**Ph.D. position for October 2022**

**Laboratory** : CEISAM (Chemistry and Interdisciplinarity: Synthesis, Analysis, Modeling), MIMM team https://ceisam.univ-nantes.fr/equipe-mimm/

**Title of the thesis topic** :
(English) : Development of structure verification methods by in-line NMR
(French) : Développements de méthodes de vérification structurale par RMN en ligne

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**Context**

The concept of an autonomous reactor for the discovery and optimization of new reactions has the potential to profoundly change organic synthesis, in academic laboratories as well as in industry, by making it faster, reducing its impact on the environment, and promoting small-scale local plants. The CEISAM laboratory is a pioneer in the development of autonomous reactors combining flow synthesis, in-line detection and control algorithms for the *optimization* of existing reactions. In order to move towards the *discovery* of new reactions, it is essential that an intelligent reactor can determine, autonomously, the outcome of a chemical reaction.

Nuclear magnetic resonance (NMR) spectroscopy is the reference method for elucidating and/or validating the structure of new molecules in organic synthesis. In particular, commercial software makes it possible to assess the compatibility between experimental spectra and structural hypotheses. However, these approaches require the pure compound of interest, and are not integrated into the operation of intelligent reactors. To make it possible to *discover* new reactions autonomously, it is necessary to verify the structure of new molecules directly from a reaction mixture, without human intervention.

The MIMM team at the CEISAM laboratory has developed ultrafast multidimensional NMR methods that efficiently separate the spectra of the compounds in a mixture (the subject of two ongoing ERC projects in the lab). A fruitful collaboration between the MIMM and CORAIL teams has led to the implementation of original high-field and low-field NMR online detection approaches for flow synthesis. These developments form the starting point for the thesis project, funded by the *Agence Nationale de la Recherche*.

**Objectives**

This project aims to develop new NMR methods to verify the structure of the products of a flow synthesis, and to integrate them into the operation of an autonomous reactor for the discovery of new reactions. Specifically, the Ph.D. student will:

- develop NMR methods to separate the 1D and 2D spectra of the compounds of a mixture, exploiting diffusion NMR and signal processing methods
- integrate automated methods for structure verification of reaction products
- The application of the methods developed to the discovery of new reactions by an autonomous flow chemistry reactor, in collaboration with researchers in organic synthesis.

These different components will benefit from the expertise of the laboratory's teams in NMR spectroscopy and flow chemistry, as well as the equipment present in the laboratory for NMR and flow synthesis.

**Environment and collaborations**

The PhD student will interact mainly with his/her supervisors who are recognized as specialists in NMR methodology and flow chemistry. 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 reaction monitoring. Training in programming, analysis and digital data processing will be an advantage. 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**

R. Mishra, A. Marchand, C. Jacquemmoz and J.-N. Dumez, Ultrafast diffusion-based unmixing of 1H NMR spectra, **Chem. Commun.** 57, 2384 (2021). DOI : 1 0.1039/d0cc07757g (https://hal.archives-ouvertes.fr/hal-03132384)

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 (https://hal.archives-ouvertes.fr/hal-02359999)

P. Giraudeau and F.-X. Felpin, Flow reactors integrated with in-line monitoring using benchtop NMR spectroscopy, **React. Chem. Eng**. 3, 399 (2018). DOI : 10.1039/c8re00083b (https://hal.archives-ouvertes.fr/hal-02140934)

B. Gouilleux, B. Charrier, E. Danieli, J.-N. Dumez, S. Akoka, F.-X. Felpin, M. Rodriguez-Zubiri and P. Giraudeau, Real-time reaction monitoring by ultrafast 2D NMR on a benchtop spectrometer, **Analyst**, 140, 7854 (2015). DOI: 10.1039/c5an01998b (https://hal.archives-ouvertes.fr/hal-02392883)