High-Resolution Structure Determination At 100kv Enabled by New Falcon-C Direct Electron Detector

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Cryo-electron microscopy (cryoEM) has become an essential tool in structural biology for determining the 3D structure of macromolecular complexes. Cryo-TEMs with 300 kV have been the standard for high-resolution cryoEM single particle analysis (SPA) experiments since th nane early 2010s, delivering the highest-resolution protein structures. Recent advances in technology have shown that 200 kV Cryo-TEMs are also capable of delivering high-resolution structures with increased throughput, owing to the development of direct electron detectors and stable energy filters that produce high-quality images.

The high cost of ownership and operation of 300kV and 200kV microscopes may make them unaffordable for many laboratories and departments. As a result, the 100kV Tundra microscope was launched in 2020 to increase accessibility of cryoEM to a wider scientific community. Although originally designed as a screening instrument, the Tundra can also produce sub-4 Å resolution structures for larger and symmetric proteins.

We are now launching a direct electron detector, Falcon-C, for Tundra. This new detector will allow collection of higher resolution data that can directly lead to biological insights. Here, we present the first highest resolution structures of different proteins, ranging from highly symmetric to sub-100kDa asymmetric proteins from obtained from this 100 kV Tundra microscope equipped with the Falcon-C direct electron detector. These results demonstrate the potential for the Tundra microscope to deliver high-quality structures, making it a valuable tool for labs and departments that cannot afford the high cost of ownership and operation of 300kV and 200kV microscopes.