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The *SIR* Program. I. Use of Negative Quartets

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Abstract

The present paper deals with the finding and the estimation of negative quartets. The use of symmetry is also discussed and the results obtained for four structures of increasing size are reported. Conditional probability distributions using magnitudes contained in the second representation of the quartets provides improved estimates of their phases.

Introduction

During recent years, direct methods have been developed to allow the crystal-structure determination of a great number of large molecules. Most of the currently available direct-method programs are based on the use of the single statistical triplet relation

$$\langle \sin(\varphi_{\mathbf{H}} + \varphi_{\mathbf{K}} + \varphi_{\overline{\mathbf{H}+\mathbf{K}}}) \rangle_{\mathbf{K}} \simeq 0,$$

from which the so-called tangent formula is derived.

The estimate of the triplet cosine invariant by statistical formulae [*e.g.* MDKS (Hauptman, 1972; Giacovazzo, 1976*a*)] is a more accurate way of using the information provided by the triplet invariants. More recently, a modification of the classical tangent formula, making use of the estimated phases of the triplet invariants (Busetta, 1976), provided a good way of determining a structure in those cases where enantiomorph discrimination is difficult. However, in order to deal with large molecules – or with very troublesome small ones – it is necessary to use the whole information provided by the complete set of structure invariants and seminvariants. This is the basic idea behind the *SIR* program. All the (sem)invariant phase relationships are estimated following the Sem Invariant Representation theory (Giacovazzo, 1977). The present available version of the program uses triplets, negative quartets and one-phase seminvariants.

The present paper, the first of a series, deals with negative quartets. The positive quartets provide information which is strongly correlated to the information contained in triplet relations. Their use requires a more complicated approach and will be analysed in a future paper. Here we intend to develop different points concerned with finding and estimating negative quartets. Until now, only the four basis vectors and the three related cross vectors have been used in their estimation (Hauptman, 1974; Schenk, 1974); we will show that the use of symmetry (Giacovazzo, 1976*b*) and of the second representation can improve these estimates.

In the estimation of quartets, seven vectors are necessary, the basis vectors $\mathbf{H}_1$, $\mathbf{H}_2$, $\mathbf{H}_3$ and $\mathbf{H}_4$ whose sum is zero and the cross vectors $\mathbf{H}_1 + \mathbf{H}_2$, $\mathbf{H}_1 + \mathbf{H}_3$ and $\mathbf{H}_1 + \mathbf{H}_4$. Of these seven vectors only three are independent. It is possible to search in different ways for negative quartets.

(1) Starting from three basis vectors with large magnitudes, $\mathbf{H}_1$, $\mathbf{H}_2$, $\mathbf{H}_3$, we may search for the fourth basis vectors $\mathbf{H}_4$ and the three corresponding cross vectors, checking if they have weak magnitudes.

(2) A second way is to start from three cross vectors **U**, **V**, **W** of weak magnitudes and to search for the four basis vectors

$$\mathbf{H}_1 = \tfrac{1}{2}(\mathbf{U} + \mathbf{V} + \mathbf{W}), \mathbf{H}_2 = \tfrac{1}{2}(\mathbf{U} - \mathbf{V} - \mathbf{W}),$$
$$\mathbf{H}_3 = \tfrac{1}{2}(\mathbf{V} - \mathbf{U} - \mathbf{W}), \mathbf{H}_4 = \tfrac{1}{2}(\mathbf{W} - \mathbf{U} - \mathbf{V}),$$

checking if all of them display large magnitudes.

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We preferred to search for negative quartets by subtracting two triplets which have a common basis vector of weak magnitude; that is to say the same way we used to build positive quartets (Busetta, 1976). This work can be done at the level of the *SIGMA*2 subroutine of the *MULTAN* (Main, Woolfson & Germain, 1971) package without requiring too many changes.

Use of the space group symmetry

Usually, the estimate of a quartet depends in its first representation on three cross vectors, but for a space group with symmetry higher than triclinic it may depend on more than three terms. This happens when one of the cross vectors is a symmetry-invariant reflexion, that is an invariant with respect to a symmetry operator, *i.e.*

$$\mathbf{H} = \mathbf{R}_S^+ \mathbf{H},$$

where $\mathbf{R}_S$ is a symmetry rotation matrix and $\mathbf{R}_S^+$ is its transpose.

For instance, if the quartet $\varphi = \varphi_{\mathbf{H}_1} + \varphi_{\mathbf{H}_2} + \varphi_{\mathbf{H}_3} + \varphi_{\mathbf{H}_4}$ (I) has a symmetry-invariant reflexion as one of its cross vectors (*e.g.* $\mathbf{H}_1 + \mathbf{H}_2$), we may define

$$\varphi' = \varphi_{\mathbf{R}_S^+\mathbf{H}_1} + \varphi_{\mathbf{R}_S^+\mathbf{H}_2} + \varphi_{\mathbf{H}_3} + \varphi_{\mathbf{H}_4}. \qquad \text{(II)}$$

Now $(\mathbf{H}_1 + \mathbf{H}_2) + \mathbf{H}_3 + \mathbf{H}_4 = \mathbf{R}_S^+(\mathbf{H}_1 + \mathbf{H}_2) + \mathbf{H}_3 + \mathbf{H}_4 = \mathbf{R}_S^+\mathbf{H}_1 + \mathbf{R}_S^+\mathbf{H}_2 + \mathbf{H}_3 + \mathbf{H}_4$ and therefore (II) is a quartet. We find

$$\varphi' - \varphi = 2\pi(\mathbf{H}_1 + \mathbf{H}_2)^+\mathbf{T}_S$$

with

$$\varphi_{\mathbf{H}_1+\mathbf{H}_2} = \varphi_{\mathbf{R}_S^+(\mathbf{H}_1+\mathbf{H}_2)} + 2\pi(\mathbf{H}_1 + \mathbf{H}_2)^+\mathbf{T}_S.$$

