dimensional extinction conditions outside the layer-group restrictions have not been included at this stage although extensive results along these lines have been produced by Tanaka, Sekii & Nagaswa (1983). Instead, we note that these extended conditions can be found from three-dimensional lattice groups formed from the same restricted set of point groups (Goodman, 1984*b*).

V. Preliminary requirements for application

The central plane approximation

Abstractly the transformation from $R^{2,2}$ to $R^{2,1}$, to the crystal-space coordinates of the layer groups, applies. We now examine the main assumption needed in order to apply this to real crystals. In the central plane approximation (CPA) it is assumed that all horizontal symmetry elements of the space group lie on the central horizontal plane of the crystal. For single symmetry elements this is an approximation which becomes exact periodically with crystal thickness, with the periodicity of the c spacing, and must always be a close approximation for crystals having many repeat distances in the z direction. This approximation is implied in all applications of space-group-determined matrices to pattern intensities. It has also been assumed in other group treatments of CBED symmetries (Tanaka, Sekii & Nagasaw, 1983; Buxton, Eades, Steeds & Rackham, 1976). Its validity was first tested specifically during the study of β-GaS belonging to the space group $P6_3/mmc$, in which horizontal diads occur at intervals of 30° around the [001] axis, separated vertically by $c/4$. In this case all horizontal symmetries were found to be active, as if they belonged to the central plane (Goodman & Whitfield, 1980).

Diffraction symmetries at a zone are higher than would otherwise be expected, owing to the increased possibilities for symmetry interaction under CPA conditions. As a result single symmetry elements can only be examined in isolation at settings sufficiently far from a zone, as illustrated in the above study in the tests for a center of symmetry.

Symmetry-group treatment overcomes the problem of such detailed analysis. Identification of a few pattern characteristics at chosen orientations, particularly if they include dynamic extinctions, has been shown to lead to unequivocal identification of space group (Tanaka, Sekii & Nagasawa, 1983; Goodman, 1984*a*).

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Triplet Phase Invariants from an Exact Algebraic Analysis of Anomalous Dispersion

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(*Received* 11 *January* 1984; *accepted* 11 *April* 1984)

Abstract

In a previous investigation, a system of exact algebraic equations was derived for any number and type of anomalous scatterers. Solution of the equations provides information concerning intensities of scattering and certain phase differences. In this paper, it is shown that when appropriate combinations of the phase differences and their values are made, the result is the evaluation of the differences of pairs of triplet phase invariants, one associated with the macromolecular structure and the second associated with the structure of the anomalous scatterers. It is usually easy to satisfy the condition that the values of triplet phase invariants associated with the structures of the anomalous scatterers be close to zero.

0108-7673/84/050526-06$01.50

This permits the evaluation of triplet phase invariants associated with the macromolecular structure. Since the structures of the anomalous scatterers are quite simple in many of the substances of interest, a theoretical and experimental study of the distribution of values for triplet phase invariants associated with simple structures has been carried out. This has provided a quantitative insight into the distribution of values of the cosines of triplet phase invariants for such structures. It has also identified useful functions, based on knowledge of the values of normalized structure factor magnitudes, that permit a reliable prediction of those triplet phase invariants that have values close to zero. In the mathematical sense, the evaluation of the triplet phase invariants for a macromolecular structure, solely from the intensity data, is exact, except for the deviation of the triplet phase invariants for the structure of the anomalous scatterers from zero. No structural information concerning the anomalous scatterers is required. In practice, of course, experimental error will affect the accuracy of the information derived from the algebraic equations. The possibility of overdeterminacy in the equations should be beneficial in reducing the effect of experimental error.

Introduction

In a previous investigation, an algebraic analysis of multiple-wavelength anomalous dispersion data resulted in a set of simultaneous equations without approximation (Karle, 1980*a*). The unknown quantities in the equations are quantities that represent nonanomalous scattering and hence are independent of wavelength. This is effected by separating the contribution of the real and imaginary parts of the atomic scattering factors from that of the normal atomic scattering factors in the defining equations for the structure factors. The resulting simultaneous equations contain the quantities representing the effects of anomalous dispersion as separate factors modifying the wavelength-independent unknown quantities. Evaluation of the factors arising from anomalous dispersion is easily obtained from the tabulated values for the real and imaginary corrections to the normal atomic scattering factors.

