Internship subject M2 or PFE engineer internship

Numerical simulation of RNAP molecular diffusion in cells

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Place: ICB Laboratory UMR 6303 CNRS (Dijon)
Duration: 16 to 24 weeks from February-March 2024

Background: **This internship is part of a more ambitious project (CAMoMill) that is supported since 2024 by the French National Research Agency (ANR) and a PhD will be funded soon to continue this work.** The aim of this ANR project is to analyze the dynamics of molecules within the cell nucleus. All cells share the same genome, but not all express the same genes: this is regulated by RNA Polymerase II molecules as shown in Figure 1. In fact, this mechanism is widely shared in living organisms, and is highly dependent on living conditions (age, stress, circadian cycle...).
However, the spatial and temporal dynamics of these molecules are still poorly understood. Indeed, they appear to be highly non-stationary, and it is difficult to capture all their subtleties with a single instrument. This is why we need to combine two modalities:

- **Single particle tracking** (SPT) which localizes precisely the positions of slow particles (as depicted in Figure 2).

- **Fluorescence correlation spectroscopy** (FCS) which is well adapted to measure fast diffusion processes but is less sensitive to slow phenomena.

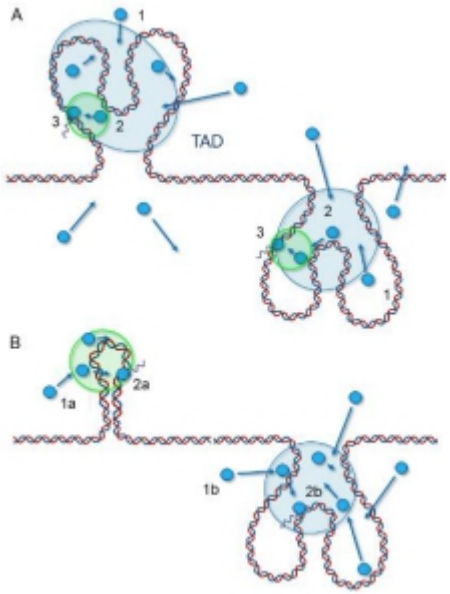

Figure 1: Models for RNAP II recruitment studied in the project. This scheme displays the two hypotheses to be verified to explain RNAP II mobilities in cells

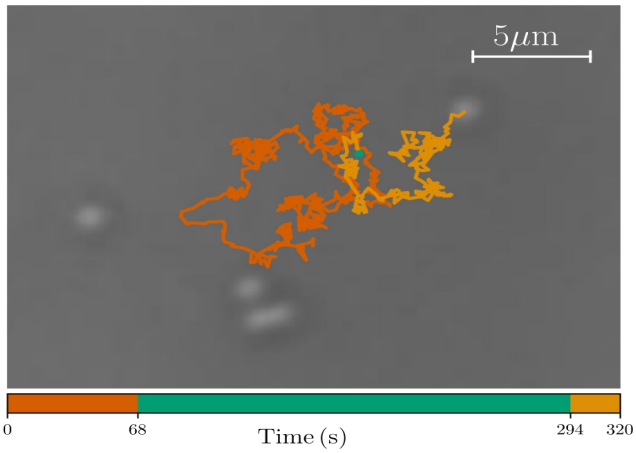

Figure 2: Example of single particle trajectory with three different stationarities (indicated by each color).

The analysis of these data is challenging because each individual technique involves complex physical models that depend on many parameters usually extracted from standard fitting methods.

Internship Description and Objectives: The main objective of this internship is to simulate RNAP diffusion models and perform numerical simulations, starting with a simple Brownian motion model, then to study more complex models by adding for example an anomaly coefficient or by drawing a non-homogeneous medium. We highlight that this internship is part of the ANR project CAMoMill (Computer Assisted Multimodal Microscopy for Quantifying Molecular Diffusion in Cells) and can lead to a PhD position in continuation of this work.
The work will be done with the collaboration of two departments of the laboratory ICB (Laboratoire Interdisciplinaire Carnot de Bourgogne - UMR CNRS 6303): NanoSciences and CO2M, with expertise in biophysics, microscopy techniques, analysis methods for biological imaging, data analysis and deep learning.

Expected profile: The ideal candidate would have an ongoing master training in physics, biophysics, applied mathematics, computer science, engineering or related fields with prior knowledge in data science. We also expect:
Taste for programming (especially in python) and experimentation.
Good level of written and spoken English and French.
Creativity, imagination and curiosity, interest in the world of academic research.

Application: Send CV + cover letter to Aymeric.Leray@u-bourgogne.fr; Renato.Martins@u-bourgogne.fr; and Cedric.Demonceaux@u-bourgogne.fr

Deadline: Please apply preferably before 17 January 2025. After that the interviews are not guaranteed, and they will be done until the position is fulfilled.

References:

[1] Fournier, M., Leclerc, P., Leray, A. et al. “Combined SPT and FCS methods reveal a mechanism of RNAP II oversampling in cell nuclei”. Scientifc Reports (13), (2023).

[2] Buchholz, J., Krieger, J., Bruschini, C., Burri, S., Ardelean, A., Charbon, E., & Langowski, J..”Widefield High Frame Rate Single-Photon SPAD Imagers for SPIM-FCS”. Biophysical journal, 114(10), (2018).

[3] M. Wachsmuth, M. Caudron-Herger, K. Rippe, “Genome organization: Balancing stability and plasticity”, Biochimica et Biophysica Acta (BBA) - Molecular Cell Research, Volume 1783, Issue 11, (2008)

[4] Bidaux, Gabriel et al. “FRET Image Correlation Spectroscopy Reveals RNAPII-Independent P-TEFb Recruitment on Chromatin”, Biophysical Journal, Volume 114, Issue 3, (2018).

[5] Furlan, Alessandro et al. “HEXIM1 Diffusion in the Nucleus Is Regulated by Its Interactions with Both 7SK and P-TEFb”. Biophysical Journal, Volume 117, Issue 9, (2019).