

**On the Application of Phase Relationships to Complex Structures.
XIX. Magic-Integer Representation of a Large Set of Phases:
The *MAGEX* Procedure**

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Abstract

Long one-dimensional magic-integer sequences are used to express the phases of 10–20 primary reflexions. The magic-integer representation of phases is extended to other secondary reflexions through strong triple-phase relationships involving one secondary and two primary reflexions. In the *MAGEX* procedure multiple magic-integer representations of the secondaries are sought and the error involved in their subsequent use in a conventional ψ map is much reduced. In view of the large number of primary reflexions the indices of the terms included in the ψ map are large and maps may be computed at up to 2^{20} points. Further reflexions, in batches of ten or so, may be added to the initial set by the further use of magic integers and small-scale ψ maps. When the base of estimated phases is sufficiently large then the phase information is extended by the controlled use of the tangent formula. Examples of the successful application of *MAGEX* are described.

Introduction

Declercq, Germain & Woolfson (1979) have described two computer-based procedures, *MAGIC* and *YZARC*, for the direct solution of crystal structures, proposing them as complementary techniques to the well established *MULTAN* system. In fact it is known to be useful, when attempting to solve complex structures, to have at hand more than one tool; if one procedure fails then an alternative one may be successful.

The present work extends and strengthens the concepts employed in *MAGIC*; the new *MAGEX* procedure can easily be linked to the *MULTAN* 78 package and will soon be available as another option to the previous methods.

The success of the random approach to structure determination (Baggio, Woolfson, Declercq & Germain, 1978) has shown that estimates of a fairly large set of

phases (typically 60 to 100), even if the estimates are fairly approximate ones, can form a strong basis for phase development and refinement. In the *YZARC* program, estimates are derived from the least-squares refinement of random phase sets. We shall now describe an alternative method, which is proving to be effective, where a large set of phases is represented by magic integers (White & Woolfson, 1975).

Long magic-integer sequences

A theory for the efficient representation of phases by magic integers has been given by Main (1977, 1978). He showed that an efficient sequence of integers m_1, m_2, \dots, m_n is one such that $2m_1 = m_n + 1$ and the differences $m_n - m_{n-1}, m_{n-1} - m_{n-2}, \dots, m_3 - m_2, m_2 - m_1$ form an integer progression of the general form

$$F_n = F_{n-1} + F_{n-k} \quad (1)$$

For $k = 1$ the series has a common ratio $r = 2$, for $k = 2$ (Fibonacci's series) r has a limiting value of 1.618 and, for higher values of k , r tends to 1. A higher accuracy in the representation of the phases is obtained with magic integers based on geometric progressions with higher common ratios. If we wish to represent a large set of phases with a r.m.s. error less than $\sim 55^\circ$ only the $r = 2$ or the Fibonacci series can be used.

However, the larger is the number of phases the larger will be the integers and in order to represent 60 to 100 phases one would need to use inconveniently large numbers. We must therefore limit the number of phases which are *directly* represented by magic integers. The information below should give a feeling for the nature of the problem.

| r | Number of phases | Maximum magic integer |
|-------|------------------|-----------------------|
| 2 | 12 | 4095 |
| | 16 | 65535 |
| 1.618 | 19 | 13529 |
| | 22 | 57313 |

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Declercq, Germain & Woolfson (1975) described a technique (the primary–secondary or *PS* method) to expand the magic-integer representation of a limited number of phases to the representation of a larger set. The phases in the secondary set are linked to two primaries by means of strong triple-phase relationships (t.p.r.'s) of the general form

$$\varphi_s \pm \varphi_{p_1} \pm \varphi_{p_2} + b \simeq 0 \pmod{1}, \quad (2)$$

where the phases are expressed in cycles. Through these t.p.r.'s the secondary reflexions may also be expressed in terms of magic integers but, because of the combined effect of the true value of the t.p.r. plus the error in magic-integer representation of phases, the precision when using a single relationship is quite low. To overcome this problem it is desirable to have more than one t.p.r. involving the same secondary reflexion but different pairs of primaries. We illustrate this idea of *multiple definition of secondaries* by the example of a secondary expressed in terms of two different pairs of primary reflexions, thus

