Phase Refinement by a Fourier Transformation of Difference Electron Density Peaks

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A method to refine phases by a numerical Fourier transformation of difference electron density peaks is described. It was tested with an artificial two-dimensional structure of $NaNO_2$. Starting from the phases of a spherical-free-atom model, those of the hypothetical true structure of aspherical atoms were reproduced fairly well after five cycles. The scale factor of the structure factors was also improved by the refinement.

Introduction

In a non-centrosymmetric structure, the phases of X-ray structure factors estimated on the basis of a spherical-free-atom model may be appreciably in error. Since these phase errors have a pronounced effect on the difference density, a quantitative analysis of the electron distribution is impossible unless the phases are further refined (Maslen, 1968; Coppens, 1974). In the present paper, we propose a method for such refinement. The phases are refined by a Fourier transformation of difference electron density peaks in this method (the FDP method).

The FDP method

Principle of the method

The principle of the FDP method can be expressed as

$$\mathbf{F}_c' = \mathbf{F}_c + \mathscr{F}^{-1}\{\Delta\varrho(\text{peaks})\}, \tag{1}$$

where $\mathbf{F}_c$ and $\mathbf{F}_c'$ are the calculated X-ray structure factors before and after phase refinement respectively, $\Delta\varrho$ is the difference electron density, and $\mathscr{F}^{-1}$ denotes the inverse Fourier transformation:

$$\mathscr{F}^{-1}\{\Delta\varrho\} \equiv V \iiint \Delta\varrho(x,y,z)$$
$$\times \exp\left[2\pi i(hx+ky+lz)\right]dxdydz, \tag{2}$$

where V is the unit-cell volume, and the integration extends over the unit cell. Although the difference peaks are usually underestimates of the true peaks in a non-centrosymmetric structure (Coppens, 1974), if we pick up only meaningful peaks, $\Delta\varrho(\text{peaks})$, and transform them, the refined $\mathbf{F}_c'$ will be a better approximation to the true structure factor than the starting $\mathbf{F}_c$.

As is evident from (1) the FDP method is analogous to the Fourier phase refinement ordinarily used for structure analysis (Hoppe, Gassmann & Zechmeister, 1970). However, in the FDP method we deal with the

difference electron density instead of the electron density; the former is almost free from the series-termination effect and is more suitable for a fine phase refinement than the latter.

Computational procedure

The FDP method is an iterative Fourier transformation method. The ith cycle consists of the following three steps.

(1) Estimate the scale factor of the observed structure factor F_o, since it is usually unknown. In the test calculations, a simple scaling with reference to F_c of the previous cycle was employed:

$$k^{(i-1)} = \sum F_c^{(i-1)} / \sum F_o, \tag{3}$$

where $F_c^{(0)}$ in the first cycle is the starting structure factor based on a free-atom model.

(2) Calculate the difference electron density with F_o phased by $\mathbf{F}_c$ (with the phase angle α_c) of the previous cycle:

$$\Delta\varrho^{(i-1)} = \mathscr{F}\{\mathbf{F}_o^{(i-1)} - \mathbf{F}_c^{(0)}\}, \tag{4}$$

where

$$\mathbf{F}_o^{(i-1)} = F_o k^{(i-1)} \exp\left[i\alpha_c^{(i-1)}\right], \tag{5}$$

and $\mathscr{F}$ denotes the ordinary Fourier synthesis. The first $\Delta\varrho^{(0)}$ is the difference density before phase refinement.

(3) Refine $\mathbf{F}_c$ by a numerical inverse Fourier transformation of difference peaks:

$$\mathbf{F}_c^{(i)} = \mathbf{F}_c^{(0)} + \mathscr{F}^{-1}\{\Delta\varrho^{(i-1)}(\text{peaks})\}. \tag{6}$$

We continue iteration cycles until the ordinary R and the changes in phase angles converge to minimum values.

