Internship + thesis proposal

Proposal date: October 2022

Internship supervisors:

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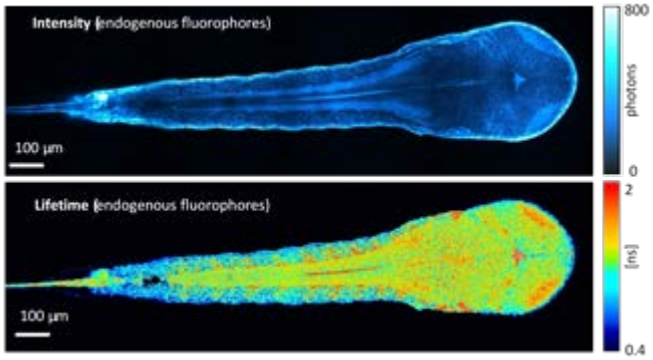
Laboratory:

Institution : Polytechnique LOB *Identification code*: LOB
Web site: https://portail.polytechnique.edu/lob/en
Address: Ecole Polytechnique, 91128 Palaiseau
Internship location: Palaiseau

Internship title: ***In vivo* nonlinear optical microscopy of nervous tissue: lipid and metabolism imaging**
Keywords: nonlinear optics; microscopy; polarization; tissues; lipids; metabolism



Nonlinear optical microscopy makes it possible to study biological tissues in 3D over depths of a few hundreds of micrometers with subcellular resolution. LOB is pioneering the use of endogenous (label-free) nonlinear optical signals to study the structure and evolution of healthy and pathological tissues (embryo, skin, brain) with sub-cellular resolution. In particular, fluorescence lifetime imaging (FLIM) provides information on the metabolic states of cells (see image) and polarized third-harmonic generation microscopy (THG) reveals morphological details and high-index structures such as lipids and myelinated axons. The goal of this project is to implement an efficient multimodal imaging method for monitoring simultaneously cell metabolism and myelin physiology in a live system.

During the master internship, the work will focus on two aspects. First, the two contrast modalities will be adapted for imaging zebrafish embryos. This will require to master and optimize an existing microscope equipped with a dual femtosecond laser source, time-resolved detection, and motorized polarization control. High-resolution multicontrast imaging will be performed in the brain and spinal cord regions. Second, the intern will explore the implementation of fast and efficient approaches to record multiparametric FLIM-based images in tissues, and the analysis of the signals in terms of cell metabolism by comparison to known data.

This work can be pursued by a PhD including a methodological and an applicative part.

On the methodological side, the aim will be to pursue the development of the FLIM-THG imaging approach. This will include the development of advanced beam and polarization shaping approaches for enhancing the sensitivity of THG to myelinated axons, and the further development of multiparametric FLIM imaging.

On the application side, these developments will be used to gain a better understanding of (de)regulation mechanisms in pathologies involving lipid and metabolic disorders using zebrafish embryos as a live model, before possibly applying it to other models (tissue slices, etc). The objective is to characterize metabolic shifts and lipid organization during demyelination in the brain and spinal cord.

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 recognized expertise in the field of multiphoton microscopies and their applications to tissue studies. The work will involve daily interactions with a group of ~3-4 people, within a local microscopy team of ~25 persons and an active collaborative network (Institut du Cerveau). The project will involve experimental nonlinear microscopy, data analysis, numerical simulations, and biological samples manipulation.

Some related references from our group: Ung, Scientific Reports (2021); Morizet, Optica (2019); Stringari, Scientific Reports (2017); Ramirez-Sanchez, J Cell Biol (2022).

https://portail.polytechnique.edu/lob/en/research/advanced-microscopies-tissue-physiology

Possibility of a PhD? Yes
Financial support for the PhD?

Requested funding	[X]	*Type of funding*	IPP, CSC