Internship subject M2 or PFE engineer internship

Deep neural networks for the analysis of 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 position will be open in the continuation of this work.** The aim of this ANR project is to analyze the dynamics of molecules within the cell nucleus (as shown in Figure 1). All cells share the same genome, but not all express the same genes: this is regulated by RNA Polymerase II molecules. 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 the WP1 top row at right of Figure 1).
- **Fluorescence correlation spectroscopy** (FCS) which is well adapted to measure fast diffusion processes but is less sensitive to slow phenomena (an scheme of FCS curves are shown in the left side in the top of Figure 1).

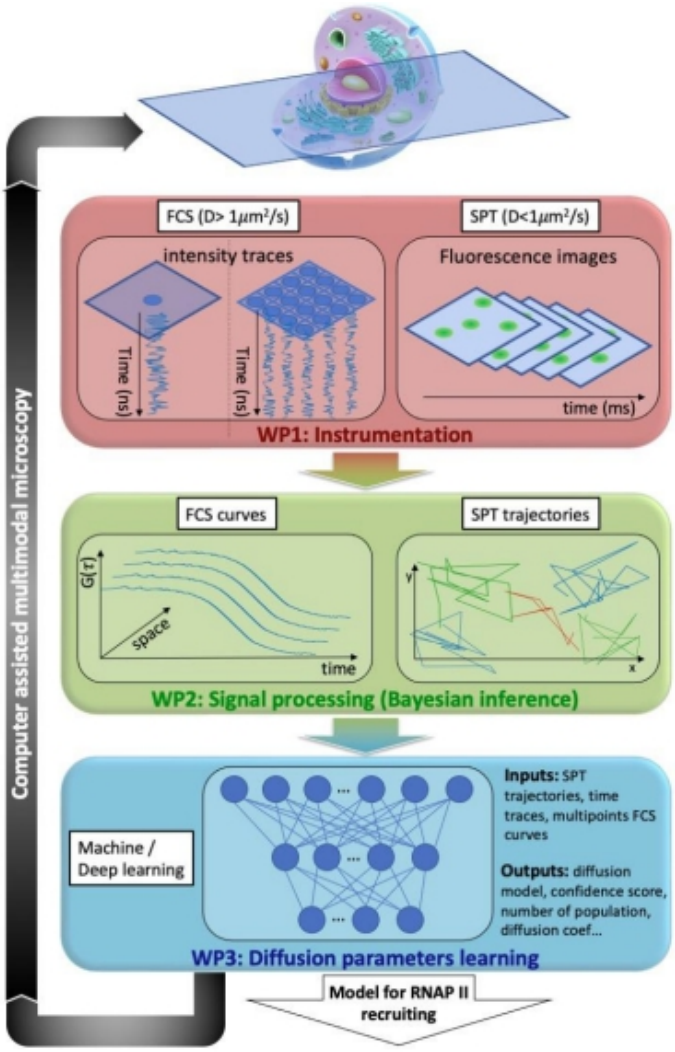

Figure 1: Overview of the learning to classify the cell diffusion type and diffusion parameters from FCS and SPT particle measurements of RNAP.

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. Moreover, the parameters of the diffusion model are dependent on the identification of the type of diffusion process that is being observed.

Internship Description and Objectives: The main objective of this internship is to exploit deep neural networks (DNN) to analyze these combined FCS and SPT measurements corresponding to different types of molecular displacement in cells (free, constrained, 2D or 3D). Our strategies will be grounded on recent tailored DL components such as of non-autoregressive transformers. We will also consider the problem of signal reconstruction from the obtained trajectories as a pretext task for improving the learning generalization of the model. The training of such models will be supported at first with simulated data. We plan to classify the different pre-treated trajectories in correlation with the FCS maps for discriminating between the different diffusion models. In order to validate the chosen architecture, both the training process and the validation will be first performed with simulated data (which will be done in parallel related internship). We will evaluate the precision and accuracy of the designed spatio-temporal deep learning algorithm for classifying the different diffusion models (Brownian, CTRW, fBm, Lw...). 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 internship 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, artificial vision, robot vision, multimodal data analysis and deep learning.

Expected profile: The ideal candidate would have an ongoing master training in machine learning (AI), computer science, computer vision, data science, physics, biophysics, applied mathematics, 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, 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] 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).

[3] Wohland, Thorsten et al. “Deep learning approaches for imaging fluorescence correlation spectroscopy parameter estimation with limited data sets”. Biophysical Journal, Volume 121, Issue 3, (2022).

[4] Héliot, L., Leray, A. “Simple phasor-based deep neural network for fluorescence lifetime imaging microscopy”. Scientifc Reports 11, (2021).

[5] Huang, L., Tan, J., Liu, J., & Yuan, J. “Hand-transformer: Non-autoregressive structured modeling for 3d hand pose estimation”. European Conference on Computer Vision (ECCV), (2020).

[6] Yufei Zhang, Jeffrey O. Kephart, Zijun Cui, Qiang Ji, “PhysPT: Physics-aware Pretrained Transformer for Estimating Human Dynamics from Monocular Videos”, IEEE/CVF Conference on Computer Vision and Pattern Recognition (CVPR), (2021).