Oral presentation

Quantum-based atomic model refinement becomes reality in Phenix

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Owing to the limited quality of experimental data, such as resolution, atomic model refinement using cryo- EM or crystallographic experimental data is often a challenging task. To make refinement practical, a priori information about model geometry is always used as chemical restraints. These restraints originate from standard libraries that are used across most structure solution software in the field, such as CCP4 and Phenix. Geometric restraints derived from these libraries suffer from at least three limitations. First, they lack information about novel molecules, such as ligands. Second, they are agnostic to non-covalent interactions such as hydrogen bonds, salt bridges, pi-interactions, and electrostatics in general. Third, the use of molecule-specific information as a source of geometric restraints, such as polypeptide chain conformations (Ramachandran plot), secondary structure, or rotameric states of amino acid side chains, requires a geometrically sound atomic model in the first place to be defined. Using quantum mechanical (QM) calculations as a source of restraints can eliminate the need for these libraries as well as the use of molecule-specific restraints altogether. However, these calculations are known to be computationally intractable for large molecules unless divide-and-conquer methods are used in conjunction with specialized QM software, some of which (the best one) is not free even for academic users. We present a novel deep learning implementation of a neural network potential that allows performing QM calculations for biomacromolecules in a timescale ranging from seconds to minutes. This, in turn, enables the use of QM- based geometry restraints in standard atomic model refinements. Preliminary results show that these methods produce refined models with much superior geometries compared to refinement using standard restraints while maintaining comparable fit to the experimental data.