

# Crystallography Times

Rigaku

Protein Crystallography Newsletter  
Volume 2, No. 11, November 2010

## Crystallography in the news



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**November 3, 2010.** Researchers at Saint Louis University School of Medicine - led by Prof. Enrico Di Cera - have revealed for the first time the [molecular structure of the zymogen](#), or inactive, form of a blood-clotting enzyme, providing a missing link between the inactive zymogen form of thrombin and the mature enzyme generated upon vascular injury.

**November 8, 2010.** Through a host of collaborators including Brian K. Kobilka and Soren G. F. Rasmussen of Stanford University, a University of Wisconsin team led by Prof. Samuel H. Gellman in conjunction with Dr. Pii Seok Chae has developed a [new class of "tunable" detergents with quaternary carbon centers](#) as an aid to crystallization of membrane proteins. In unpublished work, Kobilka's team has used one of Gellman's detergents to help obtain structures of two different forms of a membrane-spanning G-protein-coupled receptor. Gellman's and Kobilka's teams together have applied for a patent on the new amphiphiles.

**November 10, 2010.** Oryzon, a leading biomarker discovery company in Spain, announced today that it has signed a non-exclusive license with Dyax Corp. (NASDAQ:DYAX), a developer of novel biotherapeutics for unmet medical needs, to [develop therapeutic antibody products using Dyax's proprietary technology, phage display](#), based on a non-exclusive license to use Dyax's human antibody libraries to discover antibodies and the right to commercially develop such antibody products.

**November 15, 2010.** BioVisions, a scientific visualization program at Harvard's Department of Molecular and Cellular Biology, has released their most recent animation, called [Powering the Cell: Mitochondria](#), which was produced in high definition and takes viewers on a swooping roller coaster ride through the microscopic machinery of the cell.

**November 18, 2010.** NovAliX SAS, a services firm employing X-ray protein crystallography, supramolecular mass spectrometry and organic chemistry, announced that it has entered into a definitive [agreement to acquire a majority interest in Graffinity Pharmaceuticals GmbH](#) of Heidelberg, Germany, a leading fragment based drug discovery services company.

**November 22, 2010.** University of Nebraska-Lincoln biochemist Mark Wilson, whose research involves a protein believed to play a critical role in causing mitochondrial abnormalities leading to Parkinson's and some cancers, has expanding his research with a [recent \\$1.35 million grant from the National Institutes of Health's National Institute of General Medical Sciences](#).

**November 25, 2010.** Leading a team working in the lab of Marat Yusupov at the Institute of Genetics and Molecular and Cellular Biology (IGBMC) in Strasbourg, Dr. Adam Ben-Shem has published a [structure for the eukaryotic ribosome](#) based on crystals obtained from a very fast and very gentle purification technique.

## Maximum detector value: R-AXIS HTC imaging plate

With a unique high-throughput design, the Rigaku R-AXIS HTC is arguably the best imaging plate (IP) detector ever engineered as a commercial product. Nothing matches its combination of large aperture, high dynamic range and speed at such a reasonable price and low cost-of-ownership. For crystallographers needing to stretch their funding, without sacrificing either throughput or data quality, the original digital area detector technology has



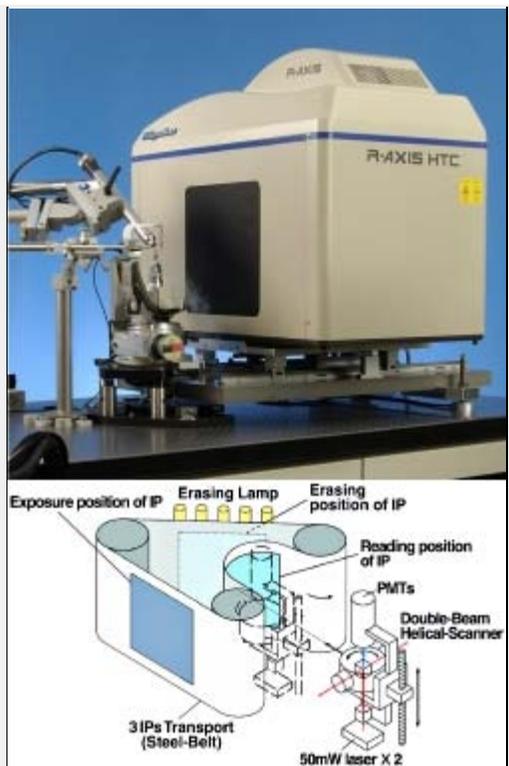
**Continuing Education Webinar**  
**Title to be Determined**  
**Presenter: Dr. Wladek Minor**  
**December 15, 2010**  
**10 AM EST (15:00 GMT)**

Wladek Minor, Professor of Molecular Physiology and Biological Physics at the University of Virginia, will provide fresh insights into the world of protein crystallography.

