x_Z agrees with the statement by Ziman, x_Z being in the range 0·2 to 0·25.

It seems that melting begins in both solids if the amplitude of vibration $(\overline{u^2})^{1/2}$ reaches a value of about 12% of the radius of the space occupied by the atom.

The melting parameters considered here have been averaged over all directions of motion, and the observed anisotropy between $\overline{u_c^2}$ and $\overline{u_a^2}$ merits further study.

Table 2. *X-ray Debye temperatures* Θ_a *and* Θ_c [*estimated in Fig.* 1(*b*)], *and* Θ_{av} [*calculated with formula* (6)], *values for r* [*defined in* (5)], *and for x and* x_Z [*defined in* (3) *and* (4)]

	Θ_a (K)	Θ_c (K)	Θ_{av} (K)	r (Å)	x	x_Z
Zn	257	158·3	206·7	1·554	0·12	0·21
Cd	161	99·0	129·4	1·740	0·12	0·21

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Phase information from anomalous-scattering measurements.

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Abstract

The fundamental basis for alternative expressions for the phase probability distributions related to anomalous-scattering measurements is examined. Exact, general expressions are derived and these are then simplified for the special situations that normally apply in practice.

North (1965) and Matthews (1966) have described methods for incorporating the phase information from anomalous-scattering measurements into the isomorphous-replacement method in a way that properly takes into account the higher accuracy that is intrinsic to measurements of anomalous differences relative to those of isomorphous differences. These methods have proven to be very effective in protein crystallography. However, uncertainty has persisted as to the correct form for the error function to be used in phase probability distributions. Although North and Matthews formulate the problem somewhat differently, after using similar approximations in their derivations they seemingly arrive at the same result. Yet, varying interpretations have been put forward regarding valid forms for use in practice.

The purpose of this note is to clarify the basic origin of the alternative error expressions and to derive the appropriate expressions without approximation. Expressions that can be cast in the simplified representation of Hendrickson & Lattman (1970) are then seen to be based on an alternative error model rather than on questionable approximations.

Moreover, the exact expressions given here may be required in neutron diffraction where anomalous-scattering effects can be quite large. Expressions appropriate to phase information from anomalous scattering without isomorphous replacement are also given.

An isomorphous-replacement experiment that includes anomalous-scattering measurements presents, for each reflection *hkl*, three observations: the structure amplitude F_P from the native or 'parent' crystal structure and the structure amplitudes F_{PH}^+ and F_{PH}^- at *hkl* and its Friedel mate $\bar{h}\bar{k}\bar{l}$

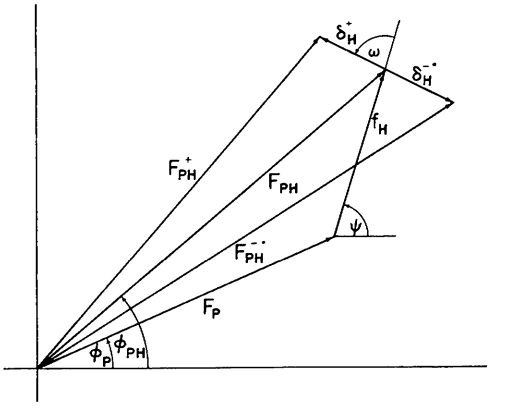

Fig. 1. Vector diagram showing relationships among the structure factors from an isomorphous-replacement experiment that include anomalous-scattering measurements. The vectors denoted $\mathbf{F}_{PH}^{-*}$ and $\boldsymbol{\delta}_H^{-*}$ are complex conjugates of structure factors for reflection $\bar{h}\bar{k}\bar{l}$ and all other vectors are structure factors for reflection *hkl*.

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respectively, from the isomorphous heavy-atom derivative. Provided that the structure is known for the isomorphously added heavy atoms in the derivative, the heavy-atom contributions to the derivative structure factors can be calculated. The contribution from the real part of the heavy-atom scattering is denoted $\mathbf{f}_H = f_H \exp(i\psi)$ and the imaginary part for hkl is $\boldsymbol{\delta}_H^+ = \delta_H \exp[i(\psi + \omega)]$ while that for $\bar{h}\bar{k}\bar{l}$ is $\boldsymbol{\delta}_H^- = \delta_H \exp[-i(\psi + \omega + \pi)]$. If all heavy atoms are of the same kind, $\omega = \pi/2$. In the absence of any errors, these data suffice to specify the desired native phase angle, φ_P. The vector relationships among these structure factors are shown in Fig. 1.