The simultaneous equations have several favorable characteristics. With appropriate definitions for the unknown quantities, the equations are linear in the variables. The unknown quantities are comprised in part of the intensities of scattering for each of the individual types of atoms present. Their values correspond to individual structures in which each type of atom would be present in isolation from the others. Additional unknown quantities are phase differences arising from the scattering from the different types of atoms. The equations retain their favorable characteristics and exactness no matter how many types of anomalous scatterers are present.

A feature of the simultaneous equations that makes them potentially valuable is the existence of the individual intensities of scattering for the various types of atoms as unknown quantities to be evaluated by use of the equations. Once the intensities are known for the anomalous scatterers from solving the simultaneous equations, it is possible to solve for the structure of the anomalous scatterers. If this structure is too complicated to be amenable to an analysis by means of a Patterson function, it is still possible to undertake a determination of the structure by direct methods. Once the structure of just one type of the anomalous scatterers is known, the information provided by the simultaneous equations permits the solution of the entire structure.

This may well be the optimal strategy for using the simultaneous equations. However, it is also possible to use the simultaneous equations to obtain evaluations of triplet phase invariants in the absence of information concerning the structure of the anomalous scatterers. It is the purpose of this paper to show how these evaluations may be obtained. In addition, it will also be seen how information from isomorphous replacement may be introduced into the simultaneous equations.

The accuracy of the evaluations of the triplet phase invariants for a substructure consisting of nonanomalously scattering atoms, for example, depends upon how closely the values of appropriate triplet phase invariants for a substructure composed of anomalously scattering atoms approximate to zero. For the simple structures that often apply to the anomalously scattering atoms, the approximation to zero is generally easily achieved. In order to obtain a more quantitative insight into this matter, some test calculations were carried out concerning the distribution of values of the cosines of triplet phase invariants for simple structures and comparisons were made with results from theoretical formulas modified to facilitate the prediction of these distributions.

Theory

A simple result from the algebraic analysis (Karle, 1980*a*) that illustrates the characteristics of the simultaneous equations described above will now be presented. It concerns a structure which is composed of atoms that scatter normally and one type of atom that scatters anomalously. A representative equation is

$$\begin{aligned}|F_{\lambda\mathbf{h}}|^2 = |F^n_{1,\mathbf{h}}|^2 &+ \{1 + (f^a_{\lambda 2,\mathbf{h}}/f^n_{2,\mathbf{h}}) \\ &\times [(f^a_{\lambda 2,\mathbf{h}}/f^n_{2,\mathbf{h}}) + 2\cos\delta_{\lambda 2,\mathbf{h}}]\}|F^n_{2,\mathbf{h}}|^2 \\ &+ 2[1 + (f^a_{\lambda 2,\mathbf{h}}/f^n_{2,\mathbf{h}})\cos\delta_{\lambda 2,\mathbf{h}}] \\ &\times |F^n_{1,\mathbf{h}}||F^n_{2,\mathbf{h}}|\cos(\varphi^n_{1,\mathbf{h}} - \varphi^n_{2,\mathbf{h}}) \\ &+ 2(f^a_{\lambda 2,\mathbf{h}}/f^n_{2,\mathbf{h}})\sin\delta_{\lambda 2,\mathbf{h}}|F^n_{1,\mathbf{h}}| \\ &\times |F^n_{2,\mathbf{h}}|\sin(\varphi^n_{1,\mathbf{h}} - \varphi^n_{2,\mathbf{h}}), \end{aligned} \tag{1}$$