Then the estimate of φ depends on five distinct cross magnitudes; three corresponding to φ,

$$|E_{\mathbf{H}_1+\mathbf{H}_2}|, |E_{\mathbf{H}_1+\mathbf{H}_3}|, |E_{\mathbf{H}_1+\mathbf{H}_4}|,$$

the other two arising from φ'

$$|E_{\mathbf{R}_S^+\mathbf{H}_1+\mathbf{H}_3}|, |E_{\mathbf{R}_S^+\mathbf{H}_1+\mathbf{H}_4}|.$$

If $(\mathbf{H}_1 + \mathbf{H}_2)$ is not a systematically absent reflexion, then $\cos\varphi$ may be expressed as $\cos\theta = I_1(B)/I_0(B)$, where

$$B = \frac{2}{N}\left|E_{\mathbf{H}_1}E_{\mathbf{H}_2}E_{\mathbf{H}_3}E_{\mathbf{H}_4}\right|[W + \sum^{5}(|E_{\text{cross}}|^2 - 1)],$$

if we use linearized formulae with $W = 1$ and N is the number of identical atoms in the unit cell.

If two cross vectors are symmetry-invariant reflexions the problem is rather more complicated, and the phase of the quartet depends on more than five vectors (Giacovazzo, 1976*b*). While in space groups of class *P*2 only the 0*k*0 reflexions are special and a limited number of quartets is affected by symmetry, for space groups of higher symmetry a significant number of quartets may be influenced by the symmetry. For instance, in the space groups $Pca2_1$ (class *Pmm*2), the three classes of reflexions 0*kl*, *h*0*l* and 00*l* are special.

If symmetry is not taken into account, all the procedures to search for negative quartets would involve unavoidable duplications. Both quartets ($\mathbf{H}_1$, $\mathbf{H}_2$, $\mathbf{H}_3$, $\mathbf{H}_4$) and ($\mathbf{R}_S^+\mathbf{H}_1$, $\mathbf{R}_S^+\mathbf{H}_2$, $\mathbf{H}_3$, $\mathbf{H}_4$) will separately appear during the search of the structure invariants. However, if the magnitudes ($E_{\mathbf{H}_1+\mathbf{H}_3}$ and $E_{\mathbf{H}_1+\mathbf{H}_4}$) and ($E_{\mathbf{R}_S^+\mathbf{H}_1+\mathbf{H}_3}$ and $E_{\mathbf{R}_S^+\mathbf{H}_1+\mathbf{H}_4}$) do not give contributions of the same sense – for instance the first two are large ($E \simeq 2{\cdot}00$) and the other two weak ($\simeq 0{\cdot}1$) – the most probable phase of the correct quartet will be between 0 and $\pi/2$; if we use both previous distinct quartets the estimated phases will be near 0 and π. It is important to take the symmetry into account in both the cases where the negative quartets are directly used during the phase expansion and where they are only used as figures of merit. To introduce into the figure of merit quartets like ($\mathbf{R}_S^+\mathbf{H}_1$, $\mathbf{R}_S^+\mathbf{H}_2$, $\mathbf{H}_3$, $\mathbf{H}_4$) for which the phase is spuriously evaluated as π instead of $\pi/2$, will certainly reduce the efficiency of such a test.

Negative quartets may also be obtained for which one of the cross reflexions, *e.g.* $\mathbf{H}_1 + \mathbf{H}_2$, is a systematic absence. Such reflexions are symmetry-invariant reflexions with the extra condition $2\pi(\mathbf{H}_1 + \mathbf{H}_2)\mathbf{T}_S \neq 0$. Then the phases of both quartets $\varphi_{\mathbf{H}_1} + \varphi_{\mathbf{H}_2} + \varphi_{\mathbf{H}_3} + \varphi_{\mathbf{H}_4}$ and $\varphi_{\mathbf{R}_S^+\mathbf{H}_1} + \varphi_{\mathbf{R}_S^+\mathbf{H}_2} + \varphi_{\mathbf{H}_3} + \varphi_{\mathbf{H}_4}$ do not differ by 2π. If $\mathbf{R}_S$ is a rotation matrix of order two, then the estimated value of φ is related to the observed cross vectors by a B term,

$$B = \frac{2}{N}|E_{\mathbf{H}_1}E_{\mathbf{H}_2}E_{\mathbf{H}_3}E_{\mathbf{H}_4}|\,|(|E_{\mathbf{H}_1+\mathbf{H}_3}|^2 - 1) \times (|E_{\mathbf{H}_1+\mathbf{H}_4}|^2 - 1) - (|E_{\mathbf{R}_S^+\mathbf{H}_1+\mathbf{H}_3}|^2 - 1) - (|E_{\mathbf{R}_S^+\mathbf{H}_1+\mathbf{H}_4}|^2 - 1)|.$$

In this case, we have $W = 0$ (Giacovazzo, 1976*b*). For instance, for the last quartet of Table 2, the four basis vectors are

$$26\,1\,2, \quad \bar{8}\,\bar{1}\,1, \quad \bar{15}\,1\,\bar{5}, \quad \bar{3}\,\bar{1}\,2.$$

