THE USE OF SIGN RELATIONSHIP IN THE
DETERMINATION OF HEAVY ATOM CONTAINING
CRYSTAL STRUCTURES

II. "COMPONENT RELATIONSHIP" AND ITS APPLICATION

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ABSTRACT

*In Part I of this article, the possibility of combining the
"heavy atom method" and the "sign relation method" was pointed out,
and a sign-refinement procedure was suggested to replace the ordinary
successive electron density syntheses. The present part deals with the
problems concerning the further combination of the previously
suggested procedure with the isomorphous replacement method or with
the anomalous scattering method in the case of noncentrosymmetric crystals.*

INTRODUCTION

In the case of noncentrosymmetric crystals, it is generally suggested
that the heavy atom method, the isomorphous replacement method, anamalous
scattering method or the like to obtain the phase angles of the structure
amplitudes. The phase angle of the heavy atom has been considered
as the basis. The author has pointed out in reference (1) the possibility
of refining the phase angle of the heavy atom by means of the sign
relationship. This possibility was further verified with respect to a
hypothetical centrosymmetric crystal. If we are able to imitate the
centrosymmetric conditions to establish a "structure amplitude component
relationship" for the noncentrosymmetric case, then we may be able to
suggest a sign-relation method to combine with the procedure of the heavy
atom method, the isomorphous replacement method or anomalous scattering
method for the noncentrosymmetric crystals.

I THE SIGNIFICANCE OF THE "COMPONENT SERIES" AND THE "COMPONENT RELATIONSHIP"

In the case of noncentrosymmetric crystals, the electron density distribution
function may be written

$$\rho(\mathbf{r}) = \Phi^{-1}(F_H) = \Phi^{-1}(A_H) + \Phi^{-1}(iB_H) \equiv \rho_A(\mathbf{r}) + \rho_B(\mathbf{r}), \qquad (1)$$

in which $\rho(\mathbf{r})$ is the electron density distribution function; F_H is the
structure amplitude with a diffraction index of H; $\Phi^{-1}(F_H)$ stands for the
Fourier inverse of F_H; A_H and B_H are the real and imaginary components of
F_H respectively; $\rho_A(\mathbf{r})$ and $\rho_B(\mathbf{r})$ can be called the real component series
and imaginary component series for the time being. It is easily seen that

$$\rho_A(\mathbf{r}) \equiv \Phi^{-1}(A_H) = \frac{1}{2}\Phi^{-1}(F_H + F_H^*) = \frac{1}{2}\rho(\mathbf{r}) + \frac{1}{2}\rho(-\mathbf{r}), \qquad (2)$$

$$\rho_B(\mathbf{r}) \equiv \Phi^{-1}(iB_H) = \frac{1}{2}\Phi^{-1}(F_H - F_H^*) = \frac{1}{2}\rho(\mathbf{r}) - \frac{1}{2}\rho(-\mathbf{r}), \qquad (3)$$

in which F_H^* is the complex conjugate of F_H.

Hence, it is seen that the electron density distribution function of the noncentrosymmetric crystals is in substance composed by the two parts, $\rho_A(r)$ and $\rho_B(r)$. The former is equivalent to a centrosymmetric structure, which contains the original structure ρ (r) and its central mirror body ρ (-r) the latter corresponding to a central anti-symmetric structure containing the original structure $\rho(r)$ and its noncentral mirror body $-\rho$ (-r). The structure amplitude of $\rho_A(r)$ is A_H; the structure amplitude of $\rho_B(r)$ is iB_H. Since A_H and B_H are all real numbers, we may anticipate the relationship of the structure amplitude of the central symmetric crystals among them.

