s1.m3.o2 **Automatic Protein Models With Flexible Fragments.** Frantisek Pavelcik, *Department of Inorganic Chemistry, Faculty of Natural Sciences, Comenius University, 842 15 Bratislava, Slovakia. E-mail: pavelcik@fns.uniba.sk*

Keywords: Protein; Automatic Building; Flexible Fragments

An automatic model building is an open challenge in the protein crystallography. Three principally different approaches have been developed so far: (i) ARP/*w*ARP is based on an interpretation of the difference electron-density in terms of oxygen globs, iteratively followed by an atomic refinement and an interpretation of the atomic coordinates in terms of a polypeptide chain. (ii) Greer devised procedures for tracing the path of the polypeptide chain and subsequent localisation of C^{α} atoms. His method is used for example in QUANTA or MAID. (iii) Direct positioning of protein fragments (helices, β-strands) in the electron density can be found e.g. in O, or SOLVE/RESOLVE. The localisation of fragments (helices) is an initial step of the model building by a computer graphics.

An advanced methodology (phased rotation and translation function) for positioning molecular fragments in an electron density was described by Friedman (1999) and Pavelcik, Zelinka & Otwinowski (2002). The refinement of fragment conformation, in a space of spherical harmonics- Bessel functions, has recently been proposed by Pavelcik (2003). Very accurate and complete protein models can be built by this approach, provided that phases are good and resolution is better than 2.1 Å. Partial results can be obtained at resolution 2.3 Å.

Protein building can be divided into well-defined steps:

(i) Expansion of crystal electron density in spherical harmonics and Bessel functions. (ii) Localisation of peptide centred Ala-Ala fragments by 6-D phased rotation and translation function. Optimisation of fragment position and orientation. Flexible and flipped refinement of fragment conformation. (iii) Sorting of fragments utilizing fragment overlap and connectivity number. Connecting individual fragments into polypeptide chain. Extending chains. Building cis-peptide bonds with cis-Ala-Pro fragment. (iv) Sequence alignment by marker and rotamer methods. Building of side chains. Refinement of side chain conformations. (v) Refinement of group temperature factors by least-squares. Building of heterogroups. (vi) Creating PDB file of protein structure.

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[2] Pavelcik, F., Zelinka, J. Otwinowski, Z. (2002). *Acta Cryst*. D**58**, 275-283.
[3] Pavelcik, F. (2003). *Acta Cryst.* A**59**, 487-494.

s1.m3.o3 **Direct Location of Individual Sulfur Atoms From Weak, Medium Resolution Sad Data**. Judit É. Debreczeni and George M. Sheldrick, *Lehrstuhl für Strukturchemie, Georg-August Universität, Tammannstr. 4, 37077 Göttingen, Germany. E-mail: gsheldr@shelx.uni-ac.gwdg.de*

Keywords: SAD Phasing; SHELX; Substructure Solution

Location of sulfur atoms in disulfide bridges represents a special case in heavy atom substructure solution, as the number of sites depends on the resolution of the anomalous data. At low resolution (lower than 2.8 Å) the two sulfur atoms of the disulfide unit coalesce to a super-sulfur atom, therefore half the real number of sulfurs should be searched. On the contrary, high resolution (better than 2.0 Å) anomalous data usually allow the direct resolution of disulfide units to single atoms [1].

The average diffraction limit of crystals from biological samples is only rarely higher than 1.5 Å and anomalous data are only reliable to 0.5 Å lower resolution. In such cases, i.e. when the anomalous signal extends to medium resolution, sulfur atoms of disulfide units cannot be resolved directly. However, modelling of the heavy atom substructure with super-sulfur atoms is not optimal and phases calculated are not sufficient to define the molecular envelope that reduces the efficiency of subsequent phase improvement steps.

This problem can be overcome by the direct location of two-atom disulfide units using the new algorithm implemented in each dual-space refinement cycle of *SHELXD*. Tests on known and previously unknown structures indicated that this innovation – apart from the marked improvement in phasing – improves the discrimination between correct solutions and noise peaks of the heavy atom substructure and allows the location of "hidden" single sulfur peaks. This approach played an essential role in successful phasing of a previously unknown structure solved recently [2].

[1] Debreczeni, J. É. *et al.* (2003). *Acta Cryst.* **D59**, 688-696.
[2] Debreczeni, J. É. *et al.* (2003). *Acta Cryst*. **D59**, 2125-2132.