

DIRECT METHODS AND ANOMALOUS DISPERSION

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by

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1. INTRODUCTION

The electron density function, $\rho(\mathbf{r})$, in a crystal determines its diffraction pattern, i.e. both the magnitudes and phases of its x-ray diffraction maxima, and conversely. If, however, as is always the case, only magnitudes are available from the diffraction experiment, then the density function $\rho(\mathbf{r})$ cannot be recovered. If one invokes prior structural knowledge, usually that the crystal is composed of discrete atoms of known atomic numbers, then the observed magnitudes are, in general, sufficient to determine the positions of the atoms, i.e. the crystal structure.

It should be noted here that the recognition that observed diffraction data are in general sufficient to determine crystal structures uniquely was an important milestone in the development of the direct methods of crystal structure determination. The erroneous contrary view, that crystal structures could not, even in principle, be deduced from diffraction intensities, had long been held by the crystallographic community prior to c. 1950 and constituted a psychological barrier which first had to be removed before real progress could be made.

2. THE TRADITIONAL DIRECT METHODS

2.1. *The phase problem.*

Denote by $\phi_{\mathbf{H}}$ the phase of the structure factor $F_{\mathbf{H}}$:

$$F_{\mathbf{H}} = |F_{\mathbf{H}}| \exp(i\phi_{\mathbf{H}}), \quad (1)$$

where \mathbf{H} is a reciprocal lattice vector (having three integer components) which labels the corresponding diffraction maximum. Then the relationship between the structure factors $F_{\mathbf{H}}$ and the electron density function $\rho(\mathbf{r})$ is given by

$$F_{\mathbf{H}} = \int_V \rho(\mathbf{r}) \exp(2\pi i \mathbf{H} \cdot \mathbf{r}) dV \quad (2)$$

and

$$\rho(\mathbf{r}) = \frac{1}{V} \sum_{\mathbf{H}} F_{\mathbf{H}} \exp(-2\pi i \mathbf{H} \cdot \mathbf{r}) = \frac{1}{V} \sum_{\mathbf{H}} |F_{\mathbf{H}}| \exp(i(\phi_{\mathbf{H}} - 2\pi \mathbf{H} \cdot \mathbf{r})) \quad (3)$$

in which V represents the unit cell or its volume. Thus the structure factors $F_{\mathbf{H}}$ determine $\rho(\mathbf{r})$. The x-ray diffraction experiment yields only the magnitudes $|F_{\mathbf{H}}|$ of a finite number of structure factors, but the values of the phases $\Phi_{\mathbf{H}}$, which are also needed if one is to determine $\rho(\mathbf{r})$ from (3), cannot be determined experimentally. If arbitrary values for the phases $\Phi_{\mathbf{H}}$ are specified in Eq. (3), then density functions $\varrho(\mathbf{r})$ are defined which, when substituted into (2) yield structure factors $F_{\mathbf{H}}$ the magnitudes of which agree with the observed magnitudes $|F_{\mathbf{H}}|$. It follows that the diffraction experiment does not determine $\rho(\mathbf{r})$. It was this argument which led crystallographers, prior to 1950, to the erroneous conclusion that diffraction intensities could not, even in principle, determine crystal structures uniquely. What had been overlooked was the fact that the phases $\Phi_{\mathbf{H}}$ could not be arbitrarily specified if (3) is to yield density functions characteristic of real crystals.

Crystals are composed of discrete atoms. One exploits this prior structural knowledge by replacing the real crystal, with continuous electron density $\rho(\mathbf{r})$, by an ideal one, the unit cell of which consists of N discrete, non-vibrating, point atoms located at the maxima of $\rho(\mathbf{r})$. Then the structure factor $F_{\mathbf{H}}$ is replaced by the normalized structure factor $E_{\mathbf{H}}$ and (1) to (3) are replaced by

$$E_{\mathbf{H}} = |E_{\mathbf{H}}| \exp(i\Phi_{\mathbf{H}}), \quad (4)$$

$$E_{\mathbf{H}} = \frac{1}{\sigma_2^{1/2}} \sum_{j=1}^N f_j \exp(2\pi i \mathbf{H} \cdot \mathbf{r}_j), \quad (5)$$

