2017-02

IC-**3i** International PhD Program

PhD thesis project

2018 Call for application

Imaging transcription in living embryos to decipher the robustness of patterning

General information

Call	2018
Reference	2017-02-DOSTATNI
Keyword(s)	Morphogen gradients, Transcriptional robustness, Chromatin dynamics, Live-imaging

Director(s) and team

Thesis director(s)	Nathalie Dostatni
Research team	Epigenetic plasticity and polarity of the embryo
Research department	UMR 3664 - Nuclear Dynamics

Description of the PhD thesis project

Morphogen gradients are used to establish polarity along embryonic axes or within organs. In these systems, positional information stems from the morphogen concentration detected by each cell in the target tissue and mediates the determination of cell identity through the expression of specific sets of target genes. Although the critical role of these gradients is now well described, how they can provide reproducible transcription patterns given the inherent stochastic nature of transcription remains unclear.

To address this question, we recently used the MS2/MCP approach to fluorescently tag RNA and study the dynamics of transcription downstream of the Bicoid morphogen gradient in living fruit fly embryos. Analysis of fluorescent time traces indicated that despite high variability in promoter functioning, loci of the main Bicoid target were able to measure their position along the length of the embryo with high precision in a very short time.

To understand how measurements of Bicoid concentration are achieved so rapidly, we will perturb the system in various genetic backgrounds and use the MS2/MCP approach to record the temporal transcription dynamics at single target locus in each nucleus of whole embryos. Using statistical physics and inference algorithms on the data collected with confocal microscopy, we will extract the characteristic parameters of the transcription kinetics of the promoter upon these perturbations. This will allow determining how maternally expressed transcription factors and/or chromatin regulators contribute to the rapid and robust responsivity of the system.

This project is highly interdisciplinary and combines cutting edge imaging with the power of fruit fly genetics. It is at the interface between molecular/developmental biology, biophysics and systems-biology.

International, interdisciplinary & intersectoral aspects of the project

Although the Bicoid morphogen is specific to the fruit fly embryo, this project includes a consequent part of cutting edge imaging and provides a clear-cut platform to quantitative measurements of differential gene expression at the single cell level upon subtle differences in transcription factor concentration changes. It is part of a long lasting collaboration with theoreticians and biophysicists at the ENS, the Institut Curie and McMaster University (Canada). It should facilitate the development of reliable technologies enabling the quantitative monitoring of biological processes including disease detection and progression, or, therapeutic efficacy. In a long term, this project might provide support for potential industrial applications.

Recent publications

1. Desponds J., Tran H., Ferraro T., Lucas T., Perez Romero C., Guillou A., Fradin C., Coppey M., **Dostatni N**., and Walczak A.M. (2016). Precision of Readout at the hunchback Gene: Analyzing Short Transcription Time Traces in Living Fly Embryos. PLoS computational biology 12, e1005256.

2. Ferraro T., Lucas T., Clemot M., De Las Heras Chanes J., Desponds J., Coppey M., Walczak A., and **Dostatni N.** (2016). New methods to image transcription in living fly embryos: the insights so far, and the prospects. WIREs Developmental Biology 5, 296-310.

3. Lucas T., Ferraro T., Roelens B., De Las Heras Chanes J., Walczak A., Coppey M., and **Dostatni N.** (2013). Live imaging of Bicoid-dependent transcription in Drosophila embryos. Current Biology 23, 2135-2139.

4. Porcher A., Abu-Arish A., Huart S., Roelens B., Fradin C., and **Dostatni N.** (2010). The time to measure positional information: maternal Hunchback is required for the synchrony of the Bicoid transcriptional response at the onset of zygotic transcription. Development 137, 2795-2804.

5. Abu-Arish A., Porcher A., Czerwonka A., **Dostatni N.**, and Fradin C. (2010). Fast mobility of Bicoid captured by fluorescent correlation spectroscopy: implication for the rapid establishment of its gradient Biophysical Journal 99, L33-L35.

Expected profile of the candidate

Applicants should have a strong motivation to explore the dynamics of gene expression in the context of development, and should show solid capacity for independent and creative thinking. Background in cell biology, developmental biology and/or genetics is strongly recommended. The project relies on microscopy and live imaging techniques, for which the applicant should have either experience or a strong motivation to learn. The project is highly interdisciplinary and the applicant should be open to interact with biophysicists and theoreticians.