

Phase Annealing in *SHELX-90*: Direct Methods for Larger Structures

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Abstract

A number of extensions to the multisolution approach to the crystallographic phase problem are discussed in which the negative quartet relations play an important role. A *phase annealing* method, related to the simulated annealing approach in other optimization problems, is proposed and it is shown that it can result in an improvement of up to an order of magnitude in the chances of solving large structures at atomic resolution. The ideas presented here are incorporated in the program system *SHELX-90*; the philosophical and mathematical background to the direct-methods part (*SHELXS*) of this system is described.

Introduction

The numerical multisolution approach to the phase problem, introduced and made popular by the program *MULTAN* (Germain, Main & Woolfson, 1970), is now involved in at least 70% of small-molecule structure determinations. In this paper we shall be concerned with the optimum application of this approach to the larger 'small-molecule' structures, given that powerful number-crunching computers with vector architectures are becoming more generally available. Since we shall be building on the experience gained with the program *SHELXS-86*, which has been described only briefly in the literature (Sheldrick, 1985; Robinson & Sheldrick, 1988), some of the ideas implemented in this program must first be introduced.

Although the original versions of *MULTAN* assigned up to four fixed phases to define the origin and enantiomorph, and then generated starting sets by permuting numerical values for several further phases, it appears that assigning random starting values to all phases is at least as effective (Furusaki, 1979; Yao Jia-Xing, 1981; Woolfson, 1987). Since it is also considerably simpler to program, random starting phases were employed in *SHELXS-86*. The iterative refinement of numerical phases using the tangent formula alone may lead to a false 'uranium-atom' solution in symmorphic space groups such as $P\bar{1}$ or $C2$, so a number of direct-methods programs (Busetta, Giacovazzo, Burla, Nunzi, Polidori & Viterbo, 1980; Gilmore, 1984; Sheldrick, 1985) now

employ a modified tangent formula which incorporates negative quartets (NQRs) as well as the triple phase relations (TPRs):

$$\text{new } \varphi_{\mathbf{h}} = \text{phase of } [\alpha - \eta]$$

where

$$\alpha = 2|E_{\mathbf{h}}|E_{\mathbf{k}}E_{\mathbf{h}-\mathbf{k}}/N^{1/2}$$

and

$$\eta = g|E_{\mathbf{h}}|E_{\mathbf{k}}E_{\mathbf{l}}E_{\mathbf{h}-\mathbf{k}-\mathbf{l}}/N;$$

N is the number of atoms (assumed equal here for simplicity) per (primitive) unit cell. Note that α and η are complex numbers in this equation and in the definition of NQUAL (below). The NQRs are characterized by large E values for the four primary terms and small E values for the three unique cross terms $\mathbf{k}-\mathbf{h}$, $\mathbf{l}-\mathbf{h}$, $\mathbf{k}+\mathbf{l}$ (Schenk, 1974; Hauptman, 1974). g is a positive constant which takes the E values for the cross terms into account; it is often set to a value larger than the theoretical value to compensate for the smaller absolute value of η compared with α . Our tests indicate that the computer time per correct solution is minimized when the total number of NQRs used is restricted to the 1000 to 8000 most reliable (depending on the size of the structure and the type of space group). For this purpose it is important to use only those quartets for which *all three* cross terms have been measured and found to be weak. On the other hand we find that it is advisable to use *all* TPRs connecting the reflections involved in the refinement, except for Σ_1 relations and TPSs consisting of three reflections with restricted phases such that the resultant phase cannot be zero (Giacovazzo, 1974).

In recent developments of the *MULTAN* system the weak reflections are used in a related manner (Debaerdemaeker, Tate & Woolfson, 1988); apparently only one of the three cross terms is required to have $|E| \ll 1$, which allows a much larger number of quartets to be used, but the individual contributors will be less reliably 'negative'. The phase-annealing method described below should be equally applicable to this approach.