From equations (2) and (3), we have

$$\frac{1}{2}[\rho_A^2(\mathbf{r}) + \rho_B^2(\mathbf{r})] = \frac{1}{4}\rho^2(\mathbf{r}) + \frac{1}{4}\rho^2(-\mathbf{r}) \equiv \rho_A^{sq}(\mathbf{r}), \qquad (4)$$

$$\rho_A(\mathbf{r})\rho_B(\mathbf{r}) = \frac{1}{4}\rho^2(\mathbf{r}) - \frac{1}{4}\rho^2(-\mathbf{r}) \equiv \rho_B^{sq}(\mathbf{r}). \qquad (5)$$

According to the principle of the Fourier transform, the Fourier transform of the product of two functions g_1 and g_2 is equal to the product of the Fourier transforms $\Phi(g_1)$ and $\Phi(g_2)$ of the two functions g_1 and g_2. Hence, obtaining the Fourier transforms for equations (4) and (5), we have

$$\frac{1}{2V}\left[\sum_{H'}A_{H'}A_{H-H'} - \sum_{H'}B_{H'}B_{H-H'}\right] = \Phi[\rho_A^{sq}(\mathbf{r})] \equiv A_H^{sq}, \qquad (6)$$

$$\frac{1}{V}\sum_{H'}A_{H'}B_{H-H'} = \frac{1}{i}\Phi[\rho_B^{sq}(\mathbf{r})] \equiv B_H^{sq}, \qquad (7)$$

in which V is the cell volume.

If there is no atomic overlapping phenomenon in $\rho(r)$, then the atomic distributions of the structures $\rho_A^{sq}(\mathbf{r})$ and $\rho_B^{sq}(\mathbf{r})$ will be the

same as the atomic distribution of $\rho_A(r)$ and $\rho_B(r)$ respectively, and only

differing in atomic forms. If $\rho(r)$ only contains two kinds, light and heavy atoms P and Q, we have [1]

$$A_H^{sq} = \frac{1}{2}\left[\frac{1}{\varphi_P} A_H + \left(\frac{1}{\varphi_Q} - \frac{1}{\varphi_P}\right)(A_H)_Q\right], \qquad (8)$$

$$B_H^{sq} = \frac{1}{2}\left[\frac{1}{\varphi_P} B_H + \left(\frac{1}{\varphi_Q} - \frac{1}{\varphi_P}\right)(B_H)_Q\right], \qquad (9)$$

in which $\varphi = f/f^{sq}$ f being the scattering factor, i.e., the Fourier transform $\Phi(\rho_j)$ of an atomic electron density distribution function ρ_j; f^{sq} is the

scattering factor of the "square atom", or $\Phi(\rho_j^{sq})$; $(A_H)_Q$ and $(B_H)_Q$ are

the real and imaginary components of the heavy atom diffraction structure amplitude. Substituting equations (8), (9) into (6) and (7), we have

$$A_H = \frac{\varphi_P}{V}\left[\sum_{H'} A_{H'} A_{H-H'} - \sum_{H'} B_{H'} B_{H-H'}\right] - \left(\frac{\varphi_P}{\varphi_Q} - 1\right)(A_H)_Q, \qquad (10)$$

$$B_H = \frac{2\varphi_P}{V}\left[\sum_{H'} A_{H'} B_{H-H'}\right] - \left(\frac{\varphi_P}{\varphi_Q} - 1\right)(B_H)_Q. \qquad (11)$$

If in addition to the absence of superposition phenomenon of $\rho(r)$ per se, there is no overlapping between $\rho(r)$ and $\rho(-r)$, then after squaring separately equations (2) and (3) and according to the above derivations, we

$$A_H = \frac{2\varphi_P}{V}\sum_{H'} A_{H'} A_{H-H'} - \left(\frac{\varphi_P}{\varphi_Q} - 1\right)(A_H)_Q, \qquad (12)$$

$$A_H = \frac{-2\varphi_P}{V}\sum_{H'} B_{H'} B_{H-H'} - \left(\frac{\varphi_P}{\varphi_Q} - 1\right)(A_H)_Q. \qquad (13)$$

Although there will be more restrictions on equations (12) and (13), yet their forms are far more simpler than those of equations (10) and (11). Prior to the use of equations (10) through (13), it is necessary to find the positions of the heavy atoms, which are not difficult to find. If there are more than one kind of heavy atoms, as long as their positions are known, it will not be difficult to add the refinement terms to the equations (10) through (13).

