

a crystal of lower quality can be accepted if only a connectivity structure is needed but the requirements are more strict when a fully publishable result is required. The number of parameters considered in determining “rank” can be large. Algorithms may include the following parameters: resolution limits, $I/\sigma(I)$, spot sharpness, indexing quality, refinement quality, mosaicity, ice-ring detection, and others. The success of the experiment can be bolstered by the amount of information provided to the system, but a truly automatic system should be able to provide the necessary results with little or no human intervention. The ability to screen large numbers of crystals also allows tests for polymorphism, autoresolution of enantiomers, phase transformations, etc.

Keywords: robotics, automation algorithms, ranking

MS.10.3

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True walk-away automation in chemical crystallography

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The recent trend in the analytical instruments market towards compact benchtop systems spawned the development of fully automated low-cost X-ray diffractometers. This was made possible in part through advances in the analytical software, specifically new and improved algorithms and decision making expert systems. This paper presents an overview of the decision tree implemented in one such system and the individual steps involved in producing publication quality structures from single-crystals without user intervention. The design of the fully automated system is targeted primarily towards users who are not expert crystallographers. In addition to all decisions being made autonomously, this means keeping the user informed about the progression of the experiment in an easily comprehensible way. Equally important is to suggest remedies in case a problem is encountered that cannot be tackled in software, such as a poorly centered crystal, radiation induced crystal decay, or a temperature induced phase transition. The expert system proceeds through the following stages: quantify the crystal quality, determine the unit cell and the crystal symmetry, select a data collection strategy, acquire and reduce the diffraction data, scale the diffraction data, determine the space group, solve the phase problem, refine and validate the molecular structure, and finally generate a report. The results are provided as a Crystallographic Information File (CIF) and as a Hypertext Markup Language (HTML) report.

Keywords: automation, chemical crystallography, software

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Rapid synchrotron X-ray crystallography for drug discovery using the SGX-CAT beamline at the APS

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SGX Pharmaceuticals, Inc., a San Diego-based oncology drug

discovery company, designed, built, and operates a protein crystallography beamline (SGX-CAT) at the Advanced Photon Source (APS). This insertion device beamline operates exclusively as a mail-in facility, providing high-throughput X-ray crystallographic data collection for SGX, its corporate partners, and APS General Users. Screening of crystal quality and diffraction data collection at SGX-CAT utilize a series of automated processes, including crystal screening and data collection, sample loop visualization/centering, removal of surface ice from the sample, crystal quality scoring, and diffraction data processing/reduction. For most samples, crystal quality is evaluated and diffraction data are recorded without human intervention. All operations are tracked using a custom database, which links beamline operations to those elsewhere in the company and provides real-time access to information from the beamline. Expert systems evaluate the contents of the database, determine the next experiments to be performed, and, via web-based displays, summarize results therefrom. With this high-throughput approach, SGX makes routine use of synchrotron-based crystallography for de novo structure determination and for its FAST fragment-based, structure-guided drug discovery platform. During 2005, 2006, and 2007, 9379, 9934, and 10895 crystals were automatically screened at SGX-CAT, respectively. The number of diffraction datasets recorded at SGX-CAT averaged in excess of 4000/annum during the same period. Rapid access to crystallographic data proved critical for discovery of SGX523, a potent, selective, and orally-bioavailable c-MET inhibitor now in Phase I clinical trials for treatment of cancer patients.

Keywords: drug discovery and design, data collection methods, protein kinases

MS.10.5

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The interdependence of wavelength, redundancy and dose on a sulfur sad experiment

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In the last decade popularity of sulfur SAD anomalous dispersion experiments spread rapidly among synchrotron users as a quick and streamlined way for solving phase problem in macromolecular crystallography. On beam line 10 at SRS (Daresbury, UK) data sets have been collected on HEWL at six wavelengths between 0.979 Å and 2.290 Å to evaluate the importance and the interdependence of experimental variables like Bijvoet ratio, wavelength, resolution limit, redundancy, and absorbed dose in the sample per image. All the crystals used for the experiments were of high quality, so that the results could be interpreted independently of that. A feature of these experiments was the use of the detector tilt capability of the beam line to preserve high diffraction resolution even at the long wavelengths we tested. Radiation damage was found to affect disulfide bridges after the crystals have been given a total dose 2.5×10^6 Gy. However with such a total dose, for all the data sets, it was possible to find a strategy to collect data to determine the sulfurs sub-structure and produce good quality phases by choosing the optimum combination of wavelength, exposure time and redundancy. $\langle |\delta_{\text{ano}}|/\sigma_{\text{ano}} \rangle$ bigger than 1.0 for all resolution shells was a necessary requirement for a successful sulfur SAD substructure location. This work expands the general vision of a single wavelength anomalous

dispersion experiment to show the relationship between some basic experimental variables and their influence on phasing and on an uninterpretable map or a map where the main chains can be auto-traced. Overall these results suggest a more optimal sulfur SAD experiment ie based on a complete description of the crystal system and the instrument to be used for data collection.

