17.2-17 ,SOLUTION OF THE PHASE PROBLEM FOR NON-CENTROSYMMETRIC CASES IN TWO STAGES. By Fan Hai-fu, Gu Yuan-xin, Xu Zhang-bao, Qian Jin-zi and Zheng Chao-de, Institute of Physics, Academia Sinica, Beijin, China.

The phase problem in noncentrosymmetric cases may be solved in such a way that the real and imaginary parts of the structure factors are treated separately and successively. The procedure includes two steps:

1. The structure is first solved on the basis of a pseudo symmetry which is higher than that of the actual one by an additional inversion centre. Signs instead of phases are then obtained for the structure factors. These signs would in fact consist of those of the real parts of the structure factors. Consequently an E-map containing both enantiomorphs can be obtained.

2. From the E-map so obtained, the real parts and the absolute values of the imaginary parts of the structure factors can be calculated approximately. Finally the signs of the imaginary parts can easily be determined and hence the phase problem can be solved with the aid of the component relation

$$B_H = (f/V) \sum_{H'} B_{H'} A_{H-H'}$$

where A denotes the real part and B the imaginary part of the structure factor; f is a function of the atomic form factor and V is the volume of the unit cell (Fan Hai-fu, Acta Physica Sinica, 21 (1965) 1114; see also J. Karle, Acta Cryst., 21 (1966) 273).

In comparison with the other methods, the procedure described above has the following advantages:

1. By executing the first step, the amount of calculation needed for permuting the phases in the starting reflection set can be reduced by a factor of about 4. Alternatively the number of reflections in the starting set can be doubled while the amount of calculation remains about the same as in the usual permutation procedure. This is valuable in the determination of complex structures.

2. The second step can strongly restrict the tendency for the whole set of phases to reduce to a centrosymmetric one. Hence the procedure has the effect of stabilizing the specified enantiomorph. This is important in the determination of structures with polar space groups like $P2_1$.

Crystal structures in space groups $P2_1$ and $P2_12_12_1$ with and without heavy atoms have been used as examples to prove the efficiency of the procedure.

17.2-18 THE PROBLEM OF MULTIPLE SOLUTIONS IN STRUCTURE DETERMINATION AND THE APPLICATIONS OF MODIFIED SAYRE'S EQUATIONS.

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Three types of crystals often lead to multiple solutions in the determination of their structures:
1. Structures composed of light atoms with polar space groups such as $P2_1$, $Pna2_1$, $P4_1$, etc.— Phase determination by direct methods in this type of structures often results in one set of centrosymmetric phases leading to an E-map containing both enantiomorphs.
2. Structures with pseudo-symmetry higher than the actual symmetry by an additional inverse centre and/or sub-periodicity of translation — Two or more structure images related by the additional symmetry would appear simultaneously in the resulting E-map or Fourier map.
3. Structures containing heavy atoms with higher symmetry than that of the whole structure by an additional inverse centre and/or sub-periodicity of translation—Two or more structure images of the light atom portion related by the additional symmetry would appear simultaneously in the resulting E-map or Fourier map.

Multiple solutions can be divided into two categories:
1. The translational multiple solutions— This leads to a systematic undetermination of certain(but not all)types of phases of the structure factors. The problem can be solved with the aid of the modified Sayre's equations (Fan Hai-fu, Acta Physica Sinica, 21(1965)1105; Fan Hai-fu, Acta Physica Sinica, 24(1975)57; Fan Hai-fu et al., Acta Physica Sinica, 27(1978)554), which have the common form of

$$F_H^o = (f/V) \sum_{H'} F_{H'}^o F_{H-H'}$$

where F^o's denote structure factors with phases systematically undetermined, F's denote structure factors with phases derivable from a pseudo structure model containing simultaneously all possible solutions, f is a function of atomic form factor and V is the volume of the unit cell.
2. The enantiomorphic double solutions— This leads to the ambiguity on signs of the imaginary components of all the structure factors (notice that the origin is fixed at the pseudo inverse centre for the reason of simplicity). This problem can be solved by making use of another type of modified Sayre's equation — component relation(Fan Hai-fu, Acta Physica Sinica, 21(1965)1114; Fan Hai-fu & Zheng Qi-tai, Acta Physica Sinica, 27(1978)169; see also J. Karle, Acta Cryst., 21(1966)273.),

$$B_H = (f/V) \sum_{H'} B_{H'} A_{H-H'}$$

where A's denote the real components of the structure factors, which can be derived from a pseudo structure model containing both enantiomorphs, while B's denote the imaginary components, of which the absolute values can be obtained as

$$|B_H| = (|F_H|^2 - A_H^2)^{1/2}$$

where $|F_H|$'s are the observed structure amplitudes.
A number of examples are given to elucidate the efficiency of the procedures in solving structures which had been difficult to solve by ordinary methods.

