Laboratory for Optics and Biosciences
CNRS UMR 7645 – INSERM U1182
Ecole Polytechnique – IP Paris
91128 Palaiseau cedex – France

M2 Internship + PhD offer (ANR funding)

SHG structural imaging of healthy and 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 enables imaging of fibrillar collagen without any labelling and with unequalled sensitivity in intact tissues [1] because this nonlinear optical process is nonzero only in non-centrosymmetrical materials. Moreover, SHG can be combined with polarimetric modalities to probe collagen disorder from sub-micrometer to millimeter scales and thus provide *in situ* quantitative mapping of collagen 3D organization. As the latter is a key distinctive feature of every tissue that governs their biophysical and mechanical properties, and thus their biological function, SHG is a unique technique to characterize the structure of complex tissues, understand their pathological dysfunctions and develop new diagnostic tools.

This research project focuses on the human cornea, which transparency and rigidity arise from the tight alignment of small fibrils in superimposed lamellae (Fig. 1.A). We have shown that polarization resolved SHG imaging provides an accurate mapping of these collagen lamellae along the full depth of healthy corneas (Fig. 1.B). It however requires proper calibration of the polarisation because of experimental issues induced by strong focusing in depth. Automated image processing is also needed to get reliable lamellae quantitation. The internship/PhD project aims first at (i) characterizing a new objective lens to mitigate polarization distorsions in depth; (ii) recording and analysing SHG images along the cornea radius in order to characterize structural variations between center and periphery. Second, the reorganization of the lamellae will be measured during inflation assays in order to provide multiscale data for refining mechanical models of the human cornea and improving refractive surgery accuracy. Finally, SHG imaging will be used to characterize pathological corneas, specifically keratoconic corneas [3].

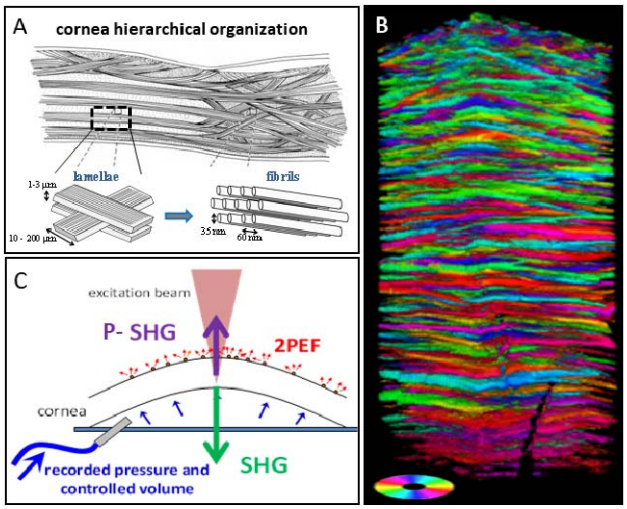

***Fig. 1**: Polarization-resolved SHG imaging of human cornea. (A) Cornea multiscale structure; (B) 3D reconstruction of collagen lamellae; (C) setup of multiphoton imaging during inflation assays.*

This project is funded by the ANR CorMecha (2022-2025) and will benefit from the experimental and numerical expertise of the LOB's advanced microscopy group and from collaborations with medical doctors at the 15-20 hospital and biomechanicians at Polytechnique. It requires skills in optics and numerical analysis and a strong interest in the interface with the biomedical field.

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] Schmeltz et al, *CD-SHG microscopy probes the polarity distribution of collagen fibrils*, Optica 7, 1469-1476 (2020)
[3] Raoux et al, *Quantitative structural imaging of keratoconic corneas using P-SHG microscopy*, Biomed. Opt. Exp. (2021)

Contact: SCHANNE-KLEIN M.-C. DR CNRS - marie-claire.schanne-klein@polytechnique.edu
LATOUR G. MCU Univ. Paris-Saclay - gael.latour@universite-paris-saclay.fr

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