Poster Presentation

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Error estimation guided rebuilding of de novo models for ab initio phasing

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Recent advancement in computational methods for protein structure prediction has made it possible to generate high quality de novo models required for ab initio phasing of crystallographic diffraction data using molecular replacement. Despite those encouraging achievements in ab initio phasing using de novo models, its success is limited only to those targets for which high quality de novo models can be generated. Here, an approach is introduced that can identify and rebuild the residues with larger errors, which subsequently reduces the overall C-alpha root mean square deviations (CA-RMSD) to the native protein structure. The error in a predicted model is estimated by the average pairwise geometric distance per residue computed among selected lowest energy coarse-grained models. This score is subsequently employed to guide a rebuilding process that focuses on more error-prone residues in the coarse-grained models. These rebuilt coarse-grained models were then turned into all-atom models and refined to produce improved de novo models for molecular replacement. This rebuilding methodology has been tested on ten protein targets that were unsuccessful with the current state-of-the-art methods. Seven diffraction datasets were successfully phased using rebuilt de novo models indicating the improved quality of these rebuilt de novo models and the effectiveness of this rebuilding process.

Keywords: ab initio phasing, structure prediction, de novo models