comprehensive implementation of the fundamentals of crystallography (symmetries, Fourier, scattering, etc). As the foundation of the macromolecular suite PHENIX, it has a certain connotation which is undeserved since the algorithms and data structures it features are correct for any crystal structure.

As part of the EPSRC grant "Age Concern" we developed a companion library, the Small Molecule Toolbox (smtbx). It shares the same philosophy as the cctbx: it is designed to make the writing of short scripts easy as well as to make it possible to build or to integrate it into large programs. It provides tools covering the whole workflow of small molecule work but we will focus on refinement in this talk.

The smtbx provides full matrix least-squares, restraints on bond lengths, angles, or dihedral angles, and special position constraints as well as the wealth of geometrical constraints available in ShelX; the both of merohedral and non-merohedral twin refinement; a solvent disorder modelling similar to the SQUEEZE procedure in PLATON.

More importantly, its modular and open design ease the addition of new features. We will present one such new tool to model water molecules.

[1] R. Grosse-Kunstleve et al, http://cctbx.sourceforge.net/

Keywords: refinement, full matrix, constraints

MS58.P09

Acta Cryst. (2011) A**67,** C594

On the refinement of routine single crystal X-ray data only to mimic single crystal neutron structural results

Wieslawa F. Sanjuán Szklarz, A. Hoser, K. Woźniak, *Chemistry Department, University of Warsaw, Pasteura 1, 02-093 Warszawa, (Poland).* E-mail: fabi.sanjuan@gmail.com

In the case of organic compounds single crystal neutron diffraction is a source of reliable structural data particularly hydrogen atom positions and their ADPs. In consequence, neutron geometry of organic molecules is usually more reliable then single crystal X-ray diffraction structural data, although no doubt this is the X-ray diffraction technique which is by far the most popular among crystallographers to acquire structural information.

One can ask then a question whether it is possible to refine single crystal X-ray diffraction data only in such a way as to mimic the geometry of molecules obtained from single crystal neutron diffraction experiments.

In this contribution will present results of our analysis focused on comparison of structural neutron and X-ray results obtained for a series of five crystals of model compounds of increasing complexity and quality of data.

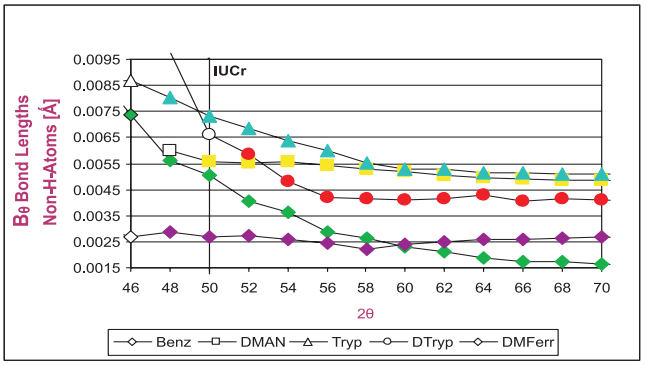

Fig. 1. Average differences between the neutron and X-ray bond lengths for the non-H-atoms obtained for a series of model compounds as a function of diffraction 2θ angle.

For each crystal, we have performed series of refinements as a function of resolution (sin θ/λ, in fact as a function of diffraction 2θ angle) using the neutron structural results as the reference ones. Will present a number of dependences of different parameters characterising the quality of X-ray data sets and average differences between particular neutron and X-ray structural parameters on 2θ diffraction angle. The results obtained influence understanding of benchmarks commonly accepted by IUCr and used in different checkcif programs, in particular 2θ limit equal to 50° for the MoKα X-ray radiation. One example of such a dependence is shown in figure below.

Keywords: neutron, X-ray, refinement

MS58.P10

Acta Cryst. (2011) A**67,** C594-C595

On a method for the absolute scaling of refined atomic B factors

Horacio Botti,[a] Lucía Bonilla,[b] Felipe Trajtenberg,[a] Rafael Radi[b] and Alejandro Buschiazzo[a] *[a]Group Redox Biology of Trypanosomes and [b]Unit of Protein Crystallography, Institut Pasteur de Montevideo. [c]Departamento de Bioquímica, Facultad de Medicina, Universidad de la República (Uruguay).* E-mail: hbotti@pasteur.edu.uy

