SCIENCES & BIOENGINEERING SCIENCES

The Research Groups
Applied Physics
has the honor to invite you to the public defense of the PhD thesis of

Rossana Bettoni

to obtain the degree of Doctor of Sciences

Title of the PhD thesis:

Exploring the link between signalling, geometry and information transmission: modelling neural fate induction in ascidian embryonic development

Supervisor:
Prof. dr. Geneviève Dupont (ULB)

Co-supervisor:
Prof. dr. Sophie de Buyl (VUB)

The defense will take place on

Monday, June 23, 2025 at 10.30 a.m.

VUB Etterbeek campus, Pleinlaan 2, Elsene, U-Residence, Green room

The defence can be followed through a live stream: link

Members of the jury

Prof. dr. Yannick De Decker (ULB, chair)
Prof. dr. Stijn Buitink (VUB)
Prof. dr. Aleksandra Walczak (Ecole Normale Supérieure, France)
Dr. Rémi Dumollard (Institut de la mer de Villefranche, France)
Dr. Isabella Graf (European Molecular Biology Laboratory, Germany)

Curriculum vitae

Rossana Bettoni obtained her MSc in Material Sciences from the University of Padova in July 2020. In November 2020, she began a joint Ph.D. program at the Université Libre de Bruxelles and Vrije Universiteit Brussel, under the supervision of Geneviève Dupont and Sophie de Buyl. Her research focuses on uncovering the mechanisms that drive cell fate specification in ascidian embryogenesis. She has authored two peer-reviewed publications, and a third is accepted for publication. She has presented her work at both national and international conferences.

Abstract of the PhD research

During embryonic development, cells adopt different identities with high spatial and temporal precision. Despite recent progress, the mechanisms governing cell fate inductions remains not completely understood. In particular, the role of the mechanics and geometry of the cells in the embryo has only recently started to be addressed. In this work we investigate the mechanisms regulating ascidian neural induction, especially addressing the impact of cell geometry on this process.

During neural induction, which occurs in ascidian embryos at the 32-cell stage, 4 out of 16 ectoderm cells adopt the neural fate, characterized by the expression of the neural marker *Otx*. This process is initiated at the extracellular level by two signalling molecules, FGF and ephrin, which control the acquisition of neural fate by a two-step process involving first the activation of the ERK pathway and second, the expression of the gene *Otx*. The combination of the two antagonistic signals (FGF activates the ERK pathway, while ephrin dampens ERK activity) tightly controls the level of *Otx* expression in all ectoderm cells. Interestingly, only a fraction of the cells exposed to the inducer FGF acquires the neural fate.

We used mathematical modelling to demonstrate that this selectivity is controlled by the quasi-invariant geometry of the embryo, which imposes upon each ectoderm cell a precise area of cell surface contact with underlying FGF-expressing cells. Our model successfully reproduces experimental observations about ERK activation and *Otx* expression obtained under normal and perturbed conditions. With the model, we investigated the role played by each signalling input as well as the role of two antagonistic transcription factors that regulate *Otx* expression.

We also investigated information transmission in neural induction and how the latter depends on the geometry of the cells. By optimizing information transmission between FGF and the number of active ERK molecules, under the constraint of a restricted total surface area with FGF-emitting cells, we found that the cell surface contacts with FGF that maximize information transmission are compatible with those measured experimentally.

Our work suggests that ascidian neural induction might be a consequence of the geometrical constraints imposed on the system via the surfaces of contact between the cells in the embryo.