— Research Internships 2022-2023 —

Probing chromosome mechanics inside living cells by magnetic micro-manipulation

Position type: **Master 1**, **Master 2** or **Engineering school internships**.
Possibilities to stay as a PhD student or as an engineer can be considered.

Location: **Institut Curie**, Paris.
'**Nuclear Dynamics**' unit (UMR3664)
'**Physical Chemistry**' unit (UMR168).

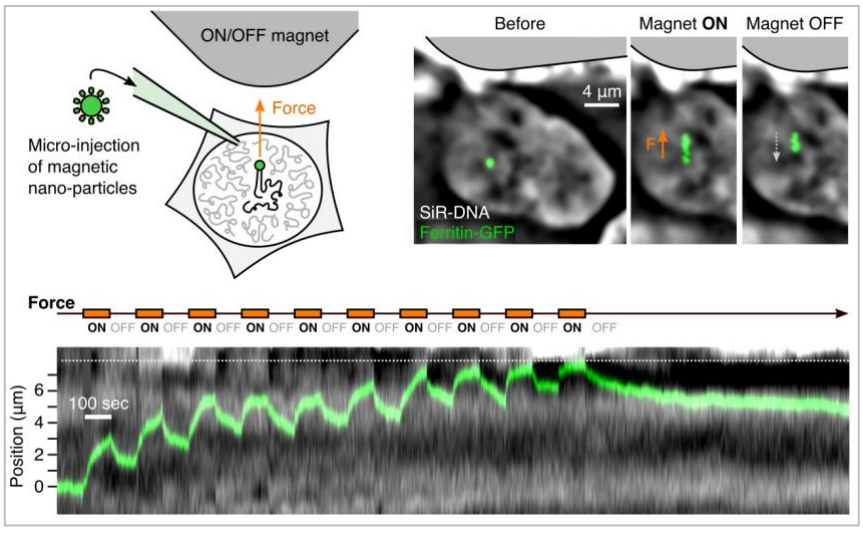
Team: http://www.coulonlab.org/

Supervisor: Antoine Coulon

Duration: Ideally, 3 to 6 months.

The physical principles governing the organization and dynamics of chromosomes in 4D inside the cell nucleus are broadly studied and central for understanding how the genome functions [1,2]. However, fundamental questions about the physical state of chromosomes and chromatin remain open, largely due to the inability to make direct mechanical perturbations and measurements on interphase chromosomes inside living cells.

To address this limitation, our team and collaborators recently developed a **new technology to mechanically micro-manipulate chromosomes inside living cells** by exerting a point force onto a targeted chromosomal locus using magnetic nanoparticles [Keizer *et al.* (2022) **Science**, 377].



This new technique gives unprecedented access to physical parameters and insight into chromatin mechanics.

In this context, we propose internships on 2 possible topics for Master 1, Master 2, or Engineering school students.

I. DETERMINANTS OF CHROMOSOME MECHANICS

Project – The student will perform chromosome micro-manipulation experiments under different biological perturbations and/or will observe specific biological responses to the mechanical perturbations.

Outcome – An understanding of how the physical nature of chromosomes relates to the biological state of chromatin (e.g. histone marks) and different genomic processes (e.g. transcription, replication), and how the cell responds to such mechanical stresses (DNA damage…).

Knowledge and skills:

- •• Mammalian cell culture
- ••• Immunofluorescence
- ••• Transfection, siRNA, drug treatments
- •• Fluorescence microscopy and image analysis
- •• Good general level of programming (Python)

II. FORCE-INDUCED DEFORMATION & REARRANGEMENT OF CHROMOSOMES

Project – The student will perform chromosome micro-manipulation experiments after fluorescent labeling of genomic elements and chromatin domains using different strategies (e.g. nucleotide incorporation, CRISPR/dCas9 based labeling, single-particle tracking).

Outcome – Following the displacement and deformation of chromosomes and genomic domains will shed light onto the physical principles organizing the genome in space and the material nature of nuclear domains.

Knowledge and skills:

- ••• Fluorescence microscopy and image analysis
- •• Good general level of programming (Python)
- •• Mammalian cell culture
- • Theoretical physics (soft matter and statistical physics)
- • Protein biochemistry and molecular biology

Context

Our team studies the **physical organization, dynamics and mechanics of chromosomes** in the mammalian nucleus and their relationship with functional genomic processes. We take a quantitative approach at the **physics-biology interface**, combining microscopy, mechanical micro-manipulation, and physical modeling. – More info: http://www.coulonlab.org/

Institut Curie is a major player in cancer research. It consists of a Research Center for basic research and Hospital group for translational and clinical research. It is an inclusive, equal opportunity employer and is dedicated to the highest standards of research integrity.

These projects will benefit from our collaborations with the Fachinetti and Coppey/Hajj teams (Institut Curie), Mirny team (MIT, USA), Pons team (ESPCI) and Giovannangeli team (MNHN).

Application

Send your CV and a letter explaining your interest in joining our lab to recruitment@coulonlab.org.

[1] Misteli, T. (2020) The Self-Organizing Genome: Principles of Genome Architecture and Function. Cell. 183, 28-45.
[2] Agbleke, A. et al. (2020) Advances in Chromatin and Chromosome Research: Perspectives from Multiple Fields. Molecular Cell. 79, 881–901
[3] Keizer V. et al. (2022) Live-cell micromanipulation of a genomic locus reveals interphase chromatin mechanics. Science, 377:489-495.

••• necessary •• recommended • considered a plus.