$$\varphi_s \simeq \varphi_{p_1} + \varphi_{p_2}$$

and also

$$\varphi_s \simeq -\varphi_{p_3} + \varphi_{p_4} + 0.5. \quad (3)$$

By substituting φ_{p_i} by its magic-integer representation $m_j x$ we have

$$\varphi_s \simeq (m_1 + m_2)x = Mx$$

and also

$$\varphi_s \simeq (-m_3 + m_4)x + 0.5 = M'x + 0.5. \quad (4)$$

We shall show how the several magic-integer definitions of the secondary reflexion are used in such a way that the effect of an individual bad definition is not important.

In order for the *MAGEX* procedure to be effective the primary reflexions must satisfy a number of criteria. Firstly, we imagine that origin-and-enantiomorph defining reflexions (*O + E*) have been chosen, either by the user or, say, by the *CONVERGENCE* routine in *MULTAN*. The *O + E* reflexions are part of the primary set and the others are chosen on the following basis:

(i) they must be strongly linked with the *O + E* reflexions so that the origin and enantiomorph are tightly defined by the phases of the complete set;

(ii) they include a large number of secondary reflexions defined by strong t.p.r.'s;

(iii) each secondary should have several definitions, but not too many to avoid the dominance of some of them in the phase-determining process. From experience the ideal number of definitions for a secondary is five, and the number should not be greater than nine, since this increases the computational effort without corresponding benefits in phase determination.

The procedure for the selection of primary and secondary reflexions according to these criteria consists of the following steps.

(a) Select *O + E* reflexions, which are part of the primary set.

(b) For each strong reflexion, regarded as a potential new primary, P_{new} , calculate

$$\Omega = \sum \kappa W_n \frac{I_1(\kappa)}{I_0(\kappa)}, \quad (5)$$

where the summation is over all relationships of the form $P_{\text{old}} P_{\text{new}} S$ for which $\kappa (= 2N^{-1/2} |E_1 E_2 E_3|) \geq \kappa_{\text{limit}} (\sim 1.0)$ and the ratio of Bessel functions, $I_1(\kappa)/I_0(\kappa)$, is the expectation value of the cosine of the t.p.r. The weight W_n is associated with the secondary which, for the primary set under consideration (including P_{new}), has n definitions. This weight is given by

$$\begin{aligned} W_n &= 0 & n \geq 10 \\ W_n &= \exp(-|n - 5|/10) \end{aligned} \quad (6)$$

which favours five, but discriminates against too many, definitions.

(c) The reflexion with the greatest Ω is added to the primary set and then (b) is repeated until the desired number of primaries has been selected.

(d) Finally only those reflexions are used as secondaries for which

$$\alpha_{\text{est}} = \sum \kappa \frac{I_1(\kappa)}{I_0(\kappa)} \geq \alpha_{\text{limit}} (\sim 1.5), \quad (7)$$

where the summation is over all relationships linking the complete *PS* reflexions which include the secondary in question.

The ψ_{big} map

Having defined the set of phases in terms of magic integers, we now have to find the most likely values of the variable x associated with the integers. This is done by means of a Fourier map, similar to the ψ map described by White & Woolfson (1975), the maxima of which correspond to the condition that the t.p.r. cosines should be as close as possible to +1.0. Before giving the expression for the ψ function, it is convenient to see how the t.p.r.'s are represented in terms of magic integers. A t.p.r. can be expressed as

$$\varphi_a \pm \varphi_b \pm \varphi_c + b = Mx + B \simeq 0 \pmod{1}, \quad (8)$$

where M is an integer combination of magic integers and B a constant angle.

There are four types of relationships involving primary and secondary reflexions (i) *PPP*; (ii) *PPS*; (iii) *PSS*; (iv) *SSS*, and the following notes refer to how they are included in the ψ map.

(i) Each relationship of this type has a single representation in magic-integer form, found by substituting for the primaries.

