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### Continuing Education Webinar



#### Structure Solution and Refinement with Phenix

Presenter: Dr. Paul Adams  
August 26th at 1PM EDT  
(16:00 GMT)

Phenix is a Python-based software system for the solution and refinement of crystallographic structures using X-ray and/or neutron diffraction data. Recent developments in Phenix, especially in the refinement program phenix.refine, are presented. These include real space target functions for refinement, the use of torsion angle constraints, and the application of additional restraints to improve structure refinement at low resolution. The integration of automated side chain rotamer correction into the refinement process will also be described.

### Grant/Funding Preparation

Times change and so do research bottlenecks. A situation and needs analysis is the first step in advancing your lab's crystallographic capabilities.



July 27, 2010. The Protein Structure Initiative (PSI) has been churning out protein structures since 2000, but its [next five-year, US\\$290-million initiative](#) will pair its 13 protein-structure research centers with a network of biologists in universities and industry in the hope of solving some of the world's most troublesome and medically relevant proteins — including the G protein-coupled receptors.

July 26, 2010. An interdisciplinary team of Boston University professors, including crystallographer Karen Allen, is launching a project to develop new ways to [target protein-protein interactions with synthetic organic drugs](#). Financed by a four-year \$1.6 million grant from the National Institutes of Health, the goal is to develop new approaches for discovering "drug-like" small molecule inhibitors against challenging protein-protein interaction (PPI) interfaces.

July 26, 2010. New investigations, initiated by research workers at CIC bioGUNE and led by Dr. Aitor Hierro, have opened possibilities for making progress in the knowledge and prediction of neurodegenerative diseases by describing the [structure of Vps54](#), one of the four proteins making up the GARP complex.

July 15, 2010. Researchers, led by assistant professor Ekaterina Heldwein at Tufts University and Gary Cohen at the University of Pennsylvania, determined the unusual [crystal structure of the gH ectodomain bound to gL from herpes simplex virus 2](#).

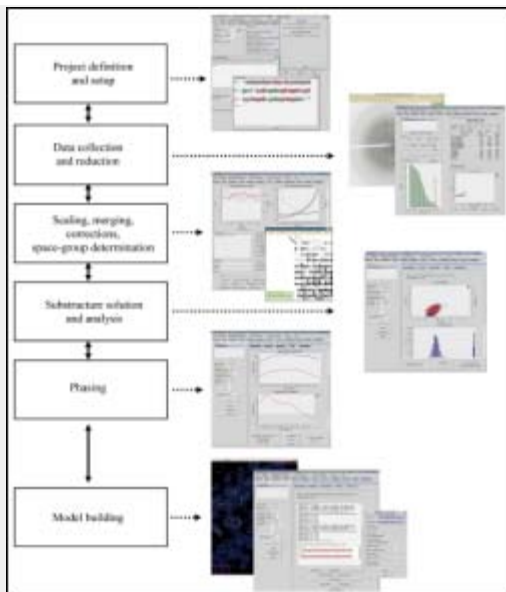
July 8, 2010. Argonne wins an R&D 100 Award for a breakthrough in protein crystallography: the [Hard X-ray Mini-beam Quad Collimator](#). Principal developers from Argonne include crystallographers: Nagarajan Venugopalan, Ruslan Sanishvili, Michael Becker and Craig Ogata, as well as Janet L. Smith from the University of Michigan.

July 1, 2010. Work by John Sutherland and his colleagues at the University of Manchester, UK provides new crystallographic evidence to support the emergence of the ["RNA world"](#) 4 billion years ago. The research pursues a long tradition, stretching back to the Miller-Urey experiments of the 1950s, of attempting to reproduce primordial pre-biotic chemistry and to generate the stuff of life spontaneously from it.

