molecular models, is more robust, provides clearer maps, and may use a smaller portion of data for the TEST set for calculation of the Rfree or leave it out completely.

Praznikar, J. & Turk, D. (2014) Free kick instead of cross-validation in maximum-likelihood refinement of macromolecular crystal structures. Acta Cryst. D70, 3124-3134.

Keywords: refinement, maximum likelihood, Rfree, macromolecule, structure accuracy

MS44-O2 MoPro software: a continual evolution and extension of algorithms from "MOlly for PROteins" to "MOlecular PROperties"

Christian Jelsch[1,2]

1. CNRS
2. Université de Lorraine. France

email: christian.jelsch@univ-lorraine.fr

There have been an increasing number of biological macromolecule structures solved at ultra-high resolution. The refinement program MoPro [1,2] dedicated to the charge density refinement at (sub)atomic resolution of structures ranging from small molecules to biological macromolecules, was therefore developed starting from MOLLY software of Hansen & Coppens [3] written in Fortran language. The program uses the multipolar pseudo-atom model [3] for the electron-density refinement. Alternative methods are also proposed later, such as modelling bonding and lone-pair electron density by virtual spherical atoms.

A charge-density database ELMAM2 [4] was constructed to enable the transfer of multipolar parameters to proteins and was later extended to model common chemical group in organic molecules. The program allows with time more and more complex refinement strategies to be written and has numerous restraints, constraints applying on the charge density or the stereochemistry. Analysis tools to compute the static electron-density and electrostatic potential are derived from the initial MOLLY secondary programs and are available in VMoPro visualisation program. Fourier electron density maps and topological charge integration were programmed from scratch while an existing FFT was incorporated. Some automation tools were programmed to spare the user's time such as local axes definition, importation, exportation, restraints and constraints preparation as well as an automatic charge density refinement strategy.

A graphical user interface MoProGUI was developed in JAVA over the years in order to guide the MoPro user and show him, by exploring the menus, the numerous options and tools available.

The last stage is the development of MoProViewer [5] written in C++, a molecular viewer which is also a Graphical User Interface of VMoPro. MoProViewer enables, in addition, to compute some properties such as the atomic charge in atomic basins from a 3D grid. Some recent tools available are the solvent accessible surface and Hirshfeld surface.

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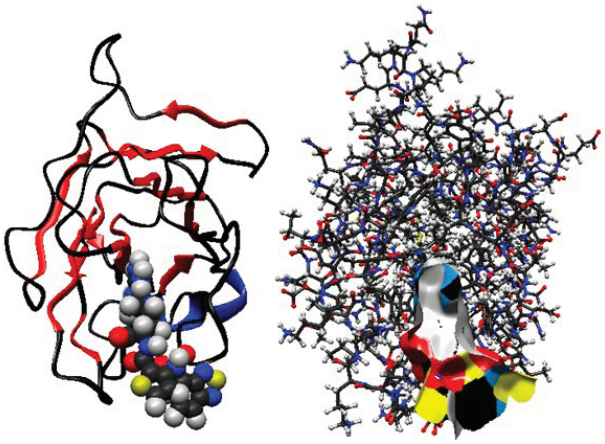

Figure 1. Left: Ribbon view of neuropilin 1, fragment b1 3D structure with bound inhibitor EG00229. Right. Hirshfeld surface of the protein/ligand interface coloured according to protein atom species.

Keywords: Charge density refinement, Restraints, Constraints, Molecular Properties, Molecular Viewer, Hirshfeld surface.

MS44-O3 Likelihood based molecular replacement model pruning in Phaser

Robert D. Oeffner[1], Airlie J. McCoy[1], Randy J. Read[1]

1. Cambridge Institute for Medical Research, University of Cambridge, Hills Road, Cambridge, CB2 0XY, United Kingdom

email: rdo20@cam.ac.uk

The use of likelihood as a target for molecular replacement (MR) calculations in *Phaser* [1] has increased sensitivity over traditional Patterson-based methods, allowing structures to be solved with smaller fragments or models derived from more distant homologues. Both the likelihood score and the probability of success are enhanced if the MR model is pruned *a priori* using tools such as Sculptor [2] or Chainsaw [3] to remove domains, loops or side chains that are predicted from the sequence alignment to be poorly conserved. However, the optimal sequence alignment and optimal pruning become more ambiguous as the sequence relationship becomes more distant, and there can be unexpected domain motions even in close relatives. In these circumstances, potential solutions can be lost because of poor signal or failure in packing tests.

A new likelihood-based *a posteriori* MR model pruning feature has been added to Phaser to deal with such problems, thereby improving clear MR solutions as well as rescuing potential solutions with poor signal-to-noise. Smoothly varying occupancies are refined along the protein chain, and then a threshold occupancy is chosen to decide which parts of the starting model should be retained. The residues discarded are typically from poorly-conserved surface loops or domains that have undergone a rigid-body motion. Removing these parts of the structure can rescue MR solutions that would otherwise be discarded by the packing test. In addition, the likelihood-based model pruning also clarifies which domains still need to be placed in multi-component structure solutions.

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Keywords: Phaser, molecular replacement, maximum likelihood, pruning