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Convolutions Applied to the Trial and Error Method of Crystal Structure Analysis

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Fourier syntheses equivalent to the convolution of the calculated electron density function and either the Patterson function or the difference Patterson function can reveal the errors in a postulated model, if the positions of some of the atoms are postulated correctly. The peak heights and the locations of the principal maxima in the distributions are derived. Generally, for a structure containing atoms of equal weight, those in correct positions are generated with greater peak heights in the convolutions relative to the corresponding peaks in the calculated electron density distribution than are the erroneous maxima, but this difference is dependent upon the fraction of correctly postulated atoms. The correct sites are indicated by new maxima in the distribution, but the magnitude of these also depends upon the 'correctness' of the model. The interpretation of these functions in terms of image and point set theory is also outlined briefly. The application of one of these functions to the solution of a projection of dihydromalvalic acid is demonstrated.

Introduction

In a crystal structure analysis by the method of trial and error, it is not uncommon for the successive Fourier refinement to terminate at an incorrect solution as a result of a gross error in a part of the model, although the remainder of the atoms are correctly placed. Often intuitive methods are used for finding the corrections, making use of known stereochemical relationships. Another well-known technique, described by Bunn (1961), makes use of the error or difference synthesis. In connection with the structure determination of some long chain compounds, which are particularly susceptible to this sort of difficulty, we have developed and applied Fourier syntheses of the type described by Ramachandran & Raman (1959) for indicating the error in a partially correct trial structure. The method is based on the convolution of the calculated electron density function with either the observed Patterson function or the difference Patterson function. Essentially it compares the postulated model with the Patterson function and, being an analytical method, is more readily adopted for use with a high speed computer than are methods which rely on chemically reasonable modifications to the trial model.

The convolutions and their properties

Consider the convolutions in (1) and (2) below

$$A(r) = \int_0^{V_c} P_0(u)\varrho_c(u+r)\,d\tau\ , \qquad (1)$$

$$B(r) = \varrho_c r + \int_0^{V_c} S[\Delta P(u)]\varrho_c(r+u)\,d\tau\ . \qquad (2)$$

Maxima occur in $A(r)$ whenever

$$r_{a'bc} = u_{a'} - u_b + u_c \qquad (3)$$

where $u_{a'}$ is the positional parameter of the ath atom in the calculated electron density function, ϱ_c, and $(u_c - u_b)$ is an interatomic vector in the observed Patterson function. The function $B(r)$ is the sum of the calculated electron density function and its convolution with the difference Patterson function ΔP, which has been sharpened and scaled by the factor S, so that the peaks in $B(r)$ are comparable to those in ϱ_c.

By the convolution theorem the Fourier expansions of equations (1) and (2) are

$$A(r) = \frac{1}{V_c}\sum_H |F_o(\mathbf{H})|^2 F_c(\mathbf{H}) \exp\left[-2\pi i \mathbf{H}.\mathbf{r}\right] \qquad (4)$$

and

$$B(r) = \frac{1}{V_c}\sum_H \left(1 + \frac{|F_o(\mathbf{H})|^2 - |F_c(\mathbf{H})|^2}{\overline{|F|^2}}\right) F_c \times \exp\left[-2\pi i \mathbf{H}.\mathbf{r}\right]. \qquad (5)$$

The term, $\overline{|F|^2}$ in (5) refers to the mean squared structure factor over an adequate range of $\sin\theta/\lambda$. These syntheses are related to the α-synthesis discussed by Ramachandran & Raman.

A distribution with maxima that are more comparable with the peak heights in the electron density map is attained by modifying the coefficients in $A(r)$ to give the series,

$$C(r) = \left(\frac{1}{V_c}\sum_H \frac{|F_o(\mathbf{H})|^2}{|F_c(\mathbf{H})|^2} F_c(\mathbf{H}) \exp\left[-2\pi i \mathbf{H}.\mathbf{r}\right] \qquad (6)$$

where

Table 1. *Peak height estimates*

Position	Series	Strength	Second order approximation
r_p	A	$(S_o^2+S_p^2)f_p$*	
r_p	B	$(S_p^2/S_o^2)f_p$	
r_p	C	$(1+S_p^2S_f^2/S_c^4)f_p$	$(1+0{\cdot}66S_p^2S_f^2/S_c^4)f_p$
r_f	A	$S_o^2f_f$	
r_f	B	f_f^3/S_o^2	
r_f	C	$(S_q^2/S_c^2+2S_p^2S_f^2/S_c^4)$	$(0{\cdot}95S_q^2/S_c^2+1{\cdot}32S_p^2S_f^2/S_c^4(f_p$
r_q	A	$S_p^2f_q$	
r_q	B	$(S_p^2/S_o^2)f_q$	
r_q	C	$(S_p^2/S_c^2)f_q$	$(1-0{\cdot}95S_f^2/S_c^2)f_q$