Schenk (1972) has described the problems that can arise when the tangent formula is applied without modification in symmorphic and polar space groups. The introduction of NQRs is a major advance, but it

is still possible for iterative phase refinement to produce an over-consistent solution, with loss of enantiomorph resolution or a single dominant peak in a subsequent Fourier synthesis. This may be a result of an inadequate number of NQRs, but can also arise in other cases. The data collection strategy for measuring the weak reflections has a considerable influence on the number and reliability of the NQRs; the worst approach is to skip the reflection if a prescan indicates that it is probably weak, but using the prescan to estimate the intensity (with a corresponding large e.s.d.) is not much better. Structures with a small number of heavy atoms also tend to give a smaller number of NQRs. Dölle (1988) and Gilmore & Brown (1988) have recommended truncating the resolution range in selecting the reflections to be used for phase refinement. We find that optimum results are obtained when a limiting resolution sphere of about 1 Å is employed. This increases the number of TPRs for a fixed number of reflections, and even more markedly increases the number and reliability of the NQRs, even though it means that some reflections with lower E values are refined.

The degradation of the tangent refinement can be handled by special action for reflections which have α greater than its expected value $\langle\alpha\rangle$ (Karle & Karle, 1966; Cascarano, Giacobozzo & Viterbo, 1987) for a correct solution. Hull & Irwin (1978) proposed a weighting scheme which down-weights these reflections; this however introduces the danger of oscillation of these weights in alternate cycles. We prefer to retain unit weights but to project α onto its expected value. A correction of $\delta\varphi$ is applied to the pure tangent formula phase φ_h (calculated without NQRs), where

$$\cos(\delta\varphi) = (\langle\alpha^2\rangle)^{1/2}/|\alpha|$$

and the sign of $\delta\varphi$ is determined by choosing the value so that the resulting φ_h is most consistent with the NQR sum (if no NQRs contribute to a particular reflection, the sign is set randomly). Thus, even if there are not many NQRs and they are not very reliable, they can make a useful contribution. This technique is very effective at driving the solution to a small R_α and a negative NQUAL (see below), but can only be applied to non-centrosymmetric structures.

The consistency of the TPR contributions can be judged by the figure of merit R_α (Roberts, Pettersen, Sheldrick, Isaacs & Kennard, 1973):

$$R_\alpha = \sum_h w[\alpha - (\langle\alpha^2\rangle)^{1/2}]^2 / \sum_h w\alpha^2$$

where w is a suitable weight, e.g. $1/(\alpha+5)$. [In *SHELXS-86* and our previous programs the denominator was $\sum w\langle\alpha^2\rangle$; the new version is more selective provided that it is used in conjunction with the α -projection technique (see above) for non-centrosymmetric structures.]

Rather than the usual criterion NQUEST (DeTitta, Edmonds, Langs & Hauptman, 1975) which represents the weighted mean cosine of the strongest NQRs, we prefer to use the correlation between α and η (Sheldrick, 1985)

$$\text{NQUAL} = \sum_h |\alpha \cdot \eta| / \sum_h |\alpha| |\eta|$$

We find that NQUAL is both more negative and also more sensitive than NQUEST for large structures, for which the larger number of NQRs involved in the summations for a given h can to a large extent compensate for the $1/N$ term in the probability expression. The two criteria can be combined to give

$$\text{CFOM} = R_\alpha \quad \text{if } Q > \text{NQUAL}$$

$$\text{CFOM} = R_\alpha + (\text{NQUAL} - Q)^2 \quad \text{otherwise,}$$

where Q is usually set to a value about 0.1 more negative than the expected NQUAL. Finally the phase set with the best (*i.e.* smallest) CFOM is used to calculate a Fourier synthesis with coefficients E and the final direct-methods phases (E map) which is searched to find potential atoms. An iterative procedure (Sheldrick, 1982), in which potential atoms are eliminated to reduce an R index (calculated for E values assuming point atoms) and the remaining atoms are used to phase the next E map, provides a further figure of merit (R_E), and facilitates the chemical interpretation of the solution.

Problem structures

The approach outlined above has now been extensively tested by users of the program *SHELXS-86*, and a number of successful applications have been reported in *Acta Crystallographica*, including several structures – often in symmorphic space groups – which had previously proved resistant to direct methods. There seem to be three general areas where problems remain:

(1) Pseudosymmetry problems, usually characterized by a number of non-equivalent solutions with approximately equally good figures of merit. Such problems are particularly prevalent in the space group $P\bar{1}$, for fused aromatic systems and for structures with heavy atoms on (almost) special positions. Lowering the E threshold and thereby increasing the number of reflections refined (Bürgi & Dunitz, 1971) often improves the discrimination of the figures of merit, but the simplest approach is to calculate E maps for all the good solutions, not just the best.

