PhD Position F/M PhD position F/M : Machine learning for 3D cryo-electron tomogram analysis: localization, identification, and spatial organization of macromolecules in cells

Le descriptif de l’offre ci-dessous est en Anglais

Type de contrat : CDD
Niveau de diplôme exigé : Bac + 5 ou équivalent
Fonction : Doctorant

A propos du centre ou de la direction fonctionnelle

The Inria Rennes - Bretagne Atlantique Centre is one of Inria’s eight centres and has more than thirty research teams. The Inria Center is a major and recognized player in the field of digital sciences. It is at the heart of a rich R&D and innovation ecosystem: highly innovative PMEs, large industrial groups, competitiveness clusters, research and higher education players, laboratories of excellence, technological research institute, etc.

Contexte et atouts du poste

The thesis will take place in the SAIRPICO project-team, which is specialized in the development of innovative methods for image restoration/reconstruction, motion analysis and computation of molecule trajectories in live cell imaging, and biophysical parameter estimation. The thesis we propose is at the frontier of applied mathematics, image processing/analysis, machine learning, and computer science. The goal is to develop generic image analysis algorithms for the analysis of 3D cryo-electron tomograms. In particular, we will investigate innovative deep learning approaches (e.g., convolutional neural networks, transformers, Generative methods) to localize and identify macromolecules with a focus on nucleosome and linkers DNA in cell nuclei. From a methodological point of a view, we will focus on hybrid methods that bring together deep learning approaches based human-expert annotations and simulated annotations. The thesis will be supervised by Charles Kervrann (Inria Rennes).

Mission confiée

CONTEXT AND MOTIVATION – Our main goal is to reveal chromatin reorganization during genotoxic stress with unprecedented resolution and analysis detail, which will be allowed by combining cryo-ET with using new deep learning approaches that will be developed. The analysis of chromatin at three structural levels – organization of chromatin domains, local geometry of nucleosome fibers, conformation and disassembly of nucleosomes – will reveal the chromatin structure-based mechanisms enabling detection and repair on UV-induced lesions in the chromatin context.

In situ cryo-electron tomography (cryo-ET) provides the ultimate quality of cell structural data available to date, because (i) biological imaged macromolecules without any chemical treatment or stain; (ii) the sampling and information quality enables structure interpretation on the near atomic scale, (iii) biological molecules are captured in their native functional environment with interaction partners, preserving their native conformational space. At the same time, in situ cryo-ET data are challenging for information extraction because of (i) a signal-to-noise ratio (SNR) that is much lower than in other imaging applications, (ii) a high crowding of molecular components in cells, (iii) incomplete angular sampling during image tilt series collection inducing missing data in 3D Fourier space and associated deformations in 3D real-space reconstruction (the so-called missing wedge (MV) problem [1, 2]); (iv) computational difficulties of dealing with 3D data. These challenges slowed down development of computational tools for in situ cryo-ET analysis, in contrast to single particle analysis of cryo-electron microscopy data obtained from purified protein complexes where the mature computational tools have been provided.

THESIS OBJECTIVE – Developing generative models and supervised DL methods for spatial localization, identification, and spatial organization of nucleosomes in situ, and simulation of cryo-ET tomograms. Automated identification of macromolecules inside cellular tomograms is challenged by noise and reconstruction artifacts, as well as the presence of many molecular species in the crowded volumes. In past works, the SERPICO team investigated supervised deep-learning and 3D CNN (DeepFinder [3]) to accurately and simultaneously localize multiple macromolecules (e.g., ribosomes, proteasomes,...) in 3D cell cryo-electron tomography images. Our results demonstrated that DeepFinder outperforms the usual
template matching algorithms and most of competitive recent deep learning methods (SHREC 2019, 2020, 2021). On cellular cryo-ET data, DeepFinder localized membrane-bound and cytosolic ribosomes (3.2MDa), Rubisco (560 kDa soluble complex), and photosystem II (550 kDa membrane complex) with an accuracy comparable to expert-supervised ground-truth annotations. In collaboration with IGBMC Strasbourg (2023), DeepFinder was trained and adapted to localize nucleosomes in denoised 3D cryo-ET images (manuscript in preparation). Nevertheless, several thousands of annotations were supplied by the experts and correspond to 3D coordinates of manually labeled macromolecules. As the number of available cellular tomograms may be limited, annotations are very expensive and represent a hard task in 3D cryo-ET, and adaptation to any microscopy set-up is not well controlled with annotated data, we will focus in this thesis on unsupervised or weakly supervised methods [4] including low-dimensional representations and simulations.

BIBLIOGRAPHY –


Compétences

Technical skills and level required :

Languages :

Relational skills :

Other valued appreciated :

Avantages

- Subsidized meals
- Partial reimbursement of public transport costs
- Possibility of teleworking (90 days per year) and flexible organization of working hours
- Partial payment of insurance costs

Rémunération

Monthly gross salary amounting to 2100 euros for the first and second years and 2158 euros for the third year

Informations générales

- Thème/Domaine : Biologie numérique
  Biologie et santé, Sciences de la vie et de la terre (BAP C)
- Ville : Rennes
- Centre Inria : Centre Inria de l’Université de Rennes
- Date de prise de fonction souhaitée : 2024-04-01
- Durée de contrat : 3 ans
- Date limite pour postuler : 2024-03-31

Contacts

- Équipe Inria : SAIRPICO
- Directeur de thèse :
  Kervrann Charles / charles.kervrann@inria.fr

A propos d’Inria

Inria est l’institut national de recherche dédié aux sciences et technologies du numérique. Il emploie
2600 personnes. Ses 215 équipes-projets agiles, en général communes avec des partenaires académiques, impliquent plus de 3900 scientifiques pour relever les défis du numérique, souvent à l'interface d'autres disciplines. L'institut fait appel à de nombreux talents dans plus d'une quarantaine de métiers différents. 900 personnels d'appui à la recherche et à l'innovation contribuent à faire émerger et grandir des projets scientifiques ou entrepreneuriaux qui impactent le monde. Inria travaille avec de nombreuses entreprises et a accompagné la création de plus de 200 start-up. L'institut s'efforce ainsi de répondre aux enjeux de la transformation numérique de la science, de la société et de l'économie.

L'essentiel pour réussir

We are looking for a candidate with an engineer or master's degree with a background in signal processing and image analysis, bioinformatics, with skills in machine learning (including deep learning) and programming (python, C++). Background in cell biology is a plus. The candidate will be expected to become knowledgeable in the field of microscopy and cellular dynamics, in order to interact with biologists.

Attention: Les candidatures doivent être déposées en ligne sur le site Inria. Le traitement des candidatures adressées par d'autres canaux n’est pas garanti.

Consignes pour postuler

Please submit online: your resume, cover letter and letters of recommendation eventually

For more information, please contact charles.kervrann@inria.fr

Sécurité défense :
Ce poste est susceptible d'être affecté dans une zone à régime restrictif (ZRR), telle que définie dans le décret n°2011-1425 relatif à la protection du potentiel scientifique et technique de la nation (PPST). L'autorisation d'accès à une zone est délivrée par le chef d'établissement, après avis ministériel favorable, tel que défini dans l'arrêté du 03 juillet 2012, relatif à la PPST. Un avis ministériel défavorable pour un poste affecté dans une ZRR aurait pour conséquence l'annulation du recrutement.

Politique de recrutement :
Dans le cadre de sa politique diversité, tous les postes Inria sont accessibles aux personnes en situation de handicap.