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On the Number of Ambiguities in Direct Methods – Anomalous Scattering Estimates of the Two- and Three-Phase Structure Invariants

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Abstract

The theoretical basis for the integration of direct methods into the single-wavelength anomalous dispersion technique is reexamined. The analysis shows that the approximations responsible for the ability to obtain unique estimates of the two- and three-phase structure invariants [Hauptman (1982). *Acta Cryst.* A38, 632-641; Giacovazzo (1983). *Acta Cryst.* A39, 585-592] or twofold estimates of the three-phase structure invariants [Kroon, Spek & Krabbendam (1977). *Acta Cryst.* A33, 382-385] are also responsible for the substantial errors observed in the applications. It is shown that, in the general case, the method of joint probability distributions leads to twofold estimates of the two-phase invariants and eightfold estimates of the three-phase invariants. Finally, it is shown that more accurately determined three-phase invariant estimates can be obtained by the use of anomalous scatterer substructure information, when available, and the use of a strategy that recognizes cases in which the eight estimates are clustered around one or two values. These cases are then distinguished from those where the eight estimates are widely scattered by a weighting function.

1. Introduction

It has been known for some thirty years that structure amplitude differences due to anomalous scattering can be used to obtain phase information. Reviews on the various proposed phasing techniques based on this approach can be found in several publications (Ramaseshan & Abrahams, 1975; Sayre, 1982; Ramachandran, 1964). Until recently, it was generally believed that, as in the single isomorphous replacement case, the single-wavelength anomalous dispersion experiment could yield only estimates of phases bearing a twofold ambiguity. Using the method of joint probability distributions, Hauptman (1982) and, subsequently, Giacovazzo (1983) obtained formulae which give unique estimates of the two-phase and three-phase structure invariants and thus unique estimates of the phases themselves. These results differ from those reported by Kroon, Spek & Krabbendam (1977), who obtained an estimate of the three-phase sine invariant, which implies of course twofold ambiguity in the estimate of the invariant itself.

While there is, at the moment, a substantial theoretical base for the integration of direct methods into the anomalous dispersion phasing technique, a number of points remain unclear. Firstly, the reasons why the one approach yields unique estimates of the invariants while the other results in a twofold ambiguity are not well understood. Secondly, in the initial applications made by Hauptman (1982) and Giacovazzo (1983), large errors persist in the invariant estimates, even when the calculations are done using error-free data. In addition, as noted by Giacovazzo (1983), the formulae tend to underestimate systematically the variance of the distributions. This suggests the presence of systematic errors in the proposed formulae and thus suggests that better estimates can be obtained once the errors are characterized and corrected.

In the present paper, the theoretical bases used by Hauptman (1982), Giacovazzo (1983) and Kroon,

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Spek & Krabbendam (1977) are reexamined. The analysis shows that both approaches used approximations which are responsible for the ability to obtain unique or twofold estimates, but are also responsible for the large errors observed. It is shown that, in general, an eightfold ambiguity remains in the estimate of the three-phase structure invariants. Finally, a strategy is proposed for the use of the eightfold estimated three-phase invariants.

2. Estimation of structure invariants by the method of joint probability distributions*

2.1. *The probabilistic theory of the two-phase structure invariant*

For a structure containing atoms that scatter anomalously, the structure factors $F_{\mathbf{H}}$ and $F_{\bar{\mathbf{H}}}$, associated with an acentric reflection **H**, generally have different amplitudes and phases. The well known diagram showing the relationships among the components of these structure factors is reproduced in Fig. 1, where

$$F_{\mathbf{H}} = F'_{\mathbf{H}} + F''_{A\mathbf{H}} \tag{1}$$

and

$$F'_{\mathbf{H}} = F_{R\mathbf{H}} + F'_{A\mathbf{H}}, \tag{2}$$

and where $F_{R\mathbf{H}}$ is the contribution from the non-anomalously scattering atoms, $F'_{A\mathbf{H}}$ is the contribution from the real part of the atomic scattering factors of the anomalously scattering atom, and $F''_{A\mathbf{H}}$ is the contribution from the imaginary part of the atomic scattering factors of the anomalously scattering atoms.

Once the substructure of the anomalously scattering atoms has been determined, the components $F'_{A\mathbf{H}}$ and $F''_{A\mathbf{H}}$ can be calculated. This information, together with the measured amplitudes $|F_{\mathbf{H}}|$ and $|F_{\bar{\mathbf{H}}}|$, leads to estimates of the phases of the structure factors $F_{\mathbf{H}}$, $F'_{\mathbf{H}}$ and $F_{\bar{\mathbf{H}}}$, $F'_{\bar{\mathbf{H}}}$ bearing a twofold ambiguity, as shown in Fig. 2. The solutions 1 and 2 are enantiomorphic with respect to the F''_{A1} vector, and $\bar{1}$ and $\bar{2}$ are enantiomorphic with respect to $F''_{A\bar{1}}$.