(2) Resolution problems. Experience with a large number of structures has led us to formulate the empirical rule that if fewer than half the number of theoretically measurable reflections in the range 1.1 to 1.2 Å are 'observed' [*i.e.* have $F > 4\sigma(F)$], it is very unlikely that the structure can be solved by direct methods. This critical ratio may be reduced somewhat

for centrosymmetric structures, and for structures containing heavier atoms. This rule simply reflects the assumption of resolved atoms, which is often invoked in direct methods. It may still be possible to solve such structures by molecular-replacement methods if a sufficiently large and accurate search fragment is available. Alternatively, the data collection can be repeated more carefully with a larger crystal at lower temperature.

(3) Large structures. The problem may be likened to that of finding a needle in a haystack. Even when using random starting phases rather than generating explicit phase permutations, the computer time per correct solution rises steeply with the number of atoms in the unit cell. The rest of this paper is concerned with this class of structure.

A technique used in *SHELXS-86* to reduce the computer time required for large structures involved dividing the phase refinement into two stages. The first stage involved about half the number of reflections used in the second, but much less than half the number of phase relations (since the number of TPRs and NQRs rises rapidly with the number of reflections used). The same general procedure was used for the selection of both phase sets. Reflections with the highest E values were selected, taking initially about 20–50% more than required. All TPRs linking these reflections were used to estimate $\langle \alpha^2 \rangle$ for each reflection. The required number of reflections with the highest $\langle \alpha^2 \rangle$ values was then selected. Further optimization of the reflection set would run the risk of accentuating pseudosymmetric features of the structure, in extreme cases by the complete elimination of weakly linked parity groups. The computer time required for phase refinement was determined primarily by the number of phase relations. On the basis of the figures of merit at the end of the first stage, only the best (say) 10% phase sets were refined further. The phase relations for the first stage could be stored in the main computer memory and did not need to be read in from the disk. With a smaller number of reflections, the reduced multimodality of phase space should increase the chances of finding the solution, but at the cost of increasing the mean phase error. For straightforward test structures this *filter* procedure did indeed reduce the average computer time per correct solution appreciably. For large structures (including some of those subsequently solved by phase annealing) it often resulted in repetition of the same wrong solution. One explanation is that the correct solution may have figures of merit at the end of the first stage that do not place it amongst the best 10%. A further explanation (if we assume that phase refinement corresponds to the minimization of some target function) is that false minima are usually broader but shallower than true minima, because the phase relations are unlikely to have their individual minima so closely in phase for an accidental solution.

If the minimization procedure cannot escape from a minimum, then the chance of random starting phases falling in the catchment area of a broad but shallow minimum will be greater than that of a narrow but deep minimum.

Phase annealing

Kirkpatrick, Gellatt & Vecchi (1983) described a very generally applicable method of combinatorial optimization which they applied to the design of computer chips and to the *travelling salesman* problem. This simulated annealing procedure may be described by analogy with statistical thermodynamics. It is necessary to define an algorithm by which the system can be brought into a state of thermodynamic equilibrium described by a temperature T . The annealing is then achieved by lowering the temperature slowly. The energy of the system is given by the sum of the potential energy (the function to be minimized) and the kinetic energy. The form taken by the kinetic energy depends on the system being considered, but involves some random behaviour of the individual contributors. The presence of the kinetic energy makes it more likely that the system will escape from broad shallow minima than from narrow deep minima, so slow cooling increases the chance of finishing in a global rather than a local minimum, consistent with the annealing analogy.