Of course, errors are not absent and must be reckoned with. Blow & Crick (1959) introduced a treatment of errors in the isomorphous-replacement method that can equally well be applied to anomalous-scattering data. Each phase value is assigned a probability of being correct,

$$P(\varphi) = N \exp[\varepsilon^2(\varphi)/2E^2], \tag{1}$$

based on the discrepancy $\varepsilon(\varphi)$ between theory and observation at the particular phase angle φ and the pertinent standard deviation of errors E. Blow & Crick define the lack-of-closure error for isomorphous replacement as

$$|\mathbf{F}_P + \mathbf{f}_H| = F_{PH} + \varepsilon_{\text{iso}}(\varphi_P), \tag{2}$$

but Hendrickson & Lattman (1970) showed that an alternative definition,

$$|\mathbf{F}_P + \mathbf{f}_H|^2 = F_{PH}^2 + \varepsilon'_{\text{iso}}(\varphi_P), \tag{3}$$

is equally plausible and has the advantage of producing a phase probability distribution that can be simply represented by four phase coefficients so that

$$P(\varphi) = N \exp(A \cos\varphi + B \sin\varphi + C \cos 2\varphi + D \sin 2\varphi). \tag{4}$$

Notice, though, that whereas the estimate of error for (2), E, is usually only slightly dependent on reflection intensity, the comparable value for (3), E', depends directly on F_{PH} and this complicates the estimation of expected error. However, Blundell & Johnson (1976) have shown (equation 12.24) that, for Gaussian distributions of error, E' is given directly by E and F_{PH}. Their result generalizes to $E'^2 = 3E^4 + 4(F_{PH}^2 + \sigma_{F_{PH}}^2)E^2$ when errors in F_{PH} are taken into account.

Alternative error definitions analogous to (2) and (3) can also be made in the case of anomalous scattering. Thus,

$$(|\mathbf{F}_P + \mathbf{f}_H + \boldsymbol{\delta}_H^+| - |\mathbf{F}_P + \mathbf{f}_H + \boldsymbol{\delta}_H^{-*}|) = (F_{PH}^+ - F_{PH}^-) + \varepsilon_{\text{ano}}(\varphi_P) \tag{5}$$

or

$$(|\mathbf{F}_P + \mathbf{f}_H + \boldsymbol{\delta}_h^+|^2 - |\mathbf{F}_P + \mathbf{f}_H + \boldsymbol{\delta}_H^{-*}|^2) = (F_{PH}^{+2} - F_{PH}^{-2}) + \varepsilon'_{\text{ano}}(\varphi_P). \tag{6}$$

In order to evaluate the lack-of-closure errors given in (5) and (6) for anomalous-scattering phase information, one must first analytically express the left-hand sides of these equations in terms of known quantities. In doing so it is helpful to abbreviate with the following definitions: $F_c \equiv |\mathbf{F}_P + \mathbf{f}_H|$, $F_c^+ \equiv |\mathbf{F}_P + \mathbf{f}_H + \boldsymbol{\delta}_h^+|$ and $F_c^- \equiv |\mathbf{F}_P + \mathbf{f}_H + \boldsymbol{\delta}_H^{-*}|$. Then, in the general case of arbitrary combinations of heavy atoms,

$$F_c^{+2} = F_P^2 + f_H^2 + \delta_H^2 + 2F_P f_H \cos(\psi - \varphi_P) + 2F_P \delta_H \cos(\psi + \omega - \varphi_P) + 2f_H \delta_H \cos\omega \tag{7}$$

and

$$F_c^{-2} = F_P^2 + f_H^2 + \delta_H^2 + 2F_P f_H \cos(\psi - \varphi_P) - 2F_P \delta_H \cos(\psi + \omega - \varphi_P) - 2f_H \delta_H \cos\omega. \tag{8}$$

Thus, the left-hand side of (6) is

$$(F_c^{+2} - F_c^{-2}) = 4F_P \delta_H \cos(\psi + \omega - \varphi_P) + 4f_H \delta_H \cos\omega. \tag{9}$$

