Laboratory for optics and biosciences
Ecole Polytechnique – CNRS – INSERM – IP Paris

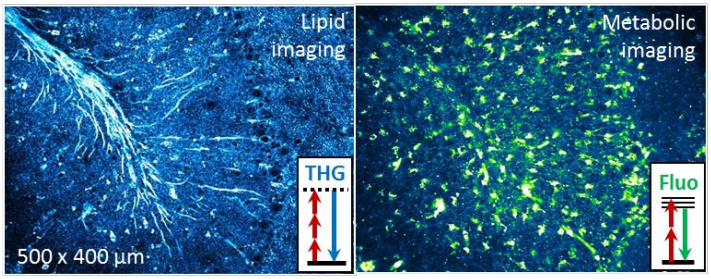
M2 / PhD internship proposal 2019-2020

Nonlinear optical microscopy of brain tissue: lipid and metabolism imaging

Keywords: nonlinear optics, microscopy, tissues, lipids, metabolism, polarization, imaging

Nonlinear optical (multiphoton) microscopy makes it possible to study biological tissues in 3D over depths of a few hundreds of micrometers with subcellular resolution. Polytechnique LOB is pioneering the use of endogenous nonlinear optical signals to study the structure and evolution of healthy and pathological tissues (embryo, brain, heart, eye).

Different optical signals provide complementary information. In particular:
-Fluorescence lifetime (FLIM) of endogenous fluorophores informs on the metabolic state of cells;
-Third-harmonic generation (THG) reveals lipidic structures such as myelinated fibers (= brain white matter).



The goal of this project is to develop multi-contrast imaging for monitoring simultaneously cell metabolism and lipid physiology in nervous and brain tissue.

During the M2 internship, the work will focus on optimizing & combining these advanced contrast modes of multiphoton imaging. The developments will be done on an existing microscope equipped with a dual femtosecond laser source and polarization controls, providing FLIM and polarized THG imaging capability. Imaging will be performed in cultured mouse brain tissues provided by Institut du cerveau et de la moelle épinière (ICM).

The work will be continued during a PhD project consisting of a technological and an applicative part. From a methodological perspective, two important goals are:
(*) to implement fast approaches for combining lipid and fluorescence-based metabolic imaging in tissues.
(*) to develop advanced polarization shaping approaches for enhancing the sensitivity of third-harmonic imaging to the sub-micron structure of samples.
On the application side, these developments will be used to gain a better understanding of (de)regulation mechanisms in brain pathologies involving lipid and metabolic disorders, in biological model systems. This will include:
(*) Measuring changes in metabolism and lipid organization during demyelination in mice brain slices
(*) Characterizing myelin distribution in pathological human tissues

Environment: The work will take place in the 'Advanced microscopies' pole of the Lab for Optics and Biosciences at Ecole Polytechnique (LOB). Our team has a well-known expertise in the field of multiphoton microscopies and their applications to tissue studies. The work will involve daily interactions with a group of ~4-5 people, within a local microscopy team of ~25 persons and an active collaborative network (ICM, Paris). The project will involve experimental nonlinear microscopy, data analysis, numerical simulations, and biological samples manipulation.

Some related references from our group:

- Morizet et al, *High-speed polarization-resolved third-harmonic microscopy*, Optica (2019);
- Stringari et al, *In vivo single-cell detection of metabolic oscillations in stem cells*, Cell Rep (2017);
- Zimmerley et al, *Probing ordered lipid assemblies with polarized THG microscopy*, Phys Rev X (2013);

LOB advanced microscopy unit web site:
https://portail.polytechnique.edu/lob/en/research/advanced-microscopies-tissue-physiology

Contact:
Applicants should have a training in optics or physics and a motivation for working at the interface with the life sciences. Send CV and enquiries to Drs Chiara Stringari (chiara.stringari@polytechnique.edu) and Emmanuel Beaurepaire (emmanuel.beaurepaire@polytechnique.edu)