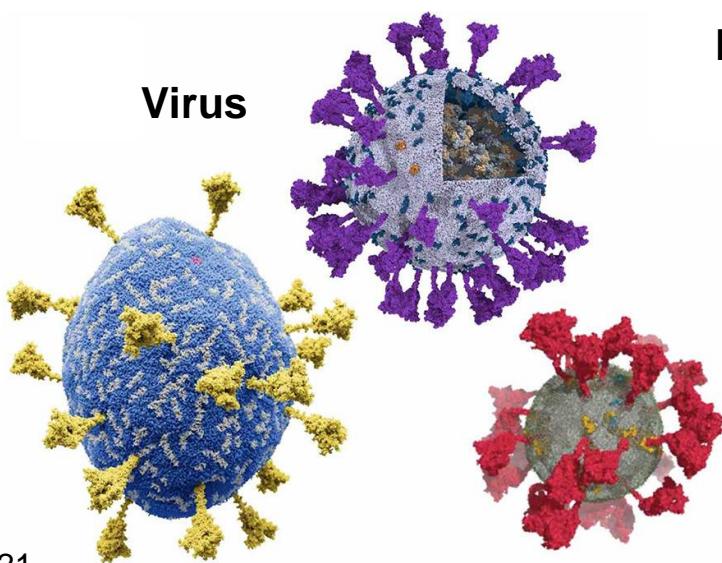


Applications for complex compartments

Vesicles



Virus



Chappa et al *J. Appl. Cryst.*, 2021

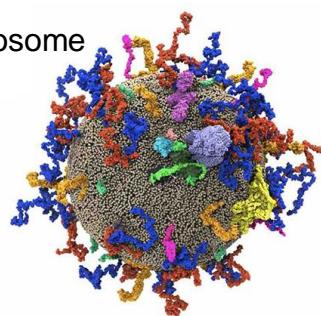
Organelles

Mitochondria



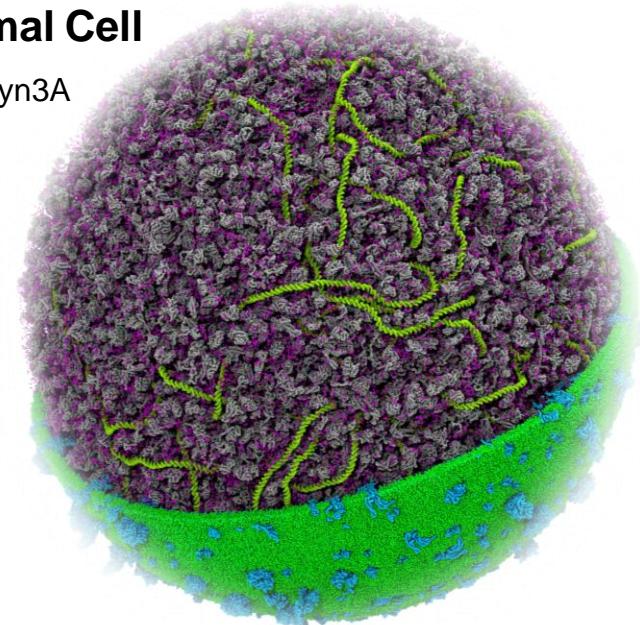
Marrink, Souza et. al *WIREs Comput. Mol. Sci.*, 2023.

Autophagosome



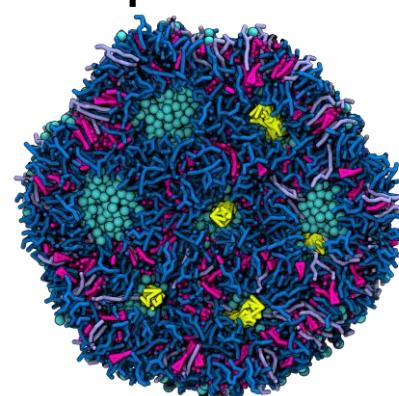
Minimal Cell

JCVI-syn3A



Stevens et al., *Front. Chem.* 2023

Lipid nanoparticles

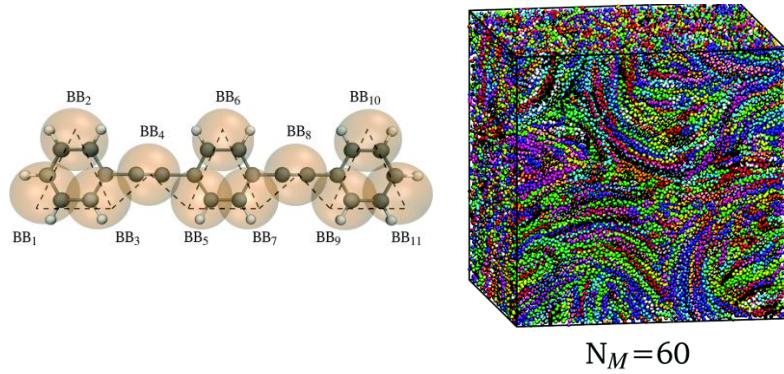


Kjølbye, et al, *JCTC*, 2026

Examples of applications in materials/ complex soft matter

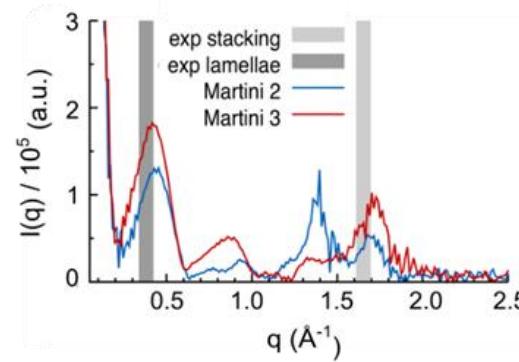
Polymer melts and nematic phases

(poly(para-phenylene ethynylene))



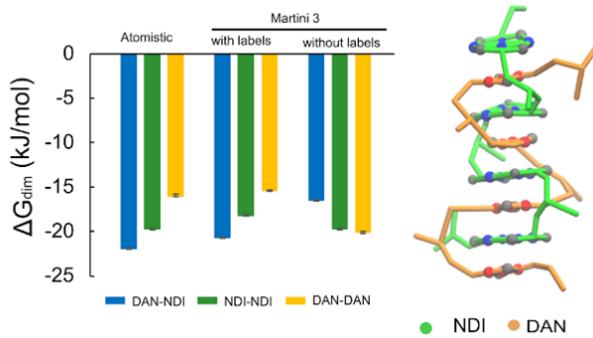
Brosz et. al *PCCP*, 2022.

