If a partial structure is not available because: (1) the Patterson synthesis is not calculated; (2) the map is calculated but it is difficult to solve; (3) a light-atom structure is studied; then the mere information on the pseudotranslational symmetry may be used in order to normalize the structure factors correctly. In the second paper of this series (Cascarano, Giacovazzo & Luić, 1985) the same information will be used in order to estimate triplet invariants.

APPENDIX

It is well known that

$$\sum_{k=0}^{n-1} \sin(x+ky) = \sin[x+(n-1)y/2]\sin[ny/2]/\sin[y/2], \qquad (A.1)$$

$$\sum_{k=0}^{n-1} \cos(x+ky) = \cos[x+(n-1)y/2]\sin[ny/2]/\sin[y/2]. \qquad (A.2)$$

From (*A*.1) and (*A*.2), (*A*.3) follows:

$$F_{p\mathbf{h}} = \sum_{j=1}^{t_p} f_j \sum_{\nu=0}^{n-1} \exp 2\pi i\mathbf{h}(\mathbf{r}_j+\nu\mathbf{u}) = \frac{\sin n\pi\mathbf{hu}}{\sin \pi\mathbf{hu}} \sum_{j=1}^{t_p} f_j \exp 2\pi i\mathbf{h}\left(\mathbf{r}_j+\frac{n-1}{2}\mathbf{u}\right). \qquad (A.3)$$

From (*A*.3) the following factorization rule follows:

$$\begin{aligned}\sum_{\nu_1=0}^{n_1-1}\sum_{\nu_2=0}^{n_2-1} \exp 2\pi i\mathbf{h}(\mathbf{r}_j+\nu_1\mathbf{u}_1+\nu_2\mathbf{u}_2) &= \sum_{\nu_1=0}^{n_1-1}\exp(2\pi i\mathbf{h}\nu_1\mathbf{u}_1)\sum_{\nu_2=0}^{n_2-1}\exp 2\pi i\mathbf{h}(\mathbf{r}_j+\nu_2\mathbf{u}_2)\\ &= \frac{\sin n_2\pi\mathbf{hu}_2}{\sin\pi\mathbf{hu}_2}\exp\left[2\pi i\mathbf{h}\left(\frac{n_2-1}{2}\right)\mathbf{u}_2\right]\\ &\quad\times\sum_{\nu_1=0}^{n_1-1}\exp 2\pi i\mathbf{h}(\mathbf{r}_j+\nu_1\mathbf{u}_1)\\ &= \frac{\sin n_1\pi\mathbf{hu}_1}{\sin\pi\mathbf{hu}_1}\,\frac{\sin n_2\pi\mathbf{hu}_2}{\sin\pi\mathbf{hu}_2}\\ &\quad\times\exp 2\pi i\mathbf{h}[\mathbf{r}_j+\tfrac{1}{2}(n_1-1)\mathbf{u}_1+\tfrac{1}{2}(n_2-1)\mathbf{u}_2].\end{aligned} \qquad (A.4)$$

References

BEURSKENS, P. T. & NOORDIK, J. H. (1971). *Acta Cryst.* **27**, 187-188.

BEURSKENS, P. T., PRICK, A. J., DOESBURG, H. M. & GOULD, R. O. (1979). *Acta Cryst.* **A35**, 765-772.

BÖHME, R. (1982). *Acta Cryst.* **A38**, 318-326.

BÖHME, R. (1983). *Z. Naturforsch.* **38**, 304-307.

BUERGER, M. (1956). *Proc. Natl Acad. Sci. USA*, **42**, 776-781.

BUERGER, M. (1959). *Vector Space.* New York: Wiley.

CASCARANO, G., GIACOVAZZO, C. & LUIĆ, M. (1984). In *Statistical Crystallography.* New York: Adenine Press. In the press.

CASCARANO, G., GIACOVAZZO, C. & LUIĆ, M. (1985). In preparation.

FAN HAI-FU, YAO JIA-XING, MAIN, P. & WOOLFSON, M. M. (1983). *Acta Cryst.* **A39**, 566-569.

GIACOVAZZO, C. (1983). *Acta Cryst.* **A39**, 685-692.

GOULD, R. O., VAN DEN HARK, TH. E. M. & BEURSKENS, P. T. (1975). *Acta Cryst.* **A31**, 813-817.

GRAMLICH, V. (1975). *Acta Cryst.* **A31**, S90.

GRAMLICH, V. (1984). Submitted to *Acta Cryst.*

HAUPTMAN, H. & KARLE, J. (1959). *Acta Cryst.* **12**, 846-850.

HEINERMAN, J. J. L. (1977). *Acta Cryst.* **A33**, 100-106.

ITO, T. (1973). *Z. Kristallogr.* **137**, 399-411.

ITO, T. & NOVACKI, W. (1974). *Z. Kristallogr.* **139**, 85-102.

JEFFERY, J. W. (1964). *Acta Cryst.* **17**, 776-777.

KARLE, J. (1970). In *Crystallographic Computing.* Copenhagen: Munksgaard.