Selection of peaks

Selection of difference electron density peaks in step 3 is most important in the present method. Since we deal with the difference density, the non-negativity criterion of electron density cannot easily be applied. However, if we confine our interests to the charge

deformation around atoms, the following two criteria for the selection of difference peaks are probably useful: (a) the difference density within spheres of radii r_{max} (or ellipsoids) centred on nuclear positions,

$$\Delta\varrho(\text{peaks}) = \Delta\varrho(r \leq r_{max}),$$

and/or (b) the difference density above a certain noise level,

$$|\Delta\varrho(\text{peaks})| > |\Delta\varrho|_{noise}.$$

Application to a model structure

The FDP method was tested with a two-dimensional model structure, an a-axis projection of $NaNO_2$ (Fig. 1). The hypothetical 'true' structure of aspherical atoms was defined as follows: the positional and thermal parameters were those determined by Kay & Frazer (1961) by neutron diffraction (Table 2); the N and O atoms were aspherical atoms with the sp^2 scattering factors of Dawson (1964), whereas the Na atom was a spherical atom. The 'observed' X-ray structure amplitudes F_o of the 32 $0kl$ reflexions (sin $\theta/\lambda < 0.78$) were assumed to be free from errors except that the scale factor was unknown; i.e. F_o was assumed to be proportional to the 'true' structure amplitude F_t.
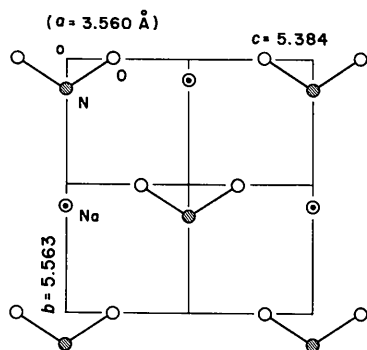
Refinement with the neutron atomic parameters

The starting structure factors $F_c^{(0)}$ of a free-atom model were calculated with the neutron atomic parameters and spherical atomic scattering factors for all the three atoms. A 'true' X − N map of the model structure, synthesized with the coefficients $F_t - F_c^{(0)}$, is shown in Fig. 2(a). A control calculation which included the 98 reflexions (sin $\theta/\lambda < 1.41$) in the synthesis showed that the series-termination effect was negligible in the map. As expected, one and two positive deformation peaks of the lone-pair electrons are seen around the N and O atoms respectively (the O and O' atoms are related by a screw diad along the b axis).

The X − N map before phase refinement $\Delta\varrho^{(0)}$, synthesized with the coefficients $F_o^{(0)} - F_c^{(0)}$, is shown in Fig. 2(b). We note that the distribution of the residual peaks is significantly deformed from that of the 'true' map, and that the peak heights are systematically reduced. According to criterion (a), the difference densities within the circles of radius 1.0 Å from the N and O nuclear positions, indicated by chain lines in Fig. 2(b), were selected as the peaks to be transformed. The Fourier transformation in (6) was performed numerically by dividing the asymmetric unit shown in Fig. 2 into 100 × 100 gridpoints. The X − N map after

Fig. 1. Structure of $NaNO_2$ in space group $Im2m$, [100] projection.

Table 1. FDP refinement of the $NaNO_2$ model structure with the neutron atomic parameters

Cycle	R	$|\Delta\alpha_c|_{av}$*	$R(\Delta\varrho)$†	$|\Delta\varphi|_{av}$	$|\Delta\alpha|_{av}$	Scale
0	0.053	–	0.55	39°	3.6°	1.017
1	0.016	1.3°	0.43	35	3.0	1.012
2	0.010	0.7	0.38	31	2.6	1.010
3	0.008	0.4	0.34	26	2.3	1.009
4	0.007	0.3	0.31	24	2.2	1.008
5	0.006	0.2	0.29	23	2.0	1.007
6	0.006	0.2	0.27	21	1.9	1.006
7	0.006	0.2	0.25	20	1.8	1.005
8	0.006	0.2	0.23	19	1.7	1.005
9	0.006	0.1	0.22	18	1.6	1.004
10	0.006	0.1	0.20	18	1.5	1.004