The reported conditional probability distribution for the two-phase structure invariant

$$\psi = \varphi_{\mathbf{H}} + \varphi_{\bar{\mathbf{H}}}, \tag{3}$$

given the two normalized structure-factor magnitudes

$$|E_{\mathbf{H}}| \text{ and } |E_{\bar{\mathbf{H}}}| \tag{4}$$

of Hauptman (1982) and Giacovazzo (1983), is unimodal, yielding, thus, a unique estimate of the invariant ψ. This result is unexpected since the ability to estimate uniquely the value of ψ is in fact equivalent to the resolution of the phase ambiguity from the magnitudes $|E_{\mathbf{H}}|$ and $|E_{\bar{\mathbf{H}}}|$ alone. This can be easily seen in Fig. 2. The sum of the phases $\varphi_{\mathbf{H}} + \varphi_{\bar{\mathbf{H}}}$ for the first solution is

$$\begin{aligned} \varphi_{\mathbf{H}} + \varphi_{\bar{\mathbf{H}}} &= \varphi'_1 + \beta_1 + \varphi'_{\bar{1}} + \beta_{\bar{1}} \\ \varphi_{\mathbf{H}} + \varphi_{\bar{\mathbf{H}}} &= \beta_2 + \beta_{\bar{2}} \end{aligned} \tag{5}$$

and for the second solution

$$\varphi_{\mathbf{H}} + \varphi_{\bar{\mathbf{H}}} = \beta_2 + \beta_{\bar{2}}. \tag{6}$$

While the sums, $\beta_1 + \beta_{\bar{1}}$ and $\beta_2 + \beta_{\bar{2}}$, have the same magnitude, they always have opposite signs owing to their enantiomorphic relationship. In one of the solutions, F and $\bar{F}$ have a phase advance with respect

* The distributions obtained by Hauptman (1982) and Giacovazzo (1983) are identical. Any references to the results of Hauptman apply as well to the results of Giacovazzo and *vice versa*. Throughout this section we shall use Hauptman's notation.

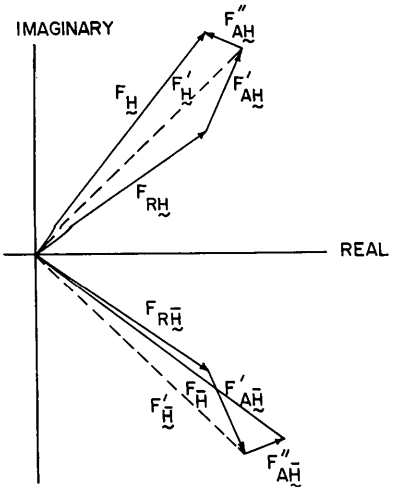

Fig. 1. Argand diagram showing the relationships among the components of the structure factors for the reflections **H** and $\bar{\mathbf{H}}$.

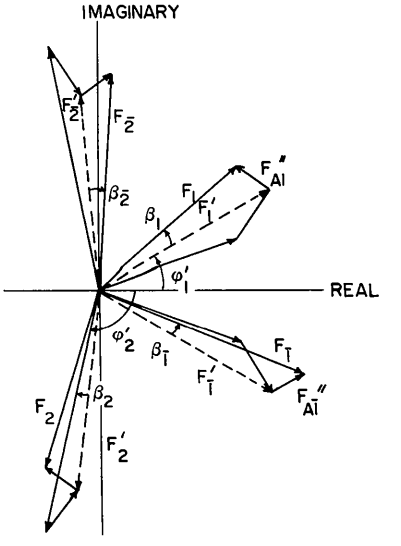

Fig. 2. The twofold ambiguity in the single-wavelength anomalous dispersion case.

to F' and $\bar{F}'$ while, in the other solution, they have a phase lag. It is thus surprising that a unimodal distribution can be obtained for the invariant $\varphi_{\mathbf{H}}+\varphi_{\bar{\mathbf{H}}}$, as it suggests that the sign ambiguity can be resolved from the magnitudes alone. This observation led us to a reexamination of the distribution so as to gain an understanding of this unexpected result.

The unimodal distribution gives the estimate

$$\varphi_{\mathbf{H}}+\varphi_{\bar{\mathbf{H}}}\simeq -\xi, \tag{7}$$

provided that the variance of the distribution is small. The angle ξ is calculated using

$$\tan \xi = -S_{\mathbf{H}}/C_{\mathbf{H}}, \tag{8}$$

where

$$C_{\mathbf{H}} = (1/\alpha_{\mathbf{H}}) \sum_{j=1}^{N} |f_{j\mathbf{H}}|^2 \cos 2\,\delta_{j\mathbf{H}}, \tag{9}$$

$$S_{\mathbf{H}} = (1/\alpha_{\mathbf{H}}) \sum_{j=1}^{N} |f_{j\mathbf{H}}|^2 \sin 2\delta_{j\mathbf{H}}, \tag{10}$$

$$\alpha_{\mathbf{H}} = \sum_{j=1}^{N} |f_{j\mathbf{H}}|^2, \tag{11}$$

$$N = \text{number of atoms in the unit cell}, \tag{12}$$

and the atomic scattering factor $f_{j\mathbf{H}}$ is expressed in the form

$$f_{j\mathbf{H}} = |f_{j\mathbf{H}}| \exp(i\delta_{j\mathbf{H}}). \tag{13}$$

For a fictional monatomic structure in which the one atom scatters anomalously, there is no ambiguity in the sign of the sum $\varphi_{\mathbf{H}}+\varphi_{\bar{\mathbf{H}}}$. For such a structure we have

$$\varphi_{\mathbf{H}}+\varphi_{\bar{\mathbf{H}}} = \delta_{\mathbf{H}}+\delta_{\bar{\mathbf{H}}} = 2\delta_{\mathbf{H}}, \tag{14}$$

$$S_{\mathbf{H}} = \sin 2\delta_{\mathbf{H}}, \tag{15}$$

$$C_{\mathbf{H}} = \cos 2\delta_{\mathbf{H}}, \tag{16}$$

and the angle ξ is uniquely and correctly defined.

