Q| R: QUANTUM-BASED REFINEMENT OF BIOMACROMOLECULES

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Protein structure determination is largely reliant on crystallography (X-ray, neutron or electron), electron cryo-microscopy (Cryo-EM) or NMR experiments. Refinement is the final step in obtaining accurate three-dimensional atomic model based on experimental data. Since the quality of the data (e.g., resolution) is rarely sufficient to utilize these data alone, this step has traditionally relied on parameterized libraries that describe stereochemistry of the molecules in question. The libraries used in major refinement packages do not describe unusual local arrangements of protein residues in Ramachandran space, novel ligands, or non-covalent interactions such as π stacking, halogen, hydrogen or salt bridges.

The methods we are developing in the Q| R project [1-4], which is our next generation open-source software package (http://github.com/qrefine), combine experimental data with chemical restraints derived from quantum-chemical methods. These procedures allow at present quantum refinement of proteins based on both X-ray crystallography or Cryo-EM experiments. Quantum refinement has shown to significantly improve model geometry, considering both the overall aspects of model and model-to-data fit statistics, as well as specific detailed structural features, in particular the hydrogen bonding.

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