

Crystallography Times

Rigaku

Protein Crystallography Newsletter
Volume 3, No. 10, October 2011

Subscribe



In this issue:

- [Crystallography news summary](#)
- [Upcoming events](#)
- [Spotlight: Prof. Stephen Curry](#)
- [Useful links for crystallography](#)
- [Product: HKL-3000R](#)
- [Professional education opportunities](#)
- [Crystallographers in the news](#)
- [Science videos of the month](#)
- [Last month's survey results](#)
- [Survey question of the month](#)
- [October crystallographic papers](#)
- [Book review](#)

Mark Your Calendar New York Structural Biology Discussion Group: Seventh Winter Meeting

Wednesday, January 25, 2012
9:30 AM - 5:30 PM

The New York Academy of Sciences, presented by the New York Structural Biology Discussion Group. Registration is free, but may be limited by room size. Rigaku believes that this is an excellent meeting and highly recommends it to anyone who has a chance to attend.

Continuing Education Webinar



Home Lab SAD phasing w/ HKL3000: From data collection to refined models in <1h.

Presenter: Dr. Jim Pflugrath
November 17, 11AM EST
(16:00 GMT)

This interactive tutorial and webinar will demonstrate how to use HKL3000 to process diffraction images, find the anomalous substructure with SHELXD, phase with SHELXC, MLPHARE, and DM, then build with ARP/wARP and refine with REFMAC (Kudos to all the authors of these programs!).

Emphasis will be on practical tips and how to interpret the output. Relatively low redundancy diffraction datasets will be used as examples to dispel some of the myths about sulfur and selenium Home Lab SAD phasing.

Crystallography in the news

October 1, 2011. Three international teams of scientists, led by researchers at the University of California San Diego, University of Michigan and Stanford University, have published a trio of papers describing in unprecedented detail the [structure and workings of G protein-coupled receptors \(GPCRs\)](#). Researchers say the improved understanding of how GPCRs interact with G proteins will likely reveal new insights that can improve how related drugs function and also present new and previously unknown therapeutic targets.

October 3, 2011. Dr. Bruce A. Beutler, the new director of the Center for the Genetics of Host Defense at UT Southwestern Medical Center, shared the [Nobel Prize in Physiology or Medicine](#) with two other scientists for their discoveries of how the immune system works. Dr. Beutler and Dr. Jules A. Hoffmann of Strasbourg University's Institut de Biologie Moléculaire et Cellulaire in France shared half the prize for their discovery of receptor proteins that recognize disease-causing agents and activate innate immunity, the first step in the body's immune response. The other half went to the late Dr. Ralph M. Steinman of Rockefeller University in New York for his discovery of the dendritic cell and its role in adaptive immunity.

October 7, 2011. Researchers from Imperial College London used intense X-rays, generated by the Diamond synchrotron and the European Synchrotron Radiation Facility (ESRF), to determine for the first time the [structure of bacterial homologue of the Apical Sodium dependent Bile Acid Transporter \(ASBT\) protein](#), a target for hypercholesterolemia drugs since it can affect the level of cholesterol in the blood.

October 14, 2011. Have you ever wondered what nanotube chemistry might look like as a dance? Or fruit fly sex? Or protein X-ray crystallography? Look no further. As part of the 2011 Dance Your Ph.D. contest, scientists who study those phenomena and more have [converted their research into dance videos for enjoyment and edification](#). The 16 finalists will compete for a \$500 prize in each category, as well as the ultimate prize: an additional \$500 and a free trip to Belgium to be crowned the overall winner at TEDxBrussels on 22 November.

October 17, 2011. US researchers have dealt a [severe blow to the idea of a single "hydrophobic effect"](#) that can help explain how all drugs dock with proteins. A team led by Harvard University's George Whitesides has shown that water structures in binding pockets can cause hydrophobic interactions with thermodynamic behavior differing from a widely used model. One conclusion from that is that there is not one hydrophobic effect but a distribution of hydrophobic effects.

October 21, 2011. Dennis Burton, study leader and a professor at The Scripps Research Institute, along with Ian Wilson, member of the Skaggs Institute for Chemical Biology at Scripps Research, Katie J. Doores, a research associate in Burton's lab, and a team of researchers, has studied an [antibody capable of neutralizing the HIV virus](#). While previous studies have found antibodies that work against many different strains of HIV, the antibody discussed in this study, called PGT 128, is much more effective and potent than those previously discovered.

