# Novel Synthetic Approaches to Probe RNA Structure and Dynamics at Atomic Resolution

## Nouvelles approches synthétiques pour sonder la structure et la dynamique des ARNs à Résolution Atomique

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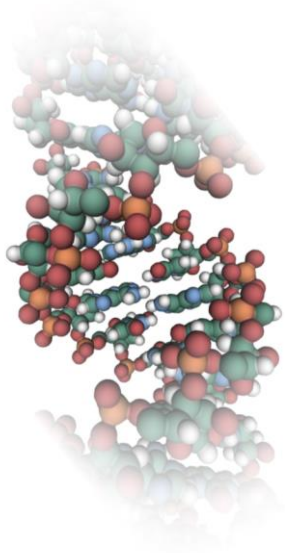
An ever-increasing diversity of biological functions for non-coding RNA has been discovered over the last decades, profoundly influencing our understanding of molecular biology. RNA functional diversity is usually triggered by complex conformational changes that critically need to be described at high resolution to link them to the biological function. Obtaining this relationship between biological function and RNA structure and dynamics will deepen our knowledge of RNA biophysics but also open new avenues for bioengineering and drug design.

Accessing a detailed picture of RNA motions has remained up to now a considerable challenge for modern biophysics. In particular, Nuclear Magnetic Resonance (NMR) spectroscopy is a tool of choice to investigate those systems but the small number of measurable data on RNA has limited its applicability.



This Ph.D. project aims at answering this challenge through the development of novel synthetic approaches that will allow to multiply the number of spectroscopic observables. Biochemical synthesis has been the method of choice for NMR studies as it allows isotope labelling at acceptable cost. However, chemical synthesis offer the possibility to surgically introduce specific reactive groups or NMR probes and thus can greatly extend the possibilities offered by classical biochemical approaches. This PhD project will aim at developing state of the art chemical synthesis to bypass the current limitations of RNA sample preparation for NMR. Different chemical and biochemical approaches will be considered and combined for the design of labeled and specifically modified RNA fragments. Those samples will then be purified and characterized by high performance liquid chromatography (HPLC) to confirm product quality and folding states. Finally, the synthetized fragments will be used for advanced NMR to describe at atomic resolution yet inaccessible flexible RNA and probe site-specific complex biological machineries.

The project will be carried between the teams of Dr. Carole Chaix (ISA) for advanced RNA synthesis and the team of Dr. Loïc Salmon (CRMN) for NMR spectroscopy analysis, in collaboration with Dr. Karine Faure (ISA) for the development of innovative HPLC characterization. The ISA and CRMN are located on the same campus and will other ample resources for RNA synthesis and purification as well as the access to a unique NMR facility, including the 1GHz spectrometer. The two institutes host word-leading research groups, provide excellent working conditions and are located in Lyon, one of the most dynamic French city, internationally recognized for its life quality.

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