

STANFIELD, R. L., FIESER, T. M., LERNER, R. A. & WILSON, I. A. (1990). Submitted.
 SUSSMAN, J. L., HOLBROOK, S. R., CHURCH, G. M. & KIM, S. (1977). *Acta Cryst.* **A33**, 800–804.

TEN EYCK, L. F. (1973). *Acta Cryst.* **A29**, 183–191.
 YEATES, T. O., KOMIYA, H., REES, D. C., ALLEN, J. P. & FEHER, G. (1987). *Proc. Natl Acad. Sci. USA*, **84**, 6438–6442.
 YEATES, T. O. & REES, D. C. (1988). *J. Appl. Cryst.* **21**, 925–928.

Acta Cryst. (1990). **A46**, 359–365

Real-Atom Grid Approximation (RAGA) – a New Technique of Crystal Structure Analysis using only Amplitudes without Determination of Phases of Reflections*

BY G. N. RAMACHANDRAN†

Mathematical Philosophy Group, Indian Institute of Science, Bangalore 560012, India

(Received 15 August 1989; accepted 27 November 1989)

Abstract

This article deals with the development of a new technique, RAGA (real-atom grid approximation), for crystal structure analysis in the initial and intermediate stages. It is particularly suited to equal-atom structures of non-centrosymmetric crystals, and especially those of the lowest symmetry $P1$, which are the most difficult to solve by conventional methods. The electron-density distribution is approximated by a set of atoms, all having the same form factor, but variable 'masses', m_i , over a grid forming a sublattice of the unit cell. In the associated computer program *RAGA*, the subroutine *GRLS*, for grid least-squares refinement, reduces the R value between the actual F structure and the approximated G structure, thus leading to a continuous sequence of structures with smaller and smaller R values. The quantities used are all in real space, although the refinement makes use of the Fourier transforms of the two structures F and G . It starts with a low resolution of the order of one third of the largest unit-cell dimension with a large temperature factor in order to wipe out intensities of reflections beyond this order of resolution, and proceeds in stages to higher resolutions, reducing the value of B in the process, and this leads to electron-density information at a resolution of twice this order. A two-dimensional example of an equal-atom structure with symmetry $P1$ is given, all atoms of which could be developed starting from a completely flat background as input. RAGA can also be used for the intermediate stages of further refinement in which atoms at unknown atomic sites can be developed using information about the known atomic sites. RAGA thus

has the potential to be developed as a valuable additional tool in the armoury of direct methods.

Genesis and principles

In X-ray crystallography, the structure factors $F(hkl) = |F| \exp(i\alpha)$ of the reflections hkl are the Fourier coefficients of the electron-density function $\rho(xyz)$ over the unit cell. Since only the intensities $I(hkl) = |F(hkl)|^2$ are available, the standard methods of proceeding from $I(hkl)$ to $\rho(xyz)$ are based on the determination of the phases $\alpha(hkl)$ by some suitable method, either of an experimental or of a theoretical nature. [For a brief account, see Chapters 3 and 4 of Dunitz (1979) and, for an extensive survey see Schenk, Wilson & Parthasarathy (1987).]. The theory behind the experimental techniques, such as the use of the presence of heavy atoms, of isomorphous crystals and of anomalous-dispersion data, is dealt with from a unified point of view in Ramachandran & Srinivasan (1970). The theoretical techniques behind *ab initio* phase determination for non-centrosymmetric crystals are mostly based on the well known tangent formula, which has been expressed as an algorithm by Main, Lessinger, Woolfson, Germain & Declercq (1977). Fourier techniques and direct methods have been combined by Beurskens *et al.* (1983) in the form of the computer program *DIRDIF*.

It is usually only in the final stages of refinement that a least-squares procedure for improving the fit with intensity data is applied for obtaining more accurate coordinates of the atoms in the structure. Among the theoretical methods, the direct methods are the ones most widely used for the initial stages of phase determination for non-centrosymmetric crystals, particularly for equal-atom structures. They are also the most difficult to solve, particularly in the case of crystal structures belonging to the space group of lowest symmetry, $P1$.

* This paper is Matphil Report No. 76 of the Mathematical Philosophy Group.

† Present address: 5, Gita, 10A Main Road, Malleswaram West, Bangalore 560055, India.