Better packing in bulk heterojunction morphology



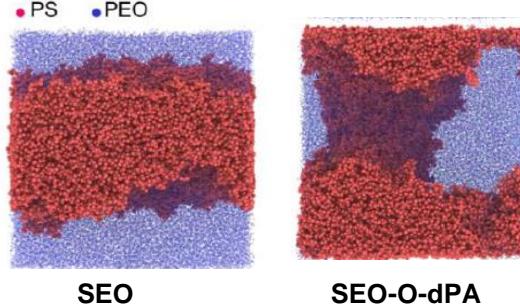
Alessandri et. al *JACS*, 2017
Souza et. al *Nature Methods*, 2021.

Specific interactions in Aedamers

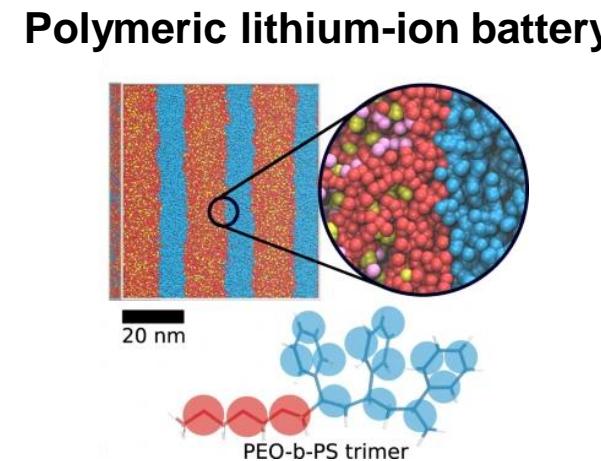


Souza et. al *Nature Methods*, 2021.

Structure in block-copolymers



Lee et. al *Science*, 2024.



Grünewald et. al *Nature Comm.*, 2022.

Take-home message

Coarse-graining

- Simple models that allow affordable, but meaningful MD simulations.

Martini, a general purpose force-field:

- Improved interactions and packing
- Great coverage of chemical space
- Applications in biological, materials and complex soft matter in general



<https://cgmartini.nl/>

Overview of the CG Module in Themosia

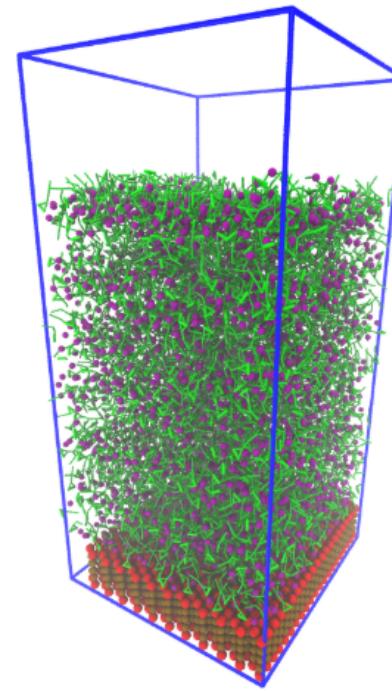
Course Scope and Objectives

The main objective of this course is to provide participants with **practical experience** in coarse-grained molecular simulations of interfaces.

Topics covered include:

- Fundamental principles of **coarse-graining**
- Overview and philosophy of the **Martini 3 force field**
- Modeling **solid surfaces** (as silica and graphite) in CG simulations
- Coarse-grained representations of **imidazolium-based ionic liquids**
- Construction of **solid-ionic liquid interfaces**
- Running CG molecular dynamics simulations
- Analysis of **interfacial and bulk structure**
- Interpretation and limitations of CG results

The emphasis is on **model construction, physical insight, and critical interpretation**, rather than force-field development.



Key question: Can surfaces induce long-range organization in ionic liquids?

First time anyone are simulating these systems in CG resolution!

The materials for the CG Module

<https://github.com/paulocts/themosia2026-cg-interfaces>

⊖ THEMOSIA Winter School 2026

⊖ Coarse-Grained Modeling of Solid–Ionic Liquid Interfaces

This repository contains the hands-on course material for the THEMOSIA Winter School 2026, focused on coarse-grained (CG) molecular modeling of solid–ionic liquid interfaces using the Martini 3 force field.

The course combines lectures and hands-on tutorials, guiding participants through the construction, simulation, and analysis of CG models for interfaces involving silica, graphite, and imidazolium-based ionic liquids.



