

## Third Year Report (2023/2024)

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### Research

I study condensed and soft matter systems at submolecular resolution using computational tools like Molecular Dynamics (MD) and enhanced sampling techniques. My Ph.D. work is part of the SUNSHINE project (EU H2020, grant no. 952924), which develops "safe and sustainable by design" strategies for high-performance nanomaterials. The project involves industrial, experimental, and theoretical partners. As a computational team, we focus on how the physico-chemical properties of nanocomposites impact their stability, nanoparticle release, and interactions with living organisms.

One SUNSHINE case study focuses on a nanocomposite used in construction, featuring silica nanoparticles (NPs) coated with silanes. In my first Ph.D. years, I studied silane-functionalized surfaces in various solvents. More recently, I've concentrated on methodological aspects of coarse-grained simulations of solvents and solid/liquid interfaces. We developed a strategy to address challenges in simulating surface-water interfaces with a popular coarse-grained force field and characterized its prediction of water surface tension (Section A).

Another SUNSHINE case study aims to develop safer, sustainable flame-retardant additives for the automotive sector, focusing on graphene oxide functionalized with chitosan. Carrying on last year's work, I continued developing a coarse-grained model of chitosan (Section B).

### Section A - Tips & Tricks for Simulating Surface-Water Interfaces with MARTINI 3

To investigate the interactions of metal oxide nanoparticles and oxide surfaces with the biological environment, I am developing, in collaboration with Prof. Giacomello's group at the University of Rome La Sapienza and Dr. Luca Monticelli at IBCP/CNRS in Lyon, a general strategy to simulate surface-water interfaces.

*Challenges in the simulation of water-surface interfaces.* Coarse-grained (CG) models, in which a group of atoms represents a single interaction center, are relevant tools in Molecular Dynamics simulations since they allow us to study systems with extended time and length scales compared to models with atomistic resolution. The Martini forcefield[1], very popular for biomolecular simulations, describes the non-bonded interactions with a 12-6 Lennard-Jones (LJ) potential and relies on a mapping scheme that groups 2, 3 or 4 heavy atoms into a single interaction center called bead. Martini also finds applications in materials science, with several polymer models available. However, simulating surfaces, especially metals and metal oxides, demands meticulous calibration, given that the top-down philosophy at the basis of the parameterization of the forcefield does not specifically target solid-state properties. A key challenge is reproducing a physically sound degree of ordering of liquid at solid surfaces. At solid-liquid interfaces, layering up to about twice the solvent diameter is a known effect, observed in experiments and explained by the theory of solvation forces[2]. At a solid-liquid interface between LJ materials with the same LJ  $\sigma$  parameter, the effect can be exacerbated by the possibility of growing ordered structures. In coarse-grained LJ models, resolution limits arise when the thickness of the real liquid's ordered layer is comparable to the size of the CG solvent beads, leading to unphysical layering.

*Guidelines for parameterizing and simulating surface-water interfaces.* We found two approaches to prevent the formation of ordered water phases on regular, compact coarse-grained surfaces: the first one exploits the introduction of disorder in the surface beads, whereas the second mitigates layering by using mixtures of differently-sized water beads. Indeed, water is available in three different sizes, i.e., regular (W) representing a cluster of four water molecules, small (SW) (three water molecules), and tiny (TW) (two water molecules). The first approach has the advantage of relying solely on regular water, thereby reducing the number of species involved and the total number of particles in the system. However, it is effective only for substrates that do not interact too strongly with water. On the contrary, using mixtures of differently-sized beads allows one to prevent water ordering regardless of the type of substrate, albeit at the cost of increasing the number of particles in the system. We then developed a strategy to parametrize metal oxide surfaces, using an implicit surface model with a fine-tuning of the hydrophobicity of the substrate by varying the density of the beads on the surface. As a test

case, we modeled an alkyl chains-grafted silica with an implicit surface, using the contact angle as a target for the parametrization.

The results of this part of the work are reported in a paper which is close to submission.

