center or not. On the other hand, the pattern does not show any difference for the diffraction groups 3 and 6 which have different vertical rotation axes. The diffraction group 3*m* cannot be distinguished from the groups 3 and 6 or from the group 6*mm* in either setting of two possible settings (see columns 1, 4, 6 and 10 of Table 3). However, it is found that most diffraction groups can be identified from one photograph, which makes a strong contrast to the method of Buxton *et al.* This fact is very important from an experimental viewpoint because symmetries obtained by comparing two photographs are unreliable in critical cases, as the photographs may be taken from different specimen areas. In the square four-beam case, the fourfold rotary inversion ($\bar{4}$) produces the symmetry 4_R in the disks *F* and *F*′. The inversion center itself does not exhibit any specific symmetry in a SMB setting, but its effect appears through the horizontal mirror plane which is automatically introduced when the inversion center is added to the vertical twofold axis (see the third row of Table 4). It is emphasized that all seven diffraction groups can be identified from one square four-beam pattern. In the rectangular four-beam case, the inversion center not only directly but also indirectly produces no specific symmetry. The rectangular four-beam pattern cannot distinguish the diffraction groups *m* and 2*mm*, since they differ only in two-dimensional symmetry elements. The diffraction group m_R has only a horizontal twofold axis. The 2_Rmm_R has a vertical mirror (m_v) and the inversion center (*i*) as well as the horizontal twofold axis. These two groups, however, cannot be distinguished from one rectangular pattern, since the pattern is insensitive to m_v and *i*. On the other hand, a rectangular four-beam pattern can distinguish the diffraction groups *m* and 2_Rmm_R and 2*mm* and $2mm1_R$, whereas the method of Buxton *et al.* requires two or three photographs to identify the groups, because the zone-axis pattern is insensitive to three-dimensional symmetry elements. A rectangular four-beam setting is also possible for the diffraction groups in which hexagonal six-beam setting or square four-beam setting was considered. Symmetries of such a rectangular four-beam pattern can be understood by finding the symmetry elements active to the pattern out of all the elements of the diffraction groups.

When a pair of symmetrical many-beam patterns are taken, all the diffraction groups are completely identified. For practical purposes, however, the use is recommended of a symmetrical many-beam pattern and the zone-axis pattern, since two-dimensional symmetries are found very easily in the zone-axis pattern. In conclusion, we emphasize again that the symmetrical many-beam method is quite an effective method to determine the point groups of crystals.

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Strengthened Translation Functions. An Automated Method for the Positioning of a Correctly Oriented Fragment by Translation Functions in *DIRDIF* Fourier Space

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Abstract

Translation functions are used to determine the position of a correctly oriented molecular fragment. Usually, translation functions are defined for the Patterson space. A new translation function is presented, which is defined as a convolution in electron-density space, and expressed as a Fourier synthesis. After expansion of the reflection data to space group *P*1, coefficients for the synthesis are obtained by direct methods on difference structure factors (the *DIRDIF* procedures). From the position of the maximum in the translation function, the

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position of the known fragment relative to symmetry elements can be obtained. The new translation function provides a fast and reliable method for the positioning of a correctly oriented fragment, if the fragment constitutes at least about 10% of the *total* scattering power of the primitive unit cell. The procedure has been automated in the computer program *TRADIR*. Examples of applications on known and unknown structures are given.

1. Introduction

Often the orientation of a molecular fragment with respect to the crystal axes is known. Usually these fragments are determined by one of two important methods:

Orientation search methods in Patterson space (Braun, Hornstra & Leenhouts, 1969; Crowther, 1972; Nordman & Schilling, 1970; Schilling, 1970).

A priori direct methods. Routine application of direct methods will often lead to an E map in which large parts of the molecule can be recognized. However, systematic phase errors may cause the fragment to be in a correct orientation but in a wrong position (Silva & Viterbo, 1980).

The next step in these known-orientation-unknown-origin cases (in all space groups but $P1$) is the determination of the translation vector, which, upon application, will position the fragment correctly with respect to the symmetry elements of the sapce group. This can be achieved by:

A. *Translation functions*, which may be designated as 'Patterson' techniques, and which are measured to fit in:

Vector space (match between model and observed Patterson map; Braun, Hornstra & Leenhouts, 1969; Huber, 1965; Nordman & Nakatsu, 1963).

Intensity space (correlation between calculated and observed intensities; Tollin, 1966; Crowther & Blow, 1967; Langs, 1975; Karle, 1972; Beurskens, 1981).

B. *Methods based on direct methods.*

The phases derived from a known fragment can be recycled in space group $P1$ with a (modified) tangent formula (Karle, 1968), to obtain an E map in space group $P1$.

A similar approach, using difference structure factors, was applied by Beurskens, Van den Hark & Beurskens (1976), using the *DIRDIF* procedures (DIRect methods on DIFference structure factors; Van den Hark, Prick & Beurskens, 1976), again in $P1$. (The resulting Fourier map is called a *DIRDIF* Fourier map.)

A careful examination of the Fourier map in space group $P1$, based on the correctly oriented fragment, may lead to the recognition of symmetry-dependent fragments (which are related to the input fragment by symmetry elements at unknown positions in the cell).

