FA1-MS10-O1

New Developments in Model Building with 'Buccaneer'. Kevin Cowtan. *Department of Chemistry, University of York, UK.*
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The 'Buccaneer' software for automated protein model building provides an effective tool for building an initial protein model into an experimentally phased electron density map. While it works at higher resolutions, it has been particularly useful in the lower resolution range, e.g. from 2.5A to 3.5A, when good phases are available[1].
The effectiveness of the procedure across a range of resolutions depends on the use of a problem-specific search function for locating likely alpha-carbon positions, where the search function is determined from a standard library structure and tailored to the resolution and data quality of the problem at hand. Some of the same methods have been implemented in the 'Coot' graphics software to allow interactive location of secondary structure features.
More recently, the focus of this work has shifted to the rebuilding of molecular replacement models. Initial results of this work will be presented. The integration of 'Buccaneer' into automation pipelines has also involved the development of a new 'classical' density modification program, 'Parrot'.

[1] Cowtan K., **2006**, *Acta Cryst*. D62, 1002-1011.

Keywords: model building; automation; protein

FA1-MS10-O2

Phasing from Unmerged Data: Exploiting the Anisotropy of Anomalous Scattering. Marc Schiltz[a], Gérard Bricogne[b]. [a]*École Polytechnique Fédérale de Lausanne (EPFL), Laboratoire de Cristallographie, 1015 Lausanne, Switzerland.* [b]*Global Phasing Ltd., Cambridge CB3 0AX, United Kingdom.*
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The space-group symmetry of a crystal structure imposes a point-group symmetry on its diffraction pattern, giving rise to so-called symmetry-equivalent reflections. We will discuss instances where the symmetry in reciprocal space is broken, i.e. where symmetry-related reflections are no longer equivalent. Such a situation occurs in the presence of anomalous scattering, when the absorbing sites display anisotropy in their local atomic environment. The genuine intensity differences between symmetry-related reflections can then be exploited to yield phase information in the structure solution process. In this approach, the usual separation of the data merging and phasing steps is abandoned. The data are kept unmerged down to the Harker construction where the symmetry-breaking effects are explicitly modelled and refined and become a source of supplementary phase information. This additional phase information essentially comes for free, i.e. without the collection of new data.

[1] G. Bricogne, S. C. Capelli, G. Evans, A. Mitschler, P. Pattison, P. Roversi & M. Schiltz, **2005**, *J. Appl. Cryst*. 38, 168-182. [2] R. Sanishvili, C. Besnard, F. Camus, M. Fleurant, P. Pattison, G. Bricogne & M. Schiltz, **2007**, *J. Appl. Cryst*. 40, 552-558. [3] M. Schiltz & G. Bricogne, **2008**, *Acta Cryst*. D64, 711-729.

Keywords: resonant diffraction; polarized resonant scattering; SAD; MAD; phase determination

FA1-MS10-O3

Molecular Replacement: A New Probabilistic Approach. Carmelo Giacovazzo[a], Rocco Caliandro[a], Benedetta Carrozzini[a], Giovanni Luca Cascarano[a], Annamaria Mazzone[a], Dritan Siliqi[a]. [a]*Institute of Crystallography-CNR, Via G. Amendola, 122/O, 70126 Bari, Italy.*
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The method of joint probability distribution functions has been applied to molecular replacement techniques. The program uses various formulas to solve the rotation and the translation problems, according to the prior information available at each step of the procedure. Several cases of prior information are studied, both for the rotation and for the translation step: e.g., the conditional probability density for the rotation or the translation of a monomer is found both for *ab initio* and when the rotation and/or the translation values of other monomers are given. The new approach has been implemented into the program *REMO09*, which is part of the package for global phasing *IL MILIONE* [1]. The new algorithms have been checked by a large set of test structures: they proved to be significantly robust in discriminating correct solutions from noise. An important design concept is the high degree of automatism: *REMO09* is often capable of offering a reliable model of the target structure without any user intervention. A brief comparison with *Phaser* and *Molrep*, two very popular and well documented programs, is made. The automatic application of the recently proposed *DEDM-EDM* procedure [2] to the molecular replacement phased data will also be described.

[1] M.C. Burla, R. Caliandro, M. Camalli, B. Carrozzini, G.L. Cascarano, L. De Caro, C. Giacovazzo, G. Polidori, D. Siliqi, R. Spagna, **2007**. *J. Appl. Cryst*. 40, 609-613. [2] Caliandro, R., Carrozzini, B., Cascarano, G.L., Giacovazzo, C., Mazzone, A.M. & Siliqi, D. **2009**. *Acta Cryst.* D65, 000-000.

Keywords: molecular replacement method; methods development; protein phasing

FA1-MS10-O4

Interpretation of Very Low Resolution X-Ray Electron Density Maps. Philipp Heuser[a], Gerrit Langer[a], Victor Lamzin[a]. [a]*European Molecular Biology Laboratory, Hamburg Unit.*
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We present a novel approach to obtain structural information from macromolecular X-ray data extending to resolution as low as 20 Å. We address the problem of interpreting low-resolution data via the segmentation of a density map into a

pre-defined number of core objects, so that each structural motif (domain) contained in the structure is represented by one such core. Rather than follow a simplistic approach of assigning the known domain structures to each segment of a low-resolution map, in this work we target a more general unbiased shape identification in terms of domains. No detailed knowledge about the composition of the low-resolution complex is required. A pattern-recognition comparative analysis which makes use of 3rd order moment invariants [1] and the radius of gyration of these shapes and those derived from structures of the unique domains from the PDB [2] results in candidate structural models that can be used for a fit into the density map. We show that the placed candidate models can be employed for subsequent phase extension up to 10-15 Å resolution.

[1] Hattne, J. & Lamzin, V. S., **2008**. *Acta Crystallogr D Biol Crystallogr* D64, 834-842. [2] Long, F., Vagin, A. A., Young, P. & Murshudov, G. N., **2008**. *Acta Crystallogr D Biol Crystallogr* 64, 125-132.

Keywords: protein structures; macromolecular crystallography; low resolution density map

FA1-MS10-O5

A Multivariate Likelihood Siras Function for Phasing and Model Refinement. Pavol Skubak[a], Garib N. Murshudov[b], Navraj S. Pannu[a]. [a]*Department of Biophysical Structural Chemistry, Leiden University, the Netherlands,* [b]*York Structural Biology Lab, York, England.*
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Previously, it has has been shown that the use of a multivariate likelihood function to optimally extract information from a single anomalous diffraction (SAD) experiment can improve the results of SAD phasing [1] and model building with iterative refinement [2].
Now a likelihood function based on the multivariate probability distribution of all observed structure factor amplitudes from a single isomorphous replacement with anomalous scattering (SIRAS) experiment has been derived and implemented for use in substructure refinement and phasing as well as macromolecular model refinement. Efficient calculation of a multi-dimensional integration required for function evaluation has been achieved by approximations based on the function's properties.
The use of the function in both SIRAS phasing and protein model building with iterative refinement was essential for successful automated model building in test cases presented.

[1] Pannu N.S., Read R.J. **2004**. *Acta Cryst*. D54, 22. [2] Skubak P., Murshudov G.N., Pannu N.S. **2004**. *Acta Cryst*. D60, 2196.

Keywords: biomacromolecule X-ray crystallography; SIRAS; experimental phases