LIPSON, H. & WOOLFSON, M. M. (1952). *Acta Cryst.* **5**, 680-682.

MAIN, P. (1976). *Crystallographic Computing Techniques*, edited by F. R. AHMED, pp. 97-105. Copenhagen: Munksgaard.

PARTHASARATHY, S. (1966). *Z. Kristallogr.* **123**, 27-50.

QURASHI, M. M. (1963). *Acta Cryst.* **16**, 307-310.

ROGERS, D. & WILSON, A. J. C. (1953). *Acta Cryst.* **6**, 439-449.

TAKÉUCHI, Y. (1972). *Z. Kristallogr.* **135**, 120-136.

TAXER, K. (1981). *Z. Kristallogr.* **155**, 1-25.

Acta Cryst. (1985). **A41**, 551-556

Use of the Fast Differentiation Algorithm for Phase Refinement in Protein Crystallography

BY V. YU. LUNIN

Research Computing Centre, USSR Academy of Sciences, 142292 *Pushchino, Moscow Region, USSR*

(*Received* 29 *October* 1984; *accepted* 7 *May* 1985)

Abstract

Additional information of various kinds on the structure, such as 'atomicity', noncrystallographic symmetry, known molecular boundaries, nonnegativity of the electron density and so forth, may be described by an equation $\rho=\tau[\rho]$ or by the corresponding system of equations for structure factors. To use this information, one tries generally to solve the 'phase' part of the structure-factor equations by simple iterations. The complete system of equations can, however, be used for phase refinement if the latter is

0108-7673/85/060551-06$01.50

defined as a minimization of the corresponding function. For the functions expressing various kinds of information gradient computation algorithms are proposed, each taking as much time as the computation of the proper function does.

Introduction

In several cases the 'experimental' moduli and the 'isomorphous' phases of structure factors do not allow the electron density distribution $\rho(\mathbf{r})$ to be calculated to the required accuracy. Therefore, it is desirable that the electron density maps should be improved by the use of additional information on the object ('atomicity', noncrystallographic symmetry *etc.*). In § 1 we shall show that in most cases this information can be represented as

$$\rho = \tau[\rho], \tag{1}$$

where $\tau[\rho]$ is a transformation of the function $\rho(\mathbf{r})$.

Equation (1) is equivalent to the corresponding system of equations for structure factors:

$$F_{\mathbf{s}} \exp(i\varphi_{\mathbf{s}}) = \mathscr{F}_{\mathbf{s}}(\tau\{(1/V) \sum_{\mathbf{u}} F_{\mathbf{u}} \times \exp(i\varphi_{\mathbf{u}}) \exp[-2\pi i(\mathbf{u}, \mathbf{r})]\}), \ \mathbf{s} \in \mathscr{R}'. \tag{2}$$

Here $\mathscr{R}'$ is the reciprocal-space lattice and $\mathscr{F}_{\mathbf{s}}\{a(\mathbf{r})\}$ is the Fourier transform of the function $a(\mathbf{r})$ at point $\mathbf{s}$:

$$\mathscr{F}_{\mathbf{s}}\{a(\mathbf{r})\} = \int_V a(\mathbf{r}) \exp[2\pi i(\mathbf{s}, \mathbf{r})] \, \mathrm{d}V_{\mathbf{r}}, \tag{3}$$

$$F_{\mathbf{s}} \exp(i\varphi_{\mathbf{s}}) = \mathscr{F}_{\mathbf{s}}\{\rho(\mathbf{r})\}. \tag{4}$$

In this paper we assume that the structure-factor moduli $\{F_{\mathbf{s}}\}$ are known from the experiment, which makes it possible to consider the system (2) suitable for determination or refinement of the phases $\{\varphi_{\mathbf{s}}\}$. The alternative variational techniques for improvement of $\rho(\mathbf{r})$ have been proposed by Navaza, Castellano & Tsoucaris (1983).

Each of the complex equations (2) is equivalent to two real equations representing the 'modulus' part of (2):

$$F_{\mathbf{s}} = |\mathscr{F}_{\mathbf{s}}(\tau\{(1/V) \sum_{\mathbf{u}} F_{\mathbf{u}} \exp(i\varphi_{\mathbf{u}}) \times \exp[-2\pi i(\mathbf{u}, \mathbf{r})]\})|, \tag{5}$$

and their 'phase' part

$$\varphi_{\mathbf{s}} = \arg[\mathscr{F}_{\mathbf{s}}(\tau\{(1/V) \sum_{\mathbf{u}} F_{\mathbf{u}} \times \exp(i\varphi_{\mathbf{u}}) \exp[-2\pi i(\mathbf{u}, \mathbf{r})]\})]. \tag{6}$$

Here $\arg z$ is the phase of a complex number z.

