PhD PROJECT PROPOSAL

CENTURI
TURING CENTRE
FOR LIVING SYSTEMS

Quantifying and modeling tissue viscoelasticity in developing embryos

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Abstract

During embryonic development, fertilized eggs undergo a series of dynamic rearrangements to adopt their adult forms. This process of form creation depends on the mechanical properties of the tissues that make up the embryo. However, since tissues are composed of cells, their viscoelasticity emerges from the physical properties and dynamic behaviors of the cells rather than being a well-defined, continuum property [1-2]. The goal of this project is to create a data-driven physical model of how tissue rheology arises from and depends on cell-scale dynamics, and how the resulting tissue properties enable the flows that drive embryo development.

To this aim, the student will combine experimentation, data analysis, and modeling to uncover how cells and tissues deform and flow to drive the development of form in *Drosophila* embryos. The resulting physical model will describe tissue behavior in control and perturbed conditions, which we will use to explore why *Drosophila* embryos develop faster in warm environments than in cool ones, but achieve the same final form. [3]

Keywords

Embryo development, tissue dynamics, physical modeling, physics inspired neural networks

Scientific question and Objectives

The key objective is to obtain data-driven models describing the dynamics of the fly embryo at the cell and tissue scale, with predictive power at the embryo scale. To this aim, it is essential to articulate experimental work, data acquisition and treatment, and data-driven modeling.

Our objectives are:

(1) Measure the cell and tissue dynamics that underlie large-scale developmental flows by performing confocal microscopy on living embryo in different perturbed conditions,

(2) Quantify the physical relationships between cell behaviors and tissue response by analysing how the deformations and rearrangements of individual cells contribute to tissue flow [4],

(3) Learn a constitutive equation of tissue rheology directly from the live-imaging data by implementing a physics-informed neural network (PINN) [5].

Proposed approach (experimental / theoretical / computational) and research plan

The project will intertwine experimental, data analysis, theoretical, and computational work. In the first semester (S1), the student will learn to work with *Drosophila* and perform confocal microscopy, benefitting from the existing expertise in the group of EG.

Starting in S2, the student will analyze the resulting movies, tracking cell position, deformation, and movement using image analysis software such as FIJI. The student will use these measurements to quantify the relationships between cell stretch (that contributes to tissue elasticity) and cell rearrangements (that contribute to tissue viscosity) and to determine how these effects contribute to tissue flow (see Figure). Establishing these relationships will allow the student to compare existing models of viscoelasticity to determine which most closely resembles the behavior of tissues. The student will be encouraged to mobilize the broad expertise in the Centuri community on this subject (e.g. Merkel, Rupprecht, Lenne groups) as well as expertise in SG's group.

In S3, the student will familiarize with using PINNs to reconstruct models from the obtained data. PINNs are adapted neural networks that can represent continuous fields from discrete, noisy data while being constrained to respect prescribed physical relations. The PINN that we set up will allow us to infer parameter values that we cannot directly measure and to quantitatively compare models and select the one that most accurately reflects our data. The student will integrate in SG's team, where PINNs are broadly used, to perform these tasks.

In S4, the pipeline will be enriched by performing experiments under different perturbations including: 1) modifying internal stress generation using genetic modifications, 2) changing the temperature at which the embryos develop, and 3) changing the energy available to power development by modifying metabolism.

S5 and S6 will consist in the exploitation and consolidation of the pipeline, systematic exploration of parameters, and interpretation of the results.

Interdisciplinarity and Implication of the two labs

This ambitious yet feasible PhD project bridges between EG's expertise on *Drosophila* embryo manipulation and imaging [6-7], and SG's expertise on data-driven physical modeling [8-9]. It is set at the interface between experimental developmental biology, bioenergetics, and fluid mechanics, and will combine advanced microscopy with cutting-edge data analysis methods. This project is thus highly interdisciplinary both in its methods and in its goals.

As described in the previous section, after a first semester of familiarization with the experimental setup, the student will integrate in both groups. We expect to have monthly joint group meetings with the two groups, as well as regular meetings with both advisors, to ensure that the student is exposed to the necessary expertise on both sides to achieve this project. Finally, we note that some goals (cell segmentation and tracking, P, full embryo development) strongly resonate with the Centuri community, and the student will be encouraged to interact and, if the opportunity arises, collaborate with other local groups.

Specify with whom the person recruited will collaborate and on what aspects

The student will work with EG on the experimental aspects of the project, will work jointly with EG and SG on the data analysis aspects, and will work with SG on setting up and implementing the PINNs.

PhD student's expected profile

We expect the student to have a physics background, with both theoretical and experimental experience in

biological physics, soft matter and/or statistical physics. The student should have lab experience, preferably including some experience with microscopy, as well as strong proficiency with theoretical tools for statistical and continuum mechanics. Experience in programming (Python) is necessary. Prior experience in image analysis (FIJI, Trackmate or alternatives), and/or in data-driven approaches / machine learning would be a plus.

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)

This is an entirely new project and collaboration. EG and SG both have ongoing ANR projects, which also involve the physical mechanisms that drive development. EG's project develops experimental capabilities that can be utilized for this PhD project. SG's project, which includes the ongoing CENTURI PhD work of M. Lardy [9], develops PINN algorithms to infer tissue rheology in embryonic organoids. In this new project, we will combine both projects' expertise to address different scientific questions and develop new technical approaches.

Two to five references related to the project

[1] Kim, Pochitaloff, Stooke-Vaughan, Campas. Embryonic tissues as active foams. *Nat Phys* **17**, 859-866 (2021).
[2] Clément, Dehapiot, Collinet, Lecuit, Lenne. Viscoelastic Dissipation Stabilizes Cell Shape Changes during Tissue Morphogenesis. Curr Biol **27** 3132-3142 (2017).
[3] Chong, Amourda, Saunders. Temporal Development of *Drosophila* Embryos Is Highly Robust across a Wide Temperature Range. *J. R. Soc. Interface* **15,** 20180304 (2018).
[4] Merkel, Etournay, Popović, Salbreux, Eaton, Jülicher. Triangles bridge the scales: Quantifying cellular contributions to tissue deformation. *Phys Rev E* **95**, 032401 (2017).
[5] Karniadakis, Kevrekidis, Lu, Perdikaris, Wang, Yang. Physics-informed machine learning. *Nat Rev Phys* **3**, 422-440 (2021).

Two main publications from each PI over the last 5 years

[6] Gehrels, E.W.*, Chakrabortty, B.*, Perrin, M.-E., Merkel, M., Lecuit, T. Curvature gradient drives polarized flow in the *Drosophila* embryo. *PNAS* **120** (6), e2214205120 (2023).
[7] Bailles, A.*, Gehrels, E.W.*, Lecuit, T. Mechanochemical principles of spatial and temporal patterns in cells and tissues. *Annu Rev Cell Dev Biol* **38**, 321-347 (2022).
[8] Gsell, Tlili, Merkel, Lenne. Marangoni-like tissue flows enhance symmetry breaking of embryonic organoids. *Nat Phys* **21**, 644-653 (2025).
[9] Lardy, Tlili, Gsell. Inferring viscoplastic models from velocity fields: A physics-informed neural network approach. J *Non Newt Fluid Mech* **346**, 105512 (2025).

Project's illustrating image