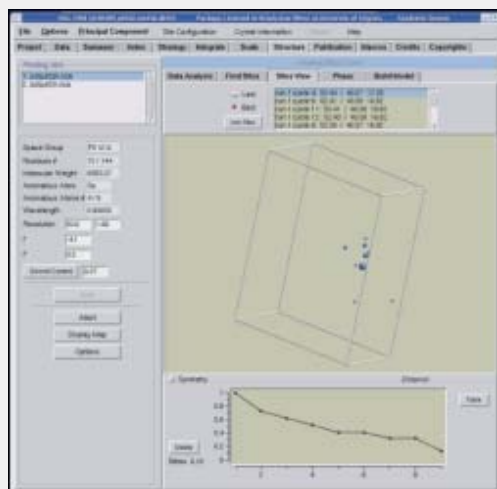
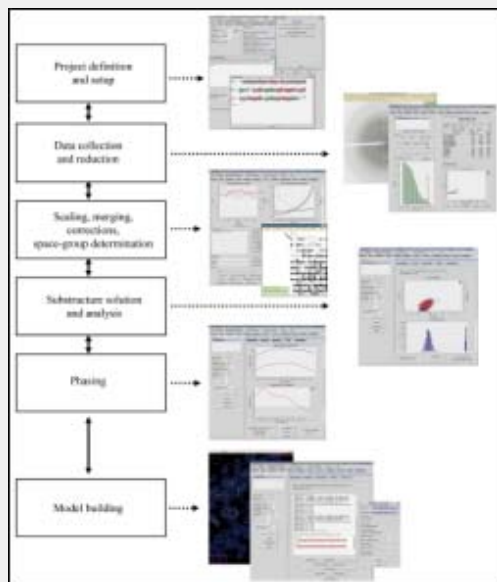
October 21, 2011. Researchers in Japan have determined the structural basis of the molecular defense system that protects insects from pathogens, which provides clarity on the molecular binding that underpins this defense system. Yoshiaki Yamaguchi of the RIKEN Advanced Science Institute and his colleagues used genetic engineering to produce the [β-glucan-binding regions of BGRPs](#) from two moth species, *Bombix mori* and *Plodia interpunctella*. They determined the structure of the receptors, both on their own and when bound to a β-glucan called laminarihexaose, using X-ray crystallography.

October 24th 2011. [Proteros biostructures GmbH](#) is further extending its business capacities by moving into a new building in Munich-Martinsried, one of the leading biotech locations in Germany. After a two-year planning period, Proteros has reached an important milestone in its development by centralizing all operations within a purpose-built facility. The 4,000m² of laboratory and office space, worth a total of about 15M€,

Macromolecular Crystallography Class

November 16-18, 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. This class will also feature a training session on processing data with HKL.



Crystallographers in the News

Dr. Rajan Sankarnarayana, senior scientist of CCMB (Center for Cellular and Molecular Biology) in Hyderabad, won the prestigious Shanti Swarup Bhatnagar award for science and technology this year. The Shanti Swarup Bhatnagar Prize for Science and Technology is awarded annually by the Council of Scientific and Industrial Research (CSIR) for notable and outstanding research, applied or fundamental, in biology, chemistry, environmental science, engineering,

has been optimally designed for Proteros' specific requirements in protein production, X-ray crystallography and kinetic analytics, as well as medicinal chemistry and own synthesis group.

October 25 2011. An international team including three Lawrence Livermore National Laboratory researchers has measured for the first time the spatial and temporal coherence of a [single femtosecond X-ray pulse generated by the first hard X-ray free-electron laser](#) (XFEL), the Linac Coherent Light Source (LCLS), at the SLAC National Accelerator Laboratory. The intense, coherent and ultra short X-ray pulses from XFELS point to new insights into biology, condensed matter physics and atomic physics. The technique has already been used to image single viruses and pointed to new approaches to protein crystallography using nanocrystals.

HKL-3000R: semi-automatic pipeline for structure determination

Rigaku customers – of new protein crystallography X-ray systems – now receive HKL-3000R, a package that runs the instrument, processes the data and provides structure solution and refinement capabilities. 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 in the spotlight: Prof. Stephen Curry

Imperial College London
Biophysics Section
Division of Cell and Molecular Biology
Department of Life Sciences
Faculty of Natural Sciences



[Stephen Curry's group](#) uses X-ray crystallography to see what the molecules of life look like and figure out how they work. Their main focus is on the molecular details of how certain RNA viruses cause infection and disease. For example, they work on cellular RNA-binding proteins such as PTB, La and Ebp1 that are press-ganged to help with viral translation. They also study viral enzymes, such as the 3C protease from foot-and-mouth diseases virus (FMDV).

Their investigations also encompass protein-drug interactions to try to understand what makes drugs stick to a particular protein target. Their work on human serum albumin (HSA), an abundant blood protein that binds and affects the action of many drugs, is helping to reveal the structural basis of its remarkably versatile binding capacity.

Useful links for crystallography

mathematics, medicine and Physics.

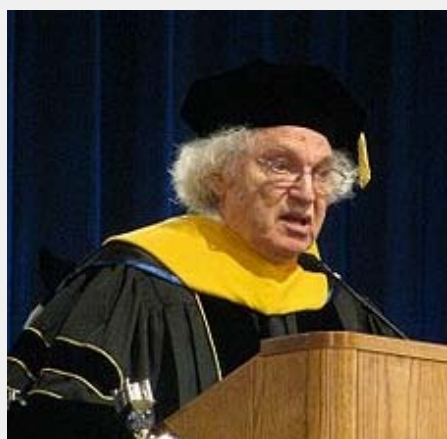
The purpose of the prize is to recognize outstanding Indian work in science and technology. It is considered the highest award for science in India. The award is named after the founder Director of the Council of Scientific & Industrial Research, Shanti Swarup Bhatnagar. It was first awarded in 1958. For Dr. Sankaranarayanan, the award recognizes his research in the field of translation of the genetic code and tuberculosis.



