

Crystallography Times

Rigaku

Protein Crystallography Newsletter
Volume 3, No. 1, January 2011

In this issue:

- [Crystallography in the news](#)
- [Crystallization, workflows and data management](#)
- [Lab spotlight: Stubbs Lab @ University of Halle](#)
- [Useful links: SAXS](#)
- [Continuing education opportunities](#)
- [European user group meeting](#)
- [Last month's survey results](#)
- [Survey question of the month](#)
- [January crystallographic papers](#)
- [Book reviews](#)



Continuing Education Webinar [Protein Crystallography: Getting in on the Ground Floor](#)

Presenter: Dr. Brian Matthews
February 23, 2011
1 PM EST (6:00 GMT)

Brian Matthews, Professor of Physics at the University of Oregon, uses X-ray crystallography, in concert with other techniques, to address some of the fundamental problems in biology: How do proteins spontaneously fold into their biologically active three-dimensional configurations? What determines the stability of these folded proteins? Can stability be improved? How do proteins interact with each other? How do proteins interact with DNA? How do enzymes interact with their substrates and act as catalysts?

Macromolecular Crystallography Training Class

March 23-25, 2011
October 26-28, 2011
The Woodlands, Texas

This class is 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, X-ray generators, and software. Class will also feature a training session on processing data with HKL.

CrystalTrak™ Workflow

Crystallography in the news



January 5, 2011. Mustafa Koeksal and David Christianson at the University of Pennsylvania, Yinghua Jin and Robert Coates of the University of Illinois and Rodney Croteau of Washington State University solved the [crystal structure of taxadiene synthase](#), an enzyme key to terpene biosynthesis in many living organisms, confirming a theoretically predicted link between two enzyme classes in the evolution of compounds such as the natural product anticancer drug Taxol.

January 10, 2011. The Alzheimer's Drug Discovery Foundation (ADDF) has awarded a \$300,000 grant to the Spanish structural biology company Oryzon for its program investigating new therapeutic approaches for Alzheimer's disease. Oryzon, a spin-off of the University of Barcelona and CSIC, employs an approach that [targets a newly discovered protein LSD1](#), which plays a role in regulating the expression of crucial genes that neurons need to keep alive.

January 17, 2011. Researchers from the Universities of Dundee and Oxford, led by Dundee Life Sciences Professor William Hunter and coordinator of the EU-funded Aeropath project, have made a significant breakthrough in understanding how resistance to antibiotics might be overcome by producing the first ever [3D molecular image of the penicillin binding protein PBP3](#) (from *Pseudomonas aeruginosa*) and showing how drugs bind to it.

January 19, 2011. Researchers led by Prof. Eric Oldfield at the University of Illinois, in collaboration with researchers in Taiwan, have determined the [structure and mechanism of the enzyme dehydrosqualene synthase \(CrtM\)](#), from the *Staphylococcus aureus* bacterium, that performs the crucial first step in the formation of cholesterol and a key virulence factor in staph bacteria.

January 20, 2011. A team of scientists at The Scripps Research Institute and the University of Virginia, led by Mark Yeager, M.D., Ph.D., a Scripps Research professor and staff cardiologist and chair of the Molecular Physiology and Biological Physics Department at The University of Virginia School of Medicine, has determined the [structure of the protein package \(capsid\) that delivers the genetic material of the human immunodeficiency virus \(HIV\) to human cells](#).

January 24, 2011. Mitegen LLC, a provider of consumables for X-ray diffraction, crystallography and protein crystallization to academic, pharmaceutical, industrial and government researchers around the world, announced that [Robert Newman](#) has been appointed to the role of chief executive officer (CEO).

January 24, 2011. Researchers at The Wistar Institute, led by Prof. Ronen Marmorstein, are the first to describe the complete atomic [structure formed by a yeast HAT, known as Rtt109, and one of its associated proteins](#). Their findings demonstrate how a particular histone acetylation event works, a crucial step to understanding epigenetics and the related processes that underlie both health and disease.

Protein crystallization, workflows and data management in CrystalTrak™

Successful use of automation in protein crystallization usually requires standardized workflows that allow for systematic testing of the chemical space. CrystalTrak is a software system that is designed around workflows that have been developed in collaboration with some of the most successful



CrystalTrak is built around the protein crystallization workflow: Experimental design, liquid dispensing, imaging and optimization.

protein crystallization facilities worldwide.

The core idea is a circular workflow of experimental design, liquid dispensing, imaging and scoring followed by optimization. Each step of the workflow allows users to interact with the automation equipment by either setting parameters or reviewing results. Another important concept of CrystalTrak is that at each step information can be captured for further use. For example, if a crystallization hit is found in a plate, it takes only one mouse click to generate a printable report that contains all information related to the hit, such as screen composition, incubation conditions, and details about the protein sample.