where $|F_{\lambda\mathbf{h}}|^2$ is the measured magnitude squared of the structure factor at wavelength λ, $|F^n_{1,\mathbf{h}}|^2$ is the magnitude squared of the structure factor for the nonanomalously scattering atoms and $|F^n_{2,\mathbf{h}}|^2$ is the magnitude squared of the structure factor for the anomalously scattering atoms, but scattering as if they were doing so normally. The measured $|F_{\lambda\mathbf{h}}|^2$ are corrected for vibrational effects and the latter are also absent from $|F^n_{1,\mathbf{h}}|^2$ and $|F^n_{2,\mathbf{h}}|^2$. The quantities $f^a_{\lambda j,\mathbf{h}}$ and $\delta_{\lambda j,\mathbf{h}}$ are defined for a particular λ,

$$f^a_{\lambda j,\mathbf{h}} = [(f'_{\lambda j,\mathbf{h}})^2 + (f''_{\lambda j,\mathbf{h}})^2]^{1/2} \tag{2}$$

and

$$\delta_{\lambda j,\mathbf{h}} = \tan^{-1}(f''_{\lambda j,\mathbf{h}}/f'_{\lambda j,\mathbf{h}}). \tag{3}$$

f' and f'' are the real and imaginary corrections, respectively, to the normal atomic scattering factor, f^n. They represent the effects of anomalous dispersion and are tabulated in *International Tables for X-ray Crystallography* (Cromer, 1974). The total atomic scattering factor is then

$$f = f^n + f' + if''. \tag{4}$$

The phase angle $\varphi^n_{1,\mathbf{h}}$ is the angle associated with the structure factor contributed by the nonanomalously scattering atoms and $\varphi^n_{2,\mathbf{h}}$ is the angle associated with the structure factor contributed by the anomalously scattering atoms, but scattering as if they were doing so normally. The subscript 1 refers to the nonanomalously scattering atoms and the subscript 2 to the anomalously scattering ones.

Closely related equations can be formed from (1) by performing anomalous dispersion experiments at various wavelengths and noting that an equation for $\mathbf{h}$ is different from that for $-\mathbf{h}$. The equations are linear if the unknown quantities are chosen to be $|F^n_{1,\mathbf{h}}|^2$, $|F^n_{2,\mathbf{h}}|^2$, $|F^n_{1,\mathbf{h}}||F^n_{2,\mathbf{h}}|\cos(\varphi^n_{1,\mathbf{h}} - \varphi^n_{2,\mathbf{h}})$ and $|F^n_{1,\mathbf{h}}||F^n_{2,\mathbf{h}}|\sin(\varphi^n_{1,\mathbf{h}} - \varphi^n_{2,\mathbf{h}})$. Having more than the algebraic minimum of equations would permit the use of least-squares methods to help compensate for experimental error. It is also possible to take advantage of the relation $\sin^2\varphi + \cos^2\varphi = 1$ and the nonnegativity of the magnitudes of the structure factors. If the anomalous scattering arises predominantly from the isomorphous addition of a heavy atom to the native structure, then measurement of the diffraction intensities for the native structure gives values for the $|F^n_{1,\mathbf{h}}|^2$, thereby reducing the number of unknowns in the simultaneous equations. In this way, information from isomorphous replacement may be combined with that from anomalous dispersion in the equations.

An evaluation of the unknown quantities in (1) gives values for the angle differences, $\varphi^n_{1,\mathbf{h}} - \varphi^n_{2,\mathbf{h}}$, and for the intensities that would be obtained for the structure of the nonanomalously scattering atoms, $|F^n_{1,\mathbf{h}}|^2$, and for the structure of the anomalously scattering atoms scattering normally, $|F^n_{2,\mathbf{h}}|^2$. Information concerning the $|F^n_{2,\mathbf{h}}|^2$ could be used to solve for the structure of the anomalously scattering atoms. With knowledge of this structure, values for the $\varphi^n_{2,\mathbf{h}}$ could be computed readily, thus leading to an evaluation of the remaining unknown quantities, the $\varphi^n_{1,\mathbf{h}}$. With this information, the computation of the structure of the nonanomalously scattering atoms is readily performed.