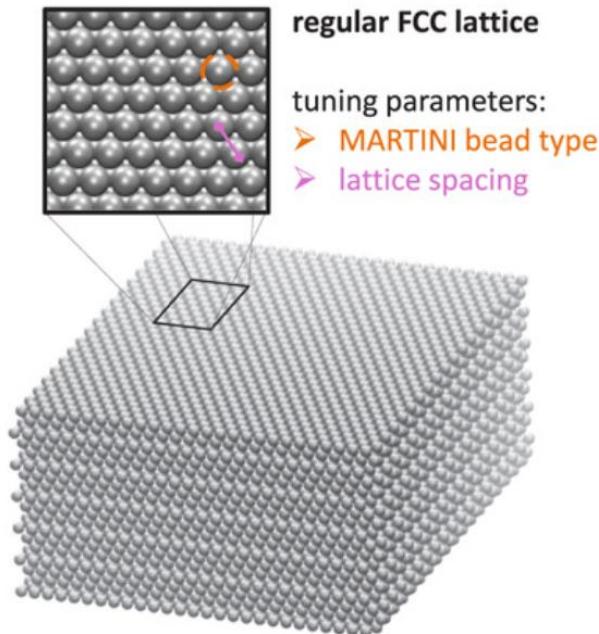
Key References

- Souza, P.C.T. et al. [Martini 3: a general purpose force field for coarse-grained molecular dynamics](#). Nature Methods 18, 382-388 (2021).
- Marrink, et al. [Two decades of Martini: Better beads, broader scope](#) WIREs Computational Molecular Science, 13(1):e1620.(2023).
- Vazquez-Salazar, L.I. et al. [Martini coarse-grained models of imidazolium-based ionic liquids: from nanostructural organization to liquid–liquid extraction](#). Green Chemistry , 22, 7376-7386 (2020).
- Shrestha, R. et al. [Martini 3 Coarse-Grained Models for Carbon Nanomaterials](#) J. Chem. Theory Comput. 2025, 21, 18, 9035–9053 (2025).
- Cambiaso, S. et al. [Solid–liquid interfaces in MARTINI 3: Modeling approaches and the case study of silica surfaces in water](#) Surfaces and Interfaces, 72, 106997 (2025).
- Alessandri, R. et al. [The Martini Model in Materials Science](#) Advanced Materials, 33, 2008635 (2021).

Hands-on 01 – Building Solid Surfaces

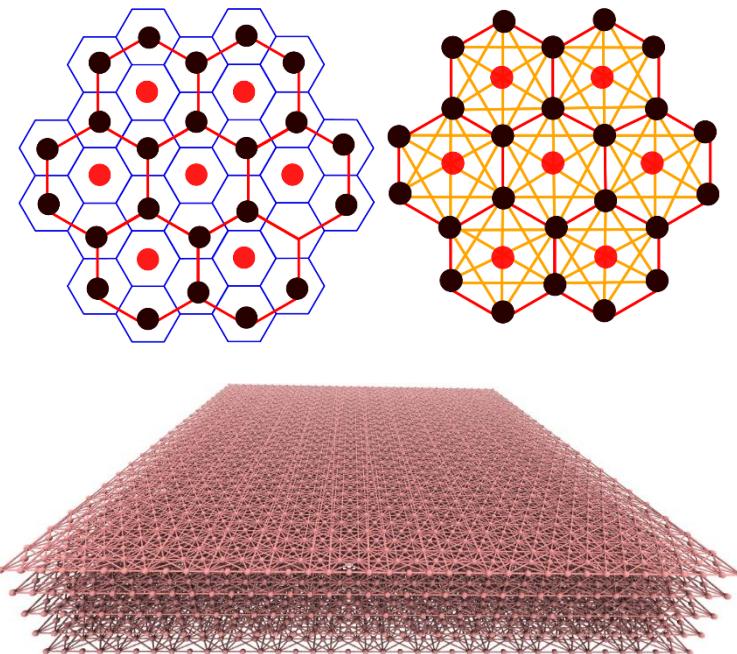
Silica: polar / hydrophilic surface

- Top-down mesoscopic surface
- Property-driven CG slab
- Tunable surface parametrization
- Effective-medium solid model



Graphite: apolar/ hydrophobic surface

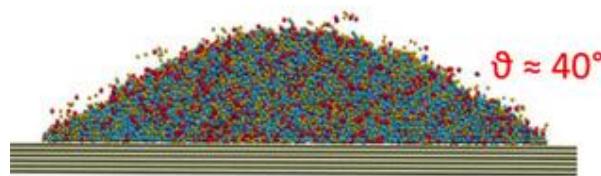
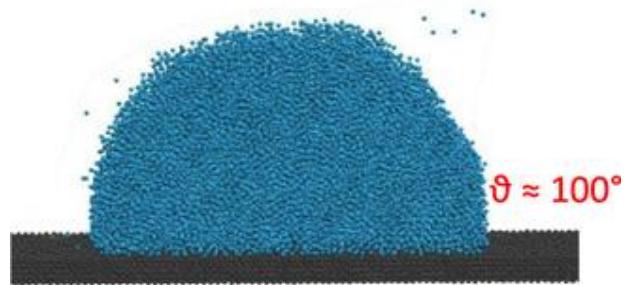
- Use Bottom-up principles
- Structure-based carbon slab
- Explicit graphene stacking
- Geometry-preserving CG solid