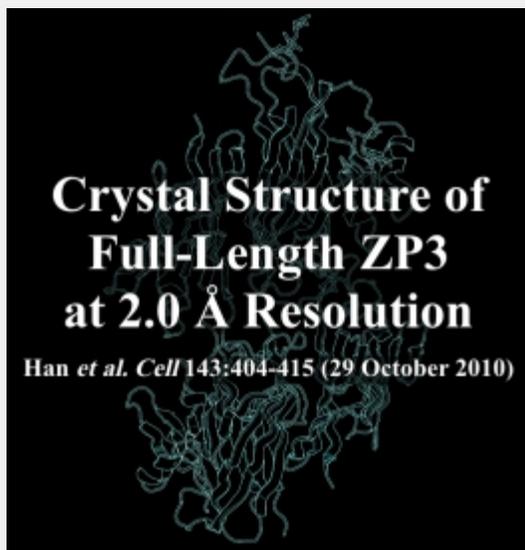
### Macromolecular Crystallography Training Class

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

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-2000** and **HKL-3000**.



Rigaku R-Axis HTC imaging plate detector (top) and operational schematic (bottom).



From the Jovine Lab at the Karolinska Institutet: insights into egg coat assembly and egg-sperm interaction from the X-Ray structure of full-length ZP3 (Han et al., 2010).

#### Reader Input on S-SAD Phasing

We are accumulating success stories for Cu S-SAD phasing and thus invite our readers to share their success stories with us. We would love to hear from you.

[Share Your Success Story](#)

much to offer.

**Three imaging plates for simultaneous expose, erase and readout**  
Imaging plates have a somewhat longer readout time as compared to CCD-based detectors. However, the R-Axis HTC's 3-plate system allows the duty cycle to be limited only by the speed of the transport of an IP from one position to the next. This makes for a detector system that is very efficient for experimental regimes where exposure times are in the range typically found within the home laboratory environment. In addition, the very large 300x300 mm aperture allows for many orders of Bragg reflections to be collected concurrently.

[Request more information](#) on the Rigaku R-Axis HTC.

### Lab spotlight: Jovine Lab @ Karolinska Institutet

Members of Dr. Luca Jovine's laboratory at the Karolinska Institutet (Department of Biosciences and Nutrition & Center for Biosciences, Huddinge, Sweden) study the molecular basis for the beginning of life. By marking the very beginning of a new individual, egg-sperm interaction at fertilization is a crucial step in the life cycle of all sexual organisms. Scanning electron microscopy pictures taken since the early 1960's have captured the collective imagination by offering low resolution glimpses of this event in humans. However, more than 40 years later, the molecular details underlying the species-specific embrace between mammalian germ cells remain obscure. The ultimate aim of their laboratory is to use structural biology to provide a definitive answer to this fundamental biological problem with important evolutionary implications.

[Luca Jovine, Ph.D.](#), group leader and EMBO young investigator has 1 postdoctoral fellow and 3 graduate students in his 6 person group. Prof. Jovine did his doctoral work at the MRC Laboratory of Molecular Biology in Cambridge with subsequent postdoctoral studies at Mount Sinai School of Medicine in New York.



### Useful links for crystallography

**Situs** is a modular and widely used software package for the integration of biophysical data across the spatial resolution scales ([review article](#)). It has been developed over the last decade with a focus on bridging the resolution gap between atomic structures, coarse-grained models, and volumetric data from low-resolution biophysical origins, such as electron microscopy, tomography, or small-angle scattering. Structural models can be created and refined with various flexible and rigid body docking strategies.

