Seminar/Talk

Cryo-electron microscopy with a laser phase plate

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Host: Mikhail Lemeshko

Cryo-electron microscopy can visualize biomolecules at high resolution in a near-native state, but the technique is limited by the low contrast of specimens together with their sensitivity to electron radiation. To maximize image contrast, a phase plate can be employed to apply an additional delay between the scattered and unscattered beams in a diffraction plane of the microscope. While this approach is widely used in optical microscopy, phase plates developed for electron microscopy have been prone to being charged by or scattering the electron beam, leading to unstable behavior and resolution loss. To overcome these limitations, we have developed a laser-based phase plate (LPP). A laser beam, amplified and focused by a Fabry-Perot optical cavity, intersects the unscattered electron beam to impart the desired phase shift. The LPP provides a stable phase shift over hours while keeping material objects far from the electron beam path to avoid scattering and decoherence. The reliability of the LPP paves the way for several future directions in cryo-electron microscopy and tomography. Improved contrast at low spatial frequencies enables detection of small particles inaccessible to conventional (defocus-based) phase contrast imaging, as well as superior correction of beam-induced motions. Additionally, the LPP eliminates the need for specimen defocus and, in combination with a spherical aberration corrector, permits near-perfect contrast transfer over many orders of magnitude in resolution (from ~100 nm to 0.1 nm). Simultaneous visualization of both small and large structural features promises to benefit cryo-electron tomography by providing high-resolution information together with larger-scale context. I will show our progress on single-particle reconstructions and tomography with the LPP and discuss prospects for the new imaging modalities enabled by the LPP based on a combination of experiments and simulations.

Wednesday, May 8, 2024 11:00am - 12:00pm
Moonstone Building, Seminar Room C

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