

EuReCa International PhD Program
PhD thesis project
2022 Call for application

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

General information

Call	2022
Reference	2022-06-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 physics 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. 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, form epithelial segments which detach periodically from one end. From a physics point of view, the process is reminiscent to the pearling instability in soft materials. Genetics has identified the biochemical pathways involved in cell fate specification allowing to reproduce the early steps of segmentation in vitro from explants or stem cells. However, the cross-talks between physics and biology, leading to the morphogenetic step of somite generation with a characteristic shape and size are not yet known.

Here, we will explore the role of tissue mechanics and the impact of the micro-environment in which the tissue evolves on the process of somitogenesis in chicken embryos.

We will develop experimental approaches inspired by soft-matter physics and novel microfluidics techniques to:

- i) assess the role of mechanical cues and mechanosensitivity as the mesoderm differentiates along the axis, in ex vivo controlled conditions, and
- ii) define the impact of the spatiotemporal morphogen gradients on somite generation.

Later, 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. "Flow dynamics of 3D multicellular systems into capillaries", **K. Guevorkian**, F. Brochard-Wyart, D. Gonzalez-Rodriguez, in *Viscoelasticity and collective cell migration*, I Pajic-Lijakovic and E Barriga (Eds). Elsevier Science, 2021.
2. "Motility-gradient induced elongation of the vertebrate embryo", I. Regev*, **K. Guevorkian***, A. Gupta*, O. Pourquié, and L. Mahadevan, bioRxiv 187443; doi: <https://doi.org/10.1101/187443>
3. "Dissecting signalling hierarchies in the patterning of the mouse primitive streak using micro-patterned EpiLC colonies", J-L Plouhinec, M. Vieira, G., J. Collignon, **Benoit Sorre**, bioRxiv 2020.11.30.404418; doi: <https://doi.org/10.1101/2020.11.30.404418>.
4. "Encoding of temporal signals by the TGF- β pathway and implications for embryonic patterning", **B. Sorre***, A. Warmflash*, A. H. Brivanlou and E. D. Siggia, *Dev. Cell*, 2014, 30, 334–342.
5. "Soft Matter Models of Developing Tissues and Tumors", D. Gonzalez-Rodriguez*, **K. Guevorkian***, S. Douezan*, and F. Brochard-Wyart, *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.