Notice that if the relationships $F_c \sin\gamma = F_P \sin(\psi - \varphi_P)$ and $F_c \cos\gamma = F_P \cos(\psi - \varphi_P) + f_H$ [equations (18) of Matthews (1966)] are used, then (9) can be expressed in terms equivalent to those in equation (16) of Matthews (1966). The left-hand side of (5) can also be expressed in terms of (7) and (8) if one notes that

$$(F_c^+ - F_c^-) = \frac{(F_c^{+2} - F_c^{-2})}{[F_c^{+2} + F_c^{-2} + 2(F_c^{+2} F_c^{-2})^{1/2}]^{1/2}}. \tag{10}$$

The numerator in (10) is given by (9) and the denominator is

$$(F_c^+ + F_c^-) = \{2F_c^2 + 2\delta_H^2 + 2[F_c^4 + \delta_H^4 + 2F_c^2 \delta_H^2 - 4F_c^2 \delta_H^2 \cos^2(\psi + \omega - \varphi_c)]^{1/2}\}^{1/2}, \tag{11}$$

where

$$F_c = [F_P^2 + f_H^2 + 2F_P f_H \cos(\psi - \varphi_P)]^{1/2}$$

and φ_c is the phase of $\mathbf{F}_P + \mathbf{f}_H$.

Equations (9), (10) and (11) provide general and exact solutions for the lack-of-closure error as defined by either alternative (5) or (6). However, simplifications apply in most practical applications. Usually all heavy atoms will be of the same kind so that $\omega = \pi/2$ and in most situations δ_H will be small compared with F_c. These simplifications result in expressions that compare with those of North and Matthews (1966).

In the case that $\omega = \pi/2$, (9) reduces to

$$(F_c^{+2} - F_c^{-2}) = -4F_P \delta_H \sin(\psi - \varphi_P). \tag{12}$$

Moreover, good approximations can be made for (11) if δ_H is small compared with F_c. The expected value with respect to angle can be used to approximate (11) and this takes on a simple form if $\delta_H^4 \ll F_c^4$. To the slightly coarser approximation that $\delta_H^2 \ll F_c^2$, (11) simplifies further:

$$(F_c^+ + F_c^-) \simeq (4F_c^2 + 2\delta_H^2)^{1/2} \simeq 2F_c. \tag{13}$$

These approximations are good to better than 1% and 2% respectively if $\delta_H < 0{\cdot}2F_c$. Then, on defining $\Delta_H = (F_H^+ - F_H^-)$ and using (12) and (13) to evaluate (5), one obtains

$$\varepsilon_{\text{ano}}(\varphi_P) \simeq -\Delta_H - \frac{2F_P \delta_H}{F_c} \sin(\psi - \varphi_P). \tag{14}$$

Apart from slight differences in notation, this is equation (9) of Matthews (1966) and is equivalent to North's equation (6). Of course, with modern computers there is little to be gained by using the approximation of (13) and the exact formula with $(F_c^+ + F_c^-)$ rather than $2F_c$ should be preferred.

If (12) is substituted directly into (6), one obtains

$$\varepsilon_{\text{ano}}(\varphi_P) = -(F_{PH}^{+2} - F_{PH}^{-2}) - 4F_P\,\delta_H \sin(\psi - \varphi_P). \qquad (15)$$

Errors from model (6) are related to those from model (5) by $\varepsilon'_{\text{ano}} = (F_c^+ + F_c^-)\,\varepsilon_{\text{ano}} + \Delta_H(F_c^+ + F_c^- - 2F'_{PH})$. On evaluating the appropriate expected values at best estimates of correct phase angles, standard deviations for use in (1) are related as $E'^2 \simeq 4\{(F_{PH}^2 + \sigma^2_{F_{PH}} + \langle \Delta F_{PH}^2 \rangle)E^2 + \langle \Delta_H^2 \rangle \langle \Delta F_{PH}^2 \rangle\}$, where $\langle \Delta F_{PH}^2 \rangle \equiv \langle (F_c - F'_{PH})^2 \rangle$. Hence, E' values will be very sensitive to intensity whereas E values are not. Another, but essentially equivalent, error can be defined by dividing through both sides of (15) with $(F_{PH}^+ + F_{PH}^-)$. Then

