To help resolve long-standing questions regarding the catalytic activity of the serine proteases the structure of porcine pancreatic elastase has been analyzed by high-resolution neutron and X-ray crystallography. In order to mimic the tetrahedral transition intermediate a peptidic inhibitor was used. Neutron and X-ray diffraction data have, for the first time, visualized a SIHB formed between catalytic residues His57 and Asp102, as well as the oxyanion located at the oxy-anion hole, and has identified strong hydrogen bonds as contributing to inhibitor recognition in PPE. These are fundamentally important structural data for the catalytic reaction and molecular recognition of an enzyme.

[1] Tamada, T., et al., *J. Am. Chem. Soc. 131*, 2009, 11033. [2] Kinoshita, T., et al., *Acta Crystallogr. F63*, 2007, 315.

Keywords: Neutron analysis, X-ray analysis, elastase

FA1-MS04-P05

MR-SAD: Phasing employing the NMR structure without model bias. Andrea Thorn[a], Franz Kerek[b], Carlos Eduardo Lima da Cunha[a], Isabel Usón[c], George M. Sheldrick[a]. [a]*Institute of Structural Chemistry, Georg-August University Goettingen, Germany.* [b]*DoNatur GmbH, Martinsried, Germany.* [c]*ICREA at Instituto de Biología Molecular de Barcelona (IMBMB-CSIC), Barcelona Science Park, Spain.*
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Molecular replacement (MR) with an NMR model is an appealing method for macromolecular phasing. However, it inevitably introduces model bias, or even errors, into the X-ray structure. In addition, the correct MR solution may be poorly discriminated from false ones. [1]
Here, we apply MR-SAD [2] to Hellethionin D from *Helleborus purpurascens*.
Molecular replacement was conducted with the NMR structure [3] as search model in a multi-solution PHASER [5] approach. Only a small fraction of all residues could be found by MR since the average rmsd between the NMR structure and the final model was 1.9 Å^2, and there were seven protein copies in the asymmetric unit. The correct solution could be discriminated by automatic chain expansion in SHELXE [4], an approach similar to ARCIMBOLDO [6]. After expansion, 36 sulfur atom positions were determined and the rest of the structure was discarded: Only the sulfur positions were used for a new run of density modification and subsequent expansion in SHELXE. The final trace contained 311 of 322 residues, with no misplaced residues present.
Despite an anomalous signal unsuitable for initial SAD phasing and only 19% of all residues traceable by MR, the methods described here resulted in an almost complete, model-bias free trace of all seven protein chains.

[1] Chen Y.W., Dodson E.J., Kleywegt G.J., *Structure* 2000, 8, R213. [2] Schuermann J.P., Tanner J.J., *Acta Cryst. D*, 2003, 59, 1731. [3] PDB 1NBL; Milbradt A.G., Kerek F., Moroder L., Renner C., *Biochemistry*, 2003, 42, 2404. [4] Sheldrick G.M., *Acta Cryst. D*, 2010, 66, 479. [5] McCoy A.J., Grosse-Kunstleve R.W., Adams P.D., Winn M.D., Storoni L.C., Read R.J., *J. Appl. Cryst.* 2007, 40, 658. [6] Rodríguez Martínez D.D., Grosse C., Himmel S., González C., de Ilarduya I.M., Becker S., Sheldrick G.M., Usón I., *Nat. Met.* 2009, 6, 651.

Keywords: phasing methods, NMR, NCS

FA1-MS04-P06

The CCP4 software suite - current status and future developments. Martyn Winn[a], Charles Ballard[b], Ronan Keegan[b], Georgios Pelios[b], Natalie Zhao[b], Eugene Krissinel[b]. [a]*STFC Daresbury Laboratory, Warrington, WA4 4AD, UK.* [b]*STFC Rutherford Appleton Laboratory, Didcot, OX11 0QX, UK.*
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CCP4 exists to produce and support a world-leading, integrated suite of programs that allows researchers to determine macromolecular structures by X-ray crystallography. CCP4 aims to develop and support the development of cutting edge approaches to experimental determination and analysis of protein structure, and integrate these approaches into the suite.
The current CCP4 software suite is on release series 6.1.x. A particular focus of these releases is the automation of significant parts of the structure solution process, including XIA2 for data processing, Crank for experimental phasing, MrBUMP and Balbes for Molecular Replacement, and Buccaneer for model building. There are also a number of new programs, including Pointless for Laue group and spacegroup determination, the new iMosflm interface, Parrot for density modification, and PISA for identification of protein-protein interfaces. We will give an overview of the additions to the CCP4 suite, as well as an update on established programs.
A major overhaul of the CCP4 suite is under development. A new graphical front-end will provide easier control of the suite, and considerable help with interpreting and evaluating the results. At the core, there will be in-built support for automation, making straightforward structures simple to solve, while continuing support for more challenging projects. Finally, usage of the suite will be underpinned by better data management, with support for database back-ends.
CCP4 also aims to enhance its functionality related to the maintenance and use of data on small molecules (ligands). Firstly, a considerably larger library of chemical compounds will be provided with the Suite. Extended search functions will be provided to allow for efficient retrieval of known compounds or their close analogs. Secondly, existing functions for generating restraint data for new ligands will be enhanced by the inclusion of relevant software, such as ProDRG, into the Suite, as well as by the development of new methods for structure reconstruction on the basis of partial similarity to structures in the library. Functionality will be available through a graphical front-end application, JLigand.

Keywords: protein crystallography, crystallographic software, automation