* $|\Delta\alpha_c|_{av} = |\alpha_c^{(i)} - \alpha_c^{(i-1)}|_{av}$.
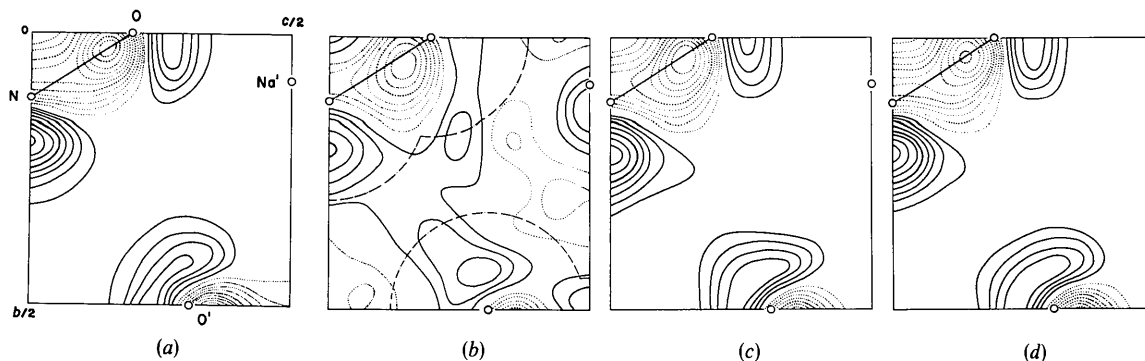† $R(\Delta\varrho) = \Sigma\Delta F_e/\Sigma\Delta F_t$.

Fig. 2. X − N maps of the model structure of $NaNO_2$. The contours are at intervals of 0.1 e Å^{-2}. Negative contours are dotted and zero contours are omitted. (a) The 'true' map, $\Delta\varrho_t(X - N)$. (b) Before phase refinement, $\Delta\varrho^{(0)}(X - N)$. The chain lines indicate the regions selected for the Fourier transformation. (c) After five, $\Delta\varrho^{(5)}(X - N)$, and (d) after ten cycles of phase refinement, $\Delta\varrho^{(10)}(X - N)$.

five cycles (Fig. 2c) reproduced the 'true' map fairly well; the map after ten cycles (Fig. 2d) was almost indistinguishable from the 'true' one.

The convergence and quantitative evaluations of the refinement are summarized in Table 1. The ordinary R value converged from the starting 0·053 to 0·006 after five cycles. The convergence of the average phase change $|\Delta\alpha_c|_{av}$ was relatively slow.

The next three columns in Table 1 show the reduction of phase errors; the relevant error quantities are defined in Fig. 3. These errors cannot of course be evaluated unless the true structure is known. The $R(\Delta\varrho)$ factor is an average ratio of the error information, ΔF_e, to the true information, ΔF_t, in the difference map; it reduced to approximately one-half and one-third after five and ten cycles respectively. The phase errors in ΔF_o and F_o also reduced to less than one-half after ten cycles. It should be noted that the former are more than ten times the latter.

The scale factor in the last column should be compared with the true scale of unity. The original 1·7% error reduced to less than one fourth after ten cycles; not only the phase but also the scale has been improved by the refinement.

Refinement with the 'X-ray' atomic parameters

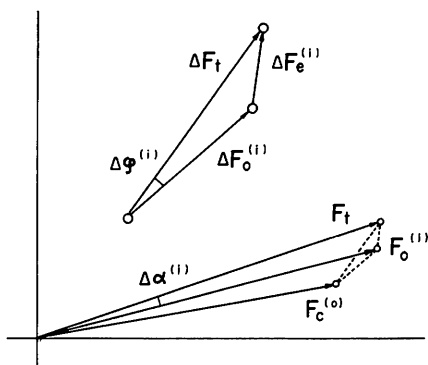As the next example, the FDP method was applied

