

# TOMOGRAPHIC RECONSTRUCTION FROM LARGE-FIELD ELECTRON MICROSCOPE IMAGES

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In recent years the electron microscopy community has been progressing toward larger format digital image detectors for the electron microscope (8K X 8K pixels or larger). These resulting high-resolution large format images play an important role in determining the three-dimensional structure and function of cells and sub-cellular organelles across a wide range of spatial scales from the whole cell to proteins and protein complexes.

In order to produce a three-dimensional tomographic reconstruction, a series of electron images are obtained at various sample orientations. The number of images is somewhat limited due to the possibility of damage by the electron beam. Also the range of sample orientations is somewhat limited, as the sample is usually a thin slab, which becomes impenetrable to electrons at high rotations out of the focal plane. Digital inversion of an appropriate ray transform produces the final reconstruction. Both the discretization of the angles and the limits on angular range are sources of reconstruction artifact and pose significant mathematical and computational challenges. Secondly, the production of high-quality reconstructions requires image alignment to sub-nanometer spatial scales. A third mathematical problem arises from the circumstance that electrons move along curvilinear trajectories rather than along straight lines through the sample. These problems all become worse as the size of the images increases.

We report on a computer code (TxBR) which incorporates recent mathematical developments in electron microscope tomography. The discretization problem may be attacked by formulation of the inverse problem as a Fourier integral operator. This operator can be factored as a backprojection followed by an appropriate spatially dependent deconvolution. The latter operator corresponds to the inverse of a pseudodifferential operator. The alignment problem may be addressed through a construction of curve envelopes, and in the case where discrete features are missing, both curve and surface envelopes. This requires a generalization of projective duality to the case of projection maps modeled on polynomial functions rather than the usual projective geometry. We will also report on a generalization to the generalized ray transform of the consistency conditions (John equations) for the classical X-ray transform, and application of these equations to the reconstruction problem.

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