Proposition de stage / Internship Proposal

Subject title: Decoding and flow of information in cellular specification

Keywords: biophysics; live imaging; transcription; stem cells; organoids; embryos
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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, often marrying theory and experiment. In particular we are interested in providing quantitative descriptions of the rich qualitative phenomena of complex biological systems with the ultimate goal to understand how they derive from general principles.

The core focus over the past several years has been to understand how cells know their identity, essentially asking about time, space and information of cellular specification: 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 dominated by genetic network activity and thus prompted us to develop tools to assess the flow of information through genetic networks at multiple temporal and spatial scales.

Expected profile of the candidate:

The ideal candidate has a strong interest for **collaborative and interdisciplinary research** and to bridge quantitative and live sciences. A background in mathematics, computer science and/or the physical sciences is a plus. Prior training in biology is not necessary but encouraged. Basic programming skills are required.

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 of the project together**. The project will center around three themes that we want to push forward over the next two to three years:

1. At the level of a **genetic network**, extract global properties and design principles from expression level measurements and analysis.
2. At the molecular level, develop mathematical models underlying the fundamental mechanisms of **transcriptional regulation**. We test these using single molecule and live measurements of the transcriptional output, and perturbative experiments using genetics and opto-genetics.
3. At the level of the **dynamics of the DNA polymer**, link the nuclear architecture with actual transcriptional activity in terms of multiple enhancers recruiting the same promoter in a given cell.

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*, in press.

Recent research presentations:

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