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An electronic detector to replace film for Electron Cryomicroscopy?

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Electron cryomicroscopy (cryoEM) is of immense importance in macro-molecular structural determination to as near atomic resolution as possible. Some recently reported structures using cryo-EM have reached 0.33 nm resolution, similar to what can be obtained with X-ray crystallography. A great deal of high resolution cryoEM data is still collected on film, which has excellent resolution, adequate size and high efficiency. A major drawback of film as a recording medium is that, since data is available only after laborious film processing, it would be extremely desirable to switch to an on-line electronic detector with immediate feedback. Although CCD detectors have been in use since the 1990s they do not provide adequate spatial resolution for the most demanding applications, namely single particle analysis of individual biological molecules, with images recorded at 200 –300 keV.
Using experience gained from earlier detectors, we present the design of a detector based on CMOS technology. Since electrons are detected directly, without going through an intermediate light conversion process as in CCDs, the resolution is expected to be superior. The detector, called Falcon, was designed to have a radiation-hard layout to withstand several years of normal cryoEM usage; it contains 4k x 4k (16 million) 14 μm pixels with an input area of 6 cms square, a fast readout and excellent detective quantum efficiency. The detector possesses most of the desirable properties needed for use in cryoEM (and indeed in other fields where electron microscopy is used). A commercial version of this detector has already been produced by the FEI Company, Eindhoven. We will discuss the results obtained at a range of electron energies between 80 and 300 keV, possibilities for biological applications and potential for further technical improvements.

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