**M2/PhD project**

**Laboratoire Physique des Cellules et Cancer**
**Institut Curie, 11 Rue Pierre et Marie Curie-75005 PARIS**

**Team: Biology-inspired Physics at MesoScales** (https://institut-curie.org/teams/buguin_silberzan)
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## Crisscross bilayering

Emerging collective behaviors observed in biological tissues are largely controlled by the structure of the underlying extracellular matrix (ECM) and its interactions with the cells. Notably, cells can deposit oriented ECM fibers which then acts as a guiding cue for neighboring cells and subsequently leads to the formation of large domains of common orientation in the cell sheet. In such monolayers, flows are actively generated at regions of large gradients of orientation corresponding to topological defects. In vitro experiments have shown that multilayers preferentially form at these spots, recapitulating the 2D-to-3D transition that is critical in several biological processes in embryogenesis or cancer development. However, the physical mechanism ruling this transition remains unclear.

Our team has recently shown that aligned ECM on a surface can be mimicked by synthetic micro-patterned grooves. Such a strategy allows to build mosaic surfaces with juxtaposed domains of uniform orientation. The angle between these domains is one of our control parameters (see Figure below where two domains are perpendicularly oriented). Culturing a cell monolayer on such substrates allows to monitor quantitatively the formation of bilayers in space and time. The obtained fields of orientation or velocity can then be compared to the predictions of active matter theories developed in parallel by our collaborators in the laboratory. This strategy will allow unraveling the mechanism of formation of bilayers from a 2D monolayer and represents a first step in our understanding of the formation of 3D tissues.

This comparison between theory and experiments will also allow measuring for the first time the physical parameters of the monolayer such as activity, aligning field, elastic constants… Potential applications can be the directed “on-chip” formation of 3D tissues from geometrical cues acting on differentiating cells.

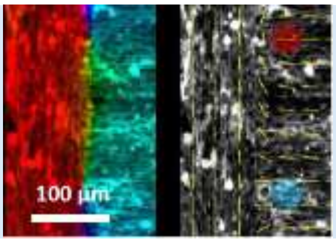


*Figure: Boundary between two perpendicularly oriented monolayers. Two representations of the same field of view. On the left panel, the colors code for the cell orientations, superimposed on a phase contrast image of the monolayer. On the right, the phase-contrast image of the monolayer is superimposed with the orientation field (yellow segments) and the topological defects (blue and red dots).*

Recent relevant references of the group (selection)

- Lacroix M et al.: *Emergence of bidirectional cell laning from collective contact guidance.* Nature Physics **20**, (2024) 1324
- 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* Physical Review. *X* **12**, (2022), 041017.
- Duclos G et al.: *Spontaneous shear flow in confined cellular nematics*, Nature Physics. **14**, (2018), 728.
- Duclos G et al.: *Topological defects in confined populations of spindle-shaped cells.* Nature Physics **13**, (2017), 58.