II POSSIBLE APPLICATIONS

1. Refinement of Heavy Atom Phase Angle

In the previous article[1] it was obvious that the discussions regarding the interrelations of the structure amplitude sign, Sayre equation and the heavy atom sign can be wholly applicable to equations (10) through (13). Hence, for non-centrosymmetric crystals, the sign-refinement procedure suggested in reference [1] may be used to replace the successive electron density syntheses. The only difference is to treat the structure amplitude separately according to its real and imaginary parts in addition to the sign-refinement of A_H and B_H during the refinement procedure as well as the successive refinement of the absolute values of A_H and B_H. Furthermore, the A_H and B_H of the first round will be approximately replaced by $\dfrac{(A_H)_0}{\sqrt{(A_H)_0^2 + (B_H)_0^2}}|F_H|$ and $\dfrac{(B_H)_0}{\sqrt{(A_H)_0^2 + (B_H)_0^2}}|F_H|$ respectively.

2. Selection of the Phase Angle in the Two Solutions by the Isomorphous Replacement Method

If we have two isomorphous crystals, in which one contains atoms P and Q_1, and the other contains P and Q_2, then their structure amplitudes are respectively

$$F_1 = F_P + F_{Q_1}, \quad F_2 = F_P + F_{Q_2},$$

therefore,

$$F_2 - F_1 = F_{Q_2-Q_1}.$$

Now, we only need to know $|F_2|$, $|F_1|$, and $F_{Q_2-Q_1}$, and we shall be able to solve for a possible pair of phase angles, which are symmetric with $_\alpha Q2\text{-}Q1$ (see Fig. 1).
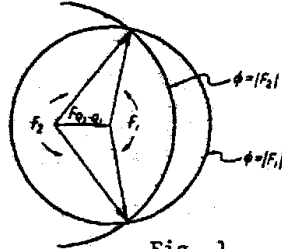

Fig. 1

In order to find the only solution, we may use anomalous scattering data or the diffraction data of a third isomorphous crystal (with the position of the replaced atom different from those of the original two crystals). However, this would enhance technical difficulties, especially the latter method mentioned above which is usually difficult to materialize except for large molecular crystals, such as proteins etc... Ramachandran and Raman[2] and Blow and Rossman[3] have independently suggested

method of combination of the isomorphous replacement method or anomalous
sattering method, which would enable to obtain the actual electron density maps
without additional experimental data. Their method, however, has failed to
solve the two-solution problem for all practical purposes, and merely taken the average
of the two phase angles. As a result of this practice, more serious errors and
distortions in the electron density maps have occurred. Furthermore, their
ethod is not applicable for those replaced atoms possessing centrosymmetric
distributions. Should we consider the equations (10) and (11), regardless of the
distribution of the replaced atoms, it is always possible to select the correct
solution. We shall state it as follows:

1) For replaced atoms with noncentrosymmetric distribution:

For every given H' we have two pairs of possible structure amplitude components
A_H, B_H and A_H, B_H. Let $\quad \langle A_{H'} \rangle = \frac{1}{2}(A'_{H'} + A''_{H'})$;

$\langle B_{H'} \rangle = \frac{1}{2}(B'_{H'} + B''_{H'})$.
Substituting the above into the A_H
and B_H, in the "Σ" of the right sides of the equations (10) and (11), we may find
the A_H and B_H on the left sides by <u>successive</u> approximations. Compare these values
with the two solutions, then the <u>closer value</u> would be the more exact solution.
In order to obtain more reliable result, we may use the successive refinement
procedure cited in reference (1). For all practical purposes, the above procedure
is essentially the combination of the isomorphous replacement method, heavy atom
method and the sign relation method.

(2) For replaced atoms with centrosymmetric distribution: From the two solutions
we may find $A_H \mid B_H \mid$ and $(A_H)_Q$ [Notice that $(B_H)_Q \equiv 0$]. Now the problem
has been narrowed down to finding the sign of B_H. Substituting the above data
into equations (10) and (11), we may find the relation among the values of B_H.
Similar to the structure amplitude sign method for centrosymmetric crystals, it
is possible to find the signs of the majority of the B_H's from which the correct
phase angle can be determined. For all practical purposes, this method is the
combination of the sign relation method and the isomorphous replacement method.

