SIMPA-Project:

Selective sugars Interactions with peptide receptors: gas phase Models and Pharmaceutical Applications

3 years PhD position at the Theoretical Biochemistry Laboratory,

Institut de Biologie Physico-Chimique, 13 rue Pierre et Marie Curie, Paris France

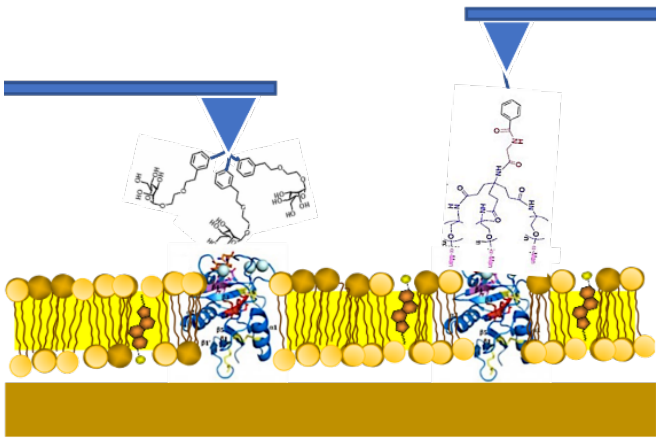
Lead PI for molecular modeling: Dr Sophie Sacquin-Mora (sacquin@ibpc.fr)/ CNRS UPR 9080 / Theoretical Biochemistry Laboratory

Experimental teams at Université Paris-Saclay: Pierre Çarçabal, ISMO, Jean-Philippe Michel, IGPS, David. Bonaffé, ICCMO

Short description

The SIMPA project (funded by the ANR) aims at **studying the interactions between sugar and peptides, ranging from gas phase models to full size pharmaceutical molecules, especially between Mannose and Mannose Receptor (MR) proteins** that are exploited in the context of targeted Photo Dynamic Therapies (PDT) by applying complementary experimental and computational physical chemistry approaches to study molecular interactions between sugars and peptides with fundamental and applied perspectives

Our goal to investigate the Sugar-MR interactions at the microscopic scale. The selectivity, strength and specificity of specific molecular recognition between the PS models and receptor proteins inserted in artificial membranes or exposed at the surface of living cells, is approached by surface science methods, at the scale of molecular subunits at the IGPS. At ISMO, the microscopic strategy is pushed one level further by studying the structural properties of complexes made of models of the subunits, either isolated in the gas phase or micro-solvated, which will be interrogated at the level of each non-covalent interaction, molecular group by molecular group. At ICMMO, the models will be synthesized and their conformational dynamics properties in an aqueous environment will be investigated by NMR spectroscopy.



The experimental work will be complemented by state-of-the-art molecular dynamics computational work, performed at LBT on the models in various environments, from the gas-phase models, to the full size systems studied at IGPS, up to the PS in interaction with a receptor protein, embedded in an artificial bilayer.

The candidate will run all-atom classical Molecular Dynamics simulations on the receptor/sugar assembly, and the analysis of the resulting trajectories will bring further insight on the dynamics and stability of the interface between the protein and the mannose group. In particular, this will give a detailed picture of the contacts formed between atoms along time, thus enabling to understand the strength of the interactions observed experimentally. This information will guide the design of new models displaying enhanced specificity for the target DC-SIGN receptor compared to MRC1. If necessary, the candidate will also develop a larger model, with the protein embedded in a lipid bilayer, using coarse-grain simulations (with the MARTINI model). Both all-atom and coarse-grain approaches will benefit from recent developments in force-field parametrization, which have made the simulation of large systems including sugar groups easily accessible. All the results from this task will systematically be compared to the experimental data obtained by the IGPS partner.

Laboratoire de Biochimie Théorique (http://www-lbt.ibpc.fr/)

The LBT has a long-standing expertise in state-of-the-art computational modeling of biomolecular systems. In particular, the group has recently focused out research on protein interactions that include disordered partners, proteins immobilized on solid surfaces, and the modeling of large biomolecular assemblies and their dynamics.

Practical information:

Qualifications: The candidate should hold a Masters degree (or plan to finish their degree in 2024) in chemistry or physics or Bioinformatics, with a strong background in modeling of biomolecular systems. Experience in classic modeling tools such as Molecular Dynamics is expected. The candidate is also expected to:

- be highly motivated by conducting a collaborative research project with experimentalists.
- have good communications skills in English (reading, writing and speaking).
- be able to present clearly their research results.
- be familiar with Linux operating system.
- have an experience with programming languages (C, Fortran, Python, Perl, bash,…)

When ? The deadline for sending the application is May 20th. The candidate should be available for starting the thesis on October 1st 2024.

How to apply: Applications should be sent to **sacquin@ibpc.fr** as early as possible.

The application should include:

- a detailed Curriculum Vitae
- 1 recommandation letter
- a motivation letter describing why you should be considered for this position.