Stage Master 2

Multi-scale Mechanics of embryo Morphogenesis

Context

Do we understand embryonic development? In 1994, the famous embryologist Lewis Wolpert wondered "**Will the egg be computable?** That is, given a total description of the fertilized egg - the total DNA sequence and the location of all proteins and RNA - could one predict how the embryo will develop?" [Wolpert 1994]. At stake is the identification of **the theoretical underpinnings of biological complexity**, and in particular collaborative processes across different scales give rise to emergent behaviors.

Traditional embryological research has primarily focused on explaining average developmental processes, often overlooking individual variation within natural populations. However, natural morphological variation is essential for both development and evolution. In this project, we aim to **link variations in morphology and in the mechanical properties driving morphogenesis**, by integrating 3D cellular dynamics and tissue mechanics. The project could form the basis of a subsequent interdisciplinary PhD project.

To reach this aim, **the project will associate two teams in Montpellier**. The team of Patrick Lemaire (Biology, CRBM) has developed over the last few years a live light-sheet imaging and segmentation pipeline to systematically reconstruct cell shapes and cell lineage during the first 9 hours of ascidian embryogenesis [Guignard 2020]. They collaborate with the statistical physics team of Prof. Madhav Mani (Northwestern University, Evanston, USA), who developed a framework to infer mechanical properties from these segmented 3D imaging data based on the hypothesis of Young-Laplace laws [Liu 2023]. The ICAR team (Computer science, LIRMM) has in parallel developed a morphogenetic browser, **MorphoNet** [Leggio 2019], to visualize, interact and manually edit 3D+t segmented datasets.

Ascidian embryos exhibit highly reproducible development, yet variation is detected at the cellular level. Our database includes cellular-resolution reconstructions of around 20 ascidian embryos, including some with experimentally manipulated development. To **characterize natural morphological variation**, we will analyze a range of geometric features, such as morphological, topological, and temporal dynamics of cells, to track the evolution of embryo morphologies. In parallel, we will seek to **identify the mechanical determinants** of this natural variation by inferring individual single-cell mechanical properties from geometric data [Liu 2023].

The student will develop a versatile framework within the MorphoNet platform to: 1) extract various morphological properties to characterize individual developmental trajectories, and 2) create a mechanical simulation platform, which integrates biomechanical models of morphogenesis to analyze the processes driving developmental variation.A major challenge will be to ensure that the nature and structuration of the data and the semantic representation of their relationships are adapted to the layer of numerical models used to explain the transitions between states and scales of organization.

Profile and skills required

The project is mostly experimental, with opportunities to contribute to the computational and statistical analysis of the acquired datasets. Applications are expected from highly motivated candidates with experience in computational and statistical analyses and in search for an interdisciplinary environment.
Ideal candidates will hold a **master's degree in computer sciences, quantitative biology or physics** (with solid experience in python). Our team has an equal opportunities employment policy.

Application procedure

Interested students should contact Dr. Emmanuel Faure (emmanuel.faure[at]lirmm.fr) and Dr. Patrick Lemaire (patrick.lemaire[at]crbm.cnrs.fr) at their earliest convenience and before January 1st 2025 by sending a detailed CV.

Compensation

Remuneration according to the legal scale for internships will be approximately €600 per month.

Publications:

- Leggio, B., Laussu, J., Carlier, A. *et al. MorphoNet*: an interactive online morphological browser to explore complex multi-scale data. *Nat Commun* 10, 2812 (2019). https://doi.org/10.1038/s41467-019-10668-1
- Guignard, L., Fiúza, U. M., Leggio, B., Laussu, J., Faure, E., Michelin, G., ... & Lemaire, P. (2020). Contact area–dependent cell communication and the morphological invariance of ascidian embryogenesis. Science, 369(6500), eaar5663.https://doi.org/10.1126/science.aar5663
- Liu, S., Lemaire, P., Munro, E., & Mani, M. (2022). A mechanical atlas for Ascidian gastrulation. bioRxiv, 2022-11.