Initially developed 1998-1999 by Willy Wriggers, in collaboration with the research groups of Ron Milligan and Andy McCammon, Situs development was later carried on at The Scripps Research Institute (1999-2003), at the University of Texas-Houston (2003-2007) and since 2007 at various laboratories. Significant contributors are Willy Wriggers, Pablo Chacon, Mirabela Rusu, Jochen Heyd, Valerio Mariani, Julio Kovacs, Paul Boyle, and Stefan Birmanns.

## September Survey Results

SAXS is becoming a popular technique in structural biology labs for studying proteins in solution. Which of the following results do you consider to be the most important contribution from the SAXS experiment to a protein crystallographer (choose one)?

Determination of whether the protein is unfolded, flexible, or aggregated.	0.0%
Determination of molecular weight or radius of gyration	8.3%
<i>ab initio</i> shape determination; modeling missing residues in high resolution structures	8.3%
Conformational changes in solution, such as those that occur on binding ligands	83.3%

## Survey Question of the Month

If you had to choose only one scientific meeting to go to in the next 12 months, what would it be?

- ASCB, Philadelphia
- IUCr in Madrid, Spain
- ACA meeting, New Orleans
- Protein Society Meeting, Boston
- Protein Society Meeting, Stockholm
- CCP4 Study Weekend, London
- ICSG, Toronto
- Other (please specify)

[Take Survey](http://www.surveymonkey.com/s/nov_survey)

or cut-and-paste

[http://www.surveymonkey.com/s/nov\\_survey](http://www.surveymonkey.com/s/nov_survey)  
into your browser.

## Quick Puck Loader

The [Quick Puck Loader](#), invented at Structural Genomics Consortium at Toronto, is designed to load crystal mounted pins into the Rigaku style puck quickly while reducing the potential for mis-seating. This tool was designed to be used with both a Rigaku Puck and Puck Tong.

## Selected recent crystallographic papers

Structural underpinnings of nitrogen regulation by the prototypical nitrogen-responsive transcriptional factor NrpR. Wisedchaisri, Goragot; Dranow, David M.; Lie, Thomas J.; Bonanno, Jeffrey B.; Patskovsky, Yury; Ozyurt, Sinem A.; Sauder, J. Michael; Almo, Steven C.; Wasserman, Stephen R.; Burley, Stephen K.; Leigh, John A.; Gonen, Tamir. *Structure* Nov2010, **18**(11): 1512-1521. DOI: 10.1016/j.str.2010.08.014.

Dynamics connect substrate recognition to catalysis in protein kinase A. Masterson, Larry R; Cheng, Cecilia; Yu, Tao; Tonelli, Marco; Kornev, Alexandr; Taylor, Susan S; Veglia, Gianluigi. *Nature Chemical Biology* Nov2010, **6**(11): 821-828. DOI: 10.1038/nchembio.452.

Raman-assisted crystallography suggests a mechanism of X-ray induced disulfide radical formation and reparation. Carpentier, Philippe; Royant, Antoine; Weik, Martin; Bourgeois, Dominique. *Structure*, Nov2010, **18**(11): 1410-1419. DOI: 10.1016/j.str.2010.09.010.

Characterisation of individual pixel efficiency in the PILATUS II sensor. Schubert, A.; O'Keefe, G.J.; Sobott, B.A.; Kirby, N.M.; Rassool, R.P. *Radiation Physics & Chemistry* Nov2010, **79**(11): 1111-1114. DOI: 10.1016/j.radphyschem.2010.06.008.

Improved fitting of solution X-ray scattering data to macromolecular structures and structural ensembles by explicit water modeling. Grishaev, Alexander; Liang Guo; Irving, Thomas; Bax, Ad. *Journal of the American Chemical Society* 11/10/2010, **132**(44): 15484-15486. DOI: 10.1021/ja106173n.

Total chemical synthesis and X-ray structure of kalitoxin by racemic protein crystallography. Pentelute, Brad L.; Mandal, Kalyaneswar; Gates, Zachary P.; Kent, Stephen B. H. *Chemical Communications* Nov2010, **46**(43): 8174-8176. DOI: 10.1039/c0cc03148h.

