appearance of the notation but affects the orientational conventions for the planes corresponding to the positions within the symbols (Whittaker, 1985). In some cases a given position in the two members of an enantiomorphic pair refers to a different subset of the set of plane orientations defined for the relevant crystal family. These changes are not listed as they can easily be derived by inspection of the hyperstereogram and consideration of the effect of a reflection of it in the *xyz* plane.

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SHORT COMMUNICATIONS

Contributions intended for publication under this heading should be expressly so marked; they should not exceed about 1000 *words; they should be forwarded in the usual way to the appropriate Co-editor; they will be published as speedily as possible.*

Acta Cryst. (1990). A**46**, 942-944

Sign distribution of two-phase structure invariants.

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Abstract

An empirical investigation of the distribution of Friedel-pair two-phase structure invariants has been reported by Guo & Hauptman [*Chin. Sci. Bull.* (1989), **34**, 137-141]. In the present paper their sign distributions are calculated for some small molecules and for a protein. The statistical figures show that there exists a strong tendency towards positive values for the signs of the two-phase structure invariants. It is anticipated that Hauptman's formula [*Acta Cryst.* (1982), A**38**, 632-641] may be good enough to estimate statistically the signs of the two-phase structure invariants for these model crystals.

Introduction

It has been known for a long time that the presence of anomalous scatterers facilitates the solution of the phase problem of macromolecular structures. Hauptman (1982) used his neighbourhood principle for integrating the techniques of direct methods with anomalous dispersion for TPSI (the two-phase structure invariant), $\Psi_2 = \varphi_{\mathbf{H}} + \varphi_{-\mathbf{H}}$, and concluded that the conditional probability distribution of the TPSI has a unique maximum at $\Psi_2 = -\xi$. If it is statistically reasonable, the new approach of direct methods may help to solve the geometric twofold phase ambiguity of a Friedel pair for a macromolecular crystal. The concise formula is

$$\Psi_2 = \varphi_{\mathbf{H}} + \varphi_{-\mathbf{H}} \approx -\xi, \tag{1}$$

where φ is the phase of the structure factor, and ξ is defined by

$$X \cos \xi = C_{\mathbf{H}}, \qquad X \sin \xi = -S_{\mathbf{H}}, \tag{2}$$

$$C_{\mathbf{H}} = \alpha_{\mathbf{H}}^{-1} \sum_{j=1}^{N} |f_{j\mathbf{H}}|^2 \cos 2\delta_{j\mathbf{H}},$$
$$S_{\mathbf{H}} = \alpha_{\mathbf{H}}^{-1} \sum_{j=1}^{N} |f_{j\mathbf{H}}|^2 \sin 2\delta_{j\mathbf{H}}, \tag{3}$$

$$\alpha_{\mathbf{H}} = \sum_{j=1}^{N} |f_{j\mathbf{H}}|^2, \tag{4}$$

where

$$f_{j\mathbf{H}} = |f_{j\mathbf{H}}| \exp(i\delta_{j\mathbf{H}}) \tag{5}$$

is the atomic scattering factor for atom *j*. As the probabilistic TPSI is of great importance to theory, Giacovazzo (1983) later obtained a similar result and suggested its practical application (Cascarano & Giacovazzo, 1984).

Fortier, Fraser & Moore (1986) correctly pointed out that since $\delta_{j\mathbf{H}}$ is positive and generally small, both $C_{\mathbf{H}}$ and $S_{\mathbf{H}}$ are positive, and thus ξ is negative; it therefore follows that Ψ_2 as estimated by (1) has a positive value. In other words, formula (1) gives the wrong sign estimate only when the true sign of Ψ_2 is negative. The author not only agrees with Fortier *et al.*, but also decided to investigate how many wrong signs of TPSI as estimated by (1) may appear in practice and how the wrong signs are distributed with relation to the magnitudes $|E|$, and thus to go further into the question whether these wrong signs may lead to serious consequences in direct methods.