It has become common practice to use (2) by solving merely their phase part (6). Usually, (6) are solved by simple iterations (Zwick, Bantz & Hughes, 1976), *i.e.* by substituting the values of phases determined in the previous iteration into the right-hand part of (6). In more detail the procedure consists in the following:

(*a*) one calculates

$$\rho(\mathbf{r}) = (1/V) \sum_{\mathbf{s}} F_{\mathbf{s}} \exp[i\varphi_{\mathbf{s}}^{(k)}] \exp[-2\pi i(\mathbf{s}, \mathbf{r})], \tag{7}$$

where $F_{\mathbf{s}}$ are the observed structure moduli and $\varphi_{\mathbf{s}}^{(k)}$ are the previously determined phases;

(*b*) one transforms

$$\rho \to \tau[\rho]$$

and calculates structure factors of the transformed electron density distribution:

$$g_{\mathbf{s}} \exp(i\psi_{\mathbf{s}}) = \int_V \tau[\rho](\mathbf{r}) \exp[2\pi i(\mathbf{s}, \mathbf{r})] \, \mathrm{d}V_{\mathbf{r}}, \tag{8}$$

taking the obtained phases as new values for the unknown ones

$$\varphi_{\mathbf{s}}^{(k+1)} = \psi_{\mathbf{s}}.$$

This procedure may generally be criticized on two points. Firstly, the 'modulus' part, *i.e.* 'half' of (2), is ignored, which sometimes leads to other solutions (the self-consistent sets of phases). Secondly, simple iterations may show divergence. In a special case, that of Sayre's equations, a complete system was used for rubredoxin (Sayre, 1972). The phases were derived from the discrepancy minimum

$$R(\boldsymbol{\varphi}) = \sum_{\mathbf{s}} |a_{\mathbf{s}} F_{\mathbf{s}} \exp(i\varphi_{\mathbf{s}}) - \mathscr{F}_{\mathbf{s}}(\{(1/V) \times \sum_{\mathbf{u}} F_{\mathbf{u}} \exp[i\varphi_{\mathbf{u}} - 2\pi i(\mathbf{u}, \mathbf{r})]\}^2)|^2. \tag{9}$$

Here $a_{\mathbf{s}}$ is a special function compensating for a truncation of the series in calculating $\rho(\mathbf{r})$. A similar approach can also be applied to any other equations of type (2). The general structure of the criterion to be minimized is described in § 2. In Sayre's minimization of criterion (5) the most difficult task was to compute the gradient ∇R and the product $\nabla^2 R\mathbf{e}$ of the matrix of second deivatives into a vector, which were necessary for the method of conjugate gradients. Later Sayre & Toupin (1975) modified the algorithms in order to simplify the computation of these values. Recently Kim, Nesterov & Cherkassky (1984) have established that for a function R all the components of the vectors ∇R and $\nabla^2 R\mathbf{e}$ require as much computation as one value. More precisely, $T(\nabla R) = O[T(R)]$ where $T(R)$ is the time of computation of R and $T(\nabla R)$ is the total time needed to compute all the components of ∇R. This algorithm has been adapted for structure refinement by Lunin & Urzhumtsev (1984, 1985). It is shown in § 3 how the algorithm of Kim *et al.* can be implemented to calculate ∇R for the general type of criterion relative to the system (2).

We shall restrict ourselves to space group $P1$.

1. Equations for the density

It will be shown in this section that a number of available methods for phase improvement are only the solution of the phase part of (2) corresponding to a transformation $\tau(\rho)$.

1.1. *Separate atoms*

Sayre (1952) obtained equations for structure factors, assuming that the density $\rho(\mathbf{r})$ is composed of the contributions of identical quite separate atoms with $\{\mathbf{r}_j\}$ coordinates:

$$\rho(\mathbf{r})=\sum_j \rho_0(|\mathbf{r}-\mathbf{r}_j|),$$

where

$$\rho_0(|\mathbf{r}-\mathbf{r}_j|)\rho_0(|\mathbf{r}-\mathbf{r}_k|)\equiv 0 \quad \text{for } j\neq k. \tag{10}$$

If we follow Sayre, we can easily prove that if this hypothesis is true for any function $\lambda(t)$ such that $\lambda(0)=0$ the following equations are valid:

$$\begin{aligned} F_{\mathbf{s}}\exp(i\varphi_{\mathbf{s}}) &= [f_0(s)/f_\lambda(s)]\mathcal{F}_{\mathbf{s}}\{\lambda[\rho(\mathbf{r})]\} \\ &= \mathcal{F}_{\mathbf{s}}\{a_\lambda(z) * \lambda[\rho(\mathbf{r})]\}, \end{aligned} \tag{11}$$

i.e. the function $\rho(\mathbf{r})$ satisfies

$$\rho=a_\lambda * \lambda(\rho). \tag{12}$$

Here

$$f_0(s)=(2/s)\int_0^\infty r\rho_0(r)\sin 2\pi sr\,\mathrm{d}r, \tag{13}$$

$$f_\lambda(s)=(2/s)\int_0^\infty r\lambda[\rho_0(r)]\sin 2\pi sr\,\mathrm{d}r, \tag{14}$$

$$a_\lambda(r)=(2/r)\int_0^\infty s[f_0(s)/f_\lambda(s)]\sin 2\pi sr\,\mathrm{d}s, \tag{15}$$

where $s=|\mathbf{s}|$ and $r=|\mathbf{r}|$, and $*$ is the convolution on $\mathbf{r}$. Note that the function $a_\lambda(r)$ does not depend on the position of atoms. Sayre's equations are derived if $\lambda(t)=t^2$. Iterative solution of their phase part (6) coincides with the tangent formula refinement and for the non-square function $\lambda(t)$ is called 'the method of electron density modification'. These approaches are now in current use (Sayre, 1980).

