M2 internship and PhD thesis

Modelization of active cellular systems: dynamics, self-organization and cohesion

Laboratory : Laboratoire Matière et Systèmes Complexes, UMR 7057, CNRS-Université Paris Cité,
10 rue A. Domon et L. Duquet, 75013 Paris.
Supervision : Marc Durand
E-mail : marc.durand@u-paris.fr
Web : https://www.marcdurand.net
Thesis possibility after internship: YES
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Summary

Confluent biological tissues can be thought of as *active multicellular systems*: they consume energy (ATP) to generate motion or change their conformation. This activity affects the cohesion and the organization of the tissue, and is at the origin of large collective motions, such as those observed during morphogenetic movements. From a macroscopic perspective, this activity allows the tissue to shift from a solid-like to a fluid-like state. Yet, biological cells are much more complex than punctual or colloidal particles: they can deform, proliferate, communicate, and adapt in ways that cannot be modelled with simple active particles. Moreover, because of their high deformability/low compressibility features, their mechanical interactions in a tissue are non-pairwise.

An essential property for the correct functioning and integrity of tissues is their capacity to maintain sharp boundaries, in spite of the noise induced by the cell renewal and cell activity. Depending on the physical (cell rigidity, cell motility,...) and biological properties (division rate, apoptosis,…) of the two cell population, the boundary can destabilize through various mechanisms (see Figure 1). In particular, we have shown in a recent study that the intrinsic stochastically of cell division and cell death (apoptosis) induces a temporal instability of the mean position of the boundary.

Using both numerical and modelling techniques, we propose to explore the "phase space" of the boundary between two cell populations and determine the domains in which the frontiers destabilize. Moreover, the characterization of the undulations of the boundary between tissues, induced by the activity and renewal of cells, could provide a non-invasive tool to measure the properties of the two tissue in contact. Such characterization is challenging in two aspects: the out-of-equilibrium nature of these undulations in one hand, and the complex rheological properties of the tissues, in between elastic solids and fluids. The transition between the two behaviours can be tracked by studying the diffusion coefficient of cells within the tissue.

Required skills: the candidate should have a strong inclination for theory (especially statistical physics) and numerical simulations.

[1] J Ranft, M Basan, J Elgeti, JF Joanny, J Prost, F Jülicher, "Fluidization of tissues by cell division and apoptosis", Proc. Nat. Acad. Sci. 107 (49), 20863-20868 (2010).
[2] D. M. Sussman, J. M. Schwarz, M. C. Marchetti, M. L. Manning, "Soft yet Sharp Interfaces in a Vertex Model of Confluent Tissue", Phys. Rev. Lett. 120, 058001 (2018).
[3] L. G. Nava, D Chekroun, I Ionescu, M. Durand, "Temporal instability of the frontier between mechanically regulated tissues", https://arxiv.org/abs/2401.07569 (2025).

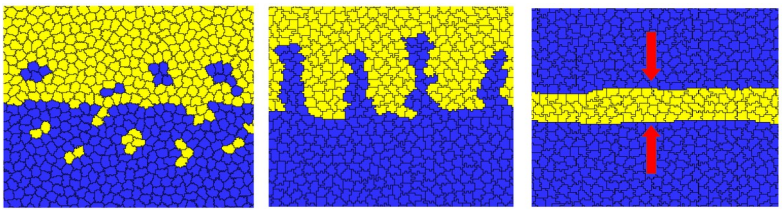

Figure 1: Mechanisms of destabilization of the boundary bewteen two tissues, depending on the mechanical and biological properties of the two cell populations: (a) mixing of cell populations ; (b) spatial instability (digitation) ; (c) temporal instability of the boundary.