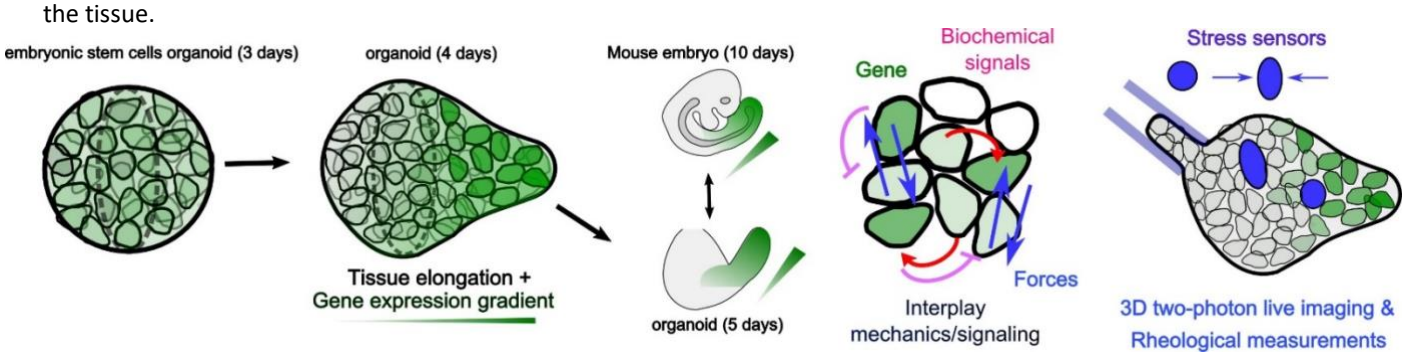
Mechanics of self-organized multicellular systems – Mechano-genetic patterns

Project for students in master or engineering school

IBDM, Turing Center for Living Systems, Marseille
Team: Physical approaches to cell dynamics and tissue morphogenesis

Team description We aim to identify the physical principles controlling the generation of tissue shapes (morphogenesis), in particular how mechanical forces sculpt tissues during embryonic development. To do so, we develop and apply quantitative approaches to observe, perturb and predict morphogenesis. We study how cell collectives generate and respond to mechanical forces, differentiate and self-organize, by probing different scales, from the molecular organization of cell-cell contacts to the global shape of tissues.

Description of the project During embryo development, **gene expression patterns encode information spatially and temporally**, such as the frequency and the localization of cellular events like cell divisions. **These events collectively generate tissue flows at the embryonic scale and heterogeneous mechanical constraints,** whose nature depends on the tissue physical properties (e.g. its rigidity and viscosity). These constraints progressively sculpt the embryonic tissues so that they gradually acquire their definitive form and function as organs.
Recent studies have shown that both mouse and human embryonic stem cells can spontaneously organize in a dish into 3D structures called embryonic organoids that recapitulate major events of early mouse and human embryogenesis. They offer a unique opportunity to study the formation of organs in mammals, which cannot be studied in a dynamic and perturbative way *in vivo*. Few days after their initial aggregation as a densely packed 3D aggregate of stem cells, these organoids self-organize and undergo a phenomenon called symmetry breaking: they evolve from a symmetrical spherical shape to an elongated shape (see Figure). Concomitantly to this tissue elongation process, genes involved in cell differentiation which were expressed in a spatially homogeneous manner progressively exhibit a heterogeneous expression following a gradient collinear to the axis of elongation of the tissue.



The project aims **to develop biophysical tools to experimentally measure both at the cell and the tissue scale the mechanical constraints** generated during the early elongation of embryonic organoids. The intern will combine deformable microspheres as stress sensors and laser ablations to measure stress in time and space within the organoid by using live imaging techniques. In addition, to measure tissue material properties, the intern will use a microfluidic device to aspire the organoids while imaging at the same time the tissue response at the cell scale. Regional differences in stress and mechanical properties will be mapped against gene expression pattern t**o dissect the gene/mechanics feedback loop responsible for the organoid early symmetry breaking.**

The project will address how mechanics and genetics interplay to pattern a self-organized multicellular system. The intern will contribute to the development/implementation of mechanical measurements, coupled with state-of-the-art microscopy approaches.

Existence of special opportunities for the intern
The project will be carried out in a biophysics lab that combines experimental and theoretical approaches
It will develop in close collaboration with teams bringing expertise in microfluidics, image analysis, and theoretical modeling in CENTURI. **The project may lead to a funded Ph.D. project.**

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Expected profile of the applicant
Physics training and desired programming skills with the motivation to perform experimental observations/measurements