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Table 1. *The statistical distribution of negative signs for true TPSI's*

The four crystals are listed in the first line. Column 1 indicates the three wavelengths Cr $K\alpha$, Cu $K\alpha$ and Mo $K\alpha$. The serial numbers are listed in descending order of $|E|$'s. The $|E|$ ranges are given by the largest and smallest $|E|$ values in the serial number range. N_n is the number of negative signs, $\Psi_2 < 0$, whose estimates by formula (1) are wrong. These numbers are also shown in Fig. 1.

	$C_{18}H_{24}NO_4I$			$C_{18}H_{24}NO_4Br$			$C_{18}H_{24}NO_4Cl$			Native protein cytochrome c_{555}		
	Serial no.	$\|E\|$ range	N_n	$\|E\|$ range	N_n		$\|E\|$ range	N_n		Serial no.	$\|E\|$ range	N_n
Cr $K\alpha$	1-100	>1·48	0	>1·48	0		>1·52	0		1-200	>1·96	7
	101-200	1·48-1·26	0	1·48-1·27	0		1·52-1·26	1		201-400	1·96-1·76	9
	201-300	1·26-1·09	0	1·27-1·11	0		1·26-1·11	5		401-600	1·76-1·62	7
	301-400	1·09-0·99	0	1·11-0·98	0		1·11-0·96	8		601-800	1·62-1·54	16
	401-500	0·99-0·90	0	0·98-0·87	0		0·96-0·84	10		801-1000	1·54-1·46	10
	501-600	0·90-0·79	0	0·98-0·76	0		0·84-0·72	17		1001-1200	1·46-1·41	15
	601-700	0·79-0·67	0	0·76-0·65	1		0·72-0·60	20		1201-1400	1·41-1·36	16
	701-800	0·67-0·56	1	0·65-0·53	4		0·60-0·47	22		1401-1600	1·36-1·31	17
	801-900	0·56-0·38	5	0·53-0·35	7		0·47-0·33	31		1601-1800	1·31-1·27	19
	901-1000	0·38-0·10	23	0·38-0·10	24		0·33-0·11	35		1801-2000	1·27-1·23	29
	1-1000	>0·10	29	>0·10	36		>0·11	149		2001-2500	1·23-1·14	56
										2501-3000	1·14-1·06	72
Cu $K\alpha$	1-100	>1·46	0	>1·47	0		>1·53	0		3001-3500	1·06-0·99	67
	101-200	1·46-1·24	0	1·47-1·27	0		1·53-1·27	2		3501-4000	0·99-0·92	80
	201-300	1·24-1·10	0	1·47-1·11	0		1·27-1·10	4		4001-4500	0·92-0·86	81
	301-400	1·10-0·99	0	1·11-0·98	0		1·10-0·96	8		4501-5000	0·86-0·80	95
	401-500	0·99-0·89	0	0·98-0·87	0		0·96-0·84	10		5001-5500	0·80-0·74	105
	501-600	0·89-0·79	0	0·87-0·77	0		0·84-0·72	17		5501-6000	0·74-0·68	110
	601-700	0·79-0·69	0	0·77-0·65	1		0·72-0·60	19		6001-6500	0·68-0·63	117
	701-800	0·69-0·58	0	0·65-0·52	6		0·60-0·47	25		6501-7000	0·63-0·57	124
	801-900	0·58-0·40	1	0·52-0·37	5		0·47-0·32	34		7001-7500	0·57-0·51	139
	901-1000	0·40-0·10	10	0·37-0·10	27		0·32-0·10	36		7501-8000	0·51-0·45	161
	1-1000	>0·10	11	>0·10	39		>0·10	155		8001-8500	0·45-0·39	159
										8501-9000	0·39-0·32	191
Mo $K\alpha$	1-100	>1·45	0	>1·48	0		>1·53	0		9001-9500	0·32-0·23	222
	101-200	1·45-1·25	0	1·48-1·27	0		1·53-1·28	2		9501-9999	0·23-0·10	209
	201-300	1·25-1·11	0	1·27-1·11	0		1·28-1·10	4		1-9999	>0·01	2133
	301-400	1·11-0·99	0	1·11-0·98	0		1·10-0·97	10				
	401-500	0·99-0·90	0	0·98-0·87	0		0·97-0·83	12		Wavelength: Cr $K\alpha$		
	501-600	0·90-0·80	0	0·87-0·77	0		0·83-0·71	19				
	601-700	0·80-0·68	0	0·77-0·65	1		0·71-0·59	16				
	701-800	0·68-0·58	0	0·65-0·52	4		0·59-0·47	27				
	801-900	0·58-0·39	1	0·52-0·35	10		0·47-0·32	33				
	901-1000	0·39-0·11	12	0·35-0·10	27		0·32-0·10	40				
	1-1000	>0·11	13	>0·10	42		>0·10	163				

