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CONTENT-AWARE IMAGE RESTORATION FOR CRYO-TRANSMISSION ELECTRON MICROSCOPY

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ABSTRACT:

Multiple approaches to use deep learning for image restoration have recently been proposed. Training such approaches requires well registered pairs of high and low quality images. While this is easily achievable for many imaging modalities, e.g. fluorescence light microscopy, for others it is not. Cryo-transmission electron microscopy (cryo-TEM) could profoundly benefit from improved denoising methods, unfortunately it is one of the latter. Here we show how recent advances in network training for image restoration tasks, i.e. denoising, can be applied to cryo-TEM data. We describe our proposed method and show how it can be applied to single cryo-TEM projections and whole cryo-tomographic image volumes. Our proposed restoration method dramatically increases contrast in cryo-TEM images, which improves the interpretability of the acquired data. Further more we show that automated downstream processing on restored image data, demonstrated on a dense segmentation task, leads to improved results.

Index Terms— image restoration, cryo-electron microscopy, deep learning, denoising

I. INTRODUCTION:

Modern cryo-transmission electron microscopy (cryoTEM) enables the observation of biological structures in their native state at high resolution. In order to prevent sample destruction during image acquisition, the total electron dose needs to be restricted . This restriction results in noisy, low contrast acquisitions. In practice, electron microscopists typically acquire defocused images to trade resolution for increased contrast. Hence, the existence of better performing image restoration methods would enable image acquisitions at low electron dose with reduced defocus and therefore also at elevated resolution. For fluorescence microscopy data, deep learning can be used for content-aware image restoration (CARE). Data for training CARE networks requires adequately imaged or synthetically generated pairs at low and high quality. The ideas presented in do not translate to cryo-TEM data, where the before mentioned electron dose prevents the acquisition of non-noisy ground truth images. Here we present cryo-CARE, a way to train contentaware restoration networks for cryoTEM data. Cryo-CARE can be trained by using registered pairs of noisy images, an idea that was recently introduced in the context of real-world RGB and MRI images. More concretely, we show how single TEM projections and whole tomographic volumes can be denoised using a strong, learned, and content-aware prior. We compare our results to simple baseline methods such as median-filtering or NAD. Despite their simplicity, these methods are widely used

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by cryo-TEM experts to improve the interpretability of their data. Furthermore, we show that automated downstream processing on restored image data leads to significantly improved results.

II. LITERATURE SURVEY:

Cryo-electron microscopy Single particle analysis (SPA): Development of cryo-EM started in 1970s, following the development of other techniques for macro molecular structure determination. X-ray crystallography is one of the most prolific methods in structural biology and was used to solve most of the known structures today. However,it has its own limitations the main of which is the requirement for a crystallized specimen. SPA was developed as an alternative tool based on TEM. It uses random 2Dprojections of individual particles which when computationally combined can generate a3D reconstruction of the target structure (Nogales and Scheres, 2015). In 1968, De Rosier and Klug managed to get a 3D electron microscopy reconstruction of the helical assembly of a T4 bacteriophage tail (De Rosier and Klug, 1968). A few years later, Henderson and Unwin determined the structure of bacteriorhodopsin at 7 Å resolution using 2D electron crystallography (Henderson and Unwin, 1975). This effort was the first glimpse on a membrane protein structure solved by EM. In fact, a few more structures came along using electron crystallography but It was limited due to difficulties in producing well- ordered 2D crystals and obtaining a sufficient high resolution in electron micro graphs at high tilt angles. In the 1980s, the concept of SPA was introduced with the ability to get a structure from micro graphs containing randomly oriented particles (Frank and van Heel, 1982; van Heel and Frank, 1981). Initially the samples were embedded in heavy metal salts (negative staining) in order to increase the contrast and make them compatible with the vacuum environment inside the TEM. However, negative staining limited the achievable resolution to about 2 nm(the staining salts grain size). The first attempt in observing hydrated samples was in 1972 by Matricide et al. They showed that fully hydrated catalase crystals can diffract electrons to high resolution (Matricardietal.,1972).

