

Signal to noise considerations in diffraction and conventional microscopy

X. Huang¹, H. Miao¹, J. Steinbrener¹, J. Nelson¹, A. Stewart¹, D. Shapiro², C. Jacobsen¹

¹Dept. Physics & Astronomy, Stony Brook University, Stony Brook, NY 11794-3800, USA

²Advanced Light Source, Lawrence Berkeley National Laboratory, Berkeley, CA 94720, USA

In x-ray diffraction microscopy, the x-ray beam diffracted by the specimen is collected directly on an area detector such as a backside-thinned CCD with high sensitivity. However, the diffracted magnitudes must be phased to obtain a real-space image. In conventional microscopy, the beam diffracted by the specimen is instead collected and phased by a lens, to yield a real-space image at the detector plane. Unfortunately, present-day x-ray lenses have finite numerical aperture cutoffs and poor efficiencies, limiting the efficiency with which the diffracted signal is exploited.

In this work we address the following question through simulations: which approach yields more information for a given exposure on an example biological specimen? This is an important consideration for radiation-sensitive specimens such as frozen hydrated cells, since in electron microscopy it is the case that radiation damage is *the* resolution-limiting factor. Factors entering into the comparison include:

- How does one expect the signal to noise ratio α of an image to scale with photon number? A simple model suggests that α scales as $N^{1/2}$.
- How do you measure the signal to noise ratio of an actual, noisy image, or pair of images of identical objects with different noise? We discuss the use of both real space and Fourier space correlation methods.

We then carry out simulations of x-ray imaging of a simulated cell consisting of a lipid membrane, low concentration protein solute, and protein bars of various diameters and orientations inside the “cell.” For diffraction microscopy, we simulate the illumination of the cell by a coherent x-ray beam, calculate the resulting diffraction intensity distribution, add simulated noise according to Poisson statistics, and reconstruct the image using finite support constraint iterative phase retrieval. For conventional microscopy, we calculate the absorption profile of the cell, convolve it with the point spread function of a representative soft x-ray zone plate, reduce the image intensity according to the efficiency of the zone plate, and add simulated photon noise to the resulting intensity image. We will discuss results of these comparative simulations and the implications for x-ray microscopy of frozen hydrated organic specimens.