UNIVERSITY: Lille, Faculty of Sciences and Technologies

Scientific field: Matter, radiation and environmental sciences

Title of the thesis: Optical detection of chiral biomolecules using π-conjugated molecular probes

Directors: Sliwa Michel, CNRS Research Director, michel.sliwa@univ-lille.fr
Mathieu Surin, Senior Research Associate FNRS, mathieu.surin@umons.ac.be

Supervisor: Bouchet Aude, Assistant Professor, aude.bouchet@univ-lille.fr

Laboratory: LASIRE (UMR 8516, team DyNaChem) / CMN (University of Mons)

Related research project (international/national/regional): IRP CNRS NANOSYNERGETICS

Expected/obtained funding: cotutelle with the University of Mons (expected)

ABSTRACT

Background - Cationic π-conjugated molecules and polymers are increasingly envisioned for applications in imaging, gene delivery and biosensing, as they combine solubility in aqueous media, strong light absorption and fluorescence emission properties. They are excellent candidates for the detection of nucleic acids because their optical properties are very sensitive to the non-covalent interactions involved in the binding to these biomolecules.[1] Recently, it has been shown that supramolecular self-assembly of a π-conjugated polythiophene with different types of DNA such as single-stranded oligonucleotides or long genomic DNA in buffered aqueous solution yields polyplexes (polymer/DNA complexes), which have been detected using circular dichroism (CD) spectroscopy. The interaction between the polymer and DNA induces a transfer of the intrinsic chirality of DNA to the polymer, inducing the CD response of the polymer. In addition, it has been shown that the (chir)optical properties of the polyplexes drastically vary whether they are in solution or in thin films.[2,3]

Goal - The goal of the proposed project is first to provide a microscopic understanding of the binding modes and self-assembly mechanisms of selected π-conjugated probes with DNA, and their impact on the chiroptical and photophysical properties of the hybrid systems. The biosensing ability of the studied π-conjugated molecular probes will be furthermore investigated in biological media, with the aim of monitoring bioreactions and to detect DNA in cells.

Job description - The work will consist in investigating the optical properties of the complexes using a set of spectroscopy and microscopy techniques available in the different laboratories involved in the project. Time Resolved Single Photon Counting (TCSPC) and Fluorescence lifetime imaging microscopy (FLIM) measurements will be conducted in order to access to the dynamics of the polymer upon interaction with DNA in solution and in thin films. Polarization-dependent FLIM measurements on the films will furthermore provide information on the orientation-dependent response of the chromophores. The chirality-induced response of the complexes will be explored using circular dichroism (CD) and circularly polarized luminescence (CPL), and the results will be rationalized by means of molecular modeling simulations. Fluorescence bioimaging will finally be performed to assess the interactions and selectivity in biological media.

Environment - The Ph.D. thesis will be jointly supervised by partners in Lille and in Mons universities: Dr. Michel Sliwa and Dr. Aude Bouchet (Univ. Lille), and Dr. Mathieu Surin (Univ. Mons). The PhD student will spend 18 months in the DyNaChem team of LASIRE in Lille (http://lasir.cnrs.fr/dynachem/) and 18 months at the Laboratory for Chemistry of Novel Materials in Mons (http://morris.umons.ac.be/). The PhD project will be conducted in collaboration with the group of Prof. Tsuyoshi Kawai in NAIST (Nara, Japan) within the frame of the CNRS French-Japanese International Research Project NANOSYNERGETICS (http://www.nanosynergetics.cnrs.fr/). Several research stays are planned in Japan for running CPL measurements.

Candidate profile - Candidates should have a Master in (bio-)physical-chemistry. He / She should be highly motivated to work in an international and interdisciplinary project. Skills in optical spectroscopy, microscopy or biomaterials would be particularly appreciated.

References - [1] C. Cui, D. H. Park, D. J. Ahn, *Adv. Mater.* **2020**, 200221. [2] M. Leclercq *et al. ChemNanoMat,* **2019**, *5*, 703. [3] M. Fosséprè *et al. ACS Appl. Bio Mater.* **2019**, 2, 2125

Planned recruitment date: Oct. 1st 2021

Contacts : Michel Sliwa : michel.sliwa@univ-lille.fr
Mathieu Surin : mathieu.surin@umons.ac.be
Aude Bouchet : aude.bouchet@univ-lille.fr