

02-Methods for Structure Determination and Analysis,
Computing and Graphics

We have assessed the relative information content of a number of bulk solvent models using cross-validation. The free R approach was generalized to study the quality of the fit for all reflections as opposed to a single test set. We compared the simple homogeneous solvent mask model (Wang, B.-C., *Methods Enzymol.* **115**,90-112, 1985), the multiple-shell model (Schoenborn, B.P., *J.Mol.Biol.* **201**,741-749, 1988; Cheng, X.D. and Schoenborn, B.P., *Acta Cryst.* **B46**,195-208, 1991), and the difference-map model (Badger, J. and Caspar, D.L.D., *Proc. Natl. Acad. Sci.*, 622-626, 1991). The relative merit of these models will be discussed.

PS-02.07.09 PHASE DETERMINATION OF MACROMOLECULAR CRYSTALS FROM MULTIPLE X-RAY DIFFRACTION USING A CONVENTIONAL LABORATORY SOURCE. By Mau-Tzai Huang, Chien-Mei Wang, and Shih-Lin Chang*, Department of Physics, National Tsing Hua University, Hsinchu, Taiwan

Coherent interaction among diffracted waves in x-ray multiple diffraction has been successfully utilized in determining phases of structure-factor multiplets for organic crystals. For macromolecular crystals, synchrotron radiation is generally believed to be an indispensable source for phasing the structure factors in multi-beam experiments, because the signal-to-noise ratio of the multiply diffracted intensities are usually very small. However, the limited synchrotron beam time and the fast deterioration of crystals under high photon flux are the disadvantages of using synchrotron radiation. To overcome this difficulty, we have used a rotating-anode x-ray generator together with a z-axis four-circle diffractometer to carry out multiple diffraction experiments. The z-axis is a vertical arm for the detector mounted perpendicular to the diffracting plane. Secondary reflections can therefore be easily detected. We have applied this geometry to observe the intensities of many 3-beam and 4-beam diffractions for lysosome crystals. The associated phases are correctly determined. The condition of observing the weak multi-beam intensities is derived and the difficulties encountered in the experiments are discussed.

PS-02.07.10

COMPARISON OF REAL-SPACE AND RECIPROCAL SPACE CRITERIA TO ASSESS THE ACCURACY OF MACROMOLECULAR CRYSTAL STRUCTURES. By J.-S. Jiang*, R.E. Hubbard and A.T. Brünger, Department of Molecular Biophysics and Biochemistry, Yale University, U.S.A.

A number of real-space and reciprocal space criteria to assess the quality of atomic models has been compared. Among the criteria are the free R value (Brünger, A.T., *Nature* **355**,472-474, 1992), the real space R value (Bränden, C.I. and Jones, T.A. *Nature* **343**,687-689, 1990), continuity of density maps (Engh, R.A. and Huber, R., *Acta Cryst.* **A47**,392-400, 1991) and satisfaction of geometric and stereochemical restraints. We have also generalized the real space R value to measure the agreement between atomic shapes of observed and computed density maps.

Two examples are presented: TAKA alpha-amylase (Swift, H., et al., *Acta Cryst.* **B47**,535-544, 1991) and the B72.3 Fab chimeric antibody fragment (Brady, R.L., et al., *J. Mol. Biol.* **227**,253-264, 1992). We compared partially incorrect models with the correct model. Results show that the various criteria are correlated to the mean phase error of the models.

PS-02.07.11 CONNECTIVITY AND THE PHASE PROBLEM IN MACROMOLECULAR CRYSTALLOGRAPHY.

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The crystallographic phase problem is indeterminate in the absence of additional chemical information. The commonly employed chemical constraints—positivity, atomicity, and a solvent boundary—leave the phase problem greatly underdetermined for Fourier data sets of moderate (2.5–3.0Å) resolution. A successful *ab initio* approach must make use of high resolution Fourier data and/or stronger chemical constraints. One such constraint is the connectivity of the macromolecule. We have developed a rapid algorithm for measuring the connectivity of a map which shows promise in reducing the multiplicity of solutions to the phase problem. We have also developed a refinement method (PRISM) which exploits the connectivity constraint to iteratively improve phases. An initial electron density map is generated with inaccurate phases derived from a partial structure or from isomorphous replacement. A linear connected skeleton is then constructed from the map using a modified version of Greer's algorithm and a new map is created from the skeleton. This "skeletonized" map is Fourier transformed to obtain new phases, which are combined with any starting phase information and the experimental structure factor amplitudes to produce a new map. The procedure is iterated until convergence is reached. The method has been applied to problems with starting phase information from either molecular replacement or isomorphous replacement and appears to be a significant improvement over solvent flattening in both cases.

PS-02.07.12 COLLAGEN FIBRIL STRUCTURE BY X-RAY SYNCHROTRON RADIATION STUDIES OF MULTIPLE ISOMORPHOUS DERIVATIVES

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Multiple isomorphous derivatives tested against the native X-ray diffraction pattern, were used to phase the (h, k, l) reflections and produce an electron density map of the collagen fibril. This allows conclusions to be drawn about the molecular packing in native fibrils and the molecular conformation of the telopeptides which contain the inter-molecular crosslinks.