* $S^2=\Sigma f^2$, the origin peak in the Patterson function of the structure indicated by the subscript.

$$\frac{F_o(\mathbf{H})^2}{F_c(\mathbf{H})^2} < N$$

and N must be chosen arbitrarily to ensure that $C(r)$ will not be dominated by a few large terms; for example, by setting it equal to the largest amplitude in the Fourier series. The $C(r)$ series is related to the β-gen series of Ramachandran & Raman (1959), which is defined as follows,

$$\beta\text{-gen} = \frac{1}{V_c}\sum_H \frac{|F_n|^2}{|F_p|^2} F_p \exp\left[-2\pi i\mathbf{H}.\mathbf{r}\right] \qquad (7)$$

where F_n is the true structure factor of the total structure and F_p is the contribution of the known atoms to the structure factor. If the experimental errors in F_o are small

$$F_o \approx F_n = F_p + F_q \qquad (8)$$

and

$$F_c = F_p + F_f \qquad (9)$$

where F_p now refers to the contribution of those atoms correctly located in the model, F_f represents the contribution by the atoms falsely located and F_q is the contribution from the corresponding atoms correctly positioned.

The Fourier coefficients in the series $C(r)$ can now be written as $F_n^2/F_p^*+F_f^*)$, demonstrating the relationship to the β-gen series.

Ramachandran & Raman have shown that the mechanism for deconvoluting the Patterson function by means of the β-gen series can be understood by recognizing that its main maxima coincide with those in the α-gen series which is the following weighted sum function,

$$\alpha\text{-gen} = \frac{1}{V_c}\sum_H |F_n|^2 F_p \exp\left[-2\pi i\mathbf{H}.\mathbf{r}\right]. \qquad (10)$$

The same relationship obtains for our $C(r)$ and $A(r)$ series.

Accordingly the deconvolution can be achieved through the superpositon or vector shift method. By applying the modulation principle (Raman) it is seen that in the $A(r)$ series the maxima of main interest coincide with those in $B(r)$ and $C(r)$ as shown in Table 1. The peak heights in $C(r)$ which have been estimated to the second order of approximation (Srinivasan) indicate that for a postulated structure composed of nearly equally weighted atoms, those in correct positions are generated with greater peak heights in both $A(r)$ and $C(r)$ relative to the corresponding peaks in the calculated electron density function than are the erroneous maxima, and that this difference becomes larger as the fraction of correctly postulated atoms in the model increases. The peak heights at the positions of the unknown atoms also increase with the fraction of correctly postulated atoms. The peak estimates given above are idealized by the assumption of completely resolved maxima with no overlap of the major with background peaks.

The $C(r)$ series differs in two respects from the β-gen series. First F_p in $C(r)$ refers only to the atoms which are correctly postulated in a trial model, while F_p in β-gen are for atoms whose positions explicitly are known, presumably from an analysis of the Patterson. Secondly, the superposition process in relation to $C(r)$ must be imagined as not restricted solely to the atoms contributing to F_p, as in β-gen, but as being extended to include all of the atoms in the postulated structure. From this point of view it is not surprising that the effectiveness of $C(r)$ in bringing out the image of the correct structure is sensitive to the fraction of correct atoms in the model, which suggests the use and scope of the method, since the criterion for determining the model error consists in making a comparison of $C(r)$ and $\varrho_c(r)$. The extent to which an atomic peak in the model is reproduced in $C(r)$ is used as an estimate of the error in the model and in favorable cases new peaks in $C(r)$ not present in ϱ_c can give the unknown positions of atoms. Unfortunately, as mentioned above, this criterion for estimating the model error is itself sensitive to the fraction of the scattering matter that has been correctly postulated in the model.

A double phased Fourier series essentially the same as the isomorphous β synthesis of Ramachandran & Raman has been described and discussed by use of the modulation principle and the vector map point of view (Kartha, 1961). However, the salient properties of the convolutions in $A(r)$ and $B(r)$ are conveniently discussed by use of the matrix theory of point sets. The peak heights and their locations in the convolutions as well as their symmetry properties are discussed from that viewpoint in the next section.

The point set representation of the convolutions

Buerger's matrix algebra for vector sets can be extended straightforwardly to a mathematical description of the point set representation corresponding to the set of maxima generated by the convolutions $A(r)$ and $B(r)$. This permits a study of the weights and locations of the points, their dependence upon coincidences brought about by the 'vector shift or superposition' operation, and the symmetry properties of the point sets.

