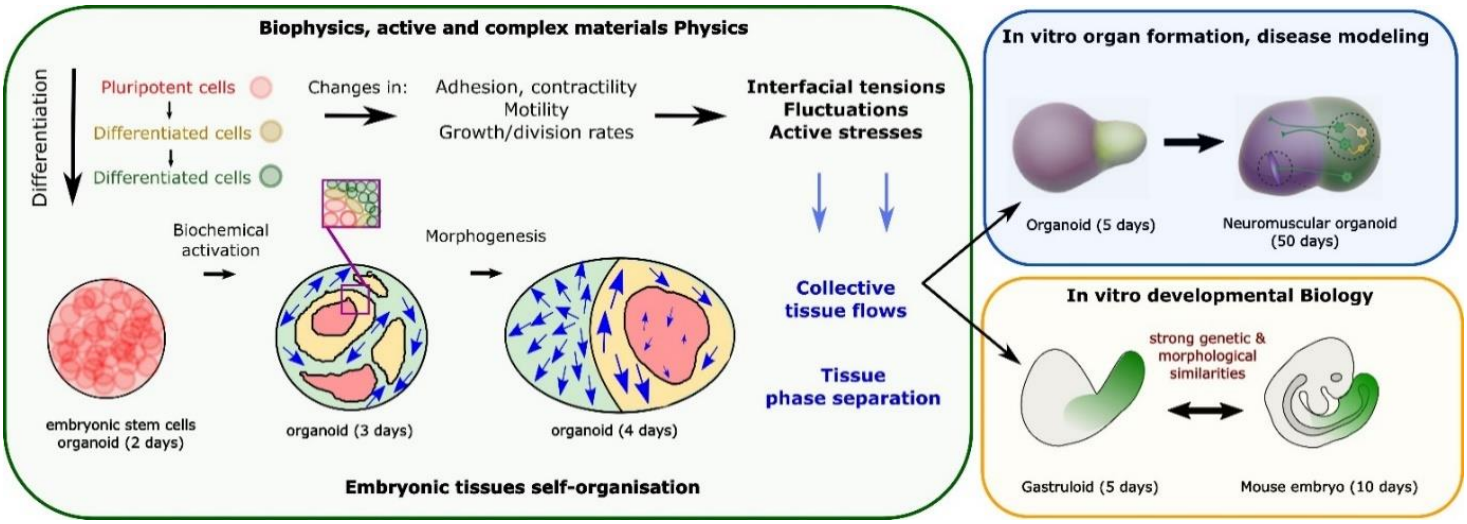
Mechanics of self-organized multicellular systems – Mechano-genetic patterns Ph.D. project (3-year fellowship)

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 animal morphogenesis, particularly **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 tissue shape.

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 properties can dramatically vary spatiotemporally within tissues due to **jamming transitions** which can be controlled by local cell packing, adhesion levels, motility and fluctuations. Emerging mechanical 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 **self-organize** *in vitro* into 3D structures called **embryonic organoids** that recapitulate major events of early 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* (see Figure).



The project aims **to develop biophysical tools to experimentally measure the mechanical constraints generated during the early elongation of embryonic organoids at the cell and the tissue scale**. The PhD. student 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 Ph.D. student 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 patterns 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 and whether jamming transitions play a role in such a process. The intern will contribute to the development/implementation of mechanical measurements coupled with state-of-the-art microscopy approaches.

Existence of unique opportunities for the Ph.D. student: 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 the Turing Center (CENTURI, MARSEILLE). **The project is funded for three years.**

Expected profile of the applicant: we are looking for a curious and enthusiastic student with a strong background in Physics/engineering motivated by undertaking an interdisciplinary project combining experiments and data analysis (and if desired theoretical modeling) at the frontier between statistical physics, biophysics and developmental biology.

Start date: September 2023.

To apply: Informal inquiries are welcome. We invite interested applicants to submit a letter of interest, a statement of prior research experience and professional interests, a CV, and contact information for 2 professional references to
Pierre-François Lenne, pierre-francois.lenne@univ-amu.fr & Sham Tlili, sham.tlili@univ-amu.fr