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A Step-by-Step Algorithm for Phase Refinement with the Aid of Sayre's Equation

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Sayre's equation is modified so as to include two kinds of atom, one kind of atom having known positions. Starting with one initial set of phases, the agreement between structure factors as calculated by Sayre's equation and the observed structure factors is systematically improved by rotating the phase angles of each of the individual structure factors through a discrete set of values; only one structure factor is rotated at a time and each is given the phase angle that produces the lowest value of the disagreement factor. This algorithm is shown to give the correct structure if some *a priori* knowledge is introduced into the initial set of phases.

Introduction

Sayre's (1952) equation: $F_{\mathbf{h}}=\theta_h\sum_{\mathbf{h}'}F_{\mathbf{h}'}F_{\mathbf{h}-\mathbf{h}'}$ gives a relation between structure factors for an equal-atom structure. Since Sayre's first application of this equation to phase determination no further attempts to use the equation have been reported. Instead, it was the related statistical formulae $U_{\mathbf{h}}=N\langle U_{\mathbf{h}'}U_{\mathbf{h}-\mathbf{h}'}\rangle$ (Cochran, 1953; Hughes, 1953) and $E_{\mathbf{h}}=N^{1/2}\langle E_{\mathbf{h}'}E_{\mathbf{h}-\mathbf{h}'}\rangle$ (Hauptman & Karle, 1954) that found successful application in a number of direct methods (*e.g.* Woolfson, 1957; Karle & Karle, 1963) and in iteration procedures for phase refinement (Karle & Karle, 1964). However, such a statistical method lacks a reliable internal consistency criterion (Karle, 1969).

In this paper we propose an algorithm for phase refinement, using the original exact form of Sayre's equation for which a reliable consistency index can be defined. In the algorithm the phase angle of each structure factor in turn is rotated over a discrete set of angles until it gives the lowest value of this consistency index. It may be considered as a reciprocal-space analogue of the real-space procedure of Bhuiya & Stanley (1963).

In order to be able to apply Sayre's equation to real structures some modifications have to be made to the equation.

Sayre's equation

We derive Sayre's equation, with the function θ_h written out in terms of the atomic scattering factors, starting from the Fourier coefficient of a squared structure:

$$\begin{aligned}\sum_{\mathbf{h}'=-\infty}^{\infty} F_{\mathbf{h}'}F_{\mathbf{h}-\mathbf{h}'} &= \sum_{\mathbf{h}'=-\infty}^{\infty}\sum_{n=1}^{N} f_n(\mathbf{h}')\exp(2\pi i\mathbf{h}'\,.\,\mathbf{r}_n)\\ &\times\sum_{m=1}^{N} f_m(\mathbf{h}-\mathbf{h}')\exp(2\pi i(\mathbf{h}-\mathbf{h}')\,.\,\mathbf{r}_m)\\ &= \sum_{n=1}^{N}\sum_{m=1}^{N}\exp(2\pi i\mathbf{h}\,.\,\mathbf{r}_m)\\ &\times\sum_{\mathbf{h}'=-\infty}^{\infty} f_n(\mathbf{h}')f_m(\mathbf{h}-\mathbf{h}')\exp\{2\pi i\mathbf{h}'\,.\,(\mathbf{r}_n-\mathbf{r}_m)\}\\ &= \sum_{n=1}^{N}\sum_{m=1}^{N} g_{nm}(\mathbf{h})\exp(2\pi i\mathbf{h}\,.\,\mathbf{r}_m) \qquad (1)\end{aligned}$$

with $g_{nm}(\mathbf{h})=0$ if $n\neq m$ and $g_{nm}(\mathbf{h})=g_m(\mathbf{h})$ if $n=m$. Then

$$g_m(\mathbf{h})=\sum_{\mathbf{h}'=-\infty}^{\infty} f_m(\mathbf{h}')f_m(\mathbf{h}-\mathbf{h}')\,. \qquad (2)$$

If all atoms are equal, then the subscript m can be omitted and equation (1) written as

$$\begin{aligned}\sum_{\mathbf{h}'=-\infty}^{\infty} F_{\mathbf{h}'}F_{\mathbf{h}-\mathbf{h}'} &= g(\mathbf{h})\sum_{n=1}^{N}\exp(2\pi i\mathbf{h}\,.\,\mathbf{r}_n)\\ &= \frac{g(\mathbf{h})}{f(\mathbf{h})}\sum_{n=1}^{N} f(\mathbf{h})\exp(2\pi i\mathbf{h}\,.\,\mathbf{r}_n)\\ &= \frac{\sum_{\mathbf{h}'} f(\mathbf{h}')f(\mathbf{h}-\mathbf{h}')}{f(\mathbf{h})}F_{\mathbf{h}}\,, \qquad (3)\end{aligned}$$

which is Sayre's equation in the desired form.*

If a structure contains P equal light atoms together with N–P heavy atoms with known positions, then the summation (1) can be separated into two parts, one involving a summation over the light atoms, the other over the heavy atoms:

$$\begin{aligned}\sum_{\mathbf{h}'} F_{\mathbf{h}'}F_{\mathbf{h}-\mathbf{h}'} &= \sum_{m=1}^{N} g_m(\mathbf{h})\exp(2\pi i\mathbf{h}\,.\,\mathbf{r}_m)\\ &= \sum_{m=1}^{P} g^L(\mathbf{h})\exp(2\pi i\mathbf{h}\,.\,\mathbf{r}_m)\end{aligned}$$