Hands-on 01 – Building Solid Surfaces

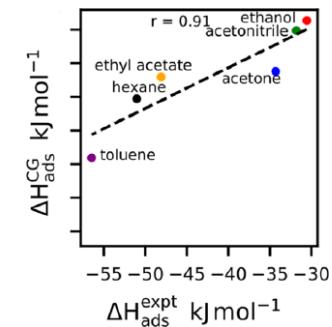
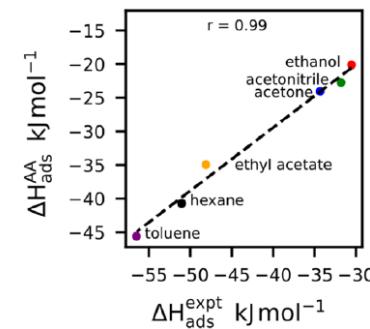
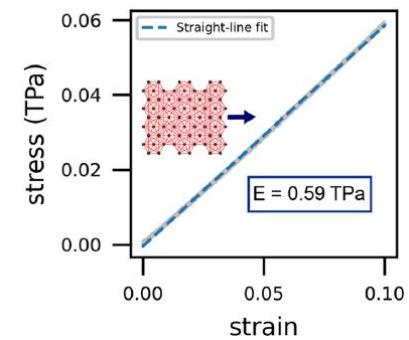
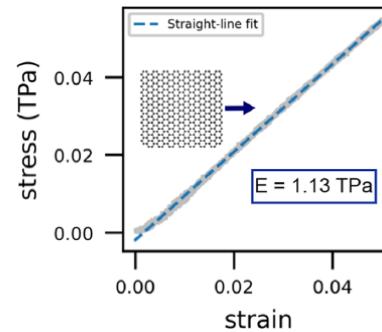
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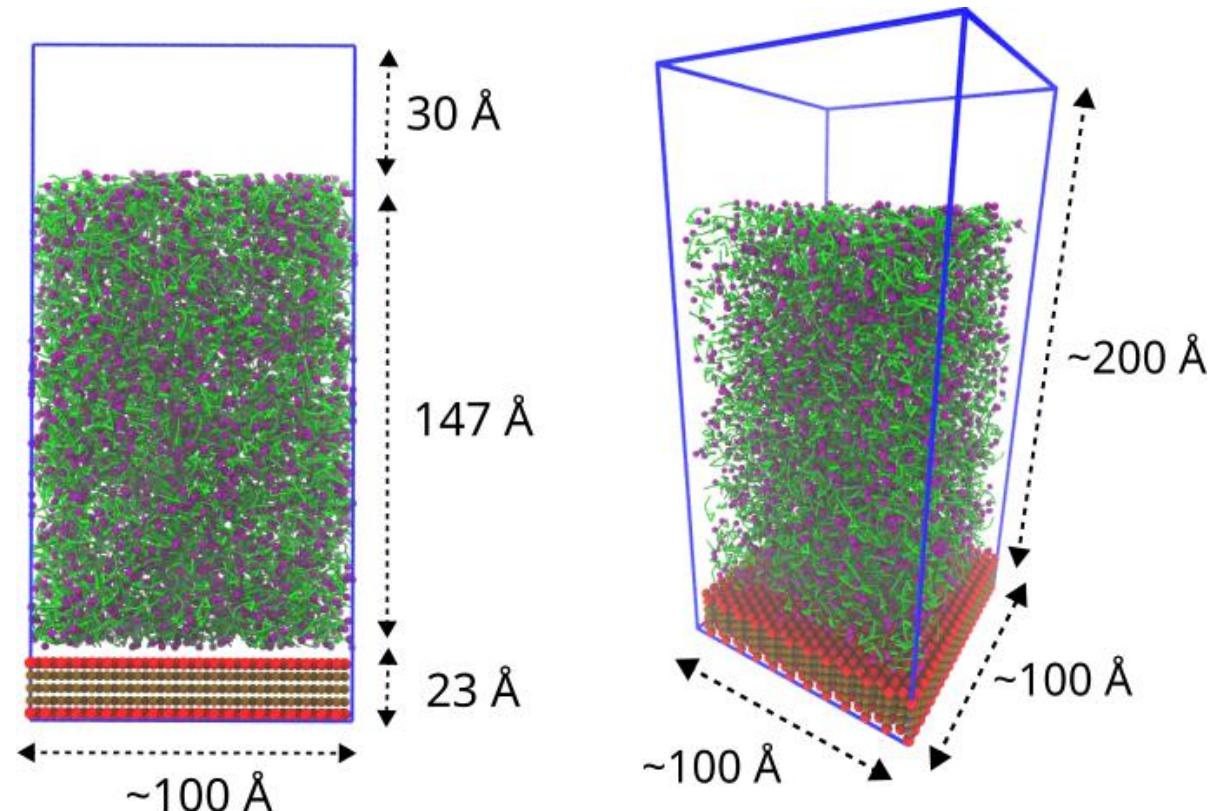