Simulated annealing has recently (Kuriyan, Brünger, Karplus & Hendrickson, 1989) established itself as an effective method for the intermediate stages of refinement of protein structures using a potential energy function which includes the X-ray data. The kinetic energy is provided naturally by a molecular-dynamics simulation of the motion of the individual atoms, and enables side-chain conformations to escape from false local minima. For systems which cannot be described in terms of continuous motion, the Metropolis algorithm (Metropolis, Rosenbluth, Rosenbluth, Teller & Teller, 1953) enables the system to approach thermodynamic equilibrium by imposing a Boltzmann distribution. Each time a parameter is changed, the energy E of the system is calculated. If the energy decreases, the jump is always made. If ΔE is positive, the probability P of the new state relative to the old is calculated from the Boltzmann formula $\exp(-\Delta E/kT)$, where k is a constant. If P is greater than a random number in the range 0 to 1, the jump is made, but if P is less the original state is retained.

To see how simulated annealing can be applied to direct methods (we shall name this *phase annealing*) it is necessary to reformulate Cochran & Wolfson's (1955) formula for centrosymmetric structures,

$$P_+ = \frac{1}{2} + \frac{1}{2} \tanh(\alpha/2),$$

where P_+ is the probability that E_h takes the sign of

α . For positive α , P_+ measures the probability of the lower-energy state, and $P_- = 1 - P_+$ is the probability of the higher state. Thus the Boltzmann ratio is given by

$$P_-/P_+ = \exp(-\alpha)$$

so all that is needed is to multiply α by β , a control variable inversely proportional to the temperature! In a slight variation of the Metropolis algorithm we take the higher-energy P_- state only if $(P_-/2P_+)$ (which must be less than $\frac{1}{2}$) is greater than a random number R in the range 0-1, otherwise we choose the lower-energy state (*i.e.* the phase given by the modified tangent formula).

In the classical applications of the Metropolis algorithm, a random change is made; for example a spin is 'flipped' (in the spin-glass problem) or two paths are interchanged (in the travelling salesman problem and in computer chip optimization). The probability of this change is then estimated *via* the Boltzmann formula and tested against a random number to see whether the change should be made or not. Often in such applications a direct refinement (*i.e.* $T=0$ in the Boltzmann formula) is known to be ineffective because of the large number of local minima; practical tests have shown that for such applications the simulated annealing algorithm is computationally much more efficient than this $T=0$ 'steepest descent' method combined with many random starting configurations. The direct-methods problem (for centrosymmetric structures) is conceptually very similar, but with a comparatively small number of local minima - otherwise multisolution tangent refinement would not be so successful - so the phase annealing approach appears promising. On the other hand, if we are designing a computer chip, a local minimum which is almost as good as a global minimum is an entirely acceptable solution; for direct methods this may not be good enough, and indeed the 'correct' solution does not necessarily correspond to the global minimum of any function which can be calculated quickly! Thus multiple-phase starting sets are still a *sine qua non*.

The above centrosymmetric formula can also be applied to restricted phases in non-centrosymmetric space groups. After testing a variety of formulae we have chosen to calculate general phases in non-centrosymmetric structures by adding $\Delta\phi$ to the phase obtained by the modified tangent formula (or projection method if $\alpha > (\alpha^2)^{1/2}$), where

$$\cos(\Delta\phi) = [4\beta\alpha + \ln(R)]/[4\beta\alpha - \ln(R)],$$

where the sign of $\Delta\phi$ is assigned at random and R is a random number between 0 and 1. Thus $\cos(\Delta\phi)$ is in the range -1 to +1 and approaches +1 in the limit of large $\beta\alpha$, as required. It should be emphasized that this formula is purely empirical, and that the numerical factor of 4 has been chosen to give similar mean

Table 1. CFOM distribution after 50 and 250 phase annealing cycles at constant temperature (initial Boltzmann factor B) for the LOG test structure

