

**DIRECT METHODS TECHNIQUES FOR SIR, MIR, SAD, MAD, SIRAS, MIRAS**

C. Giacovazzo<sup>1</sup> M. Ladisa<sup>1</sup> D. Siliqi<sup>1</sup>

<sup>1</sup>CNR-Institute of Crystallography, c/o Dipartimento Geomineralogico, Campus Universitario, Via Orabona 4, I-70125 Bari,

The method of the joint probability distribution function has been used to derive accurate phase estimates for proteins via: a) the method of the isomorphous derivatives (SIR, MIR); b) the anomalous dispersion techniques (SAD, MAD); c) the method of the isomorphous derivatives when anomalous dispersion effects are present (SIRAS, MIRAS). For SIR, MIR, SIRAS and MIRAS cases the program automatically provides phase values (and a structural model) starting from the diffraction data. In the SAD and MAD cases the program first locates the anomalous scatterers, automatically assigned structure factor phases and refines them, and lastly provides a structural model. Some experimental results will be described.

**Keywords: PROTEINS DIRECT METHODS ANOMALOUS DISPERSION**

**DIRECT PHASING IN MACROMOLECULAR CRYSTALLOGRAPHY BELOW ATOMIC RESOLUTION**

A. Urzhumtsev<sup>1</sup> N. Lunina<sup>2</sup> V.Y. Lunin<sup>1,2</sup>

<sup>1</sup>LCM3B, UMR 7036 CNRS, Universite H. Poincare, Nancy 1, Vandoevres-Nancy, France <sup>2</sup>IMPB, Russian Academy of Sciences, Pushchino, Moscow Region, Russia

Fast determination of the first crystallographic image from a single diffraction data set becomes very important with the development of the Structural Genomics projects. Such techniques would allow to get first structural ideas on the proteins under study without going to more expensive and not always possible MAD experiments to say nothing about the usual case of poorly diffracting crystals.

Our study of different criteria revealed that the search for the global minimum of some score function does not work for low resolution *ab initio* phasing in macromolecular crystallography. On contrary, a more advanced statistical approach is very efficient and allows us to solve this problem. The corresponding procedure consists in several steps: 1) generation of a random population of points (phase sets) in the search space and selection of those points which resulted in a reasonable value of the score function; 2) cluster analysis of the selected population in order to identify compact groups of the selected variants; 3) averaging variants inside every identified cluster.

One of most efficient selection criterion is based on the analysis of the connectivity of the maps calculated with generated phases and with the experimental structure factor magnitudes. Some latest results show that the image resolution at least of 4-5 Å can be reached starting from the low resolution end. Recently several practical applications to the crystals investigation for unknown structures including LDL complex confirmed the importance, robustness and power of such phasing.

**Keywords: LOW RESOLUTION, DIRECT PHASING, SECONDARY STRUCTURE**

**PROGRESS IN STRUCTURE DETERMINATION OF LARGER ORGANIC AND ORGANO-METALLIC COMPOUNDS FROM POWDER DIFFRACTION DATA**

R. Peschar<sup>1</sup> V. Brodski<sup>1</sup> E. Dova<sup>1</sup> R.A.J. Driessen<sup>1</sup> K. Goubitz<sup>1</sup> R.B. Helmholtz<sup>1</sup> A.J. Van Langevelde<sup>2</sup> M.M. Pop<sup>1</sup> H. Schenk<sup>1</sup>

<sup>1</sup>Lab for Crystallography (IMC), Universiteit van Amsterdam, Nieuwe Achtergracht 166, 1018 WV Amsterdam, The Netherlands <sup>2</sup>Crystallics BV, Zekeringstr. 29, 1014 BV Amsterdam, The Netherlands

Structure solution from powder diffraction data requires four principal steps to be carried out successfully: (i) Data collection, (ii) Indexing, (iii), Structure solution and (iv) Structure refinement. This contribution will focus in particular on steps (iii)-(iv).

In case of larger organic and organo-metallic compounds, direct space techniques are often preferable to single-crystal based techniques because of a lack of reliable single-crystal-like intensities and/or reliable phase relationships. Two direct space techniques will be discussed that have shown to be capable to deliver a suitable starting model for Rietveld refinement. The former is an optimized version of a grid-search technique [1], the latter [2] a Monte Carlo global optimization. On the basis of some recent practical cases [2-6], it will be discussed what conditions need to be fulfilled in either of the steps (ii)-(iv) to end up with a complete crystal structure model.

References:

1. Chernyshev, V.V. & Schenk, H. (1998) Z. Kristall. 213, 1-3.
2. Brodski, V., Peschar, R. and Schenk, H. (2002). In preparation.
3. Pop, M.M., Goubitz, K., Borodi, G., Bogdan, M., De Ridder, D.J.A., Peschar, R. and Schenk, H. (2002). Acta Cryst. B. In preparation
4. Helmholtz R.B, Peschar R. and Schenk H. (2002). Acta Cryst B58, 134-139.
5. Dova E., Stassen A.F., Driessen R.A.J., Sonneveld E., Goubitz K., Peschar R., Haasnoot J.G., Reedijk J. and Schenk H. (2001). Acta Cryst B57, 531-538.
6. Van Langevelde A., Peschar R. and Schenk H. (2001). Chem. Mater. 13, 1089-1094.

**Keywords: POWDER DIFFRACTION STRUCTURE DETERMINATION DIRECT SPACE**

**ELECTRON CRYSTALLOGRAPHY - STRUCTURE DETERMINATION WITH POOR-QUALITY DIFFRACTION DATA**  
T. E. Weirich

RWTH Aachen Gemeinschaftslabor fuer Elektronenmikroskopie Ahornstr. 55 Aachen D-52074 GERMANY

The invention of direct methods (DM) by Hauptman & Karle in the 50's of the past century has opened the window for routine structure determination of crystalline matter. Today DM computer programs solve several thousands inorganic and organic structures every year. Whilst the huge majority of crystal structures are solved from X-ray data, the number of structures determined per year using electron diffraction data is still insignificant small. However, electron diffraction structure analysis (EDSA) is often the only alternative if the material under investigation does not form large single crystals and it exists as one component in a polyphasic powder sample together with other unknowns. Despite all doubts that has been held against EDSA in the past (dynamical scattering!), recent research has shown that DM can yield reliable results even from standard electron diffraction data provided the structure in question is composed of elements of nearly equal scattering power and if the most significant parts of the unit-cell transform up to atomic resolution are preserved in the data (quasi-kinematical approach). The practical application of this approach is illustrated by the examples of the metal-rich compounds Ti<sub>9</sub>Se<sub>2</sub>, Ti<sub>2</sub>Se, Ti<sub>8</sub>Se<sub>3</sub>, Ti<sub>11</sub>Se<sub>4</sub> and Ti<sub>45</sub>Se<sub>16</sub> whose structures have been solved from 2D selected area electron diffraction data using DM. Finally the application of modern quantum-mechanical calculations for checking the correctness of the determined structures from electron diffraction are introduced on the examples of the two modifications of Ti<sub>3</sub>Se.

**Keywords: DIRECT METHODS ELECTRON DIFFRACTION STRUCTURE ANALYSIS ELECTRON CRYSTALLOGRAPHY**