The problems arising in the application of A ('Patterson' translation functions) are mainly due to considerable overlap in the Patterson map. The problems arising from B (based on direct methods) are mainly due to difficulties in the interpretation of the $P1$ Fourier map.

Recently, we introduced a new method to determine the position of the molecular fragment (Doesburg & Beurskens, 1981): we defined the 'strengthened' translation functions as translation functions in *DIRDIF* Fourier space. The functions do not depend on finding individual atoms but rather measure the match of unidentifiable peaks in the *DIRDIF* $P1$ Fourier map with a known search model. The method may therefore be considered as a powerful combination of the computational tools designed for methods A and B.

The present translation functions can also be applied to conventional difference Fourier maps (using ΔF's, based only on the known model); the application of *DIRDIF*, however, leads to a significant improvement of phases as well as amplitudes of the structure factors of the *difference structure*. This improvement is especially important when only a small fraction of the structure is initially known.

2. Definition of the strengthened translation function

With the rotation matrix R_s and the translation vector $\mathbf{t}_s$ of the symmetry operation s, symmetry-dependent positions $\mathbf{r}_s$ in any space group are given by

$$\mathbf{r}_s = R_s\,\mathbf{r} + \mathbf{t}_s, \qquad (1)$$

$\mathbf{r}_s$, $\mathbf{r}$ are column vectors, $\mathbf{r}$ is an arbitrary positional vector.

The symmetry-related reflections $\mathbf{h}_s$ are defined as

$$\mathbf{h}_s = \mathbf{h}R_s, \qquad (2)$$

$\mathbf{h}_s$, $\mathbf{h}$ are row vectors.

Reflections $\mathbf{h}_s$ obey

$$|F(\mathbf{h}_s)| = |F(\mathbf{h})| \qquad (2A)$$

$$\varphi(\mathbf{h}_s) = 2\pi\mathbf{h}\,.\,\mathbf{t}_s + \varphi(\mathbf{h}). \qquad (2B)$$

Usually only symmetry-independent reflections are available: reflections $\mathbf{h}_s$ are generated with (2) (excluding Friedel-related and identical reflections) and are assigned an observed structure factor:

$$|F_{\rm obs}(\mathbf{h}_s)| = |F_{\rm obs}(\mathbf{h})|.$$

After this expansion of the data, the symmetry elements are discarded, the reflections $\mathbf{h}$ and $\mathbf{h}_s$ are considered to be symmetry independent, and we have a 'symmetry-reduced' space group which is either $P1$ or a lattice-centered equivalent for non-primitive space groups.

Let $\{\mathbf{r}_p\}$ be the set of atomic positions of the known fragment with correct orientation (p = partial structure). Phases and amplitudes $F_p(\mathbf{h})$ for this fragment can be calculated in the symmetry-reduced space group:

$$F_p(\mathbf{h}) = \sum_j f_j \exp\,[2\pi i\mathbf{h}.(\mathbf{r}_p)_j].$$

$\sum_j$ includes all atoms of the partial structure. $F_p(\mathbf{h})$ is calculated for all reflections $\mathbf{h}$ and $\mathbf{h}_s$ because relations (2A) and (2B) are not applicable in the symmetry-reduced space group.

Let ρ_p be the electron-density function of a molecular fragment which is correctly oriented in the cell and, consequently, correctly positioned in the triclinic non-centrosymmetric space group:

$$\rho_p(\mathbf{r}) = \frac{1}{V}\sum_h F_p(\mathbf{h}) \exp\,(-2\pi i\mathbf{h}.\mathbf{r}). \tag{3}$$

The summation over $\mathbf{h}$ in (3) includes the generated reflections $\mathbf{h}_s$. The difference structure (the rest of the structure in the symmetry-reduced space group being the entire contents of the unit cell minus the input fragment) is expressed by the Fourier series

$$\rho_r(\mathbf{r}) = \frac{1}{V}\sum_{\mathbf{h}} F_r(\mathbf{h}) \;\exp\,(-2\pi i\mathbf{h}.\mathbf{r}). \tag{4}$$

The coefficients $F_r(\mathbf{h})$, which are the structure factors of the difference structure, are not known, and ρ_r cannot be calculated. For a conventional difference-Fourier map $F_r(\mathbf{h})$ is replaced by $\Delta F(\mathbf{h})$, based on the input fragment. The *DIRDIF*-refined coefficients, also denoted $F_r(\mathbf{h})$, are a far better approximation for the true structure factors of the difference structure, and they can be used in (4) for the calculation of a *DIRDIF* Fourier map, now denoted ρ_r.

This difference-electron-density function ρ_r does contain the molecular fragments which are related to the input fragment ρ_r by the symmetry elements of the true space group; the symmetry elements, however, are at unknown positions (relative to the position of the input fragment).

