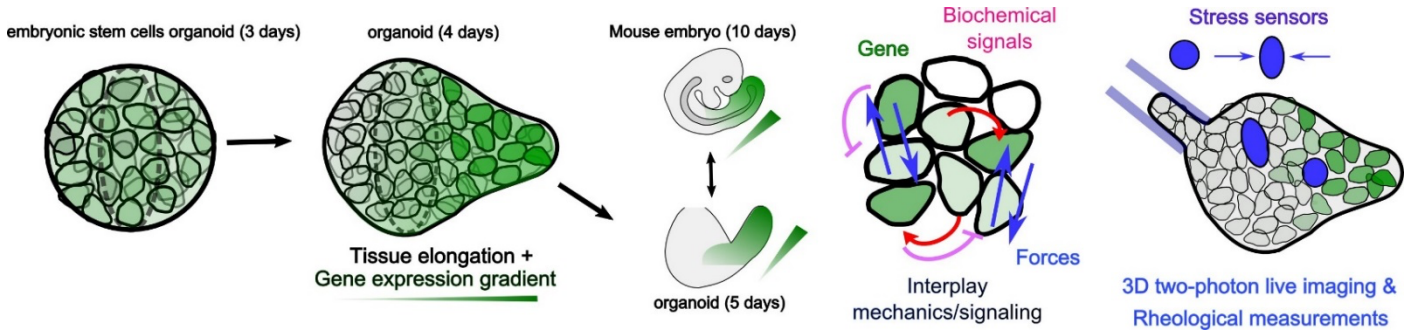
Mechanics of self-organized multicellular systems – Mechano-genetic patterns

IBDM, Turing Center for Living Systems, Marseille

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 generate collectively 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. Understanding how this biophysical feedback look between gene expression at the cellular scale and tissue mechanics is contributing to morphogenesis is a long-standing question, which is both studied quantitatively *in vivo* in embryos (such as the fruit fly embryo of the zebrafish embryo) and in *in vitro* cell cultures.

Recent studies have shown that both mouse and human embryonic stem cell**s** 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, in order 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 requires a solid background in physics and a strong interest in living systems and experiments.The project will be carried in a biophysics lab that combines experimental and theoretical approaches. This master project can eventually be continued by a PhD funded by the Turing Center for Living Systems.

Keywords: mechanics, rheology, complex systems, microfluidics, advanced microscopy, image analysis, developmental biology, stem cells, organoids, physical models

Team*: Physical Approaches to Cell Dynamics and Tissue Morphogenesis*

Contacts: PF Lenne and S. Tlili: Pierre-francois.lenne@univ-amu.fr; sham.tlili@univ-amu.fr