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PhD proposal

SHG imaging of pathological corneas.

Multiphoton microscopy has revolutionized three-dimensional (3D) imaging of biological tissues over the past 10 years. In particular, second harmonic generation (SHG) microscopy allows imaging of fibrillar collagen without any labelling and with unequalled sensitivity in intact tissues [1]. This addresses a major biomedical issue because collagen is a key element of organ architecture: the biophysical and mechanical properties of tissues, and thus their biological function, depend on the size and 3D distribution of the collagen fibrils in these tissues. For example, the opacity and flexibility of the skin are linked to a network of large entangled fibers, while the transparency and rigidity of the cornea arise from the tight alignment of small fibrils in superimposed lamellae. *In situ* imaging of the 3D organization of collagen is thus essential to characterize the structure of complex tissues, understand their pathological dysfunctions and develop new diagnostic tools.

In this context, we have shown that polarization resolved SHG imaging allows a more accurate characterization of the 3D organization of collagen [1,2]. However, experimental results are difficult to interpret in dense and heterogeneous tissues. The aim of the thesis is therefore to combine experiments and numerical simulations of polarimetric SHG signals in tissues of complex geometries. The study will focus on the human cornea (Fig. 1) to characterize the distribution of lamellae in healthy and pathological corneas (keratoconus in particular), as well as on the skin to characterize wound healing processes.

This project will benefit from the experimental and numerical expertise of the LOB's advanced microscopy group and from biomedical collaborations, notably with the 15-20 hospital and the Banque Française des yeux. It requires skills in optics and a strong interest in working at the interface with the biomedical field. The project will mainly focus on experiments or numerical simulations depending on the skills of the PhD candidate.

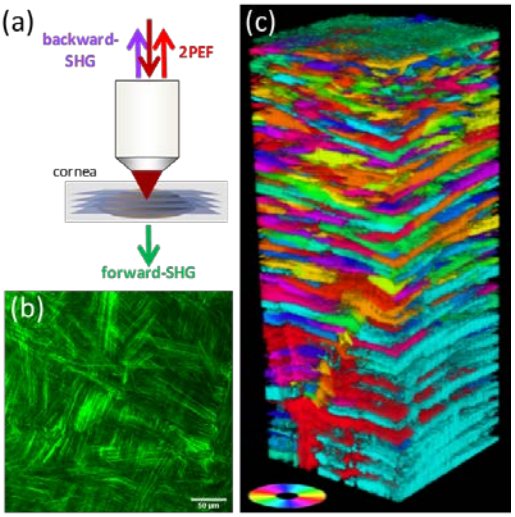

Fig. 1: Polarization-resolved SHG imaging of human cornea. (a) Setup ; (b) *en face* SHG image; (c) 3D reconstruction of collagen lamellae: the color codes for different in-plane directions of the collagen lamellae.

Recent publications (see also http://www.lob.polytechnique.fr/) :

[1] Bancelin et al, *Determination of collagen fibril size via absolute measurements of SHG signals*, Nat. Commun. 5 (2014)
[2] Ducourthial et al, *Monitoring dynamic collagen reorganization during skin stretching with fast polarization-resolved SHG imaging*, J. Biophot. 12, e201800336 (2019).

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https://portail.polytechnique.edu/lob/fr/recherche/microscopies-avancees/second-harmonic-generation-skin-and-cornea