1.2. *Local (noncrystallographic) symmetry*

The crystals of biological macromolecules are often locally symmetric. This implies that for the points of a bounded region

$$\rho(\mathbf{Gr}+\mathbf{t})=\rho(\mathbf{r}),\quad \mathbf{r}\in\Omega, \tag{16}$$

where $\mathbf{G}$ is the rotation matrix and $\mathbf{t}$ is the translation vector. In contrast to the crystallographic symmetry where (16) is valid for all $\mathbf{r}\in\mathbb{R}^3$, here it holds only for $\mathbf{r}\in\Omega$. We restrict for simplicity the function $\rho(\mathbf{r})$ to have one local symmetry transformation.

The property (16) is equivalent to (1) with

$$\tau[\rho](\mathbf{r})=\begin{cases}\rho(\mathbf{Gr}+\mathbf{t}), \mathbf{r}\in\Omega,\\ \rho(\mathbf{r}) \quad \text{for the other points in the unit cell.}\end{cases} \tag{17}$$

We can choose a more symmetric transformation $\tau[\rho]$, since the property (16) is equivalent to the pair of equations

$$\begin{cases}\rho(\mathbf{r})=\tfrac{1}{2}[\rho(\mathbf{r})+\rho(\mathbf{Gr}+\mathbf{t})],\\ \rho(\mathbf{Gr}+\mathbf{t})=\tfrac{1}{2}[\rho(\mathbf{r})+\rho(\mathbf{Gr}+\mathbf{t})],\quad \mathbf{r}\in\Omega,\end{cases} \tag{18}$$

i.e. to (1) with

$$\tau[\rho](\mathbf{r})=\begin{cases}\tfrac{1}{2}[\rho(\mathbf{r})+\rho(\mathbf{Gr}+\mathbf{t})],\quad \mathbf{r}\in\Omega,\\ \tfrac{1}{2}\{\rho[\mathbf{G}^{-1}(\mathbf{r}-\mathbf{t})]+\rho(\mathbf{r})\},\quad \mathbf{r}\in\mathbf{G}\Omega+t,\\ \rho(\mathbf{r}) \quad \text{for the other points in the unit cell.}\end{cases} \tag{19}$$

Iterative solution of the phase part of the corresponding system (2) coincides with the method of phase improvement owing to the widely used noncrystallographic symmetry electron density averaging (Argos & Rossmann, 1980).

A more general form of (1) for the local symmetry can be obtained if

$$\tau[\rho](\mathbf{r})=\begin{cases}\lambda[\rho(\mathbf{r}),\rho(\mathbf{Gr}+\mathbf{t})],\ \mathbf{r}\in\Omega,\\ \lambda\{\rho[\mathbf{G}^{-1}(\mathbf{r}-\mathbf{t}),\rho(\mathbf{r})]\},\quad \mathbf{r}\in\mathbf{G}\Omega+\mathbf{t},\\ \rho(\mathbf{r}) \quad \text{for the other points in the unit cell,}\end{cases} \tag{20}$$

where $\lambda(x,y)$ is a function such that $\lambda(x,x)=x$ [in the transformation (19) $\lambda(x,y)=\frac{1}{2}(x+y)$]. Note that (1) with $\tau[\rho]$ given by (20) is equivalent to (16).

1.3. *The known part of the distribution* $\rho(\mathbf{r})$

If it is established that the region Ω is filled by the solvent with a constant density,

$$\tau[\rho](\mathbf{r})=\begin{cases}\rho_0 \quad \text{for } \mathbf{r}\in\Omega,\\ \rho(\mathbf{r}) \quad \text{for the other points.}\end{cases} \tag{21}$$

Iterative solution of the phase part of the corresponding equations (2) was used, for example, by Hendrickson, Klippenstein & Ward (1975). There are a few cases when the electron density distribution $\rho_0(\mathbf{r})$ in the region Ω may be prescribed, for instance, as with the interpreted region of the unit cell. Then, we can determine $\tau[\rho]$ by

$$\tau[\rho](\mathbf{r})=\begin{cases}\rho_0(\mathbf{r}) \quad \text{for } \mathbf{r}\in\Omega,\\ \rho(\mathbf{r}) \quad \text{for the other points.}\end{cases} \tag{22}$$

A similar approach based on the isolation of several maximum peaks was proposed by Bukvetskaya, Shishova, Andrianov & Simonov (1977).

1.4. *Nonnegativity of* $\rho(\mathbf{r})$

The nonnegativity of the distribution $\rho(\mathbf{r})$ is equivalent to (1) where

$$\tau[\rho](\mathbf{r})=\begin{cases}\rho(\mathbf{r}) & \text{if } \rho(\mathbf{r})\geq 0,\\ 0 & \text{if } \rho(\mathbf{r})<0.\end{cases} \tag{23}$$

Iterative solution of the phase part of the corresponding equations (2) has also found application (Nixon & North, 1976). There is a more general form of the transformation (23), using the lower cut level q instead of 0 (Sirota & Simonov, 1970).