When the structure contains more than one atom, the cosine and sine terms, used for the calculation of ξ, are a weighted sum of the contributions from each of the individual atoms [(9) and (10)]. This estimate, however, is correct only for the case of a reflection for which the individual atoms' contributions to the structure factor, from the real part of their atomic scattering factors, all have the same phase angle. Physically this implies that *all* the atoms are scattering in phase, *i.e.* that all the atoms lie in the same plane. It is for this special case, and this case only, that a unique estimate of ξ can be obtained. The unimodal property of the distribution is therefore a result of an approximation which is not valid in general. This approximation leads to a poor estimate of ξ, and, in particular, does not provide any information on its sign. From (9) and (10), it can be seen that, since $\delta_{j\mathbf{H}}$ is positive and generally small, both $C_{\mathbf{H}}$ and $S_{\mathbf{H}}$ are positive, and thus ξ is negative. It is therefore implicitly assumed that the sum $\varphi_{\mathbf{H}}+\varphi_{\bar{\mathbf{H}}}$ has a positive value. From Fig. 2, it can be seen that the solution for which the sum $\varphi_{\mathbf{H}}+\varphi_{\bar{\mathbf{H}}}$ has a positive value corresponds to the solution for which the phase angles are closest to the anomalous scatterer substructure phase angles.

The notation used by Giacovazzo (1983) is different from that of Hauptman (1982). In Giacovazzo's notation, the unimodal distribution gives the estimate

$$\varphi_{\mathbf{H}}+\varphi_{\bar{\mathbf{H}}} = q \tag{17}$$

where

$$\tan q = C_2/C_1. \tag{18}$$

It can be easily shown that C_1 and C_2 correspond exactly to $C_{\mathbf{H}}$ and $S_{\mathbf{H}}$.

2.2. *The probabilistic theory of the three-phase structure invariants*

Owing to the breakdown of Friedel's law, for a triplet of reciprocal-lattice vectors, **H**, **K**, **L**, satisfying

$$\mathbf{H}+\mathbf{K}+\mathbf{L} = 0, \tag{19}$$

there exist eight three-phase structure invariants

$$\begin{aligned}
\psi_0 &= \varphi_{\mathbf{H}}+\varphi_{\mathbf{K}}+\varphi_{\mathbf{L}},\\
\psi_1 &= -\varphi_{\bar{\mathbf{H}}}+\varphi_{\mathbf{K}}+\varphi_{\mathbf{L}},\\
\psi_2 &= \varphi_{\mathbf{H}}-\varphi_{\bar{\mathbf{K}}}+\varphi_{\mathbf{L}},\\
\psi_3 &= \varphi_{\mathbf{H}}+\varphi_{\mathbf{K}}-\varphi_{\bar{\mathbf{L}}},\\
\psi_{\bar{0}} &= \varphi_{\bar{\mathbf{H}}}+\varphi_{\bar{\mathbf{K}}}+\varphi_{\bar{\mathbf{L}}},\\
\psi_{\bar{1}} &= -\varphi_{\mathbf{H}}+\varphi_{\bar{\mathbf{K}}}+\varphi_{\bar{\mathbf{L}}},\\
\psi_{\bar{2}} &= \varphi_{\bar{\mathbf{H}}}-\varphi_{\mathbf{K}}+\varphi_{\bar{\mathbf{L}}},\\
\psi_{\bar{3}} &= \varphi_{\bar{\mathbf{H}}}+\varphi_{\bar{\mathbf{K}}}-\varphi_{\mathbf{L}}.
\end{aligned} \tag{20}$$

The conditional probability distributions of each of the three-phase structure invariants, given the six magnitudes $|E_{\mathbf{H}}|$, $|E_{\mathbf{K}}|$, $|E_{\mathbf{L}}|$, $|E_{\bar{\mathbf{H}}}|$, $|E_{\bar{\mathbf{K}}}|$, $|E_{\bar{\mathbf{L}}}|$, have been derived by Hauptman (1982) and Giacovazzo (1983). The distributions obtained are unimodal, thus leading to unique estimates of the invariants in the interval 0 to 360°, and therefore unique estimates of the phases themselves.

These distributions have the form

$$\begin{aligned}
P_j &= P_j(\Omega_j \,|\, R_1, R_2, R_3, R_{\bar{1}}, R_{\bar{2}}, R_{\bar{3}})\\
P_j &= (1/K_j)\exp\{A_j \cos(\Omega_j-\omega_j)\},\\
&\qquad j = 0, 1, 2, 3, \bar{0}, \bar{1}, \bar{2}, \bar{3},
\end{aligned} \tag{21}$$

where the normalizing constant, K_j, is defined by

$$K_j = 2\pi I_0(A_j) \tag{22}$$

and where

$$R_1=|E_{\mathbf{H}}|, \quad R_2=|E_{\mathbf{K}}|, \quad R_3=|E_{\mathbf{L}}|, \quad R_{\bar{1}}=|E_{\bar{\mathbf{H}}}|, \quad R_{\bar{2}}=|E_{\bar{\mathbf{K}}}|, \quad R_{\bar{3}}=|E_{\bar{\mathbf{L}}}|. \tag{23}$$

From (21) it follows that when the variance of the distribution is small, *i.e.* when A_j is large, a reliable (and unique) estimate of ψ_j,

$$\psi_j=\omega_j, \qquad j=0,1,2,3,\bar{0},\bar{1},\bar{2},\bar{3}, \tag{24}$$

is obtained. In the initial applications made by Hauptman (1982) and Giacovazzo (1983), it was seen, however, that although unique estimates were obtained substantial errors persisted, even when the calculations were done using error-free data. The magnitude of the errors was not well predicted, as the variance of the distributions was systematically underestimated. In order to locate the source of these systematic errors, the distributions were reexamined.

