Emerging Techniques in Modern Microscopies

MIM.2.024
K2: A Super-Resolution Electron Counting Direct Detection Camera for Cryo-EM

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Direct detectors have great promise for improving resolution and sensitivity over indirectly coupled, scintillator-based cameras. However, direct detection alone does not raise the DQE at low spatial frequency significantly and falls short of its potential at high spatial frequency due to residual noise in the electron energy deposition process. An electron counting detector eliminates any signal variation between incident electrons and information about the electron path through the detector can be used to extract more precise positional information than the physical pixel size otherwise allows, similar to super-resolution methods common to light microscopy. Both electron counting and electron super-resolution require that events be physically separated and can be accomplished by providing a very fast camera readout. By counting electrons rather than integrating charge, as is done in traditional cameras, the noise of the detector can be reduced thereby increasing DQE to levels closer to unity than ever before achieved in a TEM imaging detector. Gatan, Inc., in collaboration with Lawrence Berkeley National Lab and members of the Howard Hughes Medical Institute, has developed a detector capable of acquiring electron-counted images under typical cryo-EM microscope conditions. A 3838 x 3710 sensor is read out at 400 full frames per second and images are processed in real time to identify individual electron events. The sensor is thinned to allow the electron beam to pass through the sensor without backscatter. Small-feature CMOS technology is combined with proprietary radiation hardening measures to provide a sensor lifetime of greater than 5 billion electrons per pixel.

Testing has shown a significant boost in DQE from counting and extension of the DQE to above the physical Nyquist frequency from electron super-resolution. Results will be presented that show improvements in camera performance using test samples and biological samples.