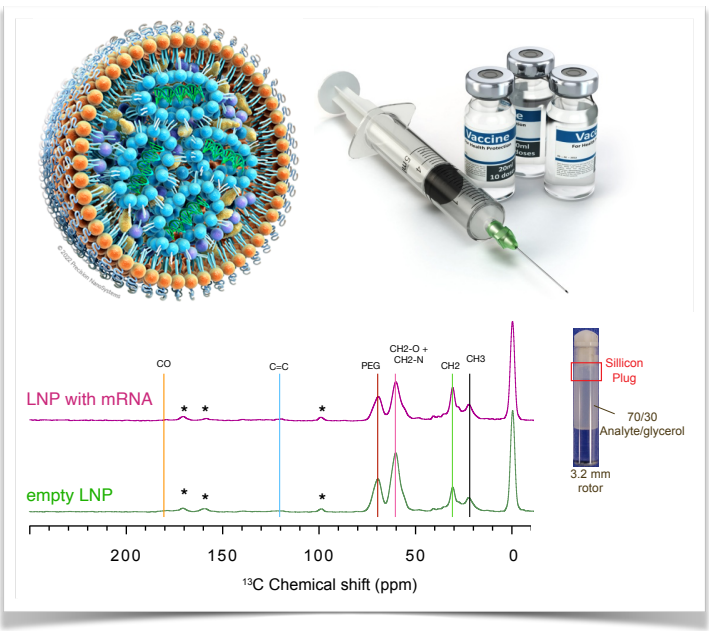
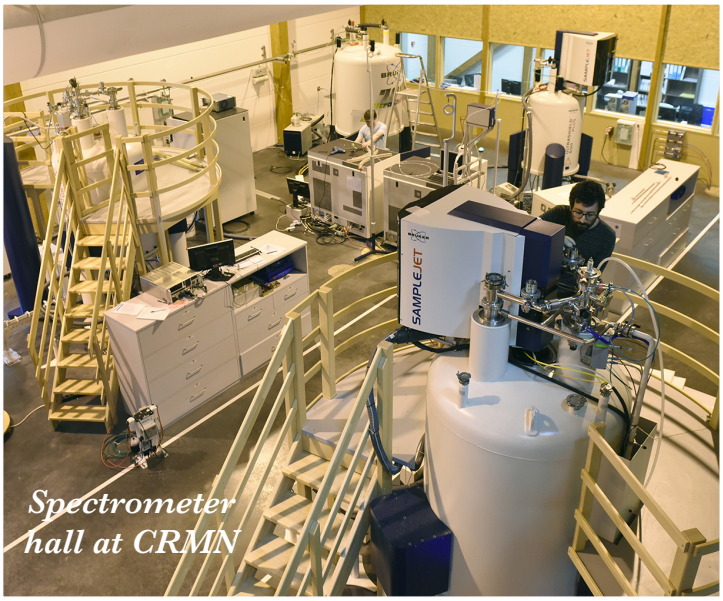
Stage de M2

Année 2024-2025

Centre Européen de RMN à Très Hauts Champs de Lyon





Spectrometer hall at CRMN

Analysing the molecular architecture of mRNA lipid nanoparticles through modern solid-state NMR methods

Context and state-of-the-art: Lipid nanoparticles (LNPs) have emerged as effective vehicles to deliver mRNA vaccines. The messenger RNA (mRNA) encapsulation and delivery properties of these nanovectors depend on their architecture. However, due their complexity and despite major research efforts recently devoted to a better understanding of their molecular organization, the structure of mRNA-loaded LNPs remains elusive. Thus, a number of aspects such as the interactions between their many components, the environment of the nucleic acid cargo or the lipid spatial distribution, are still open questions.

High-resolution solid-state NMR under magic angle spinning (MAS) has recently emerged as a powerful technique to probe with atomic-resolution the structures and dynamics of a wide range of bimolecular systems that cannot be investigated by solution NMR or X-ray crystallography. Several advances in methodology and instrumentation have addressed the traditional dual Achilles' heel of NMR in the solid-state: sensitivity and resolution. Notably, the use of very high magnetic fields and ultra-fast magic angle spinning of the sample yields significant improvement in spectral resolution. In parallel, hyperpolarization techniques such as Dynamic Nuclear Polarization (DNP) alleviate the sensitivity limitation by providing drastic enhancements of the NMR signal, opening new opportunities to investigate diluted substrates.

Project's objectives: The aim of this internship is to characterise the molecular structure of mRNA-LNPs of pharmaceutically-relevant composition by implementing and developing new MAS DNP NMR approaches. More specifically, the location of the mRNA and its interactions with the various components will be probed from samples prepared with isotopically labelled RNA. The project will encompass sample preparation, conducting NMR experiments, analyzing data, and simulating the polarization diffusion.

- The project will be carried at the High-Field NMR Center in Lyon (a laboratory of the ENS Lyon), using state of the art equipments and methods, within a research group of world-wide experts in DNP MAS NMR and in collaboration with pharmaceutical companies.

- If you want pursue your research training at the heart of a top-level NMR laboratory, in a young, friendly, truly international atmosphere, come and visit us !

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