PhD Research Proposal Form
China Scholarship Council (CSC) - ENS Group

FIELDS: Computational Biology – Physics – Computer science

Thesis subject title:

Chromosome folding: from mechanisms to functions

Name of the French doctoral school: BMIC (Biologie Moléculaire Intégrative et Cellulaire) or PHAST (Physique et Astrophysique)

Name of the Research team: Physical Biology of Chromatin
Website : http://www.ens-lyon.fr/LBMC/equipes/biologie-physique-de-la-chromatine

Name of the Supervisor: Daniel Jost, Cédric Vaillant or Jean-Michel Arbona
Email : daniel.jost@ens-lyon.fr ; cedric.vaillant@ens-lyon.fr ; jeanmichel.arbona@ens-lyon.fr

Lab Language: English & French

Research Proposal Abstract :
Our group is looking for a creative and highly-motivated PhD candidate in Computational Biology, Physics or Computer Science to work in an interdisciplinary environment on chromosome folding and regulation.

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 genome 3D organization 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 and to provide the biological and genome engineering communities with tools to define, predict, perturb and interfere with cell fate using genome structural information.

In this project, the student will develop an original research activity on the modeling of chromosome folding and dynamics in eukaryotes. In particular, he will focus on the coupling between the structure and function of chromatin by developing original models to decipher how fundamental processes like transcription, replication or DNA damage drive genome folding and reciprocally, how chromosome 3D organization impacts the regulation of these processes. The project will involve the development of biophysical models coupling statistical and polymer physics, of advanced simulation schemes, and of statistical tools to analyze modeling and experimental data. The project will be realized in close collaboration with top-leader experimental partners working on various species from yeast to human.

Key references of the research team:

Jost et al (2014) Modeling epigenome folding: formation and dynamics of topologically associated chromatin domains. Nucleic Acids Res 42, 9553-9561.
Jost, Vaillant & Meister (2017) Coupling 1D modifications and 3D nuclear organization: data, models and function. Curr Opin Cell Biol 44, 20-27.
Arbona et al (2017) Inferring the physical properties of yeast chromatin through Bayesian analysis of whole nucleus simulations. Genome Biol 18, 81.
Ghosh & Jost (2018) How epigenome drives chromatin folding and dynamics, insights from efficient coarse-grained models of chromosomes. PLoS Comput Biol 14, e1006159.
Jost & Vaillant (2018) Epigenomics in 3D: importance of long-range spreading and specific interactions in epigenomic maintenance. Nucleic Acids Res 46, 2252-2264.
Arbona et al (2018) The eukaryotic bell-shaped temporal rate of DNA replication origin firing emanates from a balance between origin activation and passivation. Elife 7, e35192.
Tortora, Salari & Jost (2020) Chromosome dynamics during interphase: a biophysical perspective. Curr Opin Genet Dev 61, 37-43.

Type of PhD:

Full PhD : Regular PhD (leading to a single French diploma)