**A Robust Bulk Solvent Correction and Anisotropic Scaling Procedure in the *CCTBX***

Pavel V. Afonine, Ralf W. Grosse-Kunstleve, Paul D. Adams, *Laurence Berkeley National Laboratory, One Cyclotron Road, BLDG 64R0121, Berkeley, CA 94720 USA*. E-mail: PAfonine@lbl.gov

Macromolecular crystals contain a large amount of disordered solvent which contributes significantly to the diffracted amplitudes at low resolution. The importance of low-resolution data has been demonstrated for many crystallographic calculations [1, 2] and hence an appropriate modelling of the bulk solvent is very important. Jiang & Brünger [1] demonstrated that a flat solvent model is the most reliable while more sophisticated models bring only marginal improvements. The combination of a bulk solvent correction and overall anisotropic scaling [3] is known to be a numerically ill behaved problem [1, 4].

In this work we describe a robust protocol for determination of bulk solvent and anisotropic scaling parameters which we have implemented in the *Computational Crystallographic Toolbox* [5]. This fully automated protocol does not require any user intervention and assures the calculation of optimal, and physically reasonable, output values for these parameters. Also we present a new maximum-likelihood target function for the determination of the flat solvent parameters and anisotropic scale matrix.

[1] Jiang J.-S., Brünger A.T., *J. Mol. Biol*., 1994, **243**, 100-115. [2] Urzhumtsev A., *CCP4 Newsl*., 2000, **38**, 38-49. [3] Sherif S., HenricksonW. A. , *Acta Cryst*., 1987, **A43**, 118-121. [4] FokineA., Urzhumtsev A., *Acta Cryst*., 2002, **D58**, 1387-1392. [5] Grosse-Kunstleve R.W., Sauter N.K., Moriarty N.W., Adams P.D., *J. Appl. Cryst.*, 2002, **35**, 126-136.

**Keywords: bulk solvent, anisotropic scaling, maximum-likelihood**