

data published for the pure metals, calibration of the X-ray camera for the measurements on the alloys was not considered necessary.

The room temperature lattice constants obtained by Hultgren & Zapffe and by Kondrashev *et al.* are compared with the values obtained in this investigation in Fig. 1. The data of this investigation are in excellent agreement with those obtained by Hultgren & Zapffe. In contrast to the observations of Kondrashev *et al.*, whose alloys were obviously not in equilibrium, the cell constants follow a smooth curve with a considerable positive deviation from Vegard's law. The molar volumes ( $V$ ) and the relative integral molar volumes ( $\Delta V^M$ , volumes of mixing), calculated from the relation

$$\Delta V^M = V - (N_{\text{Ni}}V_{\text{Ni}}^0 + N_{\text{Pd}}V_{\text{Pd}}^0),$$

where  $N_i$  and  $V_i^0$  are respectively the mole fraction and molar volume of pure component  $i$ , are also shown in Table 1. In many respects the volume of mixing presents a more realistic picture of the effects of alloying than do the cell constants, since a solution which obeys Vegard's law represents a negative deviation from the rule of mixtures in a volume sense.

In view of the recent suggestions, *e.g.* Myalikgulyev (1959) and Permanova (1961), that a superstructure exists at about 75 at.% Pd, the cell constants of the 77.7 at.% Pd alloy were determined as a function of time at 700 (7 days) and 510 °C (14 days). It was expected that if the system tended toward long-range order, the ordering reaction would be accompanied by

an increase in volume as in the similar Fe-Pd system which forms a superlattice below 800 °C (Hultgren & Zapffe, 1939). However, within the precision of the measurements, the cell dimensions remained constant at 3.868 (0) and 3.858 (4) Å respectively.

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**Solution of the phase equations representing non-crystallographic symmetry.** By MICHAEL G. ROSSMANN, *Department of Biological Sciences, Purdue University, Lafayette, Indiana, U.S.A.* and D. M. BLOW, *M.R.C. Laboratory of Molecular Biology, Hills Road, Cambridge, England*

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A set of phase relationships must be satisfied whenever the asymmetric unit contains some non-crystallographic symmetry. For instance if there are two molecules or subunits in the asymmetric unit which are related by a local twofold axis, as is the case for  $\alpha$ -chymotrypsin (Blow, Rossmann & Jeffery, 1964), there are conditions which the phase angles must fulfill if the electron density distributions of the two subunits are to be equal. The derivation of the necessary conditions has been given by Rossmann & Blow (1963) (equations (7) and (8)). These two equations may be combined to give an equation of the form

$$\sum_j A_{ij} \exp [i(\alpha_i + \alpha_j + \varphi_{ij})] = S_i \quad (1)$$

for each reflection. Here  $i$  and  $j$  identify the individual reflections, and the quantities  $A_{ij}$ ,  $S_i$  and  $\varphi_{ij}$  can be calculated from a knowledge of the structure amplitudes and the rotational and translational relationship between the two independent molecules.  $\alpha_i$  and  $\alpha_j$  are the phases of the  $i$ th and  $j$ th structure factor. In any one equation there are few terms with significantly large magnitudes  $A_{ij}$ .

Since writing the previous paper (Rossmann & Blow,

1963) we have found an alternative procedure leading towards a solution of these equations which we believe to be superior, as it considers the interdependence of each of the terms in a single equation instead of treating them independently. Also, the amount of computation involved is greatly reduced.

Let us write (1) as

$$\exp(i\alpha_i) \sum_j A_{ij} \exp [i(\alpha_j + \varphi_{ij})] = S_i \quad (2)$$

or

$$T_i \exp [i(\alpha_i + \Phi_i)] + A_{ii} \exp i(2\alpha_i + \varphi_{ii}) = S_i \quad (3)$$

where

$$T_i \exp (i\Phi_i) = \sum_{j \neq i} A_{ij} \exp [i(\alpha_j + \varphi_{ij})]. \quad (4)$$

At any stage of the refinement we have an estimate of the phase angle  $\alpha_i$  from previous results. The precision of this estimate can be expressed in terms of a figure of merit  $m_j$  (Dickerson, Kendrew & Strandberg, 1961) which varies from unity for complete certainty about the phase angle to zero when there is no phase information. We propose to replace (4) by the following expression for actual calculation:

$$T_i^c \exp(i\Phi_i^c) = \sum_{j \neq i} A_{ij} m_j \exp[i(\alpha_j^c + \varphi_{ij})]. \quad (5)$$

The right hand side of equation (4) represents a series of steps each of length  $A_{ij}$  in a direction making an angle  $(\alpha_j + \varphi_{ij})$  with the real axis on an Argand diagram. In summation (5) each step has been shortened by a factor  $m_j$ . Because  $\alpha_j$  is not accurately known, a probability distribution exists for  $\exp(i\alpha_j)$ .  $m_j \exp(i\alpha_j^c)$  is the centroid of this distribution. Similarly, the summation (5) represents the centroid of the probability distribution for  $T_i \exp(\alpha_i + \Phi_i)$ .