It occurred to the author that it should be possible to apply the least-squares procedure directly to the input data $|F(\mathbf{H})|$ ($\mathbf{H} = hkl$) and obtain the atomic coordinates by a successive series of least-squares refinements. This was first done in a study made in 1976 of the structure of a cyclic hexapeptide, *cyclo*(-Gly-Tyr-Gly-)₂, crystallizing in space group *P1* (Ramachandran & Shamala, 1976). The approximate coordinates of the atoms were obtained from molecular-packing considerations, and these were refined by least squares from a resolution of the order of 2 Å to a final resolution of 0.7 Å, reducing the *R* value from about 0.6 to 0.05 in the process. An interesting observation was made here; the refinement sequence only proceeded smoothly (even when the input structure was reasonably good) if, in the initial stages, the 'resolution' (d_{res} = lower limit of *d* values of reflections *hkl* used in the refinement) was initially made large and then reduced step by step in succeeding stages of refinement.

The present study is based on a similar approach, and is also particularly applicable to equal-atom structures in the space group *P1*. However, it is a completely general one in which no assumptions are made about the nature of the molecule, its shape or packing arrangement, and only the structure-factor data $|F(hkl)|$ are utilized to obtain the electron-density diagram at a reasonable resolution (of the order of 15 to 20% of the unit-cell dimension), in successive stages by applying least-squares formulae directly to the data without any determination of phases (Ramachandran, Thanaraj, Rajan & Varughese, 1983). This has been achieved by representing the electron density $\rho(\mathbf{r})$ as the sum of functions of a small number (i_{max}) of parameters whose values are successively refined in the least-squares cycles. Thus, the real electron-density distribution $\rho(xyz)$ of the crystal is approximated by a set of fictitious grid atoms, all of the same type, but having (variable) masses m_i , located at the grid points $i \Leftrightarrow (i_1 i_2 i_3)$, forming a sublattice consisting of $I_1 I_2 I_3$ ($= i_{\text{max}}$) grid points in the unit cell. Thus,

$$\rho(xyz) = \sum_i m_i \rho_i(x - i_1/I_1, y - i_2/I_2, z - i_3/I_3) \quad (1a)$$

where

$$\begin{aligned} i_1 &= 0 \text{ to } I_1 - 1, \quad i_2 = 0 \text{ to } I_2 - 1, \quad i_3 = 0 \text{ to } I_3 - 1, \\ i &= 1 \text{ to } I_1, I_2, I_3. \end{aligned} \quad (1b)$$

Then, the structure factors $G(hkl)$ in this approximation are given by

$$\begin{aligned} G(hkl) &= \sum_i m_i f_i[(\sin \theta)/\lambda] \exp\{-B[(\sin \theta)/\lambda]^2\} \\ &\quad \times \exp[-2\pi i(hi_1/I_1 + ki_2/I_2 + li_3/I_3)]. \end{aligned} \quad (2)$$

Here, $f_i[(\sin \theta)/\lambda]$ is the atomic scattering factor of a standard grid atom with $m_i = 1$, and *B* is the temperature factor employed, which is made large in

the initial stages of refinement to broaden the grid atoms so as to avoid termination errors when the resolution is poor. It was very soon found that the choice of such a large *B* value for both $F(hkl)$ and $G(hkl)$ is itself an excellent method of effectively reducing the degree of resolution without incurring termination errors, and this was adopted as the essential basis of the theoretical formulae and practical algorithm described below. In order to make the grid structure compatible with the real structure, a temperature factor with the same *B* value (isotropic, of the order of 10 to 30 Å² for cell dimensions of the order of 6 Å) is also applied to the input $F(hkl)$ data. We shall denote these modified values obtained after the application of an appropriate artificial temperature factor *B* by $|F(\mathbf{H})|$ and shall employ them for all refinement cycles.

We then minimize the *R* value between $|F(hkl)|$ and $|G(hkl)|$ with the same temperature factor *B* for both, as given by (3), by standard least-squares procedures to obtain the best grid approximation to the crystal structure corresponding to the given data.

$$\begin{aligned} R &= \sum |\Delta F(\mathbf{H})| / \sum |F(\mathbf{H})|, \\ |\Delta F(\mathbf{H})| &= ||F(\mathbf{H})| - |G(\mathbf{H})||. \end{aligned} \quad (3)$$

The algorithmic procedures developed for this purpose, as described below, have been found to be remarkably successful. In fact, starting from an input structure as devoid of information as a flat one with m_i being the same for all grid atoms, the real atoms of a simple non-centrosymmetric two-dimensional structure could be developed in less than 12 cycles of least squares with 57 reflections for a 5 × 5 grid. With the artificial temperature factor *B* coming down from 30 to 10 Å² in three stages (for $a \approx b \approx 6$ Å), the *R* value dropped from 0.50 to the range 0.15–0.20 (see Table 1 and remarks below). The basic theory of this and its algorithmic implementation are briefly summarized below.