Sign distribution

An example reported by Guo & Hauptman (1989) seems to indicate that (1) is reliable for sign determination of the TPSI with large $|E|$. In this paper an empirical investigation of the sign distribution of the values of the TPSI's is made systematically by means of error-free $|E_{\mathbf{H}}|$ and $\varphi_{\mathbf{H}}$ calculated from known atomic coordinates of the structures examined.

The calculations were done for cocaine methiodide, $C_{18}H_{24}NO_4I$, published by Shen & Ruble (1975), and its isomorphous crystals, $C_{18}H_{24}NO_4Br$ and $C_{18}H_{24}NO_4Cl$, having different heavy atoms, I, Br and Cl. The space group is $P2_12_12_1$, $Z=4$, and the radiations are Cr $K\alpha$, Cu $K\alpha$ and Mo $K\alpha$. All the results based on 1000 Friedel pairs, with $|E|>0{\cdot}1$, are summarized in Table 1. Similar calculations were also done for the native protein cytochrome c_{550} crystal (Timkovich & Dickerson, 1976) and about 10 000 Friedel pairs are tabulated.

Column 1 indicates the three wavelengths, column 2 lists the serial numbers in descending order of $|E|$'s, columns 3-5 show the results for each isomorphous crystal. The entries in each row are the largest and smallest $|E|$ values in the serial number range and the number of negative signs, and the sum total of negative signs in all the 1000 pairs as well.

Strictly speaking, all kinds of atoms in the unit cell always scatter anomalously (more or less). This is taken into account by the theoretical formula (1) which involves all $\delta_{j\mathbf{H}}$, from 1 to N. In order to give an accurate computational test, all the atoms are considered as anomalous scatterers and no approximate condition is introduced into (1).

The last column in Table 1 shows the results at wavelength Cr $K\alpha$ for native protein cytochrome c_{550}, which crystallizes in $P2_12_12_1$, $Z=4$, 1017 independent non-H atoms, Fe 1, S 6, O 203, N 170 and C 637. All the results in Table 1 are also shown in Fig. 1 in which all the four positive sign-distribution curves of the TPSI's tend towards Hauptman's theoretical conclusion indicated by the dotted lines when $|E|$ values are large.

For such a complex structure with 1010 light atoms and relatively weak major anomalous scatterers, 1 Fe and 6 S atoms, the statistical figures still show the positive sign tendency of TPSI. Unexpectedly, more than 95% of the TPSI's have positive signs when $|E|>1{\cdot}5$. From the original definition of (1), the light atoms may play an important role in these results. For this reason, the calculations for native protein cytochrome c_{550} were repeated assuming that only the Fe and S atoms are anomalous scatterers (all the light atoms are treated as non-anomalously scattering atoms). The results are much worse, the negative signs are

more than 30% even for $|E| > 2{\cdot}0$. It may be concluded that even though (1) can give good sign estimates for a crystal with weak anomalous scatterers or light atoms only, the useful approximate methods, *e.g.* Harker construction, cannot be used for the solution of the phase problem, because the amplitude differences would be too small to measure accurately.