$$\varepsilon''_{\text{ano}}(\varphi_P) = -\Delta_H - \frac{2F_P\,\delta_H}{F'_{PH}} \sin(\psi - \varphi_P), \qquad (16)$$

where the additional definitions that $F'_{PH} \equiv \frac{1}{2}(F_{PH}^+ + F_{PH}^-)$ and $\varepsilon''_{\text{ano}}(\varphi) \equiv \varepsilon'_{\text{ano}}(\varphi)/2F'_{PH}$ are used. This is the same expression as that suggested by North (1965) to be valid in practice and given textbook legitimacy by Blundell & Johnson (1976) (equation 12.18). Expectation values for the errors defined in (15) and (16) are related as $E''^2 = E'^2/(F_{PH}'^2 + \sigma^2_{F'_{PH}})$. Hence, provided that errors in F'_{PH} are insignificant compared with the magnitude of F'_{PH}, (16) and (15) will give identical phase probability distributions. Thus, at least in the absence of error in F'_{PH}, (16) is seen to be an exact consequence of an alternative error model rather than a questionable approximation for (14). The effect of errors in F'_{PH} is to sharpen unduly the probability distribution from (16) relative to that expected from the basic error model given by (15). It should be possible to compensate for this effect by modifying the standard deviations for use with (16) so that $E''^2 = \langle \varepsilon''^2 \rangle (F_{PH}'^2 + \sigma^2_{F'_{PH}})/F_{PH}'^2$, although the singularity at $F'_{PH} = 0$ cannot be avoided except in the absence of error.

Paralleling the analogy between (3) and (6), both (15) and (16) can be expressed in the simplified representation of (4) and the phase coefficients for (16) have already been given by Hendrickson & Lattman (1970), whereas the expressions derived from (2) and (5) cannot be so expressed. There is a practical advantage to using (16) rather than (15) since standard deviations will then be relatively independent of structure-factor amplitudes and this will facilitate the numerical evaluation of these crucial parameters. This suggests that a relationship analogous to (16) but derived from (3) might be advantageous for isomorphous-replacement information.

Error expressions analogous to (5) and (6) can also be developed for phase information from anomalous scattering without isomorphous replacement. In this case F_P is not measured and it is the phase of $\mathbf{F}_{PH}$ that is desired. The amplitude F_{PH} is also unobservable, but this can readily be estimated, from the relationship $|\mathbf{F}_{PH} + \boldsymbol{\delta}_H^+|^2 + |\mathbf{F}_{PH} + \boldsymbol{\delta}_H^{-*}|^2 = F_{PH}^{+2} + F_{PH}^{-2}$, to be

$$F_{PH} = [\tfrac{1}{2}(F_{PH}^{+2} + F_{PH}^{-2}) - \delta_H^2]^{1/2}. \qquad (17)$$

To the level of approximation that $\delta_H^2 \ll F_{PH}^2$, $F'_{PH} \equiv (F_{PH}^+ + F_{PH}^-)$ gives a good estimate of F_{PH} but F'_{PH} will always be an underestimate. In general, (17) is to be preferred both here and for use in (2) and (3) for isomorphous-replacement calculations. The relationship analogous to (9) for the case of anomalous scattering without isomorphous replacement is

$$(F_c^{+2} - F_c^{-2}) = 4F_{PH}\delta_H \cos(\psi + \omega - \varphi_{PH}). \qquad (18)$$

Then if F_{PH} is identified with F_c in (11), (11) together with (10) and (18) suffice to provide the lack-of-closure errors for this case. Results for the special case that $\omega = \pi/2$ can be found by substituting φ_{PH} for φ_P and F_{PH} for F_P and F_c in (14), (15) and (16). Then, to the level of approximation that $\sigma_H^2 \ll F_{PH}^2$, (14) and (16) both reduce to

$$\varepsilon_{\text{ano}}(\varphi_{PH}) = \varepsilon''_{\text{ano}}(\varphi_{PH}) \simeq -\Delta_H - 2\delta_H \sin(\psi - \varphi_{PH}), \qquad (19)$$

which is equivalent to equation (22) of Matthews (1970). Obviously, apart from changes in notation, (17)–(19) apply equally well to a native structure containing anomalous scatterers.

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