17.1-2   ROTSEARCH-A PATTERSON SEARCH PROGRAM FOR POSITIONING RANDOMLY ORIENTED MOLECULAR FRAGMENTS.

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ROTSEARCH is an automated Patterson Search program developed to orient and position molecular fragments with rigid geometry in the unit cell. It allows one to use the available molecular skeleton geometries e.g. from crystal structure databases, to solve undetermined crystal structures containing similar skeletons. Once the fragment is positioned, it can be used as a phasing model for the subsequent structural expansion via Fo-syntheses (large fragments) or via phases refinement (small fragments) in any of the already existing programs for crystal structure determination. In concrete, ROTSEARCH has been designed to work in connection with MULTAN-84 (Main, Germain and Woolfson). The compatibility is achieved by using the same file MULTAN. RFL and by generating the file ROTS.PKS containing the atomic coordinates of the positioned model in the same format as in SEARCH.PKS.
ROTSEARCH performs the coarse rotation search in vector space and the refinement of the fragment orientation in reciprocal space using the σ-function (Tollin, Cryst. Comp., 1976, 212-221), as described in (Rius & Miravitlles, J. Appl. Cryst., 1987, in press). The fragment positioning is accomplished using the τo- or τ- functions (Rius & Miravitlles, Acta Cryst., 1986, A42, 402-404). The combined figure of merit (CFOM) used in ROTSEARCH is a linear combination of the conventional R-index and the usual CFOM employed in direct methods calculated after a phase refinement. As the fragment size decreases, increasing weight to the direct methods CFOM is given i.e. ABS FOM, PSI ZERO and RESIDUAL.
This CFOM is computed for all the higher-ranked Patterson Search solutions and the atomic coordinates derived from the best one are stored in file ROTS.PKS. The program needs the usual crystal data, the observed structure factors and the fragment coordinates either cartesian or crystallographic (up to 100 atoms).
ROTSEARCH is written in FORTRAN/77 and should run, with a minimum of modifications, on any computer with 500 Kbytes memory and with word length of 32 bits. Its application to several representative test examples will be shown.

17.2-1
ON COMBINING PROBABILISTIC TWO-PHASE STRUCTURE INVARIANTS WITH HARKER CONSTRUCTION.

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Harker gave an elegant geometrical solution to determine protein phase angle (Harker, D. (1956) Acta Cryst. 9,1). As everyone knows, it may lead to a unique phase solution by combination of isomorphous replacement and anomalous scattering information using a single derivative (SIRAS), and to a twofold ambiguity if one wavelength anomalous scattering data of one crystal alone are used (SAS). Several SAS methods have been developed for seeking the solution of the ambiguity by some information contained in Bijvoet pairs, such as the theoretical and experimental contribution of J. Karle, H.F. Fan, M.M. Teeter, C. Giacovazzo, B.C. Wang and so on.

This presentation will focus on directly combining neighborhood theory of two-phase structure invariants (TPSI) (Hauptman, H. (1982) Acta Cryst. A38, 632 and Guo Dongyao and Hauptman, H. (1986) ACA Annual Meeting, 14, 14, 46) with Harker construction. Emphasis will be placed on geometrical relationship between TPSI and Harker construction. When the heavy-atom structure is known, the results are:

1. According to the geometrical analysis of TPSI in SIRAS case (Guo Dongyao and Hauptman, H. Mol. Struc. Inter. Sym. Beijing, Sept. (1986) 197), each value of the six TPSI is available to determine the unique phase by Harker construction provided that the accuracy of TPSI from estimates of the first neighborhood theory is at least not too bad to give the correct sign of the TPSI. It is worthy to emphasize that neighborhood theory may provide six TPSI, three are independent. In principle, the unique solution of Harker construction can be given by each of the six TPSI, therefore three unique and independent solutions may be provided for the same ambiguity. Of course, it will give a better judgement of the ambiguity.

2. In SAS case, the geometrical analysis of TPSI is much simpler than in the case of SIRAS. The simple and very important result of TPSI is useful (Hauptman, H. (1982)), as S. Fortier discussed, if the probabilistic estimate of TPSI can provide the information on its sign (Acta Cryst. (1986) A42, 149).

The computational results show that the methods described in 1 and 2 are available for solving Harker ambiguities in both SIRAS and SAS cases. The calculations were done using error-free data for $PtCl_4$ derivative of cytochrome c_{550} (Timkovich, R. and Dickerson, R.E. (1976) J. Biol. Chem. 251, 4033) in SAS case and the native in SIRAS case. It is interesting that there are 964 correct signs provided by the simple formula of TPSI (Hauptman, H. (1982) in the first 1,000 reflections, 36 wrong signs only, in SAS case.