Non-equilibrium fluctuations as drivers of tissue fluidization during embryonic development

Location: Marseille, France

Institute: <u>Centre Interdisciplinaire de Nanoscience de Marseille</u> (Aix-Marseille Université / CNRS) Host lab: Gehrels Team – "Dynamics of form creation in living systems" Lab website , email address: <u>https://gehrelslab.wordpress.com/</u> , emily.gehrels@univ-amu.fr Funding , timeline: 2.5 years of ANR funding , start date as early as January 2025

Keywords: Tissue dynamics, Embryonic development, Non-equilibrium processes

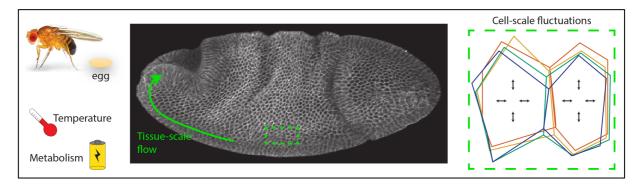
Concepts and objectives:

Embryonic development is the process by which simple fertilized eggs undergo a series of dynamic rearrangements to adopt their complex adult forms. These rearrangements depend sensitively on cellular attributes such as cell-cell adhesion, cortical tension, elasticity, and viscosity. While physical models exist that describe how tissue dynamics emerge from such cellular attributes, there is no consensus on how to treat the fact that these systems are inherently far from equilibrium. For example, the global distribution of cortical tension in the embryo has been shown to direct tissue flow, but it was recently theoretically proposed that fluctuations in local tension at cell-cell contacts are required for cells to rearrange, allowing the tissue to act as a viscous fluid instead of an elastic solid. However, there have been few experimental studies to quantify such fluctuations in biological tissue and relate them to cell rearrangements and tissue dynamics. Further, it is unknown how these energetically-costly fluctuations relate to non-equilibrium effects resulting from energy-consumption in the cells.

The aim of this project is to uncover the cellular mechanisms that drive tissue fluidization during embryonic development. Specifically, we seek to understand the effects that fluctuations in tension at cell-cell contacts play in cell rearrangements, which underlie tissue fluidization, and the dependence of said fluctuations on non-equilibrium, energy-consuming effects. To address these questions, the postdoc will pursue the following objectives:

- 1. FLUCTUATIONS: Testing whether cell-scale tension fluctuations increase tissue fluidization by correlating changes in cell-cell rearrangement rates with changes in cell-scale fluctuation dynamics at different temperatures, and consequently different developmental speeds.
- 2. ENERGY CONSUMPTION: Determining whether cells that exhibit more fluctuations consume more energy by mapping cell-scale energy consumption as a function of space and time during development.
- **3. NON-EQUILIBRIUM EFFECTS:** Decoupling thermal from non-equilibrium (energy-consuming) contributions to tissue fluidization by independently changing system temperature and perturbing metabolic rate and comparing the impact on cell-scale fluctuations and tissue-scale fluidization.

To accomplish these objectives, the postdoc will perform live imaging of embryonic development in the model organism *Drosophila melanogaster* at organism-, tissue-, and cell-scale resolution under different environmental, mutant, and drug conditions.



References:

- Bailles*, Gehrels*, Lecuit. Mechanochemical principles of spatial and temporal patterns in cells and tissues. *Annu Rev Cell Dev Biol* **38**, 321-347 (2022).
- Gehrels*, Chakrabortty*, Perrin, Merkel, Lecuit. Curvature gradient drives polarized flow in the *Drosophila* embryo. *PNAS* **120** (6), e2214205120 (2023).