Development of High-resolution TEM for Imaging Native, Radiation-sensitive Biomolecules

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Following the commercial introduction of "direct detection" cameras in ~2012, single-particle electron cryo-microscopy (cryo-EM) has produced atomic-resolution structures for a large number of biological macromolecules. This new capability requires that the native, hydrated structure be maintained during imaging, of course. This is something that, at first glance, is not compatible with putting specimens into the vacuum of the electron microscope. Furthermore, ionization damage happens so easily for such specimens that high-resolution features are too noisy to be discerned in images recorded with a "safe" exposure. While practical work-arounds have partially circumvented these problems, current results still fall well short of what is physically possible. Additional technical improvements are thus very welcome and, indeed, expected. These include reliable phase plates, which have just begun to appear, and cameras whose quantum efficiency is at least 2X-improved at high resolution.