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* It must be noted that if series-termination goes together with a considerable degree of regularity in the structure, $g_{nm}(\mathbf{h})$ in equation (1), where

$$g_{nm}(\mathbf{h})=\sum_{\mathbf{h}'} f_n(\mathbf{h}')f_m(\mathbf{h}-\mathbf{h}')\exp\{2\pi i\mathbf{h}'\,.\,(\mathbf{r}_n-\mathbf{r}_m)\}\,,$$

is not equal to zero if $m\neq n$ and thus remains a function of the atomic positions. Consequently, Sayre's equation (3) is not strictly valid in this case.

$$+\sum_{m=P+1}^{N} g_m^M(\mathbf{h}) \exp(2\pi i\mathbf{h}\,.\,\mathbf{r}_m)$$
$$=\frac{g^L(\mathbf{h})}{f^L(\mathbf{h})} F_{\mathbf{h}}^L + G_{\mathbf{h}}^M$$
$$=\frac{g^L(\mathbf{h})}{f^L(\mathbf{h})}(F_{\mathbf{h}}^L+F_{\mathbf{h}}^M)-\frac{g^L(\mathbf{h})}{f^L(\mathbf{h})}F_{\mathbf{h}}^M+G_{\mathbf{h}}^M$$
$$=\frac{1}{\theta_{\mathbf{h}}^L} F_{\mathbf{h}}-\frac{1}{\theta_{\mathbf{h}}^L}F_{\mathbf{h}}^M+G_{\mathbf{h}}^M \qquad (4)$$

in which

$g^L(\mathbf{h})$	is the scattering factor of a squared light atom
$g^M(\mathbf{h})$	is the scattering factor of a squared heavy atom
$f^L(\mathbf{h})$	is the scattering factor of a light atom
$F_{\mathbf{h}}^L$	is the contribution of the light atoms to the structure factor
$F_{\mathbf{h}}^M$	is the contribution of the heavy atoms to the structure factor
$G_{\mathbf{h}}^M$	is the contribution of the heavy atoms to the Fourier coefficient of the squared structure
$\theta_{\mathbf{h}}^L$	is equal to $\frac{f^L(\mathbf{h})}{g^L(\mathbf{h})}=\frac{f^L(\mathbf{h})}{\sum_{\mathbf{h}'} f^L(\mathbf{h}')f^L(\mathbf{h}-\mathbf{h}')}$

Equation (4) can be rewritten as

$$F_{\mathbf{h}}=\theta_{\mathbf{h}}^L \sum_{\mathbf{h}'} F_{\mathbf{h}'}F_{\mathbf{h}-\mathbf{h}'}+(F_{\mathbf{h}}^M-\theta_h^L G_{\mathbf{h}}^M)\,.$$

As $G_{\mathbf{h}}^M$ is equal to the self-convolution of $F_{\mathbf{h}}^M$, that is, as

$$G_{\mathbf{h}}^M=\sum_{\mathbf{h}'} F_{\mathbf{h}'}^M F_{\mathbf{h}-\mathbf{h}'}^M$$

we obtain:

$$F_{\mathbf{h}}=\theta_h^L \sum_{\mathbf{h}'} F_{\mathbf{h}'}F_{\mathbf{h}-\mathbf{h}'}+(F_{\mathbf{h}}^M-\theta_h^L \sum_{\mathbf{h}'} F_{\mathbf{h}'}^M F_{\mathbf{h}-\mathbf{h}'}^M). \qquad (5)$$

