Laboratory name: Genome functions in space and time
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Internship proposal

Out-of-equilibrium polymer mechanics of chromosomes
The inheritable information in all living organisms is encoded in a long polymer of DNA present in the cell nucleus. This polymer contains the “instructions” to build the constituents of the cellular body as well as to control their expression and activities. Unlike synthetic and other structural polymers, DNA is associated with a multitude of molecules that allow its efficient functioning, and contribute an additional volatile layer of information to the genetic code. The combination of DNA and these molecules is called chromatin, which is the constituent of chromosomes. Energetic processes organize chromosomes in 3D in order to colocatalize functional elements, maintaining their shape constantly out of equilibrium. Specifically to this project, we are interested in “loop extrusion” by molecular motors called cohesins: since it has been hypothesized that this governs the local conformation of mammalian chromosomes. It posits that molecular motors create and grow local DNA loops (typically < 1 Mb) until it encounters a roadblock. In particular, we are interested in the dynamical and energetic aspect of this process, and how this plays with the other sources of random fluctuations that affect the chromatin conformation.

The goal of this internship is (i) to develop an analytical theory for the dynamics of polymers undergoing loop extrusion, using the tools of out-of-equilibrium statistical mechanics, and (ii) to be able to identify "loop extrusion" in experimental data obtained in our lab and others. To study local genome conformation in the lab, we measure the 3D trajectories of genomic elements and the activity and position of individuals genes. This gives us only a partial view of what is happening inside the cell nucleus. Further, the position of such objects is dominated by variability. In order to highlight the effect of activity above the background at equilibrium chromatin, the intern will develop the following:

2. Adaptation of available numerical simulations of loop extrusion, to test the predictions obtained in point 1, in presence and absence of loop extrusion. Quantification of out-of-equilibrium effects
3. Comparison of the theory to data from our lab and from the literature: contact probability maps of chromosomes (Hi-C), distance distributions and conformation ensembles (Oligopaint DNA FISH), gene activity (RNA FISH), 3D trajectories of genomic loci.
4. explore the effect of different hypotheses in the extrusion model

Candidates should have substantial programming skills (Python preferred), knowledge in statistical physics, and a genuine interest in approaches combining theory and experiments for solving questions at the physics-biology interface.

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