# Master's Thesis Chemistry • From Jan/Feb 2020

*Group of Guillaume Stirnemann, CNRS Institut de Biologie Physico-Chimique, Paris, France*

## Conformational space of RNA duplexes: from the origins of life to ribozymes

**Subject** The idea that the early forms of life were mainly based on RNA (later coined as the RNA World hypothesis) has gained attraction in the last decades. In particular, a key characteristic of RNA is that it can ensure the function of modern DNA (i.e., store genetic information) and of proteins enzymes (i.e., catalyze chemical reactions). The catalytic properties of some RNAs (called ribozymes) are well-established but still partly unknown and not well-characterized.

The ability of RNA to self-catalyze its own synthesis by templating is an essential aspect in order to explain the appearance of "living" systems. Once copied, the template strand has to separate from its replica, which can usually occur at high temperatures only, suggesting the importance of temperature gradient cycles in the context of life's origins. The goal of this internship is to understand the molecular details of the separation between two complementary RNA strands, which is the final step of the auto-replication, and how this occurs at high temperature. The candidate will use an enhanced sampling technique that has been developed in our group. He/she will be able to characterize the conformational space of an RNA duplex, and he/she will understand how the duplex melting temperature depends on the sequence and on the structure of the duplex.

**Techniques/Methods** The candidate will gain strong experience in molecular dynamics simulations, using a well-employed and distributed code, as well as advanced technique to accelerate the sampling of the conformational space of biomolecules. Tools: Molecular dynamics simulations with state-of-the-art RNA forcefields; enhanced sampling methods; programming tools, and simulation analysis tools.

**Research environment** Research will take place in the lab of Theoretical Biochemistry of the CNRS Institute of Physical and Chemical Biology with Guillaume Stirnemann. It is located in the very stimulating research environment of the Latin Quarter, at the heart of Paris. Our group has extensive experience in applying advanced simulation and theoretical tools to tackle a variety of questions, ranging from water ultrafast dynamics in aqueous solutions to the mechanical and thermal stability of proteins. We have access to state-of-the-art computing facilities that include a local mesoscale computer cluster. More information about the lab and the research group are available here: www-lbt.ibpc.fr/people/stirnemann.

**Extension into a PhD** is possible as part of an ERC funding that is already secured. This PhD would extend what has been learnt during this internship to the study of RNA strands containing chemical defects, that are of high relevance in the context of life's origins.

**Contact information** Interested candidates should contact Guillaume Stirnemann **as soon as possible** (stirnemann@ibpc.fr), together with a curriculum vitae and contact information for one or two references.

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