### HKL-3000R: semi-auto pipeline for structure determination

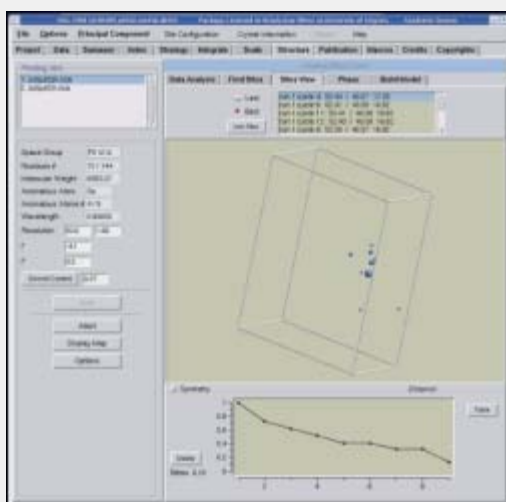
Rigaku is proud to announce a new agreement with HKL Research to integrate and distribute HKL-3000 with our protein crystallography systems. HKL-3000R represents a new approach, integrating data collection, data reduction, phasing and model building to significantly accelerate the process of structure determination and on average minimize the number of data sets and synchrotron time required for structure solution.

The system, when run in semiautomatic mode, provides the experimenter the ability to check the most important parameters defining the quality of the diffraction data and gives insight into the particular steps of the structure elucidation process. Using the default settings of the program will, in most cases, result in a highly complete model of a macromolecule. Moreover, such a semiautomatic pipeline of structure determination at every step provides feedback to the experimenter and, in the worst case, shows why a particular experiment failed, which is not possible in the case of "brute force" automation.



Raw-image data reduction and analysis is performed by the standard HKL-2000? package. For projects of known protein sequence, the system suggests the optimal input parameters for each step and provides sophisticated analysis of the outcome of each step. The analysis of results from each step is used to optimize input parameters for every subsequent step. The experimenter has the ability to adjust hundreds of parameters. Moreover, results can be sorted in several ways, one solution may be compared with others and any solution can be selected for subsequent steps.

[Request more information](#) on the new HKL-3000R software package.



## Lab spotlight: UT Southwestern Medical Center

As one of the world's foremost research institutions, UT Southwestern Medical Center (UTSWMC) is leading the way in a new era of scientific discovery in the 21st century. Their biomedical research has yielded dramatic discoveries that hold great promise for understanding the nature of human disease. For basic or clinical research, UT Southwestern — an institution that fosters multidisciplinary approaches and rigorous scientific training — provides an ideal research environment.

UTSWMC focuses on attracting and retaining pre-eminent researchers, while maintaining a culture environment that promotes research in diverse areas. They have four Nobel Laureates (three of whom are active faculty members), 18 members of the National Academy of Sciences, and 18 members of its Institute of Medicine (as of June 2009). UTSWMC also has more than 3,500 research projects under way with more than \$400 million in annual funding.

UT Southwestern Medical Center is distinguished by the quality of its biomedical research, which consistently ranks among the best in the world. Shanghai Jiao Tong's Academic Ranking of World Universities places UTSWMC 6th in the world for the impact and quality of research in the Life Sciences. Thomson Science Watch ranks UTSWMC 7th for the average quality of its research as measured by citations per paper.

Members of the structural biology department who are involved in protein crystallography include: [Johann Deisenhofer](#), [Kevin Gardner](#), [Elizabeth Goldsmith](#), [Youxing Jiang](#), [Zbyszek Otwinowski](#), [Rama Ranganathan](#), [Jose Rizo-Rey \(Josep Rizo\)](#), [Michael Rosen](#), [Diana Tomchick](#) and [Hong Zhang](#).

## Useful links for crystallography

[ProteinStructures](#) is an educational site that addresses some basic questions on the subjects of structural biology, structural bioinformatics and protein structure and function. These include the basic principles of protein structure, amino acid sequence and sequence-structure relationships, homology modeling, basic principles of drug discovery, protein crystallization and protein tertiary structure determination by X-ray crystallography. Several tutorials on sequence alignment and homology modeling are intended to help you get acquainted with various internet resources and their application in the analysis of protein structure and function.



