

## 04-Crystallography of Biological Small Molecules

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Statistical methods for determining structure factor phases have now been developed to the stage where they represent the first line of attack in the elucidation of crystal structures. Multi-solution and maximum entropy techniques have increased the power of statistical methods to the point where they provide crystal structure information semi-automatically for most 'small molecule' crystals. One factor is common to the residual structures that are more difficult to determine. The overwhelming majority of those cases have structure factor distributions differing significantly from those of random structures. That complicated the structure analysis. For example determining the basic motif in a superstructure is often quite straightforward – but deviations from the motif symmetry can be very difficult to elucidate. Symmetry, both real and approximate, and small deviations can help or hinder the elucidation of crystal structures. Such information is already utilized in many aspects of structure determination, but there may be scope for further improvement. Aspects of symmetry which could help to resolve the remaining difficulties in elucidating crystal structures will be described.

## OCM-04.03.05 THE ROLE OF THE MODEL IN X-RAY REFINEMENT

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The electron density distribution in the crystal and the diffraction pattern seem to be only a Fourier transformation apart. Since the phase problem stands no longer in the way of successful structure elucidation, there seems to be no obstacle in the process in which diffraction information is transformed into structure information. The simplest way to represent this information is to give the electron density distribution (EDD) at the  $n \times n \times n$  points of a three dimensional grid.

When the electron density distribution is obtained by straightforward Fourier summation, the many weak high order reflections seem to add more to the variance than to the distribution and the information does not increase. The series termination error adds to the problems.

The introduction of models improves the situation: every additional reflection, no matter how weak, increases the reliability of the parameters of the model. For many decades simple models sufficed, but the increase in experimental accuracy allows the use of models that have the flexibility that is required to reflect the subtle effects of chemical bonding. It should be remembered, however, that a refinement model with its large, but finite number of parameters,  $np$ , derives its use from the fact that it reduces the number of variables from  $n^3$  to  $np$ . In principle this reduction of flexibility will always be accompanied by the introduction of systematic errors, but a careful choice of model will limit these systematic errors to negligible quantities. No series termination error occurs.

Until recently the multipole refinement models were assumed to be flexible enough to introduce no errors and to contain parameters

that allow accurate representation of the various features of chemical bonding. Unfortunately this did not turn out to be true as was shown recently by Bruning (1992) for ionic charges in molecular crystals. It will be shown that a bias is introduced in the radial dependence of the atomic electron density functions with serious consequences.

In the Maximum Entropy method we have a method that yields an EDD that deviates as little from a flat distribution as is necessary to satisfy the observed structure factors. Instead of a flat distribution one can use e.g. molecules consisting spherical atoms as reference distribution. No bias is introduced and good results have been obtained in particular with respect to series termination. (Sakata & Sato (1990)). When the experimental data are not very accurate, the existing methods yield results that are not good enough for charge density studies.

The method will be illustrated by the analysis of the the bonding density in an hypothetical crystal of water dimers where calculated structure factors augmented with noise were used. It will be shown that the additional constraint of a proper  $\chi^2$  distribution is essential to obtain satisfactory results (de Vries (1993)).

Bruning, H. & Feil, D. (1992) Acta Cryst. A48, 865

Sakata, M. & Sato, M. (1990) Acta Cryst. A46, 263

Vries, R.Y. de, Briels, W.J. & Feil, D. see poster.

## OPS-04.03.06 ORIENTED INDEPENDENT ATOMS FROM X-RAY DIFFRACTION DATA. INTRA- AND INTERMOLECULAR BONDING IN ORGANIC CRYSTALS. J.E.Niu\*, L.L.Miller and W.H.E.Schwarz. Theoretical Chemistry, University of Siegen, Germany and Ames Laboratory, Iowa, USA

Electron densities in crystals are conventionally displayed in the form of deformation densities with respect to the superposition of densities of independent atoms. Independent noninteracting atoms are first to be specified by their internal state. In the case of (quasi-)degenerate ground states (i.e. open valence shells), the specification of the electron density of an independent atom comprises the *population* and *orientation* of the degenerate components of angular momentum  $l \geq 1$  (and also of their *shapes* in the case of  $l \geq 2$ ), in addition to their *vibrational ellipsoids* around their average *coordinates*. Conventionally only the latter 2 types of parameters are determined, while statistical averages of the former 2 ones are chosen. As a result, the low order reflections cause larger contributions to the R-factor than necessary for an independent atom model. Furthermore the deformation density may be significantly overlaid by the genuine multipoles of the atomic ground states.

Therefore an advanced least squares program has been developed, which refines the conventional atomic "core" parameters (coordinates, vibrations), and in addition the "valence shell" parameters (populations, orientations, shapes). It has been applied to a series of molecular crystals. The resulting genuine deformation density maps are no longer overlaid by the atomic quadrupoles, which are especially big for N, O, F and Cl atoms. The atomic orbital populations and directions as well as the genuine deformation maps are interpreted with respect to intra- and inter-molecular interactions.