PhD offer in Biophotonics

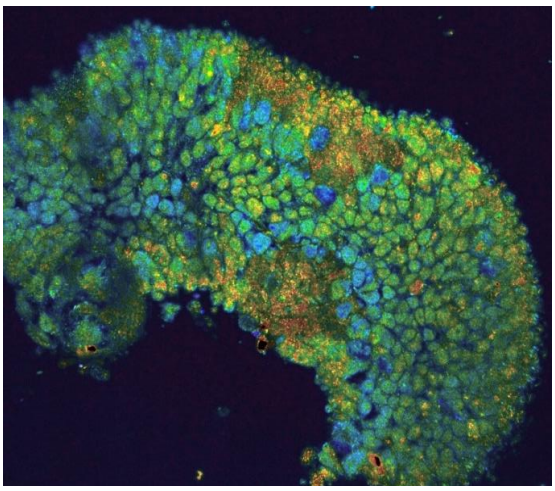
Functional and longitudinal imaging of retinal organoids with interferometric optical microscopy

Vision Institute, PARIS, FRANCE

Scientific context

Retinal organoids are 3D cell cultures that self-organize to form an **artificial retina** from induced pluripotent stem cells that could be obtained directly from patients with specific rare diseases. In general, **organoids are expected to become one of the most popular model systems for human biology**. As examples, they enable to test new drugs without extensive use of animal models or large clinical trials, or they enable the study of rare diseases in vitro with large sample numbers. The central application of this PhD project will be the study of retinal organoids with a rare ocular disease called retinitis pigmentosa, in order to understand how the disease develops and spreads over the different layers of the retina, and to test potential new treatments.
Nonetheless, **despite the growing interest for organoids in fundamental and applied research, there is still no dedicated optical microscopy method to properly characterize their growth and development without labelling**. In contrast to 2D cell cultures, label free techniques such as phase contrast or DIC microscopies fail to measure cell density and cell state in 3D organoids. Hence, the aim of this PhD project is to participate in the development of a new optical imaging technique that should enable longitudinal optical imaging of organoids.

We recently invented a technique called dynamic full field optical coherence tomography (D-FF-OCT) which is very promising for characterizing retinal organoids. FFOCT is a low coherence interferometric technique similar to digital holography but with the ability to perform optical sectioning. By analyzing the local temporal fluctuations of the scattering signals, cells can be visualized. Indeed, active transport mechanisms inside cells generate high signal fluctuations with specific time scales. By performing subtle signal analyses, physiological parameters of cells, including metabolism or mitotic state, can be measured. Hence, the physiological state of cells can be followed over time. **In brief, dynamic FFOCT is a label free optical technique that measures tissue architecture in 3D at submicron resolution. For organoids, dynamic FFOCT is very promising as it enables the visualization of the cell density and cell state in 3D, and can therefore follow the organoid development.**



Label free imaging of a retinal organoid by dynamic full field optical coherence tomography.

During this PhD project, the candidate will, among other topics, **participate in new developments of dynamic FFOCT** (to increase penetration depth, sources of contrast, etc…), **participate in the implementation of a setup at the Vision Institute,** where retinal organoids are developed, **and will investigate new potential applications.** An interesting development will be the possibility to **add a functional contrast**, i.e. to investigate how dynamic FFOCT signal is transformed during cell activity, including phototransduction in retinal organoids after visual stimulation, or neuronal activity.

This project offers several dimensions to explore depending on the interest of the candidate. **It includes optical technology development, the exploration of new biological mechanisms with this new technology, or the development of new algorithms (e.g. machine learning) for automatic quantification of samples.**

The project will be funded by an ERC Consolidator grant awarded to K. Grieve which will support a multidisciplinary team over 5 years for in vivo and in vitro retinal imaging. The PhD student will be a member of this project team and will interact with other PhD students, postdocs and researchers from the Paris Eye Imaging unit of the Vision Institute/Quinze Vingts Ophthalmology Hospital (www.pariseyeimaging.com) as well as with researchers from the Langevin Institute.

Required expertise:

The candidate should have an initial experience and affinity for optics, optical microscopy, and data analysis. Knowledge and experience in the field of biology would be highly valuable.

We expect the candidates to be familiar with programming tools, such as Matlab and/or Python, in order to participate in the development of our data acquisition and analysis workflows.

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List of a few related publications.

1. Dubois, A., Vabre, L., Boccara, A. C., & Beaurepaire, E. (2002). High-resolution full-field optical coherence tomography with a Linnik microscope. Applied optics, 41(4), 805-812.
2. Apelian, C., Harms, F., Thouvenin, O., & Boccara, A. C. (2016). Dynamic full field optical coherence tomography: subcellular metabolic contrast revealed in tissues by interferometric signals temporal analysis. Biomedical optics express, 7(4), 1511-1524.
3. Thouvenin, O., Fink, M., & Boccara, A. C. (2017). Dynamic multimodal full-field optical coherence tomography and fluorescence structured illumination microscopy. *Journal of biomedical optics*, *22*(2), 026004.
4. Thouvenin, O., Apelian, C., Nahas, A., Fink, M., & Boccara, C. (2017). Full-field optical coherence tomography as a diagnosis tool: recent progress with multimodal imaging. Applied Sciences, 7(3), 236.
5. Thouvenin O, Boccara C, Fink M, Sahel J, Paques M, Grieve K. Cell motility as contrast agent in retinal explant imaging with full-field optical coherence tomography. Invest Ophthalmol Vis Sci. 2017;58:4605–4615. DOI:10.1167/iovs.17-22375
6. Scholler et al. Opt. Lett. 45, 5901-5904 (2020)
7. Scholler et al. Nature Light Sci Appl 9, 140 (2020).