(ii) These relationships have already been used in defining the secondaries and when a secondary reflexion has only one definition the corresponding t.p.r. reduces to a trivial identity. In the case of n multiple definitions of a secondary we will have $\frac{1}{2}n(n-1)$ non-trivial and unique ways of representing by magic integers the t.p.r.'s involved. Thus, if a secondary has three definitions, we have

$$S \simeq P_1 + P_2 + b_1$$

$$S \simeq P_3 + P_4 + b_2$$

$$S \simeq P_5 + P_6 + b_3.$$

There are three non-trivial and unique representations, *viz* by substituting magic integers for primaries in

$$P_1 + P_2 + b_1 - P_3 - P_4 - b_2 \simeq 0 \quad (9)$$

$$P_1 + P_2 + b_1 - P_5 - P_6 - b_3 \simeq 0 \quad (10)$$

$$P_3 + P_4 + b_2 - P_5 - P_6 - b_3 \simeq 0. \quad (11)$$

(iii) If the secondaries have n_1 and n_2 definitions respectively then each PSS relationship, which can be expressed in terms of five primaries, can be represented by magic integers in $n_1 \times n_2$ different ways.

(iv) If the secondaries have n_1 , n_2 and n_3 definitions respectively then each SSS relationship, which can be expressed in terms of six primaries, can be represented by magic integers in $n_1 \times n_2 \times n_3$ different ways.

Associated with each representation of a relationship may be found a standard deviation σ_R which depends both on the expected error of the magic-integer representation of phases and the variances of the relationships. The analysis by which σ_R may be derived is given in the Appendix.

Each relationship is entered into the ψ map with an inverse-variance weight, *i.e.*

$$Q_R = \frac{\sum^2}{\sigma_R^2} \quad (12)$$

where $\sum^2 = 3\sigma_m^2$ (σ_m is defined in the Appendix) is a scaling constant to keep Q_R in the range 0–1. The expression used for the one-dimensional Fourier map is

$$\begin{aligned} \psi_{\text{big}}(x) = & \sum_{\text{all relationships}} \kappa \frac{I_1(\kappa)}{I_0(\kappa)} Q_R \cos \{2\pi(Mx + B)\} \\ & + W_{\text{con}} \sum_{\text{special reflexions}} C \cos \{4\pi(Kx + p - e)\}. \end{aligned} \quad (13)$$

The $\kappa[I_1(\kappa)/I_0(\kappa)]Q_R$ weights used in (13) are based on empirical, but rational, considerations.

The second summation on the right-hand side of (13) is a constraint term introduced in order to give priority to values of x for which the phases of special reflexions are close to their restricted values. In space groups belonging to the monoclinic and orthorhombic systems, for instance, some classes of reflexions have phases restricted to 0 or π or to $\pi/2$ or $-\pi/2$. If there is a phase, represented in magic-integer form as mx , which is known to be either 0 or 0.5 (in cycles) then we should expect the quantity $\cos(4\pi mx)$ to be close to +1; alternatively if mx represents a phase which is ± 0.25 then we should expect $\cos\{4\pi(mx + \frac{1}{4})\}$ to be close to +1.

In (13) $C = \kappa_{\text{max}}/\sqrt{n}$, where κ_{max} is the highest κ for the system of relationships and $n = 1$ for primaries or $n =$ (number of multiple definitions) for secondaries. W_{con} is an adjustable weight (0–1) chosen by the user. $Kx + p$ is the general representation of a phase by magic integers (for a primary, $K = m$ and $p = 0$, for a secondary, K is a combination of integers and p is a constant angle); e is one of the two possible restricted values of the phase in cycles.

Since the ψ_{big} map is calculated at an interval of $1/(4$ times the maximum index), its size is a function of the maximum value taken by M , which is an integer compounded from up to six magic integers. For long sequences it may be necessary to calculate the function at up to 2^{20} points. Use is made of a one-dimensional FFT routine and the calculation is so factorized that the routine needs only be dimensioned for 2^{15} points (Brigham, 1974). The $N(\sim 200)$ highest peaks are found by an automatic peak-search routine and their x coordinates are translated through the magic integers into trial phases for the primary reflexions. The corresponding trial phases are found for the secondary reflexions by combining different indications with the tangent formula.