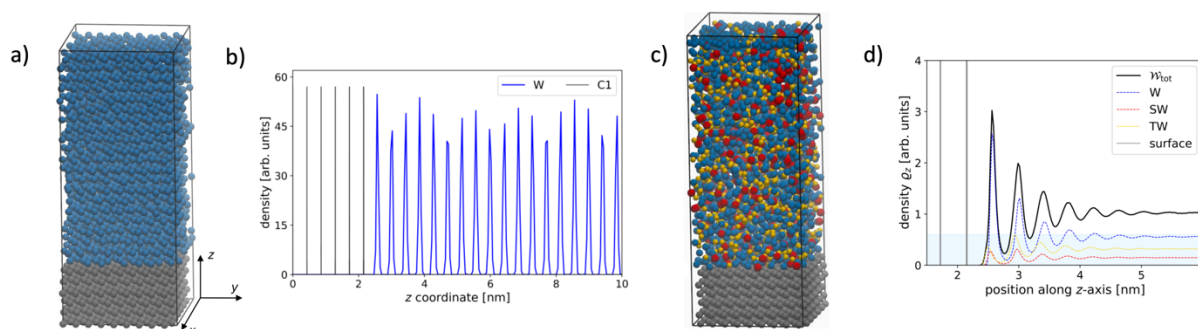


Figure 1. a) Snapshot of a simulation of regular water (W) on a surface showing that layering affects the whole water bulk, with equally spaced peaks appearing in the z density profile in panel b). c) Snapshot of a simulation of a mixture of differently sized water beads, in which only a few layers close to the surface are present (see panel d).

A second methodological work focused on the characterization of the surface tension of Martini water as a function of its composition (different mixtures of W, SW, and TW beads). This work, published on the Journal of Chemical Physics (<https://doi.org/10.1063/5.0221199>) in collaboration with the group of prof. A. Giacomello (University of Rome, Sapienza), will not be discussed in detail here.

## Section B - Development of a coarse-grained model for chitosan

Carrying on the work of my second Ph.D. year, I am developing a CG model for chitosan, a linear polysaccharide derived from chitin, which consists of a random distribution of  $\beta$ -(1 $\rightarrow$ 4) D-glucosamine (GlcN) and its acetylated derivative, N-acetyl-D-glucosamine (GlcNAc)[3].

The model is compatible with the latest Martini forcefield. Building a CG model involves three key steps: mapping atomistic structures to CG beads, parametrizing bonded interactions (within monosaccharides and polymer sequences), and selecting appropriate bead types. Due to the complexity of chitosan, which has three distinct moieties, we focused on mapping and bonded interactions, crucial for capturing polysaccharide stiffness. By reproducing bond, angle, and dihedral distributions from atomistic data, our model accurately predicted the radius of gyration for chitosan chains with different compositions and sizes, aligning well with experimental results. We validated the model in solvents with varying ionic strengths and pH and are now studying chitosan interactions with lipid monolayers for biomedical applications.

A paper is in preparation. Within the SUNSHINE project, our model polymer will be functional to the study of chitosan-graphene oxide interactions. This work has been performed in collaboration with the group of Luca Monticelli (IBCP/CNRS, Lyon), where a model of graphene oxide is being built and validated.

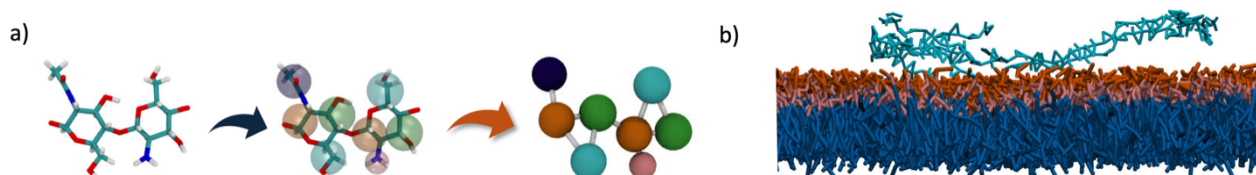


Figure 2. a) Mapping procedure of an atomistic chitosan dimer (left) into its CG corresponding (right). b) Chitosan chains (cyan) interacting with a DPPG lipid monolayer (blue: hydrophobic tails, pink and red: anionic heads).

## Attended courses

- Machine Learning Crash Course (MaLGA Center, DIBRIS and DIMA Departments, June 2024, 3 CFU)

## Conferences

- SUNSHINE 3<sup>rd</sup> annual meeting, Sofia, Bulgaria, 12-13 March 2024.

- XXVII Congresso Nazionale SIBPA 2024, Genoa, Italy, 16-20 June 2024 (Poster: *In silico study of chitosan interactions with lipid bilayers*, **best poster prize**).

## Publications

- Cambiaso S, Rasera F, Tinti A, Bochicchio D, Grosu Y, Rossi G, Giacomello A, *Local grafting heterogeneities control intrusion and extrusion in nanopores*, Communications Materials, 5(1), 100, 2024.
- Iannetti L, Cambiaso S, Rasera F, Giacomello A, Rossi G, Bochicchio D, Tinti A, *The surface tension of Martini 3 water mixtures*, The Journal of Chemical Physics, 161(8), 2024.

## References

- [1] Souza, P. C. T. et al., *Nat. Methods* **2021**, 18 (4), 382–388.
- [2] Israelachvili J.N., *Academic Press*, Intermolecular and Surface Forces, 2011
- [2] Rinaudo, M. et al., *Prog. Polym. Sci.* **2006**, 31 (7), 603–632.