CFOM range	$B=0.0$		$B=0.1$		$B=0.2$		$B=0.3$	
	50	250	50	250	50	250	50	250
	0.05-0.06	2	3	0	0	0	0	0
0.06-0.07	21	27	0	0	0	0	0	0
0.07-0.08	5	3	0	2	0	0	0	0
0.08-0.09	1	0	3	7	0	0	0	0
0.09-0.10	0	0	4	22	0	0	0	0
0.10-0.11	0	0	13	32	5	1	0	0
0.11-0.12	0	0	7	15	2	2	0	0
0.12-0.13	0	0	6	13	4	5	0	0
0.13-0.14	0	0	4	5	5	14	0	0
0.14-0.15	1	1	0	0	4	31	0	0
0.15-0.16	5	8	0	2	6	25	0	0
0.16-0.17	5	16	0	0	9	20	0	2
0.17-0.18	18	23	0	0	6	16	1	3
0.18-0.19	16	28	0	1	3	3	3	2
0.19-0.20	21	17	3	0	0	2	2	10
0.20-0.21	14	23	3	5	1	2	3	3
0.21-0.22	14	21	5	8	0	4	6	11
0.22-0.23	17	22	5	6	2	1	6	11

absolute phase shifts for general and restricted phases at the start of the phase determination (random phases).

If this phase annealing is performed with infinite β (zero T) it will correspond exactly to a phase refinement using the tangent formula as modified above. If β is zero (infinite T) the phases will simply remain random (*unconstrained* maximum entropy). If the temperature is slowly lowered, the well defined phases (high α) will be subject to smaller fluctuations than those with low α . Thus phases linked by strong phase relations will tend to become established earlier in the phase determination procedure, whilst the remaining phases are still free to explore phase space. If a 'good' (but not necessarily correct) solution is found it will remain more stable than a phase set with low mean α .

Since the appropriate value of β depends on the structure, it is more convenient to discuss the performance of the phase annealing in terms of B , the estimated initial Boltzmann ratio for random starting phases. β is estimated as $-\ln(B)$ divided by the mean (over all reflections employed) of $(\langle\alpha^2\rangle)^{1/2}$ (calculated as described by Germain, Main & Woolfson, 1970). This approximation assumes the centrosymmetric formula and ignores the contributions of the NQRs, but is adequate since only an order of magnitude is required. Table 1 illustrates the distribution of CFOM values obtained for various B values after 50 and 250 phase annealing cycles at constant 'temperature' for the loganin test structure (Jones, Sheldrick, Glösenkamp & Tietze, 1980). For $B=0$ (which corresponds to $T=0$) the correct solutions are clearly separated from the rest, but the number of correct solutions only increases a little between 50 and 250 cycles. That it increases at all suggests that it is an oversimplification to regard tangent refinement as a pure

Table 2. *Direct-methods parameters and final figures of merit for seven test structures*

Structure code Space group	LOG $P2_12_12_1$	SUOA $P2_12_12_1$	PEP1 $P2_12_12_1$	NEWQB $P\bar{1}$	BHAT Pc	MBH2 $P1$	HOPS $R3(\text{hex})$
N/cell	108	188	340	124	84	54	243
$n(E)$ for phase annealing (p.a.)	139	190	257	254	184	263	156
$n(\text{TPR})$ for p.a.	1235	1801	2634	1144	1736	1928	2233
$n(\text{NQR})$ for p.a.	191	144	896	80	637	609	494
$n(E)$ full	219	320	455	448	304	467	253
$n(\text{TPR})$ full	4625	9227	13922	5225	6333	8661	7583
$n(\text{NQR})$ full	1080	1312	2024	1147	2840	6216	2873
$n(E)$ for R_α	295	463	656	671	304	630	267
$n(\text{TPR})$ for R_α	8229	18494	27894	10472	6333	14724	8386
Final R_α	0.080	0.095	0.098	0.078	0.070	0.036	0.052
Final NQUAL	-0.70	-0.36	-0.62	-0.84	-0.74	-0.99	-0.80
Time per phase set (s)	0.13	0.19	0.34	0.05	0.22	0.31	0.23

The time corresponds to 25 cycles of phase annealing followed by four cycles of refinement (three for NEWQB). The number of reflections used in each stage $n(E)$ was chosen automatically using an empirical algorithm based on the cell volume and space group. All available TPRs were used in all tests, but $n(\text{NQR})$ was restricted in some cases. The references to the test structures are:

- LOG: Jones, Sheldrick, Glüsenkamp & Tietze (1980).
- SUOA: Oliver & Strickland (1984).
- PEP1: Antel, Sheldrick, Bats, Kessler & Müller (1990).
- NEWQB: Grigg, Kemp, Sheldrick & Trotter (1978).
- BHAT: Bhat & Ammon (1990).
- MBH2: Poyser, Edwards, Anderson, Hursthouse, Walker, Sheldrick & Walley (1986).
- HOPS: Hopf, Lehne & Jones (1990).

