

Combining Direct Methods with Isomorphous Replacement or Anomalous Scattering Data. V. Comparison of Different Phasing Methods in the OAS Case

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(Received 14 December 1984; accepted 1 March 1985)

Abstract

Different methods for resolving the phase ambiguity resulting from the OAS (one-wavelength anomalous scattering) technique are compared in the application to two model protein structures. It is concluded that the information from both Sim's and Cochran's distributions is valuable in separating the phase doublets. However, the combination of Sim's and Cochran's distributions can lead to a better result than that obtainable by using either alone.

Introduction

OAS data are important in the determination of protein structures. However, the successful use of the OAS technique relies on the discrimination of the phase doublets. Different methods have been proposed for this purpose. Hendrickson & Teeter (1981) proposed a method of resolving the phase ambiguity by making use of Sim's distribution. The method has been successfully used to solve some unknown protein structures. Fan Hai-fu (1965, 1984) suggested that triplet phase relationships may be used to break the phase ambiguity. This has been verified with a known protein structure (Gu Yuan-xin, Fan Hai-fu, Zheng Chao-de & Han Fu-son, 1985). In the present work, Sim's distribution, Cochran's distribution and the combination of Sim's and Cochran's distributions are compared for their efficiency in resolving the phase ambiguity arising from the OAS technique.

Method

The phase of a given reflection can be expressed as follows (see Fan Hai-fu & Gu Yuan-xin, 1985):

$$\varphi_{\mathbf{H}} = \varphi'_{\mathbf{H}} + \Delta\varphi_{\mathbf{H}}. \quad (1)$$

In the OAS case, if there is only one kind of anomalous scatter in the structure,

$$\varphi'_{\mathbf{H}} = \varphi_{\mathbf{H},A} + \pi/2, \quad (2)$$

where $\varphi_{\mathbf{H},A}$ is the phase of

$$\mathbf{F}_{\mathbf{H},A} = \sum_{A=1}^{N_A} (f_A + \Delta f'_A) \exp[i2\pi\mathbf{H}\cdot\mathbf{r}_A]. \quad (3)$$

The subscript A denotes the anomalous scattering atoms. $|\Delta\varphi_{\mathbf{H}}|$ can be calculated with the following expression:

$$\Delta\varphi_{\mathbf{H}} = \pm \cos^{-1}[(F_{\mathbf{H}}^+ - F_{\mathbf{H}}^-)/2F''_{\mathbf{H},A}], \quad (4)$$

where $F''_{\mathbf{H},A}$ is the modulus of

$$F''_{\mathbf{H},A} = i \sum_{A=1}^{N_A} \Delta f''_A \exp[i2\pi\mathbf{H}\cdot\mathbf{r}_A]. \quad (5)$$

As the species and positions of the anomalous scattering atoms are known, $\varphi'_{\mathbf{H}}$ and $|\Delta\varphi_{\mathbf{H}}|$ can be calculated. Hence, the problem of breaking the phase ambiguity reduces to that of finding the signs for the $\Delta\varphi_{\mathbf{H}}$'s. Three different methods for deriving the sign of $\Delta\varphi_{\mathbf{H}}$ are considered below.

1. Use of Sim's distribution

According to Sim (1959), if some part of the structure is known, the distribution of the phase difference, θ , between the phase contributed from the whole structure and that from the known part can be expressed as

$$P(\theta) = [2\pi I_0(x)]^{-1} \exp(x \cos \theta). \quad (6)$$

This can be used to predict the signs of the $\Delta\varphi_{\mathbf{H}}$'s. In the OAS case, the known part of the structure consists of anomalous scattering atoms. Hence, if we neglect the effect of anomalous dispersion on the algebraic form of Sim's distribution,

$$\theta = \varphi_{\mathbf{H}} - \varphi_{\mathbf{H},A} \quad (7)$$

and

$$x = 2E_{\mathbf{H}}E_{\mathbf{H},A} \left(\frac{\sum_j Z_j^2}{\sum_u Z_u^2} \right), \quad (8)$$

where \sum_j means sum over the entire unit cell and \sum_u means sum over the unknown part of the unit cell. The expected value of $\cos \theta$ is thus

$$\int_0^{2\pi} \cos \theta P(\theta) d\theta = I_1(x)/I_0(x), \quad (9)$$

which varies between 0 and 1 according to the value of x . Hence we can write approximately the expected value of θ as

