

04-Crystallography of Biological Small Molecules

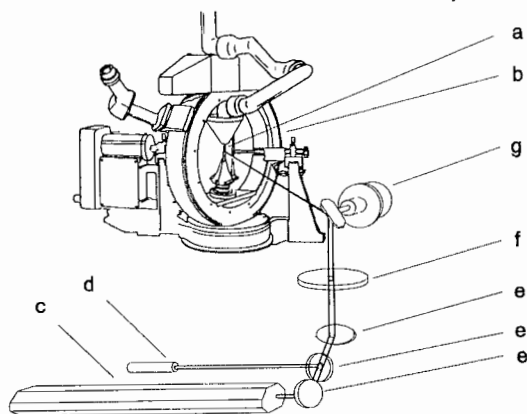


Fig. 1 *in situ*-crystallization device with IR laser: a) capillary b) Eulean cradle c) IR laser d) pilot (visible) laser e) mirror f) lens g) turnable (controlled) mirror

OCM-04.03.02 SINGLE CRYSTAL DATA WITH SYNCHROTRON RADIATION - WHAT CAN IT OFFER ?
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Synchrotron radiation has very high intensity, a continuous range of wavelengths, and very low beam divergence. These can be used with advantage for the study of microcrystals, for time resolved studies, and for a variety of other purposes.

For microcrystals, the practical problems to be faced include the quality of the small crystals (often poor), crystal mounting, radiation damage, and then distinguishing the diffraction peaks from background. The smallest crystal for which we have successfully recorded data with monochromatic synchrotron radiation and determined the structure was $10 \times 10 \times 30 \mu\text{m}$, containing a gold cluster of previously unknown constitution, and shown to be $\text{Au}_{10}(\text{PPh}_3)_7(\text{S}_2\text{C}_2(\text{CN})_2)_2$ (Cheetham, Harding, Haggitt, and Mingos, 1993, *J. Chem. Soc. Chem. Commun.* in the press). The structure of an aluminophosphate, $\text{Al}_3\text{P}_3\text{O}_{12}\text{F} \cdot \text{C}_4\text{H}_{10}\text{NO}$, was similarly determined from a crystal of dimensions $35 \times 20 \times 15 \mu\text{m}$, and in this case comparison could be made with the results of powder diffraction (Harding, Kariuki, McCusker and Simmen, 1993, in preparation for Zeolites).

White beam methods (Laue) now allow unit cell determination (Dodd, Carr and Harding, 1993, *J. Appl. Cryst.* 25, in the press) as well as intensity measurement (Helliwell et al, 1989, *J. Appl. Cryst.* B22, 483-497). Exposure times can be less than 0.1 s for normal sized crystals, and 1-5 min for very small ones; to record all the unique data, 1-10 film packs or image plates, may be required, according to the crystal symmetry.

The constitution and structure of a new organometallic complex, $\text{AuOs}_3(\text{CO})_8\text{PPh}_3\text{dppm} \cdot \text{PF}_6$, were determined from six Laue film packs - one for the unit cell and five for the intensity measurements - and structure refinement gave $R=0.075$ for 7163 unique reflections. In crystalline $\text{P}_4\text{N}_4\text{Cl}_8$ the molecule changes from a boat to a chair conformation at ca 65°C , and the crystal symmetry changes. In a preliminary time-resolved study film packs were exposed at 3 min intervals as single crystals were heated (Carr, Cheetham, Harding and Rule, 1992, *Phase Transitions*, 39, 33-43); from each film pack

200-300 reflections have been measured and used to follow the course of the change.

OCM-04.03.03 THE BACKGROUND: A NON-EVENT IN SINGLE CRYSTAL DIFFRACTOMETRY by A.T.H. Lenstra*, S. Maes & C. Van Hulle, Dept. of Chemistry, Antwerp University (UIA), Universiteitsplein 1, 2610 Wilrijk, Belgium

A net intensity I is routinely obtained by subtracting the local background $B(hkl)$ from the raw intensity $R(hkl)$:

$$I = R - B \quad (1)$$

Since the observations B and R are taken as independent, the corresponding variance is:

$$\sigma^2(I) = \sigma^2(R) + \sigma^2(B) \quad (2)$$

This classical interpretation is correct when one deals with a single observation. However, it is a very poor way to deal with the data in a single crystal analysis. Here one deals with a large set of observations, which in a hidden way includes valuable experience, notably on the background.

Let us only summarize the essential features of the observed background intensities. Within a not too large $\sin\theta/\lambda$ -interval all observed $B(hkl)$ values can be contracted into a normal distribution $N(\langle B \rangle, s^2(B))$, where $\langle B \rangle$ is the averaged background and $s^2(B)$ is the observed spread. In a standard data set one finds $\langle B \rangle s^2(B)$, which connects $B(hkl)$'s to a counting statistical distribution.

The calculated background averages in different $\sin\theta/\lambda$ -intervals appear to be interrelated by:

$$b = B(\text{ref}) \times C \quad (3)$$

where C is a theta dependent correction factor and $B(\text{ref})$ is a reference value characteristic for the whole data set. The correction C includes three component parts, viz:

i) $C_1 = f^2(O) + (Z - f^2(O))/Z$ where $f(O)$ is the scattering factor for oxygen at the diffractometer angle θ , $F^2(O)$ and $(Z - f^2(O))/Z$ are the elastic Raileigh and the inelastic Compton scattering produced by the crystal and its amorphous support.

ii) $C_2 = \cos^2 2\theta_m + \cos^2 2\theta_o$, which is the polarisation of C_1 .

iii) $C_3 = (p + q \tan^2 \theta)(r + s \tan^2 \theta)$, which connects b to the scan angle and the aperture applied during the data collection.

With $C = C_1 \times C_2 \times C_3$ it is evident that $B(\text{ref})$ is easily calculated using all available background counts in the data set. This suffices to show that the value of $B(\text{ref})$ is virtually error free. At the reciprocal lattice point (hkl) we observed a raw intensity R . Its variance is equal to R . Using (3) the local background b is given by $C \times B(\text{ref})$. Now b is an nearly error free estimate of the Bragg intensity of the crystal. An actual observation would reveal a counting statistical variance b .

When we now combine R and b as observation related to (hkl) , we get

$$I = R - b \quad \text{and} \quad \sigma^2(I) = R - b \quad (4)$$

So the background model reduces the variance of I from $I + 2B$ to I . This lowers the detection limit of your diffractometer by a factor 10 without any increase in the applied measuring time. One could even save time by skipping almost all background observations without losing accuracy.

OCM-04.03.04 WHEN AUTOMATIC STRUCTURE SOLUTION FAILS. By E.N. Maslen*, Crystallography Centre, University of Western Australia, Nedlands, Western Australia 6009

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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 χ^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.