Automated Structure Refinement for High-throughput Ligand Detection with BUSTER-TNT

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The use of crystallography for the discovery of lead compounds often involves a large number of experiments with different soaking or co-crystallization trials. The subsequent refinement and analysis of the resulting datasets can be time-consuming and tedious. Since the crystallographic parameters (resolution, space group, cell parameters) are quite often similar, this task is ideally suited for automation.

We present a method (**autoBUSTER**) that automates the refinement, solvent model update, ligand detection and analysis. Centered around the BUSTER-TNT program [1,2], it requires a minimal amount of user input. Although it can be used at any resolution and for any kind of macromolecular structure, it is tuned to the refinement of protein structures at better than 2.8 Å resolution.

The knowledge of any (possibly) bound ligand can be given (a) explicitly by supplying a PDB file of dummy atoms that describes the assumed binding site, or (b) by letting the system automatically analyze the residual density of difference Fourier maps. A unique feature of BUSTER-TNT is used, where the various masks describing the known fragment, the bulk solvent and the missing part can be given independently from each other. The results show that this can greatly enhance the capability of uniquely defining any bound ligand.

[1] Bricogne G., Irwin J., *Macromolecular Refinement: Proceedings of the CCP4 Study Weekend*, Warrington: Daresbury Laboratory, 1996, 85-92. [2] Blanc E., Roversi P., Vonrhein C., Flensburg C., Lea S. M., Bricogne G., *Acta Cryst*., 2004, **D60**, 2210-2221.

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