

MS.44.4*Acta Cryst.* (2008). A64, C81**Sulfur-SAD phasing becomes a routine approach to solve *de novo* structures**Cheng Yang¹, Aiping Dong³, Yan Liu³, Elena Evdokimova², Xiaohui Xu², Tatiana Skarina², James Pflugrath¹, Ferrara Joseph¹¹Rigaku Americas Corp, 9009 New Trails Dr., Woodlands, TX, 77381, USA, ²Midwest Center for Structural Genomics, University of Toronto, 112 College Street, Toronto, Ontario, Canada M5G1L6, ³Department of Biochemistry, University of Toronto, 1 King College circle, Toronto, Ontario, Canada M5S1A8, E-mail: cyang@rigakumsc.com

The recent application of softer X-ray radiation provides an alternative path to solve protein crystal structures in high throughput pace. In-house chromium K α radiation ($\lambda = 2.29 \text{ \AA}$) is one of the most commonly used softer X-ray radiation wavelengths in macromolecular crystallography. Chromium radiation increases the anomalous signal of many intrinsic elements or often used heavy atoms in derivatization. For example, compared to Cu radiation, the contribution to the anomalous term of sulfur and selenium atom doubles to 1.14 e and 2.28 e, respectively. These enhanced anomalous signals are sufficient to be routinely collected and processed with modern instrumentation and software packages. This work reports several examples of protein structures solved using sulfur-SAD phasing. For these proteins it was difficult to produce or crystallize the selenium-methionine substituted form, or to reproduce more of the original crystals. In other words, the native forms of these crystals had to be used to solve their structures. A single data set was collected with an in-house Cr X-ray radiation source for each protein crystal and was phased by the S-SAD phasing approach. These examples demonstrate that Cr radiation has become a routine phasing approach in the crystallographer's toolkit, which makes it possible to solve a crystal structure with native crystals only or before synchrotron data collection when selenium-methionine substituted protein is not available. This method clearly improves the productivity of macromolecular structure determination, usage of synchrotron beam time and helps enhance high throughput structure determination.

Keywords: SAD, sulfur-SAD, Cr radiation

MS.44.5*Acta Cryst.* (2008). A64, C81**Scientific inquiry and inference in macromolecular crystallography**Bernhard Rupp

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A number of recent retractions of protein structures published in high impact journals shows that not all is well in the way macromolecular crystallography is taught to students. The negative impact of severely incorrect structures extends beyond mere nuisance: crystallographic structure models carry great persuasive power - a wrong structure in a leading journal contradicting correct experimental findings makes it quite impossible for others to obtain funding for their work. With great power of modern crystallography comes great responsibility for its appropriate use, and the mistaken idea that crystallography is just a basic analytical technique only amplifies the risk of uncritical use of increasingly powerful crystallographic methods and its propagation to the next generation. The complexity of teaching a science that encompasses fundamentals of mathematics, physics, and probability theory in addition to the biological knowledge necessary

to analyze and interpret the results with an array of bioinformatics tools should not be underestimated. A closer inspection of incorrect structures shows that an even deeper and more concerning general misconception of the process of scientific inquiry lead to wrong structures and misinterpretations. These findings should be taken as an encouragement to teach crystallography in a larger framework consistently emphasizing the role of evidence and probability in inference methods. Examples range from crystallization propensities to maximum likelihood in phasing and refinement to evidence-based examination of ligand structures. In such a curriculum, even if the details of crystallographic theory are long forgotten, the fundamentals of proper inquiry and inference will remain invariably useful for the students.

Keywords: teaching, likelihood, Bayesian inference

MS.45.1*Acta Cryst.* (2008). A64, C81**Metal-organic networks designed by combination of hydrogen bonds and halogen bonds**Guillermo Minguez, Lee Brammer

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The electronic properties of inorganic halogens (M-X) differ markedly from those of organic halogens (C-X). The former are directional nucleophiles in interactions with typical hydrogen bond donors (N-H, O-H, etc.). By contrast, organic halides (C-X) can be tuned to serve as directional electrophiles; they can participate in halogen bonds, wherein the C-X group plays a Lewis acidic role, viz...X-C. Recently we have combined these two complementary environments of halogens in order to create a new type of supramolecular synthon, M-X...X-C halogen bonds, based on attractive interactions that are highly directional at both halogens. Complementary experimental and theoretical studies demonstrate that M...X-C interactions are predominantly electrostatic in nature rather than dominated by the charge transfer as might have been anticipated. These studies suggest an electronic description of halogen bonds ranging from weakest to strongest that parallels the description of hydrogen bonds. Competition between halogen bonds and hydrogen bonds has been studied in a series of compounds which are propagated by N-H...X₂M hydrogen bonds and M-X...X-C halogen bonds. The hierarchy of the interactions has been rationally modified by tuning the strength of the halogen bonds from weak isotropic to moderately strong attractive interactions and consequently the crystal packing changes depending on their strength. Finally, it has been shown that the application of isotropic perturbations such as changes in temperature or pressure produces an anisotropic response in the crystal structures due to the different behavior of non-covalent interactions, providing useful information on the intermolecular interaction potentials in molecular crystals containing hydrogen bonds and halogen bonds.

Keywords: halogen bond, hydrogen bond, high-pressure structures

MS.45.2*Acta Cryst.* (2008). A64, C81-82**A journey through the rational design of molecular solids with halogen bonding**Pierangelo Metrangolo¹, Tullio Pilati², Giuseppe Resnati^{1,2},