



In this issue:

- [Crystallography in the news](#)
- [Automated optical alignment for maximum flux](#)
- [Lab spotlight: Yigong Shi @ Tsinghua University](#)
- [Useful links for crystallography](#)
- [Hardware training courses](#)
- [Survey question of the month](#)
- [Selected recent crystallographic papers](#)
- [Book review: Biomolecular Crystallography](#)

January 11, 2010. New data from the groups led by [Daria Mochly-Rosen](#) at Stanford University School of Medicine and [Thomas Hurley](#) at Indiana University show how [Alda-1 repairs a common enzyme mutation](#) that leads to a debilitating reaction to alcohol, increases the risk of some types of cancer and might also promote some neurodegenerative diseases.

January 9, 2010. Research breakthroughs using the [LANL Protein Crystallography Station](#) (part of the Lab's LANSCE facility) to probe the [structure of cellulose](#) are making the prospect of affordable, efficient production of cellulosic fuels closer to reality. The Protein Crystallography Station is the only resource of its kind in the United States and the first protein crystallography beam line to be built at a spallation neutron source.

January 1, 2010. [Michael Kobor](#) at the University of British Columbia, working with researchers at the University of California, Berkeley, have reported the [structure and function of a key player in regulating chromatin in yeast](#) (*Saccharomyces cerevisiae*) the protein Yaf9. This is a subunit of both the essential histone acetyltransferase complex NuA4 and the ATP-dependent chromatin remodelling complex SWR1-C, which deposits histone variant H2A.Z into euchromatin. The human "equivalent" of this protein is the close relative GAS41.

December 28, 2009. Emerald BioStructures describes the application of structure-based drug design (SBDD) to engineer new allosteric [small molecule modulators of the enzyme phosphodiesterase-4](#) (PDE4) that exhibit reduced side effects. Researchers established the structural basis of PDE4 regulation through crystal structures of the PDE4 regulatory domain in contact with small molecules.

December 15, 2009. Groups led by [Dorothee Kern](#) at Brandeis University and [Tom Alber](#) at the University of California, Berkeley reported the use of ambient-temperature X-ray crystallography and nuclear magnetic resonance (NMR) techniques to directly [visualize protein structures essential for catalysis in the rare high-energy state](#).



**Continuing Education Webinar  
Processing X-ray diffraction data  
with HKL - an in depth exploration**

Presenter: Dr. Wladek Minor  
January 21st at 10AM EST  
(15:00 GMT)

Prof. Minor will explore the depths of HKL-2000 and the new HKL-3000 software packages. Designed for X-ray diffraction image processing, HKL2000 is used by more than 1200 labs worldwide. The paper: "Processing of X-ray diffraction data collected in oscillation mode" *Methods in Enzymology* (1997) 275: 307-326 that describes the program has been cited more than 19,500 times throughout the scientific literature. HKL and HKL-2000 components were written by Zbyszek Otwinowski (Professor, UT Southwestern in Dallas) and Wladek Minor (Professor, University of Virginia).

**Spring Webinar Series Focuses on Software**

Note that our continuing webinar program will feature well known expert presenters in a mini-series devoted to commonly used data processing packages.



**Automated optical alignment for maximum flux**

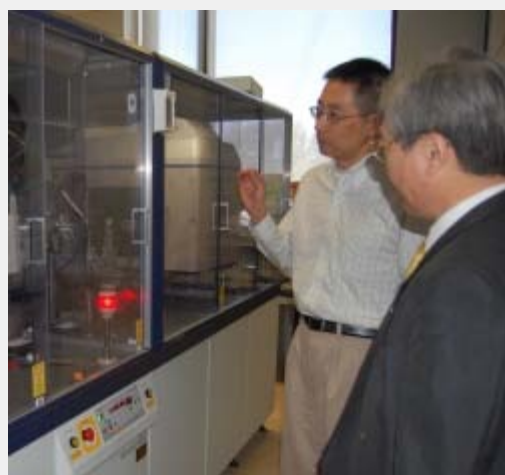
OpticAlignment™ is a computer-controlled, motorized alignment system that maximizes the X-ray flux from VariMax optics. Small Picomotor® actuators adjust the micrometers on the VariMax optic to maximize the X-ray flux measured by a PIN diode meter through a pinhole at the sample position.