The values  $T_i^c$  and  $\Phi_i^c$  calculated from (5) may now be substituted back in (3) in place of  $T_i$  and  $\Phi_i$ . Because of the error which we know exists, we do not seek an explicit value of  $\alpha_i$ , but determine how closely (3) is satisfied as a function of  $\alpha_i$ . The 'lack of closure' error (Fig. 1)

$$\varepsilon(\alpha) = |(T_i^c \exp[i(\alpha_i + \Phi_i^c)] + A_{ii} \exp[i(2\alpha_i + \varphi_{ii})] - S_i)| \quad (6)$$

may be compared with an expected root mean square error  $E$ .

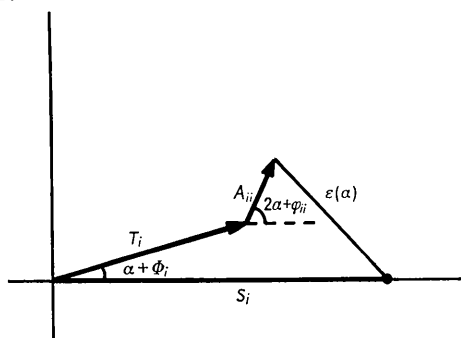


Fig. 1. Any one equation can be represented by the sum of two vectors,  $T_i^c$  and  $A_{ii}$  rotating at a speed of  $\alpha$  and  $2\alpha$  respectively. The distance  $\varepsilon(\alpha)$  between the end of the sum of three vectors and the point  $S_i$  on the real axis represents the lack of closure of that equation for any angle  $\alpha$ .

By assuming a normal distribution of error, we may now set up a probability function for the phase angle  $\alpha_i$ :

$$P_i(\alpha) = \exp[-\varepsilon^2(\alpha)/2E^2]. \quad (7)$$

To form an estimate of  $E$  we have to recognize, first, that the quantities  $A_{ij}$ ,  $\varphi_{ij}$ ,  $S_i$  which are assumed known, will contain errors due to inaccuracy in measured  $F$ 's, errors in the rotational and translational parameters, and errors in choosing an envelope for each independent subunit. The mean square contribution to  $\varepsilon$  of all these errors may be taken as some constant,  $e^2$ . A much more significant source of error is that whenever  $\exp(i\alpha_j)$  occurs in (2), we employ the approximation  $m_j \exp(i\alpha_j^c)$ . It may be shown that  $\langle (\exp i\alpha_j - m_j \exp i\alpha_j^c)^2 \rangle = 1 - m_j^2$  (see Dickerson, Kendrew & Strandberg, 1961), where the symbol  $\langle \rangle$  represents the averaging with appropriate weights over all the possibilities. Although the distribution of error for a single term will have a marked dependence on phase angle, it seems a sufficient approximation to use the sum of the squares of the magnitudes of the errors as a measure of the mean square error in the summation (5) thus:

$$E^2 = e^2 + \sum_{j \neq i} A_{ij}^2 (1 - m_j^2). \quad (8)$$

The probabilities defined by (7) can now be calculated by using (6) and (8). They may then be used to find a new phase angle and figure of merit in just the same way that this is done for the isomorphous replacement technique (Blow & Crick, 1959; Dickerson, Kendrew & Strandberg, 1961)

$$m_i \exp(i\alpha_i^c) = \frac{\int_0^{2\pi} P(\alpha) \exp(i\alpha) d\alpha}{\int_0^{2\pi} P(\alpha) d\alpha}. \quad (9)$$

When new values have been calculated for all the values of  $m_i$ ,  $\alpha_i$  by (9), a further round of refinement may be begun.

It is evident that this type of procedure will cause (1) to be better satisfied when some critical estimates of the  $\alpha_i$  exist. If the procedure is commenced with no phase information except that  $\alpha_0$ , the phase of the  $F(000)$  term, is zero, so that  $m_0 = 1$ , and all other  $m_i$  are zero, then the early stages of the procedure run closely parallel to the method described previously (Rossmann & Blow, 1963). However, the interdependence of significant terms is considered from the beginning. The method can also be used when phase information is available which would not in itself be sufficient to allow the structure to be solved, such as that obtained from a single isomorphous pair of non-centrosymmetric crystal structures. In such a case one might expect that the bimodal phase probability curves obtained from the single isomorphous replacement method would become unimodal as refinement proceeds, selecting one of the two alternative phase angles as correct.

If the arrangement of subunit centres is centrosymmetric, the necessary conditions expressed by (1) will be equally well fulfilled by the enantiomorph as by the true structure. Once, however, any one phase has been selected in favor of one enantiomorph, the solutions of the remaining phases must then all satisfy this enantiomorph. However, this last condition is difficult to achieve in practice, for no phase is known with certainty, and less still do we know in advance which phase will unequivocally distinguish between the two enantiomorphs. Thus, unless some other information is available, as for instance X-ray data for the same subunit from another crystal form, we may find our solution to be a combination of the two enantiomorph forms.

The approach described in this paper was developed while we were both on the staff of the Medical Research Council Laboratory of Molecular Biology, Hills Rd., Cambridge, England, and was tested by using computational facilities provided by the Medical Research Council.

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