Thus, unlike all the orthodox techniques in crystallography, in which the solution of the crystal structure is based on operations carried out in *Fourier* space, in our method, all operations are carried out in the *real* space of the crystal lattice, employing a *grid approximation of real atoms* – hence the name RAGA, standing for 'real-atom grid approximation'.

Basic equations and algorithm

The equations given below follow the pattern in a study made in 1983 which was written in the form of a mimeographed report (Ramachandran *et al.*, 1983), copies of which are available from the author. It was also shown therein that equations (9) below have the property of reducing the *R* value under a wide variety of circumstances, but for various reasons these could

Table 1. Example of the application of RAGA in developing a four-atom structure from a flat background

		(a) Input trial structure										(b) Output structure																
INO	RVAL	DMI	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	
RESOL = 1.00		$N = 57$	TEMP = 30.00	$w = F $																								
1-0	0.6456	—	0.32	0.32	0.32	0.32	0.32	0.32	0.32	0.32	0.32	0.32	0.32	0.32	0.32	0.32	0.32	0.32	0.32	0.32	0.32	0.32	0.32	0.32	0.32	0.32	0.32	0.32
1-1	0.5280	0.3199	0.37	0.17	0.11	0.38	0.52	0.27	0.26	0.30	0.43	0.49	0.28	0.29	0.25	0.18	0.30	0.51	0.36	0.22	0.20	0.38	0.57	0.30	0.12	0.26	0.48	
1-2	0.4597	0.1755	0.37	0.08	0.00	0.43	0.61	0.22	0.25	0.32	0.51	0.59	0.22	0.28	0.22	0.07	0.27	0.61	0.38	0.20	0.14	0.39	0.71	0.31	0.04	0.23	0.55	
1-3	0.4215	0.1185	0.34	0.03	0.00	0.45	0.65	0.16	0.27	0.35	0.57	0.66	0.16	0.27	0.21	0.00	0.24	0.66	0.39	0.20	0.11	0.40	0.78	0.32	0.00	0.21	0.56	
RESOL = 1.00		$N = 57$	TEMP = 20.00	$w = 1$																								
2-0	0.4893	—	0.32	0.00	0.00	0.46	0.66	0.12	0.29	0.37	0.60	0.71	0.11	0.26	0.19	0.00	0.22	0.69	0.38	0.22	0.09	0.40	0.83	0.32	0.00	0.20	0.55	
2-1	0.4044	0.4548	0.16	0.00	0.00	0.43	0.64	0.00	0.55	0.41	0.63	0.99	0.00	0.23	0.06	0.00	0.19	0.72	0.14	0.34	0.13	0.46	0.97	0.44	0.00	0.08	0.42	
2-2	0.3506	0.2684	0.01	0.00	0.00	0.43	0.68	0.00	0.72	0.44	0.62	1.14	0.00	0.23	0.00	0.00	0.14	0.69	0.00	0.45	0.08	0.45	1.10	0.49	0.00	0.00	0.33	
2-3	0.3293	0.1694	0.00	0.00	0.00	0.41	0.70	0.00	0.81	0.43	0.57	1.21	0.00	0.22	0.00	0.00	0.10	0.64	0.00	0.52	0.01	0.44	1.19	0.48	0.00	0.00	0.26	
RESOL = 1.00		$N = 57$	TEMP = 10.00	$w = 1$																								
3-0	0.3562	—	0.00	0.00	0.00	0.38	0.70	0.00	0.86	0.41	0.50	1.27	0.00	0.18	0.00	0.00	0.09	0.60	0.00	0.57	0.00	0.45	1.29	0.48	0.00	0.00	0.21	
3-1	0.2727	0.8925	0.00	0.00	0.00	0.21	0.71	0.00	1.17	0.30	0.13	1.68	0.00	0.00	0.00	0.00	0.00	0.44	0.00	0.86	0.00	0.42	1.81	0.27	0.00	0.00	0.00	
3-2	0.2163	0.5577	0.00	0.00	0.00	0.11	0.56	0.00	1.31	0.31	0.00	1.80	0.00	0.00	0.00	0.00	0.00	0.18	0.00	1.09	0.00	0.38	2.14	0.12	0.00	0.00	0.00	
3-3	0.1925	0.2961	0.00	0.00	0.00	0.07	0.45	0.00	1.36	0.23	0.00	1.92	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.28	0.00	0.29	2.33	0.06	0.00	0.00	0.00	
3-4	0.1837	0.2032	0.00	0.00	0.00	0.05	0.37	0.00	1.38	0.18	0.00	1.97	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.37	0.00	0.25	2.40	0.04	0.00	0.00	0.00	
3-5	0.1807	0.0802	0.00	0.00	0.00	0.04	0.32	0.00	1.40	0.15	0.00	1.99	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.42	0.00	0.21	2.42	0.05	0.00	0.00	0.00	
3-6	0.1792	0.0405	0.00	0.00	0.00	0.04	0.29	0.00	1.41	0.15	0.00	2.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.45	0.00	0.19	2.43	0.05	0.00	0.00	0.00	

