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The 4th International Conference on Electron Tomography

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This special issue of the *Journal of Structural Biology* is based on topics and presentations at the 4th International Conference on Electron Tomography that took place November 5–8, 2006, at the Paradise Point Resort in San Diego, California. The conference covered recent developments in techniques, as well as exciting applications, and the papers in this issue reflect this coverage, with about equal distribution in the two categories.

During the last decade, electron tomography has become the technique of choice for studying the three-dimensional ultrastructure of cells, organelles, and in situ macromolecular assemblies. The growth of electron tomography has been spurred by the development of convenient, automated tilt-series collection systems for the microscope, and readily available easy-to-use reconstruction software. Yet there remains considerable room for improvement, especially in algorithms for alignment of the tilt-series images and for segmentation of the reconstructed volume. Contributions to this special issue represent significant progress in these areas. The importance of electron tomography will also be furthered by integration of imaging modes such as energy-filtered TEM, which can provide enhanced contrast as well as 3-D elemental maps, and by STEM imaging, which can optimally detect nanoparticles and metallic labels.

Cryo-electron tomography is of great interest because it provides a way to study cells in a near-native state, frozen in action, but the challenges are still considerable. Dose sensitivity remains the ultimate limiting factor for resolution in cryo-tomography, and improved, low-noise imaging detectors promise to yield important improvements in low-dose imaging, and at the same time increase image pixel count for all applications. Preparation of frozen-hydrated specimens using cryo-ultramicrotomy is of great importance, because it potentially allows study of any type of specimen, and the advances in this technique that are reflected here contribute to its wider application. Nevertheless, there is still great scope for resin-embedded specimens and chemical fixation, especially for correlative studies and sophisticated labeling techniques, and the implementation of such techniques using high-pressure frozen, freeze-substituted material is important for retaining optimal structural preservation.

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One of the most attractive applications of electron tomography is in microbiology, because many bacteria and small cells can be examined as plunge-frozen whole mounts, using the intermediate-voltage, energy-filtered microscopes that are now available in many labs. Electron tomography is essential to virology, as the only way to conduct high-resolution structural studies of a virus life cycle in situ. However, cellular tomography, whether with plastic sections, frozen whole mounts of cultured cells, or cryo-ultramicrotomed sections, will remain a mainstay application.

This special issue gathers state-of the art results that exemplify the broad range of research in biological electron tomography. It represents a snapshot of the field at present, and suggests future directions.