Master 2 research internship in Integrated Structural & Cell Biology in Grenoble

Supervisor(s):
Name: Jérôme Boisbouvier
E-Mail Address: jerome.boisbouvier@ibs.fr

Host laboratory:
Lab: Institute of Structural Biology

Host group/team:
NMR of Large Assemblies group

Title of the M2 research internship:
Development of a novel biochemical approach for the atomic-scale study of highly dynamic proteins by NMR.

Project summary:
Nuclear magnetic resonance (NMR) is an ideal method for studying flexible proteins, providing valuable insights into their conformation, dynamics, and function at the atomic scale. However, NMR presents significant interconnected challenges: resolution, sensitivity, and signal assignment. These limitations restrict its application to challenging proteins, such as large intrinsically disordered proteins or complex biomolecular assemblies. To overcome these obstacles, we will develop an innovative isotope labeling method to push the biological applications of NMR beyond their current limits.
This approach holds promise for application to medically relevant proteins, including two particularly intriguing cases. The first is the well-known microtubule-associated protein tau (MAPT1, referred to as Tau), which plays a key role in neurodegenerative diseases such as Alzheimer's disease. The second is arrestin, a highly dynamic regulatory protein involved in cellular signaling through its interaction with activated G protein-coupled receptors (GPCRs), facilitating their internalization and desensitization. By applying our method to these proteins, we aim to gain deeper insights into their structural and functional properties, expanding the scope of NMR in challenging biological systems.

Keywords:
Protein biochemistry, advanced isotope labelling, cell-free protein expression Structural biology, Nuclear Magnetic Resonance

Relevant publications of the team:
1. Mas G, Guan J-Y, Crublet E, Colas Debled E, Moriscot C, Gans P, Schoehn G, Macek P, Schanda P, Boisbouvier J. Structural Investigation of a Chaperonin in Action Reveals How Nucleotide Binding Regulates the Functional Cycle. Science Advances 4, eaau4196 (2018). doi: 10.1126/sciadv.aau4196
2. Gauto D, Estrozi L, Schwieters C, Effantin G, Macek P, Sounier R, Sivertsen AC, Schmidt E, Kerfah R, Mas G, Colletier JP, Güntert P, Favier A, Schoehn G, Schanda P, Boisbouvier J. Integrated NMR and cryo-EM atomic-resolution structure determination of a halfmegadalton enzyme complex. Nature Communications (2019) doi: /10.1038/s41467-019-10490-9
3. Törner R., Kupreichyk T, Gremer L, Colas Debled E, Fenel D, Gans P, Willbold D, Schoehn G, Hoyer W, Boisbouvier J. Structural Basis for the Inhibition of IAPP Fibril Formation by the Co-Chaperonin Prefoldin. Nature Communications (2022). doi: 10.1038/s41467-022-30042-y
4. Elena-Real C., Urbanek A., Imbert L., Morató A., Fournet A., Allemand F., Sibille N., Boisbouvier J., Bernadó P. Site-Specific Introduction of Alanines for the Nuclear Magnetic Resonance Investigation of Low-Complexity Regions and Large Biomolecular Assemblies. 2023. ACS Chem. Biol., 18 (9), 2039-2049. doi: 10.1021/acschembio.3c00288
5. Henot F, Rioual E, Favier F, Macek P, Crublet E, Josso P, Brutscher B, Frech M, Gans P, Loison C, Boisbouvier J. Visualizing the Transiently Populated Closed-State of Human HSP90 ATP Binding Domain. Nature Communications (2022) doi: 10.1038/s41467-022-35399-8