RESOL(N) = resolution (Å) and number of reflections included, TEMP = B value (Å²), w = weighting function $w(H)$. The individual least-squares cycles in the three stages are numbered separately. Note that the R value for $\Delta|F|$ (RVAL) decreases continuously, and the mean proportional change in m_i (DMI) also decreases continuously with the progress of the refinement cycles in each stage. Particularly noteworthy are the purposeful changes in the individual δm_i , leading to zero values of m_i , where atoms are absent, and large values of m_i , where they are present (e.g. $i = 7, 10, 18, 21$).

not be followed up until very recently. The two-dimensional formalism developed earlier has been extended here to three dimensions.

Since $\sum |F(\mathbf{H})|$ in (3) is a constant, R is a function only of the variables m_i , apart from the parameters resolution, B value *etc.*, which are assumed for each cycle of refinement. We try to find the values of δm_i for which $\sum \Delta |F(\mathbf{H})|$ becomes zero. Each $\Delta |F(\mathbf{H})|$ can be expressed in terms of δm_i as in (4) for the index $n(\mathbf{H})$ of the reflections running from 1 to the total number of reflections N .

$$\Delta |F(\mathbf{H})| = \sum_{i=1}^{i_{\max}} -\frac{\partial |G(\mathbf{H})|}{\partial m_i} \delta m_i, \quad n(\mathbf{H}) = 1 \text{ to } N. \quad (4)$$

It also follows from (2) that

$$\frac{\partial |G(\mathbf{H})|}{\partial m_i} = p(\mathbf{H}, i) = T(\mathbf{H}) \cos [\theta(\mathbf{H}, i) - \alpha(\mathbf{H})], \quad (5)$$

where

$$T(\mathbf{H}) = f_i[(\sin \theta)/\lambda] \exp \{-B[(\sin \theta)/\lambda]^2\} \quad (6a)$$

and

$$\theta(\mathbf{H}, i) = 2\pi(\mathbf{H} \cdot \mathbf{r}_i). \quad (6b)$$

The best values of δm_i (which are i_{\max} in number) which will fit the N equations in (4) can be obtained by the standard least-squares procedure of forming the i_{\max} normal equations from (4). If we also include a suitably chosen weighting function $w(\mathbf{H})$, this leads to

$$\begin{aligned} \sum_{\mathbf{H}} w(\mathbf{H}) p(\mathbf{H}, i) p(\mathbf{H}, l) \delta m_i \\ = \sum_{\mathbf{H}} w(\mathbf{H}) p(\mathbf{H}, l) \Delta |F(\mathbf{H})| \end{aligned} \quad (7)$$

$i, l = 1 \text{ to } i_{\max}.$

This can be put in an elegant form, namely

$$\sum_{i=1}^{i_{\max}} q(l, i) \delta m_i = \Delta(l) \quad (8)$$

where

$$q(l, i) = \sum_{\mathbf{H}} w(\mathbf{H}) p(\mathbf{H}, l) p(\mathbf{H}, i) \quad (8a)$$

and

$$\Delta(l) = \sum_{\mathbf{H}} w(\mathbf{H}) p(\mathbf{H}, l) \Delta(\mathbf{H}). \quad (8b)$$