If we do not take the symmetry into account, the phase of this quartet depends on the magnitudes of three cross vectors:

$$18\,0\,3, \quad 11\,2\,\bar{3}, \quad 23\,0\,4.$$

As the first cross vector is a symmetry-invariant reflexion, the phase of the primitive quartet is also the phase of the symmetry-related one, of which the basis vectors are

$$26\,1\,2, \quad \bar{8}\,\bar{1}\,1, \quad \bar{15}\,\bar{1}\,\bar{5}, \quad \bar{3}\,1\,2,$$

so that this phase also depends on two other magnitudes corresponding to the cross vectors

$$1\,1\,0\,\bar{3} \quad \text{and} \quad 2\,3\,2\,4.$$

As the third cross vector (23 0 4) is a systematic absence, the primitive quartet is also related to another quartet:

$$26\,1\,2, \quad \bar{8}\,1\,1, \quad \bar{15}\,\bar{1}\,5, \quad \bar{3}\,\bar{1}\,2.$$

But as the translational term $2\pi\mathbf{T}_S\,\mathbf{H}$ is equal to π, the contribution of the corresponding cross vector (18 2 3) must be taken negative.

The use of quartets with a cross-reflexion which is systematically absent, may be of significant importance in direct methods. In usual procedures, systematically absent reflexions are not included in the set of diffraction data. This custom is not exceptionable when only triplet relations are used but it can give rise to a loss of information when quartets are used.

The usual programs of direct methods discard quartets as soon as one of the cross vectors is not measured so that systematic absences are dealt with in the same manner as those reflexions which are outside the sphere of measurement.

Quartets with an extinct cross-reflexion are very reliable due to the increase of the number of cross terms involved with such a symmetry-invariant reflexion (Giacovazzo, 1976*b*). Furthermore, these quartets are more likely to be enantiomorph sensitive than general quartets.

Systematic absences related to non-primitive space groups cannot provide more negative quartets than those given by the corresponding primitive space groups, as it is impossible to build triplets involving only one systematically absent reflexion. For instance, in space group $C2$ as in $P2$ there are more quartets involving systematic absences as cross vectors. The cross vector $\mathbf{H}_1 + \mathbf{H}_2$ is a systematic absence if $(h_1 + h_2) + (k_1 + k_2)$ is odd. But the basis magnitudes of the quartet must be large implying that $h_1 + k_1$ and $h_2 + k_2$ should both be even. It is therefore impossible to have $(h_1 + h_2) + (k_1 + k_2)$ odd.

Table 1. *The* 15 *most reliable negative quartets in azetidin* (*structure* IV *in Table* 3)

Each of the quartets has at least one symmetry reflexion as cross vectors and, depending on more than three cross vectors, they are more reliable than other general negative quartets.