Structural insights into substrate specificity in variants of N-acetylneuraminic acid lyase produced by directed evolution. Campeotto, Ivan; Bolt, Amanda H.; Harman, Thomas A.; Dennis, Cairiona; Trinh, Chi H.; Phillips, Simon E.V.; Nelson, Adam; Pearson, Arwen R.; Berry, Alan. *Journal of Molecular Biology* Nov2010, **404**(1): 56-69. DOI: 10.1016/j.jmb.2010.08.008.

Structures of mouse SOD1 and human/mouse SOD1 chimeras. Seetharaman, Sai V.; Taylor, Alexander B.; Holloway, Stephen; Hart, P. John. *Archives of Biochemistry & Biophysics* Nov2010, **503**(2): 183-190. DOI: 10.1016/j.abb.2010.08.014.

Structural and biochemical studies elucidate the mechanism of rhamnogalacturonan lyase from *Aspergillus aculeatus*. Jensen, Malene H.; Otten, Harm; Christensen, Ulla; Borchert, Torben V.; Christensen, Lars L.H.; Larsen, Sine; Leggio, Leila Lo. *Journal of Molecular Biology* Nov2010, **404**(1): 100-111. DOI: 10.1016/j.jmb.2010.09.013.

Surface layer protein characterization by small angle X-ray scattering and a fractal mean force concept: From protein structure to nanodisk assemblies. Horejs, Christine; Pum, Dietmar; Sleytr, Uwe B.; Peterlik, Herwig; Jungbauer, Alois; Tscheliessnig, Rupert. *Journal of Chemical Physics* 11/7/2010, **133**(17): 175102-175110. DOI: 10.1063/1.3489682.

Chemoenzymatic synthesis, inhibition studies, and X-ray crystallographic analysis of the phosphono analog of UDP-Galp as an inhibitor and mechanistic probe for UDP-galactopyranose mutase. Partha, Sarathy Karunan; Sadeghi-Khomami, Ali; Slowski, Kathryn; Kotake, Toshihisa; Thomas, Neil R.; Jakeman, David L.; Sanders, David A.R. *Journal of Molecular Biology* Nov2010, **403**(4): 578-590. DOI: 10.1016/j.jmb.2010.08.053.

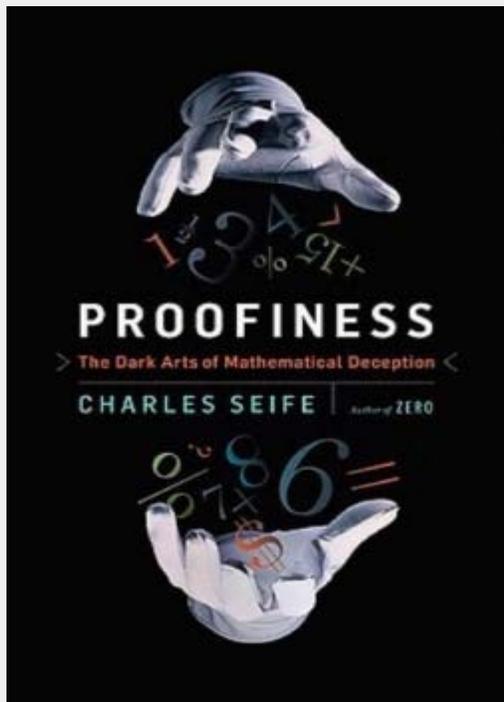
Structural characterization of the stem-stem dimerization interface between prolactin receptor chains complexed with the natural hormone. van Agthoven, Jan; Zhang, Chi; Tallet, Estelle; Raynal, Bertrand; Hoos, Sylviane; Baron, Bruno; England, Patrick; Goffin, Vincent; Broutin, Isabelle. *Journal of Molecular Biology* Nov2010, **404**(1): 112-126. DOI:



Just load pins directly into the [Quick Puck Loader](#), and then fit the Rigaku Puck right otop ... and use Puck tongs to firmly grasp and flip. Pins are perfectly seated. No more losing crystals. The device is currently used in labs from University Health Network (Canada), York University and the Structural Genomics Consortium.

The Quick Puck Loader is made of durable aluminum and comes with a 1-year warranty on the part. Colors available include red, blue and gold. Mixed colors are also available.

View [more information](#) on the new Quick Puck Loader.