So far the theory is straightforward, but in implementing (8), several precautions and restrictions have to be applied. Thus, in examples employing a grid with I_1, I_2 and I_3 in the range 4-6, the total number of reflections (N) is not much larger than the total number of δm_i to be determined (namely i_{\max}), and the solution of (8) is best obtained by employing the diagonal approximation and a fudge factor λ (~ 0.5) as in (9).

$$\delta m_i = \lambda \Delta(i) / q(i, i), \quad i = 1 \text{ to } i_{\max}. \quad (9)$$

The weighting function $w(\mathbf{H})$ may be put equal to $|F(\mathbf{H})|$ for giving higher weights for stronger reflections in the preliminary stages. Thus, the main subroutine *GRLS* for the 'grid least-squares' refinement incorporating (3)-(9) leads for each cycle to the refined value

$$m'_i = m_i + \delta m_i. \quad (10)$$

These are then pruned and normalized. In the pruning process, we make use of the fact that ρ is non-negative in X-ray diffraction, and therefore all negative m'_i values are set to zero. These are then normalized to make $\sum m'_i$ such that the total electron count for this G structure is the same as that for the actual F structure (by a subroutine named *M-NORM*) and also, if necessary, normalized once more by making $\sum |G(\mathbf{H})|^2 = \sum |F(\mathbf{H})|^2$ by the subroutine *G-NORM*.

An outline of the essential steps in the computer program *RAGA2D* incorporating the above ideas for two dimensions is shown in the flow chart in Fig. 1. In this, *SFCALC* incorporates (2) and *GRLS* (3)-(9).

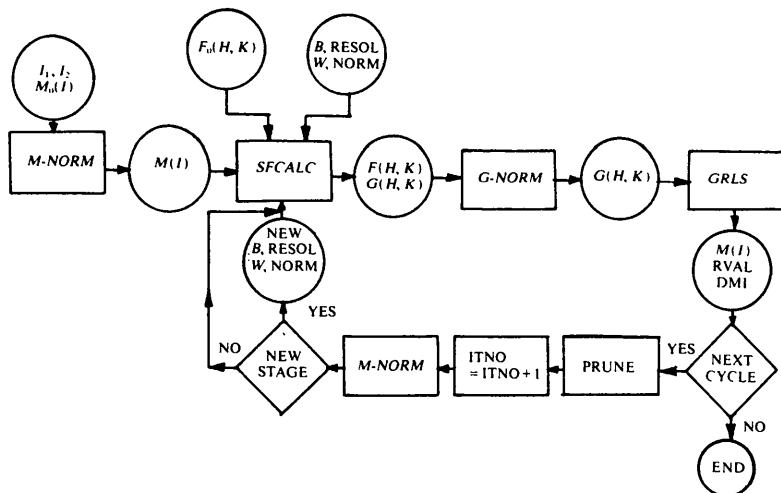


Fig. 1. Flow chart of the essential steps in the program *RAGA2D* for the technique *RAGA* applied to two-dimensional structures.

For any stage of any problem, the parameters artificial temperature factor (B), resolution (RESOL), weighting (W) and normalization (NORM) can be chosen at the discretion of the operator and any number of cycles of refinement can be carried out for each stage.

Illustrative examples

Even in 1983 it was found that RAGA had the property of reducing the R value (RVAL) between the structure amplitudes $|F(\mathbf{H})|$ of the actual F structure and $|G(\mathbf{H})|$ of the approximated grid structure in succeeding iterations. This property was confirmed for a wide variety of F structures with a number of different input trial structures which were considered to provide the best conditions for applying RAGA. These checks were done only in two dimensions on a PC/AT, but they were sufficient to give an idea of the types of problems that are likely to be solvable by this new technique. Thus, it was found that if the F structure itself had atoms located at the grid points of the chosen grid, then many homometric solutions are possible for the G structure, each of which may have an RVAL as low as 0.01 to 0.02. However, such a feature is unlikely to exist with organic crystal structures having low symmetry and therefore the examples were confined to those having all the atoms at non-grid points. A choice of values from 4 to 6 for I_1 and I_2 seems to be the most satisfactory one, and for these, the RESOL was varied in stages from one-third to one-sixth of the unit-cell dimension in three stages, e.g. with $a = b = 6 \text{ \AA}$, $\gamma = 90^\circ$. For the triclinic cells chosen in the examples given below, the three stages would correspond to RESOL = 2.0, $B = 30 \text{ \AA}^2$, RESOL = 1.5, $B = 20 \text{ \AA}^2$ and RESOL = 1.0, $B = 10 \text{ \AA}^2$.