		Basis vectors				Cross vectors					
$\cos_{est.}$	$\cos_{true}$										
−0·5545	−0·99	$\bar{2}\,\bar{2}\,6$	1·64	$4\,2\,\bar{2}$	2·18	$2\,0\,4$	0·26	$\bar{19}\,\bar{5}\,3$	0·37	$13\,1\,5$	0·13
		$\bar{17}\,\bar{3}\,\bar{3}$	2·61	$15\,3\,\bar{1}$	2·56	$\bar{19}\,\bar{1}\,3$	0·50	$13\,5\,\bar{5}$	0·31		
−0·4990	0·72	$26\,1\,2$	1·89	$\bar{8}\,\bar{1}\,1$	2·12	$18\,0\,3$	0·12	$22\,6\,\bar{4}$	0·19	$12\,\bar{4}\,5$	0·10
		$\bar{4}\,5\,\bar{6}$	2·51	$\bar{14}\,\bar{5}\,3$	1·83	$22\,4\,\bar{4}$	0·28	$12\,\bar{6}\,5$	0·16		
−0·4412*	−0·88	$\bar{1}\,\bar{3}\,4$	2·15	$9\,3\,0$	1·95	$8\,0\,4$	0·28	$\bar{10}\,\bar{6}\,\bar{4}$	0·34	$0\,0\,8$	0·33
		$\bar{9}\,\bar{3}\,\bar{8}$	2·32	$1\,3\,4$	2·15	$\bar{10}\,0\,\bar{4}$	0·63	$8\,\bar{6}\,\bar{2}$	1·15	$\bar{18}\,0\,\bar{8}$	0·41
−0·3948*	−0·67	$4\,2\,2$	2·18	$\bar{2}\,\bar{2}\,\bar{2}$	1·61	$2\,0\,0$	0·30	$8\,4\,4$	0·19	$\bar{2}\,4\,0$	0·15
		$\bar{6}\,\bar{2}\,\bar{2}$	1·84	$4\,2\,2$	2·18	$8\,0\,4$	0·28				
−0·3663	−0·91	$27\,1\,5$	1·68	$\bar{7}\,\bar{1}\,1$	1·86	$20\,0\,6$	0·27	$10\,4\,2$	0·36	$24\,\bar{2}\,2$	0·11
		$\bar{17}\,3\,\bar{3}$	2·61	$\bar{3}\,\bar{3}\,\bar{3}$	1·67	$10\,2\,2$	0·35	$24\,\bar{4}\,2$	0·47		
−0·3648	−0·97	$22\,2\,7$	2·21	$\bar{8}\,\bar{2}\,0$	2·79	$14\,0\,7$	0·30	$17\,5\,2$	0·11	$13\,\bar{1}\,5$	0·13
		$\bar{5}\,3\,\bar{5}$	1·46	$\bar{9}\,\bar{3}\,\bar{2}$	1·59	$17\,1\,2$	0·71	$13\,\bar{5}\,5$	0·31		
−0·3647*	−0·47	$6\,2\,2$	1·84	$\bar{4}\,\bar{2}\,2$	2·18	$2\,0\,4$	0·26	$8\,4\,\bar{4}$	0·19	$8\,0\,\bar{4}$	0·28
		$2\,2\,\bar{6}$	1·64	$\bar{4}\,\bar{2}\,2$	2·18	$2\,\bar{4}\,4$	0·70				
−0·3508	0·98	$2\,\bar{2}\,8$	1·62	$12\,2\,0$	2·37	$14\,0\,8$	0·25	$\bar{11}\,1\,4$	0·33	$1\,\bar{5}\,4$	0·32
		$\bar{13}\,3\,\bar{4}$	1·79	$\bar{1}\,\bar{3}\,\bar{4}$	2·15	$\bar{11}\,5\,4$	0·58	$1\,\bar{1}\,4$	0·61		
−0·3493	0·93	$18\,2\,1$	1·83	$\bar{12}\,\bar{2}\,0$	2·37	$6\,0\,1$	0·19	$13\,5\,\bar{4}$	0·34	$17\,\bar{1}\,5$	0·22
		$\bar{5}\,3\,\bar{5}$	1·46	$\bar{1}\,\bar{3}\,4$	2·15	$13\,1\,\bar{4}$	0·40	$17\,\bar{5}\,5$	0·62		
−0·3488	0·82	$7\,2\,0$	2·00	$\bar{7}\,\bar{1}\,0$	1·93	$0\,1\,0$	0·01	$6\,\bar{1}\,\bar{4}$	0·35	$8\,4\,4$	0·19
		$\bar{1}\,\bar{3}\,\bar{4}$	2·15	$1\,2\,4$	1·68	$\bar{8}\,\bar{1}\,\bar{4}$	0·60	$\bar{6}\,4\,4$	0·55		
−0·3342	−0·07	$7\,2\,5$	1·49	$\bar{1}\,\bar{2}\,1$	1·78	$6\,0\,6$	0·39	$\bar{12}\,\bar{1}\,0$	0·13	$20\,5\,4$	0·36
		$\bar{19}\,\bar{3}\,\bar{5}$	2·14	$13\,3\,\bar{1}$	2·10	$\bar{12}\,\bar{5}\,0$	0·18	$20\,1\,4$	0·38		
−0·3264	−0·78	$5\,\bar{1}\,4$	1·48	$1\,1\,2$	1·78	$6\,0\,6$	0·39	$14\,2\,0$	0·17	$\bar{10}\,\bar{4}\,2$	0·36
		$9\,3\,\bar{4}$	2·34	$\bar{15}\,\bar{3}\,2$	1·88	$14\,4\,0$	0·22	$\bar{10}\,\bar{2}\,2$	0·35		
−0·3177	−0·96	$2\,\bar{1}\,3$	1·50	$8\,1\,\bar{1}$	2·12	$10\,0\,2$	0·14	$\bar{27}\,4\,0$	0·16	$21\,2\,4$	0·29
		$\bar{29}\,\bar{3}\,\bar{3}$	2·21	$19\,3\,1$	1·61	$\bar{27}\,\bar{2}\,0$	0·12	$21\,4\,4$	0·59		
−0·3174	−0·98	$3\,\bar{1}\,2$	2·34	$7\,1\,1$	1·86	$10\,0\,3$	0·34	$\bar{5}\,5\,\bar{3}$	0·08	$1\,\bar{7}\,4$	0·16
		$\bar{8}\,6\,\bar{5}$	1·58	$\bar{2}\,6\,2$	1·54	$5\,7\,3$	0·14	$1\,\bar{5}\,4$	0·32		
−0·3149	0·02	$\bar{21}\,\bar{1}\,3$	1·54	$27\,1\,\bar{2}$	1·98	$6\,0\,1$	0·19	$\bar{31}\,\bar{3}\,0$	0·16	$\bar{17}\,1\,5$	0·22
		$\bar{10}\,\bar{2}\,\bar{3}$	1·55	$4\,2\,2$	2·18	$\bar{31}\,\bar{1}\,0$	0·15	$\bar{17}\,3\,5$	0·25		

* These three quartets are actually two-phase seminvariants, the estimated phase of which would be computed by a different formula, but the estimated phases we have here from the equivalent quartet do not seem too bad.

Experimental results

As we have seen, when the symmetry is taken into account the number of cross magnitudes may be greater than three. If all of them are weak and no systematically absent reflexion occurs, the negative indication will have great reliability. For instance, in the case of azetidin (Colens, Declercq, Germain, Putzeys & Van Meersche, 1974) we computed 652 negative quartets involving the observed reflexions. 79 of them require extra cross terms because of symmetry and they include the 15 most reliable negative quartets listed in Table 1. The 15 most reliable negative quartets for which one of the cross reflexions is a systematic absence are reported in Table 2.

In Table 3 we report the average values we obtained for the negative quartets of four different structures: the first two are steroids (I and II) (unpublished) in space group $P2_1$ and $P2_12_12_1$ with a number N of non-hydrogen atoms in the unit cell equal to 40 and 80, respectively; valinomycin (Karle, 1975) is a structure in $P1$ with $N \simeq 160$ and azetidin a $Pca2_1$ structure with $N \simeq 200$. The figures given in Table 3 are the mean values of the estimated and observed cosines when the negative quartets are grouped in sets of 20 (or 50 for azetidin) terms in ascending order of the estimated cosine.

First we notice that the reliability of the negative quartets is strongly dependent on the number of atoms in the unit cell. For the four structures we used the same threshold ($E_{max} = 0.40$) for the cross vectors and a number ($5n$) of possible basis vectors related to the number (n) of atoms in the asymetric unit (as is usually done in structure determination).

