EuReCa International PhD Program

PhD thesis project

2023 Call for application

The role of mechano-chemical cues in vertebrate axial patterning and somite generation

General information

Call	2023
Reference	2023-04-GUEVORKIAN_SORRE
Keyword(s)	Morphogenesis; Physics; Microfluidics; Tissue stress; Tissue mechanics

Director(s) and team

Thesis director(s)	Karine Guevorkian and Benoit Sorre
Research team	Dynamic Control of Signaling and Gene Expression
Research department	UMR168 - Physico-Chimie Curie Lab

Description of the PhD thesis project

We propose an interdisciplinary project, at the interface of experimental biophysics and developmental biology, to study the role of mechanical and chemical signals in tissue patterning and emergence of shapes in vertebrate embryos.

We are interested in understanding how mechanical cues and possible feedbacks between mechanics and biochemical pathways result in the formation of structures during the axial morphogenesis of vertebrate embryos. In the past, we have studied the role of tissue viscoelasticity and cell motility during axial elongation in chicken embryos. Following up on these studies, here we focus on the process of somite generation or "somitogenesis", which is a crucial tissue patterning event leading to the formation of our musculoskeletal structures. Somites emerge as cells from the posterior mesoderm differentiate under the action of morphogen gradients and undergo mesenchymal to epithelial transition along the anterior-posterior axis, forming epithelial segments which detach periodically from the anterior end. The biochemical pathways involved in cell fate specification allowing to reproduce the early steps of segmentation in vitro from explants or stem cells have been identified. However, the cross-talks between physics and genetic signalling, leading to the morphogenetic step of somite generation with a characteristic shape and size are not yet known. From a physics point of view, the process of somitogenesis is reminiscent to the pearling instability in soft materials, induced by the surface tension and rhoelogical properties of the material. It is still unknown whether a similar mechanism, although more complex due to cell activity, can be in action during somitogenesis.

To address these questions, we will develop ex vivo experiments that will allow us to assess the role of mechanical cues and mechanosensitivity as the mesoderm differentiates along the axis and study the impact of the spatiotemporal morphogen gradients on somite generation by adapting microfluidic systems recently developed in our team. Lastly, in collaboration with theoreticians, we will integrate our findings with the existing theoretical models to offer a comprehensive description of somitogenesis combining physics and biology.

International, interdisciplinary & intersectoral aspects of the project

In this project, the student will work at the interface of developmental biology, and experimental and theoretical soft and active matter physics, where she/he will develop skills in carrying out biophysical experiments, as well as techniques used in handling and characterizing embryonic tissues. We will undertake technical developments such as microfluidics and microfabrication, both using in-house facilities as well as in collaboration with a leading company in microfabrication located in Paris. Our team benefits from international collaborations with the University of Geneva, and Harvard Medical School in Boston, as well as the highly interdisciplinary and international environment offered by Laboratoire Physico-Chimie Curie, at the heart of Institut Curie.

Recent publications

1. "Activity-driven extracellular volume expansion drives vertebrate axis elongation", A. Michaut, *et al.*, bioRxiv 2022.06.27.497799; doi: https://doi.org/10.1101/2022.06.27.497799.
2. "Rectified random cell motility as a mechanism for embryo elongation", I. Regev, *et al,* Development 149 (6): 2022.
3. "Dissecting Signaling Hierarchies in the Patterning of the Mouse Primitive Streak Using Micropatterned EpiLC Colonies", J-L Plouhinec, *et al.*, Stem Cell Reports, 2022. https://doi.org/10.1016/j.stemcr.2022.05.009.
4. "Flow dynamics of 3D multicellular systems into capillaries", K. Guevorkian, *et al*, in Viscoelasticity and collective cell migration, I Pajic-Lijakovic and E Barriga (Eds). Elsevier Science, 2021.
5. "Soft Matter Models of Developing Tissues and Tumors", D. Gonzalez-Rodriguez, *et al*, Science, 338 (6109): 910-917 (2012).

Expected profile of the candidate

Applicants should hold a master's degree in one of the following areas: biophysics, bioengineering, physics, biology, or in a closely related field. Knowledge in programming and image analysis are beneficial. The applicant should have a creative mindset, capacity to work independently, team working spirit, and willingness to develop new skills at the interface of physics and biology. A good command of English is essential, both as the local working language and because of our international collaborations.