The number of peaks taken from ψ_{big} is limited more by considerations of computer time than by features of the map itself; there are usually many more substantial peaks than are selected for phase-set development. Thus the 90 sets of phases developed for ergocalciferol (see following section and Table 1) came from ψ_{big} peaks varying in height from about 1800 to 1200 while the three solutions came from peaks of heights in the lower part of the range. If a first run does not give a solution, and substantial peaks remain unexplored in ψ_{big} , then it would be sensible to make another run developing phases from a batch of next-largest peaks. This facility is not included in the present version of *MAGEX*.

Expanding the phase set

At this stage there may be 60 or less primary + secondary reflexions. Experience shows that, for many structures, expansion by the tangent formula from a

base of this size may be unsuccessful, especially when the phases have appreciable errors. In order to increase the number of phased reflexions we have used the following procedure, similar to that suggested by Woolfson (1977).

(a) A set of ten new reflexions is chosen on the basis that its members have the largest values of

$$\alpha = \sum \kappa \frac{I_1(\kappa)}{I_0(\kappa)}, \quad (14)$$

where the summation is over all relationships linking the new reflexions to these already phased ('known' reflexions).

(b) These ten phases are represented by a magic integer sequence, e.g.

89 123 144 157 165 170 173 175 176 177

and for each of the N sets of trial phases a Fourier map is calculated

$$\psi_{\text{small}} = \sum \kappa \frac{I_1(\kappa)}{I_0(\kappa)} \cos \{2\pi(Mx + B)\}, \quad (15)$$

where the summation is over all relationships involving one, two or three of the ten new reflexions and those in the 'known' set.

(c) For each of the N ψ_{small} maps the 50 highest peaks are selected. A figure of merit, given by the value of

$$F_1 = \sum_t \kappa_t \frac{I_1(\kappa_t)}{I_0(\kappa_t)} \cos \varphi_3, \quad (16)$$

or of

$$F_2 = \sum_r \left\{ \sum_s K_{rs} \cos \varphi_{3rs} - \left| \sum_s K_{rs} \sin \varphi_{3rs} \right| \right\} \quad (17)$$

is then used to select the best N' (~ 200) sets of phases from the $50N$ individual sets. In both F_1 and F_2 the φ_3 is the value of the t.p.f. with the individual phase estimates inserted; in (16) t ranges over all relationships whereas in (17) r ranges over all reflexions and s over all t.p.r.'s in which reflexion r is involved.

The process could be repeated, adding ten reflexions at each cycle, until any desired number of reflexions has been phased but in practice it has been found that it is unwise to expand for more than two cycles.

Parameter-shift refinement and tangent-formula extension

The phases obtained with the procedure described above are affected by the errors of their magic-integer representation and it is possible to improve the accuracy of their determination by a refinement process. As first suggested by White & Woolfson

(1975) a rapid and effective method is that of parameter shift. The refinement is based on the maximization of the function F_1 . Maximizing F_1 is equivalent to minimizing the weighted sum of the squares of the differences between the computed t.p.r. cosines and sines and their expected values. This would be

$$\begin{aligned} F'_1 &= \sum_t \kappa_t \left\{ \cos \varphi_3 - \frac{I_1(\kappa_t)}{I_0(\kappa_t)} \right\}^2 + \sum_t \kappa_t \sin^2 \varphi_3, \\ &= \sum_t \kappa_t \left\{ 1 + \left[\frac{I_1(\kappa_t)}{I_0(\kappa_t)} \right]^2 \right\} - 2 \sum_t \kappa_t \frac{I_1(\kappa_t)}{I_0(\kappa_t)} \cos \varphi_3, \end{aligned} \quad (18)$$

where the first sum is independent of the phases and the second term, with a negative sign, is nothing but $2F_1$.

After the refinement is complete a number (50–100) of the sets of refined phases is selected. This selection is based either on the value of F_1 or, more commonly, on F_2 . The selected sets of phases are then extended and refined with the tangent formula. In this final process the initial (60–100) phases are kept fixed until the final refinement cycle when they are allowed to relax to fit in with the overall phase set.