As an example, we consider the distribution of the ψ_0 invariant, although the discussion may be applied to any of the eight distributions. The conditional probability distribution of ψ_0 is given by

$$P_0=(1/K_0)\exp\{A_0\cos(\Omega_0-\omega_0)\}, \tag{25}$$

where

$$A_0=2B_0/[(1-X_1^2)(1-X_2^2)(1-X_3^2)], \tag{26}$$

$$B_0=[B_{0c}^2+B_{0s}^2]^{1/2}, \tag{27}$$

$$\omega_0=\tan^{-1}(B_{0s}/B_{0c}), \tag{28}$$

$$\begin{aligned}B_{0c}=&Z_0\{R_1R_2R_3\cos\zeta_0+R_{\bar{1}}R_{\bar{2}}R_{\bar{3}}\tau_1\tau_2\tau_3\cos(\xi_1+\xi_2+\xi_3+\zeta_0)\}\\&+Z_1\{R_{\bar{1}}R_2R_3\tau_1\cos(\xi_1-\zeta_1)+R_1R_{\bar{2}}R_{\bar{3}}\tau_2\tau_3\cos(\xi_2+\xi_3+\zeta_1)\}\\&+Z_2\{R_1R_{\bar{2}}R_3\tau_2\cos(\xi_2-\zeta_2)+R_{\bar{1}}R_2R_{\bar{3}}\tau_1\tau_3\cos(\xi_1+\xi_3+\zeta_2)\}\\&+Z_3\{R_1R_2R_{\bar{3}}\tau_3\cos(\xi_3-\zeta_3)+R_{\bar{1}}R_{\bar{2}}R_3\tau_1\tau_2\cos(\xi_1+\xi_2+\zeta_3)\}\end{aligned} \tag{29}$$

$$\begin{aligned}B_{0s}=&Z_0\{R_1R_2R_3\sin\zeta_0-R_{\bar{1}}R_{\bar{2}}R_{\bar{3}}\tau_1\tau_2\tau_3\sin(\xi_1+\xi_2+\xi_3+\zeta_0)\}\\&-Z_1\{R_{\bar{1}}R_2R_3\tau_1\sin(\xi_1-\zeta_1)+R_1R_{\bar{2}}R_{\bar{3}}\tau_2\tau_3\sin(\xi_2+\xi_3+\zeta_1)\}\\&-Z_2\{R_1R_{\bar{2}}R_3\tau_2\sin(\xi_2-\zeta_2)+R_{\bar{1}}R_2R_{\bar{3}}\tau_1\tau_3\sin(\xi_1+\xi_3+\zeta_2)\}\\&-Z_3\{R_1R_2R_{\bar{3}}\tau_3\sin(\xi_3-\zeta_3)+R_{\bar{1}}R_{\bar{2}}R_3\tau_1\tau_2\sin(\xi_1+\xi_2+\zeta_3)\}.\end{aligned} \tag{30}$$

All the terms used for the computation of B_{0c} and B_{0s} are defined in the publication of Hauptman (1982), to which the reader is referred. Only the terms pertinent to the present discussion will be restated.

The X_i and ξ_i terms, appearing in (26), (29) and (30), are defined by

$$X_1=(C_{\mathbf{H}}^2+S_{\mathbf{H}}^2)^{1/2}, \qquad \tan\xi_1=(-S_{\mathbf{H}}/C_{\mathbf{H}}), \tag{31}$$

$$X_2=(C_{\mathbf{K}}^2+S_{\mathbf{K}}^2)^{1/2}, \qquad \tan\xi_2=(-S_{\mathbf{K}}/C_{\mathbf{K}}), \tag{32}$$

$$X_3=(C_{\mathbf{L}}^2+S_{\mathbf{L}}^2)^{1/2}, \qquad \tan\xi_3=(-S_{\mathbf{L}}/C_{\mathbf{L}}), \tag{33}$$

where $C_{\mathbf{H}}$ and $S_{\mathbf{H}}$ are defined by (9) and (10). In view of the discussion presented in § 2.1 it is clear that significant errors are made in the computation of X_i and ξ_i and these account, in part, for the errors observed in the invariant estimates. In addition, the sign of ξ_i cannot be determined by the approximation used. In this case, however, the sign ambiguity is implicitly contained in the distribution, in the form of the τ terms.

$$\tau_i=\frac{I_1[2R_iR_{\bar{i}}X_i/(1-X_i^2)]}{I_0[2R_iR_{\bar{i}}X_i/(1-X_i^2)]}, \quad i=1,2,3, \tag{34}$$

where I_0 and I_1 are the modified Bessel functions. From equation (2.13) of Hauptman (1982) and from Hauptman (1972), it can be seen that τ_i is the expected value of the cosine of the phase sum $\varphi_i+\varphi_{\bar{i}}+\xi_i$. The equivalent cosine functions can therefore be substituted for the τ functions in the distribution.

Let

$$\cos(\varphi_i+\varphi_{\bar{i}}+\xi_i)=\cos\alpha_i, \tag{35}$$

and to simplify the discussion, let us assume that $|\alpha_2|=|\alpha_3|=0$ and $|\alpha_1|\neq 0$.

We then have

$$\begin{aligned}B_{0c}=&Z_0R_1R_2R_3\cos\zeta_0+Z_1R_1R_{\bar{2}}R_{\bar{3}}\cos(\xi_2+\xi_3+\zeta_1)\\&+Z_2R_1R_{\bar{2}}R_3\cos(\xi_2-\zeta_2)\\&+Z_3R_1R_2R_{\bar{3}}\cos(\xi_3-\zeta_3)\\&+1/2\{Z_0R_{\bar{1}}R_{\bar{2}}R_{\bar{3}}[\cos(\xi_1+\xi_2+\xi_3+\zeta_0+\alpha_1)\\&+\cos(\xi_1+\xi_2+\xi_3+\zeta_0-\alpha_1)]\\&+Z_1R_{\bar{1}}R_2R_3[\cos(\xi_1-\zeta_1+\alpha_1)\\&+\cos(\xi_1-\zeta_1-\alpha_1)]\\&+Z_2R_{\bar{1}}R_2R_{\bar{3}}\cos(\xi_1+\xi_3+\zeta_2+\alpha_1)\\&+\cos(\xi_1+\xi_3+\zeta_2-\alpha_1)]\\&+Z_3R_{\bar{1}}R_{\bar{2}}R_3[\cos(\xi_1+\xi_2+\zeta_3+\alpha_1)\\&+\cos(\xi_1+\xi_2+\zeta_3-\alpha_1)]\}\end{aligned} \tag{36}$$