If you want to learn more about CrystalTrak, we would like to point you to a recent series of videos, including an [overview](#), [setup of experiments](#), a discussion on [imaging and scoring](#) and demonstration on [fine screen optimization](#).

[Request more information](#) on Rigaku CrystalTrak.

Lab spotlight: Stubbs Lab @ Martin Luther University of Halle – Wittenberg

The main interests of [Professor Milton Stubbs' lab](#) lie in the field of "rational drug design," where they try to fuse the experimental structural data and thermodynamic measurements of protein ligand interactions in a computational framework to advance the drug discovery process. Structure determinations of various members of serine proteinases have provided a basis for computer-based drug design within this class of enzymes. In many proteins of interest, however, this course is blocked through a lack of suitable crystals. As a strategy for circumventing such problems, they are investigating the use of surrogate proteins for studying protein-ligand interactions. To test the feasibility of this approach, they have chosen bovine trypsin as a scaffold to reconstruct the ligand binding site of factor Xa.

Useful links for crystallography

[Small Angle X-ray Scattering](#) (eds. Glatter & Kratky) can be freely (and legally) downloaded. The book provides a good basic introduction to SAXS, followed by detailed fundamental theoretical and experimental aspects, as well as methods for data evaluation and description of special experimental techniques. Specific applications, for example biological macromolecules, are covered at the end of the book.

Selected recent crystallographic papers

Structural and thermodynamic characterization of metal ion binding in *Streptococcus suis* Dpr. Haikarainen, Teemu; Thanassoulas, Angelos; Stavros, Philemon; Nounesis, George; Haataja, Sauli; Papageorgiou, Anastassios C. *Journal of Molecular Biology*, Jan2011, **405**(2): 448-460. <http://dx.doi.org/10.1016/j.jmb.2010.10.058>

Alternate states of proteins revealed by detailed energy landscape mapping. Tyka, Michael D.; Keedy, Daniel A.; André, Ingemar; DiMaio, Frank; Song, Yifan; Richardson, David C.; Richardson, Jane S.; Baker, David. *Journal of Molecular Biology*, Jan2011, **405**(2): 607-618. <http://dx.doi.org/10.1016/j.jmb.2010.11.008>

Optimal molecular structures of prion AGAAAAGA amyloid fibrils formatted by simulated annealing. Zhang, Jiapu. *Journal of Molecular Modeling*, Jan2011, **17**(1): 173-179. <http://dx.doi.org/10.1007/s00894-010-0691-y>

The crystal structure of the ubiquitin-like (UbL) domain of human homologue A of Rad23 (hHR23A) protein. Chen, Yu Wai; Tajima, Toshitaka; Agrawal,



Top image is the Stubbs Lab group logo, which is borrowed from the city of Halle. The logo is based on the city's history of selling salt but "but as everyone can see, it really represents the lunes of an X-ray pattern. A recent photo of group is shown below the crest.

European User Group Meeting February 23-24, 2011 Frankfurt, Germany

The European User Group Meeting (EUGM) serves as a discussion forum between leading scientists in structural biology and Rigaku representatives, and will cover both X-ray techniques and automated protein crystallization. Speakers include Oliver Einsle, University of Freiburg; Jeremy Moore, Imperial College London; Dmitri Svergun (pictured), EMBL Hamburg; Samar Hasnain, University of Liverpool; Klaus Fütterer, University of Birmingham; Arwen Pearson, University of Leeds; and Michael McDonough, University of Oxford.



Dr. Dmitri Svergun

Wladek Minor from University of Virginia will give an introduction to structure solution in HKL-3000 alongside hands-on sessions using lab data provided by the attendees. Everybody is invited to bring their own data to take advantage of this exciting opportunity.

Attendance to the EUGM is free of charge, but space is limited.

December Survey Results

What is your most common method for solving protein structures (choose one)?

Molecular replacement	70.8%
MAD phasing from synchrotron data	4.2%
SAD phasing from synchrotron data	20.8%
SAD phasing at home	0.0%
MIR at home	4.2%

Survey Question of the Month

Some space groups are more "fun" than others. Which space group is your favorite?

☐ P2(1)2(1)2(1)

☐ P2(1)2(1)2

☐ P2(1)

☐ R32

☐ P1

☐ I4

☐ Other

[Take Survey](#)
or cut-and-paste

Seema. *PEDS: Protein Engineering, Design & Selection*, Jan2011, **24**(1/2): 131-138.

<http://dx.doi.org/10.2210/pdb2wyq/pdb>

A generic approach to evaluate how B-cell epitopes are surface-exposed on protein structures. Lollier, Virginie; Denery-Papini, Sandra; Larré, Colette; Tessier, Dominique. *Molecular Immunology*, Jan2011, **48**(4): 577-585.