The choice of the initially chosen input G structure is also quite arbitrary. Thus, it could be (a) an arbitrarily chosen set of random m_i values or (b) a single large atom at the centre of the unit cell with a relatively low flat background, or (c) with grid points over one half of the cell made to have the same finite m_i value and the other half to have $m_i = 0$, and so on. The results were not successful in every case but fragments of the real structure could be seen, as in the case of direct methods.

However, some striking successes were obtained by refining from a featureless flat input for m_i . An example is shown in Fig. 2 and Table 1, for which m_i was initially made equal to 0.41 for all $i = 1$ to 25. When this featureless input was fed along with the $|F(hkl)|$ data of the actual F structure shown in Fig. 2(a), it developed the four atoms of the F structure in approximately the correct locations in the unit cell, and these became progressively larger in m_i value until they were clearly defined as the only four atoms in the unit cell as shown in Fig. 2(b). However, as expected, the origin was not at the same place as in

Fig. 2(a) and the molecule was also found to be rotated as it developed by 180° with respect to that of the F structure, about an axis at right angles to the plane of the paper. In Fig. 2(c) this has been subjected to a linear transformation so as to have nearly the same location and orientation as that in Fig. 2(a). It can be seen that these two are very similar,

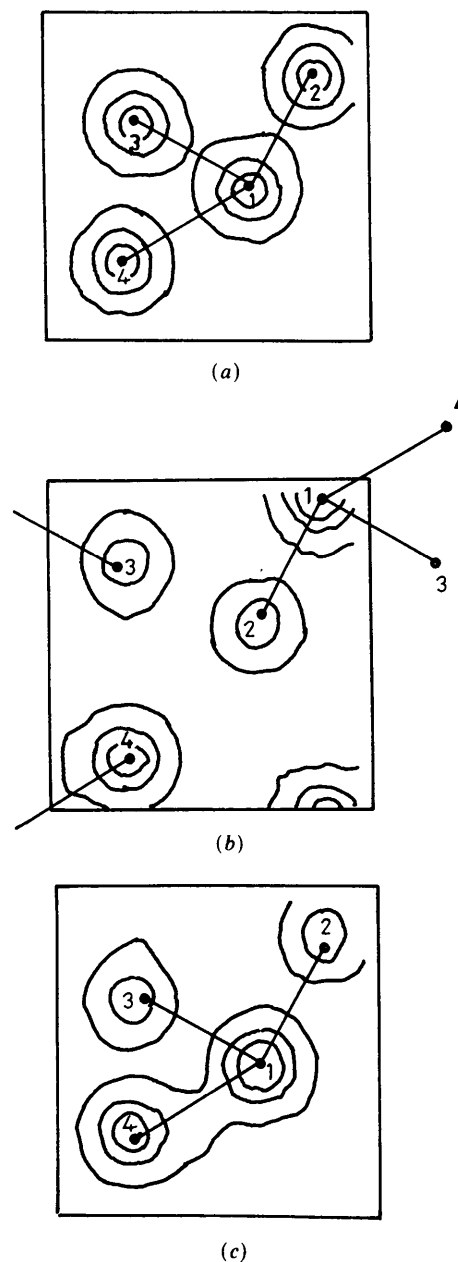


Fig. 2. Electron-density contour diagrams of the four-atom structure (a) developed by RAGA from a completely flat background, (b) is the structure as revealed and (c) is the same structure after application of inversion (rotation by 180°) and translation to bring it to the same orientation as (a). Contours are at the levels of 20, 40, 60 in arbitrary units, and are the same for all the diagrams.

and the clarity and near equality of the four atoms that have developed in Fig. 2(c) are quite striking.

The progress of the refinement is seen from Table 1, which shows not only a continuous reduction of R value for all the three stages (which were chosen in this example to have the same resolution 1.0 but having different B values of 30, 20, 10 Å²), but also a similar behaviour for DMI, the mean relative change in m_i , which also comes down with successive cycles of iteration in each stage taking as low a value as 0.04. Naturally, there is an upward jump in both RVAL and DMI when a new stage is initiated by changing the parameters B , RESOL *etc.*, for refinement.

The very low value of DMI at the end of the sixth cycle in the third stage is a clear indication that the refinement has converged (though in some other examples it converges only to a partially correct structure).

