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## Publication

## A maximum likelihood approach to two-dimensional crystals

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Maximum likelihood (ML) processing of transmission electron microscopy images of protein particles can produce reconstructions of superior resolution due to a reduced reference bias. We have investigated a ML processing approach to images centered on the unit cells of two-dimensional (2D) crystal images. The implemented software makes use of the predictive lattice node tracking in the MRC software, which is used to window particle stacks. These are then noise-whitened and subjected to ML processing. Resulting ML maps are translated into amplitudes and phases for further processing within the 2 dx software package. Compared with ML processing for randomly oriented single particles, the required computational costs are greatly reduced as the 2D crystals restrict the parameter search space. The software was applied to images of negatively stained or frozen hydrated 2D crystals of different crystal order. We find that the ML algorithm is not free from reference bias, even though its sensitivity to noise correlation is lower than for pure cross-correlation alignment. Compared with crystallographic processing, the newly developed software yields better resolution for 2D crystal images of lower crystal quality, and it performs equally well for well-ordered crystal images.

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