Never again wonder if you have the most intense beam possible from your Rigaku generator and VariMax optics. Any time you change a filament, polish the anode, or simply want to verify that you have the best possible X-ray beam, start up OpticAlignment. With the click of the mouse, and within minutes, the X-ray flux at the crystal position is maximized. OpticAlignment can be integrated with any existing VariMax optic and with all new VariMax optics.

[Request more information](#) on OpticAlignment.



Rigaku VariMax optic equipped with OpticAlignment (top) and OpticAlignment software screen image (bottom).



Professor Yigong Shi with Rigaku Chairman Hikaru Shimura after the recent installation of the 100th MicroMax-007 HF microfocus rotating anode X-ray generator, as part of a HighFlux HomeLab, at Tsinghua University.

## Rigaku Hardware Training Classes

Rigaku will hold two training sessions, at our Texas facility, tailored towards the needs of macromolecular crystallographers and their staff. Course format will be a series of short lectures on theory followed by hands-on activities with detectors and X-ray generators. Safety will be emphasized. Click for more info on upcoming sessions:

## Lab spotlight: Yigong Shi @ Tsinghua University

A leading Chinese researcher in the field of protein X-ray crystallography, [Dr. Shi](#) has determined the crystal structure of several critical apoptotic proteins, including apaf-1, DIAP1, and the BIR3 domain of XIAP. He began his independent career as an Assistant professor in the Department of Molecular Biology at Princeton University in 1998. He was promoted to the ranks of Associate Professor in 2001 and Professor in 2003. At an age of 36, he became the youngest, tenured Full Professor in the history of Princeton's Department of Molecular Biology (Warner-Lambert/Parke-Davis Professor). In June 2008, he was selected as a Howard Hughes Medical Institute investigator but instead resigned his position at Princeton University in order to pursue a career at Tsinghua University. This was in response to an [effort to repatriate Chinese scientists](#).

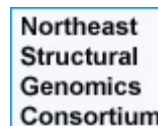


[Scientific research in Dr. Shi's laboratory](#) is aimed at understanding the structural and molecular mechanisms involved in tumorigenesis, with a focus on key regulatory components in the apoptotic pathways and other important cellular processes. He has published over 90 papers in international journals, including as corresponding author eleven in *Cell*, six in *Nature*, and three in *Science*. Dr. Shi was awarded the Irving Sigal Young Investigator Award by the Protein Society in 2003 and became the first Chinese scientist to win such honor. He has been the President of the Chinese Biological Investigators Society (CBIS) since ! 2005.

Dr. Shi was appointed a Chair Professor of Tsinghua's Department of Biological Sciences and Biotechnology in 2003 and a Tsinghua Changjiang Professor in 2006. He becomes Vice Director of Tsinghua's Institute of Biomedicine and Vice Dean of Tsinghua's Department of Biological Sciences and Biotechnology in 2007.

## Useful links for crystallography

The [Protein Crystal Structure Propensity Prediction Server](#) tool estimates the propensity of determination of a protein structure by X-ray crystallographic analysis. Analysis of data mining of the large-scale experimental results of the Northeast Structural Genomics Consortium (NSGC), and experimental folding studies to characterize the biophysical properties that control protein crystallization, has lead to the conclusion that crystallization propensity depends primarily on the prevalence of well-ordered surface epitopes capable of mediating interprotein interactions and is not strongly influenced by overall thermodynamic stability. Results identified specific sequence features that correlate with crystallization propensity and that can be used to estimate the crystallization probability of a given construct.



## Selected recent crystallographic papers

A gate-latch-lock mechanism for hormone signalling by abscisic acid receptors. K. Melcher, L. Ng, X.E. Zhou, F. Soon, Y. Xu, K.M. Suino-Powell, S. Park, J.J. Weiner, H. Fujii, V. Chinnusamy, A. Kovach, J. Li, Y. Wang, J. Li, F.C. Peterson, D.R. Jensen, E. Yong, B.F. Volkman, S.R. Cutler, J. Zhu and H.E. Xu. *Nature* **462**, 602-608 (2009).

Nonspecifically bound proteins spin while diffusing along DNA. P.C. Blainey, G. Luo, S.C. Kou, W.F. Mangel, G.L. Verdine, B. Bagchi and X.S. Xie. *Nature Structural & Molecular Biology* **16**, 1224 - 1229 (2009).

