(W/M) Postdoctoral position: Label free imaging of cerebral spheroids in acoustic levitation.

Scientific Context:

Most organs are made up of tissues organized in sheets comprising distinct layers of cells separated by basement membranes of extracellular matrix. This architecture is found in various tissues throughout the body (cardiac, pulmonary, endothelial, retinal, cerebral, etc.). The construction of complex biological tissues remains a major challenge for the future of biology and medicine, and the construction of functional organ models is becoming a crucial issue for modeling in biology and issues such as cell therapy. This calls for new techniques for assembling, structuring and culturing three-dimensional biological constructs. The construction of 3D biological tissues presents a number of challenges, including the spatial separation of cell groups, which tend to migrate and mix. Moreover, in cases where connections and/or signals are desired between different cell layers (in the case of neurons, for example), an orientation of the connections is often necessary.

To meet these challenges, the AcoustoFluidics team of the PMMH (ESPCI Paris – PSL) and the Neurosciences Paris Seine (NPS) laboratory (Sorbonne University) have developed and optimized an innovative multimodal technology combining acoustic levitation, fluidics and control of mechanical effects, aimed at fabricating, structuring culturing and stimulating complex biological tissues in acoustic levitation. They have demonstrated the possibility of simultaneously levitating and aggregating neuronal cells at the nodes and specific microstructures at the antinodes, in a hydrogel prepolymer, to form layers of cells separated by layers of biomaterial resulting in a laminar tissue once the hydrogel has set [1,2].

Such 3D structuring culture technology has brought new needs in terms of optical imaging and it has become necessary to develop new microscopes which allow the rapid visualization of cells inside such structured tissues. A third partner, the NCIS team (Nouveaux Concepts pour l'Imagerie et la Détection) at Institut Langevin (ESPCI Paris – PSL), have recently developed new label free microscopies, based on Optical Coherence Tomography (OCT), which can use the intrinsic optical properties of cells and tissues in order to reconstruct the 3D organization of biological systems and to visualize all living cells inside [3]. A recent microscope module has been recently developed to quantify cellular activity in retinal organoids, and to follow their development for several weeks [4].

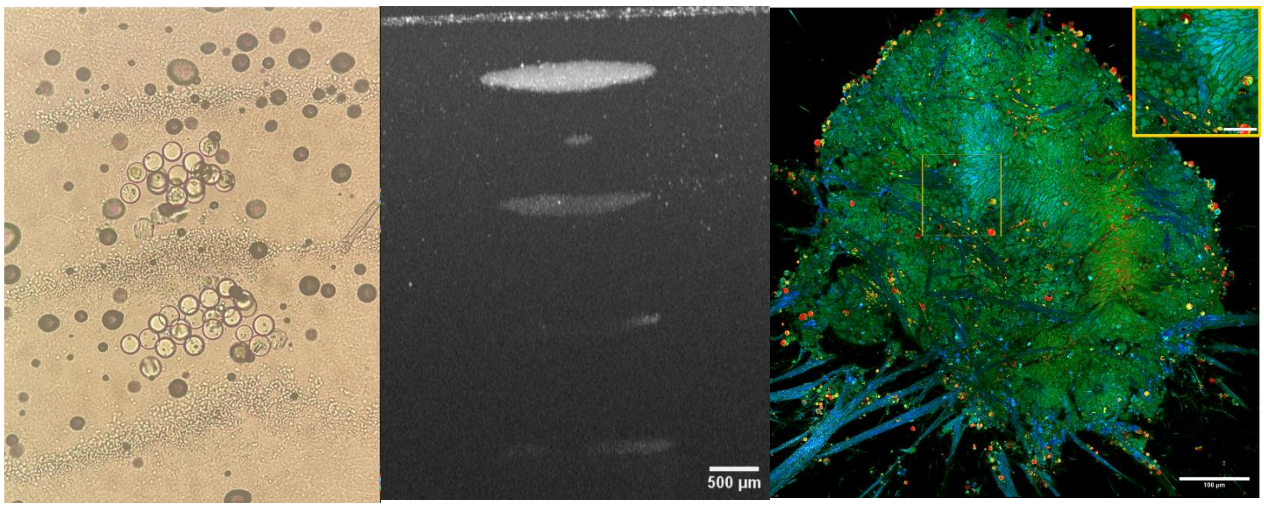

Fig. 1: Different imaging modalities to record layers of cortical primary neurons separated by layers of PDMS beads by transmission microscopy, OCT and dynamic FFOCT.