$$\begin{aligned} \langle E_{\mathbf{H}} \exp(-2\pi i \mathbf{H} \cdot \mathbf{r}) \rangle_{\mathbf{H}} &= \frac{1}{\sigma_2^{1/2}} \left\langle \sum_{j=1}^N f_j \exp [2\pi i \mathbf{H} \cdot (\mathbf{r}_j - \mathbf{r})] \right\rangle_{\mathbf{H}} \\ &= \frac{f_j}{\sigma_2^{1/2}} \text{ if } \mathbf{r} = \mathbf{r}_j \\ &= 0 \text{ if } \mathbf{r} \neq \mathbf{r}_j \end{aligned} \quad (6)$$

where f_j is the zero-angle atomic scattering factor, \mathbf{r}_j is the position vector of the atom labelled j , and

$$\sigma_n = \sum_{j=1}^N f_j^n, \quad n = 1, 2, 3, \dots \quad (7)$$

In the x-ray diffraction case the f_j are equal to the atomic numbers Z_j and are presumed to be known. From (6) it follows that the normalized structure factors $E_{\mathbf{H}}$ determine the atomic position vectors \mathbf{r}_j , $j = 1, 2, \dots, N$, i.e. the crystal structure.

In practice a finite number of magnitudes $|E_{\mathbf{H}}|$ of normalized structure factors $E_{\mathbf{H}}$ are obtainable (at least approximately) from the observed magnitudes $|F_{\mathbf{H}}|$ while the phases $\Phi_{\mathbf{H}}$, as defined by (4) and (5), cannot be determined experimentally. Since one now requires only the $3N$ components of the N position vectors \mathbf{r}_j , rather than the much more complicated electron density

function $\varrho(\mathbf{r})$, it turns out that, in general, the known magnitudes are more than sufficient. This is most readily seen by equating the magnitudes of both sides of (5) in order to obtain a system of equations in which the only unknowns are the $3N$ components of the position vectors \mathbf{r}_j . Since the number of such equations, equal to the number of reciprocal lattice vectors \mathbf{H} for which magnitudes $|\mathbf{E}_{\mathbf{H}}|$ are available, usually greatly exceeds the number, $3N$, of unknowns, this system is redundant. Thus observed diffraction intensities usually over-determine the crystal structure, i.e. the positions of the atoms in the unit cell. In short, by merely replacing the integral of Eq. (2) by the summation of Eq. (5), i.e. taking Eq. (5) as the starting point of our investigation rather than Eq. (2), one has transformed the problem from an unsolvable one to one which is solvable, at least in principle.

In summary then, the intensities (or magnitudes $|\mathbf{E}_{\mathbf{H}}|$) of a sufficient number of x-ray diffraction maxima determine a crystal structure. The available intensities usually exceed the number of parameters needed to describe the structure. From these intensities a set of numbers $|\mathbf{E}_{\mathbf{H}}|$ can be derived, one corresponding to each intensity. However, the elucidation of the crystal structure requires also a knowledge of the complex numbers $E_{\mathbf{H}} = |\mathbf{E}_{\mathbf{H}}| \exp(i\Phi_{\mathbf{H}})$, the normalized structure factors, of which only the magnitudes $|\mathbf{E}_{\mathbf{H}}|$ can be determined from experiment. Thus a "phase" $\Phi_{\mathbf{H}}$, unobtainable from the diffraction experiment, must be assigned to each $|\mathbf{E}_{\mathbf{H}}|$, and the problem of determining the phases when only the magnitudes $|\mathbf{E}_{\mathbf{H}}|$ are known is called the "phase problem". Owing to the known atomicity of crystal structures and the redundancy of observed magnitudes $|\mathbf{E}_{\mathbf{H}}|$, the phase problem is solvable in principle.

2.2. The structure invariants

Equation (6) implies that the normalized structure factors $E_{\mathbf{H}}$ determine the crystal structure. However (5) does not imply that, conversely, the crystal structure determines the values of the normalized structure factors $E_{\mathbf{H}}$ since the position vectors \mathbf{r}_j depend not only on the structure but on the choice of origin as well. It turns out nevertheless that the magnitudes $|\mathbf{E}_{\mathbf{H}}|$ of the normalized structure factors are in fact uniquely determined by the crystal structure and are independent of the choice of origin but that the values of the phases $\Phi_{\mathbf{H}}$ depend also on the choice of origin. Although the values of the individual phases depend on the structure and the choice of origin, there exist certain linear combinations of the phases, the so-called structure invariants, whose values are determined by the structure alone and are independent of the choice of origin.