For steroid I we got 230 negative quartets for which the mean value of the actual cosine invariants is quite good (−0·500).

For the other structures the quartet estimates are less accurate. We obtained: for steroid II, 180 negative quartets with a corresponding mean actual cosine equal to −0·198; for valinomycin, 310 negative quartets with a mean cosine −0·232; for azetidin, 652 negative quartets with a mean cosine −0·148.

For the last structure, belonging to a favourable space group, using the systematically absent reflexions as possible cross vectors we obtained 756 more

Table 2. *The 15 most reliable negative quartets for which at least one cross vector is a systematic absence for azetidin (structure* IV *in Table* 3)

		basis vectors				cross vectors					
$\cos_{est.}$	$\cos_{true}$										
−0·22614	−0·9167	19 1 5	1·76	$\bar{1}\,\bar{1}\,\bar{2}$	1·78	18 0 3	0·12	31 2 $\bar{3}$	0·18	$\bar{11}$ 0 10	*e*
		12 1 $\bar{8}$	1·45	$\bar{30}$ $\bar{1}$ 5	1·76	31 0 $\bar{3}$	*e*	$\bar{11}$ $\bar{2}$ 10	0·74	18 2 3	1·40(−)
−0·23091	−0·9921	29 3 3	2·21	$\bar{2}\,\bar{1}\,\bar{3}$	1·50	27 2 0	0·12	31 $\bar{2}$ 3	0·18	0 6 3	*e*
		2 $\bar{5}$ 0	1·71	$\bar{29}$ 3 0	1·61	31 2 0	1·09(−)	27 $\bar{2}$ 3	1·38(−)		
−0·23367	−0·4284	2 2 8	1·62	8 2 0	2·79	10 4 8	0·37	$\bar{5}$ 0 $\bar{1}$	*e*	$\bar{1}$ 0 9	*e*
		$\bar{7}$ $\bar{2}$ $\bar{9}$	1·96	$\bar{3}$ $\bar{2}$ 1	1·75	10 0 8	1·39(−)	$\bar{1}$ 4 9	0·52(−)	$\bar{5}$ 4 $\bar{1}$	0·54(−)
−0·23550	0·9864	8 1 1	2·12	$\bar{2}\,\bar{1}$ 0	1·52	6 0 1	0·19	29 2 $\bar{2}$	0·16	$\bar{10}$ 0 3	*e*
		21 1 $\bar{3}$	1·54	$\bar{27}$ $\bar{1}$ 2	1·98	29 0 $\bar{2}$	*e*	$\bar{19}$ $\bar{2}$ 3	0·99	6 2 1	1·39(−)
−0·24346	0·4262	12 6 6	2·43	3 $\bar{2}$ 1	1·75	15 4 7	0·36	17 0 4	*e*	$\bar{8}$ 8 1	0·19
		5 $\bar{6}$ $\bar{2}$	1·83	$\bar{20}$ 2 $\bar{5}$	1·53	$\bar{8}$ $\bar{4}$ 1	1·28(−)				
−0·24388	−0·9489	8 4 0	2·32	$\bar{3}$ $\bar{2}$ 1	1·75	5 2 1	0·18	33 0 3	*e*	$\bar{22}$ 6 $\bar{4}$	0·19
		25 $\bar{4}$ 3	1·58	$\bar{30}$ 2 $\bar{4}$	2·07	5 $\bar{6}$ 1	1·23(−)	$\bar{22}$ $\bar{2}$ $\bar{4}$	0·88(−)		
−0·24753	−1·0000	$\bar{9}$ 3 4	2·34	$\bar{3}$ $\bar{2}$ $\bar{1}$	1·75	6 1 3	0·18	25 0 8	*e*	$\bar{13}$ 5 $\bar{3}$	0·11
		16 $\bar{3}$ 4	1·53	$\bar{22}$ 2 $\bar{7}$	2·21	6 $\bar{5}$ 3	0·98(−)	$\bar{13}$ $\bar{1}$ $\bar{5}$	0·13(−)		
−0·25043	0·1080	16 3 4	1·53	12 $\bar{2}$ 0	2·37	28 1 4	0·31	$\bar{9}$ 0 1	*e*	13 5 3	0·11
		$\bar{25}$ $\bar{3}$ $\bar{3}$	2·24	$\bar{3}$ 2 $\bar{1}$	1·75	13 $\bar{1}$ 3	1·12(−)				
−0·25351	−0·6474	8 1 1	2·12	$\bar{2}\,\bar{1}$ 0	1·52	6 0 1	0·19	9 2 $\bar{1}$	0·14	1 0 2	*e*
		1 1 $\bar{2}$	1·78	$\bar{7}\,\bar{1}$ 1	1·86	9 0 $\bar{1}$	*e*	1 $\bar{2}$ 2	0·99	6 2 1	1·39(−)
−0·26378	−0·9865	14 5 4	2·74	8 $\bar{2}$ 0	2·79	22 3 4	0·38	$\bar{5}$ 0 $\bar{1}$	*e*	11 7 5	0·18
		$\bar{19}$ $\bar{5}$ $\bar{5}$	1·53	$\bar{3}$ 2 1	1·75	11 $\bar{3}$ 5	0·87(−)				
−0·26911	−0·7422	$\bar{4}$ 5 6	2·51	29 $\bar{3}$ 1	1·93	25 2 7	0·19	$\bar{25}$ 0 3	*e*	$\bar{8}$ 8 2	0·19
		$\bar{21}$ $\bar{5}$ $\bar{3}$	2·00	$\bar{4}$ 3 $\bar{4}$	1·52	$\bar{8}$ $\bar{2}$ 2	1·15(−)				
−0·27429	−0·5829	22 3 1	1·80	12 $\bar{2}$ 0	2·37	34 1 1	0·17	$\bar{3}$ 0 $\bar{2}$	*e*	13 5 3	0·11
		$\bar{25}$ $\bar{3}$ $\bar{3}$	2·24	$\bar{9}$ 2 2	1·60	13 $\bar{1}$ 3	1·12(−)				
−0·27675	0·9896	4 3 4	1·52	12 $\bar{2}$ 0	2·37	16 1 4	0·31	$\bar{13}$ 0 1	*e*	5 5 3	0·08
		$\bar{17}$ $\bar{3}$ $\bar{3}$	2·61	1 2 $\bar{1}$	1·78	16 $\bar{5}$ 4	1·33(−)	5 $\bar{1}$ 3	0·63(−)		
−0·29419	−0·6448	4 3 1	1·61	$\bar{1}\,\bar{1}$ 2	1·78	3 2 3	0·26	$\bar{23}$ 0 7	*e*	22 4 2	0·26
		$\bar{29}$ $\bar{3}$ $\bar{1}$	1·93	26 1 $\bar{2}$	1·89	3 $\bar{4}$ 3	1·28(−)	$\bar{12}$ $\bar{2}$ 5	0·35(−)		
−0·32910	−1·0000	26 1 2	1·89	$\bar{8}\,\bar{1}$ 1	2·12	18 0 3	0·12	11 2 $\bar{3}$	0·10	23 0 4	*e*
		$\bar{15}$ 1 $\bar{5}$	1·45	$\bar{3}\,\bar{1}$ 2	2·34	11 0 $\bar{3}$	*e*	23 2 4	0·95	18 2 3	1·40(−)