$$-\pi/2 \leq \theta_{\text{exp}} \leq \pi/2. \quad (10)$$

On the other hand, from (1), (2) and (7) it follows that

$$\Delta\varphi_H = \theta - \pi/2. \quad (11)$$

Accordingly we have

$$\Delta\varphi_{H_{exp}} \leq 0. \quad (12)$$

In other words, according to Sim's distribution, the 'expected' sign of $\Delta\varphi_H$ will always be negative whatever the value of x . This prediction may be mainly correct when the crystal structure contains relatively 'heavy' anomalous scatterers, but will not be reliable in other cases.

2. Use of Cochran's distribution

If the phase doublet information is incorporated into Cochran's distribution (Cochran, 1955), then the probability for $\Delta\varphi_H$ to be positive is given by (Fan Hai-fu, Han Fu-son & Qian Jin-zi, 1984):

$$P_+(\Delta\varphi_H) = \frac{1}{2} + \frac{1}{2} \tanh [2\sigma_3\sigma_2^{-3/2} E_H \sin |\Delta\varphi_H| \times \sum_{H'} m_H m_{H-H'} E_{H'} E_{H-H'} \times \sin (\Phi_3' + \Delta\varphi_{H'_{best}} + \Delta\varphi_{H-H'_{best}})], \quad (13)$$

where

$$m_H = \exp(-\sigma_H^2/2) \{ [2(P_+ - \frac{1}{2})^2 + \frac{1}{2}] \times (1 - \cos 2\Delta\varphi_H) + \cos 2\Delta\varphi_H \}^{1/2} \quad (14)$$

and

$$\tan (\Delta\varphi_{H_{best}}) = 2(P_+ - \frac{1}{2}) \sin |\Delta\varphi_H| / \cos \Delta\varphi_H. \quad (15)$$

The calculation should start with substituting $P_+ = \frac{1}{2}$ into (14) and (15), then a new set of $P_+(\Delta\varphi_H)$ can be obtained using (13). Unlike the method described above, the sign of $\Delta\varphi_H$ derived by (13) will obviously not always be negative. Moreover, with (13), the sign of a given $\Delta\varphi_H$ is determined by a large set of reflections ranging over the reciprocal space and not by quantities just related to only one reflection. On the other hand, there is a weak point in (13), i.e. no modification to Cochran's distribution has been made in order to take into account the *a priori* knowledge of the anomalous scatterers. This may give rise to a non-negligible error, if the anomalous scatterers are rather 'heavy' or numerous.

3. Use of the combined information contained in Cochran's and Sim's distributions

If Cochran's and Sim's distributions are combined to deal with the OAS data, we have instead of (13) the following expression (Fan Hai-fu & Gu Yuan-xin, 1985):

$$P_+(\Delta\varphi_H) = \frac{1}{2} + \frac{1}{2} \tanh \{ [2\sigma_3\sigma_2^{-3/2} E_H \sin |\Delta\varphi_H| \times \sum_{H'} m_H m_{H-H'} E_{H'} E_{H-H'} \times \sin (\Phi_3' + \Delta\varphi_{H'_{best}} + \Delta\varphi_{H-H'_{best}})] + x \}. \quad (16)$$

Table 1. Results for the calculation of signs of $\Delta\varphi_H$'s for the 1000 largest E 's from Hg-APP

%: percentage of reflections with the sign of $\Delta\varphi_H$ correctly determined.

ER: averaged phase error in degrees.

Group	Number of reflections	Method 1		Method 2		Method 3	
		%	ER	%	ER	%	ER
1	200	88.0	11	87.0	16	100.0	0
2	400	88.8	10	74.3	31	97.8	2
3	600	89.0	9	67.5	37	96.3	4
4	800	87.9	10	64.0	40	93.3	8
5	1000	86.1	12	60.4	40	87.1	11

The use of (16) is similar to that of (13). When the crystal contains relatively 'heavy' anomalous scatterers, then x in (16) becomes non-negligible, and (16) may give a better result than that obtained by (13). On the other hand, if the anomalous scatterers are relatively 'light', the result from (16) will be nearly the same as from (13).

