Ph.D. position for October 2023

Laboratory : CEISAM (Chemistry and Interdisciplinarity: Synthesis, Analysis, Modeling), MIMM team

Title of the thesis topic :
(English) : Development of fast NMR methods for the real-tim analysis of out-of-equilibrium mixtures
(French) : Développements de méthodes RMN rapides pour l'analyse en temps réel de mélanges hors équilibre

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Context

Mixtures of small molecules are ubiquitous, and the detection, identification and quantification of molecules in mixtures is important for applications ranging from chemical synthesis to biomedical science. Nuclear magnetic resonance (NMR) spectroscopy is a powerful tool for the analysis of mixtures, especially thanks to 2D methods that provide higher resolution as well as important structural information. However, classic 2D NMR methods require experiment durations of several minutes or more. This is a limitation for the analysis of mixtures that evolve in time, such as chemical reactions, or mixtures that have been hyperpolarized to detect dilute components.

The MIMM team at the CEISAM laboratory develops original fast 2D NMR methods towards the analysis of out-of-equilibrium mixtures. In particular, we develop ultrafast 2D NMR approaches, inspired by magnetic resonance imaging concepts, that provide a complete 2D spectrum in a single scan of less than one second. We have notably introduced the concept of ultrafast multiple-quantum NMR, which results in the simplification of mixture spectra, as well as the separation of compound-specific spectra for aromatic compounds. Recent proof-of-principle experiments have illustrated the relevance of UF MQ NMR for the analysis of out-of-equilibrium mixtures, but this promising area remains largely unexplored so far.

The MIMM team works on two main types of out-of-equilibrium mixtures. The first concerns application in organic chemical synthesis, through the monitoring of chemical reactions by continuous flow NMR. This approach is highly relevant, as it provides real-time monitoring data in experimentally relevant conditions. It is also challenging, because sample flow can interfere with NMR data acquisition. The second concerns the detection of dilute compounds thanks to hyperpolarisation methods that significantly increase NMR signals by several orders of magnitude. The team notably hosts a state-of-the art apparatus for dissolution dynamic nuclear polarisation (D-DNP), a method that transiently enhances nuclear spin polarisation by up to four orders of magnitude. Be it for reacting or hyperpolarised mixtures, novel NMR experiments are required to extract more chemical information.

Objectives

This project aims to develop novel NMR methods for the real-time analysis of out-of-equilibrium mixtures, and apply them to the monitoring of organic chemical reactions by continuous-flow NMR, and to the sensitive detection of dilute compounds using hyperpolarisation. Specifically, the Ph.D. student will:

- develop NMR methods for the fast acquisition of 2D NMR spectra, and in particular multiple-quantum spectroscopy methods, that are applicable to flowing and/or hyperpolarised samples

- develop data-analysis methods to extract compound-specific spectra and identify mixture components, based on a maximum-quantum analysis of MQS 2D spectra
- apply these methods to the online monitoring of organic chemical reactions, and to the analyis of mixtures that are hyperpolarised by D-DNP.

These different components will benefit from the expertise of the laboratory's teams in NMR spectroscopy, hyperpolarisation and reaction monitoring, as well as the corresponding equipment present in the laboratory, which includes high-field and benchtop spectrometers.

Environment and collaborations

The PhD student will interact mainly with his/her supervisors who are specialists in the development and applications of NMR methods for mixture analysis. The thesis work will be carried out in the stimulating collaborative environment of the MIMM team, involving many PhD students in NMR methodology. The applications will benefit from the collaborative environment of CEISAM (especially in synthesis).

CEISAM is the molecular chemistry laboratory of Nantes University and gathers 5 research teams recognized in theoretical, physical and analytical chemistry, and in organic synthesis. The NMR platform of the CEISAM laboratory is the largest NMR platform in the west of France. It has a large facility, including 6 high field spectrometers (400 - 700 MHz) and 3 compact NMR spectrometers. Moreover, it is part of the national research infrastructure MetaboHub. CEISAM is located in the dynamic environment of the city of Nantes, close to the Atlantic coast and South Brittany.

Profile

The candidate has a background in chemistry (preferably physical or analytical chemistry) or physics, and must be strongly interested in the development of NMR methods and their application to mixture analysis. Due to the highly collaborative nature of the project, good writing and communication skills in French and English are required. The recruited Ph.D. student will be required to train other students (Master, Ph.D.) and to present his work in international conferences.

References

A. Le Guennec, P. Giraudeau, S. Caldarelli and J.-N. Dumez, *Ultrafast double-quantum NMR spectroscopy*, **Chem. Commun.** 51, 354 (2015). DOI : 10.1039/C4CC07232D

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C. Jacquemmoz, F. Giraud and J.-N. Dumez, *Online reaction monitoring by single-scan 2D NMR under flow conditions*, **Analyst** 145, 478 (2020). DOI : 10.1039/C9AN01758E

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