1.5. *Functions with a finite set of values*

In a number of cases the function $\rho(\mathbf{r})$ can be approximately assumed to have only a finite set of values. For instance, Vainshtein & Khachaturyan (1977) considered that

$$\rho(\mathbf{r})=\{0 \text{ or } 1\}. \tag{24}$$

Let $\lambda(t)$ be a function such that

$$\lambda(t)=t \quad \text{only if } t=0 \quad \text{or if } t=1. \tag{25}$$

It is evident that in this case the condition (24) is equivalent to (1) with

$$\tau[\rho](\mathbf{r})=\lambda[\rho(\mathbf{r})]. \tag{26}$$

In a more general case the function $\rho(\mathbf{r})$ can have a finite set of values $P_1,\ldots,P_k$ so that

$$\rho(\mathbf{r})=\{P_1 \text{ or } P_2,\ldots,\text{or } P_k\}, \tag{27}$$

which is equivalent to (1) with $\tau[\rho]$, defined by the equality (26), where the function $\lambda(t)$ is such that

$$\lambda(t)=t \quad \text{only if } t=P_1, \text{if } t=P_2,\ldots,\text{if } t=P_k. \tag{28}$$

Note that the phase part of (2) with $\tau[\rho]$ defined by (26) coincides with that of (11) obtained for the case of separate atoms. The 'method of electron density modification' may thus imply the search for not only a function satisfying the condition (10) but also for those having a finite number of values determined by the condition (28), and the prescribed structure moduli. In particular, the functions satisfying the conditions (10) and (24) would both be solutions of the phase part of Sayre's equations.

2. Structure of the minimized criterion

2.1. It has been shown in the previous section that a great number of methods for phase refinement may be interpreted as the iterative solution of the phase part of (2). Sayre (1972) noted that the complete system (7) with $\lambda(t)=t^2$ provides a more successful calculation than its phase part taken alone. Similarly, the other cases considered in § 1 can be expected to give better results if the information of (2) is used completely. As far as computations are concerned, the solution of an overdetermined system, such as system (2) containing twice as many equations as unknowns, usually implies the minimization of a function representing the discrepancy in these equations. Further, we shall give the general form of such a function but beforehand it is worth mentioning briefly why it is desirable to consider the minimized function in a general form.

In all the cases equations (2) are approximate. Firstly, this is because the initial hypotheses concerning the properties of the function $\rho(\mathbf{r})$ are approximate. These hypotheses may be realized if one introduces weight functions in the calculation of $\rho(\mathbf{r})$. For instance, the application of normalized structure factors may give a better atomic separation in (10), the use of syntheses weighed by the figure of merit may result in a more precise equality (16) *etc.* Therefore, we shall assume that the function $\rho(\mathbf{r})$ is calculated by the more general formulae (32) rather than by (7).

Secondly, errors in (2) may result from truncations of Fourier series in calculating $\rho(\mathbf{r})$. The values of the errors may be reduced if we properly correct (2). For example, criterion (9) applied to rubredoxin (Sayre, 1974) gave the following correction for the modulus part of (2):

$$a_{\mathbf{s}}=(\alpha-\beta s-\gamma s^2)\,Vf_{\lambda}(s)/f_0(s). \tag{29}$$

By modifying the tangent formula, Olthof, Sint & Schenk (1979) introduced a correction into the phase part of Sayre's equations to compensate for low resolution.

Generally, phase information is used as the probability distributions $P(\varphi,\mathbf{s})$ for the values of phase φ. These distributions are usually written in a more general form (Hendrickson & Lattman, 1970):

$$P(\varphi,\mathbf{s})\sim\exp\{A_{\mathbf{s}}\cos\varphi+B_{\mathbf{s}}\sin\varphi + C_{\mathbf{s}}\cos 2\varphi+D_{\mathbf{s}}\sin 2\varphi\} \tag{30}$$

and can be used for further stabilization of the phase values in solving system (2). In this case the minimized function of type (9) is appended by

$$-\sum_{\mathbf{s}}\{A_{\mathbf{s}}\cos\varphi_{\mathbf{s}}+B_{\mathbf{s}}\sin\varphi_{\mathbf{s}}+C_{\mathbf{s}}\cos 2\varphi_{\mathbf{s}}+D_{\mathbf{s}}\sin 2\varphi_{\mathbf{s}}\} \tag{31}$$

(Lunin & Urzhumtsev, 1984). Therefore, instead of criterion (9) we shall take the more general criteria (35).