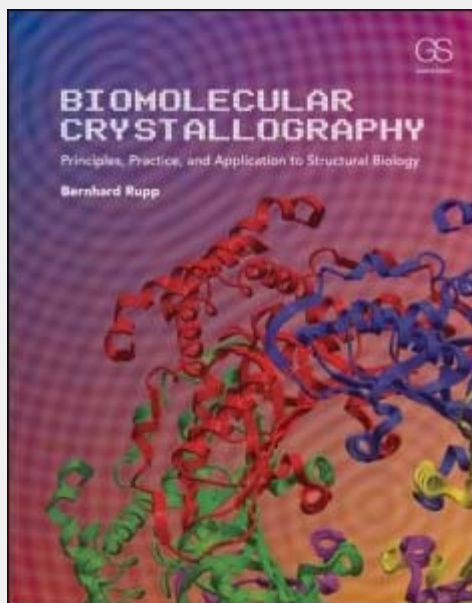
- March 24-26, 2010
- October 27-29, 2010

### Survey Question

**When purchasing new instrumentation for your lab, what is the most important factor in your decision?**

- Price
- Capabilities/functionality
- Feedback from reference customers
- Ease-of-use
- Reliability
- Other (please specify)

[Click to take survey](http://www.surveymonkey.com/s/MXJX765)  
 or cut-and-paste  
[www.surveymonkey.com/s/MXJX765](http://www.surveymonkey.com/s/MXJX765)  
 into your browser.



Biomolecular Crystallography

X-ray structure, symmetry and mechanism of an AMPA-subtype glutamate receptor. A.I. Sobolevsky, M.P. Rosconi and E. Gouaux. *Nature* **462**, 745-756 (2009).

The abscisic acid receptor PYR1 in complex with abscisic acid. J. Santiago, F. Dupeux, A. Round, R. Antoni, S. Park, M. Jamin, S.R. Cutler, P.L. Rodriguez and J.A. Márquez. *Nature* **462**, 665-668 (2009).

Structural basis of abscisic acid signalling. K. Miyazono, T. Miyakawa, Y. Sawano, K. Kubota, H. Kang, A. Asano, Y. Miyauchi, M. Takahashi, Y. Zhi, Y. Fujita, T. Yoshida, K. Kodaira, K. Yamaguchi-Shinozaki and M. Tanokura. *Nature* **462**, 609-614 (2009).

RNA polymerase II-TFIIB structure and mechanism of transcription initiation. D. Kostrewa, M.E. Zeller, K.J. Armache, M. Seizl, K. Leike, M. Thomm and P. Cramer. *Nature* **462**, 323-330 (2009).

Crystal Structure of the Catalytic Core of an RNA-Polymerase Ribozyme. D.M. Shechner, R.A. Grant, S.C. Bagby, Y. Koldobskaya, J.A. Piccirilli and D.P. Bartel. *Science*, Vol. 326, **5957**, 1271-1275 (2009).

#### Book review: *Biomolecular Crystallography*

**by Bernhard Rupp**

This book has been referred to as an "epic tome" by Judith Flippen-Anderson, the next "Blundell & Johnson" by Jim Pflugrath and a paperweight by the author. I found this book to be a much needed compilation of the current state of the art of X-ray crystallography for structural biology. BMX is destined to become a classic and worth reading cover-to-cover.

Some of the features include an extensive and descriptive main body, side bars with loads of useful information and a key concepts section at the end of every chapter. The book provides many, many historical and current references. It is a first edition and there are a few typos and some awkward language, but I found only one math error and one historical error. It is very clear the community is supporting this book and has been most helpful in discovering the [errata](#).

The only real complaint I have is that page numbers are not associated with figures and such, so it sometimes takes a while to find a non-adjacent figure or table. The book has thirteen chapters (no Triskaidekaphobia here):

Chapter 1: This chapter is an abstract of the entire book, covering all the concepts and provides an outline for beginning your trek through a crystal structure analysis.

Chapter 2: Protein Structure. Basic protein structure is described here, although the chapter does include the basics of DNA and membrane protein structure.

