# M2+PhD: Inference of cell rearrangements & theory of active phase separation in cell assemblies

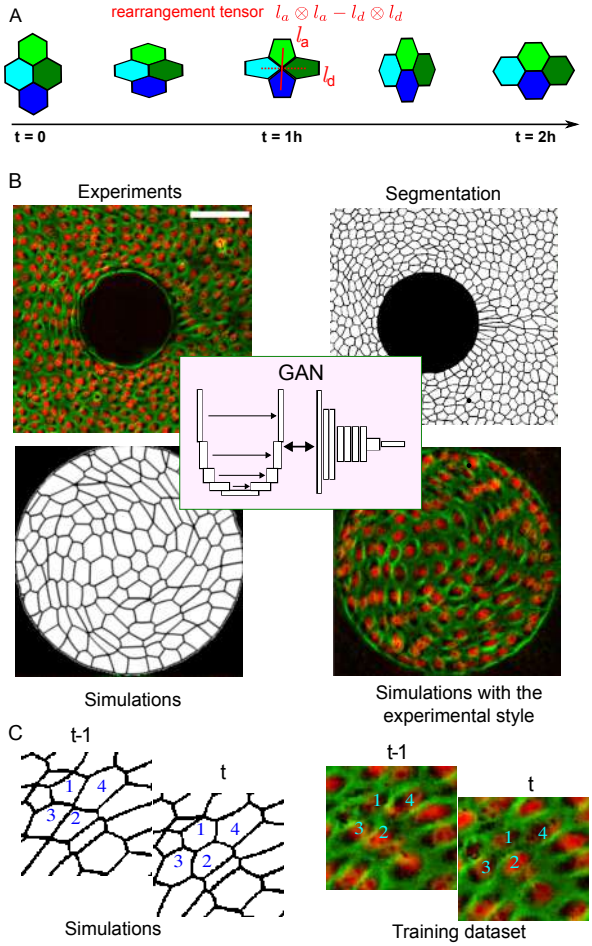
Embryonic development is a complex hydrodynamic problem. Global flows stem from individual cell-cell rearrangements, see Fig. A. These rearrangements can either resist or drive, embryonic flows. Tracking their location and orientation is crucial to understanding morphogenesis, yet it remains a challenging task. On the theoretical side, we observe that modulation in the rates cell-cell rearrangements triggers phase separation between cell types, but we seek to develop simplified analytical models to account for this effect.

**Objective of the internship** Currently, the detection of cellular rearrangements in biological tissues relies on an extremely difficult step: the segmentation and tracking of cell-cell interfaces. In this internship, we propose bypassing this step and inferring the positions and directions of the rearrangement directly from time-lapse images. We will readapt a method that our team initiated to locate cell divisions (Karnat et al. bioRxiv 2024). This internship serves as the starting point to PhD in Physics, aimed at understanding the phase separation in tissues according to their fluidity, with applications to the symmetry breaking in 3D gastruloids – a model system for embryogenesis.

**The team** Jean-François Rupprecht is a theoretician building continuum (active nematics, Prasad et al. Science 2024) and cell-based (vertex, Lin et al. PRL 2023) models. We closely collaborate with Sham Tlili, a physicist, leading model, analysis & experiments for gastruloids (Gsell et al., Nat. Phys. 2024).

**Context** Rearrangements are represented by a tensorial quantity (Graner et al. 2008). Maps of these tensors have been obtained in the context of the development of the thorax and wing of Drosophila in the pupa stage (Guirao Science 2016). However, the ideal conditions of the Drosophila pupa are rarely met: in most cases, the real-time imaging of biological tissues is limited by constraints such as phototoxicity in fluorescence microscopy, which restricts temporal and spatial resolution. Constraints on cell segmentation are even greater in most cases, as in 2D MDCK in Fig. B, or 3D.

In this M2 internship, we propose to directly detect the positions and orientations of rearrangements using dedicated networks (see Fig 1A), based on the preliminary results obtained during the PhD of Marc Karnat. To bypass the tedious task of building a training dataset through manual annotation in experimental movies, we recently adapted a generative adversarial network (GAN) to transfer the style of experimental images to the binary tissue masks obtained by vertex




simulations (Fig B). These simulations are then used to build a training dataset (Fig. C) Our preliminary results are very promising: many rearrangements are correctly detected in our experimental data of collective migration of MDCK cells around obstacles.

**Overall Ph.D. subject** Analysis of the rearrangement tensor enables the quantification of tissue fluidity. We propose a Ph.D. subject on cell sorting based on fluidity modulations, which builds upon our recent success in modelling tissues according to their viscosity levels (Fu et al. PNAS 2024). We will **balance between conceptual, analytical and simulations work**.

**Possible PhD funding:** Yes, I have fundings available. ***We do not require any previous experience in deep learning nor in biology.***

**Location**: Marseille Luminy, arguably the most beautiful campus in the world, right in the middle of the Calanques National Parc.

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