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Iterative Methods in Large Field Electron Microscope Tomography

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Electron tomography is an emerging technology for the three dimensional imaging of cellular ultrastructure. In combination with other techniques this technology can provide three dimensional reconstructions of protein assemblies, correlate 3D structures with functional investigations at the light microscope level and provide structural information which extends the findings of genomics and molecular biology. Because of rapid advances in instrumentation and computer-based reconstruction, the routine imaging of molecular structure in context appears to be likely within the next few years.

Tomographic reconstruction from large format electron microscope images requires special procedures to handle geometric distortions arising from electron optics as opposed to light-ray optics. In particular, electrons travel in curvilinear paths through the sample, defocus and other aberrations can be more severe. We have developed a software package, TxBR, which is based on a generalization of the inverse problem associated with the ray transform. This software compensates for instrument optics, sample degradation, and other deleterious effects.

TxBR utilizes a filtered backprojection algorithm for reconstruction, so geometric compensation for curvilinear electron paths should also be accompanied by a filtering algorithm which is accurate for the three dimensional optics. This would require a pointwise treatment of the filtering problem, which is, in effect, a six-dimensional kernel. At present we employ an image warping technique which gives a usable approximation to the correct kernel and reduces the problem to one dimension. Further improvements would require alternative inversion algorithms which bypass the filtering problem. Algorithms which employ iterative techniques constitute an attractive class of alternatives. In this case it is

necessary to code corrections for the beam geometry into the projections.

We present an adaptive simultaneous algebraic reconstruction technique (ASART) in which a modified multilevel access scheme and an adaptive relaxation parameter adjustment method are developed to improve the quality of the reconstructed 3D structure. The reconstruction process is facilitated by using a column-sum substitution approach. This modified multilevel access scheme is adopted to arrange the order of projections so as to minimize the correlations between consecutive views within a limited angle range. In the adaptive relaxation parameter adjustment method, not only the weight matrix (as in the existing methods) but the gray levels of the pixels are employed to adjust the relaxation parameters so that the quality of the reconstruction is improved while the convergence process of the reconstruction is accelerated. In the column-sum substitution approach, the computation to obtain the reciprocal of the sum for the columns in each view is avoided so that the needed computations for each iteration can be reduced.