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Difference Map Denoising to Model Low-Occupancy Populations in Crystallographic Data with METEOR

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ABSTRACT: Uncovering low-occupancy species is essential for a number of structural biology applications, such as detecting time-evolving intermediates and bound ligands. In protein crystallography, difference maps reveal changes in electron density between a reference and a perturbed dataset. Current methods to generate difference maps, however, rely heavily on manually tuned parameters and can fail to extract clear, chemically interpretable signals from noisy data. We introduce the use of negentropy to find parameters that maximize the deviation of difference map's electron density distribution from a Gaussian.

We then robustly evaluate different map-generation strategies using map negentropy, improving automation and reducing user bias. This allows us to apply an image restoration technique, total variation denoising, to crystallographic difference maps. Total variation denoising filters out high-frequency noise and improves phase estimates for low occupancy states: this significantly enhances high-resolution signal detection compared to current methods.