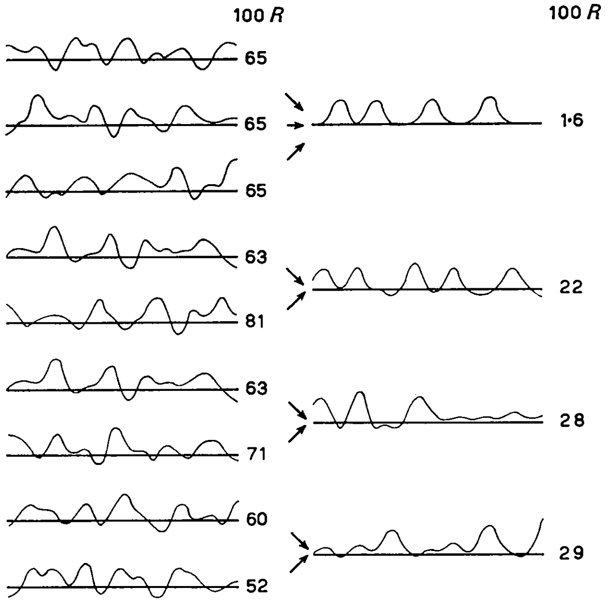

Fig. 1. The sign-reversing procedure applied to a one-dimensional structure. The 'structure' with random signs (left), and with signs after iteration (right).

If the heavy atoms are equal too, then

$$G_{\mathbf{h}}^M=g^M(\mathbf{h}) \sum_{m=P+1}^{N} \exp(2\pi i\mathbf{h}\,.\,\mathbf{r}_m)$$
$$=\frac{g^M(\mathbf{h})}{f^M(\mathbf{h})} \sum_{m=P+1}^{N} f^M(\mathbf{h}) \exp(2\pi i\mathbf{h}\,.\,\mathbf{r}_m)$$
$$=\frac{1}{\theta_h^M} F_{\mathbf{h}}^M, \qquad (6)$$

in which

$f_{\mathbf{h}}^M$ is the scattering factor of a heavy atom,

$$\theta_h^M=\frac{f^M(\mathbf{h})}{g^M(\mathbf{h})}=\frac{f^M(\mathbf{h})}{\sum_{\mathbf{h}'} f^M(\mathbf{h}')f^M(\mathbf{h}-\mathbf{h}')}\,.$$

Then equation (5) finally becomes

$$F_{\mathbf{h}}=\theta_h^L \sum_{\mathbf{h}'} F_{\mathbf{h}'}F_{\mathbf{h}-\mathbf{h}'}+F_{\mathbf{h}'}^M\left(1-\frac{\theta_h^L}{\theta_h^M}\right)\,. \qquad (7)$$

In equations (5) and (7) the known heavy-atom contribution is separated from the part containing the unknown phases.

Equation (5) can also be derived by writing down Sayre's equation for the light-atom part of the structure (Appendix).

Algorithm

The problem is to find an algorithm which, starting with one initial set of phases, searches for those phases that match the structure factors as calculated by equations (3) or (7) to the observed structure factors as closely as possible. For the non-centric case Sayre's equation (3), for computational reasons without the function θ_h, consists of two parts:

$$A_{\mathbf{h}}=\sum_{\mathbf{h}'} F_{\mathbf{h}'}F_{\mathbf{h}-\mathbf{h}'} \cos(\varphi_{\mathbf{h}'}^0+\varphi_{\mathbf{h}-\mathbf{h}'}^0)$$
$$B_{\mathbf{h}}=\sum_{\mathbf{h}'} F_{\mathbf{h}'}F_{\mathbf{h}-\mathbf{h}'} \sin(\varphi_{\mathbf{h}'}^0+\varphi_{\mathbf{h}-\mathbf{h}'}^0) \qquad (8)$$

with a consistency index defined as:

$$R=\frac{1}{\sum_{\mathbf{h}} \frac{|F_{\mathbf{h}}|}{\theta_h}} \sum_{\mathbf{h}} \left[\left(\frac{|F_{\mathbf{h}}|}{\theta_h}\cos\varphi_{\mathbf{h}}^0-A_{\mathbf{h}}\right)^2 + \left(\frac{|F_{\mathbf{h}}|}{\theta_h}\sin\varphi_{\mathbf{h}}^0-B_{\mathbf{h}}\right)^2\right]^{1/2} \qquad (9)$$

in which $\varphi_{\mathbf{h}}^0$ belongs to the initial set of phases.

We propose to improve the phases by the following algorithm: The initial phases are first rounded off to one of the values $\frac{n\,.\,360^\circ}{n_{\max}}$, with $n=0(1)\,n_{\max}-1$. Execute the summations (8) and calculate R. Next take one structure factor $F_{\mathbf{p}}$ and let its phase angle $\varphi_{\mathbf{p}}$ run through the values $\varphi_{\mathbf{p}}^0+\frac{n\,.\,360^\circ}{n_{\max}}$, with $n=1(1)\,n_{\max}-1$. Calculate for each value of n the corresponding value of $A_{\mathbf{h}}(n)$ and $B_{\mathbf{h}}(n)$ with the aid of the formulae:

$$A_{\mathbf{h}}(n)=A_{\mathbf{h}}(n=0)+2\,|F_{\mathbf{p}}|\,|F_{\mathbf{h}-\mathbf{p}}|$$

