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Denoising of Electron Tomograms

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1. INTRODUCTION

The crucial problem inherent to electron tomography is radiation damage or, related to this, the choice of the correct electron dose: an excessive dose destroys the specimen, especially biological ones, while an insufficient dose results in images that are noisy and lack information. Sophisticated and highly automated techniques have been developed both for data acquisition with the aim of keeping the electron dose as low as possible, and for image processing, in order to extract reliable information from the

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recorded data. However, the tolerable dose is very small, especially for unstained, frozen-hydrated specimens. As a rule of thumb, 5000 e/nm^2 are tolerable for such specimens. According to the dose fractionation theorem (Hegerl and Hoppe, 1978), the total tolerable dose has to be divided by the number of projection views in order to find the dose allowed for each image of a tilt series. In addition, the low scattering power of biological material results in low-contrast images. For instance, assuming a tilt series of 50 images, a pixel size of 1 nm^2, phase contrast imaging with a contrast of 10%, and considering only the shot noise of the electrons, the signal-to-noise ratio (SNR defined as energy of signal over energy of noice) in the projection images is in the order of 1. An increase in the number of projection images, a decrease of the pixel size and additional noise arising from the image recording system push the SNR below 1. The noise in the raw images propagates into the final tomogram; the resulting noise distribution in the tomogram strongly depends on the type of reconstruction algorithm used, e.g. the choice of weighting function in the case of weighted back-projection. Due to the incompleteness of information typical for tomography of the cell, the SNR of the final density map may be of the same order of magnitude as that of the raw images, at least when no additional filtering is used.

The low SNR creates severe problems for the visualization and interpretation of the 3D density maps reconstructed from tilt series. Typically, the maps are inspected first by displaying slices through the reconstruction. Even though our brain is very skillful in recognizing 2D structures in a noisy environment, we have difficulties recognizing small, arbitrarily sliced, 3D structures. Iso-surface representation and volume rendering are powerful tools to represent 3D structures; however, the interpretation of the output is frequently impossible without further processing of the map. Quantitative analysis of the reconstruction, e.g. by automatic segmentation (see Chapter 12 of this volume), and subsequent measurement of structural parameters is an even more demanding task and requires powerful tools for noise reduction.

There is a growing interest in developing new techniques for noise reduction. Looking around at other fields concerned with image analysis, for instance medical imaging or astronomy, we see much activity. Studying the literature is inspiring and helps in developing new ideas or adapting existing approaches to the needs of electron tomography, but it also has to be pointed out that most existing techniques require data with a SNR much higher than 1, and therefore are of no use for electron tomography. Furthermore, most of the presently available techniques have been developed for 2D images and need to be extended to 3D.

For structure analysis based on electron microscopy with a resolution in the nanometer range, noise reduction is absolutely essential. The impressive results obtained by electron crystallography (Fujiyoshi, 1998) as well as by single-particle analysis (Frank, 2002) are attributed to noise reduction by averaging. In both cases, the signal is highly redundant and averaging is