Deep learning approaches for data analysis in limited-angle cryo electron tomography and application to reconstruction of cellular filament systems

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Abstract:

Deciphering structure and function/dysfunction of macromolecular assemblies in a cellular context using cryo electron tomography (cryo-ET) is hampered by bottlenecks at all image processing steps. Among the most important challenges is the limited-angle data collection geometry that induces deformations on the 3D reconstructed biological scene, which is referred to as Missing Wedge (MW) problem. Also, objects of interest have to be recognized and segmented within a noisy and crowded cellular environment. These challenges make a reliable extraction and interpretation of structural information difficult and, in many cases, impossible.

This PhD project aims at developing strategies for image processing, based on deep learning algorithms, for a reliable extraction and interpretation of information from cryo-ET datasets. First, we will develop a new approach for MW correction. MW-corrected tomograms are expected to facilitate downstream processing tasks such as segmentation and classification. The project will leverage likelihood-based generative learning algorithms called Diffusion Models (DMs). DMs have shown great results for denoising, segmentation, and classification of natural images. Yet, they were not used with challenging cryo-ET data (a lower signal-to-noise ratio than in natural images). The thesis will explore the potential of DMs, not only for MW correction, but also for denoising, segmentation, and classification of cryo-ET data.

Using the new approaches, the project will address two challenging biological questions where the geometry and absence of symmetry make data processing particularly difficult. The new methods will be used to decipher septin-membrane interaction mechanisms and the nature of ESCRT proteins promoting different macroscopic ultra-structures. Both questions are related to 3D reconstruction of cellular filament systems. They will serve as proof of concept of the utility of the new methods.

The thesis will be co-supervised by S. Jonic, ED 130 (image processing methods development) and A. Bertin, ED 515 (cryo-ET of septins and ESCRTs).