UTSWMC's four Nobel Laureates: Alfred Gilman, Joseph L. Goldstein, Johann Deisenhofer, Michael S. Brown.

## Rigaku Hardware Training Courses

Rigaku has scheduled our next training session, 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.

### Software Webinars Available On-demand

Our Spring 2010 webinar program featured well known expert presenters in a mini-series devoted to commonly used data processing packages.

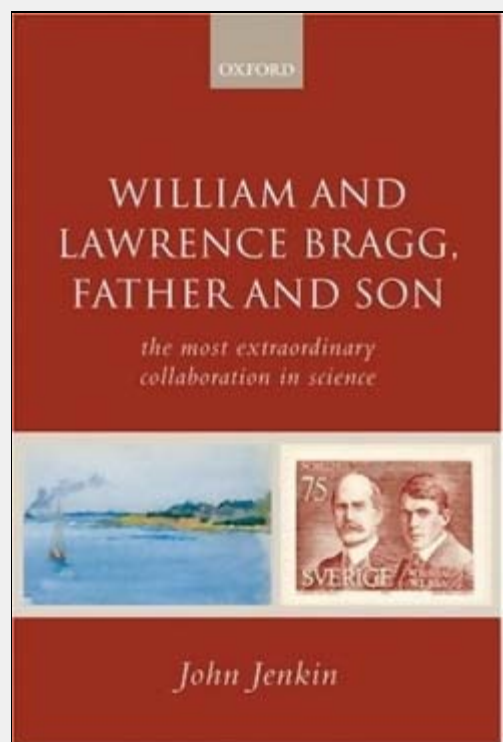
## SURVEY QUESTION

**What do you consider to be the most influential book in macromolecular crystallography?**

- Protein Crystallography, Blundell & Johnson
- Practical Protein Crystallography, McRee
- Principles of Protein Crystallography, Drenth
- Crystallography Made Crystal Clear, Rhodes
- Biomolecular Crystallography, Rupp

[Take survey](http://www.surveymonkey.com/s/julysurvey1)  
or cut-and-paste

<http://www.surveymonkey.com/s/julysurvey1>  
into your browser.



## Selected recent crystallographic papers

HKL-3000: the integration of data reduction and structure solution — from diffraction images to an initial model in minutes. Minor W, Cymborowski M, Otwinowski Z and Chruszcz M. *Acta Crystallogr D Biol Crystallogr.* 2006; **62**: 859-866.

To automate or not to automate: this is the question. M. Cymborowski, M. Klimecka, M. Chruszcz, M. D. Zimmerman, I. A. Shumilin, D. Borek, K. Lazarski, A. Joachimiak, Z. Otwinowski, W. Anderson and W. Minor. *J Struct Funct Genomics.* 2010; DOI 10.1007/s10969-010-9092-9.

Biochemistry: old gate gets a new look. Simone Weyand and So Iwata. *Science.* 2010; **329** (5988): 151-152.

Slow cooling and temperature-controlled protein crystallography. Matthew Warkentin and Robert E. Thorne. *Journal of Structural and Functional Genomics.* 2009; **11** (1): 85-89.

Protein crystallography reveals a role for the F50 cluster of *Escherichia coli* nitrate reductase a (NarGHI) in enzyme maturation. RA Rothery, MG Bertero, T Spreter, N Bouromand, NCJ Strynadka and JH Weiner. *The Journal of Biological Chemistry.* 2010; **285**: 8801-8807.

Prediction of protein crystallization outcome using a hybrid method. FH Zucker, C Stewart, J dela Rosaa, J Kima, L Zhanga, L Xiaoa, J Rossa, AJ Napulia, N Muellera, LJ Castaneda, SR Nakazawa Hewitta, TL Arakakia, ET Larsona, E Subramaniana, CLMJ Verlindea, E Fana, FS Bucknera, WC Van Voorhisa, EA Merritta and WGJ Hol. *Journal of Structural Biology.* 2010; **171** (1): 64-73.

