PS03.03.09 THE PROTEIN PROGRAM SYSTEM: REAL SPACE TECHNIQUES USING FOURIER AND PATTERSON MAPS. Wolfgang Steigemann, Max-Planck-Institut für Biochemie, Computing Center, D-82152 Martinsried, Germany

Recently implemented modules and features in the PROTEIN program system will be in focus that provide high flexibility in the area of density modification and manipulation in real space.

Real space techniques have been an important issue in PROTEIN from its very beginning. Original goals of the "search methods" in the field of molecular replacement have been the correlation of maps for the exploration of non-crystallographic symmetry (Patterson self rotation), positioning of known molecular models in unknown structures (cross rotation, translation) both in Patterson and Fourier map, location and refinement of local axes in Fourier map, calculation of "mean Fourier maps", and rotated density maps.

The widely used density modification techniques like molecular averaging and solvent flattening aiming at phase improvement and interpretability of density maps have required further extension and flexibility of these capabilities. Following the principles of PROTEIN, this has been acchieved by implementing additional modules and features (e.g. simple map algebra incl. rotation and superposition, unit-cell generation from an asymmetric unit, mask calculation by convolution techniques). In this way tools are provided to the user he can combine with the already present elements to powerful procedures on the level of PROTEIN's flexible command language.

PROTEIN itself has been ported to a variety of platforms and is available for the most prominent Unix systems incl. DEC Alpha, Silicon Graphics, IBM RS/6000, Sun and Hewlett Packard, as well as OpenVMS on VAX and AXP, on particular request

The Web page *http://www.biochem.mpg.de/PROTEIN/home.html* provides detailed information about the package's capabilities, availability, new features, examples, a mailing list for the user community, etc.

PS03.03.10 COMPARISON OF MODEL WITH ELECTRON DENSITY: REFINEMENT, MODEL-BUILDING, QUALITY ASSESSMENT IN CRYSTALLOGRAPHY & EM. Xie, Q.; Blanc, E., Zhou, G., Tong, J. & Chapman, M.S., Department of Chemistry and Institute of Molecular Biophysics, Florida State University, Tallahassee, FL 32306-3015, USA

A function has been derived through which it is possible to calculate from an atomic model, the appearance of an electron density map at any arbitrary experimental resolution [Chapman (1995) Acta Crystallogr. **A51**: 69-80]. This serves as the basis of a stereochemically restrained refinement protocol that is very fast when applied to local regions and overcomes many of the problems with previous implementations of real-space refinement. This method has been used in the refinement of 3 virus structures [Chapman & Rossmann (1996), Acta Crystallogr. *in press*; Balaji & Caspar, *in prep.*; Blanc *et al.*, IUCR abstract]. The method shows promise for protein crystallography in bridging between model building and reciprocal space refinement, to help bring an initial model within the convergence radius of conventional refinement. The results of ongoing systematic tests with maps of various qualities will be presented. The same mathematical models of electron density are being used for the improvement of indices that measure the quality of a model on a residue-by-residue basis. They are also being used at low (~20 Å) resolution in the development of methods to orient and position domains of known structure within electron micrograph images of large assemblies. The authors will summarize the theoretical foundation common to all of these applications, and present some of the recent results that demonstrate the success of this approach.

PS03.03.11 AN IMPROVED CROSS-VALIDATION METHOD DENSITY MODIFICATION. APPLICATION TO PHASE REFINEMENT AND EXTENSION. J.-S. Jiang, A. T. Brünger, The Howard Hughes Medical Institute and Department of Molecular Biophysics and Biochemistry, Yale University, New Haven, CT 06520, USA

The cross-validated or free R value is correlated with the phase accuracy of an atomic coordinate model in the course of model building and refinement (Brünger, 1993, *Nature*, **355**, 472-474). Application of cross-validation to phase improvement by density modification causes difficulties in the absence of an atomic model (Roberts & Brünger, 1995, *Acta Cryst.*, **D51**, 990-1002). The underlying reason can be found in the removal of partial information from the iterative electron density map calculation required in density modification schemes. This problem can be partially overcome by complete cross-validation albeit at a significant computational expense.

An improved cross-validation scheme with a single test set is proposed for phase refinement and extension in density modification schemes, such as solvent flattening, histogram matching, Sayre's equation, skeletonization, and noncrystallography symmetry averaging. It is based on "interpolating" the test set when computing electron density maps from working sets. This interpolation method which is commonly used for density modification when only partial diffraction data are available appears to improve the reliability of the free R value for density modification. The free R value computed with the new scheme shows more correlation to mean phase error than the original scheme when a single test set is used.

PS03.03.12 MAGICSQUASH: ITERATIVE MULTIPLE DOMAIN AND MULTIPLE SPACE GROUP NCS AVERAGING. David J. Schuller, Department of Molecular Biology, University of California, Irvine, CA, 92697-3900 USA.

The simultaneous application of multiple constraints such as non-crystallographic symmetry (NCS) averaging, solvent levelling, histogram matching and Sayre's equation has proven to be very effective for phase refinement and extension. An existing program, SQUASH, exists for carrying this out in a fast, automated and iterative manner [1]. Modifications have been made to this program to allow the averaging of multiple domain and multiple space group NCS while retaining the ease of use and automation, resulting in program MAGICSQUASH [2]. The averaging algorithms of MAGICSQUASH are described, and examples of structures solved with MAGICSQUASH are described, including some with multiple domain or multiple space group NCS.

[1] K.D. Cowtan & P. Main (1993) Acta Crystallogr. D49, 148-157.
[2] D.J. Schuller (1996) Acta Crystallogr. D. in press.