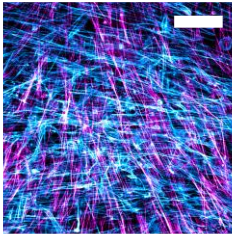


## M2 project

Laboratoire PhysicoChimie Curie  
Institut Curie, 11 Rue Pierre et Marie Curie-75005 PARIS

Team: Biology-inspired Physics at MesoScales ([https://institut-curie.org/teams/buguin\\_silberzan](https://institut-curie.org/teams/buguin_silberzan))  
Supervisor: Pascal Silberzan (pascal.silberzan@curie.fr)

### 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., Yashunsky V., Brézin L., Blanch Mercader C., Aryaksama T., Lacroix M., Risler T., Joanny J.-F., Silberzan P.: Crisscross multilayering of cell sheets, *PNAS Nexus*, **2**, (2023), pgad034
- Yashunsky V., Pearce D.J.G., Blanch-Mercader C., Ascione F, Silberzan P., Giomi L.: Chiral Edge Currents in Nematic Cell Monolayers *Physical Review. X* **12**, (2022), 041017.
- Duclos G., Blanch-Mercader C., Yashunsky V., Salbreux G., Joanny J.-F., Prost J., Silberzan P.: *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