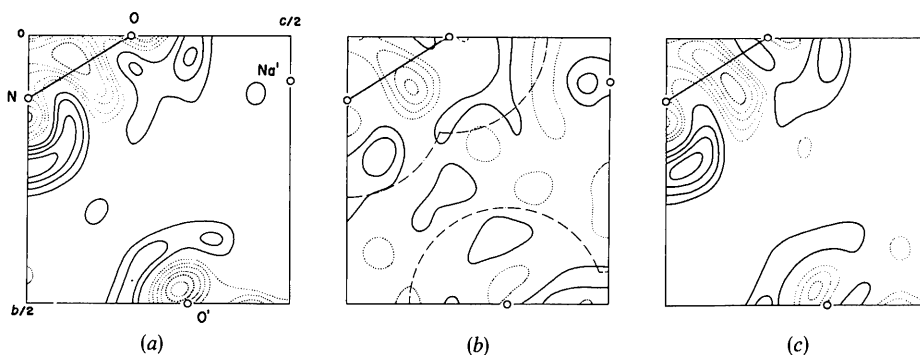Fig. 3. Definitions of various errors after the ith cycle of phase refinement.

to a case where the neutron atomic parameters were not available. The 'X-ray' atomic parameters of the model $NaNO_2$ structure were obtained from a spherical least-squares refinement of the true structure using the same set of F_o as was used in the preceding example. The shifts of the atomic parameters from the neutron values are shown in Table 2; the atomic parameters of the Na atom were not varied in the refinement. The positions of the N and O atoms shifted toward the lone-pair directions, and the thermal parameters of the N atom changed significantly.

Table 2. *Shifts of atomic parameters in a least-squares refinement*

		Neutron (Kay & Frazer, 1961)	Shift
Na	y	0·5853	
	B_{22}	1·29	Fixed
	B_{33}	1·10	
N	y	0·1200	+0·0032 (0·018 Å)
	B_{22}	1·03	+0·48
	B_{33}	1·23	−0·45
O	y	0·0000	−0·0034 ⎫ (0·026 Å)
	z	0·1941	+0·0034 ⎭
	B_{22}	2·01	+0·05
	B_{33}	1·00	−0·05
	B_{23}	0·10	+0·17

The starting structure factors $F_c^{(0)}$ (X-ray) of a free-atom model were calculated with the 'X-ray' atomic parameters. Fig. 4(a) is a 'true' X-ray difference electron density map, synthesized with the coefficients $F_t - F_c^{(0)}$ (X-ray). Although the map is qualitatively similar to the 'true' $X - N$ map (Fig. 2a), the residual peaks are significantly deformed from the 'true' ones; it illustrates the limitations of an X-ray difference map in the analysis of the lone-pair deformation. The ordinary X-ray difference map before phase refinement is shown in Fig. 4(b). All the lone-pair peaks reduced almost to the noise level; even a qualitative analysis is hardly possible.

The FDP refinement was performed in a similar way as in the preceding example. The difference map

Fig. 4. X-ray difference maps of the model structure of $NaNO_2$. The scale is the same as in Fig. 2. (a) The 'true' map, $\Delta\varrho_t$ (X-ray). (b) Before phase refinement, $\Delta\varrho^{(0)}$ (X-ray). (c) After ten cycles of phase refinement, $\Delta\varrho^{(10)}$ (X-ray).

after ten cycles of refinement is shown in Fig. 4(c). Again, the map reproduced fairly well the 'true' X-ray difference map (Fig. 4a). The results of the refinement are summarized in Table 3. The average phase error $|\Delta\alpha|_{av}$ reduced from the original 4·2 to 2·1° after ten cycles. However, the various errors after ten cycles are larger than those of the previous X−N refinement (Table 1).

Table 3. *FDP refinement of the* $NaNO_2$ *model structure with the X-ray atomic parameters*

Cycle	R	$|\Delta\alpha_c|_{av}$	$R(\Delta\varrho)$	$|\Delta\varphi|_{av}$	$|\Delta\alpha|_{av}$	Scale
0	0·029	–	0·79	55°	4·2°	1·017
1	0·012	0·8°	0·68	44	3·7	1·014
2	0·010	0·5	0·63	39	3·4	1·013
3	0·009	0·4	0·59	36	3·1	1·012
4	0·008	0·3	0·56	34	2·8	1·012
5	0·007	0·2	0·54	33	2·6	1·011
6	0·007	0·2	0·52	32	2·5	1·011
7	0·007	0·2	0·50	31	2·4	1·011
8	0·006	0·1	0·49	30	2·3	1·010
9	0·006	0·1	0·48	29	2·2	1·010
10	0·006	0·1	0·47	28	2·1	1·010

Discussion

The present Fourier method may be compared with aspherical least-squares methods based on more flexible models than a free-atom model (Hirshfeld, 1971; Jones, Pautler & Coppens, 1972; Stewart, 1973). The FDP method has the advantage that it is free from an assumption of the analytical expression for charge deformation. Therefore, it will be useful for a structure in which the nature of the charge deformation is hard to predict, and also for a preliminary refinement to look for an appropriate analytical expression. On the other hand, the FDP method does not refine the atomic parameters; accurate atomic parameters must be known beforehand in order to obtain a reliable difference map.