The symmetry-related fragments are now used as a search model in the *DIRDIF* Fourier space. This search model ρ_{ps} is defined, for any symmetry element, as

$$\rho_{ps}(\mathbf{r}_s) = \rho_p(\mathbf{r}). \tag{5}$$

Thus each search model is defined as a result of applying on ρ_p the symmetry operators R_s and $\mathbf{t}_s$, where s runs from 2 to n, with n = total number of symmetry operations. The search model can, in principle, be calculated by

$$\rho_{ps}(\mathbf{r}) = \frac{1}{V}\sum_{\mathbf{h}} F_{ps}(\mathbf{h}) \exp\,(-2\pi i\mathbf{h}.\mathbf{r}). \tag{6}$$

In this expression, F_{ps} is defined as

$$F_{ps}(\mathbf{h}) = \sum_j f_j \exp\,[2\pi i\mathbf{h}.(\mathbf{r}_s)_j]$$

for given s. Summation over j is over symmetry-related atomic positions $\mathbf{r}_s$. Using (1) and (2), we obtain

$$F_{ps}(\mathbf{h}) = F_p(\mathbf{h}_s) \exp\,(2\pi i\mathbf{h}.\mathbf{t}_s). \tag{7}$$

Analogously to translation search methods in Patterson space, ρ_{ps} is translated, now in the *DIRDIF* Fourier space, to find the maximum fit with the rest structure. From the coordinates of the resulting vector, the translation vector $\mathbf{t}_0$ can be obtained.

A general translation function is defined by Argos & Rossmann (1980); for our purpose we define this translation function $Q_s(\mathbf{q})$ as a measure of fit for ρ_{ps} in ρ_r:

$$Q_s(\mathbf{q}) = \int\limits_{\text{unit cell}} \rho_{ps}(\mathbf{r}-\mathbf{q})\,\rho_r(\mathbf{r})\,\mathrm{d}\mathbf{r}. \tag{8}$$

$Q_s(\mathbf{q})$ will be maximal for exact coincidence of ρ_{ps} and ρ_r at $\mathbf{q} = \mathbf{q}_0$.

After substitution of (6) and (4) into (8) and integrating term by term, the result is

$$Q_s(\mathbf{q}) = \frac{1}{V}\sum_{\mathbf{h}} F^*_{ps}(\mathbf{h})\,F_r(\mathbf{h}) \exp\,(-2\pi i\mathbf{h}.\mathbf{q}), \tag{9}$$

where F^* is the complex conjugate of F. Equation (9) can also be derived by considering it to be the convolution of two electron-density functions. The functions to be convoluted are the rest structure, ρ_r, and the inverted search fragment ρ^i_{ps}. According to properties of convolutions, this will give, in reciprocal space, a multiplication of the Fourier coefficients of the two electron-density functions, which is identical to (9). This expression is used for the actual calculation of the translation functions. It can simply be evaluated by standard fast Fourier transform (FFT) techniques. For all reflections partial structure factors $F_p(\mathbf{h})$ are calculated. For a given symmetry operation s, transformation (7) readily gives $F_{ps}(\mathbf{h})$ values for all reflections. The *DIRDIF* results [refined $F_r(\mathbf{h})$ values] are not used as coefficients for the calculation of a *DIRDIF* Fourier map, but are multiplied by $F^*_{ps}(\mathbf{h})$, which, after Fourier transformation, leads to the translation function for the specified symmetry element. The *DIRDIF* refinement is executed only once: the calculation of $Q(\mathbf{q})$ is repeated for each of the $(n-1)$ symmetry elements.

Note: A perfect overlap of a search model with a completely correct rest structure will lead to

$$Q(\mathbf{q}_0)=\frac{1}{V}\sum_{h}|F_p(\mathbf{h})|^2\equiv Q_0.$$

A relative measure of fit is defined as $Q(\mathbf{q})/Q_0$.

3. The translation vector $\mathbf{t}_0$

The desired translation vector $\mathbf{t}_0$, over which the original set of atomic coordinates $\{\mathbf{r}_p\}$ is to be shifted, is related to $\mathbf{q}_0$ in a symmetry-dependent way. If the set $\{\mathbf{r}_0\}$ is the correctly located set, the next equation holds for corresponding positions in the two sets:

$$\mathbf{r}_0=\mathbf{r}_p+\mathbf{t}_0. \qquad (10)$$

The position of the true-symmetry-related set $\{\mathbf{r}_s\}$ (*not* identical to the atomic positions of ρ_{ps}) is defined by

$$\mathbf{r}_s=R_s\,\mathbf{r}_0+\mathbf{t}_s=R_s(\mathbf{r}_p+\mathbf{t}_0)+\mathbf{t}_s. \qquad (11)$$

Application of *DIRDIF* in $P1$ on the basis of $\{\mathbf{r}_p\}$ will yield a set of positions $\{\mathbf{r}_r\}$, which contains subsets of correctly oriented symmetry-related fragments $\{\mathbf{r}_s\}$. A shift over $\mathbf{t}_0$ will superimpose these sets:

$$\mathbf{r}_s=\mathbf{r}_r+\mathbf{t}_0. \qquad (12)$$

Equation (12) is the symmetry-related analogon of (10).

