Ph. D. in Chemistry at Centre de Biophysique Moléculaire, Orléans (France)

Development of contrast agents for selective Cu^{2+} detection via frequency encoded ParaCEST/Parashift MRI

Project : Physiological cations, in particular copper, play a key role in the organism and their concentrations are highly regulated. Misregulation have been connected to several pathologies such as cancers, neurodegenerative disorders, or Wilson and Menkes diseases.
Visualising these cations in vivo in real time would enable us to better understand their role, fate, biodistribution and to detect pathologies at an early stage. MRI (Magnetic Resonance Imaging) is a choice technique thanks to its excellent resolution. It suffers however from a lack of sensitivity which can be compensated by the introduction of a contrast agent, which can be rendered specific to a given biomarker through a careful design. Most of the Cu^{2+} responsive contrast agents developed so far are T_1-based contrast agents and therefore Gd^{3+} complexes. However, it remains difficult to achieve a good selectivity for Cu^{2+} vs Zn^{2+}, with keeping a desired affinity and response. Here, we propose a fundamentally different approach based on the paramagnetic-induced hyperfine shift properties of Ln^{3+} ions (other than Gd^{3+}). We will take advantage of the spectral selectivity of this detection and the different magnetic properties of Cu^{2+} (paramagnetic) vs Zn^{2+} (diamagnetic).
The PhD student will be in charge of:
(1) the **synthesis of the Ln^{3+} complexes**,
(2) the **in vitro characterization** of these complexes in the presence of various metal ions by NMR, UV-visible and luminescence spectroscopies mainly.
The PhD student will also be able to participate to the **EPR characterization** of the complexes and **DFT calculations**, that will be performed by the partners of the project.

The candidate will work in the **"Metal complexes and MRI" group of the Centre de Biophysique Moléculaire in Orléans**. CBM has all the state-of-the-art equipment necessary for the synthesis and characterization of these contrast agents. The candidate will benefit from the large national and international collaborative network of the host group. The project is within the frame of an ANR project in collaboration with Serge Gambarelli (CEA Grenoble) and Anne-Laure Barra (LNCMI, Grenoble). Both teams are part of the national Infranalytics research network.

Student profile : The candidate should have a strong background in organic chemistry (synthesis and characterization). Some experience in coordination chemistry and physical chemistry (NMR and optical spectroscopies) is not mandatory but would be a plus.

Contact : please send your resume, academic records and two references to celia.bonnet@cnrs.fr and jean-francois.morfin@cnrs.fr

Deadline 15th of April 2025