2.2. The problem of phase refinement based on the equations of type (1) can now be reduced to the minimization of the criterion $R(\varphi)$ calculated as the following chain of transforms:

(*a*) *Calculation of the 'density' for* $\mathbf{r} \in U_\rho$.

$$\rho_\mathbf{r} = \operatorname{Re}\left\{\sum_{\mathbf{s}\in S_0} B_\mathbf{s} \exp(i\varphi_\mathbf{s}) \exp[-2\pi i(\mathbf{s},\mathbf{r})]\right\} = \sum_{\mathbf{s}\in S_0} B_\mathbf{s} \cos\{-2\pi(\mathbf{s},\mathbf{r}) + \varphi_\mathbf{s}\}. \quad (32)$$

Here S_0 is the set of reflexions with refinable phases (we assume that all the phases are refined independently); U_ρ is a grid in the unit cell; $\rho_\mathbf{r}$ is the electron density $\rho(\mathbf{r})$ at point $\mathbf{r}$ of the grid U_ρ [we write $\boldsymbol{\rho} = \{\rho_\mathbf{r}\}_{\mathbf{r}\in U_\rho}$ for the set of values of the function $\rho(\mathbf{r})$ at points of the grid U_ρ]; $B_\mathbf{s}$ are the known values including weights, experimentally determined moduli $F_\mathbf{s}$, factor $2/V$ *etc.*

(*b*) *Transformation of the density.*

$$\tau_\mathbf{r} = \tau_\mathbf{r}(\boldsymbol{\rho}), \quad \mathbf{r} \in U_\tau. \quad (33)$$

Here U_τ is a grid in the unit cell, which may disagree with U_ρ; $\tau_\mathbf{r}(\boldsymbol{\rho})$ are given functions determining values of the transformed density at grid points $\mathbf{r} \in U_\tau$.

(*c*) *Calculation of the 'modified' structure factors.*

$$g_\mathbf{s}^R + i g_\mathbf{s}^I = C \sum_{\mathbf{r}\in U_\tau} \tau_\mathbf{r} \exp[2\pi i(\mathbf{s},\mathbf{r})], \quad \mathbf{s} \in S_1. \quad (34)$$

Here the set of structure factors S_1 can differ from the set S_0.

(*d*) *Calculation of the criterion.*

$$R = \sum_{\mathbf{s}\in S_1} q(\varphi_\mathbf{s}, g_\mathbf{s}^R, g_\mathbf{s}^I; \mathbf{s}). \quad (35)$$

Here $q(\psi, u, v; \mathbf{s})$ are given functions including the corrections. For criterion (9) these are

$$q(\varphi_\mathbf{s}, g_\mathbf{s}^R, g_\mathbf{s}^I; \mathbf{s}) = |a_\mathbf{s} F_\mathbf{s} \exp(i\varphi_\mathbf{s}) - (g_\mathbf{s}^R + i g_\mathbf{s}^I)|^2. \quad (36)$$

3. Gradient computation

When minimizing a complex function of a large number of variables, the most difficult task is generally to compute the gradient of this function and the product of the matrix of second derivatives into a vector. For the function (9) Sayre & Toupin (1975) suggested an effective algorithm that could in particular compute the gradient ∇R as fast as the value of R. For an arbitrary criterion determined by the chain of transforms (32)-(35) a similar algorithm can also be obtained by the fast differentiation (Kim *et al.*, 1984; Lunin & Urzhumtsev, 1985). In this paper we restrict ourselves to the general case of the algorithm for the computation of ∇R (for R, see § 2).

The fast computation algorithm implies that the minimized function can first be represented as a chain of substitutions of variables that should be as simple as possible. Further computation will only involve transformation of the gradient with respect to one set of variables into that with respect to the others.

Thus, we begin with computing the gradient with respect to the variables $\varphi_\mathbf{s}$, $g_\mathbf{s}^R$, $g_\mathbf{s}^I$, assuming them to be independent in (35). This computation does not present any difficulty

$$\begin{cases} \tilde{\Phi}_\mathbf{s} = \dfrac{\partial}{\partial\varphi_\mathbf{s}} \sum_\mathbf{u} q(\varphi_\mathbf{u}, g_\mathbf{u}^R, g_\mathbf{u}^I; \mathbf{u}) = \dfrac{\partial}{\partial\varphi_\mathbf{s}} q(\varphi_\mathbf{s}, g_\mathbf{s}^R, g_\mathbf{s}^I; \mathbf{s}), \\ G_\mathbf{s}^R = \dfrac{\partial}{\partial g_\mathbf{s}^R} R = \dfrac{\partial}{\partial g_\mathbf{s}^R} q(\varphi_\mathbf{s}, g_\mathbf{s}^R, g_\mathbf{s}^I; \mathbf{s}), \\ G_\mathbf{s}^I = \dfrac{\partial}{\partial g_\mathbf{s}^I} R = \dfrac{\partial}{\partial g_\mathbf{s}^I} q(\varphi_\mathbf{s}, g_\mathbf{s}^R, g_\mathbf{s}^I; \mathbf{s}), \mathbf{s} \in S_1. \end{cases} \quad (37)$$

