



PhD thesis

# Registration of multiple point clouds in a deep learning framework

## Application to single molecule localization microscopy

Fluorescence microscopy has been revolutionized by the recent development of super-resolution techniques that overcame the resolution limits of conventional optical microscopes. It is now possible to image the protein structure of small fundamental cellular units such as macromolecular assemblies, which were not observable in live cells until recent years. This opens a new field of investigation that has been growing very rapidly [1, 2]. However, intrinsic physical and biological limitations still restrict the impact of these techniques: Firstly, the 3D resolution in fluorescence microscopy is strongly anisotropic (the axial resolution is 3 to 5 times lower than in the lateral plane), and secondly, the fluorescent proteins do not cover uniformly the structures of interest such that the observation of a particle is incomplete.

To overcome these issues, we will adopt the single particle reconstruction paradigm [3, 4]: several replicates of a given particle are imaged at random orientations, and we reconstruct a single particle that represents a model of these multiple observations. The combination of multiple views yields high isotropic resolution, and compensates for the partial labelling in the input data. The main challenge comes from the absence of *a priori* knowledge about the orientations of the particles and their shape. We have already proposed a reconstruction method dedicated to a certain class of imaging modalities covering confocal and stimulated emission depletion (STED) microscopy [4, 5]. In this project, we want to extend single particle reconstruction to another type of microscopy called single molecule localization microscopy (SMLM), which is able to reach the best resolution in fluorescence imaging.

The data acquired in SMLM differs from the images that are considered in [4, 5]: it is composed of point clouds with uncertainties associated to each point. In this setting, the problem essentially amounts to the joint registration of multiple point clouds. In [6], several traditional (without machine learning) point matching algorithms are presented, and some of them have already been tested in our team. We want now to develop a point cloud registration method based on a deep learning framework and adapted to the specificity of SMLM data. In this context, the objective of the PhD thesis is threefold:

- Several deep architectures have already been proposed to model graphs and point sets, such as the graph neural network [7], dynamic graph convolutional neural network [8], PointNet [9], Deep Closest Point [10]... They are mainly designed for classification and segmentation but they can also be used for registration purposes [10, 11]. The first task will consist in an experimental evaluation of the potential of some of these state-of-the-art methods.
- Then, we would like to adapt the deep learning architectures to our application. In particular, each point is associated to a known uncertainty that should be integrated in the algorithm to guide the

registration process. Another specificity of our problem is the joint registration of multiple point sets without target reference, contrary to most methods dedicated to pairwise registration. Finally, we often have a strong biological prior on the shape of the particle that could be imposed as a constraint. In particular, we will focus on particles with cylindrical symmetry of order  $n$  ( $n$  is known).

- The ultimate goal is to apply the algorithm to real data to decipher the architecture of the centriole, which is an organelle present in most eukaryotic cells essential for cilia, flagella and centrosomes formation. This part of the project will be carried in collaboration with the microscopy group of Pr. Markus Sauer in University of Würzburg (<https://www.biozentrum.uni-wuerzburg.de/super-resolution/startseite/>).

## Working environment

The student will be a member of the IMAGeS team (<http://images.icube.unistra.fr/>) in the ICube laboratory in Illkirch. The PhD thesis will start between September and November 2021.

Supervisors: Denis Fortun ([dfortun@unistra.fr](mailto:dfortun@unistra.fr)), and Sylvain Faisan ([faisan@unistra.fr](mailto:faisan@unistra.fr)).

## Profile of the candidate

- Master diploma in one of the following fields: computer science, applied mathematics, machine learning
- Good programming skills (the coding language will be Python)
- Interest for biomedical applications

## References

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