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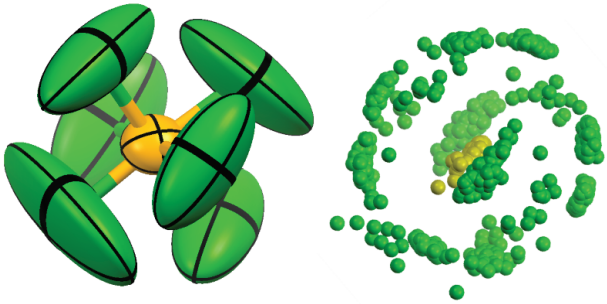

Figure 1. Conventional a.d.p. model of disordered PF_6 anion (left); ensemble of partially occupied molecular models (right) revealing more detailed orientational disorder.

Keywords: disorder, a priori chemical information, solvent

MS45-O2 Use of chemical restraints in Phenix

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The models obtained from crystallography can be improved by the use of prior chemical knowledge. Phenix (Adams, 2010) makes use of previously obtained experimental data and also predictive methods such as quantum chemistry (QC) to improve the accuracy of crystallographic models.

The electronic Ligand Builder & Optimization Workbench (eLBOW) (Moriarty, 2009) is used in Phenix to generate geometries and restraints for use in structure refinement. These can be determined by the using built-in semi-empirical QC methods, including RM1 and AM1, or via third party QC packages. It can also interface with the experimental geometries available via the Mogul program (Bruno, 2004). Libraries of restraints can be generated automatically, however, validation is essential to ensure accurate results. These range from simple checks to ensure topological correctness to detailed checks that highlight limitations of the generation method.

The Phenix structure refinement program, phenix.refine (Afonine, 2012), can make use of prior and predictive chemical methods in multiple ways to improve molecular models. The geometry of the protein can be improved using the Conformation Dependent Library (Moriarty, 2014) to adjust the main chain geometry based on the conformation of the backbone. Macromolecular geometry can also be improved by using more physically realistic potentials from molecular mechanics, such as Amber (Case, 2014). Finally, ligand geometries can be improved by the application of molecular modeling force fields (MMFF) or semi empirical QC (PM6) gradients from the AFITT program (Wlodek, 2006), or the use of QC methods from the DivCon library (Borbulevych, 2014).

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Keywords: ligands, restraints, quantum chemistry, force fields, ligand libraries, validation