Laboratoire d'Optique et Biosciences
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M2 internship + PhD project in biomedical optics

Polarization-resolved Second Harmonic structural imaging of collagen remodeling.

Multiphoton microscopy has revolutionized three-dimensional (3D) imaging of biological tissues over the past 10 years. Notably, second harmonic generation (SHG) microscopy enables imaging of collagen fibrils (10-300 nm diameter) without any labelling and with unequalled sensitivity in intact tissues [1]. This is directly related to the property of SHG to be nonzero only in dense and non-centrosymmetrical materials. Nevertheless, the build-up of this coherent nonlinear signals in heterogeneous collagen-rich tissues (skin, artery, lung, bone…) is a complex issue and proper analysis of SHG images requires complementary information. We have therefore combined SHG with polarimetry, which enables measurements of collagen orientation in each pixel and thus provides *in situ* quantitative mapping of collagen 3D organization [2, 3]. We have also shown theoretically and experimentally that polarization-resolved SHG (pSHG) is highly sensitive to the disorder of the collagen fibrils within the focal volume, at sub-micrometer scale [2,4]. This is highly relevant as the size and 3D distribution of collagen fibrils governs the biophysical and biomechanical properties of each tissue, and therefore their biological function: opacity and compliance for skin, transparency and rigidity for cornea, stiffness for artery or cervix, etc… pSHG therefore appears as a unique technique to characterize the structure of complex tissues, understand their pathological dysfunctions and develop new diagnostic tools.

This project focuses on the distribution of collagen in the cervix and its remodelling during pregnancy. Collagen is indeed a key component of the cervix, organized like a rope closing the os before delivery. Recent pSHG experiments coupled with automated image processing have evidenced strong variations in the collagen distribution before delivery (paper in redaction). The aim of this project is to automate acquisition and processing of pSHG images of murine cervix and to explore new polarimetric modalities sensitive to collagen remodeling. Based on these optimized methods, series of pSHG images will be recorded in a murine model of pre-term birth and new metrics of collagen structure will be designed and evaluated.

This project will benefit from the experimental and numerical expertise of the advanced microscopy group at the LOB and from a close collaboration with Ass. Prof. J. Ramella-Roman at the Florida International University (FIU, USA), who will provide the murine cervical samples. It requires a strong background in physics (nonlinear optics, light-matter interaction, polarimetry) and in numerical analysis and a strong interest in the interface with the biomedical field. The master internship can be followed by a PhD that will involve short stays at FIU.

Related recent publications (see also http://www.lob.polytechnique.fr/) :
[1] Bancelin et al, Nat. Commun. 5 (2014) - 10.1038/ncomms5920
[2] Schmeltz et al, Optica 7 (2020) - 10.1364/OPTICA.399246
[3] Raoux et al, Light Sci Appl 12 (2023) - 10.1038/s41377-023-01224-0
[4] Schmeltz et al, Sci. Adv. 7 (2021) - 10.1126/sciadv.abg1090

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