For the small structures it is seen that the sign distributions shown in Table 1 are only moderately influenced by the halogens. If the I, Br or Cl atom is replaced by F or even by H, the sign estimates for these light-atom crystals are still good; however, intensity differences of Friedel pairs may be too small to be measured accurately and no atom can be considered as a satisfactory anomalous scatterer for phasing by Harker construction.

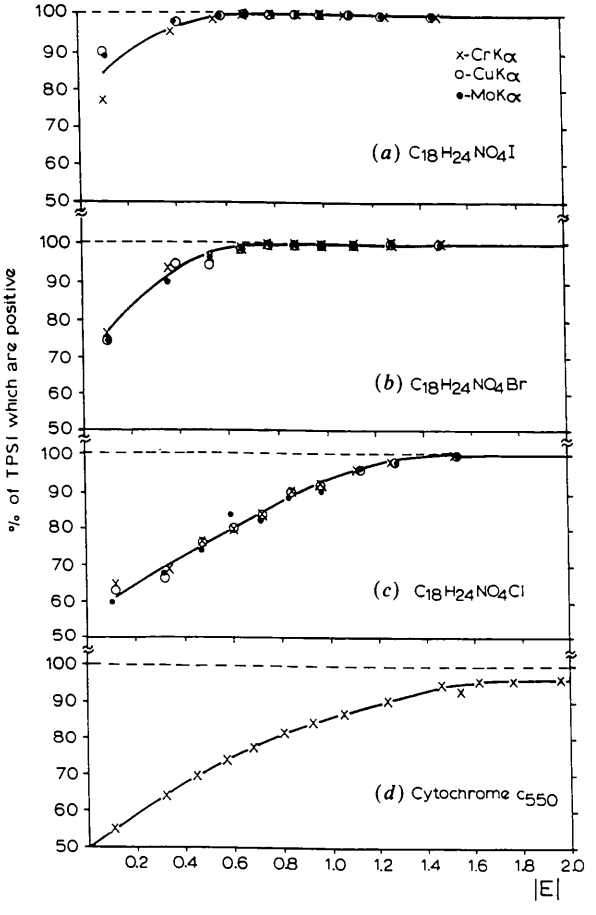

Fig. 1. Percentage of the TPSI's which are positive as a function of $|E|$.

Concluding remarks

The expectation of Hauptman's theory for estimating the TPSI signs, employing the chemical composition only, has been compared with the computational results for a series of crystals and wavelengths. The entries in Table 1 and the curves in Fig. 1 show that: (i) there exists a strong tendency towards positive signs of TPSI, and, as expected, the larger the $|E|$ values the more reliable are the sign estimates; (ii) the distributions are essentially independent of wavelength for the three small structures; (iii) the sign distributions do not strongly depend on the major anomalous scatterer I, Br, Cl *etc.* A detailed paper on the application of this procedure to protein structures is in preparation.

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Books Received

The following books have been received by the Editor. Brief and generally uncritical notices are given of works of marginal crystallographic interest; occasionally a book of fundamental interest is included under this heading because of difficulty in finding a suitable reviewer without great delay.

Acta Cryst. (1990). A**46**, 944

Biomineralisation: chemical and biochemical perspectives. Edited by S. MANN, J. WEBB and R. J. P. WILLIAMS. Pp. xiv+541. Weinheim, New York: VGH Verlag, 1988. Price DM 274.00. A review of this book, by S. K. Chapman, has been published in the August 1990 issue of *Acta Crystallographica*, Section B, pages 575-576.

A revolution in biotechnology. Edited by JEAN L. MARX. Pp. 227. Cambridge University Press, 1989. Price £25.00, US $44.50. A review of this book, by J. R. Helliwell, has been published in the August 1990 issue of *Acta Crystallographica*, Section B, page 576.