Master Internship / PhD Thesis Proposal

Subject title: Genome organization and transcription in development

Keywords: biophysics; live imaging; transcription; stem cells; organoids
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Presentation of the laboratory and its research topics:

The Unit for the Physics of Biological Function at Institut Pasteur works at the interface between physics and biology, combining theory and experiment. We are interested in quantitative descriptions of the rich qualitative phenomena of complex biological systems with the ultimate goal to understand how they derive from general principles. Over the past several years the core focus has been on cellular specification in multicellular organisms: how does a cell know where it is, what it is, and when does it know that? This problem is at the heart of bridging the formation of macroscopic patterns in multi-cellular organisms to the molecular events that govern the underlying decisions in individual cells. These decisions are controlled by genetic network activity and gene regulation, and we have developed quantitative tools centered on microscopy and statistical physics to tackle this problem.

Expected profile of the candidate:

The ideal candidate has a strong interest for **collaborative and interdisciplinary research** and in bridging quantitative and live sciences. A background in mathematics, computer science and/or the physical sciences is a plus. Prior training in biology is encouraged. Good programming skills are a must.

This thesis offer is directed towards energetic and assertive students willing to take initiatives. It is of prime importance to me that the student feels ownership over her/his project, and we will thus **define the specifics together**. The project will center around three themes that we want to push forward over the next few years:

1. Develop mathematical models underlying the mechanisms of **transcriptional regulation**. We test these models using single molecule and live measurements of the transcription, and perturbative experiments with genetics and opto-genetics.
2. Investigating the **dynamics of the DNA polymer** using **embryonic stem cells**, linking nuclear architecture and genome organization with transcriptional activity in terms of multiple enhancers recruiting the same promoter in a given cell.
3. Quantification of **reproducibility** and developmental **precision** in **synthetic mouse embryos**.

Recent example publications:

- Zoller et al. (2018). Diverse Spatial Expression Patterns Emerge from Unified Kinetics of Transcriptional Bursting. *Cell* 175(3):835–847.
- Chen *et al*. (2018). Direct visualization of transcriptional activation by physical enhancer-promoter proximity. *Nature Genetics* 50(9):1296–1303.
- Petkova et al. (2019). Optimal decoding of cellular identities in a genetic network. *Cell* 176(4), *844–855*.

Recent research presentations:

- https://www.youtube.com/watch?v=VE5z21Eut_8
- https://www.youtube.com/watch?v=C-_8DTUU9OM