Equating (11) and (12) gives

$$R_s r_p+\mathbf{t}_s=\mathbf{r}_r+(I-R)\,\mathbf{t}_0, \qquad (13)$$

where I is the unity matrix. Interpretation of (13) in terms of the electron-density functions defined in § 2 tells us that the left-hand side of (13) represents ρ_{ps}, and that $\{\mathbf{r}_r\}$ constitutes ρ_r. The last term of (13) with a minus sign thus gives the expected position $\mathbf{q}_0$ of the maximum of $Q_s(\mathbf{q})$, when the model and structure exactly overlap:

$$\mathbf{q}_0=-(I-R_s)\,\mathbf{t}_0. \qquad (14)$$

From (14) three components of $\mathbf{t}_0$ can be determined if R_s is the rotation matrix for inversion or rotation–inversion. In the case of a rotation of screw axis the component in the direction of the axis is undetermined. Mirror or glide planes only allow the determination of one component of $\mathbf{t}_0$, perpendicular to the plane; the other two components are undetermined. An unknown component of $\mathbf{t}_0$ may become available from the Q map for a different symmetry element. If only one twofold symmetry element (2, 2_1, m, a, b, c, n) is present (*e.g.* $P2_1$, Pc) the model can be translated freely in one or two directions with undetermined components. In such space groups the undetermined components are assigned an arbitrary value of zero. For triclinic, monoclinic and orthorhombic space groups each translation vector $\mathbf{t}_0$ can be reduced modulo $(\frac{1}{2},\frac{1}{2},\frac{1}{2})$:

$$\mathbf{t}_0=[X_o(\mathrm{mod}\,\tfrac{1}{2}),\,Y_0(\mathrm{mod}\,\tfrac{1}{2}),\,Z_0(\mathrm{mod}\,\tfrac{1}{2})]. \qquad (15)$$

This reduction describes eight possible vectors (0 or $\frac{1}{2}$, in three directions) that correspond merely to a shift of the coordinate system from one permissible origin to another (see Hauptman, 1972). In, say, $P2_1$, (15) takes the form

$$\mathbf{t}_0=[X_0(\mathrm{mod}\,\tfrac{1}{2}),\,0,\,Z_0(\mathrm{mod}\,\tfrac{1}{2})].$$

For space groups with symmetry higher than orthorhombic, the additional translational symmetry can be determined according to the rules given by Hall (1970) and is contained implicitly in *International Tables for X-ray Crystallography* (Karle, 1974). For example, in $P3_1$, (15) becomes $\mathbf{t}_0=[X_0(\mathrm{mod}\,\frac{1}{3}),\,Y_0(\mathrm{mod}\,\frac{1}{3}),\,0]$, with the condition that $X_0(\mathrm{mod}\,\frac{1}{3})=2Y_0(\mathrm{mod}\,\frac{1}{3})$.

4. The *TRADIR* procedure

In this section we will briefly describe the *TRADIR* (TRAnslation function in DIRdif Fourier space) procedure. After expansion of the reflection data, the normal *DIRDIF* facilities are used as in space group $P1$. After the determination of scaling and separate temperature factors for partial and rest structure, pseudo-normalized structure factors E_1 are defined as the normalized equivalent of the conventional difference structure factors $(|F_{\mathrm{obs}}|-|F_p|)\exp i\varphi_p$ (see Beurskens, Prick, Doesburg & Gould, 1979). By using E_1 values and phases as input to a weighted tangent refinement procedure, new reliable indications for the phases of the rest structure factors are obtained. Accordingly, $|F_r|$ values are calculated by the vector relationship: $F_{\mathrm{obs}}=F_p+|F_r|\exp(i\varphi_r)$. The resulting phased F_r values are stored for the calculations of the Fourier coefficients given in (9). Now, the position of the input fragment has to be determined relative to $(n-1)$ symmetry elements. Accordingly, $(n-1)$ summations of type (9) have to be calculated and resulting Q maps interpreted. The Q map for a centre of symmetry or for a $\bar{3}$ or $\bar{4}$ axis has three-dimensional character, because the position of the inversion centre has to be fixed in three directions. In the case of n-fold rotation or screw axis, only two components for $\mathbf{t}_0$ need to be determined. For mirror- and glide-plane operations, a one-dimensional Fourier summation will suffice. This reduction of the problem of finding $\mathbf{t}_0$ is also noticed in Patterson-search translation functions (sum function; Tollin, 1970).

In the present procedure each of the $(n-1)$ Q maps is searched for peak maxima. As it is expected that small partial structures will lead to Q maps in which the strongest peak may not represent $\mathbf{t}_0$, several peaks are collected from each of the Q maps. The coordinates of the peaks in the respective maps are reduced to components of $\mathbf{t}_0$ by the use of (14). After all searches have been completed, it is attempted to combine the various indications for the components of $\mathbf{t}_0$ resulting from the $(n - 1)$ searches into one, if possible, three-dimensional vector, which is consistent in its components for each of the searches (see § 5 for an actual example).

More than one possible solution for $\mathbf{t}_0$ may arise. Because the heights of the peaks in the Q maps are given on an identical scale, various results for a component of $\mathbf{t}_0$ can be compared, weighted according to their corresponding peak heights. The reliability of different three-dimensional results for $\mathbf{t}_0$ can be estimated according to the summed peak heights. In space groups in which $n = 2$ such a combination of results, which is a reinforcement of individual results, is not possible and only one indication for a three-dimensional ($P\bar{1}$) or two- or one-dimensional vector (*e.g.* $P2_1$, Pc) is obtained.