The next step is to transform the derivatives with respect to $\{g_\mathbf{s}^R, g_\mathbf{s}^I\}$ into those with respect to $\{\tau_\mathbf{r}\}$ making up (34). It is clear that

$$T_\mathbf{r} = \frac{\partial}{\partial\tau_\mathbf{r}} R = \sum_{\mathbf{s}\in S_1} \left[\frac{\partial R}{\partial g_\mathbf{s}^R}\frac{\partial g_\mathbf{s}^R}{\partial\tau_\mathbf{r}} + \frac{\partial R}{\partial g_\mathbf{s}^I}\frac{\partial g_\mathbf{s}^I}{\partial\tau_\mathbf{r}}\right] = C \operatorname{Re}\left\{\sum_{\mathbf{s}\in S_1} (G_\mathbf{s}^R + iG_\mathbf{s}^I) \exp[-2\pi i(\mathbf{s},\mathbf{r})]\right\}, \quad \mathbf{r} \in U_\tau. \quad (38)$$

Then, by (33), we can determine the derivatives of R with respect to $\{\rho_\mathbf{r}\}$ through the values $\{T_\mathbf{r}\}_{\mathbf{r}\in U_\tau}$:

$$P_\mathbf{r} = \frac{\partial}{\partial\rho_\mathbf{r}} R = \sum_{\mathbf{r}'\in U_\tau} \frac{\partial R}{\partial\tau_{\mathbf{r}'}}\frac{\partial\tau_{\mathbf{r}'}}{\partial\rho_\mathbf{r}}, \quad \mathbf{r} \in U_\rho. \quad (39)$$

Let us detail the last equality for some special cases.

If $\tau[\rho] = \lambda(\rho)$ and $U_\tau = U_\rho = U$, then

$$\frac{\partial\tau_{\mathbf{r}'}}{\partial\rho_\mathbf{r}} = \begin{cases} \lambda'(\rho_\mathbf{r}) & \text{for } \mathbf{r} = \mathbf{r}' \\ 0 & \text{for } \mathbf{r} \neq \mathbf{r}' \end{cases} \quad (40)$$

so that $P_\mathbf{r} = \lambda'(\rho_\mathbf{r}) T_\mathbf{r}$.

Let $\tau[\rho]$ be given by (20). We assume that $U_\rho = U_\tau = U$ and $\mathbf{Gr+t}$ is a point of the grid U if $\mathbf{r}$ is a grid point. Practically, one cannot obtain direct hits of $\mathbf{Gr+t}$ at a grid point, therefore one has to interpolate the values at the nearest points, which leads to an additional linear transform in the chain (32)-(35) with a sparse matrix. Let us write

$$\lambda_1(u, v) = \partial\lambda(u, v)/\partial u, \; \lambda_2(u, v) = \partial\lambda(u, v)/\partial v. \quad (41)$$

Then, (22) assumes the form

$$\begin{cases} P_\mathbf{r} = \lambda_1(\rho_\mathbf{r}, \rho_{\mathbf{Gr+t}})[T_\mathbf{r} + T_{\mathbf{Gr+t}}], & \mathbf{r} \in \Omega; \\ P_{\mathbf{Gr+t}} = \lambda_2(\rho_\mathbf{r}, \rho_{\mathbf{Gr+t}})[T_\mathbf{r} + T_{\mathbf{Gr+t}}], & \mathbf{r} \in \Omega; \\ P_\mathbf{r} = T_\mathbf{r} \quad \text{for the other points.} \end{cases} \quad (42)$$

In particular, if the local symmetry averaging (19) is used

$$\begin{cases} P_\mathbf{r} = \tfrac{1}{2}[T_\mathbf{r} + T_{\mathbf{Gr+t}}], & \mathbf{r} \in \Omega; \\ P_{\mathbf{Gr+t}} = \tfrac{1}{2}[T_\mathbf{r} + T_{\mathbf{Gr+t}}], \mathbf{r} \in \Omega; \\ P_\mathbf{r} = T_\mathbf{r} \quad \text{for the other points.} \end{cases} \quad (43)$$

and transform (39) coincides with transform (19).

It is obvious that for transform (22) formulae (39) are

$$P_\mathbf{r} = \begin{cases} 0 & \text{for } \mathbf{r} \in \Omega \\ T_\mathbf{r} & \text{for the other points.} \end{cases} \quad (44)$$

For transform (23) they are

$$P_{\mathbf{r}} = \begin{cases} T_{\mathbf{r}} & \text{if } \rho_{\mathbf{r}} \geq 0, \\ 0 & \text{if } \rho_{\mathbf{r}} < 0. \end{cases} \tag{45}$$

Finally, we are to pass to the gradient of R with respect to the variables $\{\varphi_{\mathbf{s}}\}$, with both the direct dependence between R and $\{\varphi_{\mathbf{s}}\}$ and the complex dependence between $\boldsymbol{\rho}$ and $\boldsymbol{\varphi}$ taken into account:

$$\begin{aligned} \Phi_{\mathbf{s}} = \frac{\partial}{\partial \varphi_{\mathbf{s}}} R &= \tilde{\Phi}_{\mathbf{s}} + \sum_{\mathbf{r} \in U_\rho} \frac{\partial R}{\partial \rho_{\mathbf{r}}} \frac{\partial \rho_{\mathbf{r}}}{\partial \varphi_{\mathbf{s}}} \\ &= \tilde{\Phi}_{\mathbf{s}} + \operatorname{Im}\Big\{ B_{\mathbf{s}} \exp(-i\varphi_{\mathbf{s}}) \sum_{\mathbf{r} \in U_\rho} P_{\mathbf{r}} \\ &\quad \times \exp[2\pi i(\mathbf{s}, \mathbf{r})] \Big\}, \mathbf{s} \in S_0. \end{aligned} \tag{46}$$

It is easy to see that the chain of transforms (37)-(46) requires as much computation as the chain of transforms (32)-(35) needed to compute the criterion $R(\boldsymbol{\varphi})$.

