High Throughput Protein-Ligand Complex Structure Solution with Phenix

Nigel W. Moriarty[a] and Paul D. Adams[ab]

[a]Molecular Biosciences and Integrated Bioimaging, Lawrence Berkeley National Laboratory, Berkeley, CA 94720, USA

[b]Department of Bioengineering, University of California, Berkeley, CA, 94720, USA

Solving structures quickly in the academic or industrial setting is a high priority. The Phenix suite of programs (Adams *et al.*, 2010) provides a number of tools for automation of structure solution in addition to tools that allow for highly accurate results.

A tool for pipelining the protein-ligand complex structure solution known as phenix.ligand_pipeline (Echols *et al.*, 2014) combines a number of Phenix tools to provide a solution from minimal inputs and minimal intervention. The procedures includes a check of the experimental data using xtriage; an optional molecular replacement step using Phaser (Bunkoczi *et al.*, 2013); a ligand restraints generation step using eLBOW (Moriarty *et al.*, 2009); fitting of the ligand using LigandFit (Terwilliger *et al.*, 2006) or Guided Ligand Replacement (Klei *et al.*, 2014); and several rounds of refnement using various strategies in phenix.refne (Afonine *et al.*, 2012). Several custom tools are deployed during the run to improve the results.

eLBOW is a fexible tool that can be easily added to any pipeline. It takes a large number of chemical inputs can produced restraints for the ligand including all it's isomers. The geometry can be minimised using the AM1/RM1 shipped with Phenix as well as plugins for several quantum chemical packages including GAMESS.

Refnement in phenix.refne can use AFITT (Janowski *et al.*, 2016) to provide gradients for the ligand or Amber (Case *et al.*, 2016) for the entire protein-ligand complex to improve hydrogen bonding and clashscores.

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