

18 months postdoctoral position

Development of biocompatible redox-responsive fluorescent probes

In the frame of an ANR-funded project, an 18 month postdoc position is available in the Laboratory of Biomolecules (Chemistry department, Ecole Normale Supérieure, Paris, France) under the supervision of Dr. Jean-Maurice Mallet and Dr. Blaise Dumat to work on the design of fluorescent probes to monitor local variations of the cellular redox state.

Starting date: Fall 2024

Duration: 18 months

Employer: Ecole Normale Supérieure (ENS)

Salary: ≈ 2100€ net/month

Project:

The project is a collaboration with the team of Olivier Buriez (electrochemistry, PASTEUR laboratory, ENS) and Ilaria Ciofini (Theoretical chemistry, i-CLeHS, Chimie Paristech) and aims at developing metallocene-based probes to study variation in the redox cellular state for instance in the context of oxidative stress that is involved in various pathologies. Contrary to reaction-based probes for reactive oxygen or nitrogen species (ROS, RNS) that accumulate irreversibly, redox-responsive fluorophores are reversible and can monitor variation of the redox potential over time.¹ In this project, the fluorescence of the probes will be reversibly controlled by a photoinduced electron transfer (PeT)

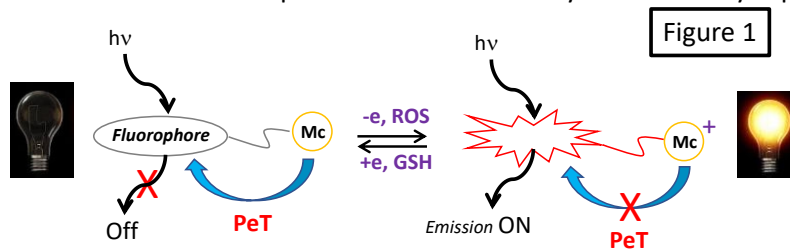


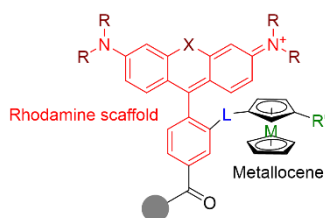
Figure 1

process between the metallocene and the fluorophore (Figure 1). To control their localization, the probes will be targeted to the cell membrane or to various organelle thanks to genetically-encoded protein tags. Overall, these probes

should lead to a finer understanding in space and time of variations of the redox cell state.

A first proof of concept has been published by the team based on a rhodamine fluorophore.^{2,3} The project will continue on the rhodamines scaffold and will aim at diversifying the structure to optimize

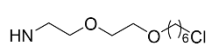
R (= alkyl) and X (= C, O, Si, PO₂, SO₂): Tuning of absorption/emission wavelengths and redox potential to optimize the PeT process



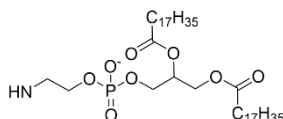
Metal M (= Fe and Ru) and R' group: modulation of redox properties

Linker L: Modulation of distance and orientation to optimize the PeT process

● Targeting moiety



Chloroalkane: Genetic targeting of HaloTag fusion proteins



Phospholipids: Membrane insertion

the sensitivity and enable the targeting of various subcellular structures. This will be supported by previous work of the team on genetically-targeted fluorescent probes and sensors.^{4,5}

The design of new probes will be guided by theoretical calculations to optimize the photoinduced electron transfer and is expected to yield valuable guidelines for the general

design of PeT-based sensors. In collaborations with electrochemists, the probes will be characterized and applied in cellular imaging.

References:

- (1) Lou, Z.; Li, P.; Han, K. Redox-Responsive Fluorescent Probes with Different Design Strategies. *Acc. Chem. Res.* **2015**, *48*, 1358–1368.
- (2) Čížková, M.; Cattiaux, L.; Pandard, J.; Guille-Collignon, M.; Lemaître, F.; Delacotte, J.; Mallet, J.-M.; Labbé, E.; Buriez, O. Redox Switchable Rhodamine-Ferrocene Dyad: Exploring Imaging Possibilities in Cells. *Electrochem. commun.* **2018**, *97*, 46–50.
- (3) Čížková, M.; Cattiaux, L.; Mallet, J.-M.; Labbé, E.; Buriez, O. Electrochemical Switching Fluorescence Emission in Rhodamine Derivatives. *Electrochim. Acta* **2018**, *260*, 589–597.
- (4) Coïs, J.; Bachollet, S. P. J. T.; Sanchez, L.; Pietrancosta, N.; Vialou, V.; Mallet, J.-M.; Dumat, B. Design of Bright Chemogenetic Reporters Based on the Combined Engineering of Fluorogenic Molecular Rotors and of the HaloTag Protein. *Chem. – A Eur. J.* **2024**, *30* (32).
- (5) Bachollet, S. P. J. T.; Pietrancosta, N.; Mallet, J.; Dumat, B. Fluorogenic and Genetic Targeting of a Red-Emitting Molecular Calcium Indicator. *Chem. Commun.* **2022**, *58* (46), 6594–6597.

Laboratory:

The laboratory of Biomolecules is affiliated to Sorbonne Université, CNRS and Ecole Normale Supérieure (ENS). It thus benefits from an outstanding scientific environment at the center of Paris.

The postdoctoral fellow will work in the team “[peptides, glycoconjugates and metals in biology](#)” and will be located at the chemistry department of the ENS. In January 2025, the LBM will merge with the PASTEUR laboratory also part of the ENS chemistry department to form the Chimie Physique et Chimie pour le Vivant (CPCV) research unit that will thus become a major laboratory in the field of chemistry at the interface of biology.

Research projects in the team span various aspects of chemical biology from oligosaccharides synthesis and fluorescent probes development. The recently refurbished labs are fully equipped for chemical synthesis, analysis and purification (NMR, automated flash chromatography, HPLC, LC-MS...) as well as for biology and biophysics (UV and fluorescence spectroscopies, cell culture, microscopy).

Mission and profile

This is a multidisciplinary and collaborative project and the work will consist in:

- i) Multistep organic synthesis of the molecular probes
- ii) Characterization of the probes by UV-visible absorption and fluorescence spectroscopies

The candidate will also be able to participate in early biological evaluation in cellular imaging by confocal microscopy. The successful candidate should hold a PhD in chemistry (defended less than 3 years ago) with a strong background in multi-step organic synthesis. Experience in biological or biophysical chemistry would be a plus and the candidate should have a taste for interdisciplinary and collaborative work. Good communication and writing skills in English are required.

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To apply, send CV (with 2 references) and motivation letter.