$$\times\ \left\{\cos\left(\varphi^0_{\mathbf{P}}+\frac{360n}{n_{\max}}+\varphi^0_{\mathbf{h}-\mathbf{P}}\right)-\cos\left(\varphi^0_{\mathbf{P}}+\varphi^0_{\mathbf{h}-\mathbf{P}}\right)\right\}$$
$$+2\,|F_{\mathbf{P}}|\,|F_{\mathbf{h}+\mathbf{P}}|$$
$$\times\ \left\{\cos\left(\varphi^0_{\mathbf{P}}+\frac{360n}{n_{\max}}-\varphi^0_{\mathbf{h}+\mathbf{P}}\right)-\cos\left(\varphi^0_{\mathbf{P}}-\varphi^0_{\mathbf{h}+\mathbf{P}}\right)\right\},\quad(10)$$

$$B_{\mathbf{h}}(n)=B_{\mathbf{h}}(n=0)+2\,|F_{\mathbf{P}}|\,|F_{\mathbf{h}-\mathbf{P}}|$$
$$\times\ \left\{\sin\left(\varphi^0_{\mathbf{P}}+\frac{360n}{n_{\max}}+\varphi^0_{\mathbf{h}-P}\right)-\sin\left(\varphi^0_{\mathbf{P}}+\varphi^0_{\mathbf{h}-\mathbf{P}}\right)\right\}$$
$$-2\,|F_{\mathbf{P}}|\,|F_{\mathbf{h}+\mathbf{P}}|$$
$$\times\ \left\{\sin\left(\varphi^0_{\mathbf{P}}+\frac{360n}{n_{\max}}-\varphi^0_{\mathbf{h}+\mathbf{P}}\right)-\sin\left(\varphi^0_{\mathbf{P}}-\varphi^0_{\mathbf{h}+\mathbf{P}}\right)\right\},\quad(10)$$

only if $\mathbf{P}\neq\mathbf{h}-\mathbf{P}$, and $\mathbf{h}\neq\mathbf{0}$.
Also

$$A_{\mathbf{h}}(n)=A_{\mathbf{h}}(n=0)$$
$$+|F_{\mathbf{P}}|^2\left\{\cos\left(2\varphi^0_{\mathbf{P}}+2\frac{360n}{n_{\max}}\right)-\cos\left(2\,\varphi^0_{\mathbf{P}}\right)\right\}$$
$$+2|F_{\mathbf{P}}|\,|F_{\mathbf{h}+\mathbf{P}}|$$
$$\times\ \left\{\cos\left(\varphi^0_{\mathbf{P}}+\frac{360n}{n_{\max}}-\varphi^0_{\mathbf{h}+\mathbf{P}}\right)-\cos\left(\varphi^0_{\mathbf{P}}-\varphi^0_{\mathbf{h}+\mathbf{P}}\right)\right\},\ (11)$$

$$B_{\mathbf{h}}(n)=B_{\mathbf{h}}(n=0)$$
$$+|F_{\mathbf{P}}|^2\left\{\sin\left(2\varphi^0_{\mathbf{P}}+2\frac{360n}{n_{\max}}\right)-\sin\left(2\varphi^0_{\mathbf{P}}\right)\right\}$$
$$-2|F_{\mathbf{P}}|\,|F_{\mathbf{h}+\mathbf{P}}|$$
$$\times\ \left\{\sin\left(\varphi^0_{\mathbf{P}}+\frac{360n}{n_{\max}}-\varphi^0_{\mathbf{h}+\mathbf{P}}\right)-\sin\left(\varphi^0_{\mathbf{P}}-\varphi^0_{\mathbf{h}+\mathbf{P}}\right)\right\}\quad(11)$$

if $\mathbf{P}=\mathbf{h}-\mathbf{P}$ and $\mathbf{h}\neq\mathbf{0}$. The factors of 2 do not occur in the second terms because here $\mathbf{h}'$ and $\mathbf{h}-\mathbf{h}'$ simultaneously become equal to $\mathbf{P}$. Calculate for every n the corresponding values of the disagreement factors $R(n)$. Let $F_{\mathbf{P}}$ finally assume the phase angle $\varphi^0_{\mathbf{P}}+\frac{360n}{n_{\max}}$ corresponding to the lowest value of $R(n)$.

This procedure is repeated for all structure factors, taking the larger ones first. This causes the consistency index to decrease gradually. After a number of cycles every change in phase angle will increase R. The process then ends.

For the non-centric case we have tested this procedure for a one-dimensional structure. An example will be given.

If the reciprocal net contains mirror planes or rotation axes, then there are equivalent reflexions, the phases of which have to be changed simultaneously, taking into account the phase relations. Equations (10) and (11) then contain correspondingly more terms.

