

M2 internship/PhD position in biological physics:

Phase-separation in nucleo and the formation of chromatin compartments

Our group is looking for a Master student/PhD candidate in biological physics or computational biology to work on chromosome folding in close collaboration with experimentalists.

Context: Inside the cellular nucleus, DNA is tightly packed into a polymer-like structure called chromatin. Characterizing how chromatin self-organizes is one of the major challenges faced in recent years by biology. During the last decade, thanks to the development of advanced experimental techniques, major progresses have been realized in our understanding of the multi-scale chromosome organization during interphase. An increasing number of experimental evidences has suggested that the spatio-temporal organization of the genome may play a decisive role in the regulation of gene expression and in diseases. It is therefore of high importance to better characterize the mechanisms driving such organization. In particular, the coordinated recruitment of architectural molecules at specific genomic gives rise to a wide variety of spatial compartments. In recent years, the physical mechanism of liquid-liquid phase separation (LLPS) has been increasingly proposed as a key paradigm to explain their formation. However, the difficulty of quantitatively and unequivocally distinguishing LLPS from alternative self-organization processes in vivo has generated disputes about its biological relevance. In this project, we aim to address this question in the context of heterochromatin – the silenced part of the genome – condensates formation using biophysical modeling in close collaboration with experimental biologists.

Objectives: The student will develop a research activity on the modeling of complex phase separation inside cell nuclei to characterize the biophysical properties of heterochromatin compartments. It will involve the development of original models coupling statistical and polymer physics, of efficient simulation schemes, and of statistical tools to analyze experimental data. The project will be realized in close

collaboration with the experimental groups of Giacomo Cavalli (CNRS, IGH, France) and Gary Karpen (UC Berkeley, USA). This work will provide grounds to a wide spectrum of totally-novel investigations on how cells regulate their nuclear organization.

Environment: The candidate will integrate our group 'Physical Biology of Chromatin' that mainly focuses on understanding the fundamental bases of chromatin and gene regulation using physical modeling and computational approaches. Our innovative research is conducted in close interaction with top-leader experimental partners. The group is integrated within the Laboratory of Biology and Modeling of the Cell that aims to characterize the molecular bases underlying the organization and functioning of cellular processes in normal and pathological conditions. It is based at Ecole Normale Supérieure de Lyon, a French top-leading research and educational institute.

Profile of the candidate: We are looking for a creative and highly motivated candidate with a background in statistical or polymer physics, in computer science or in computational biology. Advanced skills in programming is required and a previous interdisciplinary experience in connection with biological issues would be a plus.

To apply, please send your CV and a motivation letter to Daniel Jost at daniel.jost@ens-lyon.fr