It follows readily from Eq. (5) that the linear combination of three phases

$$\psi_3 = \Phi_{\mathbf{H}} + \Phi_{\mathbf{K}} + \Phi_{\mathbf{L}} \quad (8)$$

is a structure invariant (triplet) provided that

$$\mathbf{H} + \mathbf{K} + \mathbf{L} = 0; \quad (9)$$

the linear combination of four phases

$$\psi_4 = \phi_{\mathbf{H}} + \phi_{\mathbf{K}} + \phi_{\mathbf{L}} + \phi_{\mathbf{M}} \quad (10)$$

is a structure invariant (quartet) provided that

$$\mathbf{H} + \mathbf{K} + \mathbf{L} + \mathbf{M} = 0 ; \quad (11)$$

etc.

2.3. The structure seminvariants

If a crystal possesses elements of symmetry then the origin may not be chosen arbitrarily if the simplifications permitted by the space group symmetries are to be realized. For example, if a crystal has a centre of symmetry it is natural to place the origin at such a centre while if a two-fold screw axis, but no other symmetry element is present, the origin would normally be situated on this symmetry axis. In such cases the permissible origins are greatly restricted and it is therefore plausible to assume that many linear combinations of the phases will remain unchanged in value when the origin is shifted only in the restricted ways allowed by the space group symmetries. One is thus led to the notion of the structure seminvariant, those linear combinations of the phases whose values are independent of the choice of permissible origin.

If the only symmetry element is a centre of symmetry, for example (space group $\overline{\text{P1}}$), then it turns out (again from Eq. (5)) that a single phase $\phi_{\mathbf{H}}$ is a structure seminvariant provided that the three components of the reciprocal lattice vector \mathbf{H} are even integers; the linear combination of two phases $\phi_{\mathbf{H}} + \phi_{\mathbf{K}}$ is a structure seminvariant provided that the three components of $\mathbf{H} + \mathbf{K}$ are even integers; etc.

If the only symmetry element is a two-fold rotation axis (or twofold screw axis) then one finds from Eq. (5) that the single phase $\phi_{\mathbf{hkl}}$ is a structure seminvariant provided that h and l are even integers and $k = 0$; the linear combination of two phases

$$\phi_{h_1k_1l_1} + \phi_{h_2k_2l_2}$$

is a structure seminvariant provided that $h_1 + h_2$ and $l_1 + l_2$ are even and $k_1 + k_2 = 0$; etc.

The structure invariants and seminvariants have been tabulated for all the space groups (Hauptman and Karle 1953, 1956, 1959; Karle and Hauptman 1961; Lessinger and Wondratschek 1975). In general the collection of structure invariants is a subset of the collection of structure seminvariants. If no element of symmetry is present, that is the space group is P1 , then the two classes coincide.

2.3.1. Origin and enantiomorph specification

The theory of the structure seminvariants leads in a natural way to space group dependent recipes for origin and enantiomorph (i.e. the handedness, right or left) specification.

In general the theory identifies an appropriate set of phases whose values are to be specified in order to fix the origin uniquely. For example, in space group PI (no elements of symmetry) the values of any three phases

$$\phi_{h_1k_1l_1}, \phi_{h_2k_2l_2}, \phi_{h_3k_3l_3}, \quad (12)$$

for which the determinant Δ satisfies

$$\Delta = \begin{vmatrix} h_1k_1l_1 \\ h_2k_2l_2 \\ h_3k_3l_3 \end{vmatrix} = \pm 1, \quad (13)$$

may be specified arbitrarily, thus fixing the origin uniquely. Once this is done then the value of any other phase is uniquely determined by the structure alone. For enantiomorph specification it is sufficient to specify arbitrarily the sign of any enantiomorph sensitive structure invariant, i.e. one whose value is different from 0 or π . (See Hauptman 1972, pages 28-52, for further details.)