For a centrosymmetric structure* we define

$$F^C_{\mathbf{h}}\equiv\textstyle\sum_{\mathbf{h}'}F_{\mathbf{h}'}F_{\mathbf{h}-\mathbf{h}'}$$

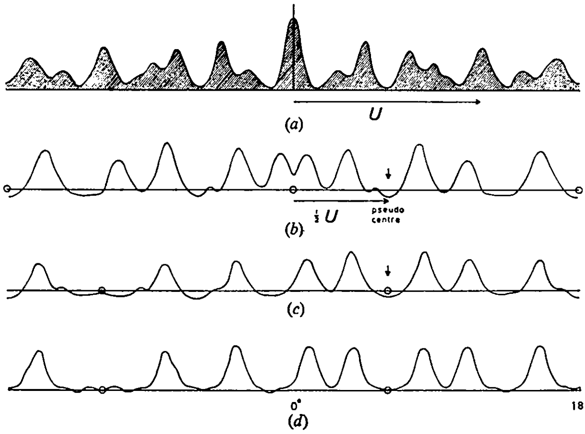

Fig. 2. Interpretation of a false structure. (*a*) Patterson function; (*b*) false structure, $R=0{\cdot}22$; (*c*) minimum function, $R=0{\cdot}17$; (*d*) correct structure, $R=0{\cdot}016$.

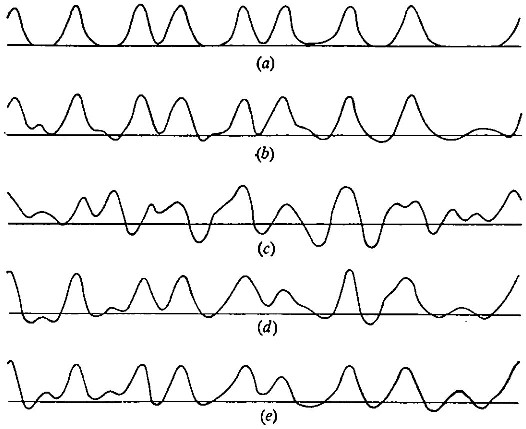

Fig. 3. Centrosymmetric structure treated as acentric. The 'structure' deduced with (*a*) correct phases, $R=0{\cdot}013$; (*b*) correct phases rounded off to discrete values 0°, 45°, . . . ; (*c*) random phases, $R=0{\cdot}839$; (*d*) cycle 1, $R=0{\cdot}364$; (*e*) Cycle 8, $R=0{\cdot}286$.

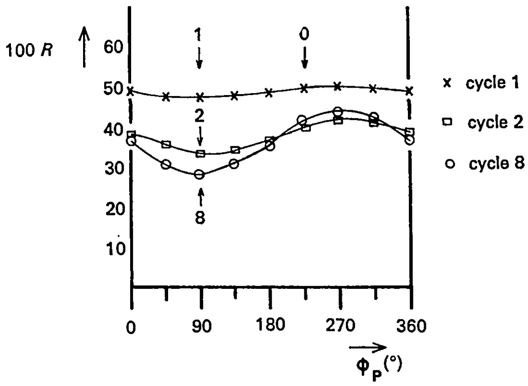

Fig. 4. R as a function of the phase angle $\varphi_{\mathbf{P}}$ of one reflexion $F_{\mathbf{P}}$.

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* Cochran & Douglas (1955) proposed a similar algorithm for systematic sign changing, but their criterion – maximalization of the sum of triple products – appeared to be insufficiently stringent.

and the disagreement factor (9) reduces to

$$R=\sum_{\mathbf{h}}\left|\frac{F_{\mathbf{h}}}{\theta_h}-F_{\mathbf{h}}^C\right|/\sum_{\mathbf{h}}\frac{|F_{\mathbf{h}}|}{\theta_h}\,.$$

With $n_{\max}=2$, which corresponds to increments in phase angle of 180°, equation (10) is greatly simplified:

$$F_{\mathbf{h}}(n=1)=F_{\mathbf{h}}(n=0)-4F_{\mathbf{P}}F_{\mathbf{h}-\mathbf{P}}-4F_{\mathbf{P}}F_{\mathbf{h}+\mathbf{P}}. \qquad (12)$$

When the vector $\mathbf{P}$ in the reciprocal net is related by symmetry to a vector $\mathbf{P}'$ then $F_{\mathbf{P}'}$ will change sign if $F_{\mathbf{P}}$ changes sign. If it does:

$$F_{\mathbf{h}}(n=1)=F_{\mathbf{h}}(n=0)-4F_{\mathbf{P}}F_{\mathbf{h}-\mathbf{P}}$$
$$-4F_{\mathbf{P}}F_{\mathbf{h}+\mathbf{P}}-4F_{\mathbf{P}'}F_{\mathbf{h}-\mathbf{P}'}-4F_{\mathbf{P}'}F_{\mathbf{h}+\mathbf{P}'}\,. \qquad (13)$$

