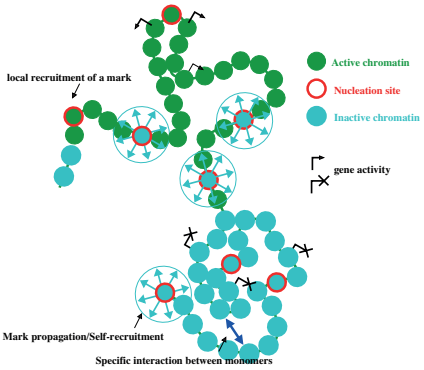
Field of the Master: Physics, Computer science, Computational biology
Level: M2/PhD thesis
Required skills: computer programming, statistical physics, polymer physics
Duration: 3 to 6 months for M2 internships, 3 years for PhD thesis
Period: any periods between January and July 2016 for M2 internships

Title of the research project: Coupling 3D organization to local biochemical state dynamics: application to chromatin folding

Names of the supervisors: Daniel Jost (daniel.jost@imag.fr) & Cédric Vaillant (cédric.vaillant@ens-lyon.fr) - Lab. TIMC-IMAG, CNRS, Université Grenoble Alpes & Lab. de Physique, CNRS, ENS Lyon

Context: Inside the cellular nucleus, DNA is tightly packed into a polymer-like structure called chromatin. The 3D organization of chromatin is not random and distinct patterns of contacts between chromatin loci are observed. Recently, we propose and test that such organization is mainly driven by the profile of the local biochemical states (the epigenomic state) along the chromatin through physical contact-interactions. In this previous work, we hypothesized that such profile was constant. However, increasing number of experimental evidence suggests that the local state is highly dynamic and that 3D organization might play an important role in the establishment and stabilization of the epigenomic state.



Objectives: In this project, we aim to better understand the crosstalk between 3D chromatin organization and the epigenomic state dynamics by introducing a generic modular framework, the living chromatin model, that allow to couple the polymeric properties of the chromatin to the local fluctuations of the biochemical state. Based on our previous works, the student will have to develop the general formalism. Since we aim to study very long polymer chains (up to 10^6 monomers), the student will build an efficient algorithm of simulation using parallelization techniques on GPU architecture. After analyzing the generic physical properties of the model on toy examples, the student will apply the formalism to concrete biological examples like the phenomenon of dosage compensation of sexual X chromosomes in worms (in collaboration with the experimental group of Peter Meister, University of Bern) or the heterochromatization of telomeres in yeasts (in collaboration with the experimental group of Angela Taddei, Institut Curie, Paris). In particular, the student will have the opportunity to visit our collaborators to learn and perform experiments suing cell-imaging techniques for example.

Expected results: The living chromatin model is an original formalism that is modular and applicable to many different biological contexts where structure and function are coupled. We expect such formalism to answer generic and specific questions about the relation between 3D chromatin organization and the epigenomic state. In parallel, the development of the simulator of polymers on GPU would be innovative and should pave the way of efficient simulations of very long polymers.