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Density modification for macromolecular and small molecule phasing. George M. Sheldrick[a]. [a]*Lehrstuhl für Strukturchemie, Georg-August-Universität, Göttingen, Germany.*
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Experimental phasing of macromolecules almost always requires a step known as ***density modification*** [1-4], in which the electron density is modified iteratively so that it looks more like that expected for a macromolecule, before an interpretable map can be obtained. The quality of the resulting map depends on the quality of the initial phases, the resolution of the native data and the solvent content. Modern direct methods of solving small molecule structures also often involve a density modification step, but with the important differences that the initial phases may be random and that the data are expanded to the space group P1 and the true space group is determined after solving the ***phase problem*** [5-8]. A particularly effective form of density modification is simply to set negative density to zero [9] but the radius of convergence can be increased by using additional criteria for modifying the density [2-4,10,11] and by perturbing the density in some way, e.g. by ***charge flipping*** [12-14]. However care is needed when this approach is applied to the solution of small molecule structures because both the extension to space group P1 and the perturbation of the density can degrade the quality of the electron density maps, especially when the experimental data do not extend to high resolution. This talk will discuss a new implementation of ***random omit maps*** [8], a robust alternative to charge flipping for solving small molecule structures, and the incorporation of chemical information with the help of the ***sphere of influence algorithm*** [10] and ***iterative chain tracing*** [15] in the experimental phasing of macromolecular structures. It is to be expected that some of the density modification algorithms that have proved useful for phasing macromolecules will also assist the solution of small molecule structures and *vice versa*.

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Keywords: density modification, direct methods, SAD phasing

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XPRESSO: Automation in Routine Crystallography. Holger Ott[a], Joerg Kaercher[b]. [a]*Bruker AXS GmbH, Karlsruhe, Germany.* [b]*Bruker AXS Inc, Madison, WI, USA.*
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Single crystal X-ray diffraction (SC-XRD) has become a routine tool for structure validation in analytical chemistry. Due to tremendous improvements in available hardware, smaller and more weakly diffracting crystals can now be measured. In consequence, the workload of staff crystallographers has increased significantly. At the same time software tools became available for processing data files more easily, e.g. for structure solution, structure refinement and absorption correction. In particular on routine data sets these tools allow for quick processing of the entire data set based on reasonable defaults and some clever decisions of an experienced user. In many cases only little crystallographic knowledge is required for successful processing. However, the routine work delays investigation of crystallographically more challenging samples and problems in a number of cases.

To alleviate experienced crystallographers from day-to-day routine work an automated software interface (XPRESSO) is available as part of the APEX2 software. This software builds a layer on top of established programs, such as SAINT, SADABS and the SHELXTL suite, which makes a number of crystallographic decisions to attempt for a successful structure solution, refinement and validation.

XPRESSO (Figure 1) also provides an entirely automated process from an initial quality check to the fully refined structure for processing previously collected data. A general description of the program flow and a number of examples will be presented.

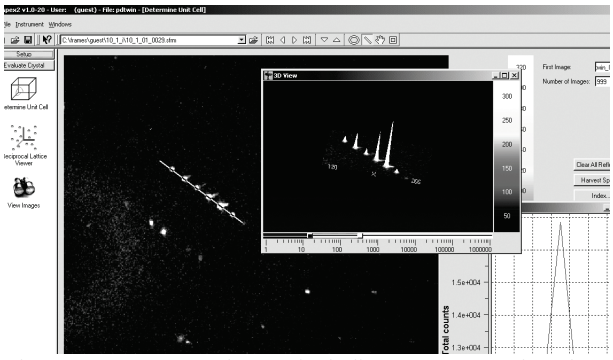

Figure 1: APEX2 software including XPRESSO interface, facilitating routine crystallography

Keywords: automation in chemistry, crystallographic software development, service crystallography

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Technologies for structural determination and validation using the CSD. Tracy Allgood, Ian Bruno *Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, UK*
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The inclusion of the half-millionth structure into the Cambridge Structural Database highlights the rate of growth of the CSD in recent years, the growing body of structural knowledge this provides, and the challenges this amount of information represents in terms of validation and maintenance. This talk will describe the processing and validation of X-ray crystal structures at the CCDC and the development of tools to enhance this process. These tools include assigning chemistry to crystal structure data, indicating reliability of assignments, and the use of the existing database to enhance future processing. Further developments that will aid this growing body of structural knowledge to be exploited in a range of external applications and the provision of additional services that can assist the scientific community will also be illustrated.

Keywords: Cambridge Structural Database, validation

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CATS & G-ROB: 6-AXIS robotic-arm-based AUTOMATED systemS for crystallography.

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CATS and G-Rob systems were developed on protein crystallography beamline FIP-BM30A at the ESRF. CATS [1] is a sample changer currently now installed on various synchrotrons (SLS, BESSY, DLS, APS, ...). G-Rob, also a 6-axis robotic arm based system, is a fully integrated device for crystallography beamlines and laboratories. G-Rob is an "all in one" system, since it integrates the following functions:

- sample changer,
- goniometer for frozen samples, capillaries, … [2],
- crystallization plates/micro-chips screening for *in situ* analysis of diffraction condition and data
- collection [3],
- goniometer for non-classical sample environments (high pressure cells, …),
- beam monitoring.

G-Rob provides unique features. It is automated: thanks to its tool changer, it goes automatically from one application to another. CATS and G-Rob are also highly flexible: if a new application or a new sample format emerges in the community, a new tool can be designed to implement it. They are highly reliable systems, based on well-known, industrial quality equipments, with reduced maintenance.
They are currently in use on beamline FIP-BM30A. It was made available to the research community in 2005 and up to now, users have expressed an unprecedented high degree of satisfaction. The crystallization plates screening capability for example appears to be a precious tool in several cases (crystals too small to be fished, or too fragile, of when there is no good cryoprotectant).
Several results obtained on FIP-BM30A are presented, such as *in situ* screening of membrane proteins, ribosome, high pressure protein diffraction, etc. Recent experiments demonstrated also the possibility of the automated structural screening for the Fragment Based Drug Design strategy: the same crystal was reproduced in presence of a library of fragments. Systematic *in situ* data collection has shown some of the fragments present in the active site, without having to manipulate the crystals individually. Movies are available on www.natx-ray.com.

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Keywords: robot goniometer, X-ray screening automation

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What can the Bruker SMART X2S do for me?

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The Bruker Smart X2S is a completely automated instrument designed for routine chemical crystallography for the non-specialist, encompassing all stages of data collection, structure solution and refinement.
Advances in automation can lead to greater awareness and uptake of a technique, although this can come at a cost, namely, reduction in the practical knowledge and understanding of the underlying scientific theory, as well as in the awareness of the difficulties and limitations of the technique in question. Indeed, a major criticism of such advances is that they often lead to a "black box" philosophy, characterized by a non-critical appraisal and over reliance on the results obtained.
In this presentation we wish to discuss our experiences with the Bruker SMART X2S, by presenting data for a representative range of samples in inorganic, organic and pharmaceutical chemistry, highlighting its successes and challenges.

Keywords: chemical crystallography, automation