Laboratoire d'Optique et Biosciences
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Internship/PhD project in nonlinear optical microscopy

Second Harmonic Generation imaging of heterogeneous tissues.

Non-linear optical microscopy has revolutionized three-dimensional (3D) imaging of biological tissues over the last 10 years. In particular, second harmonic generation microscopy (SHG) enables the visualization of fibrillar collagen without any labeling and with an unequalled sensitivity in intact tissues [1]. However, the interpretation of this SHG signal is complex due to its coherent nature and to the intricate geometry of biological tissues. In this context, we have shown that polarization-resolved imaging allows a more complete characterization of the 3D organization of collagen [2,3] because the SHG signal is higher when the excitation electric field is parallel to the dipoles responsible for the nonlinear response. However, the signal from heterogeneous materials remains poorly understood whereas most collagen-rich tissues are highly heterogeneous (cornea, skin, bone, arteries, ligaments...).

The internship aims at characterizing polarization-resolved SHG signals in complex geometries. Numerical simulations will first be carried out to reproduce the strong focussing and model the non-linear coherent signals. They will aim at understanding the effect of vertical and horizontal interfaces on SHG signals that are excited with linear or circular polarizations. It will be necessary to introduce magnetic dipole contributions to model circular dichroism signals [3]. These simulations will then be compared to experiments on intact tissues, mainly SHG images of human corneas (Fig 1). Indeed, the transparency and stiffness of the cornea come from a lamellar organization that must be accurately characterized in order to better diagnose structural pathologies such as keratoconus. Experiments will also be carried out on the skin, which is characterized by a dense and disordered network of large fibers, in order to characterize healing defects on a microscopic scale.

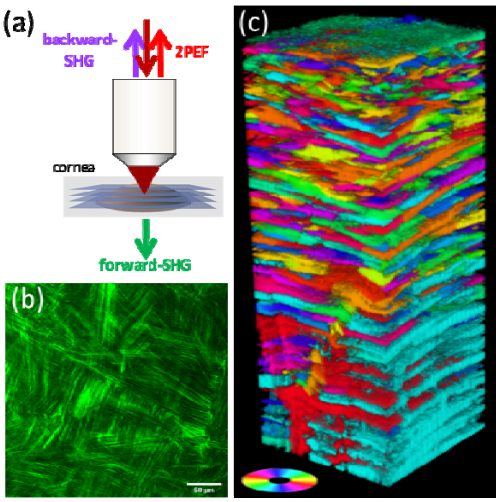

Fig 1: Polarization-resolved SHG image of a human cornea. (a) Experimental setup; (b) en face SHG image; (c) 3D reconstruction of the collagen lamellae: the color codes the orientation.

This project is based on the expertise in experimental optics and numerical simulations of the LOB's advanced microscopy group and on biomedical collaborations, notably with the 15-20 hospital and the Banque Française des yeux. It requires skills in optics and a strong interest in interfacing with the biomedical field. It is possible to continue with a PhD.

Related recent publications (see also http://www.lob.polytechnique.fr/) :
[1] Bancelin et al, Nat. Commun. 5 (2014) - 10.1038/ncomms5920
[2] Ducourthial et al, J. Biophot. 12, e201800336 (2019) - 10.1002/jbio.201800336
[3] Schmeltz et al, Optica (2020) - 10.1364/optica.399246

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