Hands-on 02 – Building Solid–Ionic Liquid Interfaces

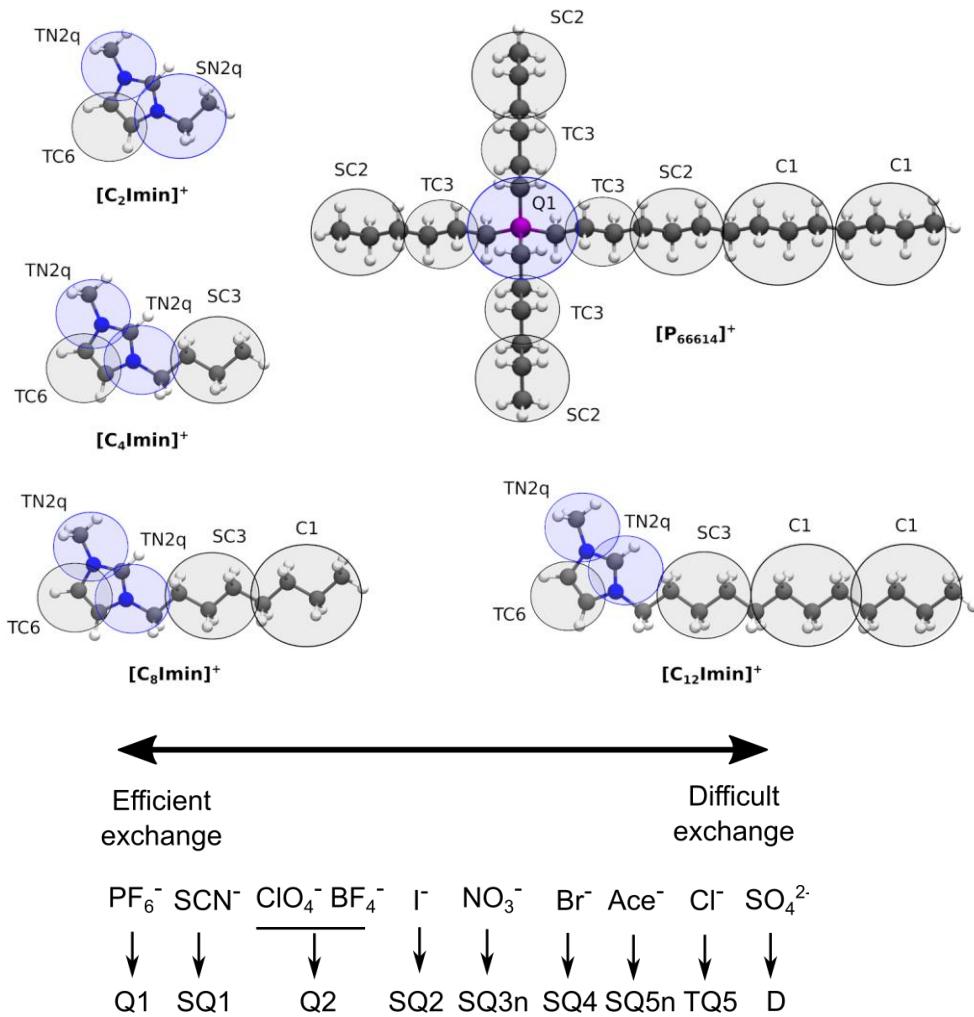
PACKMOL



- Explore different box sizes and compositions



Ionic liquids – Bead Types



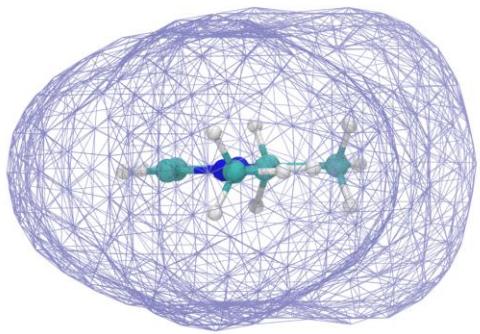
Partial charges label (q)

- Large charged molecules
- partial charges distributed between beads.
- Computed via QM preserving dipoles/quadruples

Q beads

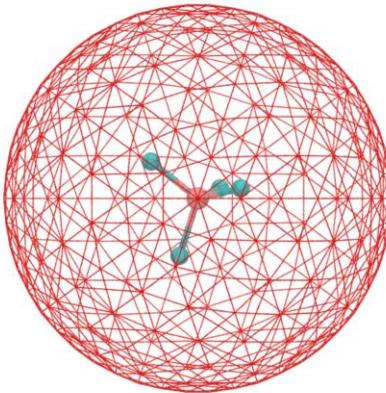
- Smaller ions/charged molecule charge value ± 1 in one bead.
- Different types and sizes capturing differences in “hydrophilicity”

Ionic liquids – Molecular Volume and Density

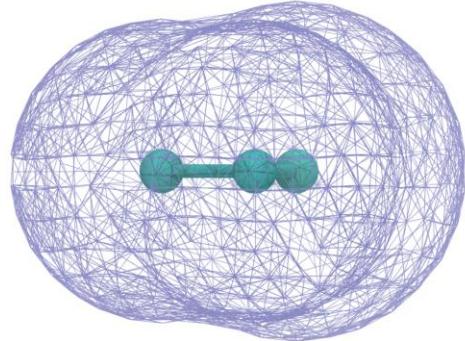


$[C_2\text{ mim}]^+ = C2$

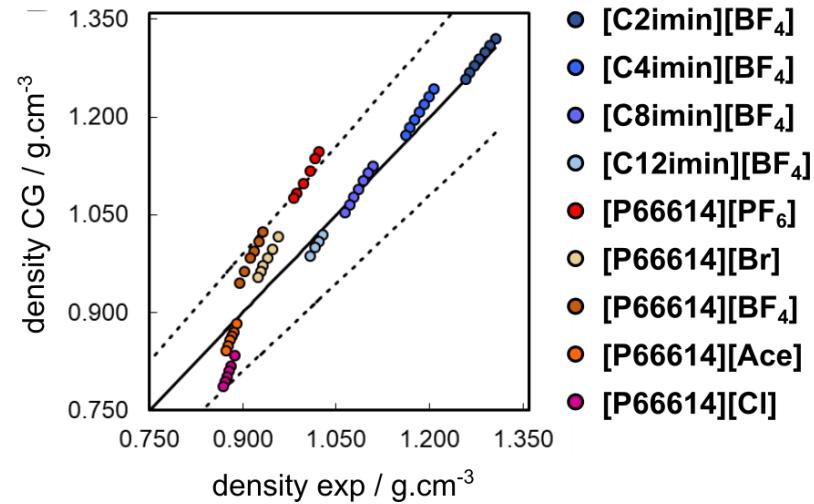
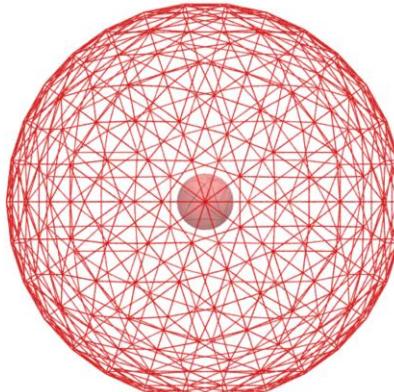
Atomistic



