Funded PhD Thesis Biophysics/Chemistry

Groups of Jérôme Hénin and Guillaume Stirnemann, CNRS,
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Response of membrane proteins and lipid bilayers to high pressures characterized by atomistic simulations

Subject High pressure can be used experimentally to modulate the conformational landscape of proteins, in particular in NMR experiments that can capture the structural and dynamic changes upon changes in pressure. On a broader perspective, understanding the impact of pressure on protein structure and dynamics is important to get a better comprehension of the evolutionary pathways that have led to pressure resistance in some organisms that thrive in extreme pressure conditions.

Preliminary experimental results of our collaborators (E. Lescop, ICSN, and Laurent Catoire, IBPC) suggest that high pressure affects both the local dynamics of transmembrane proteins and their interactions with lipids. All-atom simulations are the ideal tool to produce a high-resolution description of these phenomena, leading to better physical understanding. The goal of this project is to use molecular dynamics simulations to model the pressure response (0-2500 bar range) of transmembrane proteins embedded in lipid membranes. Both the protein dynamics and the lipid bilayer response will be characterized in detail, and results will be compared with experimental observables, validating the simulation approach in the process.

Methods The candidate will gain strong experience in molecular dynamics simulations (no previous experience is required), using a well-employed and distributed code, as well as advanced techniques to accelerate the sampling of the conformational space of biomolecules. Tools: Molecular dynamics simulations with state-of-the-art RNA forcefields; enhanced sampling methods; programming tools, and simulation analysis tools.

Research environment Research will take place in the Theoretical Biochemistry Lab of CNRS' Institute of Physical-Chemical Biology, with Jérôme Hénin and Guillaume Stirnemann. It is located in the very stimulating research environment of the Latin Quarter, in the heart of Paris. Our group has extensive experience in applying advanced simulation and theoretical tools to tackle a variety of questions, ranging from the mechanical and thermal stability of proteins to the modulation of membrane receptors by lipids and other molecules. We have access to state-of-the-art computing facilities that include a local mesoscale computer cluster. More information about the lab and the research groups are available here: www-lbt.ibpc.fr/people/henin and www-lbt.ibpc.fr/people/stirnemann. This project will take place within a funded collaboration between our lab and two experimental labs specializing in high-pressure NMR of membrane systems, with frequent interactions between the three partners.

Requirements Candidates should have a Master's degree in Physics, Chemistry, Biology, Computer Science, or at the interface of those domains, and be proficient in molecular dynamics simulation, numerical analysis using Python and other programming languages, and the Linux command line.

Contact information Interested candidates should contact Jérôme Hénin (jerome.henin@cnrs.fr) and Guillaume Stirnemann (stirnemann@ibpc.fr), together with a curriculum vitae and contact information for two references.

Calendar The position is funded for **three years**, and can start at any time **April to September 2023**.