## PROPOSITION DE STAGE & THESE

# Thermodynamics of chromatin fiber

**Laboratoire**: Laboratoire de Physique de l'ENS Lyon

**Adresse :** ENS Lyon, 46 Allée d'Italie 69007 Lyon

**Responsable de stage/thèse:** Cédric Vaillant

**Collab.:** P. Carrivain, R. Everaers (Lab Phys), Daniel Jost (LBMC)

**Email :** cedric.vaillant@ens-lyon.fr

**Profil recherché:** Statistical Physics, Numerical simulations**,** Computational biology

**Durée : (Internship)** between 4 and 6 months.

**Financement: (PhD thesis)** Ecole Doctorale de Physique (ED-Phast)

**Lieu :** ENS de Lyon (Laboratoire de Physique, Centre Blaise Pascal)

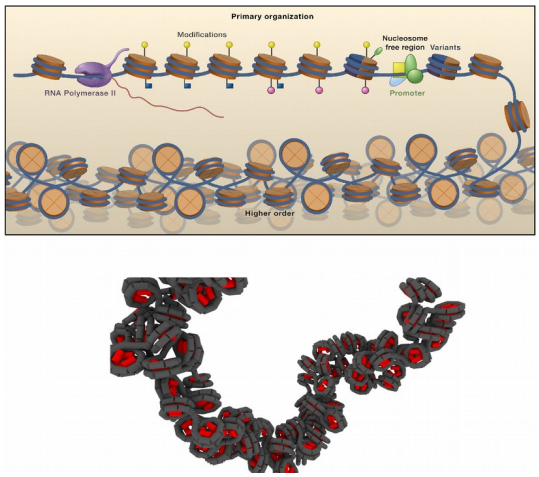


*Figure 1 : Chromatin : from nucleosome positioning to 3D chromatin fiber*

**Context:** Eukaryotic chromosomes are packaged in condensed chromatin structures whose primary unit, the nucleosome, is composed of about 147 DNA base pairs wrapped around a histone octamer (Figure 1 Top). Nucleosomes, as well as the enzymes that remodel and modify them, are key regulators of genome activity. Nucleosome positioning can affect the accessibility of underlying DNA to the nuclear environment and as such plays an essential role in the regulation of cellular processes such as gene transcription, replication, repair and insertion of transposable elements.

**Objectives:** Recent high-resoluted mappings of nucleosome positions along chromosomes in different species, cell types as well as in various *in vitro* experiments have revealed a non-random distribution along the genome which has been shown to result from the interplay between intrinsic properties of the DNA sequence (such as flexibility or natural bending of adjacent base pairs), enzyme activity and nucleosome-nucleosome interactions. Current models of nucleosome formation mostly consider a simple unidimensional fluid of hard-rods at equilibrium (Tonks gas) in an inhomogeneous adsorption potential (1). However nucleosome positioning and stability is likely to affect their higher-order folding into the so-called chromatin fiber (Figure 1 ), whose local 3D topology might also influence DNA accessibility and play a role in the control of large scale conformations (2). Hence, the general objectives of the internship and thesis will be to extend these 1D models to 3D models by taking into account the spatial constraints and then investigate the thermodynamical properties of the chromatin fiber (local compaction/accessibility, elastical properties...) as function of the different control parameters such as the genomic sequence, global nucleosome density and enzyme activity.

**Expected Results:** By implementing efficient Monte-Carlo simulations of chromatin fiber models (Figure 1 bottom), the objective of the internship will be (i) to study the conformation of the chromatin fiber at equilibrium, given a “fixed” distribution of nucleosomes taken from experimental datas (ii) to perform similar studies but now with a “fluid” distribution of nucleosomes (Tonks gas with 3D constraints). The objective of the PhD thesis will be to extend this work to the non equilibrium situation, ie to study the relaxation dynamics of the chromatin fiber when perturbed following transcription or replication activities.

**References:** (1) Chevereau et al. Thermodynamics of intragenic nucleosome ordering. *Phys. Rev. Lett.* **103**: 188103 (2009) Influence of the genomic sequence on the primary structure of chromatin. *Frontiers in Life Science* **5**:29-68 (2011). (2) Mergell, B., Everaers, R., and Schiessel, H. Nucleosome interactions in chromatin : fiber stiffening and hairpin formation. *Phys. Rev. E: Stat. Nonlin. Soft Matter Phys.* **70**: 011915 (2004).