At this stage figures of merit are found, E maps are computed and interpreted using the programs of the *MULTAN* system.

Some applications of *MAGEX*

The *MAGEX* procedure has been tested on several known structures and on some unknown ones. The main features of the structure solution for some of these compounds are outlined in Table 1.

Let us now consider two examples in more detail. The first is the structure of ergocalciferol (Hull, Leban, Main, White & Woolfson, 1976), which was first solved with great difficulty by *MULTAN*, but so far has resisted all attempts at solving it in a straightforward way.

The space group is $P2_12_12_1$ and the formula $C_{28}H_{44}O$ with $Z = 8$. With the *MULTAN* system the 350 reflexions with largest E values were selected and 5000 unique \sum_2 relationships generated. The outcome of the convergence map indicated three *origin-fixing* reflexions. The enantiomorph was not fixed in this *MAGEX* run but the procedure is not affected by the initial lack of enantiomorph definition.

Twelve *primaries* were selected with the algorithm described in § 2, which gave 32 *secondaries* defined by 85 *PPS* t.p.r.'s. The magic-integer sequence was based on Fibonacci's series. The total number of relationships used in calculating the ψ_{big} map was 1336, plus 35 constraint terms ($W_{\text{con}} = 0.1$, $\kappa_{\text{max}} = 5.71$) and the maximum index in the Fourier summation was 2630.

Table 1. *Some details of structure solutions by MAGEX*

| Structures | Primaries | | Secondaries | ψ_{big} maps | | Number of expansion reflexions | Number of good solutions | Fraction of atoms in best E maps | Time on DEC System 10 computer (min) |
|--|-----------|--------|-------------|---------------------------|-------------|--------------------------------|--------------------------|------------------------------------|--------------------------------------|
| | $O + E$ | Others | | Independent relationships | Constraints | | | | |
| Ergocalciferol $C_{28}H_{44}O$ $P2_1, Z = 8$ | 3 | 12 | 32 | 1336 | 35 | | 3 | 45/58 | 27 |
| MUNICH1 $C_{20}H_{16}$ $C2, Z = 8$ | 3 | 14 | 38 | 1019 | 19 | | 1 | 39/40 | 17 |
| TURSCHI1 $C_{15}H_{24}O_4$ $P2_1, Z = 4$ | 3 | 17 | 37 | 241 | 14 | | 1 | 33/38 | 34 |
| Cortisone $C_{21}H_{28}O_5$ $P2_1, Z = 4$ | 4 | 10 | 37 | 514 | 22 | 11 | 38 | 25/26 | 41 |
| TRIPRO $C_{21}H_{33}N_3O_6$ $P2_1, Z = 4$ | 4 | 13 | 28 | 332 | 14 | 20 | 38 | 29/30 | 44 |
| SCHWZ1 $C_{54}H_{88}O_{18}$ $P2_1, Z = 2$ | 4 | 13 | 47 | 261 | 21 | | 1 | 33/72 | 31 |

No expansion of the phase sets by the ψ_{small} maps was carried out. A total of 90 sets of 47 phases corresponding to the highest maxima in ψ_{big} were refined by parameter shift and then entered into the *MULTAN* 78 system for tangent-formula extension. The five sets with a combined figure of merit greater than 2.0 were

| Set number | ABSFOM | ψ_0 | RESID | CFOM | Solution |
|-------------|--------|----------|-------|--------|----------|
| 68 | 0.8723 | 1.303 | 38.05 | 2.1669 | YES |
| 69 | 0.8882 | 1.659 | 37.19 | 2.1087 | NO |
| 70 = set 69 | | | | | |
| 43 | 0.8633 | 1.249 | 38.61 | 2.1073 | YES |
| 47 | 0.8663 | 1.278 | 38.83 | 2.0676 | YES. |

Sets 68 and 47 gave similar maps with two correct fragments which could have been completed by weighted-Fourier recycling, but set 43, with the lowest ψ_0 , yielded a better map with two almost complete molecular fragments as shown in Fig. 1 together with the actual structure of the molecule.