Table 3. *Number of correct solutions per 10 000 tries as a function of the initial Boltzmann factor B for a cooling schedule of 25 cycles with the temperature multiplied by 0.95 after each cycle, followed by four cycles of phase refinement (three for NEWQB)*

Structure code	LOG	SUOA	PEP1	NEWQB	BHAT	MBH2	HOPS
$B = 0.0$	206	6	1	1	26	469	56
0.1	488	42	17	11	77	1015	201
0.2	564	44	17	16	91	942	211
0.3	644	50	25	20	97	825	184
0.4	724	48	18	21	77	707	180
0.5	718	25	10	14	47	619	144
0.6	566	2	5	8	38	474	82

minimization procedure. As B increases all the CFOM values increase, and the percentage of correct solutions grows with the number of cycles performed. Finally for $B = 0.3$ or higher it is no longer possible to distinguish the correct solutions from the rest because all CFOM values are high (high kinetic energy). In addition, the fluctuations of the distribution from one cycle to the next increase appreciably with B .

Computational efficiency

The reliability of individual phase relations decreases with increasing N , so we need to use more phase relations per reflection in the final refinement to obtain the same phase accuracy and quality of figures of merit for larger structures. Since the phase annealing stage will be rate determining and we are deliberately introducing noise into it, it makes sense to perform it using only the 50–60% of reflections with the largest $\langle \alpha^2 \rangle$ values. In contrast to the filter procedure described above, all phase sets are then finally refined for three cycles (centrosymmetric) or four (non-centrosymmetric) with the full number of phases and relations. The selectivity of R_α can be improved further by including summations for reflections additional to those used for the phase refinement.

The modified tangent formula and phase annealing procedure are particularly suitable for vector processing on modern computers with parallel architectures. All that is necessary is to process a suitable number M (we usually use 128) of phase sets in parallel. All rate-determining stages can be formulated as vectorizable loops over the M phase sets. Even on scalar machines, this brings an appreciable bonus, because various overheads such as reading phase relations from the disk occur only once per K phase sets. All the tests reported here were performed on an IBM-3090 300E computer (with vector processor), using the FORTV2S2 compiler which automatically vectorized the critical loops. The vectorized version was about 3.7 times faster than the non-vectorized for these loops and about 3.0 times faster for the complete structure solution run. Preliminary tests with Cray and Convex computers also resulted in automatic vectorization of the critical loops.

Practical tests

Tables 2 and 3 illustrate some practical tests using seven structures selected from a test bank of direct-methods structures that is available from the author. The first three were chosen to illustrate the effect of

varying the size of the structure for a given (well behaved) space group, the remaining four to illustrate symmorphic and/or polar space groups. In all seven cases it was known from extensive tests that the correct solution could be recognized on the basis of the figures of merit alone. Chance can play a considerable role in direct methods, so to obtain a statistically significant number of solutions about 10 000 (or more) phase sets were refined for each of the entries in Table 3. Although increasing the number of phase annealing cycles increases the number of correct solutions, there comes a point where it would be more efficient in terms of computer time to process different random starting phase sets instead. So for each entry in Table 3, 25 cycles of phase annealing were performed starting with the given Boltzmann ratio B (for random phases) and multiplying the temperature by 0.95 after each cycle. It can be seen that this is a good general strategy with an initial B in the range 0.2 to 0.4; the exact value of B is not very critical. Further tests confirmed the trend that a smaller initial B gives slightly better results in polar space groups, and showed that the number of phase annealing cycles could be reduced in such cases. Doubtless the cooling schedule could be tuned for each individual structure, but this would require knowing the structure.