17.2-19 FALSE MOLECULAR IMAGES IN DIRECT AND HEAVY ATOM PHASE DETERMINATIONS. By W. Wong-Ng and S. C. Nyburg, Department of Chemistry, University of Toronto, Toronto, Ontario, Canada M5S 1A1.

We have found, in several instances, that direct methods or heavy atom methods can lead to false solutions in which two images of the true molecules overlap. In all cases some of the atoms of the two images were superimposed. Methods of unravelling the true structure will be illustrated with examples.

17.2-20 A REAL APPROACH TO DETERMINATION OF PHASES, By D.F.Grant and R.C.G.Killean, Physics Department, University of St.Andrews, North Haugh, St.Andrews, Fife KY16 9SS, Scotland.

It is well known that trivial solutions to phase determination in the centrosymmetric case yield a maximimum value for $\int \rho^3 dv$ for x-ray data. A procedure has been devised for obtaining non-trivial solutions which gives maximum values of this integral for certain restricted sets of structure factors. The contribution of each structure factor to the integral is evaluated in turn and then the structure factors are arranged in order of importance. This order is used to build up sets of phases giving the maximum value of the integral. Procedures have been evolved for handling the different parity groups and for terminating the process with a limited number of sets of phases. The technique operates in real rather than reciprocal space, uses the observed structure factors, and involves no statistical arguments. The method will be illustrated by reference to a number of three-dimensional data sets in the space group $P\bar{1}$.

17.4-01 RESTRAIN: THE PRACTICAL APPLICATION OF A RESTRAINED LEAST SQUARES REFINEMENT PROGRAM IN PROTEIN CRYSTALLOGRAPHY. By D. S. Moss, Laboratory of Molecular Biology, Birkbeck College, London, U.K. and A.J. Morffew, IBM United Kingdom Ltd., Scientific Centre, Winchester, Hampshire, UK

A restrained least-squares procedure is described that has been designed for refining protein structures in conjunction with an interactive computer graphics facility. By allowing the assignment of relative weights to individual atoms in the graphics database, the user can interact with the refinement program.

The sum of residuals minimised in RESTRAIN is a function of structure amplitudes, phases and target geometry. The normal equations are solved by the Gauss-Seidel method with Δ^2 acceleration and the under-determined case is solved by the Levenberg-Marquardt method. It is the 'Marquardt factor' that has been adapted to apply the individual relative weights to the atoms.

The methods, strategy and some results of this program are described.

17.4-02 A ROBUST/RESISTANT TECHNIQUE FOR CRYSTAL STRUCTURE REFINEMENT. W. L. Nicholson, Battelle Pacific Northwest Laboratories, Richland, WA 99352, U. S. A., E. Prince, National Measurement Laboratory, National Bureau of Standards, Washington, DC 20234, U. S. A., J. Buchanan and P. Tucker, Battelle Pacific Northwest Laboratories, Richland, WA 99352, U. S. A.

A refinement technique is "robust" if it works well over a broad class of error distributions in the data, and "resistant" if it is not strongly influenced by any small subset of the data. Least squares possesses neither property. A more robust/resistant procedure is to minimize, instead of a simple sum of squared differences, a sum of terms of the form $\rho(x) = (x^2/2)[1 - (x/a)^2 + (1/3)(x/a)^4]$ for $|x| \leq a$, $\rho(x) = a^2/6$ for $|x| > a$. Here $x = r_i(\theta)/s$, where $r_i(\theta) = w_i^{1/2}[|F_{oi}| - m_i(\theta)]$, $m_i(\theta) = |F_{ci}(\theta)|$, and s is a measure of the width of the error distribution based on the results of the previous cycle. a is a constant chosen so that extreme data do not influence the solution. The function $\rho(x)$ behaves like the sum of squares for small x, but is constant for large x, so that the effect of large differences is deemphasized. Most least-squares refinement programs can easily be modified to be more robust/resistant. Both weighted least squares and the modification are examples of a class of estimation methods which, for crystal structure refinement, take the form, minimize the loss function, $f(\theta) = \Sigma\rho[r_i(\theta)/s]$ by selecting θ so the normal equations $\nabla f = 0$ are satisfied. Let $\phi(x) = (1/x)\rho'(x)$ and $\omega(x) = \rho''(x)$. Linearization of the normal equations gives the iteration formula

$$\Delta\theta_j^{q+1} = \sum_{k=1}^{p} C^{jk} \sum_{i=1}^{N} \phi[r_i(\theta^q)/s^q] w_i^{1/2} r_i(\theta^q) \frac{\partial m_i(\theta^q)}{\partial \theta_k}$$

for updating parameter estimates. Here C^{jk} is an element of the inverse to the linearized Hessian matrix, whose typical element has the form