Post doctoral project:

The work corresponds to the first part of a collaborative ANR project (between the 3 partners described above) to study cerebral spheroids under acoustic levitation and induced mechanical stress. In particular, this will allow

investigating the impact of mechanics on neuronal growth and function, possibly in the context of chronic traumatic encephalopathy. The postdoctoral project is focused on the development of the microscope itself. In particular, a new microscope module will be developed to enable label-free imaging of neuronal spheroids in acoustic levitation. The module will combine 3 imaging modalities, including a new one invented at the Institut Langevin:

-Dynamic full-field OCT to reveal all the cells in a tissue or culture without labeling by analyzing temporal fluctuations of full-field OCT signals (Fig. 1 right)
-Spectral OCT for visualization of spheroid volume (Fig. 1 center)
-Fluorescence imaging (e.g. calcium imaging, and nanoparticle tracking)

The post-doctoral candidate will develop the module, connect it to a commercial microscope, and develop a sample holder for imaging samples in acoustic levitation. He/she will interface with two teams of collaborators developing levitating cell cultures to integrate their needs into the imaging system. The development of the module will be facilitated through a long-term collaboration between the Institut Langevin, and the Institut de la Vision, and a start-up is being created to commercialize a dynamic FF-OCT module. If this is of interest, the post-doctoral candidate may work in collaboration with the start-up.

Activities:
-Design and production of an imaging module
-Development of automated data processing algorithms
-Production of acoustic levitation chips and microscope integration. Realization of mechanical interfaces and 3D printing to make the interface
-Imaging of biological samples and discussion with physicists and biologists to optimize imaging.
-Bibliographical work and writing of scientific articles
-Regular presentation of results
-Participation in the scientific life of the team and collaboration with other team members

Skills:
-A PhD in biophotonics, or equivalent, is expected.
-The candidate must master basic and advanced microscopy concepts. Experience in label-free imaging or Optical Coherence Tomography would be appreciated.
- The candidate must be able to present his/her work to an interdisciplinary audience of biologists/physicists and physicians. An interest in interdisciplinarity is required to successfully complete this project.
-An advanced level of programming (ideally Matlab or Python) is required.
-The candidate is expected to master the skills needed to carry out a research project (bibliographical research/article writing/presentation of results/project organization).

Location: Institut Langevin And PMMH, 1 rue Jussieu, Paris, France

Application: Don't hesitate to contact me olivier.thouvenin@espci.fr, ideally with a CV, relevant cover letter, and a few references. However, the official application needs to go through the CNRS website: https://emploi.cnrs.fr//Offres/CDD/UMR7587-OLITHO-005/Default.aspx

Bibliography :
[1] N. Jeger-Madiot *et al.*, « Self-organization and culture of Mesenchymal Stem Cell spheroids in acoustic levitation». *Scientific reports* 11.1: 8355, 2021, doi: 10.1038/s41598-021-87459-6
[2] N. Jeger-Madiot *et al.*, « Controlling the force and the position of acoustic traps with a tunable acoustofluidic chip: Application to spheroid manipulations », *Journal of the Acoustical Society of America*, vol. 151, nº 6, p. 4165, 2022, doi: 10.1121/10.0011464.
[3] S. Azzollini, et al., "Dynamic optical coherence tomography for cell analysis", *Biomed. Opt. Express,* 2023.doi: https://doi.org/10.1364/BOE.488929
[4] T. Monfort, et al. « Dynamic full-field optical coherence tomography module adapted to commercial microscopes allows longitudinal in vitro cell culture study". *Communications Biology*, *2023* doi: https://doi.org/10.1038/s42003-023-05378-w