$$\begin{aligned}B_{0s}=&Z_0R_1R_2R_3\sin\zeta_0-Z_1R_1R_{\bar{2}}R_{\bar{3}}\sin(\xi_2+\xi_3+\zeta_1)\\&-Z_2R_1R_{\bar{2}}R_3\sin(\xi_2-\zeta_2)\\&-Z_3R_1R_2R_{\bar{3}}\sin(\xi_3-\zeta_3)\\&-1/2\{Z_0R_{\bar{1}}R_{\bar{2}}R_{\bar{3}}[\sin(\xi_1+\xi_2+\xi_3+\zeta_0+\alpha_1)\\&+\sin(\xi_1+\xi_2+\xi_3+\zeta_0-\alpha_1)]\\&+Z_1R_{\bar{1}}R_2R_3[\sin(\xi_1-\zeta_1+\alpha_1)\\&+\sin(\xi_1-\zeta_1-\alpha_1)]\\&+Z_2R_{\bar{1}}R_2R_{\bar{3}}[\sin(\xi_1+\xi_3+\zeta_2+\alpha_1)\\&+\sin(\xi_1+\xi_3+\zeta_2-\alpha_1)]\\&+Z_3R_{\bar{1}}R_{\bar{2}}R_3[\sin(\xi_1+\xi_2+\zeta_3+\alpha_1)\\&+\sin(\xi_1+\xi_2+\zeta_3-\alpha_1)]\}.\end{aligned} \tag{37}$$

Equations (36) and (37) show that a twofold ambiguity is implicitly contained in the distribution. Since the sign of α_1 is unknown, both signs are considered equally probable and their contributions are averaged.

In the general case where $|\alpha_1|$, $|\alpha_2|$ and $|\alpha_3|$ are all non zero, there exist eight possible sign combinations in the α's. By extension from (36) and (37), it can be seen that the use of the τ_i functions results in an averaging of these eight possible cases and, as a consequence, a unique estimate of the invariant is obtained. The accuracy of the estimate, however, may be poor. In addition, since X_i tends to be nearly equal to one, the argument of the Bessel functions (used for the evaluation of τ_i) tends to be large and thus τ_i itself tends to be nearly equal to one. As a consequence, the ambiguity in the sign of the ξ_i is removed. As was shown in the previous section, ξ_i generally has a negative sign and, thus, it is implicitly assumed that the sum $\varphi_i+\varphi_{\bar{i}}$ has a positive value. Substantial errors are made in the invariant estimates, particularly when one of the ξ has a positive sign, *i.e.* when one of the three sums $\varphi_{\mathbf{H}}+\varphi_{\bar{\mathbf{H}}}$, $\varphi_{\mathbf{K}}+\varphi_{\bar{\mathbf{K}}}$ or $\varphi_{\mathbf{L}}+\varphi_{\bar{\mathbf{L}}}$ has a negative value, as shown in Table 1.

The use of the τ functions accounts for the ability to obtain a unique estimate of the invariants; it also, however, accounts for the substantial systematic errors observed. If, instead of using the τ functions, the ξ_i angles are allowed to take their two possible signs, and the distribution is calculated for each of the eight sign combinations, eight possible estimates of the invariant are obtained.

As shown in Table 2, large differences may exist between the eight estimates. It is thus precisely in those cases that the distributions of Hauptman (1982) and Giacovazzo (1983) fail to give an accurate estimate of the invariants.

3. Estimation of sine invariants from geometrical considerations*

The first results on the use of the integrated direct methods–anomalous dispersion technique for the estimation of the three-phase structure invariant were presented by Kroon, Spek & Krabbendam (1977). By extending the method proposed by Peederman & Bijvoet (1956), Ramachandran & Raman (1956) and Okaya & Pepinsky (1956) to the three-phase structure invariant, they showed that three-phase sine invariants can be estimated using

$$\sin\bar{\varphi}_{\mathbf{hk}}=(|\tau_{\mathbf{hk}}|^2-|\tau_{\bar{\mathbf{hk}}}|^2)/4\tau''_{\mathbf{hk}}|\tau^0_{\mathbf{hk}}|, \tag{38}$$

where

$$\mathbf{hk}=\mathbf{h}+\mathbf{k}+(-\mathbf{h}-\mathbf{k}), \tag{39}$$

$$\bar{\varphi}_{\mathbf{hk}}=1/2(\varphi_{\mathbf{hk}}-\varphi_{\bar{\mathbf{hk}}}), \tag{40}$$

$$|\tau_{\mathbf{hk}}|=|E_{\mathbf{h}}||E_{\mathbf{k}}||E_{-\mathbf{h}-\mathbf{k}}|, \tag{41}$$

$$|\tau_{\bar{\mathbf{hk}}}|=|E_{\bar{\mathbf{h}}}||E_{\bar{\mathbf{k}}}||E_{\mathbf{h}+\mathbf{k}}|, \tag{42}$$

$$|\tau^0_{\mathbf{hk}}|=\{1/2[|\tau_{\mathbf{hk}}|^2+|\tau_{\bar{\mathbf{hk}}}|^2]-\tau''^2_{\mathbf{hk}}\}^{1/2}. \tag{43}$$

