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Directing cell populations with multiscale environments

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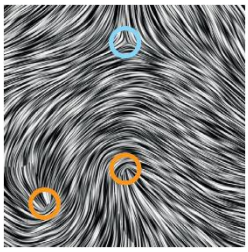
Internship summary:



The behavior of a biological tissue results from the coordinated actions of the cells that constitute it. *In vivo*, these cell populations cope with their microenvironment, including physical and biochemical cues exerted by the extracellular matrix but also by neighboring cells. Importantly, these environments are complex and include different lengthscales from molecular sizes (the biopolymers of the Extra Cellular Matrix (ECM)) to multicellular guiding cues (such as the large scale heterogeneities in the ECM gel). Therefore, experiments aiming at mimicking these situations *in vitro* should include this complexity in the form of guiding cues, physical boundaries, and confinement.

In the last years, our group has addressed different aspects of collective behaviors of cells with a physics approach. In particular, we have studied various aspects of collective migration in confluent cell sheets in different situations including for instance spontaneous laminar flows, global oscillations or migration over a free surface (wound-healing) under confinement.

In the present project, we propose to increase the complexity of these experiments by designing multiscale structures and studying the impact of the different lengthscales that can act independently or synergistically on high-density cell populations. From these experiments and their theoretical interpretation, we expect to be able to quantitatively extract several relevant parameters such as the cell-substrate effective friction. In a second time, acting on the relevant signaling pathways will allow relating these physical global parameters with the cell molecular players.

To address these questions practically, we combine microfabrication, micropatterning, innovative microscopy techniques and image analysis, with cell biology techniques. Physical quantities such as the cell flows or the mechanical traction forces exerted on the substrate are quantitatively measured at all scales in parallel with biological activity.

This interdisciplinary project is developed in close collaboration with groups of biologists and theoreticians at Institut Curie and ENS.

Recent references (selection)

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- Duclos G., Erlenkämper C., Joanny J.-F., Silberzan P.: *Topological defects in confined populations of spindle-shaped cells.* Nat. Phys. **13**, (2017), 58.
- Hakim V., Silberzan P.: *Collective cell migration: a physics perspective.* Rep. Prog. Phys. **80**, (2017), 076601
- Reffay M., Parrini M. C., Cochet-Escartin O., Ladoux B., Buguin A., Coscoy S., Amblard F., Camonis J., Silberzan P.*: Interplay of RhoA and mechanical forces in collective cell migration driven by leader cells*. Nat. Cell. Biol. **16**, (2014), 217.

This internship can be continued in a thesis