e is for systematic absence.

(−) indicates the cross vectors for which the translational term $\exp[i2\pi\mathbf{T}_S\mathbf{H}] = -1$.

Table 3. *Some averages of negative estimated quartets for four test structures*

Structure I
(steroid) $P2_1$, $N \simeq 40$,
230 negative quartets

estimated	observed
−0·302	−0·263
−0·340	−0·273
−0·362	−0·307
−0·396	−0·591
−0·413	−0·274
−0·461	−0·602
−0·484	−0·633
−0·506	−0·784
−0·531	−0·517
−0·560	−0·610
−0·695	−0·741
⟨cos⟩ = −0·500	

Structure II
(steroid) $P2_12_12_1$, $N \simeq 80$,
180 negative quartets

estimated	observed
−0·110	−0·102
−0·135	−0·105
−0·160	−0·109
−0·190	−0·054
−0·214	−0·438
−0·241	−0·371
−0·260	−0·271
−0·302	0
−0·338	−0·334
⟨cos⟩ = −0·198	

Structure III
(valinomycin) P_1, $N \simeq 160$,
310 negative quartets

estimated	observed
−0·061	−0·019
−0·080	0·055
−0·095	−0·222
−0·108	−0·269
−0·138	−0·054
−0·161	−0·120
−0·180	−0·484
−0·204	−0·165
−0·228	−0·347
−0·250	−0·132
−0·282	−0·309
−0·308	−0·238
−0·343	−0·112
−0·395	−0·476
−0·462	−0·625
⟨cos⟩ = −0·232	

Structure IV
(azetidin) $Pca2_1$, $N \simeq 200$

756 negative quartets with systematic absences		652 negative quartets without systematic absences	
estimated	observed	estimated	observed
−0·009	0·101		
−0·016	0·079		
−0·023	−0·141		
−0·032	−0·189		
−0·042	−0·148		
−0·054	−0·069		
−0·066	−0·035		
−0·076	−0·104		
−0·088	0·039	−0·080	0·038
−0·101	−0·159	−0·096	−0·183
		−0·107	0·013
−0·115	−0·244	−0·115	−0·068
−0·130	−0·141	−0·125	−0·128
		−0·134	−0·170
		−0·142	−0·226
−0·149	−0·097	−0·151	−0·047
−0·173	−0·160	−0·163	−0·137
		−0·178	−0·146
		−0·195	−0·148
−0·224	−0·228	−0·224	−0·347
		−0·307	−0·376
⟨cos⟩ = −0·100		⟨cos⟩ = −0·148	

negative quartets. If such quartets involve at least four observed cross vectors, the term $W = 0$ instead of $W = 1$ explains a less reliable determination (mean cosine −0·100).

In Tables 1 and 3, another aspect of the quartet estimate may be noticed. For steroids I and II and for valinomycin, we have a smaller number of negative quartets and we rank them in groups of 20 quartets. The differences between the observed and the estimated mean cosine invariant for each group are greater in these cases (mean difference 0·10) than for azetidin where we could use groups of 50 quartets (mean difference 0·06). Thus for a sufficiently large number of quartets corresponding to the same range of the estimated cosine, this value is a good estimation of the actual cosine invariant. But for the four structures within each group the mean difference between this mean estimated cosine and the actual cosine of each individual is always very high (about 0·60). In each group we have a great number of positive quartets and a great number of negative ones in such a way that the actual cosine is, on average, equal to the estimated cosine, but there is almost no quartet whose cosine is equal to the estimated value. The small list we give of the most reliable cosines for azetidin is a good example of what happens.