BF_4^-



Coarse-Grained

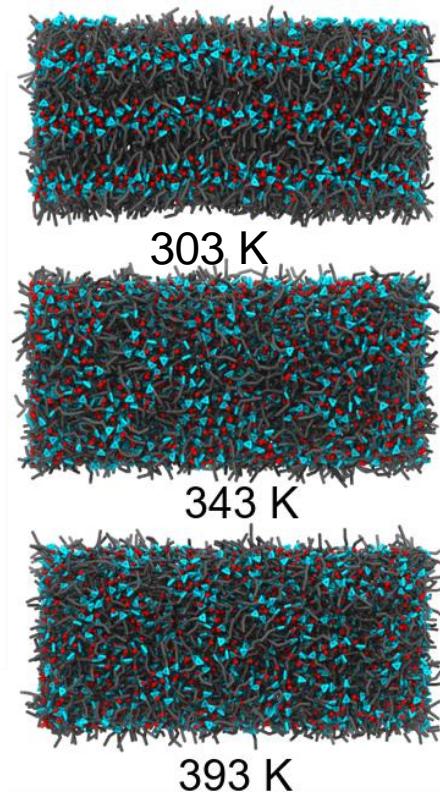
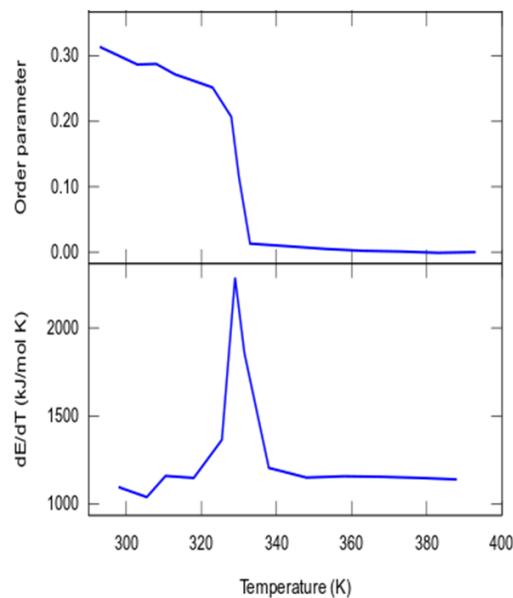
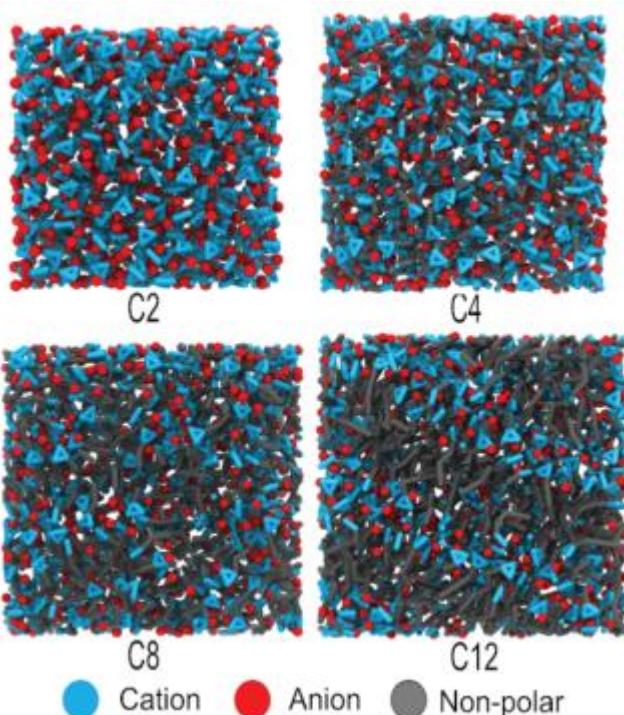


Q beads

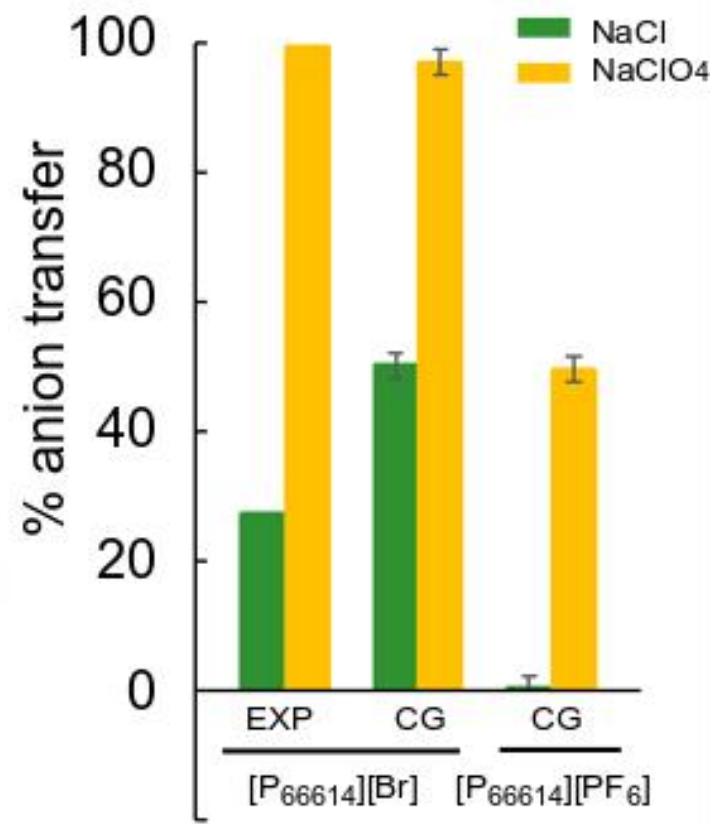
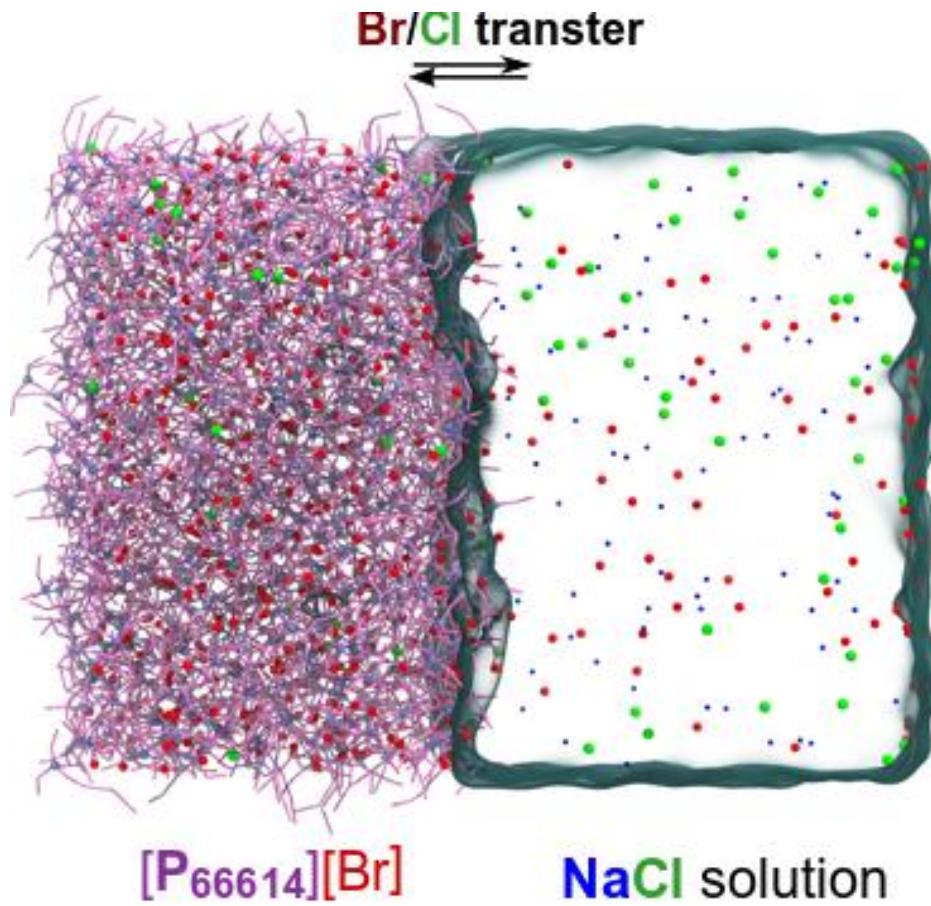
- Very good, with improvements for large charged molecules.
- Less improvements of size (in particular for anions modelled only with 1 Q-bead)

