LOCATING SMALL STRUCTURAL FRAGMENTS USING A VECTOR-SEARCH ROTATION FUNCTION

J. Borge C. Alvarez-Rua S. Garcia-Granda
Departamento de Quimica Fisica y Analitica. Facultad de Quimica. Universidad de Oviedo. C/ Julian Claveria, 8. 33006 Oviedo. SPAIN

Image Seeking Functions (ISFs) were originally designed to deconvolute Patterson maps automatically by making use of the following property: a Patterson map can be considered as a sum of images of the molecules in the crystal unit cell. These functions also appeared to perform well as rotation functions in molecular replacement, because of their ability to detect a vector set from the search model in the Patterson map of the target structure. The basis of these functions is that the Patterson synthesis is strictly the vector set of the electron density of the crystal. Actually, a Patterson map differs from being a set of discrete points, rather it is a continuously variable function, with multiple overlapping peaks. However, these maps tend to have a discrete behavior as the resolution of the data used for computing them increases. The performance of ISFs when used as rotation functions benefit from the availability of high-resolution data. Nowadays, it is almost routine - at least for small proteins - to obtain data up to atomic resolution in synchrotron sources. This has made possible a new application of a vector search rotation function program (OVIONE)(1): the determination of the correct orientation of molecular fragments representing only a small percentage of the total scattering matter in the unit cell (less than 10%). This allows the use of secondary structure motifs (like an ideal α-helix) as search models. Potential applications of this methodology are connected with the idea that there is a list of structural fragments from which all proteins can be assembled.

References

(1) Alvarez-Rua, C., Borge, J. & Garcia-Granda, S. (2000). J. Appl. Cryst. 33, 1436-1444.

Keywords: MOLECULAR REPLACEMENT, ROTATION FUNCTION, SMALL FRAGMENT SEARCHES

EXPANDING THE POWER OF SIR2001

M.C. Burla[1] B. Carrozzini[2] G.L. Cascarano[2] C. Giacovazzo[2,3] G. Polidori[1]
[1]Dipartimento di Scienze della Terra, Universita' di Perugia, P.za Universita', I - 06100 Perugia, Italy [2]Istituto di Cristallografia, CNR, c/0 Dipartimento Geomineralogico, Campus Universitario, I - 70125 Bari, Italy [3]Dipartimento Geomineralogico, Campus Universitario, I - 70125 Bari, Italy

Direct Methods are able (at times) to drive random sets of phases to the correct ones, provided the resolution of the diffraction data is not worse than 1.2 Å. The density of the favorable trials is quite small, and decreases with the structural complexity, therefore making the *ab-initio* procedure a potentially very time consuming technique. In case of failure, the structural information is often hidden in electron density distribution, which roughly corresponds to a translated model. A new procedure, named RELAX, has been implemented in SIR2001 in order to overcome such a problem. Real space techniques are used to translate the model in the correct position. This procedure is able to increase the solution density of SIR2001 at least by a factor of 2-3.

Keywords: PROBABILITY THEORY DIRECT METHODS PROTEINS

DIRECT-METHODS IMPROVED MAD PHASING

H. F. Fan Y. X. Gu B. D. Sha F. Jiang
Institute of Physics, Chinese Academy of Sciences #8 Southern 3rd St. Zhong Guan Cun P.O. Box 603 BEIJING 100080 CHINA

New phasing procedure DMAD, which combines direct methods (D) and multi-wavelength anomalous diffraction (MAD), has been proposed and tested. Encouraging results were obtained. The main points are as follows. (i) Conventional MAD phasing is first performed and, only the MAD phases with a figure of merit greater than a certain limit, say 0.99, are accepted as the input to the following step. (ii) The MAD data are divided into n-sets (n equals the number of wavelengths used) of SAD (Single wavelength Anomalous Diffraction) data, each set of which is treated by direct methods separately to break the phase ambiguity with starting phases from step (i). (iii) Direct-method phases of different sets of SAD data are combined to give a unique set of phases. (iv) Resultant phases from step (iii) are further combined with that of step (i) to give the final set of phases. Extensive test calculations have been made with the experimental four-wavelength MAD data from a known protein, the yeast Hsp40 protein Sis1 (residues 171-352). It turned out that, even a 2-wavelength DMAD phasing could lead to evidently better results than that from a 4-wavelength conventional MAD phasing.

Keywords: **DIRECT-METHODS MAD PHASING**

ON INTEGRATING THE TECHNIQUES OF DIRECT METHODS AND SIRAS. I. THE THEORETICAL BASIS

H. Hauptman[1, 2] H. Xu[1, 2]
[1]Hauptman-woodward Medical Research Institute, 73 High Street, Buffalo, NY 14203-1196, USA [2]Department of Structural Biology, SUNY at Buffalo, USA

Let S and T be a pair of isomorphous structures. In the SIRAS case, normal diffraction data are available for S and single wavelength anomalous diffraction data are available for T. One example of the SIRAS case is that S is a sulfur containing native protein and T is obtained from S by replacing some (or all) of the sulfur atoms in S by selenium atoms. Another example is the case that S is a known heavy-atom substructure of T in which case our theory would lead to a method for going from a known substructure (S) of T to the whole structure T when anomalous data are available only for T. The realization of this goal is particularly important since a method for determining the heavy atom substructure of a macromolecule by combining Shake-and-Bake phasing [1] with single wavelength anomalous diffraction data, even at a resolution of 3-4 Å, has recently been elucidated [2].

In the SIRAS case there are three normalized structure factors associated with each reciprocal lattice vector and three related two-phase structure invariants (doublets). The joint probability distribution of the three structure factors leads directly to the major results of this paper: 1. the conditional probability distributions of the doublets, given selected magnitudes and 2. the conditional probability distribution of a single phase, given selected magnitudes, when a heavy-atom substructure is known. The accompanying paper [3] describes the first applications.

This Research was supported by grants GM-46733 (NIH) and ACI-9721373 (NSF).

References

1. Weeks, C.M. & Miller, R. (1999). J. Appl. Cryst. 32, 120-124.
2. Deacon, A.M. et al. (2000). Structure 8, 453-462.
3. Xu, H & Hauptman, H.A. 19th Congress and General Assembly, August 2002, Geneva, Switzerland.

Keywords: **DIRECT METHODS PROBABILITY DISTRIBUTIONS ISOMORPHOUS REPLACEMENT**