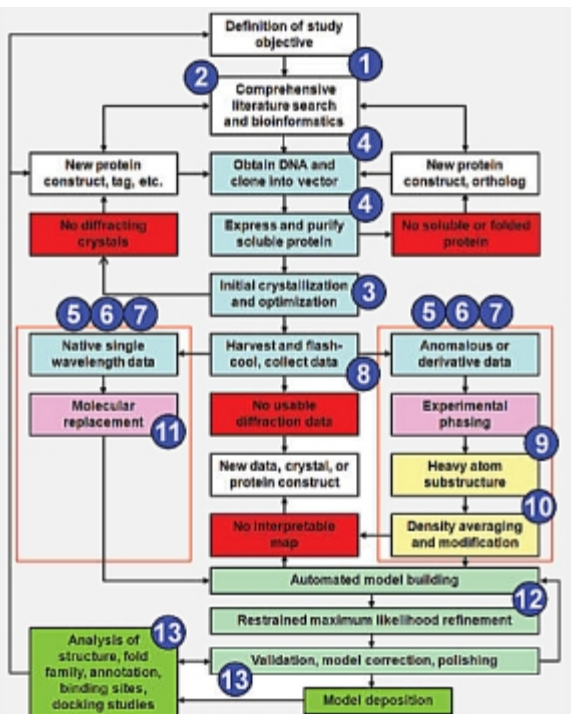
Chapter 3: Protein Crystallization. I found this chapter to be a good survey of modern crystallization techniques with a good section the physical chemistry of crystallization.

Chapter 4: Proteins for Crystallography. Provides a comprehensive listing of the methods available when the information in Chapter 3 is insufficient for success.

Chapter 5: Crystal Geometry. Here we learn about crystal geometry, crystal symmetry and the relationship of the symmetry of the real space lattice to the reciprocal space lattice.

Chapter 6: Diffraction Basics. This chapter provides a detailed description of the relationship of the real space lattice and reciprocal space lattice, hence the relationship between the electron density in the crystal and diffraction data.





Chapter Flow Chart



Dr. Bernhard Rupp

Chapter 7: Statistics and Probability in Crystallography. I thought this was the best chapter because it provides a lucid discussion of the often misunderstood concepts in statistics and probability. Furthermore, the examples, as related to crystallography, make for easier understanding of these concepts.

Chapter 8: Instrumentation and Data Collection. While this is a good basic chapter on the subject, it is here that I found the historical error: imaging plates are reported as predating multiwire proportional counters, but to the best of my knowledge that is not true. A good description of crystal handling methods and cryocrystallography is provided. Described are both synchrotron and home lab data collection, both useful with an excellent section on data processing with modern tools.

Chapter 9: Reconstruction of electron density and the phase problem. Covers the solution of the phase problem and provides background information for the next two chapters.

Chapter 10: Experimental phasing. Here is the current state of the art in phasing methods, MAD, SAD, SIR, SIRAS, MIRAS, initial refinement and density modification.

Chapter 11: Non-crystallographic symmetry and molecular replacement. Provides a description of NCS and its usefulness in the solution and refinement stages. Also described is molecular replacement, the most popular method solving the phase problem.

Chapter 12: Model building and refinement. The penultimate chapter describes in detail the refinement and model building stages using a couple of good examples and current software packages. A review of chapter 7 is appropriate for this chapter.

Chapter 13: Structure analysis, validation and presentation. This final chapter details the pitfalls and traps of polishing and publishing a structure. Furthermore, a recent example of a falsified structure is presented with an explanation of the telltale signs of which every crystallographer should be aware.

Joseph D. Ferrara, Ph.D.



RuppWeb.org Site



To subscribe to this newsletter or cancel your subscription, [e-mail the webmaster](#).

**Rigaku Americas**

e-mail: [info@Rigaku.com](mailto:info@Rigaku.com)

Tel: (281) 362-2300

**Rigaku Europe**

e-mail: [info@Rigaku.com](mailto:info@Rigaku.com)

Tel: +[44] 1732 763 367

**Rigaku Corporation**

e-mail: [rinttyo@rigaku.co.jp](mailto:rinttyo@rigaku.co.jp)

Tel: +[81] 3-3479-0618

**Rigaku China**

e-mail: [info@rigaku.com.cn](mailto:info@rigaku.com.cn)

Tel: +[86] 010-82800840