Suppose that V_o is the vector set matrix analogue of the observed Patterson function and that F_c is the fundamental set corresponding to the calculated electron density function, then $A(r)$ can be represented by the point set matrix F_cV_o. Each point in F_cV_o is a triple, $a'bc$, corresponding to a particular maximum in $A(r)$, for example $r_{a'bc}$ in equation (3). The complete set, F_cV_o, is generated by multiplying each element of V_o on the left by an element in F_c.

$$\begin{aligned} F_cV_o &= a'V_o + b'V_o + \ldots \\ &= a'(aa+ab+ac+\ldots)+b'(aa+ab+ac+\ldots)+ \quad (11) \end{aligned}$$

If V is the vector set of F, then FV becomes the cubed point set, where

$$C = FV = F^3. \quad (12)$$

If F contains n points and is non-centric, then the point set C contains at most $\frac{1}{2}(n^3-n^2+2n)$ points and is also non-centric. Interestingly the number of points in C for the centric case is $\frac{1}{6}(n^3+8n)$.

Images in the cubed set matrix

The image theory by Wrinch (1939) can be extended to the cubed set matrix by following the same method that Buerger (1950) used in applying it to the vector set matrix. The feature of particular interest here is the occurrence of $2n$ images of the fundamental set polygon in the cubed set matrix. On aV, the first layer of the C matrix, consider the first row, $a(aa+ab+ac\ldots)$ which represents the image of the fundamental set polygon in the point a. Clearly, on each layer of the cubed matrix there is found one row with this image property. Therefore n images of this kind occur in the cubed set and these coincide.

Next consider the linear array of matrix elements that run perpendicular to the layer aV and that intersect the main diagonal. One such array is comprised of the points $(aaa+baa+caa+daa+\ldots)$, but this file of matrix elements possesses image properties identical with those of the row described in the preceding paragraph, since $baa = aab$. Evidently a total of $2n$ images of the fundamental set occur in the cubed set matrix and these coincide. However, the number of points in the cubed set matrix that coincide at each point of the fundamental set is $2n-1$, for although $2n$ images coincide, every pair of images has a diagonal element as a common point.

The effect of the coincident images that occur in the cubed set is to make the weight at each of the image points equal to the sum of the weights contributed by each of the coinciding images. For example, the weight of the point in the cubed set coincident with the point a in the fundamental set is $\sum_i^n 2W_i^2W_a - W_a^3$, where W_i is the weight of the ith point in a fundamental set of n points and the summation over the coincident points makes allowance for the fact that although $2n$ images coincide, every pair of images contains a cubed set matrix element and therefore one point in common. The weights at other typical points in the non-centric case are, for example, $W_a^2W_b$ at aba and $2W_aW_bW_c$ at abc (coincides with cba). In the centrosymmetric cubed set matrix, on the other hand, there are $3n-3$ coinciding images of the fundamental set, while systematic coincidences at other typical points number 1 at $aa\bar{a}$, 3 at bab and 6 at abc. The vector shift or superposition method can be considered to be the mechanism for bringing the various images manifested in the cubed set matrix into coincidence. The same result is predicted if the principle of modulation is applied to an equivalent Fourier series with coefficients $F_n|F_n|^2$.

Symmetry properties in the cubed point set

By a transformation of the cubed set matrix into the so-called condensed matrix, it can be shown that if the fundamental set contains a given symmetry element, it is also contained in the cubed set (Sax, 1961). Furthermore, the presence of the inversion center in the vector set does not imply one in the cubed set.

In the same way the matrix representation of the point set F_cV_o can be transformed into a condensed matrix for the purpose of studying the symmetry properties of that point set (Sax, 1961). These considerations lead to the following results:

If the vector set V_o contains the symmetry elements that are present in the vector set V_c, then the space group of F_cV_o is the same as the one assumed for F_c.

If a symmetry element in V_c is not present in V_o, the space groups of F_cV_o and F_c differ.

Finally, if a symmetry element that is contained in V_o is not present in V_c, the corresponding element (present of course in F_o) will not be present in F_cV_o.

The point set representation of the convolution $B(r)$

The point set analogue of the convolution $B(r)$ is given by

$$M = F_c + F_c(V_o - V_c)g\ . \quad (13)$$

The factor g places the weight of certain points in $F_c(V_o-V_c)$ on a basis comparable with the fundamental point weights and is given here by the equation

$$g^{-1}=n\sum_{1}^{N}W^2(a_j) \tag{14}$$

where $W(a_j)$ is the weight of the jth point in the asymmetric unit of F which may be designated by A_i and that contains N points. The subscript i denotes a symmetry related unit and runs from 1 to n.

