The Principal of Aberration Corrected 300 kV Cryo-EM and Its Application to Thick Specimens in Biology

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High-resolution 3D structures of cells, tissue, virus, or other biological macromolecules complex in their native environment can be achieved by Cryo-ET *in situ* and is considered to be a bridging between molecular biology and cellular biology. Compared with Cryo-EM SPA (single particle analysis), Cryo-ET is not perfect in many aspects and has no mature workflow with some technical bottlenecks that need to be solved urgently. One major matter is the degradation of image quality when the sample thickness increase. In general, the thickness of biological sample suitable for Cryo-ET study is limited to 150~200 nm. This is because when the electron beam travel through a thick sample, the inelastic scattering occurs due to the energy loss. As sample thickness increases, more and more inelastic scattering will generate. The electrons with various wavelength arriving at the back focal plane of the objective lens have different cross-over, caused the chromatic aberration (Cc) which decrease the image quality dramatically. CEOS Cc-corrector is one of the most important inventions in the electron microscope history. It can significantly improve the information limit and reduce the focus spread caused by energy loss. Cc-corrector also affects the envelope function of contrast transfer of the instrument. The successful application of Cc-corrector in material science inspires us on introducing a Cc corrector to the Cryo-EM community. We report here the progress and preliminary results of the world's first 300kV cryo-electron microscope equipped with CEOS Cs/Cc aberration corrector and TFS selectris imaging filter in the Cryo-Electron Microscope Center at the Southern University of Science and Technology.