PhD thesis title: **Advanced EPR studies of molybdenum enzymes for CO_2 valorization**

Laboratory: Bioenergetics and Protein Engineering – BIP – Aix-Marseille University & CNRS (France)

Team: Biophysics of metalloproteins (Prof. B. Guigliarelli) - http://bip.cnrs-mrs.fr

Supervisor: Dr. Stéphane Grimaldi, HDR (Email: stephane.grimaldi@univ-amu.fr), Phone: +33 (0)4 91 16 45 57

Description of the PhD project:

Mononuclear molybdenum active sites in which the metal ion is coordinated by one or two pterin ligands play central biological roles [1]. They are found in a large family of enzymes that catalyze a wide diversity of redox and non-redox reactions including hydroxylations or oxygen or sulfur atom transfer. The ability of some members of the family (i.e. formate dehydrogenases or FDHs) to be able to reversibly convert CO_2 in mild conditions into formate ($HCOO^-$), a precursor for the synthesis of hydrocarbons, has attracted much attention in the context of the search for new energy sources alternative to fossil fuels. However, the understanding of the molecular factors that drive the reactivity, the efficiency, the specificity and the catalytic directionality of mononuclear molybdenum enzymes (MOEs) in general and of FDHs in particular remains limited.

The aim of this project is to address these issues by providing a detailed description of the molybdenum active sites in different catalytically-relevant or inhibited states of carefully selected MOEs. For this purpose, a state-of-the-art experimental approach based on multi-frequency EPR spectroscopy, including pulsed hyperfine spectroscopy (ESEEM, ENDOR, HYSCORE) will be used to characterize the magnetic properties of key Mo(V) intermediates, including the detection and analysis of weak magnetic and nuclear quadrupole interactions to nearby magnetic nuclei [2]. Uniform or specific isotope enrichment strategies of natural or engineered enzymes, or of their substrates or inhibitors will be developed to provide a deep understanding of the active site reactivity. The data will be interpreted by computer-assisted theoretical modeling relying on structure-based DFT calculations and/or QM/MM hybrid approaches. Such combination of approaches aims at providing new insights into how the protein environment tunes MOEs reactivity as well as clues for the rationale design of bio-inspired Mo-based artificial catalysts optimized towards the reduction of CO_2 in mild conditions.

The student will be hosted in the BIP lab in Marseille for a 3-year PhD contract from Aix-Marseille to begin in October 2018. The BIP lab has a strong expertise in spectroscopic and theoretical studies of metallo-enzymes (see e.g. [3]). It hosts one of the major French EPR facilities of the national EPR network that includes continuous wave and pulsed EPR spectrometers operating at various frequencies (3 GHz, 9 GHz, 34 GHZ and 94 GHz) and equipped with multi-resonance capabilities.

Candidate profile:

The applicant must have a Master of Science in Chemistry or Physics with honors and some experience in spectroscopy. An interest in theoretical approaches such as DFT calculations is welcome. Highly motivated, independent and dynamic, he/she should be able to work in a multidisciplinary team.

Please send applications including (i) a detailed CV, (ii) official transcripts of master and undergraduate studies, (iii) an application and motivation letter, and (iv) a recommendation letter of the Master's internship supervisor by e-mail at stephane.grimaldi@univ-amu.fr

Application deadline: 6th June 2018 – Interview in Marseille (doctoral school): **19th June 2018**.

References:

[1] S. Grimaldi, B. Schoepp-Cothenet, P. Ceccaldi, B. Guigliarelli & A. Magalon (**2013**) *Biochim. Biophys. Acta - Bioenergetics*, 1827, 1048-1085
[2] E. L. Klein, A. V. Astashkin, A. M. Raitsimring & J. H. Enemark (**2013**) *Coord. Chem. Rev.*, 257, 110-118
[3] J. Rendon, F. Biaso, P. Ceccaldi, R. Toci, F. Seduk, A. Magalon, B. Guigliarelli & S. Grimaldi (**2017**) *Inorg. Chem.*, 56, 4422-4434