Institut Pasteur

Physics of Biological Function – UMR 3738

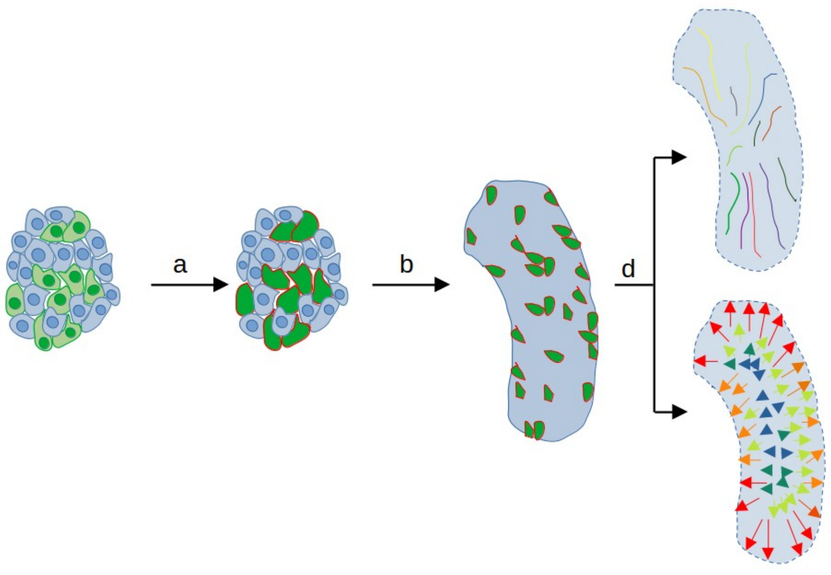
Quantitative study of the morphological changes and the patterning of gastruloids

Basile Poutier

Supervised by Thomas Gregor

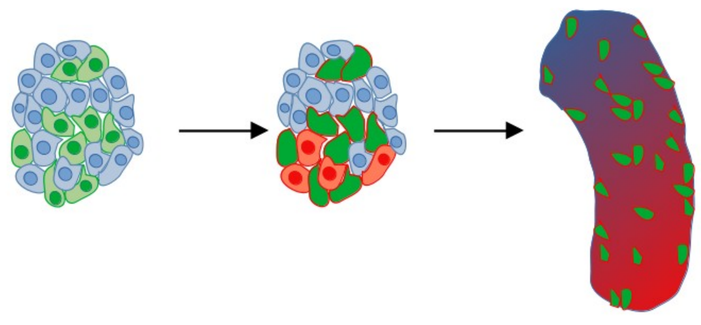
Abstract:

The development of a single cell into a complex multicellular embryo is largely mediated by signaling and mechanical cues. Biochemical signals can induce cell reshaping, or movement and then act on the mechanical properties of the embryo. On the other hand, mechanical cues are sensed at multiple levels and can tune the gene expression or enzymatic activity. However, we still don't know how these two cues are coupled in space and time during the development, and more especially in mammals because of the difficulties to access the embryo and the lack of reproducibility. The recent ability to generate gastruloids *ie* mES cells aggregates that mirror the early mouse development (which break symmetry, polarize their gene expression, specify their AP and DV axis, and undergo a gastrulation-like process) provides a powerful system to study quantitatively the coupling between morphogenesis and gene patterning. Indeed, the hosting lab demonstrated the high precision and reproducibility of the self-organization of gastruloids. The aim of my internship is to gather imaging data and develop a image analysis pipeline to measure precisely the spatiotemporal setting up of the patterning and the shaping of gastruloids. These results might shed a new light on the dynamical coupling between patterning and morphogenesis.



Quantitative study of gastruloid morphogenesis :
Preparation of mosaic gastruloid by aggregating mES cell constitutively tagged or not, and live imaging. Analysis of the imaging data :
a. 3D segmentation and labeling of the tagged cells
b. 3D cell tracking during the gastruloid development
c. (Up) Individual cell trajectories. (Down) Multicellular deformation

These results should help us understanding precisely how the gastruloid shape is acquired. Is the reshaping done by localized cell growth? Individual or collective migration? Large scale deformation?



Coupling between patterning and morphogenesis :
Same system + tagging of a patterning gene (Brachyury for example). With the green tag we can measure cell movements and deformations. With the red tag, we have the expression dynamics of a patterning gene.

These results give some insight into the coupling between the patterning of the gastruloid and its morphogenesis. We will study the expression of Brachyury (Bra) which specifies the mesoderm. Its expression is localized in the posterior part of the gastruloid. This experiment will enable us to understand the interaction between the localized expression of Bra and the different morphological changes.

Depending on the results of these experiments, different perspectives can be imagined to understand further how the gene patterning deal with the morphogenesis. The perturbative experiment currently envisaged is the artificial modification of the gastruloid size by fusion or section: we already know that the pattern scale with the size but we don't know how the size impacts the morphogenesis.