The $\tau^0_{\mathbf{hk}}$ and $\tau''_{\mathbf{hk}}$ correspond to the sum of the contributions to the $E_{\mathbf{h}}E_{\mathbf{k}}E_{-\mathbf{h}-\mathbf{k}}$ vector from the real and imaginary parts of the atomic scattering factors. While $|\tau_{\mathbf{hk}}|$ and $|\tau_{\bar{\mathbf{hk}}}|$ can be calculated from the magnitudes alone, the term $\tau''_{\mathbf{hk}}$ cannot be calculated directly since it depends on the atomic positions. In the method proposed by Kroon, Spek & Krabbendam (1977), the value of $\tau''_{\mathbf{hk}}$ is estimated using

$$\tau''_{\mathbf{hk}}=(\alpha_{\mathbf{h}}\alpha_{\mathbf{k}}\alpha_{\mathbf{h+k}})^{-1/2}\sum_{i=1}^{N}|f_i(\mathbf{h})f_i(\mathbf{k})f_i(\mathbf{h}+\mathbf{k})|$$
$$\times\sin\{2\pi[\delta_i(\mathbf{h})+\delta_i(\mathbf{k})+\delta_i(\mathbf{h}+\mathbf{k})]\}, \tag{44}$$

where

$$\alpha_{\mathbf{h}}=\sum_{i=1}^{N}|f_i(\mathbf{h})|^2 \tag{45}$$

and similarly for $\alpha_{\mathbf{k}}$ and $\alpha_{\mathbf{h+k}}$.

The atomic scattering factor $f_i(\mathbf{h})$ is defined as

$$f_i(\mathbf{h})=|f_i(\mathbf{h})|\exp[2\pi i\delta_i(\mathbf{h})]. \tag{46}$$

The nature of the approximation used can be understood by considering the imaginary part of the product of the normalized structure factors $E_{\mathbf{h}}E_{\mathbf{k}}E_{-\mathbf{h}-\mathbf{k}}$. Let

$$E_{\mathbf{h}}=|E_{\mathbf{h}}|\exp(2\pi_i\varphi_{\mathbf{h}}). \tag{47}$$

The imaginary part of the triple product $E_{\mathbf{h}}E_{\mathbf{k}}E_{-\mathbf{h}-\mathbf{k}}$ is

$$\tau_{\mathrm{im}}=|E_{\mathbf{h}}||E_{\mathbf{k}}||E_{-\mathbf{h}-\mathbf{k}}|\sin[2\pi(\varphi_{\mathbf{h}}+\varphi_{\mathbf{k}}+\varphi_{-\mathbf{h}-\mathbf{k}})]. \tag{48}$$

According to the notation used in § 2.1, equation (5), we define

$$\begin{aligned}\varphi_{\mathbf{h}}&=\varphi'_{\mathbf{h}}+\beta_{\mathbf{h}}\\ \varphi_{\mathbf{k}}&=\varphi'_{\mathbf{k}}+\beta_{\mathbf{k}}\\ \varphi_{-\mathbf{h}-\mathbf{k}}&=\varphi'_{-\mathbf{h}-\mathbf{k}}+\beta_{-\mathbf{h}-\mathbf{k}}\end{aligned} \tag{49}$$

and

$$\tau_{\mathrm{im}}=|E_{\mathbf{h}}||E_{\mathbf{k}}||E_{-\mathbf{h}-\mathbf{k}}|$$
$$\times\sin[2\pi(\varphi'_{\mathbf{h}}+\varphi'_{\mathbf{k}}+\varphi'_{-\mathbf{h}-\mathbf{k}}+\beta_{\mathbf{h}}+\beta_{\mathbf{k}}+\beta_{-\mathbf{h}-\mathbf{k}})]. \tag{50}$$

For a monoatomic structure in which the one atom scatters anomalously, there is no ambiguity in the signs of the $\beta_{\mathbf{h}}$, $\beta_{\mathbf{k}}$, $\beta_{-\mathbf{h}-\mathbf{k}}$ angles. The structure-factor magnitudes $|E_{\mathbf{h}}|$, $|E_{\mathbf{k}}|$ and $|E_{-\mathbf{h}-\mathbf{k}}|$ are equal to one and, since the atom is by necessity located at the origin, the angles $\varphi'_{\mathbf{h}}$, $\varphi'_{\mathbf{k}}$ and $\varphi'_{-\mathbf{h}-\mathbf{k}}$ are equal to zero.

* Throughout this section, the notation of Kroon, Spek & Krabbendam (1977) is used. Note, in particular, that the quantity represented by the τ symbol is *not related* to that of § 2.2.

Table 1. *Ten representative estimates of the structure invariants ψ_j for the $PtCl_4^{2-}$ derivative of cytochrome c_{550} obtained using Hauptman's (1982) distributions*

$\lvert E_{\mathbf{H}}\rvert$	$\lvert E_{\bar{\mathbf{H}}}\rvert$	$\lvert E_{\mathbf{K}}\rvert$	$\lvert E_{\bar{\mathbf{K}}}\rvert$	$\lvert E_{\mathbf{L}}\rvert$	$\lvert E_{\bar{\mathbf{L}}}\rvert$	A_j	Estimated value of ψ_j (°)	True value of ψ_j (°)	Estimated signs of $\xi_1\xi_2\xi_3$	True signs of $\xi_1\xi_2\xi_3$
1·91	2·06	1·57	1·41	1·20	1·08	8·02	84	14	− − −	+ − −
1·81	1·93	1·11	0·97	1·41	1·57	7·16	−61	−16	− − −	− + −
1·98	2·07	1·91	2·06	1·20	1·08	5·48	−51	−164	− − −	+ + −
2·36	2·48	1·56	1·69	0·82	0·68	4·52	52	2	− − −	− − +
1·34	1·48	1·34	1·22	1·25	1·16	3·76	−72	−126	− − −	+ − −
1·85	1·94	0·85	0·67	0·78	0·92	4·21	56	42	− − −	− − −
2·17	2·04	0·92	1·04	0·86	0·70	4·10	146	148	− − −	− − −
1·39	1·28	0·85	0·67	0·87	0·75	4·02	−72	−68	− − −	− − −
1·88	1·98	1·28	1·15	0·85	0·67	3·87	104	96	− − −	− − −
1·56	1·69	1·41	1·57	0·98	0·90	3·72	73	78	− − −	− − −

