Ph.D. topic for early october 2022

Laboratory : CEISAM (Chimie et Interdisciplinarité : Synthèse, Analyse, Modélisation), MIMM team https://ceisam.univ-nantes.fr/equipe-mimm/

Title of the thesis subject :
Methods development in compact NMR to analyze complex mixtures

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Context

Nuclear magnetic resonance (NMR) at high magnetic field (≥ 300MHz in ^{1}H) is a tool of choice to identify and quantify molecules in complex mixtures (reaction mixtures, food matrices, biofluids...). However, the purchase and operating costs of high field NMR spectrometers remain high and they require a dedicated space due to their bulkiness. Moreover, high field spectrometers have a high environmental impact (liquid helium in particular). In parallel, another type of NMR spectrometers called "compact" or "benchtop" have emerged for more than a decade. These instruments are less expensive to purchase, smaller and therefore transportable on a laboratory bench, under a fume hood or even on a production line. They are particularly suitable for on-line and real-time monitoring of chemical or biological transformations. However, this miniaturization of the instrument is associated with a reduction of the magnetic field (from 40 to 100 MHz in ^{1}H) which generates strong overlaps between signals and a loss of sensitivity. These major limitations make the performance of these spectrometers reduced compared to those with higher magnetic fields.

In this context, the CEISAM laboratory has been one of the pioneers since 2015 in developing methods to improve the separation of signals from complex mixtures on NMR spectra obtained on transportable devices. In this framework, different tools [1] have been implemented to analyze complex mixtures such as ultrafast 2D NMR, 2D DOSY and Pure-Shift methods. Thus, we have shown that these methods can make compact devices more efficient to detect the adulteration of edible oils [2], to monitor chemical reactions [3] and bioprocesses involving microalgae [4]. However, these techniques need to be improved by optimizing and combining them, for example, to make them faster, more sensitive and informative and thus extend their applicability to complex mixtures. Other promising methodological approaches can also be explored, such as the development of sequences incorporating selective pulses.

Objectives

The aim of this Ph.D. project is to develop and optimize multi-pulse NMR experiments to improve the performance of compact NMR for complex mixtures such as compounds from chemical syntheses or food matrices, and to evaluate their potential for quality control and process monitoring. This project stands at the interface between NMR spectroscopy and analytical chemistry, which will require both a significant investment in the understanding and development of compact NMR tools and their applications in chemical synthesis and food sciences.

More specifically, the PhD student will be in charge of:

- Developing and optimizing advanced strategies on a compact NMR spectrometer, via the implementation of approaches combining experiments, theory and numerical simulations,
- Evaluating the analytical potential of these approaches for quality control of food matrices and reaction monitoring,
- Analyzing the obtained results with a critical view of analytical chemistry, and comparing them to those obtained by usual methods.

Environment and collaborations

The PhD student will interact mainly with his/her supervisors who are recognized as specialists in the development of pulse sequences. 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.

Profil

The candidate has a background in chemistry (preferably physical or analytical chemistry) or physics, and should have a strong interest in the development of NMR analytical methods and their application to quality control and reaction monitoring. A strong interest in understanding and developing NMR pulse sequences is essential. An interest for programming, analysis and numerical data processing will be an advantage. Due to the highly collaborative nature of the project, good writing and communication skills in English are required. The recruited PhD student will be required to transmit his/her knowledge to other students (Master, PhD) and to present his/her work at international conferences.

References

1 - Gouilleux, B.; Farjon, J.; Giraudeau, P. Gradient-Based Pulse Sequences for Benchtop NMR Spectroscopy. *Journal of Magnetic Resonance* **2020**, *319*, 106810. https://doi.org/10.1016/j.jmr.2020.106810.

2 - Gouilleux, B.; Marchand, J.; Charrier, B.; Remaud, G. S.; Giraudeau, P. High-Throughput Authentication of Edible Oils with Benchtop Ultrafast 2D NMR. *Food Chemistry* **2018**, *244*, 153–158. https://doi.org/10.1016/j.foodchem.2017.10.016.

3 - Gouilleux, B.; Charrier, B.; Danieli, E.; Dumez, J.-N.; Akoka, S.; Felpin, F.-X.; Rodriguez-Zubiri, M.; Giraudeau, P. Real-Time Reaction Monitoring by Ultrafast 2D NMR on a Benchtop Spectrometer. *Analyst* **2015**, *140* (23), 7854–7858. https://doi.org/10.1039/C5AN01998B.

4 - Bouillaud, D.; Drouin, D.; Charrier, B.; Jacquemmoz, C.; Farjon, J.; Giraudeau, P.; Gonçalves, O. Using Benchtop NMR Spectroscopy as an Online Non-Invasive in Vivo Lipid Sensor for Microalgae Cultivated in Photobioreactors. *Process Biochemistry* **2020**, *93*, 63–68. https://doi.org/10.1016/j.procbio.2020.03.016.