10.1016/j.jmb.2010.09.036.

Structure and flexibility of the complete periplasmic domain of BamA: The protein insertion machine of the outer membrane. Gatzeva-Topalova, Petia Zvezdanova; Warner, Lisa Rosa; Pardi, Arthur; Sousa, Marcelo Carlos. *Structure* Nov2010, **18**(11): 1492-1501. DOI: 10.1016/j.str.2010.08.012.

The structural basis for membrane binding and pore formation by lymphocyte perforin. Law, Ruby H. P.; Lukoyanova, Natalya; Voskoboinik, Ilia; Caradoc-Davies, Tom T.; Baran, Katherine; Dunstone, Michelle A.; D'Angelo, Michael E.; Orlova, Elena V.; Coulbaly, Fasséli; Verschoor, Sandra; Browne, Kylie A.; Ciccone, Annette; Kuiper, Michael J.; Bird, Phillip I.; Trapani, Joseph A.; Saibil, Helen R.; Whisstock, James C. *Nature* 11/18/2010, **468**(7322): 447-451. DOI: 10.1038/nature09518.

## Book review:

*Proofiness: The Dark Arts of Mathematical Deception*

by Charles Seife, Viking, ISBN-13: 978-0-670-02216-8

I saw this book at the store and bought it for my wife. We had both read and enjoyed an earlier book by the same author, *Zero: The Biography of a Dangerous Idea*, and I expected this to be just as good. It was better - it is also the first "math" book I have ever read that made me laugh out loud. In all seriousness, though, it lays down a basis for interpreting mathematical information in the correct context. For crystallographers, this should be very familiar, but this interpretation applies to society in general, not just to scientific inquiry.

Seife first defines proofiness: "the art of using bogus mathematical arguments to prove something that you know in your heart to be true - even when it's not". He then cites numerous examples that we've all experienced in our lifetimes. In Chapter 1, "Phony Facts, Phony Figures" Seife defines disestimation as "the act of taking a number too literally, understating or ignoring the uncertainties that surround it" and provides several examples. In addition he demonstrates the problem with fruit picking data to give the answer one desires. Chapter 2, "Rorschach's Demon", Seife coins the word causuistry, "where the fault in the argument comes from implying that there is a causal relationship between two things when in fact there isn't any such linkage" and randomness: "in which one insists there is order when there is only chaos". Again examples are given, most from Nature and one from the The Wall Street Journal.

Chapter 3, "Risky Business" takes a look at understanding risk. Comparing the shuttle program and air traffic safety is one example. If the aviation industry had the same record as the shuttle program there would be 275 airplane crashes a year. This chapter also summarizes nicely the Enron affair and the current financial mess. The next two chapters, "Poll Cats" and "Electile Dysfunction" (not a typo!), are very interesting. The former introduces random and systematic error, and how they bias the results of polls. The latter analyzes the 2008 Minnesota Senate election, which resulted in a recount in favor of Franken vs. Coleman, which was really quite humorous, and the 2000 Bush vs. Gore recount in Florida. In the end, Seife suggests that the counts in Florida were much too close and a flip of a coin would have adequately reflected the will of the people.

Chapter 6, "An Unfair Vote," should upset you. It details the process of gerrymandering and how redistricting of the type that dilutes the will of the people will happen with the publication of the 2010 census. Chapter 7, "Alternate Realities" looks at how lawyers and judges are able to turn numbers upside down to win cases that would make no sense to anyone who actually paid attention to the numbers. The O.J. Simpson trial is given as one example of how lawyers confuse juries with bad statistics. In the last chapter, "Propaganda by the Numbers," Seife reviews the string of victories in Vietnam that led to the US pullout and why buying a Hummer 3 is greener than buying a Prius. Three appendices, "Statistical Error", "Electronic Voting" and "The Prosecutor's Fallacy," supplement the main text with detailed discussion on the particular topic. My wife says, "Believe nothing you hear and only half of what you see." This book will help you decide what half of what you see to believe.

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Joseph D. Ferrara, Ph.D.

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The Rigaku logo consists of the word "Rigaku" in a bold, blue, sans-serif font. The letter "R" is significantly larger and more stylized than the other letters, which are in a standard weight.

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