In the event of higher symmetry, equation (13) contains correspondingly more terms. However, care must be taken not to subtract invariant terms, such as $F_{\mathbf{P}}^2(\mathbf{h}=\mathbf{0})$, $F_{\mathbf{P}}^2(\mathbf{h}=2\mathbf{P})$ or $F_{\mathbf{P}}F_{\mathbf{h}-\mathbf{P}}$ (if $\mathbf{h}-\mathbf{P}=\mathbf{P}'$, where $\mathbf{P}'$ is related to $\mathbf{P}$ by symmetry). The latter will occur if the vector $\mathbf{h}$ is in a mirror plane or if $\mathbf{h}$ coincides with a rotation axis.

Program

The algorithm was programmed in Algol for triclinic, monoclinic and orthorhombic centrosymmetric space groups, using formula (7). To test the applicability to non-centrosymmetric space groups also an acentric one-dimensional program was devised.

One can give a list with signs to the program. If the sign of a certain structure factor is not in the list, then this structure factor will be given the sign of the heavy-atom contribution (or of the known light-atom contribution, as the case may be). If there is no contribution of known atoms to a particular structure factor and its sign is not in the list, then it is given a sign chosen at random.

The program offers the possibility of sharpening the observed structure factors. The influence of sharpening on θ_h^L and θ_h^M is then accounted for.

It is also possible to change the signs of only those structure factors for which $F_{\mathbf{h}}/\theta_h$ exceeds a certain value; this value can gradually be lowered.

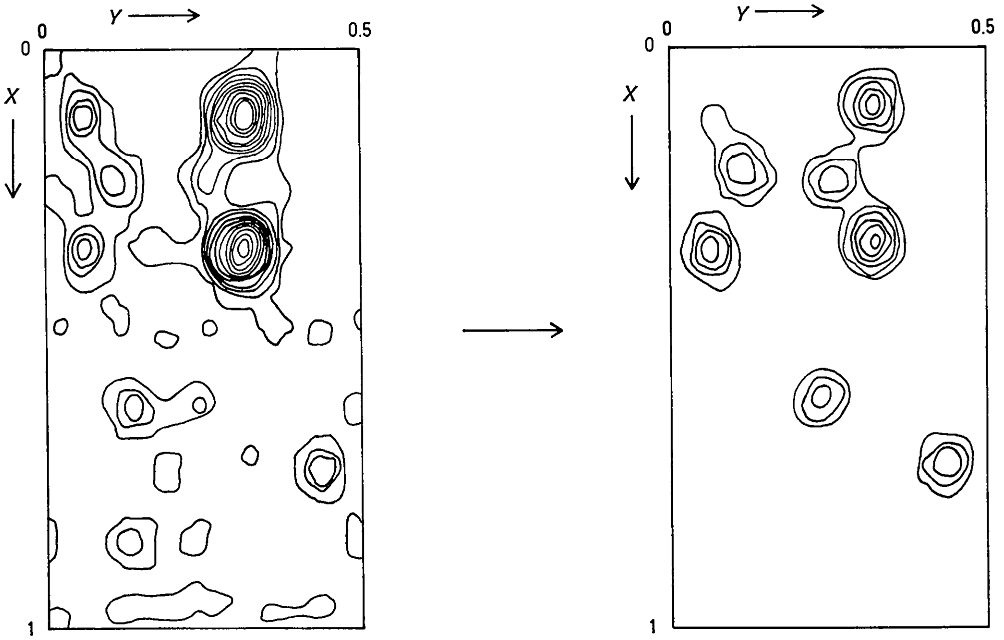
As the computing time depends linearly on the number of equations the number of equations used in the process may be restricted too.

Examples

1. *Starting with random signs*

A one-dimensional example (Sayre, 1952), is shown in Fig. 1. Starting with 30 different combinations of signs, 10 of them resulted in the correct structure. The other sets stopped in subsidiary minima. Some of the results are shown in Fig. 1. As can be seen from Fig. 1, the process tends to create structures with small negative areas, but certainly some discrete peaks.

In trying to find a method for restarting the sign-reversing procedure after the deadlock in a subsidiary minimum, we notice a resemblance to atomic distances between the correct structure and a false one. In order to find a relation between the two structures, we tried to imagine how a false structure could be built up if



(a) (b)

Fig. 5. Glycollic acid, Fourier sections at $z=0{\cdot}25$, with (a) signs obtained from the positions of two oxygen atoms. R (Sayre) = 0·470; (b) signs resulting from the sign-reversing procedure. R (Sayre) = 0·083.

we start from the correct one, keeping in mind that:

(i) the correct and a false structure both correspond to the same Patterson function;

(ii) a false structure corresponds to a solution of Sayre's equation, which means that it will contain a number of equal peaks.

