

For the remaining 377 reflexions, or 60 per cent of the data, the choice of phase angle rested between two ambiguous values. It is to this last class of reflexions that we have applied the phase angles which were derived from the positions of the heavy atoms and were therefore intermediate between the ambiguous values.

In spite of these approximations in the phase angles, the plot of this Fourier contained interesting features which appear to have some significance. The $Ta_6Cl_{12}^{++}$ ion was roughly spherical, and the contours throughout the remaining portions of the plot showed continuous regions of high density which suggested portions of a polypeptide chain, possibly in the α -helix configuration.

The second three-dimensional Fourier was calculated in an attempt to reduce the effects of the errors in phase angles present in the first Fourier. In this calculation the values of $A_0(LTa)$ and $B_0(LTa)$ were weighted with a factor $\cos^3 \varphi$ in which φ is the difference between the phase angle of the heavy-ion contribution and the ambiguous phase angles of the total lysozyme- $Ta_6Cl_{12}^{++}$ complex. From the terms $A_c(Ta-Nb)$, $B_c(Ta-Nb)$, and $|\Delta F_c|$ defined here, and the observational results from the two types of crystals, $|F_0(LTa)|$ and $|F_0(LNb)|$, the ambiguous phase angles of the reflexions from LTa and LNb crystals were calculated; from these the values of φ and $\cos^3 \varphi$ were computed. The effect of this weighting factor, $\cos^3 \varphi$, is to compensate in some degree for the errors inherent in the first Fourier by giving relatively high weight to those reflexions for which the true phase angle differs little from the assumed phase angle and causing the weight to fall off rapidly as this difference increases.

In the calculation of both Fourier syntheses the F_{000} terms were omitted, and in the plots the contours were drawn at equal but arbitrary intervals. The plot of the weighted Fourier (Fig. 1) is conspicuously clearer than that of the unweighted one. The $Ta_6Cl_{12}^{++}$ ion is very close to spherical, although slightly flattened in the direction of the c axis. The continuous regions of high density in other portions of the plot are also better defined, and more suggestive of coiling or folding of polypeptide chains than are those in the unweighted plot. A photograph of a portion ($z = 0$ to $1/2$) of the plot of the weighted three-dimensional Fourier is shown in Fig. 1. The positions of the complex ions are clearly shown as spherical groups of contours near the four-fold screw axes at the bottom and left side of the figure.

Fig. 2 is a photograph of a 'Styrofoam' model of the regions of relatively high density in one asymmetric unit selected with a view to represent the volume perhaps occupied by a single molecule of lysozyme. The position of the $Ta_6Cl_{12}^{++}$ ion is shown by the dark sphere, Ta, near the top of the figure. Although the presence of continuous regions of high electron density is strongly suggestive of a polypeptide chain in a folded configuration, the analysis must be carried much further before this interpretation can be considered to be established.

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A 6 Å Model of Triclinic Lysozyme

WE have recently calculated in this laboratory a three-dimensional structure of triclinic lysozyme nitrate to a resolution of 6 Å, using three isomorphous heavy atom derivatives: HgI_4^- , $HgBr_4^-$ and $PtCl_6^-$. The space group is $P1$ with one molecule per unit cell, and there were found to be five, six and six heavy atom occupancy sites per molecule respectively for this crystal form. The mean figure of merit from the centroid phase determination is 0.85, and the mean lack-of-closure error of the phase triangles or 'R factor' as defined by Kraut¹ is 6-7 per cent for each derivative.

This is the first time that the multiple isomorphous replacement method has been tried with structures having no centrosymmetric projections and with multiple-site derivatives of this nature. Two questions of fundamental importance have been raised about such an analysis: (a) To what extent can one be sure of obtaining the correct heavy atom positions from three-dimensional $(\Delta F)^2$ -type approximate Patterson functions in the absence of centrosymmetric projections to serve as a check?

(b) With the large number of sites per molecule and hence with a large number of parametric degrees of freedom, can one exclude the possibility of falling into a false structure which would still produce reasonable phase circles and a high figure of merit? As part of a programme to test these points, work is now in progress which will lead to a redetermination of the structure using the most favourable new derivatives selected from a screening of about two dozen. It is hoped that this work will resolve questions concerning both the structure and the validity of the methods used.

A complete account of this structure will be presented at a later date.

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