Structure of full-length class I chitinase from rice revealed by X-ray crystallography and small-angle X-ray scattering. Y Kezuka, M Kojima, R Mizuno, K Suzuki, T Watanabe and T Nonaka. *Proteins: Structure, Function, and Bioinformatics.* 2010; **78**: 2295-2305.

Crystal growth procedure of HIV-1 protease-inhibitor KNI-272 complex for neutron structural analysis at 1.9 Å resolution. N Shimizu, S Sugiyama, M Maruyama, Y Takahashi, M Adachi, T Tamada, K Hidaka, Y Hayashi, T Kimura, Y Kiso, H Adachi, K Takano, S Murakami, T Inoue, R Kuroki, Y Mori and H Matsumura. *Crystal Growth & Design.* 2010; **10** (7): 2990-2994.

## Book reviews:

*William and Lawrence Bragg, Father and Son:  
the most extraordinary collaboration in science*

by John Jenkin, Oxford University Press, 2008,  
ISBN: 978-0-19-923520-9

I remember seeing *William and Lawrence Bragg* just after its publication in 2007 but had forgotten about it until I recently found a copy on Amazon. I learned a lot from this book about the origins of X-ray crystallography, history that predates the last biography I read about a crystallographer: *J. D. Bernal: The Sage of Science* by Andrew Brown.

While William Bragg was a brilliant scientist in his own right—for example, he applied the Fourier transform to diffraction data in later years—it was his son Lawrence who explained Max von Laue's experimental results, deriving in 1912 what we today call Bragg's Law. Even more amazing to me is the fact that he did this during his first year as a fellow at Cambridge. Lawrence is the youngest scientist to have won a Nobel Prize, awarded when he was just twenty-five years old.

The first half of the book chronicles William's life until he returned to his homeland, England, after twenty-three years at the University of Adelaide. Author Jenkin goes on to describe the overlapping lives of William and his

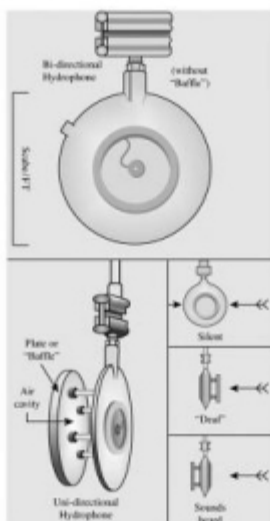


Fig. 17.5 Two forms of the portable directional hydrophone developed by the British during The Great War. (top) Mark II developed by Commander Ryan and the Navy, (below) Mark I due to Professor Bragg and the RBR. (From Sir William Bragg, *The World of Sound*, Bell & Sons, 1920, p. 175.)

William generously invited Ryan to join him in applying for a patent for the Mark I PHL,<sup>254</sup> and he also honoured the earlier work of the RBR by joining Rutherford in a patent application for the simple hydrophone.<sup>255</sup> In May

<sup>254</sup>W. H. Bragg and C. P. Ryan, 'Improvements in apparatus for detecting the direction of sounds in water', British patent no. 364,067, 1908, Patent Office, London.  
<sup>255</sup>W. H. Bragg and E. Rutherford, 'Improvements in apparatus for detecting the direction of sound in water', British patent no. 125,446, 1916, Patent Office, London.

sons Lawrence and Robert, who was killed at Gallipoli during World War I. Unlike the first half, this part of the book is not laid out in chronological order, so you have to pay attention to the dates.

The most exciting part of the book is the final third. Students of crystallography could learn just about everything they need from this section. Jenkin, a retired physicist from La Trobe University in Melbourne, Australia, shows how Lawrence formulated the theory of diffraction and began to solve structures by inspection. During WWI, Lawrence contributed to the war effort by developing sounding methods for locating German artillery.

As director of the Cavendish Laboratory at Cambridge, Lawrence cultivated the crystallography program in the UK. Among his proudest moments were the 1962 Nobel prizes in Chemistry for the structures of hemoglobin and myoglobin, and in Physiology or Medicine for the structure of DNA, both awarded to members of labs he headed.

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