If we build up a false structure by superimposing the correct structure on its image, obtained by inverting the correct one through one of its pseudo-centres, we shall fulfil more or less conditions (i) and (ii). In this way false Patterson peaks are introduced, but not many of them if the pseudo-centre is pronounced enough. As Patterson (1949) has pointed out pseudo-centres in a structure are situated relative to the centre of symmetry at points halfway along the Patterson vectors. The pseudo-centres are more like real centres the higher the corresponding Patterson peaks. In Fig. 2 we demonstrate how we find the correct structure by searching for an appropriate pseudo-centre in the false structure, by reversing the above procedure. Fig. 2(*a*) shows the Patterson function with one of its highest peaks at u; Fig. 2(*b*) shows the false structure (Fig. 1, $R=0{\cdot}22$) with a pseudo-centre at $\frac{1}{2}u$. In Fig. 2(*c*) the pseudo-centre of Fig. 2(*b*) is changed into a real centre by taking the minimum of the values of the calculated electron density ($R=0{\cdot}22$) at corresponding points to the left and right of the pseudo-centre. The minimum function thus determined has a close resemblance to the real structure [Fig. 2(*d*)]. The Fourier transform of this minimum function resulted in new signs ($R=0{\cdot}17$ in Sayre's equation). After applying the sign-reversing procedure to this set R decreased to 0·0147, indicating that the correct structure had been found.

In this example, given in Fig. 2, the appropriate pseudo-centre was found by trial and error. So, if we are going to include the above procedure in the sign-reversing algorithm we should have to systematize the detection of the appropriate pseudo-centres in false structures. We believe that the foregoing illustrates the nature of a false structure.

2. *Starting with random phases*

Using the same one-dimensional centrosymmetric example with the origin shifted away from the centre of symmetry, it was shown that, provided we start with phases chosen at random from the discrete set $360n/8$, the method again produced the more-or-less correct set in one third of the cases. An example is shown in Fig. 3. Apparently increments in phase angle of 45° are accurate enough to make the algorithm work.

It also appeared that in the majority of cases R, as a function of the phase angle of one reflexion, has one minimum and one maximum 180° apart (Fig. 4). It is noteworthy that after the first cycle no great changes in phase angle were observed.

3. *Signs obtained from direct methods*

Glycollic acid (Pijper, 1971) has been solved by the correlation method of de Vries (1965). The method resulted in 8 sets of signs; the correct set was found after inspection of the Fourier syntheses. We applied

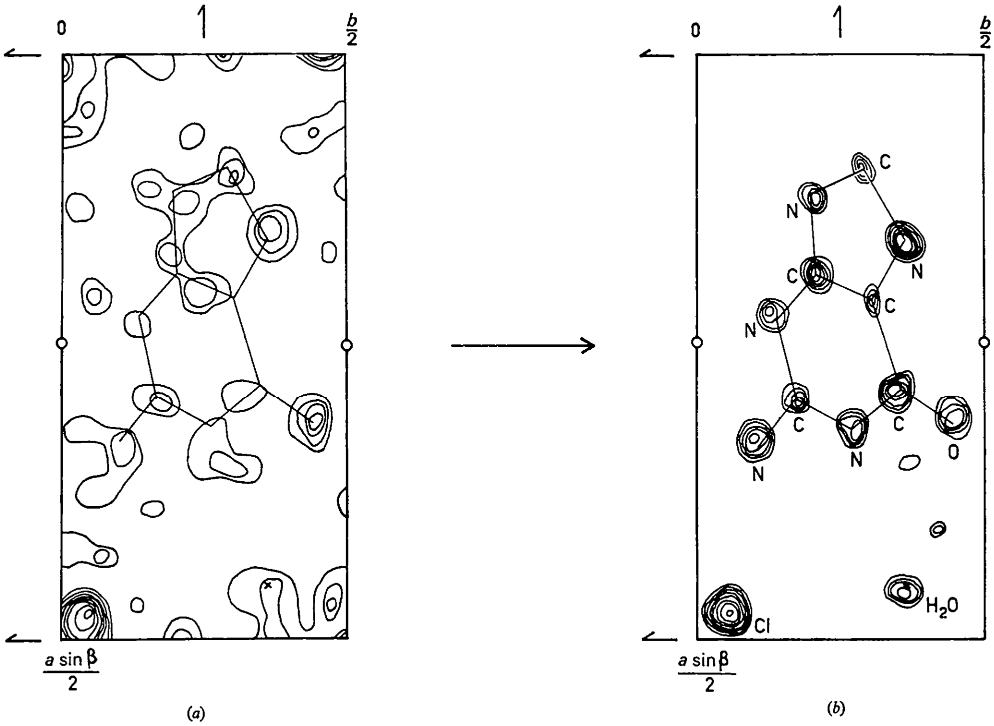


Fig. 6. Guanine hydrochloride monohydrate. Electron density projection along the c axis (*a*) With signs obtained from the chlorine contribution. R (Sayre)$=0{\cdot}25$; (*b*) with signs after the sign-reversing procedure. R (Sayre)$=0{\cdot}18$.

our sign-reversing procedure to these eight sets. Before the refinement the *R*'s were high with no indications for the correct set. After the refinement the correct set was indicated by the lowest *R* value (Table 1).

