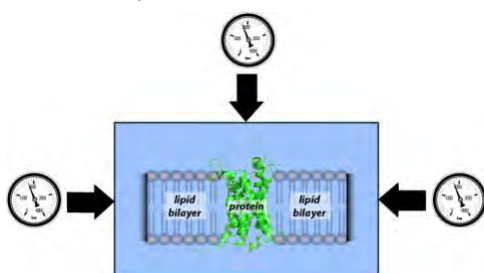


Funded PhD position for probing lipid/protein interactions under High-Pressure NMR at ICSN Gif-sur-Yvette (Univ Paris-Saclay) and IBPC Paris

We are looking for a motivated PhD candidate in the field of structural biology to probe lipid/protein interactions under high hydrostatic pressure NMR for a start in fall 2023 or earlier. The PhD is funded by a French ANR PhD fellowship.



The PhD student will be involved in a highly interdisciplinary research project at the frontiers of Chemistry, Biology and Physics. The aim is to continue the development of high-pressure NMR techniques to understand how membrane proteins affect lipid dynamics and how lipids affect protein dynamics in lipid bilayers.

PhD context and objective: Lipids and proteins are the main components of cell membranes. Although their mutual interactions and dynamics govern many cellular functions, we are still far from having a complete description. In our two CNRS laboratories (ICSN/IBPC), we have started to explore a new and original way to probe lipid/protein interactions within lipid bilayers using high hydrostatic pressure [1]. We will aim to demonstrate the existence of coupling between lipid and protein dynamics by NMR at pressures ranging from 1 to 3000 bar at various temperatures. We already identified strong lines of evidence of coupled motions but we will characterize at much higher details (timescales, ...) the interactions by combining NMR relaxation data but also SAXS, fluorescence on different types of membrane proteins, including G protein-coupled receptors (GPCRs) and lipid bilayers systems. Notably, we will deeply analyze the lipid dynamics and phase transitions in nanometric particles.

The PhD student will be trained during the PhD thesis in the production and purification of isotopically enriched membrane proteins in nanodiscs (at IBPC), as well as in state-of-the-art NMR spectroscopy (ICSN) in two laboratories that are world experts in their fields. He/she will have privileged access to ICSN's exceptional NMR equipment (ten spectrometers up to 950 MHz including the High-Pressure setup, <https://icsn.cnrs.fr/en/platforms/ir-rmn>). The two labs are closely located, with IBPC in Paris downtown (near Pantheon) and ICSN in the green area of Gif-sur-Yvette in Univ Paris-Saclay with a village spirit. Both labs are directly connected by the RER B train (~1h door to door), thus allowing to experience two radically different atmospheres. Complementary experiments will be collected at Soleil synchrotron (2km away from ICSN) in neighboring platforms at Paris-Saclay. In parallel, another PhD thesis will cover the molecular modelling aspect of the project under the supervision of J. Héning/G. Stirnemann also at IBPC.

References:

- [1] Pozza et al. (2022) Exploration of the dynamic interplay between lipids and membrane proteins by hydrostatic pressure. *Nat Commun.* 13(1):1780. doi: 10.1038/s41467-022-29410-5.
- [2] Casiraghi et al. (2018) Illuminating the Energy Landscape of GPCRs: The Key Contribution of Solution-State NMR Associated with *Escherichia coli* as an Expression Host. *Biochemistry* 57(16):2297-2307. doi: 10.1021/acs.biochem.8b00035.
- [3] Casiraghi et al. (2016) Functional Modulation of a G Protein-Coupled Receptor Conformational Landscape in a Lipid Bilayer. *J Am Chem Soc.* 138(35):11170-5. doi: 10.1021/jacs.6b04432.

Required background: The candidate should ideally have a background in biochemistry, chemistry, physical-chemistry, biophysics, molecular biology and/or structural biology or a related discipline. A strong interest in structure-dynamics-interaction-function studies of proteins/lipids, in the



physical-chemistry of biological systems and in collecting and analyzing data on biomolecular dynamics will be appreciated. Experience in protein expression and purification and/or NMR would be a plus.

Application: Interested and motivated candidates can apply by email to ewen.lescop@cnrs.fr and Laurent.catoire@ibpc.fr. Please provide:

- your CV
- a motivation letter
- Master (M1/M2) marks and ranking

More information about our groups at <https://icsn.cnrs.fr/en/research/cbsa/structural-biology-and-chemistry> and <http://umr7099.ibpc.fr/research-themes/molecular-signalisation-pathway-of-gpgrs/>