The strengthening of negative quartets from the second representation

The estimation of an n-phase invariant may be written as (Giacovazzo, 1977)

$$\langle \cos \varphi \rangle = G_1/N^{n/2-1} + G_2/N^{n/2} + G_3/N^{n/2+1} + \cdots,$$

where G_1 is a function which depends on the basis and cross magnitudes of the first representation of φ, G_2 is a function which depends on the basis and cross magnitudes of the second representation of φ, *etc.*

In the case of quartets the first representation, which we used in the first part of this paper, involves seven or more magnitudes (first phasing shell) according to whether one or more cross vectors are of special type. The second representation of any general quartet $\varphi_{\mathbf{H}_1} + \varphi_{\mathbf{H}_2} + \varphi_{\mathbf{H}_3} - \varphi_{\mathbf{H}_1+\mathbf{H}_2+\mathbf{H}_3}$ is the set of special sextets

$$\varphi_{\mathbf{H}_1} + \varphi_{\mathbf{H}_2} + \varphi_{\mathbf{H}_3} - \varphi_{\mathbf{H}_1+\mathbf{H}_2+\mathbf{H}_3} + \varphi_{\mathbf{K}} - \varphi_{\mathbf{K}},$$

whose phases may be estimated from 22 magnitudes (second phasing shell). Seven of these already belong to the first phasing shell. The other ones have indices

$$\mathbf{K},\ \mathbf{H}_1 \pm \mathbf{K},\qquad \mathbf{H}_2 \pm \mathbf{K},\qquad \mathbf{H}_1 + \mathbf{H}_2 + \mathbf{H}_3 \pm \mathbf{K},$$

$$\mathbf{H}_1 + \mathbf{H}_2 \pm \mathbf{K},\ \mathbf{H}_2 + \mathbf{H}_3 \pm \mathbf{K},\ \mathbf{H}_1 + \mathbf{H}_2 + \mathbf{H}_3 \pm \mathbf{K},$$

In this work, we only used a subset of the 22 magnitudes, with the following notation:

$$\begin{array}{ccccccc} \mathbf{H}_1 & \mathbf{H}_2 & \mathbf{H}_3 & \mathbf{H}_1+\mathbf{H}_2+\mathbf{H}_3 & \mathbf{K} & & \\ (\varepsilon_1) & (\varepsilon_2) & (\varepsilon_3) & (\varepsilon_7) & (\varepsilon_8) & & ; \\ \mathbf{H}_1+\mathbf{H}_2 & \mathbf{H}_1+\mathbf{H}_3 & \mathbf{H}_2+\mathbf{H}_3 & \mathbf{H}_1+\mathbf{K} & \mathbf{H}_2+\mathbf{K} & & \\ (\varepsilon_4) & (\varepsilon_5) & (\varepsilon_6) & (\varepsilon_9) & (\varepsilon_{10}) & & \\ \mathbf{H}_3-\mathbf{K} & \mathbf{H}_1+\mathbf{H}_2+\mathbf{K} & \mathbf{H}_1+\mathbf{H}_2+\mathbf{H}_3+\mathbf{K} & & & & ; \\ (\varepsilon_{11}) & (\varepsilon_{12}) & (\varepsilon_{13}) & & & & \end{array}$$

where ε_i stands for $(|E_i|^2 - 1)$.

The cosine invariant can again be expressed by a ratio of two modified Bessel functions $I_1(G)/I_0(G)$ but when using the second representation, the argument is given by (Giacovazzo, 1979)

$$G = \frac{2}{N}|E_1 E_2 E_3 E_7|\,[|E_4|^2 + |E_5|^2 + |E_6|^2 - 2 + (1/N)f]/(1 + Q/2N),$$

where

$$\begin{aligned} Q = {} & \varepsilon_1\varepsilon_2\varepsilon_4 + \varepsilon_1\varepsilon_3\varepsilon_5 + \varepsilon_1\varepsilon_6\varepsilon_7 + \varepsilon_2\varepsilon_3\varepsilon_6 + \varepsilon_2\varepsilon_5\varepsilon_7 \\ & + \varepsilon_3\varepsilon_4\varepsilon_7 + \varepsilon_1\varepsilon_8\varepsilon_9 + \varepsilon_1\varepsilon_{10}\varepsilon_{12} + \varepsilon_2\varepsilon_8\varepsilon_{10} \\ & + \varepsilon_2\varepsilon_9\varepsilon_{12} + \varepsilon_3\varepsilon_8\varepsilon_{11} + \varepsilon_3\varepsilon_{12}\varepsilon_{13} + \varepsilon_4\varepsilon_8\varepsilon_{12} \\ & + \varepsilon_5\varepsilon_9\varepsilon_{11} + \varepsilon_5\varepsilon_{10}\varepsilon_{13} + \varepsilon_6\varepsilon_9\varepsilon_{13} + \varepsilon_6\varepsilon_{10}\varepsilon_{11} \\ & + \varepsilon_7\varepsilon_8\varepsilon_{13} + \varepsilon_7\varepsilon_{11}\varepsilon_{12} \end{aligned}$$

(Q is set to 0 when this expression becomes negative) and

$$\begin{aligned} f = {} & \tfrac{1}{2}[(\varepsilon_8\varepsilon_9 + \varepsilon_{10}\varepsilon_{12})\varepsilon_1 + (\varepsilon_8\varepsilon_{10} + \varepsilon_9\varepsilon_{12})\varepsilon_2 \\ & + (\varepsilon_8\varepsilon_{11} + \varepsilon_{12}\varepsilon_{13})\varepsilon_3 + (\varepsilon_8\varepsilon_{13} + \varepsilon_{11}\varepsilon_{12})\varepsilon_7] \\ & \times (\varepsilon_4 + \varepsilon_5 + \varepsilon_6 + 1) - [(\varepsilon_8\varepsilon_9 + \varepsilon_8\varepsilon_{10})(\varepsilon_{11} + \varepsilon_{12} + \varepsilon_{13}) \\ & + (\varepsilon_{11} + \varepsilon_{13})(\varepsilon_8\varepsilon_{12} + \varepsilon_9\varepsilon_{12} + \varepsilon_{10}\varepsilon_{12})]. \end{aligned}$$

This expression is more accurate if all the magnitudes corresponding to the **K** vectors are large. In practice we used the 100 largest normalized structure factors and their symmetry-related vectors in the estimate. However, our computer program was not able to avoid duplications of contributions to f and Q (they easily occur because **K** is a free vector). This reduces the efficiency of the probabilistic approach, so that we used it only as a means to discard negative quartets which were suspected to be positive.