For the test structures in Tables 2 and 3, a 'correct' solution is one which (a) had a CFOM value which clearly separated it from the 'incorrect' solutions, and (b) after the usual Fourier recycling gave a peak list in which all atoms were higher than any spurious peaks. Criterion (b) was relaxed a little for PEP1, since one phenyl ring and the solvent molecules showed appreciable thermal motion; a typical final map for PEP1 had 78 of the expected 80 unique non-solvent atoms in the top 80 peaks, and about half of the solvent also present in the peak list. Almost all one-phase seminvariants had identical signs for different 'correct' solutions of a given structure.

We also tested the three structures in the space group $P2_12_12_1$, without NQRs in the phase annealing stage; the results were always inferior to those reported in Table 3, but for the PEP1 structure the differences were not significant. It is to be expected that the NQRs will become relatively less reliable the larger the structure, because of the $1/N$ term in the probability expression compared to $1/N^{1/2}$ for TPRs. The NQRs are however essential for symmorphic space groups.

For the $P1$ test structure (MBH2) the increase in the number of solutions obtained with phase annealing was only sufficient to compensate for the extra computer time required (compared with the $B=0$ run). For the other six structures the phase annealing produced significant dividends, and for the largest structure studied (PEP1) increased the chance of finding a correct solution by more than an order of magnitude.

Concluding remarks

In addition to performing at least as well as our previous programs on each of the structures in the full test data bank, the phase annealing method has already been successful in solving eight large structures with up to 180 atoms in the asymmetric unit which had resisted all previous efforts using a variety of programs including *SHELXS-86*.

Phase annealing is also appropriate for the expansion of a partial structure which is too small for successful elucidation by tangent expansion followed by E -map recycling. Preliminary tests indicate that, instead of using a small number of fixed partial structure phases plus random starting values for the rest, it is more effective for all attempts to start from the *same* partial structure phases for all reflections. The inherent randomness of the phase annealing approach then ensures that each phase set follows a different refinement path, leading to effective exploration of phase space in the vicinity of the partial structure solution. The cooling schedule should be just 'warm' enough to ensure that not too many solutions are the same.

The program described here is available in source form from the author as part (*SHELXS*) of the *SHELX-90* system. Although designed with vectorizing computers in mind it is written entirely in Fortran 77 and runs on a wide variety of computers with little or no modification. A precompiled version is available for personal computers running the MSDOS operating system.

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On the Determination of Quasicrystal Structures

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Abstract

A possible approach to direct phasing of quasicrystal diffraction data is described. The data are first converted to a set of structure-factor amplitudes of a multidimensional crystal. The Patterson function of the quasicrystal is used to derive the converting factor. A direct method is then used to solve the phase problem in multi-dimensional space. The method has been tested with a hypothetical one-dimensional quasicrystal yielding a satisfactory result.

Introduction

The recently discovered quasicrystals (Shechtman, Blech, Gratias & Cahn, 1984) belong to a new kind of substance between the crystalline and amorphous states. They have long-range orientational order as well as long-range quasiperiodicity. The inconsistency of their symmetry with classical crystallography has drawn great attention from condensed-matter physicists and chemists. Determination of quasicrystal structures is important for understanding the properties or for exploring the applications of quasicrystals. So far quasicrystal structure determination has mainly been performed by trial-and-error methods. One must first propose a structure model,

calculate the diffraction intensities and then compare with the experimental data. This is a tedious process; it resembles the structure analysis of crystals in the early days. During the last two decades X-ray analysis of crystal structures has achieved great progress owing to the development of direct methods (Woolfson, 1987). Hence it is worth trying to apply direct methods to quasicrystal structures. However, the task is far from straightforward, since quasicrystals do not possess periodicity in the sense of classical crystallography. Use of direct methods in quasicrystal structure analysis was proposed by Li Fang-hua, Wang Li-chen & Fan Hai-fu (1987). A structure-factor relation for quasicrystals has been derived and a preliminary test result has been obtained. In the previous study, the shape factor for constructing a quasicrystal from a multi-dimensional (MD) crystal is assumed to be known in advance. However this is not true in practice. In order that direct methods can be useful in practice, this problem remains to be solved. In this paper, a method which makes use of the Patterson function is proposed to determine the shape factor. This enables the conversion of diffraction data from a three-dimensional (3D) quasicrystal to the corresponding MD crystal. Direct methods can then be used to solve the phase problem in MD space.