It is possible to generalize the result given in (1) to any number of types of atoms, all treated as anomalous scatterers (Karle, 1980*a*). If there are q types of atoms, the general result is

$$\begin{aligned}
|F_{\lambda\mathbf{h}}|^2 = {} & \sum_{i=1}^{q} |F^n_{i,\mathbf{h}}|^2 + 2\sum_{i<j}^{q} |F^n_{i,\mathbf{h}}||F^n_{j,\mathbf{h}}| \cos(\varphi^n_{i,\mathbf{h}} - \varphi^n_{j,\mathbf{h}}) \\
& + \sum_{i=1}^{q} (f^a_{\lambda i,\mathbf{h}}/f^n_{i,\mathbf{h}})^2 |F^n_{i,\mathbf{h}}|^2 \\
& + 2\sum_{i<j}^{q} (f^a_{\lambda i,\mathbf{h}}/f^n_{i,\mathbf{h}})(f^a_{\lambda j,\mathbf{h}}/f^n_{j,\mathbf{h}})|F^n_{i,\mathbf{h}}||F^n_{j,\mathbf{h}}| \\
& \times \cos(\varphi^n_{i,\mathbf{h}} - \varphi^n_{j,\mathbf{h}} + \delta_{\lambda i,\mathbf{h}} - \delta_{\lambda j,\mathbf{h}}) \\
& + 2\sum_{i=1}^{q} (f^a_{\lambda i,\mathbf{h}}/f^n_{i,\mathbf{h}})|F^n_{i,\mathbf{h}}|^2 \cos \delta_{\lambda i,\mathbf{h}} \\
& + 2\sum_{i<j}^{q} |F^n_{i,\mathbf{h}}||F^n_{j,\mathbf{h}}|[(f^a_{\lambda i,\mathbf{h}}/f^n_{i,\mathbf{h}}) \\
& \times \cos(\varphi^n_{j,\mathbf{h}} - \varphi^n_{i,\mathbf{h}} - \delta_{\lambda i,\mathbf{h}}) \\
& + (f^a_{\lambda j,\mathbf{h}}/f^n_{j,\mathbf{h}}) \cos(\varphi^n_{i,\mathbf{h}} - \varphi^n_{j,\mathbf{h}} - \delta_{\lambda j,\mathbf{h}})].
\end{aligned} \tag{5}$$

The equations represented by (5) retain the features noted for the simple case represented by (1). They are exact and, if the unknown quantities are chosen in a fashion similar to the four described for (1), the equations are linear in the unknowns. Study of (5) shows that, after evaluation of the unknown quantities, the determination of only one of the substructures corresponding to one type of anomalous scatterer by use of the appropriate $|F^n_{i,\mathbf{h}}|$ would permit the evaluation of all the phases required for the determination of all the remaining substructures.

This may well be the procedure of choice in the future. There is, however, an alternative to solving for some substructure since it is possible to obtain evaluations of triplet phase invariants by means of the algebraic equations and a simple probabilistic argument without any need to determine a substructure. This matter will now be discussed.

Triplet phase invariants

The derivation of triplet phase invariants may be illustrated by considering the case of a structure composed of essentially nonanomalous scatterers and one type of anomalous scatterer represented by (1). It is apparent that solution of the equations to evaluate the unknown quantities would give values for the

phase differences, $\varphi^n_{1,\mathbf{h}} - \varphi^n_{2,\mathbf{h}}$. From the values of many of the phase differences, it is possible to form the sums of suitably chosen ones,

$$\varphi^n_{1,\mathbf{h}} + \varphi^n_{1,\mathbf{k}} + \varphi^n_{1,(\bar{\mathbf{h}}+\bar{\mathbf{k}})} - \varphi^n_{2,\mathbf{h}} - \varphi^n_{2,\mathbf{k}} - \varphi^n_{2,(\bar{\mathbf{h}}+\bar{\mathbf{k}})} = A_{\mathbf{hk}}, \quad (6)$$