5. A theoretical and practical example in $P2_1/c$

In this section the practical use of formulae presented in § 4 is illustrated for a specific space group, $P2_1/c$. Also, details of the actual calculation will be shown. Table 1 lists the equivalent positions for $P2_1/c$. Symmetry-related reflections are hkl, $\bar{h}k\bar{l}$, $\bar{h}\bar{k}\bar{l}$ and $h\bar{k}l$. Reflection data were expanded for space group $P1$ by generating an $\bar{h}\bar{k}\bar{l}$ reflection for each hkl, except for $0k0$ or $h0l$ reflections. A partial structure with correct orientation and incorrect position must be translated with respect to three symmetry elements. These symmetry elements are ignored during structure-factor calculations and *DIRDIF* refinement of the difference structure factors, but will explicitly be used in the calculations of the translation functions.

Consider the positioning of the fragment with respect to the 2_1 axis, *i.e.* the determination of the vector components X_0 and Z_0 of $\mathbf{t}_0$ which shift the fragment to the correct position with respect to the 2_1 axis. Formulae (7) and (9) are now rewritten for the case of a 2_1 axis.

Table 1. *An example of a possible combination of results of different searches in space group $P2_1/c$, where $-\mathbf{t}_0$ is the vector over which the correctly located fragment was misplaced*

Equivalent position	Expression for expected maximum in Q map	Possible consistent three-dimensional result
$-x, \frac{1}{2}+y, \frac{1}{2}-z$	$-(2X_0, 0, 2Z_0)$	
$-x, -y, -z$	$-(2X_0, 2Y_0, 2Z_0)$	$(X_0, Y_0, Z_0) = \mathbf{t}_0$
$x, \frac{1}{2}-y, \frac{1}{2}+z$	$-(0, 2Y_0, 0)$	

For the symmetry-related reflections hkl and $\bar{h}k\bar{l}$ (7) becomes:

$$\text{for } \mathbf{h} = hkl\text{: } F_p(\mathbf{h}) = F_p(hkl);\ F_{ps}(hkl) = F_p(\bar{h}k\bar{l}) \exp \pi ik$$
$$\text{for } \mathbf{h} = \bar{h}k\bar{l}\text{: } F_p(\mathbf{h}) = F_p(\bar{h}k\bar{l});\ F_{ps}(\bar{h}k\bar{l}) = F_p(hkl) \exp \pi ik.$$

The two reflections enter (9) as the sum:

$$F_p^*(\bar{h}k\bar{l})\,(-1)^k\,F_r(hkl) \exp\left[-2\pi i(hx_q + ky_q + lz_q)\right] + F_p^*(hkl)\,(-1)^k\,F_r(\bar{h}k\bar{l}) \exp\left[-2\pi i(\bar{h}x_q + ky_q + \bar{l}z_q)\right]. \tag{16}$$

Actually, the results of (16) are summed over k and stored as two-dimensional Fourier coefficients $G(hl)$ and will be used for the calculation of a two-dimensional search function:

$$Q_s(x_q, z_q) = \frac{1}{V} \sum G(hl) \exp\left[-2\pi i(hx_q + lz_q)\right].$$

The position of the expected maximum in this Q function gives the components X_0 and Z_0 of the translation vector $\mathbf{t}_0$. The flow chart (Fig. 1) gives a summary of the calculations for the 2_1 axis.

The translation functions for $\bar{1}$, 2_1 and c are calculated in parallel, *i.e.* after the execution of

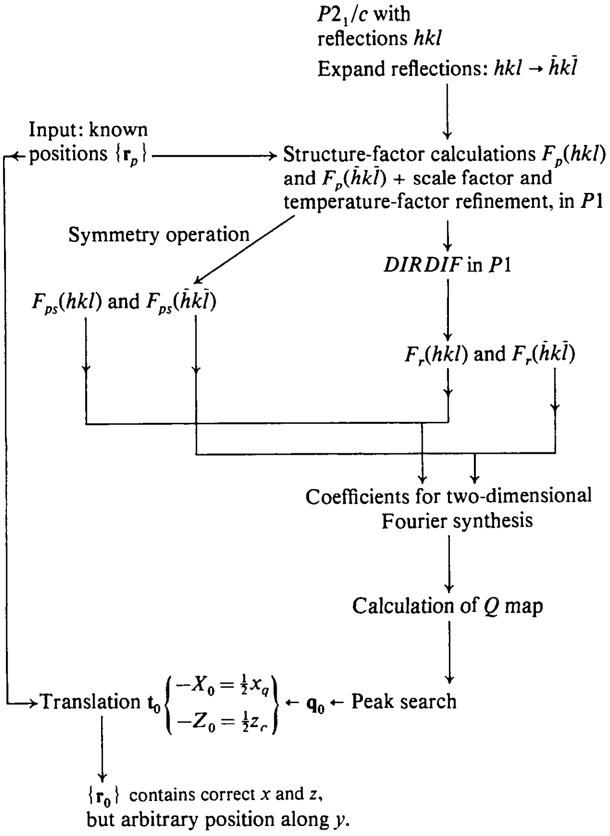


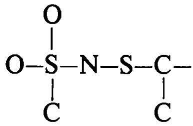
Fig. 1. Flow chart of the *TRADIR* system, for a translation search for the 2_1 axis in $P2_1/c$.

