INTERNSHIP PROPOSAL

Laboratory name: Laboratoire PhysicoChimie Curie – Team Biology-inspired Physics at MesoScales
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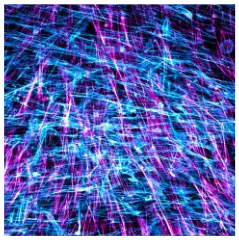
Internship location: Institut Curie, Paris

Thesis possibility after internship: YES
Funding: To be discussed

Multiscale control of active multicellular tissues



Emerging collective behaviors observed in multicellular biological tissues are controlled by the activity of the cells that make them up and by their mutual interactions. Such collective phenotypes include collective cell migration or organized supracellular tissue architectures; and span 2D and 3D geometries. However, *in vivo*, cell populations also strongly interact with their microenvironment via the physical and biochemical cues resulting from the presence of extracellular matrix (ECM) and neighboring tissues.

These complex environments therefore span different length scales from subcellular microscales (molecular sizes of the biopolymers of the ECM), to supracellular mesoscales (large scale heterogeneities, such as physical confinement between other tissues). The two situations are very different since subcellular cues act on all cells, whereas supracellular confinement defines tissue boundaries and relies on cell self-organization. There is therefore a need for *in vitro* experiments in which cells experience guiding cues at well-controlled length-scales.

In the present project, we propose to expose active cell populations to well-defined multiscale environments. To achieve these conditions, we will design and fabricate microstructures encompassing several length-scales ranging from subcellular guidance cues to supracellular confinement. Interestingly, these microscale and mesoscale features can act antagonistically or synergistically on the tissue. These experiments will allow quantitative measurements of key physical parameters, such as activity or rheological parameters that can then be related to biological functions.

In the longer run, such structures will be used to explore tissue-scale interactions between cancer cells and associated fibroblasts, or to promote the formation of well-controlled 3D tissues with potential applications to "on-chip" cell differentiation.

This interdisciplinary experimental project relies practically on microfabrication, cell biology and image analysis including machine learning methods. It is developed in collaboration with groups of biologists and theoreticians.

Recent references of the group (selection) Sarkar T. et al. Crisscross multilayering of cell sheets, *PNAS Nexus*, **2**, (2023), pgad034; Yashunsky V et al. Chiral Edge Currents in Nematic Cell Monolayers *Phys Rev. X* **12**, (2022), 041017; Duclos G. et al. *Spontaneous shear flow in confined cellular nematics*, *Nature Physics*. **14**, (2018), 728

Figure: Organized "crisscross" bilayer of muscle cells developing at a topological defect. Actin labeling (magenta=layer1; cyan=layer2). Bar=50µm

Please, indicate which speciality(ies) seem(s) to be more adapted to the subject:
Condensed Matter Physics: NO Soft Matter and Biological Physics: YES
Quantum Physics: NO Theoretical Physics: NO