From the discussion in the preceding section it follows that the symmetry of M provides a first check upon the correctness of the assumed model. If the symmetries of M and F_c differ, the assumed symmetry must be incorrect.

One procedure for analyzing the behavior of the points in M that coincide with loci of points in F_c or F_o is first to consider the number and location of points corresponding to the matrix elements of (V_o-V_c) and secondly, to repeat the process for the matrix $(F_cV_o-C_c)$. This procedure is followed below.

Let the N points in the general asymmetric unit of F be designated by $A_i=(a_i+b_i+\ldots)$. Then the square matrix (V_o-V_c) can be partitioned into n^2 matrices $\Delta_{11}+\Delta_{12}\ldots\Delta_{nn}$, where n is the number of general equivalent positions and $\Delta_{ij}=(A_iA_j)_o-(A_iA_j)_c$. Since a typical element in Δ_{ij} is $(c_ie_j)_o-(c_ie_j)_c$ evidently an element is zero if it contains points in F_o or F_c that coincide. In general Δ_{ij} and Δ_{ii}, however, will contain $2Nx-x^2$ and $2Nx-x^2-x$ non-zero elements respectively, where x is the number of points in A_i for which $(a_i)_o\neq(a_i)_c$.

The cubed matrix $F_c(V_o-V_c)$ can be expanded in the form

$$\begin{aligned}(F_cV_o-C)&=(A_1+A_2+\ldots+A_n)_c(\Delta_{11}+\Delta_{12}+\ldots\Delta_{nn})\\&=(A_1\Delta_{11}+A_1\Delta_{12}+\ldots+A_i\Delta_{jk}+\ldots+A_n\Delta_{nn})\,. \quad (15)\end{aligned}$$

Inspection of the individual terms in this expression shows that the points in (F_cV_o-C) that coincide with points in F_o or F_c occur only in the matrix sets $\Sigma A_i\Delta_{ii}$ and

$$\sum_{j\neq i}\Sigma A_i\Delta_{ij}\,.$$

If, then, a_i is contained in both F_o and F_c or in F_o only, $n(2N-x)$ points in (F_cV_o-C) coincide at the locus of a_i with a net weight equal to $(S_p-g^{-1})Wa_i$, where

$$S_p=\sum_{i}^{N-x}W^2(a_i)$$

and where the summation is taken over the square of the point weights of those points that are both in F_o and F_c. If a_i is contained in F_c only, $(Nn-1)$ points in (F_cV_o-C) coincide at its locus with weight equal to $-Wa_i(Wa_i^2-g^{-1})$. For the centric case the number and net weight of the points in (F_cV_o-C) coinciding at the locus of a particular point, a_i, in F_o are $(4nN-2nx)$ and $(S_p-g^{-1})Wa_i$ respectively. At a_i contained in F_c only, the number and net weight are $(2Nn-3)$ and $(3Wa_i-g^{-1})Wa_i$ in the centric case.

On the basis of these results, the important properties of M in equation (14) can be deduced straightforwardly. For the non-centric case the weight of a point in M coincident with a in F_o is gS_pW_a, but if the point is contained in F_c only, its weight is gW_a^3. For the centric case the net weight of points in M coinciding at the locus of a is $(2gS_p-1)Wa$ if a is in F_o and F_c. The weight of the coinciding points equals $2S_pgW_a$, if a is in F_o only. If it is in F_c only, the weight is $(3g-1)W_a$. These results agree with those predicted by the modulation principle. In a centrosymmetric space group, negative minima may occur in $B(r)$ at the erroneously postulated atomic positions.

