Laboratory for Optics and Biosciences
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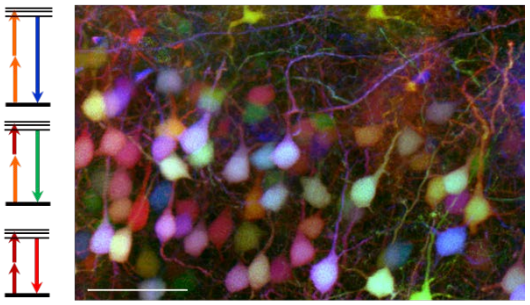
M2 Research internship proposal / Proposition de stage 2019

Large-volume multicolor multiphoton microscopy for studying brain development

Keywords : nonlinear optics, microscopy, brain development, big data



Nonlinear optical microscopy can probe biological tissues in 3D over depths of a few hundreds of micrometers with micron-scale resolution. With this unique capability, it becomes possible to study the development of neuronal/sensory networks with sub-cellular precision. In collaboration with Institut de la Vision (IDV, J. Livet team), our team at Polytechnique LOB is developing and pioneering new methods to address this challenge.
To uniquely distinguish cells or groups of cells, IDV is developing multicolor labeling approaches ('brainbow') based on the combined expression of different fluorescent proteins. At LOB, we have recently developed a new imaging system for mapping large volumes of brainbow tissue with micrometric resolution. This system (Abdeladim 2018) is based on multicolor multiphoton excitation through two-beam mixing (Mahou 2012), automated tiling and sectioning, and post-acquisition data reconstruction. We have now started to use this technology to map with subcellular resolution the structure of nervous circuits at different development stages.

However, one acquisition currently takes several days for a volume comprising 20*10^9 pixels. In order to be able to analyze and compare multiple samples, we would like to accelerate multicolor image acquisition by a factor of 5-8 times. The Master project will concentrate on the following strategies to achieve this goal:
(i) Reducing the chromatic mismatch between the excitation lasers during beam scanning, by implementing an active correction. This will result in larger tiles size, requiring less sample motion and faster acquisition;
(ii) Optimizing the mosaic acquisition strategy to minimize dead times.
These developments will then be used to record large-scale images of a neural circuit involved in vision, in collaboration with IDV.
The internship can be followed by a PhD thesis concentrating on one or several of the following aspects: (i) building a next-generation high-speed system based on light-sheet (parallelized) excitation; (ii) improving / developing data analysis pipelines for extracting biological measurements from large-scale data; (iii) application to developmental neuroscience; (iv) exploration of the potential of large-scale nonlinear imaging for other applications.

Environment: The work will take place in the «Advanced microscopies» pole of Polytechnique Lab for Optics and Biosiences (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 ~20 persons and an active collaborative network (Institut de la Vision, IOGS, etc). The project will involve experimental nonlinear optics, mounting of biological tissues for imaging, and image processing.

Some related references from our group:
Guesmi, Light Sci App (2018); Abdeladim, PhD thesis (2018); Mahou, Nature Methods (2012);
https://portail.polytechnique.edu/lob/en/research/advanced-microscopies-tissue-physiology

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