Comparison

1. Data

Error-free data from two model structures, Hg-APP (Hg derivative of avian pancreatic polypeptide) and RFC (rice ferricytochrome C), were used for the comparison.

APP crystallizes in space group $C2$ with $a = 34.18$, $b = 32.9$, $c = 28.44$ Å, $\beta = 105.30^\circ$ and $Z = 4$. There are about 2100 independent reflections at 2.1 Å resolution for Hg-APP.

RFC crystallizes in space group $P6_1$ with $a = 43.78$, $c = 110.05$ Å and $Z = 6$. The structure contains Fe atoms as anomalous scatterers. There are about 6000 independent reflections at 2 Å resolution.

1000 largest E 's and 60 000 strongest \sum_2 relationships from each structure were used in the test calculation.

2. Results

Table 1 shows the results of the three methods using the data of Hg-APP. For method 1, the 1000 reflections were arranged in descending order of the value of x and then cumulated into five groups, which contain the top 200, 400, 600, 800 and all reflections, respectively. For methods 2 and 3, the reflections were arranged in descending order of $|P_+ - \frac{1}{2}|$ and cumulated as above. In this example, the anomalous scatterers (Hg) are comparatively heavy. Method 1 gives better results than method 2. However, the best result came from method 3.

Table 2 shows the results from RFC. In this example, the contribution of the anomalous scatterers (Fe) is not as significant as that of Hg in the above

Table 2. Results for the calculation of signs of $\Delta\varphi_H$'s for the 1000 largest E 's from RFC

%: percentage of reflections with the sign of $\Delta\varphi_H$ correctly determined.

ER: averaged phase error in degrees.

Group	Number of reflections	Method 1		Method 2		Method 3	
		%	ER	%	ER	%	ER
1	200	70.0	29	92.0	11	93.5	8
2	400	65.0	31	82.3	20	89.5	12
3	600	64.2	31	76.2	24	78.8	21
4	800	60.9	34	70.0	28	72.8	24
5	1000	56.9	38	65.9	27	67.8	25

example. The results of methods 2 and 3 are nearly the same and both are better than that of method 1.

It is concluded from the comparison that method 3 is the best among the three.

The authors are indebted to Professor N. Tanaka and FHF is indebted to Professor T. L. Blundell for making available the RFC and APP data, respectively.

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Structure Analysis of Displacively Modulated Molecular Crystals

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(Received 29 October 1984; accepted 8 March 1985)

Abstract

A structure-factor formalism for incommensurate modulated structures is derived. It allows for several simultaneous translational and rotational displacements of molecules or molecular segments, which are considered as being rigidly displaced. It incorporates treatment of several displacement waves in the crystal and makes full use of the four-dimensional symmetry description of de Wolff, Janssen & Janner [*Acta Cryst.* (1981), **A37**, 625-636]. A computer program based on the formalism has been applied to existing data sets on phenothiazine-TCNQ [Kobayashi (1974). *Acta Cryst.* **B30**, 1010-1017] and biphenyl [Baudour & Sanquer (1983). *Acta Cryst.* **B39**, 75-89], and to a new data set on [bis(ethylenedithio)-TTF]₂I₃ [Leung *et al.* (1984). *J. Am. Chem. Soc.* **106**, 7644-7646].

Introduction

It has become increasingly clear in the past years that modulated crystal structures are more common than

previously expected. In particular the recent interest in conducting organic solids has led to the discovery of a great many incommensurate phases of molecular crystals, each stable in a certain temperature domain, which can be described with formalisms developed for application to minerals, alloys and other inorganic solids. In many cases the transition to the modulated structure corresponds to a change from a metallic to an insulating state (*i.e.* a Peierls transition), in others the transport properties are much less affected. In all cases a knowledge of the geometry of the distortion is important for the understanding of the mechanism of the transition and the transport properties in the modulated state. Intermolecular distances and molecular overlap, for example, may show large local variations from the average over the whole crystal.

Scattering formalisms for modulated structures have been discussed by Overhauser (1971), de Wolff (1974), Axe (1980) and Yamamoto (Yamamoto, Nakazawa & Tokonami, 1979). They take into account substitutional or displacive modulations of each of the atoms in the crystal. In molecular crystals, however, a translational or rotational displacement of a molecule, or one of its segments, is more likely because of the stiffness of the intramolecular linkages between atoms. Such a *rigid body displacement analy-*

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