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Segmentation of Cell Components Using Prior Knowledge

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1. INTRODUCTION

Electron tomography is a method for determining 3D structure by electron microscopy, using multiple tilt views of the specimen (Lucic *et al.*, 2005; McEwen and Marko 2001; McIntosh *et al.*, 2005). Since electron

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tomography does not employ averaging or require the presence of symmetry, it can be used in biological applications to image single copies of subcellular components *in situ*. When specimen preparation is optimized by use of rapid freezing, and imaged either directly in the frozen-hydrated state, or after freeze substitution and plastic embedding, electron tomography provides a relatively high-resolution view of biological structure in a native, or near-native, cellular context.

To realize the full potential of this powerful breakthrough, investigators must be able to identify and segment components of interest from the complex and densely packed cellular environment characteristic of well-preserved biological specimens. This is particularly challenging because, in addition to the crowded environment they portray, images of biological specimens have inherently low contrast and a low signal-to-noise ratio (SNR). As a result, segmentation of cellular components has been dominated by manual procedures that rely on the expert knowledge of biologists to recognize specific structures. However, such manual procedures are time-consuming, subjective and ill suited to handling the data throughput required to make statistical correlations among data sets recorded under differing functional conditions.

Many semi-automatic and fully automatic segmentation methods have been developed to overcome the limitations of manual segmentation, and some of these have been adapted for electron tomographic volumes. In this chapter, we first review segmentation work in the field of electron tomography, and then discuss the rationale for using prior knowledge to improve the segmentation of a 3D reconstruction portraying a densely packed cellular environment with a high amount of noise present (low SNR). This is followed by a detailed description of our implementation of prior knowledge-based segmentation, including practical applications, experimental results and evaluations.

2. REVIEW OF VOLUME SEGMENTATION IN ELECTRON TOMOGRAPHY

Quantitative analysis of cell components in an electron tomographic volume has become an important tool at the frontier of structural biological research. This analysis often involves segmenting cell components, measuring their dimensions, locating critical points and determining spatial relationships among the components (e.g. Harlow *et al*., 2001; Marsh *et al*., 1998; Perkins *et al*., 1997; Renken *et al*., 2002; Scorrano *et al*., 2002). In a number of applications, segmentation was achieved primarily by stacking the manually traced contours from the individual slices to construct the 3D model (He *et al*., 2003; McEwen and Marko 1999; Tregear *et al*., 2004). Several software packages can be used to contour electron tomographic data sets, including: SYNU (Perkins *et al*., 1997), IMOD (Kremer *et al*., 1996), SPIDER/STERECON (Frank *et al*. 1996; Marko and Leith, 1996) and NIH Image (Rasband and Bright, 1995).