DIRDIF three types of coefficients are calculated simultaneously. After all Fourier syntheses, which give the *Q* maps, have been calculated and interpreted, the results for the three searches are combined. Table 1 illustrates the combination of different indications for the components of $\mathbf{t}_0$.

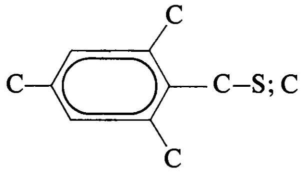
Test calculations

As a test of the procedure a known structure was shifted over an arbitrary but known vector. Starting with the complete structure, smaller fragments were used also to test the performance of the translation function as a function of known scattering power. The test structure is: (*Z*) – *S*′-phenyl-*S*′-(*p*-toluenesulphonamido)-2,4,6-trimethyldithiobenzoate, $C_{23}H_{23}NO_{23}$; space group $P2_1/c$, $Z = 4$; $a = 9.223$, $b = 16.210$, $c = 15.282$ Å, $\beta = 100.83°$; abbreviated as THIM (Prick, 1978). Number of reflections: 2084. After expansion: 4060 reflections. Refined positional parameters were shifted over a fixed vector for each of the following THIM fragments.

I. One complete molecule, excluding H atoms: $C_{23}NO_2S_3$.

II.

$$\mathrm{O{-}\overset{\overset{\displaystyle O}{|}}{\underset{\underset{\displaystyle C}{|}}{S}}{-}N{-}S{-}\underset{\underset{\displaystyle C}{|}}{C}{-}S};\ C_3NO_2S_3$$

III. Three S atoms (relative positions may be available from Patterson synthesis).

IV.

$C_{10}S$.

We define the fractional scattering power p^2 of a fragment as: p^2 = average of $|F_p|^2/(\sum_j f_j^2)$, $\sum_j$ = sum over all atoms. The calculations were performed by *DIRDIF* (Beurskens *et al.*, 1981).

Table 2 gives the results for the separate searches on every symmetry element and the combined results which yield a vector that is suitable for translation. From this table it can be concluded that for all fragments the correct vector is found as the combined vector with the highest sum of the peak maxima from the individual searches. Furthermore, it shows that indications for a component of $\mathbf{t}_0$ which are obtained from a one-dimensional search (mirror or glide symmetry) are very strong compared to results from a two-, or even more, a three-dimensional search. Especially for small fragments, such as fragment IV for which $p^2 < 0.10$, the correct answer for $\mathbf{t}_0$ is only obtained as the fourth peak in the three-dimensional *Q* map. However, the first three peaks from this map can be excluded since they cannot combine with any of the indications resulting from the other *Q* maps. The computing times needed for the translation searches are indicated in Table 3.

Table 2. *Application of the strengthened translation functions Q*(**q**) *to some fragments of THIM*

Locations and peak heights of main maxima in the *Q* maps are listed. The true vector is (0·20, 0·10, 0·30).

			Symmetry element													
			2_1 axis at $(0,y,\frac{1}{4})$			$\bar{1}$ at (0,0,0)				*c* at $(x,\frac{1}{4},z)$		Combined vector			
Fragment	p^2	Q_0	q_x	q_z	Max.	q_x	q_y	q_z	Max.	q_y	Max.	$-X_0$	$-X_0$	$-Z_0$	Max. sum
I	0·26	400	0·40	0·60	372	0·40	0·20	0·60	274	0·20	373	0·20	0·10	0·30	1019
			0·78	0·46	84	0·40	0·32	0·10	113	0·69	15	0·23	0·10	0·35	525
			0·52	0·55	75	0·11	0·67	0·22	99	0·89	9				
			0·46	0·71	72	0·76	0·35	0·95	95						
			0·64	0·52	70	0·40	0·54	0·10	94						
II	0·18	271	0·40	0·60	315	0·40	0·20	0·60	197	0·20	281	0·20	0·10	0·30	793
			0·03	0·74	78	0·40	0·32	0·10	117	0·72	27				
			0·53	0·55	69	0·76	0·36	0·95	112	0·88	15				
			0·26	0·65	66	0·41	0·38	0·10	111	0·84	8				
			0·77	0·46	66	0·04	0·36	0·25	100						
III	0·14	221	0·40	0·60	240	0·40	0·20	0·60	144	0·20	242	0·20	0·10	0·30	625
			0·53	0·54	87	0·13	0·72	0·23	104	0·72	24				
			0·17	0·69	67	0·76	0·36	0·96	96	0·89	16				
			0·47	0·86	54	0·26	0·47	0·22	92						
			0·48	0·71	50	0·16	0·44	0·13	91						
IV	0·09	189	0·40	0·60	49	0·22	0·03	0·82	113	0·19	62	0·20	0·10	0·30	174
			0·55	0·09	45	0·27	0·28	0·72	69	0·40	30	0·30	0·20	0·04	140
			0·15	0·84	42	0·64	0·43	0·08	65	0·69	28	0·10	0·35	0·17	96
			0·92	0·95	39	0·41	0·20	0·60	63	0·89	25				
			0·94	0·77	38	0·36	0·78	0·20	61						

Table 3. *Computing time* (s) *for translation searches on some fragments of THIM for different steps of the procedure on an IBM* 4341, *model* 2

Fragment (see Table 2)	Expansion of reflection data	Structure-factor calculation and normalization	Tangent refinement on difference structure factors	Calculation Q maps and interpretation	Total
I	9·6	71·4	120·5	40·8	242·3
IV	9·6	51·0	49·2	41·4	151·2

6. Further *TRADIR* experiences

The *TRADIR* procedure has been automated and incorporated in the *DIRDIF* program system; it has been tested and used on a number of known (test) and unknown structures. In this section results are summarized. A review of the structures, with code names and crystal data, is given in Table 4.