Table 1. *Glycollic acid*

Eight sets of signs, obtained by the correlation method of de Vries (1965), subjected to the sign-reversing procedure.

Set	Initial *R* (× 100)	Number of cycles	Final *R* (× 100)	
1	51	11	28	
2	47	8	29	
3	51	10	17	correct set
4	43	10	26	
5	50	11	23	
6	51	9	29	
7	51	9	24	
8	46	9	27	

4. *Signs obtained from the contribution of some light atoms in the equal-atom case*

Before the structure of glycollic acid was found by direct methods much searching of the Patterson function had been done, resulting only in the finding of the positions of two oxygen atoms (out of a total of 10 atoms). We applied the sign-reversing procedure to the signs obtained from these two atoms; it resulted in the correct structure. In Fig. 5 a relevant section through the three-dimensional Fourier shows the structure before and after refinement.

Another example is methylmalonic acid (Derissen, 1970). From the Patterson function two possible configurations were found, which differed only in the position of the methyl group. One configuration did refine by the least-squares method and gave the correct structure; the other configuration did not refine. We applied the sign-reversing procedure to the two sets of signs obtained from the atomic positions in the two configurations. In both cases the same correct solution resulted.

5. *Signs obtained from the contributions of heavy atoms*

Applying the sign-reversing procedure to guanine hydrochloride monohydrate (Broomhead, 1951), we found that this procedure gave the correct structure only if sharpened amplitudes were used (Fig. 6). This is explained by the fact that the contributions of the heavy atoms to the structure factors are greater for the higher-order reflexions.

We thank Professor A. F. Peerdeman for valuable discussions and suggestions. We are grateful to Mr D. Kaas for writing the computer program.

APPENDIX

Equation (5) is identical to Sayre's equation for the light-atom part of the structure alone, as will now be shown.

Sayre's equation for the light-atom part is

$$F^L_{\mathbf{h}} = \theta^L_h \textstyle\sum_{\mathbf{h}'} F^L_{\mathbf{h}'} F^L_{\mathbf{h}-\mathbf{h}'}$$

or

$$\begin{aligned} F_{\mathbf{h}} - F^M_{\mathbf{h}} &= \theta^L_h \textstyle\sum_{\mathbf{h}'} (F_{\mathbf{h}'} - F^M_{\mathbf{h}'})(F_{\mathbf{h}-\mathbf{h}'} - F^M_{\mathbf{h}-\mathbf{h}'}) \\ &= \theta^L_h (\textstyle\sum_{\mathbf{h}'} F_{\mathbf{h}'} F_{\mathbf{h}-\mathbf{h}'} - 2\textstyle\sum_{\mathbf{h}'} F_{\mathbf{h}'} F^M_{\mathbf{h}-\mathbf{h}'} \\ &\qquad + \textstyle\sum_{\mathbf{h}'} F^M_{\mathbf{h}'} F^M_{\mathbf{h}-\mathbf{h}'}). \end{aligned}$$

$\sum_{\mathbf{h}'} F_{\mathbf{h}'} F^M_{\mathbf{h}-\mathbf{h}'}$ is the Fourier coefficient of the product of the electron density corresponding to the complete structure, and the electron density corresponding to the heavy-atom structure. However, this product is equal to the squared heavy-atom structure with Fourier coefficient $\sum_{\mathbf{h}'} F^M_{\mathbf{h}'} F^M_{\mathbf{h}-\mathbf{h}'}$.

So

$$\textstyle\sum_{\mathbf{h}'} F_{\mathbf{h}'} F^M_{\mathbf{h}-\mathbf{h}'} = \textstyle\sum_{\mathbf{h}'} F^M_{\mathbf{h}'} F^M_{\mathbf{h}-\mathbf{h}'}.$$

Therefore

$$\mathrm{F}_{\mathbf{h}} - F^M_{\mathbf{h}} = \theta^L_h (\textstyle\sum_{\mathbf{h}'} F_{\mathbf{h}'} F_{\mathbf{h}-\mathbf{h}'} - \textstyle\sum_{\mathbf{h}'} F^M_{\mathbf{h}'} F^M_{\mathbf{h}-\mathbf{h}'})$$

which is identical with equation (5).

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