Poster Presentation

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Better maps for better models

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Atomic models are the ultimate result of the cryo-EM structure determination process. Yet, interpretation of high-resolution cryo-EM density maps with atomic models remains challenging due to inherent contrast loss and resolution variation. Resolution variation combined with global contrast restoration procedures generates maps that are inapt in representing local detail accurately and thus are prone to hamper or misguide atomic model building and refinement. Here, we introduce a general procedure that iteratively improves cryo-EM density maps such that the resulting map faithfully restores local structural features. The method (LocScale) employs prior knowledge of structure factor properties of biological macromolecules to optimize contrast in cryo-EM density maps. We integrated the procedure with atomic model refinement and tested it on three published cryo-EM structures as part of the EMDB model challenge, TRPV1 , β-galactosidase , γ-secretase [1] and on RNA polymerase III [2]. We demonstrate that LocScale maps improve existing models and reveal novel structural insight. The presented approach enhances the interpretability of single-particle cryo-EM density maps and provides an implementation that efficiently combines iterative density improvement with atomic model refinement, reminiscent to procedures commonly used in X-ray crystallography.

[1] http://challenges.emdatabank.org/?q=model_challenge
[2] Hoffmann, N. A. et al. (2015). Nature 528, 231–236 .

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