The comparison of crystallographic models representing different functional and/or physical states of the same protein might seem easy if big conformational differences are detected by simple visual inspection. The precision of the models must be immediately considered if subtle structural changes are at play or if the aim is to evaluate small internal changes that occur in combination with for example large scale rigid-body changes. While the estimation of the positional uncertainty of crystallographic models has been extensively studied and a few methods have been developed to perform error-inclusive coordinate comparisons, the comparison of isotropic atomic B factors (Bi) has received less attention. One problem is to estimate standard uncertainties for refined Bi, but in addition, it is known that direct quantitative comparisons of Bi are flawed by several sources of model-specific variations (such as refinement strategies, data resolution, etc) ultimately contributing to a general scaling problem (inaccuracy). Precise and accurate comparison of Bi among several (frequently many) models would represent a rich source of information about dynamics and plasticity, often neglected in crystallographic approaches, despite the general acceptance of using Bi as a critical parameter in model refinement. The development of new methods to bring refined B factors to a common absolute scale would thus represent a genuine contribution, especially relevant to tackle the problem of "protein allostery without conformational change" (i.e. without a change in the shape: conformational entropy modulation). In this work we propose a method to compare atomic B factors, based on Cruickshank's approach to predict atomic positional standard uncertainties (psu's) in crystallographic models [1]. The method we are now proposing uses Cruickshank's psu's to build a correction index that, once applied to invididual refined atomic B factors, generates a set of scaled B factors to be used for comparison purposes. This approach assumes that the psu's integrate all sources of position uncertainty: dynamic (temperature-dependent), static and model error. Among other interesting applications, direct comparison of room and cryogenic temperature models are possible. Different sets of protein models consisting of apo and complexed forms revealed a previously overlooked inverse relationship between Bavg and Rfree, warning about the need for adequate and complete model refinement strategies to ensure accurate structural comparisons. We show evidence supporting that the Wilson B factor value can act as a universal attractor leading to inaccurate models. As a practical example we have used

this method of atomic B factor scaling to analyze the redox-dependent allosteric communication between the Cys34 thiol site and Sudlow's drug binding site I in Human Serum Albumin.

[1]. D.W. Cruickshank, *Acta Crystallogr D Biol Crystallogr* **1999***, 55*, 583.

Keywords: plasticity, dynamics, accuracy

MS58.P11

Acta Cryst. (2011) A**67,** C595

Improving molecular replacement solutions with SHELXE

Andrea Thorn, George M. Sheldrick, *Department of Structural Chemistry, Georg-August-Universität, Tammannstr. 4, Göttingen (Germany).* E-mail: athorn@shelx.uni-ac.gwdg.de

The program SHELXE [1],[2] was originally designed for *experimental phasing* of macromolecules followed by improvement of the resulting map by *density modification* using the *sphere of influence* [2] and *free lunch* [3], [4], [5] algorithms. The latest beta-test version iterates between density modification and generation of a *poly-Ala trace* [6], enabling an interpretable map to be obtained from even weaker initial phase information.

This phase information must not necessarily originate from anomalous scattering. An MR solution representing a rather small percentage of the total scattering power can be a sufficient starting point for iterative density modification and poly-Ala tracing in SHELXE, given native data to good resolution.

In small molecule direct methods, a multi-solution approach is often attempted, using random or somewhat better-than-random phases obtained by *Patterson seeding*. By analogy, our approach starting from many potential molecular replacement solutions could be called *MR seeding*. When and if longer chains can be traced (with a correlation coefficient to the native data better than 25%), one can be sure the structure is solved. This approach is also exploited in the program ARCIMBOLDO, [7] where a large number of possible MR solutions for small fragments such as α-helices are expanded with SHELXE running on a computer cluster.

If anomalous data is available, but the anomalous signal is too weak for the immediate location of the anomalously scattering atoms by direct and Patterson methods, a molecular replacement (MR) solution can provide starting phases for the SHELXE density modification. An anomalous map is calculated in order to locate the heavy atoms as starting point for further iterative density modification and poly-Ala tracing. With this MR-SAD approach [8], phase information from anomalous scatterers, molecular replacement and density modification can be combined in SHELXE. Model bias, a major problem with MR, is also substantially reduced.

Here, we will present general guidelines, remarks and examples of these applications of SHELXE, with particular reference to MR-SAD involving native sulfur atoms as the anomalous scatterers.

