PhD position : 2020-2023

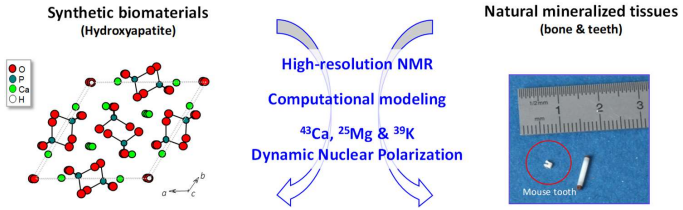
The observation of low gyromagnetic ratio nuclei in biomaterial environments through hyperpolarization enhanced magnetic resonance

Context : Elements such as Ca and Mg are of key importance in many synthetic and natural materials, including bones and teeth, and yet their structural and biological roles are only partly understood. The intrinsic structural complexity of these materials calls for the development of original and advanced characterization techniques, notably in the field of NMR spectroscopy.[1-3] In a new and promising proof-of-concept study, the chemical environments around Ca^{2+} ions have been probed by ^{43}Ca DNP (Dynamic Nuclear Polarization)-enhanced NMR (Nuclear Magnetic Resonance) at natural abundance (0.14%).[2] Circumventing the ultra-low sensitivity of ^{43}Ca, it allowed the surface and core sites in nanomaterials to be distinguished.

Objectives : The proposed PhD thesis aims at optimizing ^{43}Ca DNP NMR for the analysis of Ca environments in synthetic biomaterials, and then extending this new technique to the in-depth study of bones of normal and genetically engineered mice, in view of expanding our understanding of human bone pathologies. Moreover, the investigation of other poorly-sensitive cations of biological relevance (Mg^{2+}, K^{+}) using these new DNP methods will be looked into, to gain additional information on the structure of biomaterials.

A first part of the work will be dedicated to the synthesis of a variety of model calcium-phosphate samples, starting from purely hydroxyapatite phases (the main inorganic component of bones and teeth) and then switching to surface-grafted compounds and more biologically-relevant and biomimetic hybrid materials. Each of these compounds will be elaborated by using or adapting previously-published protocols and fully characterized by standard analytical techniques, including "conventional" multinuclear solid state NMR, before moving to DNP analyses. Moreover, for each phase, computational models will be developed, involving first principles calculations of NMR parameters, to ensure a proper interpretation of the DNP spectra.

A second part will be focused on the study of local cation environments in pathological mice bones using DNP NMR experiments. Here, the objective will be to highlight the variability of the calcium environments at the collagen/mineral interface when comparing healthy and impaired tissues, and to establish the link between NMR descriptions at the molecular level and the changes in functional properties in bones of pathological mice, or, in other words, at determining which are the molecular-level changes that could impact bone density and resistance to fracture.



References :

(1) « Recent directions in the solid-state NMR study of synthetic and natural calcium phosphates », C. Gervais, C. Bonhomme, D. Laurencin, *Solid State Nuclear Magnetic Resonance*, 107 (2020) 101663

(2) « Interfacial Ca^{2+} environments in nanocrystalline apatites revealed by dynamic nuclear polarization enhanced ^{43}Ca NMR spectroscopy », D. Lee, C. Leroy, C. Crevant, L. Bonhomme-Coury, F. Babonneau, D. Laurencin, C. Bonhomme, G. De Paëpe, *Nature Communications* 8 (2017) 14104

(3) « Pushing the limits of sensitivity and resolution for natural abundance Ca-43 NMR using ultra-high magnetic field (35.2 T) » C. Bonhomme, X. Wang, I. Hung, Z. Gan, C. Gervais, C. Sassoye, J. Rimsza, J. Du, M. E. Smith, J. V. Hanna, S. Sarda, P. Gras, C. Combes, D. Laurencin, *Chemical Communications* 54 (2018) 9591

Research environment

The PhD will take place between the Laboratoire de Chimie de la Matière Condensée de Paris in Sorbonne Université (https://lcmcp.upmc.fr/site/smiles/) and the Institut Charles Gerhardt in Montpellier (https://www.icgm.fr/imno). Part of the work will also be performed in strong collaboration with CEA Grenoble for DNP experiments, and the Centre de Physiopathologie Toulouse Purpan for studies on pathological mice bones.
The project is funded by the Agence Nationale de la Recherche (ANR).
The prefered starting date is between October and December 2020.

Research team

Supervisors: Prof Christel GERVAIS (LCMCP, Sorbonne Université)
Prof Christian BONHOMME (LCMCP, Sorbonne Université)
Co-supervisor: Dr Danielle Laurencin (ICGM, Université de Montpellier)
Collaborators: Dr Gaël de Paëpe (CEA Grenoble),
Dr Sara Dalicieux (INSERM-Toulouse)

Candidate Profile

This PhD offer is open to candidates with a **Masters degree in Materials Chemistry or Physical Chemistry**. The study is interdisciplinary and different profiles can be adapted but the candidate must have a high interest in **solid state NMR** (a first experience in this field would be really appreciated) and for **advanced characterization methodologies**. Moreover, knowledge in DFT calculations will be seen as a plus.

How to apply

Interested candidates should email their CV, an application letter, and the names of 3 references to:

- Pr Christel GERVAIS (LCMCP, christel.gervais_stary@sorbonne-universite.fr)
- Pr Christian BONHOMME (LCMCP, christian.bonhomme@sorbonne-universite.fr)
- Dr Danielle Laurencin (ICGM, danielle.laurencin@umontpellier.fr)

Pre-selected candidates will be interviewed.
The application process remains open until a suitable candidate is found.