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## 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 have 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 current limitation of RNA sample preparation for NMR. Different chemical and biochemical approaches will be considered for the design of labeled and structured RNA fragments. Those samples will then 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 hold in collaboration between the teams of Dr. Carole Chaix at the ISA for advanced RNA synthesis and the team of Dr. Loic Salmon for NMR spectroscopy analysis. The two institutes are located on the same campus and will offer ample resources for RNA synthesis as well as the access to the unique NMR facility of the CRMN, including the 1GHz spectrometer. The ISA and CRMN host world-leading research groups, provide excellent working conditions and are located in Lyon, one of the most dynamic French city, internationally recognised for its life quality.

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