Maximizing recovery of information from noisy cryo-EM images

Oleg Kuybeda, National Institutes of Health (NIH)

The recent introduction of direct electron counting detectors has led to a new wave of improvements in the use of cryo-electron microscopy (cryo-EM) technology for determining protein structures. The combination of advances in microscope hardware, detector technology and image processing algorithms have now enabled determination of structures in selected instances close to ~2Å resolution, almost at the level of resolving individual atoms in the protein. The type of data that is now collected routinely poses interesting and important challenges of direct interest to the image processing community. Cryo-EM images are recorded at very low signal-to-noise (SNR) ratios to minimize damage from the incident electron beam. With direct electron detectors, this poor SNR is further aggravated by the scarcity of specimen electron scattering events, which combined with a high image acquisition frame-rates, result in images with only a small number of non-zero pixels. Moreover, these pixel values no longer represent continuously valued densities of the specimen, but rather a set of randomly and deeply quantized measurements with most non-zero values corresponding to either single electron, or a small number of electrons. Classical image processing methods, commonly used in the field, that postulate a dense continuous signal, fixed/deterministic signal quantization, or an additive noise model are therefore suboptimal. In this talk, we will address the effect of the new challenges in the context of common image processing tasks such as registration, classification and CTF correction, which are important building blocks in the single particle reconstruction paradigm.