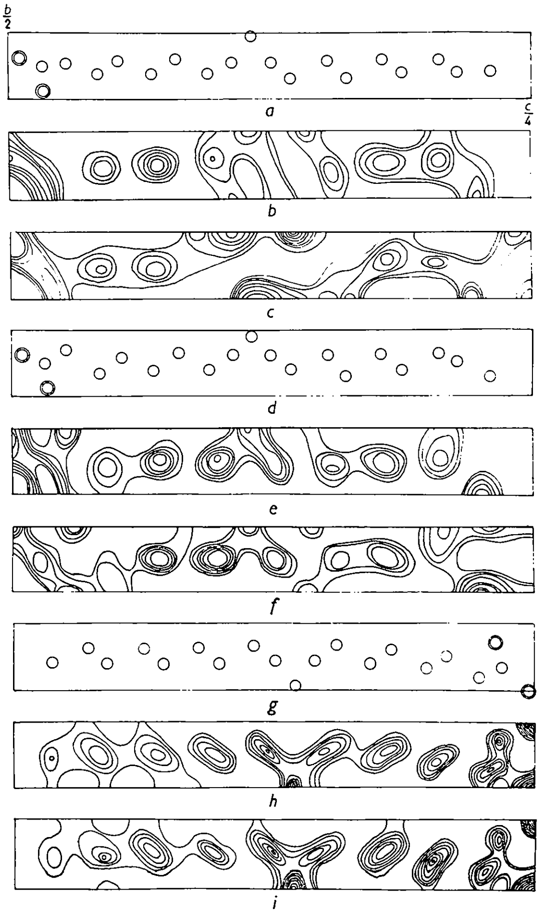

Fig. 1. Comparison of observed electron density and $C(r)$ functions at different stages in the structure determination of dihydromalvalic acid, $0kl$ projection.

(*a*) Model, R 0·61 for forty non-axial reflections.
(*b* Electron density map assuming model in *a*.
(*c*) $C(r)$ map assuming model in *a*.
(*d*) Model, R 0·52 for forty non-axial reflections.
(*e*) Electron density map assuming model in *d*.
(*f*) $C(r)$ map assuming model in *d*.
(*g*) Correct model, R 0·20 for 220 reflections.
(*h*) Electron density distribution based upon *g*.
(*i*) $C(r)$ map based upon *g*.

The maxima giving the corrected sites appear with doubled strength relative to the non-centric case but the maxima at the sites of the correctly postulated atoms are more sensitive to errors in the structure than in the non-centric case, since the rate of fall off in the peak height with the number of erroneously placed atoms of equal weight is doubled.

An application of the function

A brief description of our experience with the function, $C(r)$ as defined in (6), when applied to the crystal structure analysis of dihydromalvalic acid, $C_{18}H_{34}O_2$, will illustrate some of its properties. The function was applied to the $(0kl)$ projection when a satisfactory trial model had not been obtained.

The data consisted of 40 axial reflections $(00l)$ whose signs were known from the $(h0l)$ projection (Craven & Jeffrey, 1960) and twenty each of the low order $01l$ and $02l$ terms. The agreement factor, R, was 0·61 excluding the axial reflections and there was no indication of convergence to a correct solution.

The initial trial model is shown in Fig. 1(*a*) where concentric circles represent oxygens and circles are the carbon positions. The corresponding electron density and $C(r)$ maps are shown in Figs. 1(*b*) and 1(*c*) respectively. The most obvious discrepancies between the model and $C(r)$ were at the center of the molecule, near the cyclopropyl ring, and at the terminal methyl group. Some minor changes in the chain direction and the terminal configuration improved R to 0·52. The model, $\varrho(r)$, and $C(r)$ maps are shown in Fig. 1(*d*), (*e*) and (*f*). The discrepancies again indicated errors at the ends of the molecule, and suggested a reversal of the model. This corresponded to a shift of z coordinates to $\frac{1}{4}-z$, with the carboxyl groups dimerized by hydrogen bonding across a symmetry center at $(\frac{1}{4}, \frac{1}{4})$ instead of the origin of the space group $A2/a$. The correct model is shown in Fig. 1(*g*). Successive Fourier refinement proceeded normally to give an agreement of about 0·20 and the electron density projection shown in Fig. 1(*h*) which contained 220 terms. The corresponding $C(r)$ map appears in Fig. 1(*i*).

A comparison of map (*h*) with the maps (*b*), (*c*), (*e*) and (*f*) shows quite clearly that the $C(r)$ functions gave a better indication of the true atomic positions which were not included in the model than did the electron density functions.

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Analysis of Three-Dimensional Patterson Maps Using Vector Verification

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A new path from the Patterson map to an electron density map has been investigated. The procedure is called vector verification and involves testing all points in x, y, z space. Harker vectors are generated for each point and their presence is sought in the Patterson map. If all vectors are present, the point may be an atomic position. In most cases, over 95% of the positions in x, y, z space are at once eliminated. It has been demonstrated that by using one known atomic position the remaining atomic positions could be determined. One method which may be used to determine the position of a 'known' atom involves the selection of a vector from the vector set, and the use of this vector in a verification procedure leading to the position of an atom in the fundamental set.

Introduction

Most crystal structures are solved by conversion of vector sets to the corresponding fundamental sets. This step is usually the most difficult and time-consuming in the structure determination of a compound, and is especially difficult when heavy atoms