Open position for master students (M2)

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NMR and computational methods for protein ligand structure determination

Proteins exert diverse functions on the cells that can be modulated by their interactions with other bio-macromolecules or ligands. Then, a detailed atomistic description of the protein-ligand structures is a must to understand how proteins and ligands interplay. Thus far, the most very well-known experimental methods to reach this goal are X-ray crystallography and NMR spectroscopy, which both present advantages and drawbacks. For example, several protein-ligand structures are not solvable by X-ray crystallography (e.g. in the cases of low affinity binders or highly dynamic proteins). NMR in its counterpart, is very well suited for analysing these kinds of systems, but is limited by the often difficult task to assign all the atoms to their corresponding chemical shifts. Unfortunately, this very time-consuming task is necessary for the structure calculation procedure.

The goal of the project relies on developing methods to obtain a protein/ligand structure from NMR data without performing a detailed assignment of the protein. In this sense, one of the main bottleneck presented by NMR will be surmounted.

For that purpose, different techniques need to be integrated, as for example the previous knowledge of the protein structure that can be provided by X-ray crystallography or computational models (e.g. homology modelling or alpha-fold), computational tools to predict binding pockets and protein-ligand docking calculations integrated with experimental data.

This project will be performed in a very collaborative way between CNRS and the pharma company SERVIER.

M2 position context and goals

In our lab we have started to collect NMR experimental data on a serine/threonine kinase and we have deployed an initial computational pipeline that allows us to integrate the experimental data with advances computational modelling tools in a computational high-throughput format.

The specific goals of the master student will be to continue the computational pipeline development, test the protocol on different examples and take the challenge to integrate new experimental data in order to improve the accuracy of the method.

Scientific environment

The position will be held in the structural biology and chemistry NMR group, at the *Institut de Chimie des Substances Naturelles* (ICSN) in Gif-sur-Yvette, France. The laboratory has all the equipment for the recombinant protein production, purification and characterization, manage a very well equipped high-field NMR platform, and has all the necessary computational tools for the development of the project. We also have access to different NMR very high field spectrometers (especially for solid-state NMR) in the context of the National NMR infrastructure (IR-RMN), to national high-performance computing centre (e.g. GENCI) and to complementary equipment (e.g. high-field EPR, synchrotron SOLEIL and biophysical platforms).
In addition, the ICSN and more in general, the Paris-Saclay region, will bring interesting opportunities to meet with chemists, structural biologist and biologist to promote fruitful discussions and collaborations.