MS4-05 **Zinc-binding to protein surface and its application to phase determination.** Sun-Shin Cha[a,b], Young Jun An[a], Chang-Sook Jeong[a], Min-Kyu Kim[a], Sangmin Lee[a] [a]*Marine Biotechnology Research Center, Korea Ocean Research & Development Institute, Ansan 426-744, Republic of Korea.* [b]*Department of Marine Biotechnology, University of Science and Technology, Daejeon 305-333, Republic of Korea.*
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Zinc is a suitable metal for anomalous dispersion phasing methods. Crystal structure determination using anomalous scattering from zinc has been limited to proteins with intrinsically bound zinc(s). Herein we report that multiple zinc ions can be charged on the surface of proteins and used for structure determination of proteins with no intrinsic zinc-binding site. The discovery of facile zinc-binding to proteins without an intrinsic zinc-binding site opens a new avenue to the usage of zinc anomalous signal for structure determination.

Keywords: Zinc, anomalous signal, phasing

MS5-01 **Better ligand representation in BUSTER protein-complex structure determination.** Oliver S. Smart, Andrew Sharff, Claus Flensburg, Peter Keller, Wlodek Paciorek, Clemens Vonrhein, Thomas O. Womack, Gérard Bricogne *Global Phasing Ltd., Sheraton House, Cambridge CB3 0AX, UK*
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The generation of reliable restraints for novel small-molecule ligands in macromolecular complexes is of great importance for both ligand placement into density maps and subsequent refinement. This has led us to develop Grade, a ligand restraint generator whose main source of restraint information is the Cambridge Structural Database (CSD) of small-molecule crystal structures, queried using the MOGUL program developed by the CCDC. Where small-molecule information is lacking, GRADE uses quantum mechanics (QM) procedures to obtain the restraint values. Grade automatically produces restraints that are compatible with the Engh and Huber EH99 restraints used for the protein during building and refinement. Grade was released to academic users as part of the Buster package in July 2011 and has proved popular. However, a problem for some academic users has been that, in order to get the best restraints from GRADE, a CSD system license is necessary to use MOGUL. To provide easy access to Grade a public Web server was launched in March 2012 [1]. The GRADE WEB SERVER is free to use but should not be used for confidential projects. It has proved popular with users as the restraint dictionaries produced can be used with BUSTER, COOT, REFMAC and many other programs. Recent advances in Grade will be described including provision of better QM methods and support for a wider range of input formats. An alternative to conventional stereochemical restraint functions is provided by the direct use of QM to compute the potential energy of the ligand. This involves invoking a QM program, such as Gamess, to provide the QM energy and its gradients for the ligand conformation in each cycle of BUSTER refinement. The use of a weighted-QM representation for a ligand in refinement provides for a means of accurately modelling its stereochemical properties, albeit at some computational cost. In particular weighted-QM for ligands allows the assessment of conformational strain energy, together with the identification of what degrees-of-freedom are involved. It will be shown how conformational strain assessment by weighted-QM for ligands is complemented by methods, such as MOGUL, based on the comparison with CSD structural information.

[1] Grade Web Server http://grade.globalphasing.org

Keywords: refinement methods; protein ligands; quantum chemistry