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Denoising and Covariance Estimation of Single Particle Cryo-EM Images Tejal Bhamre Department of Physics, Princeton University, Jadwin Hall, Washington Road, Princeton, NJ 08544-0708, USA

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abstract The problem of image restoration in cryo-EM entails correcting for the effects of the Contrast Transfer Function (CTF) and noise. Popular methods for image restoration include 'phase flipping', which corrects only for the Fourier phases but not amplitudes, and Wiener filtering, which requires the spectral signal to noise ratio. We propose a new image restoration method which we call 'Covariance Wiener Filtering' (CWF). In CWF, the covariance matrix of the projection images is used within the classical Wiener filtering framework for solving the image restoration deconvolution problem. Our estimation procedure for the covariance matrix is new and successfully corrects for the CTF. We demonstrate the efficacy of CWF by applying it to restore both simulated and experimental cryo-EM images. Results with experimental datasets demonstrate that CWF provides a good way to evaluate the particle images and to see what the dataset contains even without 2D classification and averaging.