Keywords: SAD, wavelength, radiation damage

MS.11.1

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Hands-on crystallographic teaching: The Zurich School of Crystallography - Bring your own crystals

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The Zurich School of Crystallography, initiated by the authors in 2007, teaches the theory of small-molecule crystallography, and offers full hands-on experience from data collection to structure refinement and analysis of results. Our speciality is to give students the opportunity to bring crystals of a compound of interest in their current research and to return home with their completed structure. This ambitious concept relies on several key conditions:

Know what you want to achieve: Our aim is to introduce non-specialists to routine single crystal structure determination, rather than to create the next generation of expert crystallographers. The students learn to conduct routine structure analyses competently and to recognise when to ask for expert advice.

Know what you want to teach: We focus on small-molecule crystallography and inform applicants of the course content in order to avoid false expectations. Participation of students specifically interested in macromolecular or powder methods is discouraged.

Ensure students understand the objectives of the school: We make it clear beforehand that we do not run a data collection service nor solve problem structures. We ask for the students' crystals in advance, screen them for suitable quality and didactical usefulness and collect preliminary data.

Maximize the motivation of the students: Working on their own crystals ensures strong interest by the students. Access to a diffractometer of the student's choice and individual computing facilities are important. A student:tutor ratio of 2:1 ensures no-one gets left behind. Consequently, we limit the school to 20 students.

Have the equipment available: 5 diffractometers (4 different types) are used. There is one personal computer per student with all of the required software.

Keywords: crystallographic teaching, teaching of crystallography, structure determination

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Conquering superspace - A beginner's guide to modulated structures

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In the daily routine of a crystallographer modulated structures are often still perceived as an unpleasant disturbance. Their diffraction pattern, characterized by the existence of additional (satellite) reflections, requires (3+d) indices for an integer indexing, a complication usually resulting in an immediate dismissal of the crystal under study. Another obstacle may be the unfamiliarity with the so-called superspace approach, a concept developed to overcome the above mentioned loss of 3-dimensional periodicity and allow for a correct description of modulated structures. The theoretical foundation for the superspace approach is well-established by now. Also considerable efforts have been put into making the software package JANA2006 which can conveniently handle data and structures of modulated compounds available and user-friendly [1]. What still seems to be missing somehow are illustrative examples of molecular compounds which can be used to demonstrate in a comprehensible way how to approach modulated structures. In this context we will present a selection of cases from our pharmaceutical service lab along with a detailed recipe how to handle the modulated structure of a typical organic compound [2]. Having established a working knowledge of the concept and terminology of the superspace approach we will discuss various aspects of indexing, data processing and scaling as well as structure solution, refinement and interpretation details. Finally, the validity of a (classical 3-dimensional) superstructure approach and additional quality control features in JANA2006 are described.

[1] V. Petricek, M. Dusek, L. Palatinus, JANA2006, Institute of Physics, Praha, Czech Republic (2006).

[2] T. Wagner, A. Schoenleber, K. Baumann, *Acta Crystallogr.* A63, s51 (2007).

Keywords: modulated structure, superspace, teaching

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Sustaining crystallography in the 21st century: Education policies and use of cyberinfrastructure

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The USNC/Cr conducted two surveys to determine the status of crystallography education and training in the US, in both physical and life sciences. The ACA and USNC/Cr then held an education summit, the outcome of which is a consensus policy statement on crystallography education and training that makes recommendations for a comprehensive re-evaluation of crystallography education, provides guidelines to professional societies and academic departments for crafting future crystallography curricula, and suggests ways to develop in the broader scientific community an appreciation for the value of crystallographic information. With the migration of academic crystallography from a research specialty to a technique employed by a wide community of users, instruction in crystallography is increasingly relegated to non-curricular resources, such as web-based tutorials. While such tutorials often are well-constructed and provide a valuable resource to the broader scientific community, they generally do not provide practical experience needed to appreciate the value of crystallographic information and correctly interpret and judge the quality of crystallographic results. We can now exploit advances in cyberinfrastructure to effectively broaden access to instrumentation, data handling and analysis. These advances can develop in the wider user community a sufficient working knowledge of the field, enabling them to answer specific