Ionic liquids - Temperature dependent phase transition

- Non-homogeneous IL depending on the tails length.
- Transition from lamellar to isotropic phase for C12, in agreement with experimental findings

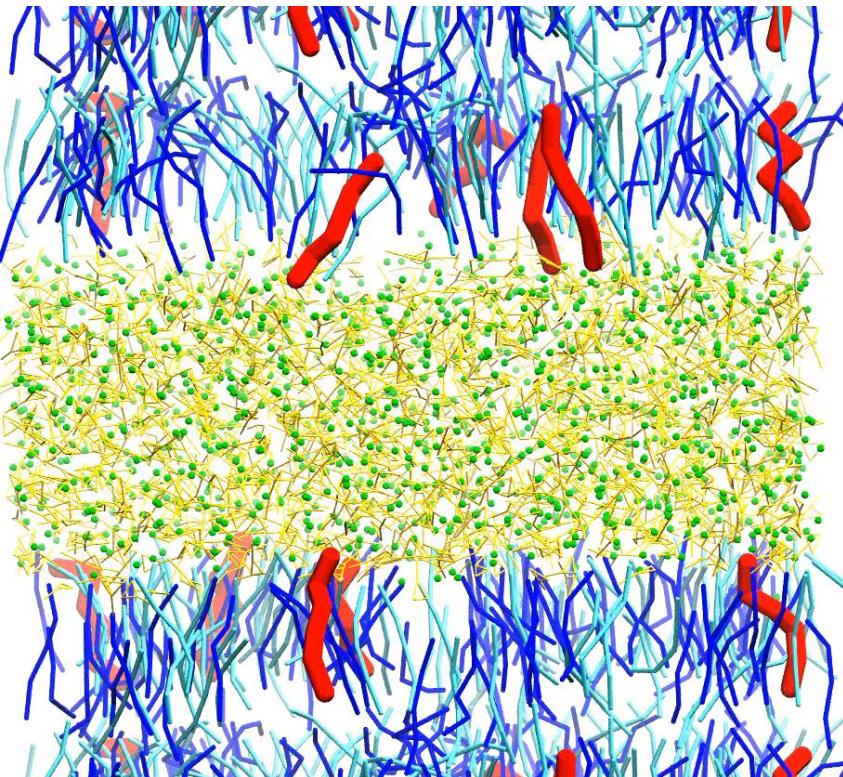


Ionic liquids and ion transfer in relation to salt water solution



Ionic liquids – Extraction 2

Omega 3 from Fish Oil Model

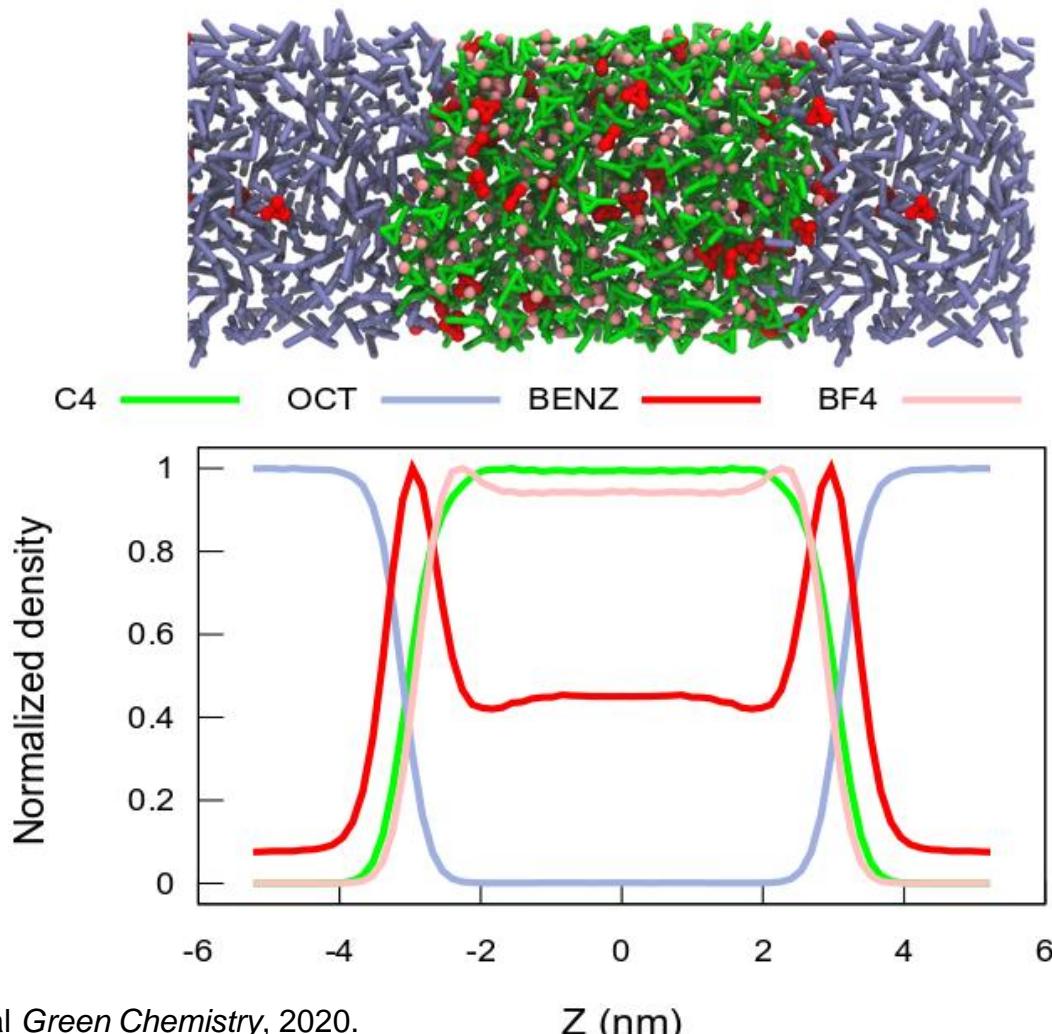


- Fish oil model (salmon):
 - 48% **palmitic acid**
 - 48 % **oleic acid**
 - 4% **docosahexaenoic acid**
(omega 3)
- Ionic liquid: **C4 + BF4**
- Simulation of the extraction of docosahexaenoic acid from fish oil model during 1 μ s.
- Co-solvent effect in the miscibility with oil

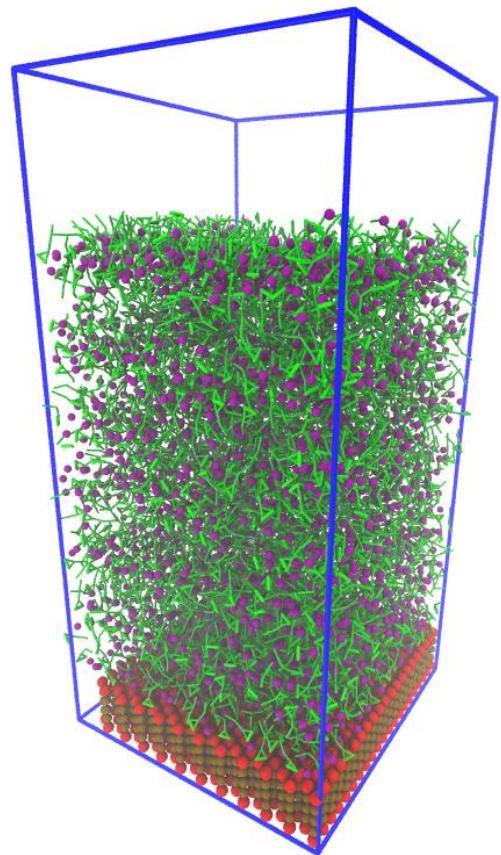
Ionic liquids – Extraction

Aromatic rings from Petroleum Oil Model

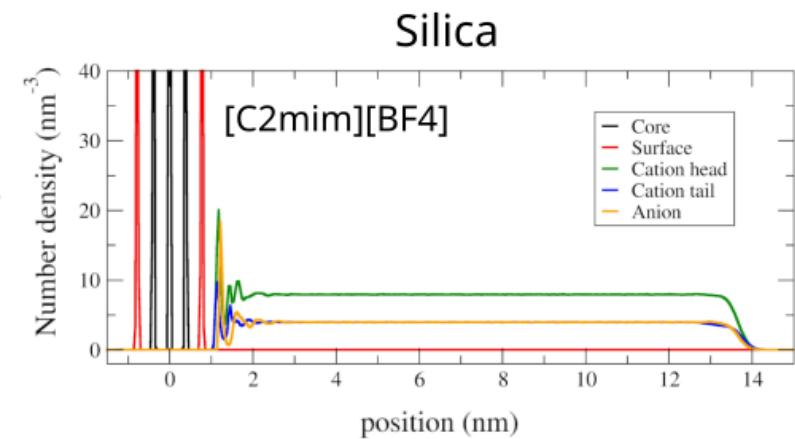
- Benzene is selectively enriched in the IL phase, in agreement with experimental findings
Ferreira et al. Ind Eng. Chem. Res. 2012



Hands-on 03 – Running CG MD Simulations and Analysis



FAST. FLEXIBLE. FREE.
GROMACS 



Evaluation for the Master Students

What to submit: A mini-report (PDF), maximum 1–2 pages (total of 3 points)

Suggested content of the mini-report:

- **At least one plot (1.0 pt)** e.g. density profile(s) along z, including a comparison of two systems (*examples: C2 vs C8 on silica, or silica vs graphite for the same ionic liquid*).
- **Short interpretation (1.0 pts)**, answering briefly:
 - Do you observe layering / ordering at the interface?
 - How does it change with alkyl chain length and/or different surfaces?
- **Atomistic vs coarse-grained MD discussion (0.5 pt)** : Discuss advantages and limitations of CG MD compared to atomistic MD
- **Perspective (0.5 pt)** : suggest one idea to improve the CG model or setup if you identify limitations.

Submission deadline - Friday 23/01/2026 — 17:00

Thanks! Merci!