For the four test structures we used, the efficiency of our procedure to detect positive quartets in a set of negative ones is strongly dependent on the number of atoms N, as may be expected from the mathematical expression.

For structure I ($N = 40$), 15 quartets are discarded from the initial 230 negative quartets, with an actual mean cosine equal to 0·113 compared with the mean cosine equal to −0·500 for all 230 quartets.

For structure II ($N = 80$), 38 quartets are discarded from the initial 180 negative ones with a mean cosine equal to −0·085 instead of −0·198.

For structure III ($N = 160$), 32 quartets are discarded from the initial 310 negative ones with a mean cosine equal to −0·030 instead of −0·232.

For structure IV ($N = 200$), no tentative partition between the negative quartets gives any improvement.

The results presented here are sufficiently encouraging for us to expect that quartet estimations will be improved as soon as more accurate mathematical formulae have been derived for the second representation and more efficient computing procedures become available.

Discussion

It is well known that the use of negative quartets as figures of merit in the multisolution process instead of the usual *PSI ZERO* test is a fairly good improvement when the set of reflexions used in the phase determination are divided into unrelated subsets (*i.e.* the so-called island problem; see for instance Busetta, 1973). In that way, we may avoid troubles which are usually related to the presence of independent molecules or to the peculiar nature of the space group ($P\bar{1}$, $P2_1\ldots$). When only the island problem occurs, all the phases of the unrelated subsets of reflexion can be estimated from strong triplet relations. Between the reflexions of the different subsets there are no or only poorly estimated triplet relations. Conversely, well estimated phases of quartets involving reflexions from the different subsets can be used to solve the final problem of the phase determination.

In this paper we have shown that the negative quartets for which one or several cross vectors are symmetry-invariant reflexions are more accurately estimated than the other quartets because they depend on more than three cross-vector magnitudes. The resolution of the island problem, which is strongly related to the negative quartets, should be easier for space groups of high symmetry than for triclinic. We also showed that the use of systematic absences as possible cross vectors provides an important number of well determined negative quartets, and space groups having glide planes would give a significant number of quartets.

But if this study shows which kind of negative quartets must be preferentially used as figures of merit, nevertheless the number of well determined negative quartets remains too small to allow their successful use beside the triplet relations in the phase refinement. In particular, they cannot balance the disastrous influence of the triplet relations in the case of structures for which there is an acute enantiomorph problem and further improvement of the quartet estimations should be worthwhile in that way.

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Triplet and Quartet Relations: Their Use in Direct Procedures

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Abstract

A phase relationship involving triplet and quartet contributions is given. It is able to take account of the correlation between triplet and quartet relations. The information exploited by the formula is discussed and compared with that exploited by phase relationships arising from the properties of the Fourier transform of periodic positive functions. In particular, the information contained in a Karle–Hauptman determinant of low order is briefly considered.

1. Introduction

The properties and the use of quartet relations in direct procedures can be approached from two basic points of view: (*a*) the properties of the Fourier transform of periodic positive functions (*i.e.* the electron density function); (*b*) the application of joint probability distribution methods. We show in this paper that phase relations based on (*a*) hold only if some restrictive conditions are satisfied. On the other hand, phase relations based on (*b*) can be extensively applied in the usual procedures for phase solution. In practice, the probabilistic approach can provide phase relations more useful than those provided by (*a*).

Triplet and quartet relations can be used together in phase-determination processes. Since a quartet is the sum of two triplets, a strong correlation may exist between the sets of estimated triplets and quartets. Unfortunately, triplets and quartets have been used so far as independent relationships. In practice this assumption can lead to undesirable effects, *e.g.* to the 'squaring' effect of Σ_2 relationships the 'cubing' effect of quartet relations is added. In this paper a formula is given, involving triplet and quartet relations, which is able to take account of the correlation between the two kinds of phase relationships.

The value of Karle–Hauptman determinants of low order is mostly determined by triplet and quartet contributions. We discuss the information contained in such determinants and briefly compare it with the information exploited in our probabilistic approach.

2. Phase relations arising from the Fourier transform of $\rho^n(\mathbf{r})$

For a structure containing atoms which are fully resolved from one another the operation of raising $\rho(\mathbf{r})$ to the nth power retains the conditions of resolved atoms but changes the shape of each atom. In practice it is possible to substitute, with an accuracy quite sufficient for the purpose of structure analysis, $\rho(\mathbf{r})$ by a sum of N spherically-symmetrical atomic functions:

$$\rho(\mathbf{r}) = \sum_{j=1}^{N} \rho_j(\mathbf{r} - \mathbf{r}_j).$$

$\rho_j(\mathbf{r})$ is an atomic function and $\mathbf{r}_j$ is the coordinate of the center of the atom. When a function is periodic, its nth power is periodic with the same unit cell but with a

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