In the space group PI one again specifies arbitrarily the value (0 or π) of three phases (12), but now the condition is that the determinant Δ [defined by (13)] be odd. Similar recipes for all the space groups are now known and are to be found in the literature cited.

2.4. *The fundamental principle of direct methods*

It is known that the values of a sufficiently extensive set of cosine seminvariants (the cosines of the structure seminvariants) lead unambiguously to the values of the individual phases (Hauptman 1972). Magnitudes $|E|$ are capable of yielding estimates of the cosine seminvariants only or, equivalently, the magnitudes of the structure seminvariants; the signs of the structure seminvariants are ambiguous because the two enantiomorphous structures permitted by the observed magnitudes $|E|$ correspond to two values of each structure seminvariant differing only in sign. However, once the enantiomorph has been selected by specifying arbitrarily the sign of a particular enantiomorph sensitive structure seminvariant (i.e. one different from 0 or π), then the magnitudes $|E|$ determine both signs and magnitudes of the structure seminvariants consistent with the chosen enantiomorph. Thus, for fixed enantiomorph, the observed magnitudes $|E|$ determine unique values for the structure seminvariants; the latter, in turn, lead to unique values of the individual phases. In short, the structure seminvariants serve to link the observed magnitudes $|E|$ with the desired phases ϕ (the fundamental principle of direct methods). It is this property of the structure seminvariants which accounts for their importance and which justifies the stress placed on them here.

By the term "direct methods" is meant that class of methods which exploits relationships among the structure factors in order to go directly from the observed magnitudes $|E|$ to the needed phases ϕ .

2.5. *The neighborhood principle*

It has long been known that, for fixed enantiomorph, the value of any structure seminvariant ψ is, in general, uniquely determined by the magnitudes $|E|$ of the

the applications; and yet (32) is severely limited because it is capable of yielding only the zero estimate for ψ_3 , and only those estimates are reliable for which A is large, the favorable cases.

