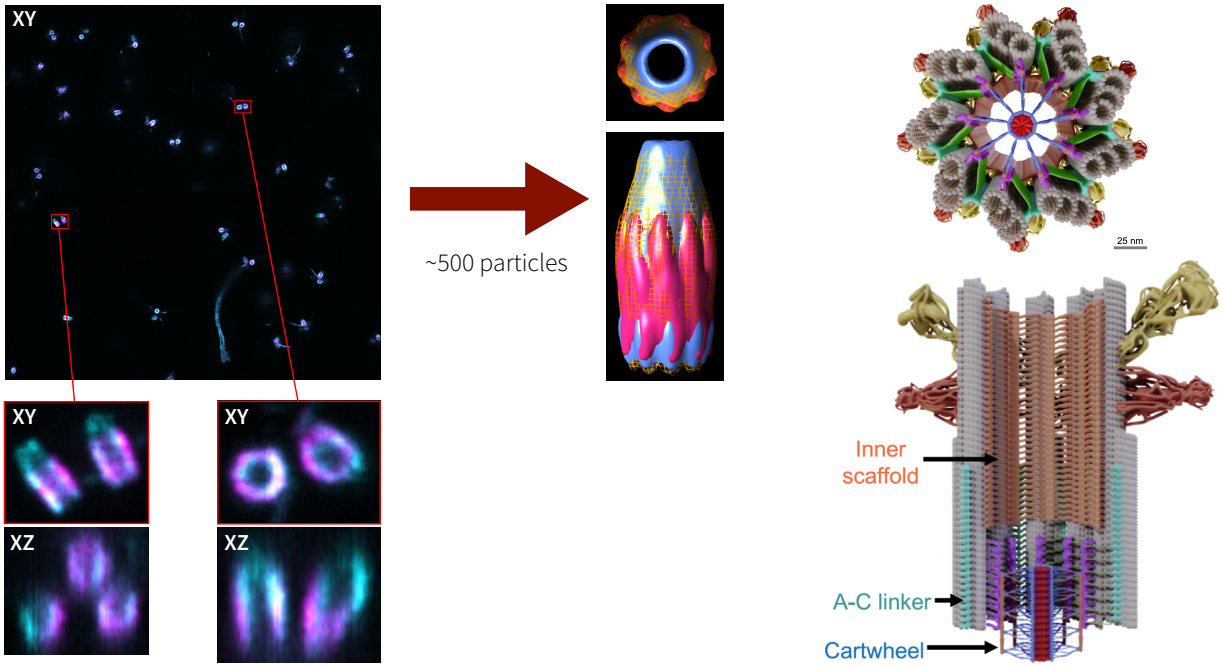
Master 2 Internship

Reconstructing heterogeneous conformations in single-particle fluorescence imaging: application to centriole growth

Thanks to recent advancements in super-resolution and expansion microscopy, it is now possible to observe macromolecular assemblies with near-nanometric resolution in fluorescence imaging. These techniques have motivated the exploration of fluorescence microscopy in the field of structural biology, in particular through the development of single particle reconstruction methods (SPR). SPR consists in reconstructing the structure of a particle from acquisitions of a large number of instances of that particle observed in random positions and containing complementary information about its structural composition (see Fig.1.a).



(a) (b)

Figure 1: (a) General principle of SPR. Left: example of acquired volume containing multiple centrioles with random orientations [8]; right: reconstruction of a model of the centriole with the method described in [3]. (b) Structure of the centriole in top and side view, determined in cryoEM [6].

A few SPR methods have been specifically proposed for fluorescence imaging modalities [5, 9], and our IMAGeS team has been developing a comprehensive and generic reconstruction pipeline for several years,

aiming to address all aspects of SPR [3, 4, 8, 2, 1]. These existing works have primarily focused on reconstructing particles in a single conformation. However, in practice the structure of the observed particles has a conformational variability related to their functions in cellular mechanisms. In this context, we aim at reconstructing a continuous set of particle conformations, and not only a single structure. The general objective of this internship is to extend the methods developed in the IMAGeS team to this heterogeneous case.

More precisely, we will focus on adapting reconstruction algorithms to the specific case of the centriole growth. The centriole is an organelle that has a crucial role in microtubule organization and mitosis. It is characterized by a cylindrical ninefold symmetry structure illustrated in Fig.1.b. While the structure of the mature centriole has been extensively studied [6], we aim in this internship at deciphering its growth dynamics. Therefore, the primary goal is to develop a method for reconstructing a continuous series of centriole growth states, in order to visualize and elucidate the different steps of its construction.

Phase 1: Amortized heterogenous reconstruction based on implicit neural network representation

We have initiated a work on heterogenous reconstruction in the context of the PhD thesis of Thibaut Eloy. Our method directly estimates a conformation variable from the acquired particles with a regression neural network, and jointly estimates the poses and the volume to reconstruct with an implicit representation parameterized with another neural network. It is inspired by similar works in another imaging modality named cryo-electron microscopy [7]. The fist step of the internship will be to finalize this work, with a particular focus on enhancing the accuracy of particle pose estimation and tailoring each stage of the method to suit our real centriole data.

Phase 2: Adaptation to the case of centriole growth dynamics

The second step will focus on the development of centriole-specific adaptations, building upon the basis method established in the first phase. The first adaptation will consist in enforcing the ninefold cylindrical symmetry of the centriole within the reconstruction process, which can drastically improve the reconstruction result. Another potential adaptation is to simplify the problem by imposing parametric growth model, to ensure physically plausible deformation of the growing centriole.

Working environment

The intern will be a member of the IMAGeS team (`http://images.icube.unistra.fr/`) in the ICube laboratory in Illkirch. The internship will begin between January and May 2024, for a period of 6 months. Supervisors: Denis Fortun (CNRS researcher, `dfortun@unistra.fr`), Etienne Baudrier (Assistant Professor , `baudrier@unistra.fr`).

Profile of the candidate

We are seeking a motivated M2-level student enrolled in a program specializing in computer science, machine learning and deep learning. Proficiency in the programming language Python is required. An interest in biology and microscopy would be advantageous but is not required. The successful candidate will

work closely with our team, benefiting from collaboration with biologists.

Application

Send a CV and a short description of your motivation, as well as the transcript of marks for the past 2 years to Denis Fortun (`dfortun@unistra.fr`), and Etienne Baudrier (`baudrier@unistra.fr`).

References

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