Table 2. *Estimates of the structure invariant ψ_j as a function of the ξ_1, ξ_2 and ξ_3 signs for the $PtCl_4^{2-}$ derivative of cytochrome c_{550}*

$|E_{\mathbf{H}}| = 2{\cdot}36$, $|E_{\bar{\mathbf{H}}}| = 2{\cdot}48$, $|E_{\mathbf{K}}| = 1{\cdot}56$, $|E_{\bar{\mathbf{K}}}| = 1{\cdot}69$, $|E_{\mathbf{L}}| = 0{\cdot}82$, $|E_{\bar{\mathbf{L}}}| = 0{\cdot}68$.

Signs of ξ_1	ξ_2	ξ_3	Estimated value of ψ_j using the estimated $\lvert\xi_i\rvert$ magnitudes (°)	Magnitude of the error (°)	Estimated value of ψ_j using the true $\lvert\xi_i\rvert$ magnitudes (°)	Magnitude of the error (°)
+	+	+	141	139	132	130
+	+	−	166	164	180	178
+	−	+	94	92	87	85
+	−	−	119	117	135	133
−	+	+	69	67	53	51
−	+	−	93	91	100	98
−	−	+*	24	22	10	8
−	−	−	48	46	57	55

* Signs corresponding to the true ξ_1, ξ_2 and ξ_3 signs.

We have, therefore,

$$\tau_{\text{im}} = \sin\left[2\pi(\beta_{\mathbf{h}} + \beta_{\mathbf{k}} + \beta_{-\mathbf{h}-\mathbf{k}})\right]. \qquad (51)$$

In this case $\beta_{\mathbf{h}} = \delta(\mathbf{h})$, and similarly for $\beta_{\mathbf{k}}$ and $\beta_{-\mathbf{h}-\mathbf{k}}$, and we have $\tau_{\text{im}} = \tau''_{\mathbf{hk}}$.

Equation (44) corresponds to a weighted average of the contributions from the individual atoms. This approximation is valid only for the special case of a triplet $\mathbf{h}$, $\mathbf{k}$, $-\mathbf{h}-\mathbf{k}$ for which the individual atoms' contributions, from the real part of their atomic scattering factors, all have the same phase angle. It is only in this case that the $\varphi'_{\mathbf{h}}$, $\varphi'_{\mathbf{k}}$ and $\varphi'_{-\mathbf{h}-\mathbf{k}}$ can be neglected and that the $\beta_{\mathbf{h}}$, $\beta_{\mathbf{k}}$ and $\beta_{-\mathbf{h}-\mathbf{k}}$ have a unique value. Again, in the general case, there are eight possible sign combinations in the β's which result in an eightfold ambiguity in the determination of $\bar{\varphi}_{\mathbf{hk}}$. In the method proposed by Kroon, Spek & Krabbendam, (38) corresponds to considering two of these combinations, namely (+++, −−−). This accounts for the twofold ambiguity in the determination of the invariant estimates. The method thus should work best when the true β's are either all positive or negative. Kroon, Spek & Krabbendam's approach has been further refined, in particular in the calculation of better estimates of the $\tau''_{\mathbf{hk}}$ term (Pontenagel, 1983). All of the approximations, however, still yield only a twofold estimate of the invariants. In addition, it was predicted, and confirmed, by Pontenagel (1983) that the method fails for macromolecular structures.

4. Proposed strategy for the use of eightfold estimated three-phase invariants

It was shown in § 2.2 that there are two main sources of errors in the estimates of the three-phase structure invariants from the presently available probabilistic theory. The first one comes from the inability to estimate reliably the magnitudes of the ξ angle terms appearing in the formulae; the second one results from the fact that, in the distributions, the ξ angles are, in general, assumed to have a negative sign. The first source of errors can be eliminated easily, once the anomalous scatterer substructure has been determined. It is then possible to calculate the magnitudes of the ξ angles and to incorporate this information into the distributions. Table 3 shows a few examples of invariants estimated using the true ξ angles. For the purpose of comparison, the invariants selected are the same as those used by Hauptman (1982, Table 1). From these calculations, it is apparent that a remarkable gain in accuracy is obtained by incorporating the true ξ values into the formulae. These calculations, however, are of a purely theoretical nature. In practical applications, once the anomalous scatterer substructure has been determined the magnitudes of the ξ angles can be calculated, but their signs remain unknown. Thus, in the general case, eight possible estimates of the invariant are obtained, one of which can be expected to be close to its true value,

Table 3. *Twenty-one estimates of the structure invariants ψ_j sampled from the top 2000 for the $PtCl_4^{2-}$ derivative of cytochrome c_{550}*

The $|E|$ magnitudes, associated with the ψ_j invariants, are given by Hauptman (1982), Table 1.