The second illustration in Fig. 3 and Table 2 is that of another useful property of RAGA, namely for refinement at intermediate levels of structure analysis, when some atoms have been recognized and other atoms are absent. The normal procedure in such cases is to employ Fourier refinement. However, if the input G structure is made that of the partially known F structure, which we may denote by F_p , then the RAGA refinement has the property of developing the atom(s) at the unknown atomic sites (which we may denote by F_Q). In the example illustrated in Fig. 3, the three atoms 1, 2, 3 shown in Fig. 3(a) were taken to be known and the fourth atom 4 to be unknown. The former were given m_i values of 2.0 as in Table 2(a) and on applying RAGA for three stages (12 cycles), as for Table 1, the outputs of the three stages were those indicated in Tables 2(b), (c) and (d). It will be seen that the m_i value at the fourth location continuously increases with its stage. In fact, the electron-density contour diagram for the final output is illustrated in Fig. 3(a), and it will be seen that a fairly good atom has appeared at location 4, corresponding to the unknown atom. (Incidentally, it was also verified during our study that if a wrong atom was put in after a non-centrosymmetric group of correct atoms has been identified, the m_i values of these wrong atoms go down in the succeeding cycles of refinement using RAGA.)

The power of RAGA in Fig. 3(a) is brought out particularly well by comparing it with Fig. 3(b) which is the result of a standard Fourier refinement using $\gamma' = |F(\mathbf{H})| \exp i\alpha_p(\mathbf{H})$ with the same assumptions as in Fig. 3(a) [see Ramachandran (1964) for the definition of γ' synthesis]. It will be seen that although atom 4 has developed, it is not at all as clear as the results obtained with RAGA.

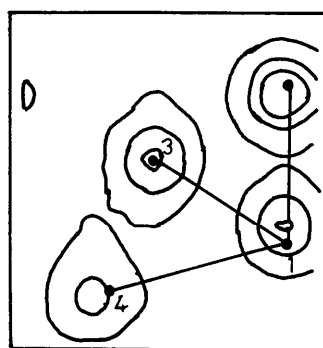
In connection with this, it was also thought worthwhile to verify the power of the β synthesis first proposed by Ramachandran & Raman (1956) [see

Ramachandran (1964) for a systematic treatment]. It had been shown by Kalyanaraman, Parthasarathy & Ramachandran (1969) that the undesirable peaks in the β synthesis are mostly eliminated by using the Sim weighting function (Sim, 1960), which is given by

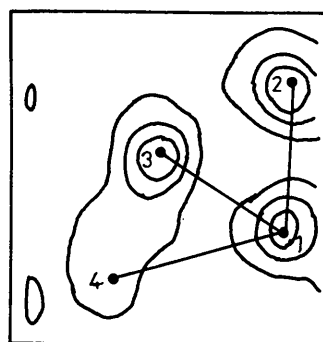
$$W = I_1(2X)/I_0(2X), \quad (11a)$$

where

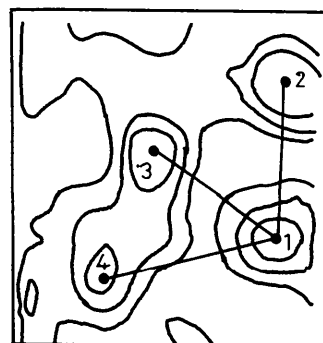
$$X = |F| |F_p| / \sum f_{Qj}^2, \quad (11b)$$



(a)



(b)



(c)

Fig. 3. Development of atom 4 from the partial information regarding atoms 1, 2 and 3 by three different techniques; (a) RAGA, (b) Fourier synthesis and (c) $W^2\beta$ synthesis (RESOL = 1.0, $B = 10$ Å², $a = b = 6$ Å, $\gamma = 90^\circ$, symmetry $P1$). [Contours as in Fig. 2, at the same levels for (a), (b) and (c).]