<http://dx.doi.org/10.1016/j.molimm.2010.10.011>

Regulation and structure of YahD, a copper-inducible α/β serine hydrolase of *Lactococcus lactis* IL1403. Martinez, Jacobo; Mancini, Stefano; Tauberger, Eva; Weise, Christoph; Saenger, Wolfram; Solioz, Marc. *FEMS Microbiology Letters*, Jan2011, **314**(1): 57-66.

<http://dx.doi.org/10.1111/j.1574-6968.2010.02144.x>

Nickel-quinolones interaction. Part 4 — Structure and biological evaluation of nickel(II)-enrofloxacin complexes compared to zinc(II) analogues. Skyrianou, Kalliopi C.; Psycharis, Vassilis; Raptopoulou, Catherine P.; Kessissoglou, Dimitris P.; Psomas, George. *Journal of Inorganic Biochemistry*, Jan2011, **105**(1): 63-74.

<http://dx.doi.org/10.1016/j.jinorgbio.2010.09.007>

Challenges in the determination of the binding modes of non-standard ligands in X-ray crystal complexes. Malde, Alpeshkumar K.; Mark, Alan E.. *Journal of Computer-Aided Molecular Design*, Jan2011, **25**(1): 1-12.

<http://dx.doi.org/10.1007/s10822-010-9397-6>

Crystal structure of the zinc-, cobalt-, and iron-containing adenylate kinase from *Desulfovibrio gigas*: a novel metal-containing adenylate kinase from Gram-negative bacteria. Mukhopadhyay, A.; Kladova, A.; Bursakov, S.; Gavel, O.; Calvete, J.; Shnyrov, V.; Moura, I.; Moura, J.; Romão, M.; Trincão, J. *Journal of Biological Inorganic Chemistry*, Jan2011, **16**(1): 51-61.

<http://dx.doi.org/10.1007/s00775-010-0700-8>

A hybrid structural model of the complete *Brugia malayi* cytoplasmic asparaginyl-tRNA synthetase. Crepin, Thibaut; Peterson, Francis; Haertlein, Michael; Jensen, Davin; Wang, Cheng; Cusack, Stephen; Kron, Michael. *Journal of Molecular Biology*, Jan2011, **405**(4): 1056-1069.

<http://dx.doi.org/10.1016/j.jmb.2010.11.049>

Amyloid fibril recognition with the conformational B10 antibody fragment depends on electrostatic interactions. Haupt, Christian; Morgado, Isabel; Kumar, Senthil T.; Parthier, Christoph; Bereza, Magdalena; Hortschansky, Peter; Stubbs, Milton T.; Horn, Uwe; Fändrich, Marcus. *Journal of Molecular Biology*, Jan2011, **405**(2): 341-348.

<http://dx.doi.org/10.1016/j.jmb.2010.10.059>

Benchmarking membrane protein detergent stability for improving throughput of high-resolution X-ray structures. Sonoda, Yo; Newstead, Simon; Hu, Nien-Jen; Alguet, Yilmaz; Nji, Emmanuel; Beis, Konstantinos; Yashiro, Shoko; Lee, Chiara; Leung, James; Cameron, Alexander D.; Byrne, Bernadette; Iwata, So; Drew, David. *Structure*, Jan2011, **19**(1): 17-25.

<http://dx.doi.org/10.1016/j.str.2010.12.001>

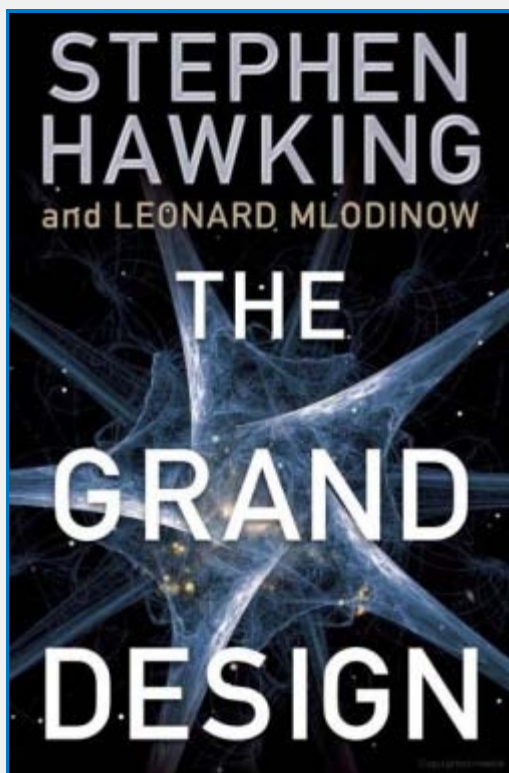
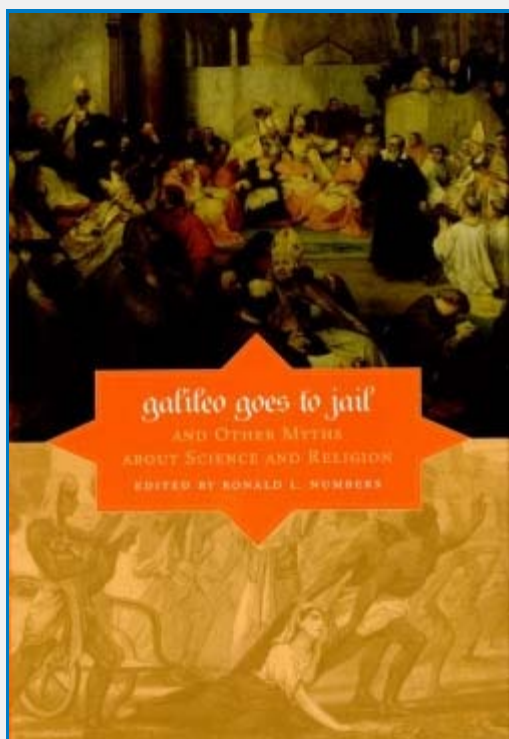
Atomic-level modelling of the HIV capsid. Pornillos, Owen; Ganser-Pornillos, Barbie K.; Yeager, Mark. *Nature*, 1/20/2011, **469**(7330): 424-427.

