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# Analysis of the Performance of an 8k x 8k Lens Coupled Detector for Wide-field, High-resolution Transmission Electron Microscopy (TEM).

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Film has long been regarded as the gold standard for image recording. With a modest dynamic range of 3 orders of magnitude, a format of approximately 8k x 6.5k can be expected for film, thereby, far exceeding the performance current digital detection systems produced to date. While film provides excellent modulation transfer functions (MTF), especially as compared with commercial CCD cameras, it requires several post-acquisition steps like development and digitizing that are cumbersome and time-consuming. For example, J. Frank et al. estimated that to get a 10 Å structure of a large protein complex like the ribosome, one would need to collect 100,000 images (Frank 2000). To alleviate the burden of developing and digitizing such large data sets, we have developed a design that will match the resolution and format of film with a far superior high accelerating dynamic range.

This presentation will outline the details of putting together this system from the ground up. There are many facets to such a large complicated assembly. We start by describing the scintillator technology which converts electron energy to light energy. In this case, the scintillator is a self-supported design deposited on a stretched, aluminized kapton membrane (figure 1). The scintillator resides in the vacuum of the camera chamber of the TEM. The scintillator is the bottleneck in producing a high-resolution system. We describe how MTFs are measured in our scintillator technology and how they relate to total system performance. Below the scintillator sits a leaded glass window The purpose of the window is two fold, first, to end the vacuum and provide mediation of the x-rays produced in an intermediate voltage electron microscope (IVEM) running at 300-400keV and also, to allow the scintillator to be imaged from outside the vacuum. Below the leaded glass window, we have placed a beam splitter to divide the scintillator image into four separate sub-images, each relayed across high NA lenses designed to provide single electron sensitivity (a critical point for the cryo-EM community) and maximum contrast transfer to the image recording devices. We will present the optical design in the context of providing the necessary MTF to transfer excellent resolution to the final image. We have chosen the lens-coupled design for its high-resolution performance at higher accelerating voltages and for the ease involved in separating the scintillator image into four sub-images. Moreover, lens coupled systems using demagnification lend themselves well to matching the electron footprint of the scintillator to the pixel pitch of the CCD camera. For high-energy electrons at 300keV and above, it starts to become important to move away from fiber optical relays which produce backscattering into the scintillator causing a large plume of light at the scintillator, thereby, degrading resolution (Fan et al. 2000, Fan and Ellisman, 1996, Fan et al., 1994). Moreover, it is very difficult to produce a seamless mosaiced imaging system using fiber coupling of the scintillator to the butted

CCD detectors. In order to provide single electron sensitivity, it is important to properly mange the electron to photon light budget in the context of the scintillator design, the lens efficiency, the CCD quantum efficiency, and the CCD readout characteristics. To record the images, custom fabricated 4k x 4k CCD chips are used to provide 14-15 bits of "real" dynamic range, while achieving low readout noise characteristics. We will discuss the readout characteristics, the noise characteristics of these cameras, and the high-speed data acquisition system to readout the data.

We will discuss the detailed physics and obvious engineering challenges related to the detector's ultimate resolution, format, dynamic range, and stability for each level of the system.

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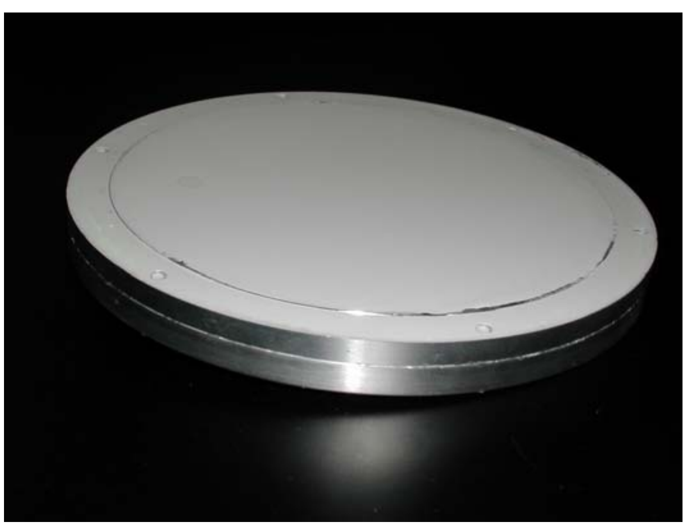

**Figure 1** A self-supported scintillator screen of P20 phosphor stretched across an aluminized kapton membrane. Self-supported scintillators provide improved resolution at

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