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Advances in energy filtered electron tomography for quantitative 3-D phosphorus imaging of cell nuclei MARIA A. ARONOVA, GUOFENG ZHANG, RICHARD D. LEAPMAN, NIH — Electron tomography (ET) is an established and valuable tool for determining three-dimensional subcellular structure at a macromolecular scale. Contrast in conventional tomograms is generated through high-angle elastic scattering of the incident electrons by heavy atoms in stained plastic sections or through phase differences of elastic scattering in frozen hydrated specimens. Energy filtered transmission electron microscopy (EFTEM) has undergone recent developments to provide an improved capability for quantitative mapping of elemental distributions. We have developed a new approach where specific chemical elements in biological systems can be imaged in three dimensions. This method of collecting electron tomograms with inelastically scattered electrons combines ET and EFTEM. We have applied this technique to analyze unstained sections of rapidly frozen, freeze-substituted and embedded cells. Using intrinsic phosphorus as a label for nucleic acid, we have investigated the distribution of DNA in nuclei of *Drosophila* larvae. We show that quantitative analysis of the three-dimensional phosphorus distribution has the potential to provide new information about the DNA packing density of chromatin.

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