In order to see the effect of errors in F_o on the performance of the method, the first example was repeated with F_o data in which random errors of 1·0% were introduced. The refinement proceeded almost as well as in the first example; the average phase error after ten cycles (1·7°) was only a little higher than that (1·5°) attained in the first example. Thus, in this case the FDP method was found to be sufficiently resistant to errors in F_o, if they are random.

The FDP method depends much on appropriate selection of the difference peaks. In this respect an extreme case without peak selection may be worth mentioning. If we transform the difference density of the whole unit cell, relation (1) gives, from a fundamental theorem of the Fourier transform, a trivial result:

$$\mathbf{F}_c' = \mathbf{F}_c + \mathscr{F}^{-1}\mathscr{F}\{\mathbf{F}_o - \mathbf{F}_c\} = \mathbf{F}_o. \quad (7)$$

That is, the phase is not refined at all, although R reduces to zero. We note, therefore, that elimination of ghost peaks is as important as selection of meaningful peaks.

The above case shows also that a zero R value or a featureless difference map* after refinement is no guarantee that the phase is correct. It should be noted that the situation is also more or less the same in methods with flexible models. Unless the flexibility is confined toward the true asphericity of the electron distribution around the atoms, reduction of R after least-squares refinement may be deceptive. In fact, by refining the 'X-ray' atomic parameters in the second example, R decreased from 0·053 to 0·029, and the corresponding X-ray difference map (Fig. 4b) showed fewer features than the original X−N map (Fig. 2b); and yet the average phase error $|\Delta\alpha|_{av}$ increased from 3·6 to 4·2° (Tables 1 and 3).

Computing time may give rise to a problem in the application of the present method. The computing time (CPU time) on a FACOM 230-75 computer was 13 s cycle^{-1} for the test examples in which 32 reflexions were refined with grid intervals of about 0·03 Å (100 × 100 gridpoints). Intervals of about 0·06 Å gave essentially the same results with a CPU time of 4 s cycle^{-1}. Intervals of about 0·1 Å still proved useful with a CPU time of 1 s cycle^{-1}, but the convergence was somewhat poorer. Appropriate intervals are, of course, problem dependent; relation (7) will be useful for checking the accuracy of the numerical integrations of a given problem. Combined use of criteria (a) and (b) for peak selection reduced the computing time significantly because a level check was much less time-consuming than a distance check. The fast Fourier algorithm of Cooley & Tukey (1965) will also be useful in speeding up the computation.

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* The difference map in this context is the ordinary difference map synthesized with the coefficients $F_o^{(i)} - F_c^{(i)}$.

References

COOLEY, J. W. & TUKEY, J. W. (1965). *Math. Comput.* **19**, 297–301.
COPPENS, P. (1974). *Acta Cryst.* B**30**, 255–261.
DAWSON, B. (1964). *Acta Cryst.* **17**, 997–1009.
HIRSHFELD, F. L. (1971). *Acta Cryst.* B**27**, 769–781.
HOPPE, W., GASSMANN, J. & ZECHMEISTER, K. (1970). *Crystallographic Computing*, edited by F. R. AHMED, pp. 26–36. Copenhagen: Munksgaard.
JONES, D. S., PAUTLER, D. & COPPENS, P. (1972). *Acta Cryst.* A**28**, 635–645.
KAY, M. I. & FRAZER, B. C. (1961). *Acta Cryst.* **14**, 56–57.
MASLEN, E. N. (1968). *Acta Cryst.* B**24**, 1172–1175.
STEWART, R. F. (1973). *J. Chem. Phys.* **58**, 1668–1676.