Post-acquisition super resolution (and breaking other limits too) in cryo-electron microscopy.

Raymond N. Burton Smith and Kazuyoshi Murata
National Institute for Physiological Sciences

For researchers studying giant viruses by cryo-electron tomography, or in situ cryo-electron tomography, one significant challenge is efficiently acquiring sufficient data with a large enough field of view. Decreasing the magnification with which data are acquired is one solution, but until recently this imposed limits on maximum resolution. With the introduction of fast direct electron detectors, capable of an advanced acquisition-time pixel sub-sampling method, called “super resolution”, this physical limit could be exceeded. However, acquiring with super resolution sampling dramatically increases data storage requirements while failing to guarantee commensurate improvements in attained resolution, due to the myriad other factors which influence biological cryo-EM analysis. This work demonstrates application of a dithering technique originally applied in astrophotography to cryo-electron microscopy data to “break” the sampling limit of acquired data. We show with multiple sample types from multiple possible microscopes and detectors that it is possible to exceed this limit.

In a related, but separate investigation, we demonstrate how far past the Nyquist limit data can reach, reaching 92% of the super resolution Nyquist limit with a 200 kV microscope, and 113% of super resolution Nyquist with a 300 kV microscope.