Master 2 internship proposal

Physique et Mécanique des Milieux Hétérogènes - ESPCI Paris
Institut de Neurosciences - IBPS - Sorbonne University

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Internship location: Laboratoire PMMH de l'ESPCI Paris and Laboratoire de Neurosciences, Institut de Biologie Paris Seine (IBPS), Sorbonne Université, Campus Jussieu, in Barre Cassan, 7-9 quai Saint Bernard, 75005 Paris.

Construction of a three-dimensional cortical column using acoustic levitation

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, cerebral, etc.). In the Central Nervous System, the retina is composed of layers of epithelial cells and neurons interconnected in a complex manner, found in other brain structures such as the cortical layers, the cerebellum or the hippocampus. 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. The 2D approach to microfluidics is faced with these same problems, and numerous approaches, both chemical and biological, have been explored. Among these, those involving conduit topology are particularly promising.

The team of JM Peyrin has demonstrated the possibility of using asymmetric channels between two chambers of a microfluidic chip to reconstruct a directed neural network. The adoption of this topological approach is of interest for 3D tissue structuring. Coupled with acoustic levitation, this approach opens up a vast field of possibilities. To meet these challenges, the AcoustoFluidics team of the PMMH (ESPCI Paris) started a collaboration with the Neurosciences Paris Seine (NPS) laboratory (Sorbonne University). This new scientific consortium has made it possible to develop and optimize 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. In this context, and with the aim of controlling the interactions of acoustically structured cells, the PMMH and NPS teams have developed a patent-pending acoustofluidic system based on the acoustic properties of materials. Indeed, while most cells levitate at pressure nodes in a stationary acoustic field, materials with negative acoustic contrast have the remarkable property of levitating at pressure antinodes. The AcoustoFluidics team at PMMH and NPS at SU 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.

Ojectives
The aim of the Master 2 internship will be to capitalize on the results obtained in the laboratory by carrying out the three-dimensional reconstruction of a minimalist cortical column using acoustic levitation as a tool to manipulate and organize the cell layers. The model will then be composed of several layers of cortical neurons separated by porous layers of microbeads. The first objective will be to build and culture the cortical columns. The second objective will be to monitor and study the modalities of axonal connections between cortical layers. Finally, the project will benefit of the collaboration with a third partner, the NCIS team (New Concepts for Detection and Imaging) at Institut Langevin (ESPCI Paris Ð PSL), who develops an innovative visualization technique called Optical Coherence Tomography (OCT), which allows the rapid visualization of cells inside living tissues. The final objective of the internship would be to run preliminary OCT measurements on a cortical column.
A Ph D. is possible through an ANR project gathering the three partners.

a)

b)

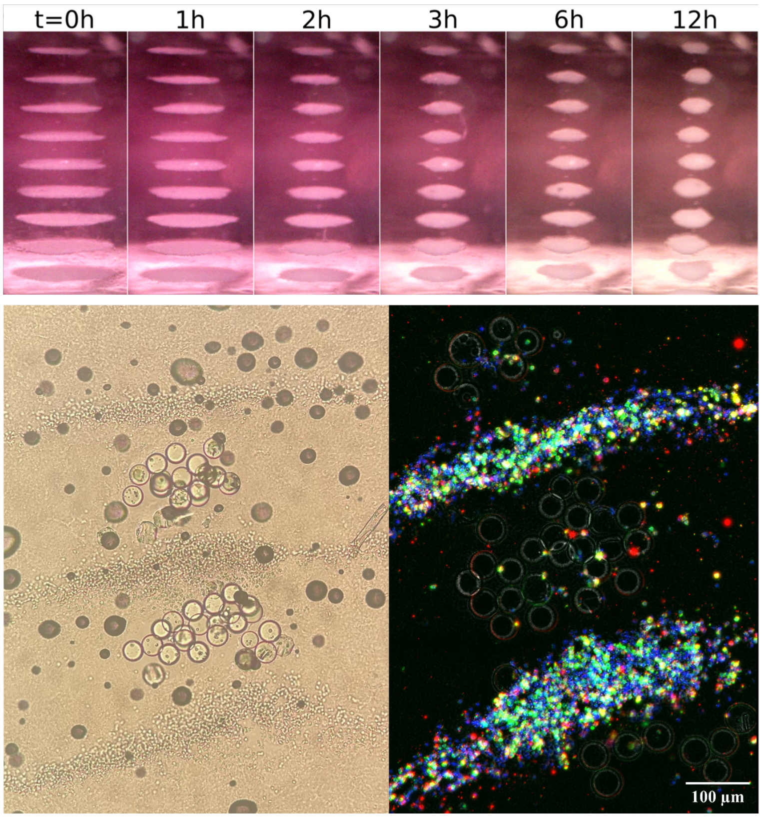

Fig. 1 : a) Rapid formation of MSCs cell sheets in acoustic levitation ($t = 0$). Within a few hours, the cell sheets have spontaneously turned into spheroids that can be maintained in acoustic levitation. b) Formation of a layers of neurons separated by PDMS beads using the acoustic force.

Expected skills: Master 2 in biophysics. Knowledge in microfluidicis, fluorescence microscopie, cell culture. Strong motivation for experimental work and interdisciplinary subjects.

Références

[1] Jeger-Madiot, N., Arakelian, L., Setterblad, N., P. Bruneval, M. Hoyos, J. Larghéro, J.-L. Aider, Self-organization and culture of Mesenchymal Stem Cell spheroids in acoustic levitation. Nature Sci. Rep. 11, 8355 (2021). https://doi.org/10.1038/s41598-021-87459-6