The procedure was applied in the structure determination of six unknown structures:

in two cases the orientation of a fragment of the structure was determined from the Patterson synthesis (PENTAN and AUP1). *TRADIR* was used to find the position of the fragment in the cell.

in four cases a molecular fragment or some possible atomic positions were obtained from *MULTAN* (Main, 1980) (TERMIN, TMPPA, SYDNON and NAHMAL), but the complete structure could not be determined with routine methods. In one case (TERMIN) the correct position was found by *TRADIR*. In the three remaining cases *TRADIR* was used to prove that the position was correct (translation vector equals null vector) and the complete structure was obtained after careful application of various methods.

Approximately 12 known structures were used to investigate the specific properties of the procedure, four of which are listed in Table 4. Special attention was given to the following points of interest:

TRADIR results for small fragments. The influence of the size of a correctly oriented fragment was tested, using data of HEPTA as a trial structure. Preliminary results have been published (Beurskens, 1981). It should be mentioned that the *TRADIR* results, given therein, greatly improve if the number of tangent refinement cycles for the difference structure factors is varied. By optimization of this number, smaller fragments (eight C atoms out of a total of 120) could be correctly located.

Tests were performed also in space groups with Laue symmetry higher than orthorhombic (DIAMBE). The same lower limit of 10% for p^2 for reliable answers was observed.

It appeared to be possible to position a single medium–heavy atom in a moderately small organic structure (one S atom in MONOS, $p^2 = 0{\cdot}07$). Application of *TRADIR* in such a special case causes an enantiomorph-fixation problem (Prick, Beurskens & Gould, 1978), as one known atom constitutes a centrosymmetric model structure in $P1$. Consequently, 'enantiomorph-related' peaks will also appear in the Q maps, although with lower densities after the enantiomorph-fixation procedure used in DIRDIF.

TRADIR results if a false orientation is used as input. Peaks in the Q map will have very low densities compared to the expected maximum density. In addition, it will be difficult, if not impossible, to build a three-dimensional translation vector that is consistent for all searches. The successful determination of a combined vector is highly indicative for the correctness of the orientation. Preliminary *DIRDIF* results (refinement of temperature factors, R values) can also support the supposed correctness of an orientation. It should be noticed that if a wrong model is used as input, the null vector is not present in any of the Q maps.

Relative strength of different searches. A good

Table 4. *Some of the crystal structures which served as examples for the TRADIR procedure*

Code name	Molecular formula	Known/unknown structure	Space group	Z	Number of non-H atoms in unit cell	Reference
THIM	$C_{23}H_{23}NO_2S_3$	known	$P2_1/c$	4	116	(*a*)
HEPTA	$C_{30}H_{18}$	known	$P2_1$	4	120	(*b*)
MONOS	$C_{15}H_{16}N_2O_2S$	known	$P2_12_12_1$	4	80	(*c*)
DIAMBE	$C_{13}H_{12}N_2O$	known	$P3_1$	3	48	(*d*)
PENTAN	$C_{14}H_{14}N_2O_2$	unknown	$Pbca$	8	144	(*e*)
AUP1	$C_{126}H_{105}Au_7P_7$	unknown	$P\bar{1}$	8	1120	(*f*)
TMPPA	$C_{20}H_{27}F_3O_3$	unknown	$P2_1$	2	52	(*g*)
TERMIN	$C_{27}H_{21}Na$	unknown	$P\bar{1}$	2	92	(*h*)
SYDNON	$C_7H_7N_3O_2$	unknown	$P2/c$	8	96	(*i*)
NAHMAL	$C_4O_5H_5Na$	unknown	Pa	4	40	(*j*)

References: (*a*) Prick (1978); (*b*) Beurskens, Beurskens & Van den Hark (1976); (*c*) Noordik, Beurskens, Ottenheijm, Herscheid & Tijhuis (1978); (*d*) Van der Velden & Noordik (1980); (*e*) Doesburg, Noordik & Beurskens (1983); (*f*) Bosman, Beurskens, Van der Velden & Noordik (1982); (*g*) Doesburg, Petit & Merckx (1982); (*h*) Noordik, Doesburg & Prick (1981); (*i*) Hasek *et al.* (1982); (*j*) Lenstra & Doesburg (1983).

indication of the relative strength was given by the determination of PENTAN. In this space group seven Q maps have to be calculated. Four independent determinations for each component of $\mathbf{t}_0$ can be expected. It was noticed that the searches for the three glide planes gave the strongest indications for components X_0, Y_0 and Z_0 of $\mathbf{t}_0$.

