M2 INTERNSHIP AND/OR THESIS PROPOSAL

Statistical inference of tissue rheology

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Thesis possibility after internship: Yes

Rheology is the study of the flow of matter. When cell-cell adhesion is strong, living tissues form a cohesive material, amenable to hydrodynamic descriptions. When cells are motile, their collective migration spontaneously generates tissue flow. During morphogenesis, tissue size and shape emerge through multi-scale feed-backs involving both genes and mechanics. As a first, crucial step, one needs to determine the tissue rheology, or how cell-generated displacements and forces produce tissue deformations. Tissue rheology involves mechanical ingredients, but must often take into account additional biological ingredients, such as contractility, polarity, cell proliferation and cell death, or the densities of relevant proteins such as morphogens and molecular motors [1].

Direct modeling approaches postulate a tissue rheology, then compare predictions with data. Since Bayesian inversion now allows to estimate the tissue stress field [2,3], we propose to investigate inverse approaches to tissue constitutive equations, and to determine tissue rheology from experimental data thanks to statistical inference. This approach has been successful for homogeneous cellular aggregates: we wish to extend it to epithelial cell monolayers where spatial degrees of freedom are relevant.

The first objective of the project is to combine stress field estimates with kinematic quantifiers of tissue dynamics to infer the constitutive equations of a tissue in physiological conditions, and determine the relevant material parameters. We will use experimental data measured in *in vitro* (cell monolayers) and/or *in vivo* systems (epithelia of developing organisms), as well as numerical data from simulations of cell-based models of epithelia.

This internship/thesis will involve analytical and numerical calculations, as well as experimental data analysis, at the interface between theoretical soft matter physics, mechanobiology, and statistics. No prior knowledge of the biology of tissues is required. The project will necessitate a strong desire to collaborate with experimentalists.

[1] S. Tlili, C. Gay, F. Graner, P. Marcq, F. Molino and P. Saramito, *Mechanical formalisms for tissue dynamics*, Eur. Phys. J. E **38**, 33 (2015)

[2] S. Ishihara and K. Sugimura, *Bayesian inference of force dynamics during morphogenesis*, J. Theor. Biol. **313C** 201-211 (2012)

[3] V. Nier, S. Jain, C.T. Lim, S. Ishihara, B. Ladoux and P. Marcq, *Inference of internal stress in a cell monolayer*, Biophys. J. **110** 1625-1635 (2016)