Master Project:

Ultra-High Field NMR Spectroscopy of microRNA: from Biophysics to Biological Function

Host Institute: CRMN-FRE2034, CNRS, ENSL, UCBL, Lyon University

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Micro-RNAs (miRNAs), are short non-coding RNA, that play essential roles in RNA induced gene silencing. Discovered nearly two decades ago, it is now known that miRNAs play an essential role in gene regulation in plants and animals. In humans, hundreds of miRNAs have been identified and are estimated to target up to 60% of the protein coding genes. They are involved in signaling, developmental timing and apoptosis. miRNAs also appear to be increasingly implicated in diseases, especially in cancer, and are currently seen as promising drug targets.

miRNA biological function is triggered by complex and flexible interactions with the messenger RNA (mRNA). However despite the fundamental importance of this process, the mechanism by which miRNA recognizes and interacts with the mRNA remains quite elusive. Describing this process at atomic resolution is crucial for understanding miRNA biological function and will open new avenues for molecular biology, bioinformatics and rational drug design again oncomirs, a key class of miRNA involved in cancer.

Nuclear Magnetic Resonance (NMR) spectroscopy is an extremely powerful tool to investigate biological systems, as it is the only method that can be performed in close to physiological conditions, while providing atomic resolution, sensitivity to motions covering the timescales of all biological motions and the possibility to probe even weak interactions. Modern NMR spectroscopy is also a very multidisciplinary field, that combine: advanced sample preparation based on the latest development in biology and chemistry, state of the art spin physics and instrumentation as well as advance data analysis and modeling.

In that context we are proposing several Master projects focusing a variety of aspects and systems. Those topic includes: (i) novel chemical strategies for preparing uniquely labelled RNA and revel yet inaccessible atomic information on flexible RNA, (ii) development of novel NMR strategy to efficiently probe low populated states in RNA and (iii) numerical approaches to probes RNA dynamic at timescales inaccessible by state of the art classical molecular dynamics. To discuss in more details the possibility of joining the lab, please contact me to discuss or visit the lab.

Figure 1: Ultra high-resolution description of RNA motions using site-specific NMR information and advanced molecular modeling.

The project will take place in a young and dynamic team, recently started and supported by an ERC Grant. It will take place at the Very High Field NMR Center (CRMN), a unique multidisciplinary NMR center, offering the best opportunities to study complex biological systems. The CRMN biomolecular NMR researchers are leading several projects where the latest development in hardware and methodologies in NMR are combined to address important functional questions inaccessible to other methods of structural biology, in particular using the 1GHz spectrometer, the highest magnetic field available for NMR as of today.

Boudet et al. Cell 2019 176:154-166