where $A_{\mathbf{hk}}$ is known from the values of the three individual phase differences comprising (6). It is seen that (6) consists of the difference of two triplet phase invariants, one for the structure consisting of non-anomalously scattering atoms, and the second for the anomalously scattering atoms (heavy-atom structure). Values for the $|F^n_{2,\mathbf{h}}|$ indicate which of the triplet phase invariants for the heavy-atom structure are associated with large products, $|F^n_{2,\mathbf{h}} F^n_{2,\mathbf{k}} F^n_{2,(\bar{\mathbf{h}}+\bar{\mathbf{k}})}|$. Such structures are usually rather simple, so that when the products of the magnitudes of the structure factors are large the triplet phase invariants for the heavy-atom structure can quite reliably be set equal to zero. This gives, under the conditions of large products of structure factor magnitudes for the heavy-atom structure,

$$\varphi^n_{1,\mathbf{h}} + \varphi^n_{1,\mathbf{k}} + \varphi^n_{1,(\bar{\mathbf{h}}+\bar{\mathbf{k}})} \simeq A_{\mathbf{hk}}, \quad (7)$$

an evaluation of triplet phase invariants for the unsubstituted structure.

The evaluation of a sufficient number of triplet phase invariants by use of (7) could obviate the necessity for determining the heavy-atom structure, since phase determination could, in principle, proceed from knowledge of the values of the triplet phase invariants.

Triplet phase invariant distributions

Calculations were made of the distributions of triplet phase invariants in simple equal-atom structures, three- and nine-atom structures in space group $P1$ and three- and nine-atom structures in the asymmetric unit of space group $P2_12_12_1$. The atoms were distributed at random with suitable separations between them. This is appropriate for the heavy-atom substructures that occur, for example, in heavy-atom substitution structures.

For the various structures, thousands of cosines of triplet phase invariants, $\cos(\varphi_{\mathbf{h}} + \varphi_{\mathbf{k}} + \varphi_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}) \equiv \cos \Phi_{\mathbf{hk}}$, were computed and their values were ordered according to the values of the products of associated normalized structure factors, $2N^{-1/2}|E_{\mathbf{h}}E_{\mathbf{k}}E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}|$, where N is the number of atoms in the unit cell. Groups of five thousand cosine invariants in the ordered sequence were averaged to give $\langle \cos \Phi_{\mathbf{hk}} \rangle$ and plotted against the average value of the corresponding $2N^{-1/2}|E_{\mathbf{h}}E_{\mathbf{k}}E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}|$. Plots of the results for two of the structures are shown in Figs. 1 and 2.

Values for $\langle \cos \Phi_{\mathbf{hk}} \rangle$ were also computed from four different theoretical formulas with the objective of determining which of the formulas can best represent the observed distributions. A general formula for the expected value of a cosine invariant is

$$\langle \cos \Phi_{\mathbf{hk}} \rangle = I_1(t|E_{\mathbf{h}}E_{\mathbf{k}}E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}|)/I_0(t|E_{\mathbf{h}}E_{\mathbf{k}}E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}|). \quad (8)$$

The four different theoretical formulas are represented in (8) by different definitions for the quantity t. The definitions corresponding to the data points shown in Figs. 1 and 2 are as follows:

$$S: \qquad t = 2N^{-1/2}; \quad (9)$$

$$J: \quad t = 2N^{-1/2} + 2N^{-3/2}(|E_{\mathbf{h}}|^2 + |E_{\mathbf{k}}|^2 + |E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}|^2 - 3) + 2N^{-5/2}[|E_{\mathbf{h}}|^4 + |E_{\mathbf{k}}|^4 + |E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}|^4 + (11/4)(|E_{\mathbf{h}}E_{\mathbf{k}}|^2 + |E_{\mathbf{h}}E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}|^2 + |E_{\mathbf{k}}E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}|^2) - (9/2)(|E_{\mathbf{h}}|^2 + |E_{\mathbf{k}}|^2 + |E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}|^2) + 2]; \quad (10)$$

$$I: \qquad t = 2N^{-1/2}/q_1, \quad (11)$$

where

$$q_1 = 1 + 2|U_{\mathbf{h}}U_{\mathbf{k}}U_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}| - |U_{\mathbf{h}}|^2 - |U_{\mathbf{k}}|^2 - |U_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}|^2, \quad (12)$$

$$U = EN^{-1/2}; \quad (13)$$

$$D: \qquad t = 2N^{-1/2}V_{3,p}, \quad (14)$$

where

$$V_{3,p} = \frac{(1-|U_{\mathbf{h}}|^2) + (1-|U_{\mathbf{k}}|^2) + (1-|U_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}|^2)}{3(1-|U_{\mathbf{h}}|^2)(1-|U_{\mathbf{k}}|^2)(1-|U_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}|^2)}. \quad (15)$$

