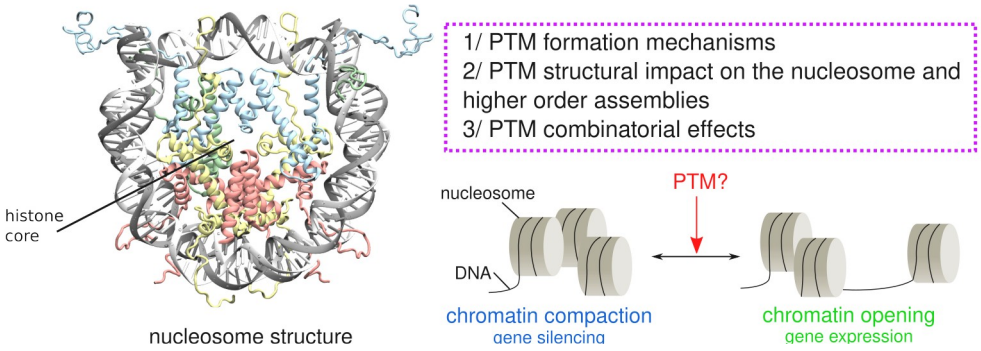
Computational study of DNA compaction regulatory mechanisms using multi-scale approaches

Scientific description

In cells, gene activity is tightly controlled by reversible chemical modifications called epigenetic marks. These are of various types and modulate gene accessibility without affecting the DNA sequence. The modification of the histone proteins, responsible for DNA compaction in the nucleus, is one of them. Understanding how these changes impact DNA compaction (from nucleosome to chromatin structures) and genome functioning is a timely area of research, yet several aspects suffer from a critical lack of data and remain elusive to experimental tools.

This doctoral project aims at elucidating the impact of post-translational modifications of histone proteins on chromatin dynamics, by means of molecular modeling and simulations. Owing to an ambitious multi-scale methodology featuring molecular dynamics simulations and Quantum Mechanics/Molecular Mechanics approaches, the formation mechanisms of these modifications, their structural impact on the nucleosome architecture, and their combinatorial effect will be scrutinized. This research will provide important insights into the histone modifications regulatory role on DNA compaction and gene expression, opening invaluable perspectives for understanding epigenetic mechanisms and for the design of next-generation drugs targeting these key-processes.



The candidate will work at the Laboratoire de Physique et Chimie Théorique in Nancy (France), in collaboration with experts in Protein Structural Networks analysis (Y. Karami, LORIA) and CryoEM (G. Papai, IGBMC).
The LPCT laboratory is committed to promoting an inclusive workplace.

Searched profile

Master-completed student or equivalent, with a background in computational biochemistry or biophysics.
A strong interest for applications to biological systems, and an experience with at least one molecular dynamics software (AMBER, NAMD, or GROMACS) are required from the candidate.
Good programming skills and knowledge of QM softwares (Gaussian...) and QM/MM approaches would be preferred but are not required.

PhD advisors

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Send us a CV and a cover letter, transcripts of Master grades, and a reference letter (Master's supervisor, internship supervisors, etc.) or the contact details of one referee.