The second example refers to the structure of 9,10,11,12-dibenzopentacyclo [6.2.2.0^{2,6}.0^{2,7}.0^{3,7}]dodeca-9,11-diene (Szeimies-Seebach, Harnisch, Szeimies, Van Meerssche, Germain & Declercq, 1978). This structure which was given the code name MUNICH1, has space group $C2$ with formula $C_{20}H_{16}$ and $Z = 8$. All previous attempts at solving the structure by *MULTAN*, *MAGIC78* or *YZARC78* had failed and the structure was first solved by Patterson-search techniques. With 300 reflexions related by 2800 relationships the *CONVERGENCE* map plus user intervention gave two origin and one enantiomorph-defining reflexion, which were used as a basis to

generate 14 primaries and 38 secondaries (defined by 81 *PPS* t.p.r.'s). Magic-integer values, based on Fibonacci's series, were assigned to the primaries and

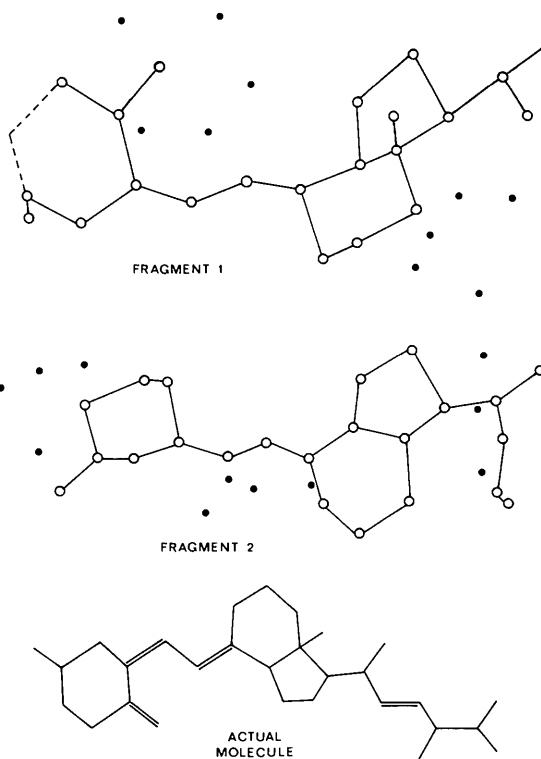


Fig. 1. Set 43 for ergocalciferol. The black dots are false peaks from the E map.

the number of relationships used in ψ_{big} was 1019 plus 19 constraint terms ($W_{\text{con}} = 0.1$, $\kappa_{\text{max}} = 4.81$); the maximum index was 4836. No expansion by ψ_{small} maps was performed, 100 sets of 55 phases were refined by parameter shift and then input into *MULTAN78* for tangent-formula extension. Set number 65 with the highest CFOM ($\psi_0 = 1.078$, ABSFOM = 1.0966 and RESID = 23.24) produced an *E* map showing all but one of the atoms of the two molecules in the asymmetric unit, as shown in Fig. 2.

As far as the solutions of the other structures in the table are concerned we just add a few comments:

- TURSCHI1** Braekman, Daloze, Dupont, Tursch, Declercq, Germain & Van Meerssche (1981). This structure was first solved by *MAGIC78*.
- Cortisone** $17\alpha,21\beta$ -Dihydroxy-4-pregnene-3,11,20-trione (Declercq, Germain & Van Meerssche 1972). This is the test structure issued with the *MULTAN* system.
- TRIPRO** *N*-*tert*-butyloxycarbonyl-L-prolyl-D-prolyl-L-proline methyl ester (Giordano & Silva, 1981). This was an unknown structure and was solved at the same time both by *MAGEX* and by *MULTAN80*, the most recent version of *MULTAN*.

