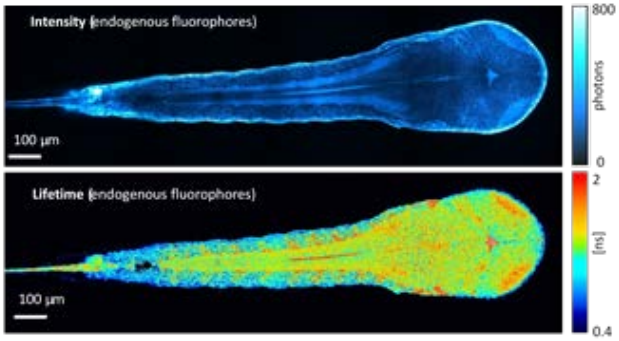
Master/PhD thesis proposal

Laboratoire d'Optique et Biosciences
Ecole Polytechnique, Palaiseau

Nonlinear optical microscopy of nervous tissue: lipid and metabolism imaging

Keywords: *nonlinear optics; microscopy; polarization; tissues*

Project: 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 label-free nonlinear optical signals to study the structure and evolution of biological tissues (embryo, skin, brain) with sub-cellular resolution. In particular, fluorescence lifetime imaging (FLIM) provides information on the metabolic state of cells (see image) and polarized third-harmonic generation microscopy (THG) reveals high-index structures such as myelinated axons. The goal of this project is to develop an efficient imaging approach for quantifying cell metabolism and myelin distribution in nervous tissues.



During the master internship, the work will focus on two aspects. First, the two contrast modalities will be adapted for imaging immobilized zebrafish larvae. This will require to optimize an existing lab-built microscope equipped with a tunable femtosecond laser source, time-resolved detection for FLIM, and polarization control. High-resolution FLIM-THG images will be recorded in the spinal cord region. Second, the intern will develop myelin and metabolic scores based on these images.

This work can be pursued by a PhD including a methodological and an applicative part. On the methodological side, the aim is to pursue the development of FLIM-THG imaging. This will include the development of polarization and beam shaping methods for enhancing the sensitivity of THG to myelinated axons, and the acceleration of FLIM imaging with improved detectors. On the application side, these developments will be used (i) to better understand lipid and metabolic disorders using zebrafish embryos as a live model, and (ii) to record large-area maps of myelin distribution in ex vivo healthy and pathological tissue samples. Image analysis methods will be implemented to extract scores at scales ranging from sub-micrometer to centimeter.

Profile**:** The candidate should have a background in physics, and a motivation to work in an interdisciplinary environment. Programming skills are important. Knowledge in image/signal processing will be an asset. The work will involve microscope alignment and acquisitions, data analysis, numerical simulations, and basic biological samples manipulation.

Environment: The project will take place in the 'Advanced microscopies' pole of the Lab for Optics and Biosciences at Ecole Polytechnique (LOB). The work will involve daily interactions with a group of 3-4 people, within a microscopy team of ~25 persons and in collaboration with the Paris Brain & Spine Institute. The project involve experimental optics, data analysis, numerical simulations, and biological samples manipulation.

Some related references: (THG) Gleeson, ACS Photonics (2024); Morizet, Optica (2021); Morizet, Optica (2019); (FLIM) Gottlieb, Biol Im (2023); Stringari, Scientific Reports (2017). https://lob.ip-paris.fr/recherche/microscopies-avancees-physiologie-des-tissus

Techniques/methods: Nonlinear optical microscopy. Image analysis. Numerical simulations. Samples handling.
Applicant skills: Experimental optics. Programming. Taste for interface work (physics/ biology/ informatics). Good level of English.
Internship supervisor(s): Chiara Stringari, chiara.stringari@polytechnique.edu; Emmanuel Beaurepaire, emmanuel.beaurepaire@polytechnique.edu
Internship location: LOB, Ecole Polytechnique, Palaiseau
Possibility for a Doctoral thesis: Yes