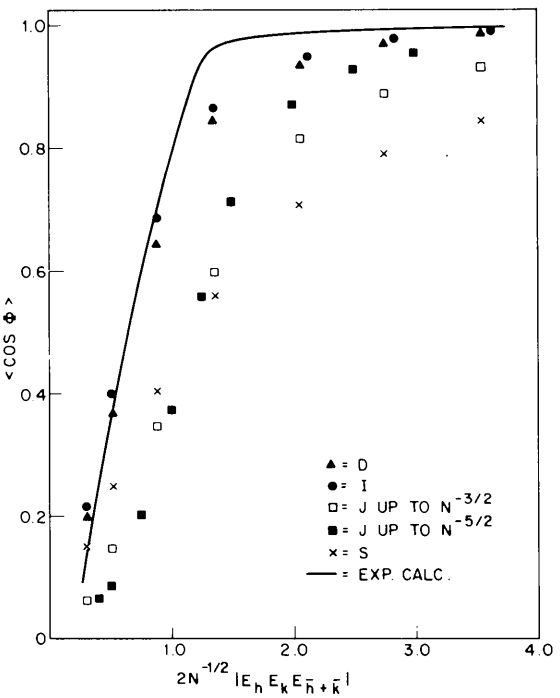

Fig. 1. Variation of the expected values of the cosines of triplet phase invariants with $2N^{-1/2}|E_{\mathbf{h}}E_{\mathbf{k}}E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}|$ for a three-atom structure in space group $P1$. The solid line is drawn among values computed experimentally from a large number of cosine invariants. Values from various theoretical formulas are plotted by means of symbols. The best fits to the larger values of $2N^{-1/2}|E_{\mathbf{h}}E_{\mathbf{k}}E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}|$ are given by functions I and D. There is a region, however, in which even these functions give estimates that are significantly too low.

In order to compute (10), (11) and (14) for given values of $|E_{\mathbf{h}}E_{\mathbf{k}}E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}|$, as required for Figs. 1 and 2, it was assumed that $|E_{\mathbf{h}}| = |E_{\mathbf{k}}| = |E^{*}_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}| = |E_{\mathbf{h}}E_{\mathbf{k}}E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}|^{1/3}$.

The expected value formula labelled S comes from the probability distribution for a cosine invariant derived by Cochran (1955) with the use of the central limit theorem. Formula J comes from the exponential form of the conditional joint probability distribution for a cosine invariant (Karle, 1972; Karle & Gilardi, 1973), a form designed to diminish the effect of asymptotic convergence when normalized structure factors of large magnitude are present. The first term in J corresponds to S and the second and third terms are higher-order corrections. Formulas I and D have a heuristic origin and are intended to correct for the fact that formula S underestimates the distribution when the products of normalized structure factor magnitudes $|E_{\mathbf{h}}E_{\mathbf{k}}E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}|$ are large. Formula I is derived from characteristics of a third-order determinantal inequality (Karle, 1972) and formula D is derived from a joint probability distribution expressed in terms of the determinants that are associated with the non-negativity of electron density distributions in a crystal (Karle, 1978; Karle, 1980*b*).

