2018-01

IC-**3i** International PhD Program

# PhD thesis project

2018 Call for application

## The geometry of developmental time – Dissecting temporal cell-fate acquisition during C. elegans development

## General information

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| **Call** | 2018-2019 |
| **Reference** | 2018-01-KEIL_BUGUIN |
| **Keyword(s)** | Quantitative developmental biology, C. elegans, Microfluidics, Live imaging, Mathematical modelling |

## Director(s) and team

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| **Thesis director(s)** | Wolfgang Keil |
| **Research team** | Quantitative Developmental Biology |
| **Research department** | UMR168 – Physico-Chimie |

## Description of the PhD thesis project

Development is the process by which the fertilized egg, a single cell, transforms into a fully functional multicellular organism. During this fascinating transformation, all basic cellular processes – from the cycle of each cell division to the formation of individual organs – need to be precisely coordinated in time and space. Our team is interested in how this is achieved. We are driven by the conviction that mathematical and physical concepts are indispensable for a deeper understanding of how the collective action of gene networks and environmental factors drives the emergence of precise and reproducible biological shapes and patterns.

Developmental studies often focus on mechanisms of patterning tissues in space. How cells “know” when to execute a certain developmental program is much less understood. In this project the PhD student will quantitatively study temporal patterning of the skin and egg-laying organ in the model organism Caenorhabditis elegans (C. elegans). To this end, the student will use a novel microfluidics technology for long-term live confocal microscopy of C. elegans that our team has recently developed. The student will follow temporal cell-fate acquisition through large-scale cell lineaging in both tissues and correlate the observed fates with spatiotemporal expression dynamics of timing genes at single-cell resolution.

To conceptualize this novel kind of data, the student will develop and test mathematical models for temporal cell-fate decisions of vulval and skin precursor stem cells. These models will be able to, for instance, predict the temporal cell-fate statistics in various genetic backgrounds, including within and across-tissue coordination. This approach will provide the first quantitative picture of temporal patterning in a multicellular organism, and offer a unique interdisciplinary training to the student.

## International, interdisciplinary & intersectoral aspects of the project

This thesis project aims to resolve a fundamental biological question using a highly interdisciplinary approach that combines:

1. state-of-the-art bioengineering (microfluidics/microfabrication)
2. high-resolution long-term live confocal microscopy and image analysis
3. molecular and cell biology
4. physical and mathematical modeling

Skills in automated image analysis of high-throughput microscopy data are in high demand from pharmaceutical companies performing high-content screens. Similarly, microfluidics is a booming technology that forms the basis of many modern-day biomedical commercial applications.

The student will strongly benefit from our network of collaborators and contacts, both in Paris (ENS, Curie) and in the US East coast (Cold Spring Harbor, Rockefeller).

## Recent publications

1. Katz M, Corson F, **Keil W**, Singhal A, Bae A, Lu Y, Liang Y, Shaham S.
Glutamate spillover in C. elegans triggers repetitive behavior through presynaptic activation of MGL-2/mGluR5 (2018); bioRxiv 415828; doi: https://doi.org/10.1101/415828

2. Kutscher LM, **Keil W**, Shaham S (2018)
RAB-35 and ARF-6 GTPases Mediate Engulfment and Clearance Following Linker Cell-Type Death, Developmental Cell, 47:2; doi: 10.1016/j.devcel.2018.08.015

3. **Keil W**, Kutscher LM, Shaham S & Siggia ED (2017)
Long-term high-resolution imaging of C. elegans larval development with microfluidics Developmental Cell 40:2; doi: 10.1016/j.devcel.2016.11.022

## Expected profile of the candidate

Applicants should have a strong interest in quantitatively understanding biological processes. Background in physics, biophysics or bio-engineering will be a plus. Critical thinking, analytical skills, creativity, and a drive for quality is needed. The project heavily relies on imaging and image analysis for which the applicant will require programming experience or a strong motivation to acquire such.

Finally, a sense of humor, and excitement about joining a supportive new team of researchers with diverse backgrounds and interests is a prerequisite.