Optimizing the Electron Energy for Cryomicroscopy

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Biologically relevant specimens can be imaged in the transmission electron microscope, but electrons also cause damage which limits the information that can be gained. Both the ultimate resolution and the effort required to achieve a particular resolution are therefore determined by the amount of information gained per particle image. This physical limit caused by damage becomes more important as improvements are made in software and hardware for cryomicroscopy.

In recent work [1] we have measured how the elastic and inelastic cross-sections for carbon depend on the accelerating voltage of the electrons, in the energy range typically used in transmission electron microscopy, and made quantitative comparisons to two-dimensional crystals of paraffin and bacteriorhodopsin at 100 keV and 300 keV.

By determining the carbon cross-sections for elastic an inelastic scattering (Fig. 1) and measuring the difference in the rates of damage accumulation to the two-dimensional crystals at 300 keV and 100 keV, we estimate the potential to gain 25% more information per unit damage operating at 100 keV rather than 300 keV for typical biological specimen.

Using these measurements, we have introduced an information coefficient which expresses the information gain per unit damage as a function of a specimen thickness and electron energy (Fig. 2). This allows us to determine the optimal energy (accelerating voltage) to use for a given thickness specimen. From these calculations we conclude that 100 keV represents the highest potential for information in single particle cryomicroscopy.

Other limits to reducing the operating energy have already been addressed [2-4], so it seems in the future 100 keV will become the best choice for single particle cryomicroscopy [5].

References:

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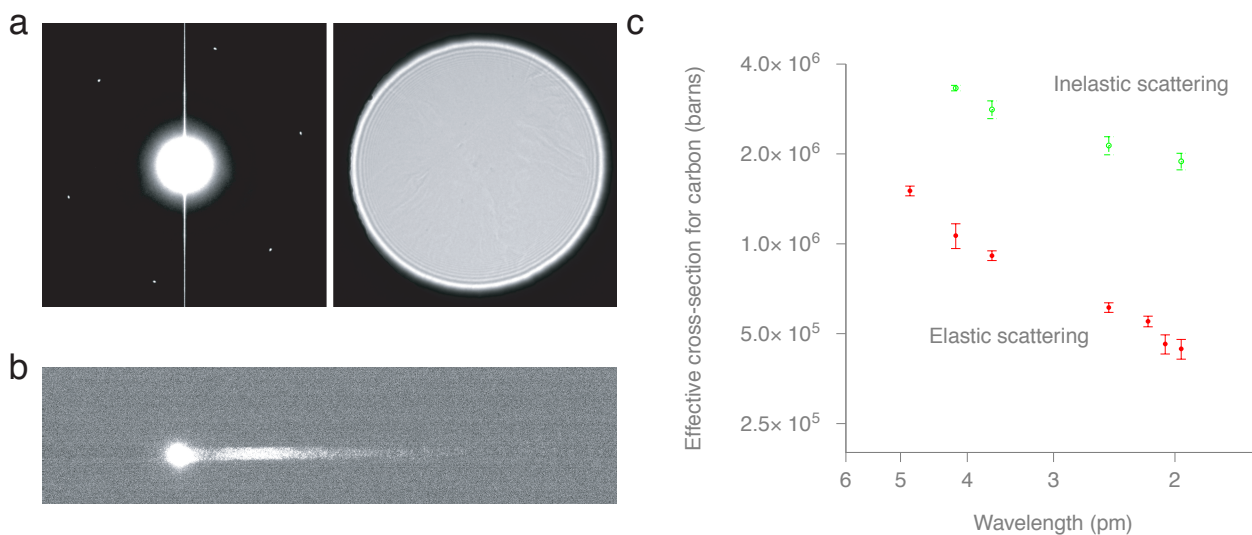
Figure 1. **(a)** Measurement of elastic, and **(b)** inelastic cross-sections of the electrons were made as a function of accelerating voltage in the electron microscope **(c)**.
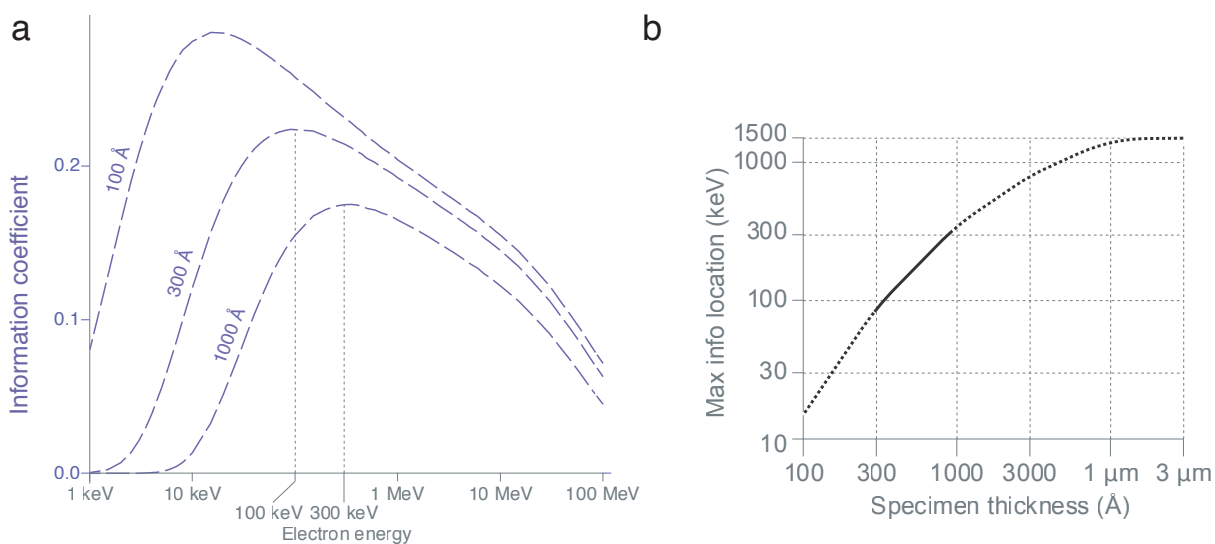
Figure 2. (a) We calculate an Information coefficient as a function of energy and **(b)** the shift in optimum voltage with specimen thickness.