

Class Averaging in Cryo-Electron Microscopy

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Class averaging is a crucial initial step in cryo-electron microscopy single particle reconstruction, because the signal to noise ratio (SNR) of raw projection images is typically too low for ab initio modeling. Class Averaging amplifies the SNR by averaging noisy images of similar viewing directions. The averaged images form the input to ab initio reconstruction algorithms to determine the 3D electron density map of a macromolecule. Without prior knowledge of the particle, identifying images from similar viewing directions is challenging at low SNR. Our class averaging procedure is fast (near linear running time in the number of images) and succeeds at remarkably low levels of signal-to-noise ratio. It uses steerable PCA, Wiener filtering, rotational invariant representation of 2D images with bispectrum, fast randomized SVD, fast randomized nearest neighbors search, vector diffusion maps, and fast 2D alignment of images.