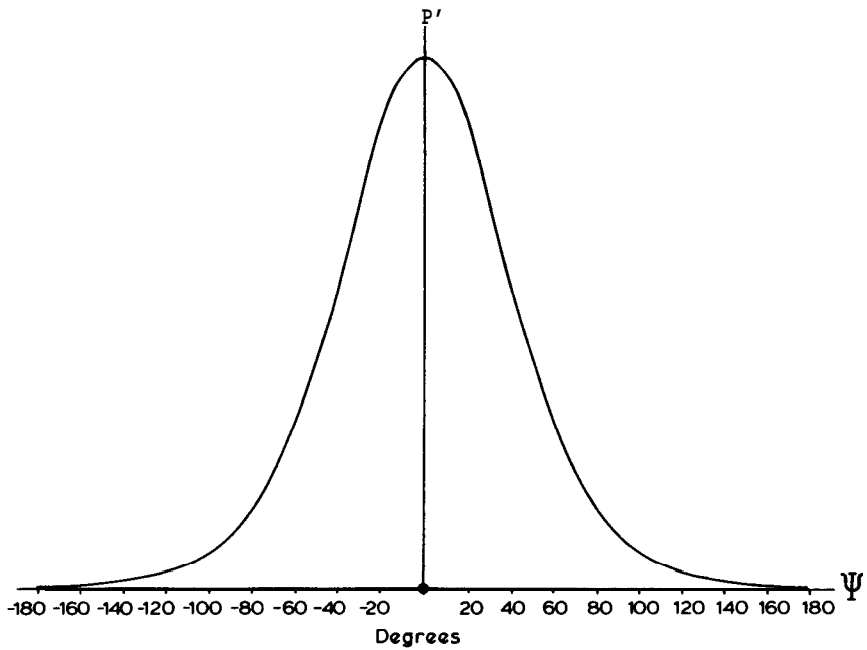


Figure 1. The distribution $P_{1/3}$, equation (30), for $A = 2.316$

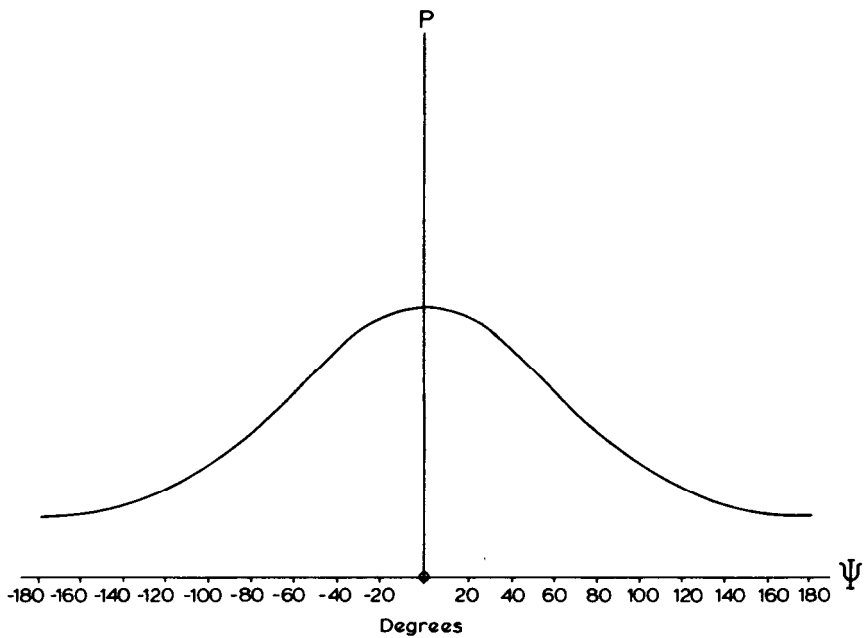


Figure 2. The distribution $P_{1/3}$, equation (30), for $A = 0.731$

Table 1. Twenty-one estimates ω_j (in degrees) of the structure invariants ψ_j sampled from the top 2,000 for the Pt Cu_4 2^- derivative of Cytochrome c_{550} .

Serial No.	$ E_H $	$ E_H $	$ E_H $	$ E_H $	$ E_H $	$ E_L $	$ E_L $	A_j	Estimated value ω_j of ψ_j	True value of ψ_j	Mag. of the Error $ \omega_j - \psi_j $
1	2.17	2.04	1.03	0.89	0.85	0.67	6.92	- 58°	- 88°	30°	
100	1.91	2.06	1.49	1.61	0.85	0.67	5.62	148	130	18	
200	1.91	2.06	2.06	1.96	1.41	1.57	4.83	- 79	- 121	42	
300	2.36	2.48	1.69	1.56	0.82	0.68	4.52	52	2	50	
400	2.17	2.04	1.48	1.34	1.28	1.15	4.31	79	96	17	
500	1.85	1.94	0.67	0.85	0.78	0.92	4.21	56	42	14	
600	2.17	2.04	1.04	0.92	0.86	0.70	4.10	146	148	2	
700	1.39	1.28	0.67	0.85	0.87	0.75	4.02	- 72	- 68	4	
800	1.41	1.57	1.49	1.61	0.71	0.85	3.93	70	50	20	
900	1.88	1.98	1.15	1.28	0.85	0.67	3.87	104	96	8	
1,000	1.29	1.43	0.71	0.79	0.85	0.67	3.80	- 88	- 138	50	
1,100	1.34	1.48	1.22	1.34	1.25	1.16	3.76	- 72	- 126	54	
1,200	1.56	1.69	1.57	1.41	0.98	0.90	3.72	73	78	5	
1,300	1.98	2.07	1.94	2.08	1.08	1.21	3.68	- 161	- 124	37	
1,400	1.56	1.67	1.57	1.41	1.24	1.33	3.63	- 72	- 3	69	
1,500	2.38	2.50	2.06	1.91	0.74	0.64	3.59	84	77	7	
1,600	1.91	2.06	1.22	1.34	0.72	0.83	3.55	- 64	- 94	30	
1,700	1.91	2.06	2.12	2.02	2.15	2.24	3.51	- 64	- 72	8	
1,800	2.38	2.50	1.49	1.61	0.78	0.90	3.46	78	82	4	
1,900	2.38	2.50	1.70	1.63	1.81	1.93	3.43	63	123	60	
2,000	0.85	0.67	0.83	0.97	1.02	1.09	3.42	- 96	- 126	30	

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