7. Discussion and conclusions

From the results of applying *TRADIR* on both known and unknown structures, several important conclusions can be drawn with regard to the reliability and applicability of the technique.

Symmetry considerations

In high-symmetry space groups, in which the total number of symmetry operations can be larger (say eight), there is often only one way in which the results of the (seven) searches can be combined into one three-dimensional translation vector. A large number of symmetry operations implies a rapid decrease of the known scattering fraction upon reduction to the non-centrosymmetric triclinic space group. At first sight this seems a considerable disadvantage of the technique. However, the larger number of searches counter balances this effect.

The correct vector is usually obtained with the largest probability from the one-dimensional search. The answer coming from the three-dimensional search gives smaller (correct peak height)/(lower peak height) ratios. Therefore, it is recommendable to give a large weight to the results from the one- and (slightly less) two-dimensional searches. Though every search (1D, 2D, 3D) involves a shifting of a three-dimensional fragment in the three-dimensional *DIRDIF* Fourier space, for a 1D search (2D search), the search is executed in a fixed plane (along a fixed line). This avoids disturbance by overlapping densities from other (unknown) fragments, which, in a three-dimensional search can happen quite frequently.

Once a consistent answer for $\mathbf{q}_0$ is obtained, $\mathbf{t}_0$ can be calculated in a straightforward way from $\mathbf{q}_0$ and is now uniquely determined. An ambiguity concerning the sign of the parameter shift may arise in other types of translation functions (Karle, 1972), because of the high symmetry of the Patterson space, in which the search is done. In the functions presented here, no such ambiguity exists.

Comparison with other methods

The major drawback of the translation functions defined in the Patterson space is the amount of overlap of interatomic peaks, even if sharpened coefficients are used. Since the present function is defined in Fourier space, no such overlap exists.

Other methods for locating fragments in Fourier space (tangent recycling, *DIRDIF*, or Fourier methods) executed in $P1$ are based upon identification of atoms. In *TRADIR*, electron-density functions are fitted to each other, and correlations will occur even in regions where no clearly separated atomic densities are visible and this will give a considerable contribution to $Q(\mathbf{q})$.

Computing time

The computing time needed for a conventional Patterson translation search is strongly dependent on the number of symmetry elements, the number of vectors used in the search, and the setting of various program parameters. Although time limits for the several types of translation function are not frequently specified, and, if available, are hard to compare because of different computer properties, it is our experience that some Patterson-search translation functions are very computer-time consuming, especially if additional optimization is required. When comparing the times given in Table 3 with those for conventional programs running on our computer (*DIRDIF*, *MULTAN*, *FC-step* of XRAY), it is found that the time for the execution of *TRADIR* is of the same order of magnitude. It is, in any case, negligible compared with the time needed for the refinement of the structure.

Number of reflections

A possible reduction of the number of reflections, leading to a reduction of computing times, may be considered. In R criteria (Petit, Lenstra & Van Loock, 1981) or in rotation functions (Tollin & Rossman, 1966), this reduction was investigated. A threshold on $|E|$ values is often applied. Obviously, in our type of translation functions, the tangent refinement of the difference structure factors plays an important role, and in the *DIRDIF* method all reflections participate in the procedure.

In certain cases, however, a limit on $\sin\theta/\lambda$ values can be applied to discard high-order reflections, which may suffer severely from errors in the model. In addition this can also lead to a more stable refinement of temperature factors and scale factors, which should be determined optimally to arrive at a good starting point for the tangent refinement.

Small fragments

From the experimental results, it can be concluded that if at least about 10% of the total scattering power is known, the method will provide a reliable answer for

$\mathbf{t}_0$. If less is known, alternative answers can be evaluated by normal *DIRDIF* use.

It appears that the procedure is not very sensitive to small errors in the fragment or the orientation of the fragment.

Applications

The main application of the strengthened translation functions is the determination of a correctly oriented molecular fragment in the unit cell with respect to the symmetry elements.

In some applications (*e.g.* TMPPA) a very strong indication for the null vector as a solution of $\mathbf{t}_0$ was obtained. It appeared that this is a very strong indication for the correctness of the original position of the molecular fragment.

In some cases, only a very poor fragment is available (bad geometry, or inaccurate orientation, or an uninterpretable collection of peaks from an E map). In such cases relatively large peaks in the strengthened translation functions are very probable indications for the correctness of large parts of the model structure (*e.g.* TMPPA, TERMIN). Such 'model verification' may be followed by *DIRDIF* in order to modify the model (small atomic shifts, removal of some atoms); thereafter *DIRDIF* will usually lead to a rapid development of the structure.

In principle, the *TRADIR* procedure can also be used to position two independent fragments in space group $P1$: F_{ps} [in (9)] is simply to be replaced by the calculated structure factors for the second fragment; the interpretation of the Q map is straightforward. Alternatively, two *DIRDIF* results can be convoluted.

The application of the strengthened translation functions on protein structure analysis has not been tested so far. Some preliminary tests of the application of *DIRDIF* on protein molecules are in progress (Parthasarathi & Beurskens, 1982). If satisfactory results are obtained, *TRADIR* will be tested on its applicability to protein structures.

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