Table 2. Refinement of a structure employing RAGA from the partial data shown in (a)

(a) Input partial structure					(b) Output of first stage				
0.000	0.000	0.000	0.000	0.000	0.228	0.213	0.114	0.059	0.107
0.000	0.000	0.000	0.000	2.000	0.013	0.000	0.012	0.000	2.128
0.000	0.000	2.000	0.000	0.000	0.000	0.000	2.075	0.000	0.000
0.000	0.000	0.000	0.000	2.000	0.000	0.195	0.139	0.000	1.945
0.000	0.000	0.000	0.000	0.000	0.227	0.364	0.182	0.000	0.000
(c) Output of second stage					(d) Output of third stage				
0.141	0.140	0.050	0.000	0.021	0.000	0.000	0.000	0.000	0.000
0.381	0.028	0.166	0.000	1.944	0.199	0.041	0.164	0.000	2.356
0.000	0.000	1.652	0.000	0.000	0.000	0.000	1.799	0.000	0.000
0.000	0.360	0.417	0.000	1.626	0.000	0.214	0.136	0.000	1.693
0.248	0.639	0.183	0.000	0.004	0.074	1.148	0.175	0.000	0.000

The outputs of the three stages are tabulated as 5×5 grids in (b), (c) and (d). Note that the three input atoms continue to have large m_i (~ 2.0), while there is a continual increase in the value of m_i at the location of the unknown atom as shown by the rules.

in the form

$$W^2\beta = W^2(|F|^2/|F_P|) \exp i\alpha_P. \quad (11c)$$

This function was tested in the example studied here and the resulting diagram, shown in Fig. 3(c), is very interesting. It brings out the peak at the location of the unknown atom 4 in a very distinctive way with a peak height comparable to those of the known input atoms 1, 2 and 3.

Thus RAGA appears to be a procedure that should be investigated further and checked for its capabilities not only in revealing preliminary data about non-centrosymmetric equal-atom structures at the initial stages of crystal structure analysis, but also for its application at intermediate stages where these data are developed further to identify more atoms at relatively low resolution. It is our conviction that RAGA deserves further scrutiny and examination with structures in three dimensions where it would be expected to have greater power, provided the computational aspects are properly taken care of.

The author wishes to acknowledge the excellent computational assistance that was provided by Mr Ravi Upadhyaya, who implemented all these studies on a PC/AT. The work was carried out during the author's tenure of the Indian National Science Academy Albert Einstein Professorship at the Indian Institute of Science. The latter provided him with the personal computer. Thanks are due both to INSA

and IISc for finances, equipment and other facilities provided.

References

- BEURSKENS, P. T., BOSMAN, W. P., DOESBURG, H. M., VAN DEN HARK, TH. E. M., PRICK, P. A. J., NOORDIK, J. H., BEURSKENS, G., GOULD, R. O. & PARTHASARATHI, V. (1983). In *Conformation in Biology*, edited by R. SRINIVASAN & R. H. SARMA, pp. 389–406. Guilderland, New York: Adenine Press.
- DUNITZ, J. D. (1979). *X-ray Analysis and the Structure of Organic Molecules*. Ithaca: Cornell Univ. Press.
- KALYANARAMAN, A. R., PARTHASARATHY, S. & RAMACHANDRAN, G. N. (1969). In *Physics of the Solid State*, edited by S. BALAKRISHNAN, M. KRISHNAMURTHY & B. RAMACHANDRA RAO, pp. 63–76. London: Academic Press.
- MAIN, P., LESSINGER, L., WOOLFSON, M. M., GERMAIN, G. & DECLERCQ, J.-P. (1977). *MULTAN77. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.
- RAMACHANDRAN, G. N. (1964). *Fourier Syntheses for Partially-Known Crystal Structures*. In *Advanced Methods in Crystallography*, edited by G. N. RAMACHANDRAN, pp. 25–65. London: Academic Press.
- RAMACHANDRAN, G. N. & RAMAN, S. (1956). *Acta Cryst.* **12**, 957–964.
- RAMACHANDRAN, G. N. & SHAMALA, N. (1976). *Acta Cryst.* **A32**, 1008–1009.
- RAMACHANDRAN, G. N. & SRINIVASAN, R. (1970). *Fourier Methods in Crystallography*. New York: Wiley-Interscience.
- RAMACHANDRAN, G. N., THANARAJ, T. A., RAJAN, S. S. & VARUGHESE, K. I. (1983). *Matphil Reports*, No. 31, pp. 1–37. Mathematical Philosophy Group, Indian Institute of Science, Bangalore, India.
- SCHENK, H., WILSON, A. J. C. & PARTHASARATHY, S. (1987). Editors. *Direct Methods, Macromolecular Crystallography and Crystallographic Statistics*. Singapore: World Scientific.
- SIM, G. A. (1960). *Acta Cryst.* **13**, 511–512.