		Protocol 1*			Protocol 2†		
Serial no.	True value of ψ_j (°)	A_j	Estimated value of ψ_j (°)	Magnitude of the error (°)	A_j	Estimated value of ψ_j (°)	Magnitude of the error (°)
1	−88	6·92	−58	30	6·16	−86	2
100	130	5·62	148	18	7·39	138	8
200	−121	4·83	−79	42	6·77	−113	8
300	2	4·52	52	50	5·17	10	8
400	96	4·31	79	17	4·47	97	1
500	42	4·21	56	14	6·12	46	4
600	148	4·10	146	2	4·36	157	9
700	−68	4·02	−72	4	3·95	−69	1
800	50	3·93	70	20	6·64	54	4
900	96	3·87	104	8	3·88	93	3
1000	−138	3·80	−88	50	4·71	−146	8
1100	−126	3·76	−72	54	6·39	−119	7
1200	78	3·72	73	5	4·32	58	20
1300	−124	3·68	−161	37	4·69	−129	5
1400	−3	3·63	−72	69	5·01	−2	1
1500	77	3·59	84	7	2·90	94	17
1600	−94	3·55	−64	30	4·12	−72	22
1700	−72	3·51	−64	8	3·50	−60	12
1800	82	3·46	78	4	5·43	100	18
1900	123	3·43	63	60	2·44	100	23
2000	−126	3·42	−96	30	5·22	−132	6
				Av. 27°			Av. 9°

* In protocol 1, the estimates were obtained using Hauptman's (1982) original distributions.
† In protocol 2, the true $\varphi_i + \varphi_r$ values were incorporated into Hauptman's distributions from which the ψ_j estimates were then obtained.

Table 4. *Ten representative estimates of the structure invariantss ψ_j for the $PtCl_4^{2-}$ derivative of cytochrome c_{550} showing a reduction from an eight- to a twofold ambiguity*

$\|E_H\|$	$\|E_{\bar{H}}\|$	$\|E_K\|$	$\|E_{\bar{K}}\|$	$\|E_L\|$	$\|E_{\bar{L}}\|$	A_j	True value of ψ_j (°)	Twofold estimates of ψ_j (°)
2·06	1·91	1·61	1·50	0·85	0·67	7·75	−124	−132 (3)*, −32 (3)
2·04	2·17	0·89	1·03	0·85	0·67	6·27	−87	−79 (6), −111 (6)
0·91	1·04	0·46	0·31	0·26	0·41	5·62	−30	−43 (13), −139 (13)
0·59	0·46	0·15	0·32	0·41	0·26	5·00	85	73 (8), 110 (8)
0·15	0·32	0·40	0·24	0·19	0·10	4·80	123	118 (17), 64 (17)
1·91	2·06	1·42	1·55	1·21	1·10	4·68	−62	−49 (13), −135 (13)
1·39	1·28	0·85	0·67	0·75	0·87	4·08	71	66 (8), 118 (8)
1·91	2·06	1·81	1·93	1·49	1·37	3·87	−63	−63 (17), −121 (17)
0·46	0·31	0·41	0·26	0·56	0·46	3·46	−68	−66 (12), −108 (12)
0·57	0·41	0·46	0·31	0·41	0·51	3·06	99	116 (10), 64 (10)

* The value in parentheses corresponds to the maximum difference between the cluster's average and its individual contributors.

provided that the variance of the distribution is small, or the A value is large. Those estimates can be obtained easily by calculating the distributions for each of the eight possible sign combinations.

Naturally, invariant estimates bearing an eightfold ambiguity are of little or no use in the determination of the individual phases. However, while in principle eight possible estimates of the invariant are obtained, in practice these estimates are often clustered around two values. In particular, if one of the ξ angles is large as compared to the remaining two, then the eightfold ambiguity reduces to a twofold ambiguity as shown in Table 4. This suggests a phasing strategy, analogous to the one proposed for the single isomorphous replacement case (Fortier, Moore & Fraser, 1985). The eight possible estimates obtained by calculating the distribution for each of the eight sign combinations are divided into two clusters, and the average value for each of the two clusters is calculated. Differences between each cluster's average estimate and its contributors are computed, and the cosine of the largest difference is then used as a weight in the estimation of the associated A magnitude, *i.e.*

$$A(\text{av., wtd}) = \tfrac{1}{8}\sum A_i \times \cos\,(\text{max.}\,|\text{cluster estimate} - \text{contributor estimate}|),$$
$$i = 1, 2, 3, \ldots, 8. \qquad (52)$$

In this manner, the A magnitudes obtained reflect correctly the accuracy of the twofold invariant esti-

mate. The individual phases can then be determined from the twofold estimated invariants, provided that there exists a redundant set of accurately estimated invariants.

5. Concluding remarks

The presently available theory for the estimation of the three-phase structure invariants, *via* combined direct methods - anomalous dispersion techniques, has been reexamined. The analysis shows that these techniques do not yield one or two but rather eight possible estimates of the invariants. This, naturally, appears at first to limit severely the applicability of these techniques. Preliminary test calculations indicate, however, that in many cases the eight possible estimates are clustered around one or two values. Distinguishing these cases from those in which the eight estimates are widely scattered results in a significant gain in accuracy. Extensive calculations, based on the strategy described in § 4, are now in progress. Their results will be presented in the near future.

Details of the test calculations

All of the calculations were done using calculated diffraction data for the $PtCl_4^{2-}$ derivative of cytochrome c_{550} (Timkovich & Dickerson, 1973, 1976). The coordinates were obtained from the Protein Data Bank (Bernstein *et al.*, 1977). The calculations were done on a 16-bit PDP11/23 computer. The programs used were written by S. A. Potter and C. M. Weeks of the Medical Foundation of Buffalo, Inc., and adapted by Nancy J. Moore.

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Single-Crystal Structure of Rapidly Cooled Alloys with Icosahedral Symmetry. I. Experimental Analysis

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Abstract

Crystallographic analysis is applied to a set of electron diffraction patterns taken from a rapidly cooled Al-Mn alloy to construct reciprocal-lattice patterns in agreement with the observed icosahedral results. The analysis leads to a proposed atomic scale model which is derived from two sets of experimental modulations, each of which has six independent modulation vectors. The underlying structure has a lattice, the unit cell of which involves 32 atomic sites with the required symmetry properties. The appearance of the experimental electron diffraction patterns is explained either by the coherent arrangement of this