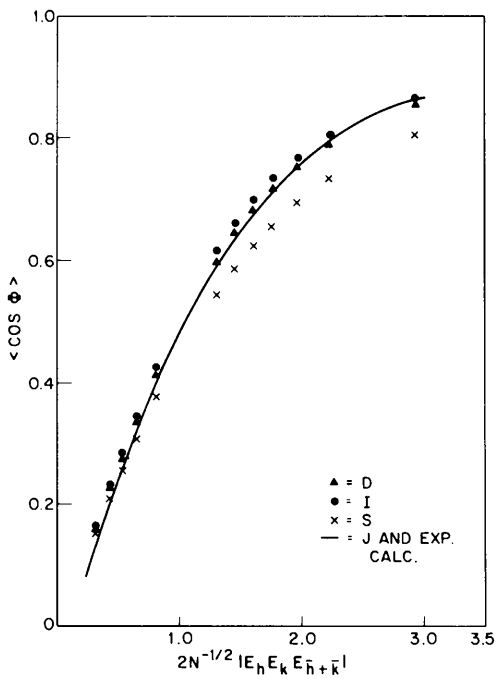

Fig. 2. Variation of the expected values of the cosines of triplet phase invariants with $2N^{-1/2}|E_{\mathbf{h}}E_{\mathbf{k}}E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}|$ for a nine-atom structure in the asymmetric unit of a unit cell in space group $P2_12_12_1$. The solid line is drawn among values computed experimentally from a large number of triplet phase invariants. Values from various theoretical formulas are plotted by means of symbols. The function J is not explicitly plotted since it coincides with the experimental curve. The function S gives estimates that are too low for the values of the cosine invariants for the larger values of $2N^{-1/2}|E_{\mathbf{h}}E_{\mathbf{k}}E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}|$. The function D is a good fit to the experimental curve in the latter region while function I has a tendency toward modest overestimation as the values of $2N^{-1/2}|E_{\mathbf{h}}E_{\mathbf{k}}E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}|$ decrease.

The results of the computations for a three-atom structure in space group $P1$ are shown in Fig. 1. It is seen that the distribution for the structure composed of just three atoms is not well represented by S or even by J, the joint distribution carried out to higher-order terms in the exponential form. There are actually two plots for J given in Fig. 1, one that omits the term of order $N^{-5/2}$ and one that includes it. Quite favorably for the assumption leading to (7) from (6), the distribution of the cosine invariants is much closer to unity than predicted by S or J. The theoretical formulas I and D give a better fit, but the actual distribution is still quite apparently closer to unity in the range $2N^{-1/2}|E_{\mathbf{h}}E_{\mathbf{k}}E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}| = 1$–3 and greater.

At the other extreme of complexity in the test problems is the nine-atom structure in space group $P2_12_12_1$. The results of the computations for this structure are shown in Fig. 2. It is seen that the function S again predicts values here that are too low. The functions J, I and D give a rather good fit to the experimental curve. The points for J are omitted in Fig. 2. They fit the experimental curve quite precisely except below $2N^{-1/2}|E_{\mathbf{h}}E_{\mathbf{k}}E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}| \sim 0{\cdot}4$ where the calculation of J gives values that are slightly high.

Experimental calculations of the averages of cosines of triplet phase invariants were made for a second three-atom structure in space group $P1$ and a second nine-atom structure in space group $P2_12_12_1$ to determine whether significant deviations from the distributions observed for the first structures would occur. None were observed.

For the nine-atom structure in $P1$ and the three-atom structure in the asymmetric unit of $P2_12_12_1$, J fitted the large values well down to a value of about 0·86 for the average of the cosines of the triplet phase invariants but S underestimated seriously the larger values of the cosines of the triplet phase invariants. J underestimated the cosine invariants between values of about 0·45 and 0·86. Below 0·45, it again continued to fit well. The possibility that the term of order $N^{-7/2}$ would improve this was not tested. The calculations I and D fitted well from the largest values for the cosine invariants down to a value of about 0·60 after which they overestimated the values.

In some additional test calculations, it was found that, for a two-atom structure in space group $P1$, the average values of experimentally calculated triplet cosine invariants were unity until the value of $2N^{-1/2}|E_{\mathbf{h}}E_{\mathbf{k}}E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}|$ fell below about 0·55, at which point the values decreased precipitously toward zero and slightly negative numbers. In the region below $2N^{-1/2}|E_{\mathbf{h}}E_{\mathbf{k}}E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}| = 2$, all the theoretical functions, D, I, J and S underestimated badly the experimental

calculations. The functions I and D were better than J and S. For a one-atom structure in the asymmetric unit of space group $P2_12_12_1$, the values of the exponentially calculated cosine invariants were fairly well represented by I and D down to $2N^{-1/2}|E_{\mathbf{h}}E_{\mathbf{k}}E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}| \sim 0{\cdot}6$, after which they overestimated the values of the cosine invariants. The estimates from functions S and J were systematically too low.