4. Efficiency of the algorithm

In conclusion, we shall discuss the efficiency of our algorithm compared with the known methods. For the transform $\rho(\mathbf{r}) \rightarrow \lambda[\rho(\mathbf{r})]$ applied to atomic separation or a function with a finite number of values, and for the transforms (22) and (23) the steps (33), (35), (37) and (39) need too little time to be compared with the Fourier transforms (32), (34), (38) and (46). Therefore the computation of R and ∇R is here reduced essentially to the four FFTs, as in the Sayre-Toupin case.

The transforms (18) and (43) may be less efficient than $\rho \rightarrow \rho^2$, as they sometimes require to interpolate the values of ρ to points $\mathbf{Gr}+\mathbf{t}$, not at the grid points. The speed of such transforms does not, however, exceed that of FFTs, so the entire computational cost increases only by less than 1·5 times compared with the Sayre-Toupin algorithm for (9).

If we compare our algorithm to the method of electron density modification, we can see that the function R and the gradient ∇R require approximately twice as much computation as the modification $\varphi \rightarrow \rho \rightarrow \varphi'$. But in this paper we have used the complete system of equations (5)-(6) and avoided the shortcomings of the method of simple iteration mentioned in the *Introduction*.

References

ARGOS, P. & ROSSMANN, M. G. (1980). In *Theory and Practice of Direct Methods in Crystallography*, edited by M. F. C. LADD & R. A. PALMER. New York: Plenum Press.

BUKVETSKAYA, L. V., SHISHOVA, T. G., ANDRIANOV, V. I. & SIMONOV, V. I. (1977). *Kristallografiya*, **22**, 494-497.

HENDRICKSON, W. A., KLIPPENSTEIN, G. L. & WARD, K. B. (1975). *Proc. Natl Acad. Sci. USA*, **72**, 2160-2164.

HENDRICKSON, W. A. & LATTMAN, E. E. (1970). *Acta Cryst.* B**26**, 136-143.

KIM, K. V., NESTEROV, YU. E. & CHERKASSKY, B. V. (1984). *Dokl. Akad. Nauk SSSR*, **275**, 1306-1309.

LUNIN, V. YU. & URZHUMTSEV, A. G. (1984). *Acta Cryst.* A**40**, C18.

LUNIN, V. YU. & URZHUMTSEV, A. G. (1985). *Acta Cryst.* A**41**, 327-333.

NAVAZA, J., CASTELLANO, E. E. & TSOUCARIS, G. (1983). *Acta Cryst.* A**39**, 622-631.

NIXON, P. E. & NORTH, A. C. T. (1976). *Acta Cryst.* A**32**, 325-333.

OLTHOF, G. J., SINT, L. & SCHENK, H. (1979). *Acta Cryst.* A**35**, 941-946.

SAYRE, D. (1952). *Acta Cryst.* **5**, 60-65.

SAYRE, D. (1972). *Acta Cryst.* A**28**, 210-212.

SAYRE, D. (1974). *Acta Cryst.* A**30**, 180-184.

SAYRE, D. (1980). In *Theory and Practice of Direct Methods in Crystallography*, edited by M. F. C. LADD & R. A. PALMER. New York: Plenum Press.

SAYRE, D. & TOUPIN, R. A. (1975). *Acta Cryst.* A**31**, S20.

SIROTA, M. I. & SIMONOV, B. I. (1970). *Kristallografiya*, **15**, 681-685.

VAINSHTEIN, B. K. & KHACHATURYAN, A. G. (1977). *Kristallografiya*, **22**, 706-710.

ZWICK, M., BANTZ, D. & HUGHES, J. (1976). *Ultramicroscopy*, **1**, 275-277.

Acta Cryst. (1985). A**41**, 556-559

Self-Crystallizing Molecular Models. VII. Plant-Virus Coat Protein

BY TARO KIHARA

Department of Physics, Meisei University, Hodokubo Hino-shi, Tokyo 191, *Japan*

(*Received* 22 *March* 1985; *accepted* 28 *May* 1985)

Abstract

The strong tendency to aggregate of coat protein molecules of simple plant viruses has been represented by means of self-assembling molecular models. These models are made of ferrite magnets and are similar to molecular models designed for the purpose of simulating crystal structures. Capsid structures of isometric viruses are simulated by assembling dipolar spheres. The double-disk and helix structures of tobacco mosaic virus protein are simulated by assembling dipolar molecular models in a characteristic shape.

0108-7673/85/060556-04$01.50