

Postdoctoral fellow in DNP-enhanced solid-state NMR

18 months postdoctoral position is open for a highly motivated candidate in the laboratories: Modélisation et Exploration des Matériaux (MEM) and Laboratoire Chimie et Biologie des Métaux (LCBM), in Grenoble.

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| Laboratories | <p>MEM and LCBM are research units of the Interdisciplinary Research Institute of Grenoble (IRIG), which brings together fundamental research in biology, health, nanoscience, cryotechnology and new technologies for energy and the environment. The MEM laboratory brings together a unique and coherent set of cutting-edge techniques for materials exploration, such as electron microscopy, synchrotron X-ray diffraction, neutron diffraction, advanced simulations and theories, as well as solid-state and hyperpolarized NMR (DNP, Dynamic Nuclear Polarization). The LCBM conducts research at the interface between chemistry and biology. Their work focuses on studying the structure, activity and regulation of complex biological systems that transport and use metal ions, and on exploiting this knowledge to develop bio-inspired systems with similar structures and/or functions.</p> |
| Team | <p>Within MEM, the Magnetic Resonance Laboratory's DNP-NMR group focuses on developing DNP-NMR instrumentation and methodology to push back the limits of the technique's sensitivity and resolution, in order to tackle challenging systems ranging from materials science to life sciences. The DNP-NMR solid-state team (https://nmr-dnp-grenoble.net/home/) is headed by Gaël De Paëpe and currently comprises 3 researchers, 3 PhD students and 1 postdoc. Sabine HEDIGER (CNRS Research Director) is an expert in solid-state NMR, with a particular focus on methodological developments in hyperpolarization by DNP and their application to biomolecular systems. Gaël DE PAËPE (Research Director at CEA, Head of the Magnetic Resonance Laboratory) is an expert in solid state NMR and DNP, including instrumental and methodological developments and application to materials science and biomolecules.</p> |
| Location | CEA Grenoble |
| Context and scientific objectives | <p>We propose to solve the problems of resolution, sensitivity and selectivity associated with in-cell DNP experiments by developing an innovative approach based on the combination of bio-orthogonal chemistry and selective DNP (SeIDNP). The methodology will be applied on mammalian cells for the study of Atox1, a copper (Cu) chaperone involved in Cu homeostasis.</p> |
| Project name | Methodological development for protein-selective DNP-enhanced NMR in mammalian cells |
| | <p>Based on preliminary results, the methodology will be developed in stages, first on purified proteins, and then on the protein in mammalian cells. The first step will be to optimize experimental conditions for selective DNP (SeIDNP) on Atox1 and to determine the best targeting strategy (including polarizing agent) that allows detecting sub-micromolar concentrations in cell lysates. This knowledge will then be used to target and detect Atox1 directly in the mammalian cell, using bio-orthogonal chemistry to introduce the spin label for</p> |

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| Project description | SeIDNP. SeIDNP is a methodology developed over the last few years in our group. It enables the production of high-resolution DNP-enhanced NMR subspectra specific to a predefined region of the protein, determined by the position of the spin label. Demonstrated so far only on purified proteins, the methodology is very promising for targeting a biomolecule in the crowded environment of the cell, but as well for removing the cell background signal, which become significant at low protein concentrations. |
| Mission | The candidate will work mainly in NMR and DNP with the project leader, but depending on his/her expertise in biochemistry, he/she may assist the co-leader in protein production and labeling. |
| Responsibilities | The work in NMR and DNP will include the specific DNP preparation of labeled protein samples in cells or cell lysates, the autonomous use (after training) of the DNP-NMR spectrometer, the recording and processing of multi-dimensional biomolecular DNP-NMR experiments, including selective DNP, and the assignment and interpretation of spectra. The candidate will participate actively in the development of the strategy used throughout the project, and in the writing of research articles describing the results. |
| Expected results | Methodological development for intracellular DNP is a major challenge, and the project should provide new insights and innovative perspectives on the ability to characterize a target protein in cells by NMR. All results will be published in leading journals in the field. |
| Skills | <ul style="list-style-type: none"> ● Use of NMR spectrometers, theoretical and practical knowledge of biomolecular NMR and tools for processing and assigning spectra, basic knowledge in biochemistry, production of labeled proteins. ● Fluency in written and spoken English. ● Ability to communicate and work as part of a team. ● Interest in methodology. |
| Experience | From 2 to 5 years |
| Education | Thesis in liquid- or solid-state biomolecular NMR |
| Applications Close | 31/05/2024 |
| How To Apply | Send the application including CV, cover letter and at least one letter of recommendation to the project leader: sabine.hediger@cea.fr |
| Funding | Labex Arcane: https://arcane.univ-grenoble-alpes.fr |