<http://dx.doi.org/10.1038/nature09640>

Packing space expansion of protein crystallization screening with synthetic zeolite as a heteroepitaxial nucleant. Michihiro Sugahara; Yuko Kageyama-Morikawa; Naoki Kunishima. *Crystal Growth & Design*, Jan2011, **11**(1): 110-120.

<http://dx.doi.org/10.1021/cg100987g>

High-throughput evaluation of the critical micelle concentration of detergents. Jumpertz, Thorsten; Tschapek, Britta; Infed, Nacera; Smits, Sander H.J.; Ernst, Robert; Schmitt, Lutz. *Analytical Biochemistry*, Jan2011, **408**(1): 64-70.



<http://dx.doi.org/10.1016/j.ab.2010.09.011>

Assisted crystal growing by tempering metastable vapor-liquid fluids.
Odriozola, Gerardo; Jiménez-Ángeles, Felipe; Orea, Pedro. *Chemical Physics Letters*, Jan2011, **501**(4-6): 466-469.
<http://dx.doi.org/10.1016/j.cplett.2010.11.076>

Book review:

Galileo Goes to Jail and Other Myths about Science and Religion

edited by Ronald L. Numbers, Harvard University Press, 2009
ISBN: 978-0674033276

I don't know what I was thinking when I picked this book up. It is a set of twenty-five essays on how religion has not negatively impacted science. The fourth myth "That Medieval Islamic Culture Was Inhospitable to Science" seemed to have the properties of what I understand to be true so I thought there was promise. Myth 7, "That Giordano Bruno was the First Martyr of Modern Science" just about drove me mad.

The essayist, Jole Shackelford, makes the following arguments that debunk the myth. If you remember, Bruno was a priest who adopted the Copernican view and taught that the earth might not be the only planet with life, among other things. Shackelford suggests that Bruno wasn't the first scientist martyr because he wasn't a scientist, that this form of capital punishment was common practice anyway, and finally, that he was a priest and the Church could do what it wanted with him.

The essays give the appearance of being well researched but I felt as if I were reading a skit by a partisan political pundit purporting to provide a fair and balanced viewpoint. Moving onto a more interesting book, in my humble opinion.

The Grand Design

by Stephen Hawking and Leonard Mlodinow, Bantam Books, 2010
ISBN: 978-0553805376

From a technical perspective this book is a relatively easy read. It has lots of good pictures and no math, except a definition of p similar to the Indiana legislature's old value. However, don't be fooled, as the philosophical implications are profound. The authors start by introducing the question of why does the universe behave the way it does. Next they pass through history and the development of the laws that we think describe the behavior of the universe: Aristotle's, Newton's, Einstein's and Feynman's theories, to string theory and ultimately M-theory, which is a combination of all the theories necessary to describe the behavior of the universe. The difficulty arises in the concepts of free will and causality.

Do we, as human beings, our brains driven by chemical reactions, which are further described by quantum fluctuations in our brains, have "free will"? Is my typing of this document a series of random probabilities? The other mind bender is the idea that observing an event forces the path of the event to become evident. In other words, observing the present impacts the past. I first came across this concept five years ago in Davies' *Cosmic Jackpot*. It still does not sit well.

Joseph D. Ferrara, Ph.D.

Tel: +[86] 010-82800840
FAX: +[86] 010-82800864

Tel: +[44] 1732 763 367
FAX: +[44] 1732 763 757