PhD PROJECT PROPOSAL

Computational Fluid Dynamics to infer embryonic tissue rheology

Lead supervisor: Simon Gsell (IRPHE)
Co-supervisor 1: Sham Tlili (IBDM)
If appropriate: Co-supervisor 2:

Abstract (10 lines)

Multi-cellular morphogenesis relies on the ability of tissues to generate internal stresses resulting in large tissue deformation. At the tissue scale, those stresses can be effectively described through continuum models for active materials [1]. However, tissue rheology, i.e. the way these stresses translate into large scale irreversible tissue deformation, remains poorly understood. Experimentally, the growing ability to engineer in-vitro functional tissues [2], together with the development of microfluidic techniques [3], open the way to new perturbative approaches to determine tissue mechanical properties. New theoretical and computational approaches are however crucially needed to infer tissue rheology from such experiments. This project aims at developing new inference approaches based on non-Newtonian Computational Fluid Dynamics (CFD) [4]. This will allow us to bridge a crucial gap in the understanding of the mechanics of morphogenesis, and will pave the way to the development of predictive computational models for tissue mechanics.

Keywords

Tissue morphogenesis; Active matter; Rheology; Computational Fluid Dynamics (CFD)

Objectives (5 lines)

The PhD project aims to use computations to develop new rheological models for embryonic organoids. (1) We will determine the main fields (e.g. key protein concentrations) controlling tissue rheology. (2) We will propose simple rheological models recapitulating heterogeneous mechanical properties of embryonic organoids. (3) These models will be applied to the computational modeling of embryonic organoid morphogenesis, in collaboration with a postdoc in the group (ANR-JCJC submitted by Simon Gsell).

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Proposed approach (experimental / theoretical / computational) (10 lines)

Sham Tlili (ST) will perform rheological experiments where embryonic organoids are aspired through microfluidic channels [3], while being imaged at the subcellular scale using multi-photon microscopy. The experimental data will consist in heterogeneous velocity and cell deformation fields, obtained for various tissue types ranging from homogeneous stem cell aggregates to differentiated organoids. The PhD student will (i) contribute to the experimental data analysis and (ii) develop a CFD program based on the lattice-Boltzmann method able to simulate such tissue flows, given some prescribed rheological properties. He/She will perform extensive simulations coupled to a Bayesian inference algorithm [5] in order to determine the rheological parameters that best predict experimental tissue velocity fields. By applying our algorithm to various homogeneous tissues, we will determine the impact of tissue biochemical properties on rheology. Our tissue-dependent rheological models will finally be applied to fully developed heterogenous organoids.

Interdisciplinarity (10 lines)

This project is at the interface between developmental biology, biophysics, soft matter physics and computational physics. It is specifically designed to address a fundamental question regarding multi-cellular morphogenesis (How can mechanical properties shape tissues ?) and to synergize with emerging experimental techniques (microfluidic experiments on embryonic organoids). The project is at the confluence of expertise present at IRPHE (Theoretical fluid dynamics, Computational physics) and IBDM (embryonic tissue culture/ engineering, microfluidics and 3D imaging) resulting in an original inter-disciplinary program. The use of Computational Fluid Dynamics in the field of developmental biology is an emergent trend that may pave the way to the development of new computational tools to better understand and engineer tissue morphogenesis. Heterogeneous mechanical properties emerge in other biological tissues such as tumors and spheroids: for this reason we expect this project to have spin-off in other fields such as cancer biophysics.

PhD student's expected profile

Applicants should have a background in physics, mechanics or applied mathematics, with some experience in programming and numerical simulations. They should have a strong interest in biological physics/mechanics and be motivated by inter-disciplinary research. Some theoretical knowledge/experience in rheology, active matter, image analysis and/or computational fluid dynamics would also be appreciated.

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Is this project the continuation of an existing project or an entirely new one?
In the case of an existing project, please explain the links between the two projects (5 lines)

During his CENTURI postdoc from 2020 to 2022, Simon Gsell (SG) developed computational models recapitulating early morphogenetic flows in embryonic organoids, assuming that tissues behave as simple viscous fluids. However, this hypothesis is not valid anymore for more advanced morphogenesis stages, where tissues exhibit complex visco-elasto-plastic mechanical behavior, which is likely to be modulated by cell differentiation. Both new experimental (ST) and numerical (SG) tools need to be developed to tackle this new question.

2 to 5 references related to the project

[1] Jülicher et al., 2018, Reports on Progress in Physics, doi:10.1088/1361-6633/aab6bb
[2] Simunovic & Brivanlou, 2017, Development, doi:10.1242/dev.143529
[3] Tlili et al., 2022, Development, doi:10.1242/dev.200774
[4] Gsell et al., 2021, Journal of Computational Physics, doi:10.1016/j.jcp.2020.109943
[5] Ran et al., 2023, Journal of Rheology, doi:10.1122/8.0000556

3 main publications from each PI over the last 5 years

Simon Gsell

(i) Loiseau et al., 2020, Nature Physics, doi:10.1038/s41567-020-0980-z
(ii) Gsell et al., 2020, Scientific Reports, doi:10.1038/s41598-020-64695-w
(iii) Gsell & Merkel, 2022, Soft Matter, doi:10.1039/D1SM01647D

Sham Tlili

(i) Tlili et al., 2019, PNAS, doi:10.1073/pnas.1900819116
(ii) Tlili et al., 2020, Physical Review Letters, doi:10.1103/PhysRevLett.125.088102
(iii) Hashmi et al., 2022, eLife, doi:10.7554/eLife.59371