III. EXISTING METHODOLOGY:

In this section, we introduce the proposed model for depth map restoration. We first introduce the detailed formulation of our model. Then, we provide a task driven training method to learn stage-wise model parameters. With the learned stage-wise parameters, guided depth restoration can be achieved in only a few iterations

Weighted analysis sparse representation model :

How to take full advantage of the information from the guided image is the key issue in guided image restoration. Many previous optimization-based methods promote discontinuity between intensity and depth maps by using guidance related weights to regularize pixel-pair wise differences. To better model the dependency between intensity and depth images, we propose the following weighted analysis prior model:

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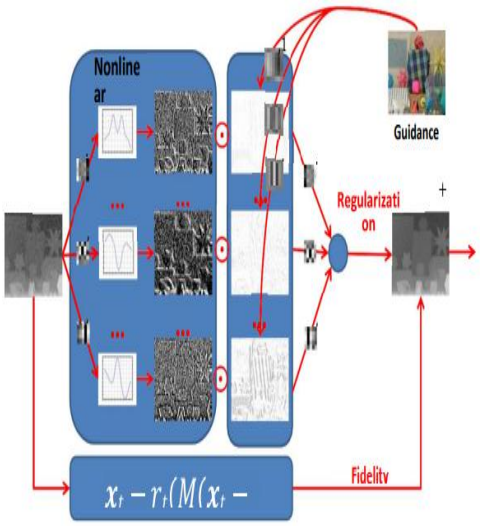

Fig 1. Flowchart of the proposed method.

where w, p denotes the standard inner product. The weight wi ∈ RN is a column vector associated with each pixel in the intensity image g, which is controlled by the parameter βi. ρi(x; pi, αi) is also a column vector by point-wisely applying the penalty function ρi to the filter response pi x, i.e.,

ρi(x; pi, αi) = (ρi((pi x)1), ⋯ , ρi((pi x)N))T ∈ RN

Nonline are Guidance Image Fidelity 7 where denotes the convolution operator, and the penalty function ρi is parameterized by αi. Note that in a standard analysis prior model, the weight wi is given as a constant. However, in our proposed model, wi is defined based on the local structure of intensity image, such that wi → 1 at homogeneous regions, and wi → 0 at edges. As a consequence, the resulting weighted analysis model will penalize high depth discontinuities at homogeneous regions and allow sharp depth jumps at the corresponding edges. By plugging the proposed analysis prior model (2.3) into a variational framework, we arrive at the following functional Most penalty functions used for natural image restoration as well as guided depth map refinement favour small filter responses, and accordingly smooth image edges. While, Chen et al. [26] found that the behaviour of penalty functions learned from training data is actually very complex. Though most of the penalty functions tend to shrink the filter response to promote smoothness, there are also some penalty functions which will enlarge filter responses in certain ranges. Such an expansion behaviour is helpful to generate sharper image edges. In order to generate high-quality depth map with sharp edges, we follow [26] and investigate penalty functions with flexible shapes. As in both training and test phases (e.g., see (2.10)), the proposed model explicitly involves the first-order derivative of the penalty function ρi, we alternatively focus on the derivative function φi = ρ J i , which is known as the influence function [26] and can be parameterized.

IV. PROPOSED METHODOLOGY:

Image restoration, including image denoising, super resolution, inpainting, and so on, is a well-studied problem in computer vision and image processing, as well as a test bed for low-level image modelling algorithms. In this work, we propose a very deep fully convolutional auto-encoder network for image restoration, which is a encoding-decoding framework with symmetric convolutional-deconvolutional layers. In other words, the network is composed of multiple layers of convolution and de-convolution operators, learning end-to-end mappings from corrupted images to the original ones. The convolutional layers capture the abstraction of image contents while eliminating corruptions. Deconvolutional layers have the capability to up sample the

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feature maps and recover the image details. To deal with the problem that deeper networks tend to be more difficult to train, we propose to symmetrically link convolutional and deconvolutional layers with skip-layer connections, with which the training converges much faster and attains better results.

V. CONCLUSION AND RESULT:

In this publication we show how content-aware image restoration can successfully be applied to cryo-TEM data. EM experts are currently using relatively simple filtering techniques, i.e. NAD, before manually investigating acquired data. CryoCARE, as we have shown, leads to highly contrasted and well resolved 2D and 3D data. Our experiments also show that P2P reconstructions are not ideal for tomographic reconstructions. Nevertheless, with T2T we can offer a simple and powerful tool for content-aware tomographic restorations. We therefore believe that cryo-CARE will facilitate manual data browsing, a step that can hardly be underestimated when many and/or large volumes have to be browsed for regions of interest. Additionally we showed that cryo-CARE restorations can lead to highly improved automated analysis results. a preprocessing step that does not need human labels and a analysis stage that is likely to require lesser amounts of training data. We are confident that cryo-CARE will rapidly find application in the cryo-EM field. It improves data-browsing, creates well contrasted, high SNR images for improved visualization of single projections/tomograms, and improves the performance of automated analysis pipelines, hence it enables to work efficiently on much larger bodies of data.

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