[1] G.M. Sheldrick, *Acta Cryst***. 2008**, *A64*, 112-122. [2] G.M. Sheldrick, *Z. Kristallogr* **2002**, *217*, 644-650. [3] R. Caliandro, B. Carrozzini, G. Cascarno, L. De Caro, C. Giacovazzo, D. Siliqi, *Acta Cryst.* **2005**, *D61*, 556-565. [4] Y. Jia-xing, M.M. Woolfson, K.S. Wilson, E.J. Dodson, *Acta Cryst.* **2005**, *D61*, 1465-1475. [5] I. Usón, C.E.M. Stevenson, D.M. Lawson, G.M. Sheldrick, *Acta Cryst.* **2007**, *D63*, 1069-1074. [6] G.M. Sheldrick, *Acta Cryst.* **2010**, *D66*, 479-485. [7] D.D. Rodriguez, C. Grosse, S. Himmel, C, Gonzáles, I.M. de Ilarduya, S. Becker, G.M. Sheldrick, I. Usón. *Nature Methods,* **2009**, *6*, 651-653. [8] J.P. Schuermann, J.J. Tanner, *Acta Cryst.* **2003**, *D59*, 1731-1736.

Keywords: experimental phasing, molecular replacement, MR-SAD

MS58.P12

Acta Cryst. (2011) A**67,** C595

New approach to structure determination: Envelop-based Phase Extension

Weizhe Zhang, Hongmin Zhang, Quan Hao *Department of Physiology, LKS Faculty of Medicine, The University Of Hong Kong (Hong Kong).* Email: zhangwz@hku.hk

A new method is proposed to solve the Crystallographic Phase Problem utilizing the protein envelope information[1] obtained from small-angle X-ray scattering (SAXS) or electron-microscopy (EM) data.

The method involves three steps.(1) Once SAXS scattering pattern has been collected, the three-dimensional molecular envelope will be recovered from this one dimensional pattern using the spherical harmonics method or Mont Carlo method. (2) FSEARCH is able to perform a real space search for orientation and translation of envelope within the crystallographic unit cell, which provides low resolution phases for a starting point of phase extension.(3) The last step is to extend low resolution phases to higher resolution ones by applying the genetic algorithm(GA) or iterative-projections method.

Three types of data has been tested as input: coordinate data, real SAXS spherical harmonics data, and calculated solution scattering data.[2] As coordinate input, atoms have been fuzzed to create a mask while spherical harmonics input can be used as envelope directly. Three known protein structures have been used as test models: SOD, Cyclase, and HMG. SOD and Cyclase are crystal structures while HMG is an NMR structure. An Input-Output Algorithm [3] is applied on phase retrieving. Phase errors against known structures are introduced to monitor iterative quality, as well as several other adjustable parameters, aiming on finding out best optimization process that leads to correct structure solution.

In our tests, FSEARCH was able to find the proper orientation and translation of envelope in the crystallographic unit cell. Furthermore, our phase extension program was used to extend low resolution phases to a higher level within an acceptable phase error.

[1] Q. Hao, *Acta Cryst*. **2001** *D57*, 1410-1414 [2] D.I. Svergun, C. Barberato, M.H.J. Koch, *J. Appl. Cryst.* **1995,** *28,* 768-773. [3] J.R.Fienup, *Applied Optics*, **1982**, *21(15).*

Keywords: envelope, phase, extension

MS58.P13

Acta Cryst. (2011) A**67,** C595-C596

BORGES a tool to generate customised, secondary structure libraries for phasing

Massimo Sammito,[a] Dayté Rodríguez Martínez,[a] Kathrin Meindl,[a] Iñaki Martínez de Ilarduya,[a] Isabel Usón,[a,b]. [a]*Departament of Structural Biology, Instituto de Biología Molecular de Barcelona (IBMB-CSIC) Barcelona Science Park, (Spain).* [b] *ICREA (Spain).* E-mail: massimo.sammito@ibmb.csic.es

Macromolecular crystallography is computationally intensive. In the midst of the vertiginous increase in computation speed experienced in the last years, crystallography, unlike modelling, has largely turned its back on the use of massive calculations and large scale parallelisation. In our group, we intend to exploit this aspect to tackle the phase problem with multi-solution methods, relying on the information available in the databases. BORGES is an interactive tool, whose aim is to generate pdb-based, customized, secondary structure fragment libraries, to be used as search fragments by our *ab Initio* crystallographic phasing program ARCIMBOLDO [1], which performs parallel model fragment