3. Selection of the Phase Angle in the Two Solutions by the Anomalous Scattering
   Method

If the crystal contains the atoms P and Q, and Q produces anomalous scattering
with respect to the incoming wave, then the structure amplitude can be divided
into two components - one being the normal contributions from all the atoms plus
the anomalous correction of the real part of the Q atom; the other component being
the anomalous correction of the imaginary part of the Q atom, i.e.

$$F(H) = F'(H) + F''_Q(H),$$
$$F(\overline{H})^* = F'(\overline{H})^* + F''_Q(\overline{H})^* = F'(H) - F''_Q(H),$$

therefore

$$F(H) - F(\overline{H})^* = 2F''_Q(H),$$

in which F* is the complex conjugate of F.

Now, if we only know $|F(H)|$, $|\overline{F(H)}|$ and F''(H), a pair of possible phase angle can be solved, which are antisymmetric with respect to $F_Q(H)$ -- the normal structure amplitude of a Q atom (Fig. 2). There are various methods to eliminate the two-solution. For instance, use the diffraction data of another kind of wavelength, or use those of an isomorphous crystal. But this tends to complicate the experimental work. Raman[4,5] has pointed out that in the light of not increasing the experimental data, this problem can be solved by means of the "Double Phase Angle Syntheses" or the "Heavy Atom Identification" method. However, the result is not yet satisfactory. It is possible to improve the degree of reliability of Raman method with the aid of the equations (10) and (11). We shall consider the following two cases:

(1) If the anomalous atoms have a noncentrosymmetric
      distribution:

Now, similar to the case by the isomorphous replacement method, it is possible to find two pairs of the components of A_H' and B_H' for every given H'. But at this moment the two solutions due to their antisymmetry to $F_Q(H)$ has at least one pair of A_H, and B_H, which is closer to $F_Q(H)$. Substituting such values of A_H and B_H' into the "Σ" on the right side of the equations (10) and (11), A_H and B_H can then be found by successive approximation. After a cyclic refinement procedure more reliable results can be obtained.
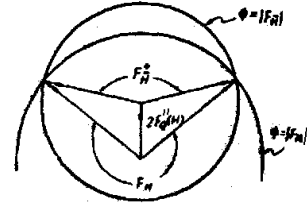

Fig. 2

(2) If the anomalous atoms have a centrosymmetric
      distribution:

From the two solutions we may find A_H, B_H and $(A_H)_Q$ notice that $(B_H)_Q = 0$. Now, the problem has been narrowed down to finding the sign of A_H. By substituting the above data into the right side of equation (10), the sign of A_H, equal to that of $(A_H')_Q$, and A_H can be calculated. After cyclic refinement procedure, the correct sign of A_H can be found.

The two procedures mentioned above are equivalent to using Raman's "heavy atom identification" method to find the initial A_H and B_H, further refined with equations (10) and (11).

4. To Find the unknown phase angle from a known one

There is an obvious use for equations (10) and (11), i.e., when the majority of the phase angles are known, the unknown A_H and B_H can be successively computed by substituting the corresponding A_H' and B_H'. If necessary, cyclic refinement can also be carried out. This is useful to supplement the heavy atom method, since certain occasional distributions of the heavy atoms often make the phase

angles of a portion of the diffraction spots (sometimes involving a large quantity of diffraction spots) difficult or even failed to yield any clue from the positions of the heavy atoms. Now, by using the equations (10) and (11), great improvement on the electron density maps may be made. The author will make detailed discussions in another article, regarding the application in this respect.

In the procedures mentioned above, and if the non-overlapping condition of $\rho(r)$ and $\rho(-r)$ can be satisfied, we may replace equation (10) by the equations (12) and (13). If the non-overlapping condition cannot be fully satisfied, we may also use equations (12) and (13) to find an approximate result in order to simplify computations.

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<div align="center">REFERENCES</div>

[1] Fan Hai-fu, Acta Physica Sinica, 21 (1965), 1105
[2] Ramachandran, G.N. and Raman, S. Acta Cryst., 12 (1959), 957
[3] Blow, D. M. and Rossman, M.G., Acta Cryst., 14 (1961), 1195
[4] Raman, S. Proc. Ind. Acad. Sci., 47A (1958), 1.
[5] Raman, S.,Z. Krist., 111 (1959), 301.

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