The calculations indicate that for the simple structures that are expected to occur in heavy-atom derivatives of macromolecules, it should be easy to satisfy the criterion for (7), namely that triplet phase invariants for the heavy-atom structure have values close to zero for the larger values of $2N^{-1/2}|E_{\mathbf{h}}E_{\mathbf{k}}E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}|$ appropriate to the heavy-atom structure. The calculations also show that the functions I and D provide a satisfactory description of the distributions except for an underestimation of the distribution for two and three-atom structures in space group $P1$ in the range $2N^{-1/2}|E_{\mathbf{h}}E_{\mathbf{k}}E_{\bar{\mathbf{h}}+\bar{\mathbf{k}}}| = 1$–3. The three-atom test example implies that, for very simple structures, the distribution of triplet invariants is closer to zero than even theoretical formulas improved to take account of the effect of large values of the magnitudes of the normalized structure factors would predict, a rather favorable circumstance. I and D can often be used as theoretical estimators of the closeness to zero of triplet phase invariants for simple structures. Alternatively, a few calculations such as the ones performed here can be used as a guide to the validity of (7). The reliability of (7) will depend, in addition, on the accuracy with which the $A_{\mathbf{hk}}$ can be obtained from experimental data.

Concluding remarks

This paper shows that the values of triplet phase invariants can be obtained from an exact algebraic analysis of anomalous dispersion data. This can be achieved with very high accuracy in the mathematical sense since the only uncertainty would derive from deviations from zero of triplet phase invariants associated with the structure of the anomalous scatterers. For macromolecules, the latter structures are usually quite simple and it is readily possible to satisfy the requirement for (7) to be valid, namely that the triplet phase invariants associated with the structure of the anomalous scatterers have values close to zero. The accuracy of the triplet phase invariants obtained from (7) is then mainly dependent upon the accuracy with which $A_{\mathbf{hk}}$ in (7) can be obtained from experimental data. It is easy to imagine circumstances in a multi-wavelength experiment in which the number of equations can exceed the number of unknowns by a factor of two or more. This has the potential to reduce the effect of experimental error and thereby improve the accuracy.

It was also noted that the algebraic equations, from which the theoretical results of this paper follow, were of a form that permitted intensity information from isomorphous replacement experiments to be easily introduced into the equations, thus reducing the number of known quantities to be determined.

Use of the algebraic equations to provide the values of triplet phase invariants may not be the optimal way to derive phase information from them. In order to obtain phase information from the equations otherwise, however, it would be necessary to solve for the structure of at least one type of anomalous scatterer from knowledge of the corresponding intensities that occur as unknown quantities in the equations. If for some reason this structure determination falters, it may be possible to proceed with the use of the values of the triplet phase invariants.

There are some additional virtues of the anomalous dispersion technique that are worth noting. Essentially, the power of the method does not deteriorate with complexity. The power depends upon the contribution of the anomalous scatterers to the measured intensities relative to that of the nonanomalous scatterers. So long as a favorable ratio is maintained, complex systems remain accessible. A second point of interest concerns the fact that the number of atoms in a structure that are strong anomalous scatterers in the usual systems of interest is a rather small fraction of the total. It is therefore appropriate to expect that a rather large amount of data would be obtained from an anomalous dispersion experiment relative to the number of atoms that scatter anomalously. This facilitates the determination of the structure of the anomalous scatterers by use of the corresponding intensities that are obtained from the solution of the algebraic equations. It also facilitates the evaluation of a large number of triplet phase invariants from (7) because with many data the criterion for the validity of this equation, namely values close to zero for the triplet phase invariants associated with the structure of the anomalous scatterers, is readily satisfied in a large number of instances.

I wish to thank Mr Stephen Brenner for writing the appropriate programs and making the computations reported here.

This research was supported in part by USPHS grant GM30902.

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