Hyperpolarized Solid-State NMR Spectroscopy: Advanced Polarizing Sources and Experimental Methodologies.

Direction Dr Anne Lesage (anne.lesage@ens-lyon.fr),

Centre de RMN à Hauts Champs de Lyon (FRE 2034, CNRS/ ENS Lyon/ UCB Lyon)

The Achille's heel of NMR spectroscopy is the low sensitivity of the method, which restricts its use to concentrated samples. In situ dynamic nuclear polarization (DNP) at cryogenic temperatures has recently developed as a key approach to overcome the sensitivity limitation of Magic Angle Spinning (MAS) solid-state NMR spectroscopy. Notably surfaces were previously inaccessible to NMR. In 2010, the group at CRMN Lyon has shown that by transferring polarization from electrons to nuclei, NMR signals from surfaces can be observed with high sensitivity, opening up an entirely new form of spectroscopy: Surface Enhanced NMR Spectroscopy (1).

DNP relies on a microwave-driven polarization transfer from electron spins to nearby protons. The electrons are usually introduced into the sample in the form of stable organic free (bi)radicals dissolved in a glass-forming solution. It has been realized since the early days of the renaissance of high-field DNP in the 2000s that the structure of the polarizing agent was crucial to obtain high signal enhancement factors. Notably, recent progress highlighted the key role of the electron dipolar and spin exchange magnetic interactions, of the electronic relaxation properties, of the width and shape of their EPR line in polarization (and depolarization) mechanisms, and pointed out the importance of a careful design and optimization of the structure of free biradicals for efficient DNP. In parallel several polarization transfer schemes have been recently revisited at high magnetic fields to further improve signal enhancement factors. Record enhancements of 180 have been recently reported at the CRMN Lyon at a field of 18.8 T (800 MHz proton frequency) using tailor-designed hybrid biradicals (2).

However, despite these tremendous efforts to develop even more efficient polarizing agents and to evaluate different polarization transfer schemes, the sensitivity of many DNP experiments is still in practice often insufficient, preventing many relevant applications. This is partly because:

- **i)** today's signal enhancement factors are still far from the theoretical maximum value (660 for 1H), in particular at very high magnetic field,
- **ii)** the polarization transfer schemes from the electrons to the nuclei are not yet fully understood and optimized,
- **iii)** the formulation used today to impregnate or wet substrates are far from being ideal.

We will address these key fundamental issues preventing a widespread use of solid-state DNP through i) developing new electron sources by rationally fine-tuning their chemical structures; (ii) developing new simulation tools to get a deeper knowledge on parameters that control spin dynamics and polarization transfer mechanisms; (iii) developing innovative chemical and experimental NMR approaches to provide higher signal enhancements on surfaces; The project will be developed at the High Field NMR Center of Lyon (CRMN Lyon). The center accommodates a 400 MHz (9.4 T) and a 800 MHz (18.8 T) wide bore spectrometers, fully equipped for DNP in the solid-state. With two MAS probes of diameter 3.2 and 1.3 mm, these spectrometers offer unique DNP capabilities worldwide, at the forefront of DNP hardware, to test new radicals and develop new experimental DNP approaches. The project will be developed in collaboration with leading groups in radical chemistry (Dr O. Ouari at Aix-Marseille University) and in NMR spectroscopy, at EPFL (Prof. L. Emsley) and at the University of Florence (Prof. M. Lelli).

(1) Berruyer, P.; Emsley, L.; Lesage, A. DNP in Materials Science: Touching the Surface. *eMagRes* **2018**, *7*, 93–104.

(2) Wisser, D.; Karthikeyan, G.; Lund, A.; Casano, G.; Karoui, H.; Yulikov, M.; Menzildjian, G.; Pinon, A. C.; Purea, A.; Engelke, F.; Chaudhari, S. R.; Kubicki, D.; Rossini, A. J.; Moroz, I. B.; Gajan, D.; Copéret, C.; Jeschke, G.; Lelli, M.; Emsley, L.; Lesage, A.; Ouari, O. BDPA-Nitroxide Biradicals Tailored for Efficient Dynamic Nuclear Polarization Enhanced Solid-State NMR at Magnetic Fields Up to 21.1 T. *J. Am. Chem. Soc.* **2018**, *140* (41), 13340–13349.