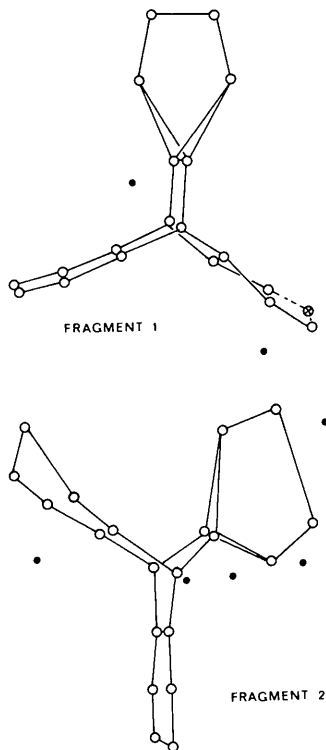


Fig. 2. Set 65 for MUNICH1. The missing atom is filled in with a cross and black dots correspond to false peaks.

SCHWZ1 Azalomycin B (Schweizer, 1980). Several direct-methods attempts had failed with this structure but a version of *MULTAN* under development and *MAGEX* both gave fragments which could be developed by weighted Fourier refinement.

General comments

The underlying process of *MAGEX* combines two important features of *MAGIC* and *YZARC* – the use of magic integers to represent the phases and the preparation of a large starting set before entering into tangent-formula expansion. As shown by Main (1977, 1978), magic integers provide an efficient way of exploring phase space, and even when the error in the magic-integer representation of the phases is rather large it is always less than random. The *MAGEX* procedure, by using magic integers based on high-*r* progressions and a strengthened definition of secondary reflexions, tends to minimize the errors in the representation, so that the sets of phases corresponding to the largest peaks in the ψ_{big} map are, in principle, substantially better than random phase sets.

It is common experience that tangent-formula expansion and refinement starting from a small set of phases sometimes has a tendency to drift away from the correct solution. This is especially true when the enantiomorph is not strongly defined and the phases tend to the values corresponding to a centrosymmetric structure containing both images of the structure. Schemes have been designed to prevent such drift (e.g. Hull & Irwin, 1978) but a very effective method is to use the tangent formula with a large set of phases which are kept fixed until the last cycle of refinement. The large set acts as a strong anchor to prevent the drift of phases towards values without enantiomorph discrimination or corresponding to a one-or-two-large-peaks situation ('uranium solution'). One final cycle of refinement will then just adjust the phases to better self-consistency.

When the initial set of primary and secondary reflexions is not large enough the expansion procedure used in *MAGEX* is designed to avoid convergence to a unique but wrong solution. The selection of 50 peaks from the ψ_{small} map gives a multiplicity of solutions, one of which is likely to be correct.

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APPENDIX

Consider a single *PPP* relationship of the form

$$Z = \varphi_1 + \varphi_2 + \varphi_3 \approx 0. \quad (A1)$$

The quantity $X = (m_1 + m_2 + m_3)x$ which represents the relationship can be written as

$$\begin{aligned} X &= Z + (m_1 x - \varphi_1) + (m_2 x - \varphi_2) + (m_3 x - \varphi_3) \\ &= Z + \delta_1 + \delta_2 + \delta_3 \end{aligned} \quad (A2)$$

where $\delta_1, \delta_2, \delta_3$ are the errors in representing the phases by magic integers. Each of the quantities on the right-hand side of (A2) has an expectation value of zero and a known theoretical standard deviation. Hence X , the sum of these quantities, has an expectation value of zero and a probability density with variance

$$\sigma_R^2 = V + 3\sigma_m^2, \quad (A3)$$

where V is the variance associated with the relationship (Karle & Karle, 1966) and σ_m the r.m.s. error in representing a phase for the magic-integer sequence being used (Main, 1977). If one or more primaries in the t.p.r. are *O + E* reflexions then they are given zero σ_m .

The same idea can be extended to other types of relationships. The variance associated with the definition of a secondary reflexion from two primaries by means of a t.p.r. will be

$$\sigma_S^2 = V' + 2\sigma_m^2 \quad (A4)$$

and therefore the σ_R^2 for the other types of relationships will be

$$PPS \quad \sigma_R^2 = V + V' + 4\sigma_m^2$$

$$PSS \quad \sigma_R^2 = V + V' + V'' + 5\sigma_m^2$$

$$SSS \quad \sigma_R^2 = V + V' + V'' + V''' + 6\sigma_m^2$$

σ_m is set to zero if the corresponding primary is an *O + E* reflexion.

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