INTERNSHIP PROPOSAL

Laboratory name: Physics of Biological Function
CNRS identification code: UMR 3738
Internship director'surname: GREGOR
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Web page: https://research.pasteur.fr/en/team/physics-of-biological-functions/
Internship location: Institut Pasteur; 24 rue du Dr. Roux; 75015 Paris

Thesis possibility after internship: YES
Funding: YES If YES, which type of funding: ERC, ANR, Pasteur

Title: Self-organized patterning in mammalian stem-cell aggregates

Keywords: machine learning; cell differentiation; microscopy; image analysis; organoids

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? At the heart of this problem are decisions for individual genes in a genetic network to be active or inactive. These decisions are governed by molecular events and thus prompted us to develop tools to assess the flow of information through genetic networks and in particular through individual gene loci at multiple temporal and spatial scales. We are currently implementing these questions and approaches in mammalian organoids, both experimentally and theoretically.

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 thesis, and we will thus **define the specifics of the thesis project together**. The project will center around three themes that we want to push forward over the next three years:

1. Determine the biophysical strategies and design principles that lead mammalian embryonic stem cells to self-organize into a developing structure that resembles an actual mouse embryo.
2. Develop mathematical models underlying the emergence of positional and correlative information in differentiating stem-cell aggregates.
3. Linking models and experiments, comparing dynamic information flow between different developing systems (i.e., fly embryos and mammalian stem-cell aggregates).

Recent publications of relevance for the internship:

- Brückner et al. (2023). Stochastic motion and transcriptional dynamics of pairs of distal DNA loci on a compacted chromosome. *Science* **380**, 1357–62.
- Merle et al. (2023). Precise and scalable self-organization in mammalian pseudo-embryos. *Nature SMB*
- Tkačik G, Gregor T (2021). The many bits of positional information. *Development* 148: dev176065.
- Petkova et al. (2019). Optimal decoding of cellular identities in a genetic network. *Cell* 176(4): 844–855.
- Chen *et al*. (2018). Direct visualization of transcriptional activation by physical enhancer-promoter proximity. *Nature Genetics* 50(9):1296–1303.

Please, indicate which speciality(ies) seem(s) to be more adapted to the subject:

Condensed Matter Physics:	YES	Soft Matter and Biological Physics:	YES
Quantum Physics:	NO	Theoretical Physics:	NO