Master 2: *International Centre for Fundamental Physics*

INTERNSHIP PROPOSAL: Probing the diffusion landscape in the nucleus of living cells

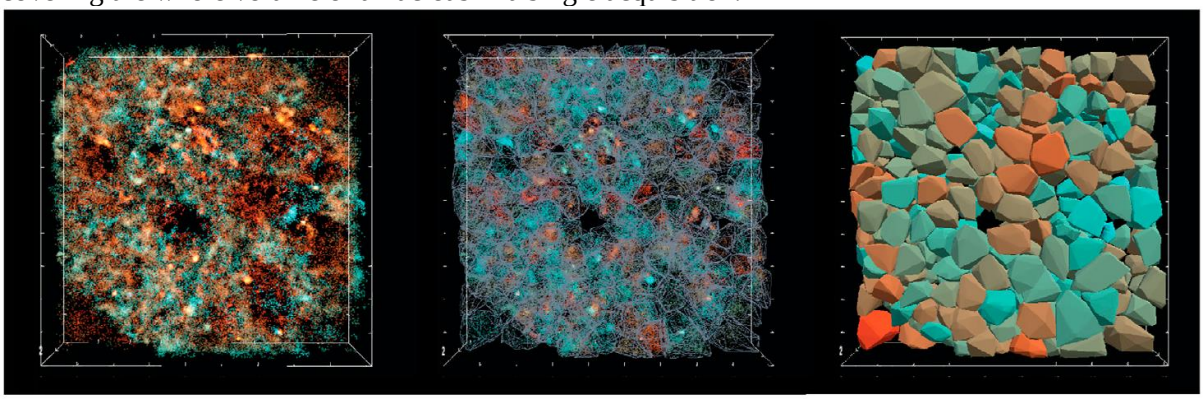
Laboratory name: Laboratoire Physico Chimie Curie
CNRS identification code: UMR168
Internship director'surname: Bassam HAJJ
e-mail: bassam.hajj@curie.fr Phone number: 01 56 24 63 15
Web page: https://institut-curie.org/team/coppey
Internship location: Laboratoire Physico Chimie Curie, Institut Curie, 11 rue Pierre et Marie Curie, 75005 Paris

Thesis possibility after internship: YES
Funding: Maybe

Title Probing the diffusion landscape in the nucleus of living cells

Single-molecule localization microscopy (SMLM) offers a means to visualize (super-resolution) and follow (single-particle tracking) the dynamics of biological entities at the molecular scale. Within the nucleus, SMLM imaging revealed that biomolecules self-assemble and organize into condensates and compartments to perform specific tasks (e.g. transcription) or play a specific role (e.g. maintaining of genetic information), thus linking organization with function [1]. It is known that DNA organization and compaction play a role in orchestrating the different nuclear functions and gene expression by restricting the accessibility of nuclear players to specific genes. In cancerous cells, it was shown that DNA compaction and chromosome territories are massively altered. However, a single cell characterization of the physical property of the cell nuclear environment is still missing. The purpose of this internship is to **map such environment at molecular scale by following the dynamics of inert particles of different sizes injected inside the nucleus**.

Efficient 3D tracking of single particles in the nucleus will be performed using Multifocus microscopy (MFM) [2]. MFM allows simultaneous acquisition of 9 different focal planes on the same camera, thus covering the whole volume of a nucleus in a single acquisition.



During the internship, particles with different sizes and surface functionalization will be tracked in 3D inside the nucleus of living cells. Advanced analysis developed in the team will allow to extract physical property maps in 3D and relay it to local chromatin compaction [3,4]. We aim to fully characterize the effect of chromatin compaction on the particle diffusion, characterize the effect of surface functionalization on the recorded diffusion and characterize the typical size threshold above which the particles are trapped. We will extract the typical sizes of open and close regions of chromatin in different cell lines. We hope to shade light on the difference of compaction at the molecular scale between normal and cancerous cells and in cells under mechanical or chemical stress.

References

[1] Cisse, II, et al.Science, 2013. [2] Hajj, B., et al. Proc Natl Acad Sci U S A, 2014. [3] Blanc, T., et al. Nature Methods, 2020. [4] Blanc, T., et al. Front. Bioinform., 2022

Please, indicate which speciality(ies) seem(s) to be more adapted to the subject:

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