



## PhD on In-vivo flow NMR lipidomics - development of innovative NMR methods for whole-cell lipid profiling of microalgae

**Context:** Microalgae are a source of biomass rich in various high value-added compounds such as lipids (mainly fatty acid triglycerides), carbohydrates, vitamins and proteins, with industrial applications ranging from food to health and energy. In this context, the project aims to develop the potential of Nuclear Magnetic Resonance (NMR) for on-line monitoring of the biochemical quality of microalgae. Among these, spirulina or *Limnospira platensis* (LP) is recognized for its nutritional properties as superfood. Moreover, it will be possible to offer this on-board method, which will not only control the physiological condition of these life support systems, but also their edibility.

The CEISAM and GEPEA laboratories at Nantes University have been collaborating for over 6 years now. As part of the AMER-METAL project, they demonstrated that NMR can be used to precisely determine the identity and quantity of microalgal lipids [1], directly on whole biomass, using high-field magnetic instruments. Investigations were also carried out into the capabilities of compact, lower-field NMR instruments [2] for monitoring the production of microalgae lipids.

**Objectives:** The main aim of the project is to develop a miniaturized system based on compact NMR for on-line monitoring of high-nutrient metabolites from microalgae grown in photobioreactors. Improving the analytical performance of compact NMR systems is essential for better on-line simultaneous analysis of several families of metabolites: LP lipids as well as carbohydrates. With this in mind, the PhD student's mission will be to characterize the diversity of nutritive metabolites produced by LP using high-field NMR (700 MHz at CEISAM in Nantes), identifying the various lipids but also sugars. Firstly, LP extracts will be studied, but also whole cells *in vivo*, which represents a real challenge. In this context, we will implement advanced methodologies to make signals more resolute, sensitive and accelerate their acquisition, but also capable of overcoming intracellular inhomogeneities. The high repeatability of NMR makes it a tool of choice for quantifying metabolites identified in mixtures in culture media and cells. Compact 80 MHz devices (available at CEISAM and GEPEA sites in St Nazaire) will also be evaluated with advanced methods in a second phase to validate their performance in identifying and quantifying LP lipids and sugars, compared with information obtained at 700 MHz. Finally, the coupling with a photobioreactor will be set up to monitor on-line and in real time the accumulation of metabolites of high nutritional interest in LP cells under cultivation.

### References:

- [1] Dylan Bouillaud, these de doctorat, 2017-2020, Multiscale NMR analysis of the microalgae metabolism
- [2] Castaing-Cordier, T.; Bouillaud, D.; Farjon, J.; Giraudeau, P. *Recent Advances in Benchtop NMR Spectroscopy and Its Applications*. In Annual Reports on NMR Spectroscopy; Academic Press, **2021**. <https://doi.org/10.1016/bs.arnmr.2021.02.003>.
- [3] Bouillaud, D.; Heredia, V.; Castaing-Cordier, T.; Drouin, D.; Charrier, B.; Gonçalves, O.; Farjon, J.; Giraudeau, P. Benchtop Flow NMR Spectroscopy as an Online Device for the in Vivo Monitoring of Lipid Accumulation in Microalgae. *Algal Research* **2019**, *43*, 101624. <https://doi.org/10.1016/j.algal.2019.101624>.
- [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>.

**Environment of work:** The project is being carried out in collaboration between two CNRS laboratories: CEISAM (Chimie Et Interdisciplinarité : Synthèse, Analyse, Modélisation) for the analytical development side, and the GEPEA (Environnement - Agroalimentaire) process engineering laboratory for the development of processes for microalgae cultivation. CEISAM's MIMM team is renowned for its development of liquid-state NMR techniques, applying these tools to the analysis of complex mixtures, and GEPEA's BAM team for its development of breakthrough, high-productivity culture systems.

**Profile: Candidates must have an Engineer or a Master's degree in (Bio)Analytical Chemistry or Physical Chemistry and have a solid theoretical knowledge in NMR.** Previous experience in this field (internship) is appreciated but not essential. The engineer will also need to be open-minded, given the interdisciplinary and collaborative nature of the project, carried out between two laboratories in the Nantes area. This recruitment will offer a unique opportunity to an engineer or a master 2 student to invest in innovative developments in high and low field NMR, at the interface between spectroscopy, analytical chemistry, biology and process engineering, to a better understanding of the metabolism of microalgae.

The net monthly salary is between 1,500 € and 2,000 € for 36 months.

**Application procedure:** Candidates shall submit **before the 14<sup>th</sup> of July 2024** their complete Curriculum Vitae, a motivation letter, Master / Engineer degree transcripts as well as two recommendation letters to:

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