Master Internship – 6 months

Single particle reconstruction in single molecule localization microscopy

Fluorescence microscopy has been revolutionized by super-resolution methods that overcame the resolution limits of conventional optical microscopes, and for which the Nobel prize was awarded in 2014. 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 have been growing very rapidly in recent years [3, 4]. However, intrinsic physical and biological limitations of fluorescence microscopy still limit 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 only label small parts of the structures of interest.

To overcome these issues, we have recently proposed a multiview reconstruction method based on the single particle reconstruction paradigm [1, 2]: we image several replicates of a given particle at random orientation, and we reconstruct a single particle that represents a model of these multiple observations (Fig.1). The combination of multiple views allows us to obtain high isotropic resolution, and to compensate for the partial labelling in the input particles. The method described in [1] is restricted to a specific class of microscopy modalities, covering confocal and stimulated emission deplection (STED) microscopy. In this project, we want to extend the single particle reconstruction to a new class of modalities 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 [1, 2]: it is composed of point clouds with uncertainties associated to each point. The reconstruction has to be adapted to this new acquisition model. To this end, the trainee will have to implement a point clouds registration method inspired by computer graphics works, taking into account the individual uncertainties modeling the physics of the microscope. He will take advantage of the optimization framework developed in [1]. The reconstruction will be first realized on idealized synthetic data with gradually increasing complexity. The final goal is to apply the algorithm to real data to decipher the architecture of the centriole, an organelle present in most eukaryotic cells essential for cilia, flagella and centrosomes formation, in the context of the on-going collaboration with the Centriole Lab in University of Geneva [2] (`http://guichardpaul.wixsite.com/centriolelab`).

Working environment

The student 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 2019, for a period of 6 months.
Supervisor: Denis Fortun (`dfortun@unistra.fr`)

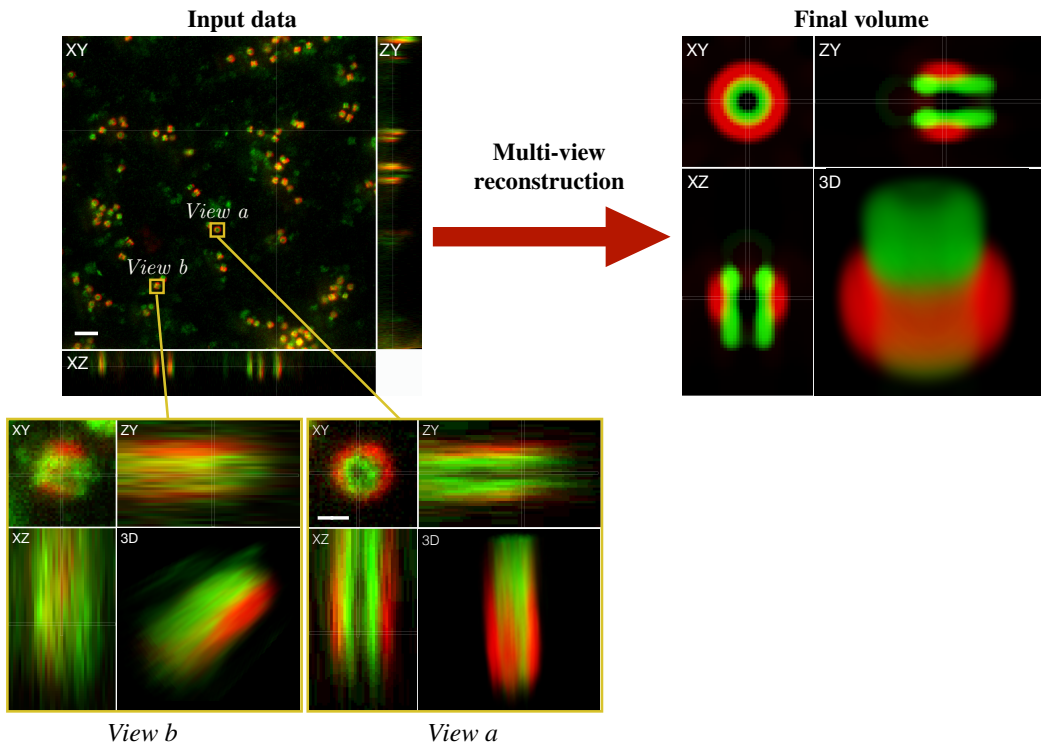

Figure 1: Input data (left) and reconstruction result(right) of the protein Cep63 (red channel) and tubulin (green channel) in the centriole [1].

Profile of the candidate

- Last year of Master studies in one of the following fields: computer science, applied mathematics, biomedical engineering
- Strong background in signal and/or image processing
- Good programming skills (the coding language will be Python)
- Interest for biomedical applications
- An experience with inverse problems is preferable (but not required)

Application

Send a CV and a short description of your motivation to Denis Fortun: `dfortun@unistra.fr`

References

[1] D. Fortun, P. Guichard, V. Hamel, C. Sorzano, N. Banterle, P. Gonczy, and M. Unser. Reconstruction from multiple particles for 3d isotropic resolution in fluorescence microscopy. *IEEE Transactions on Medical Imaging*, 37(5):1235–1246, 2018.

[2] D. Gambarotto, F. U. Zwettler, M. Cernohorska, D. Fortun, J. Borgers, S. andHeine, J. G. Schloetel, M. Reuss, M. Unser, E. Boyden, M. Sauer, V. Hamel, and P. Guichard. Imaging beyond the super-resolution limits using ultrastructure expansion microscopy (ultraexm). *Nature Methods*, page in press, 2018.

[3] D. Salas, A. Le Gall, J. Fiche, A. Valeri, Y. Ke, P. Bron, G. Bellot, and M. Nollmann. Angular reconstitution-based 3d reconstructions of nanomolecular structures from superresolution light-microscopy images. *Proceedings of the National Academy of Sciences*, 114(35):9273–9278, 2017.

[4] C. Sieben, N. Banterle, K. Douglass, P. Gonczy, and S. Manley. Multicolor single particle reconstruction of protein complexes. *Nature methods*, 15:777–780, 2017.