Senior scientist of CCMB Rajan Sankaranarayanan (right) with CCMB Director Ch. Mohan Rao (left).

— Obituary —

Herbert Aaron Hauptman, an American mathematician and crystallographer, died on October 23, 2011, at the age of 94. Hauptman was a co-winner of the Nobel Prize in Chemistry in 1985 for developing mathematical methods for deducing the molecular structure of chemical compounds.



Science Video

Scientists share their thoughts and stories with Stephen Curry about how they got interested in science, what keeps them going and what makes a good scientist. The trailer will get you interested and you won't be able to stop watching the film.

How to Write a Scientific Masterpiece by Ushma S. Neill, Executive Editor, The Journal of Clinical Investigation (Published December 3, 2007).

"I've been asked several times to give talks about various aspects of the scientific publishing enterprise, and sometimes to comment specifically on how to write a manuscript that will have maximal impact. While many in my audiences have felt that my presentations are designed for students and trainees, I hope everyone listens, as sometimes even established scientists are prone to making mistakes. I hope here to outline a few pointers that will help your manuscripts skate through the submission and peer review process. Some points may be elementary, but all bear repeating."

Selected recent crystallographic papers

Advances in Structural and Functional Analysis of Membrane Proteins by Electron Crystallography. Wisedchaisri, Goragot; Reichow, Steve L.; Gonen, Tamir. *Structure*, Oct2011, Vol. 19 Issue 10, p1381-1393. <http://dx.doi.org/10.1016/j.str.2011.09.001>

New developments in protein structure-function analysis by MS and use of hydrogen-deuterium exchange microfluidics. Landreh, Michael; Astorga-Wells, Juan; Johansson, Jan; Bergman, Tomas; Jörnvall, Hans. *FEBS Journal*, Oct2011, Vol. 278 Issue 20, p3815-3821. <http://dx.doi.org/10.1111/j.1742-4658.2011.08215.x>

In Vitro Evolved Non-Aggregating and Thermostable Lipase: Structural and Thermodynamic Investigation. Kamal, Md. Zahid; Ahmad, Shueb; Molugu, Trivikram Rao; Vijayalakshmi, Amash; Deshmukh, Mandar V.; Sankaranarayanan, Rajan; Rao, Nalam Madhusudhana. *Journal of Molecular Biology*, Oct2011, Vol. 413 Issue 3, p726-741. <http://dx.doi.org/10.1016/j.jmb.2011.09.002>

Recent contributions from solid-state NMR to the understanding of membrane protein structure and function. Judge, Peter J; Watts, Anthony. *Current Opinion in Chemical Biology*, Oct2011, Vol. 15 Issue 5, p690-695. <http://dx.doi.org/10.1016/j.cbpa.2011.07.021>

Cryo-electron tomography: gaining insight into cellular processes by structural approaches. Yahav, Tal; Maimon, Tal; Grossman, Einat; Dahan, Idit; Medalia, Ohad. *Current Opinion in Structural Biology*, Oct2011, Vol. 21 Issue 5, p670-677. <http://dx.doi.org/10.1016/j.sbi.2011.07.004>

Crystal Structure of Cardiac Troponin C Regulatory Domain in Complex with Cadmium and Deoxycholic Acid Reveals Novel Conformation. Li, Alison Yueh; Lee, Jaeyong; Borek, Dominika; Otwinowski, Zbyszek; Tibbits, Glen F.; Paetzel, Mark. *Journal of Molecular Biology*, Oct2011, Vol. 413 Issue 3, p699-711. <http://dx.doi.org/10.1016/j.jmb.2011.08.049>

Engineering an Ultra-Thermostable β_1 -Adrenoceptor. Miller, Jennifer L.; Tate, Christopher G. *Journal of Molecular Biology*, Oct2011, Vol. 413 Issue 3, p628-638. <http://dx.doi.org/10.1016/j.jmb.2011.08.057>

Structure of the Food-Poisoning *Clostridium perfringens* Enterotoxin Reveals Similarity to the Aerolysin-Like Pore-Forming Toxins. Briggs, David C.; Naylor, Claire E.; Smedley, James G.; Lukyanova, Natalya; Robertson, Susan; Moss, David S.; McClane, Bruce A.; Basak, Ajit K. *Journal of Molecular Biology*, Oct2011, Vol. 413 Issue 1, p138-149. <http://dx.doi.org/10.1016/j.jmb.2011.07.066>

Kinemage of action — Proposed reaction mechanism of glutamate-1-semialdehyde aminomutase at an atomic level. Sorensen, John L.; Stetefeld, Jörg. *Biochemical & Biophysical Research Communications*, Oct2011, Vol. 413 Issue 4, p572-576. <http://dx.doi.org/10.1016/j.bbrc.2011.09.003>

Biosynthesis, purification and characterization of β -fructofuranosidase from *Bifidobacterium longum* KN29.1. Jedrzejczak-Krzepkowska, Marzena; Tkaczuk, Karolina L.; Bielecki, Stanislaw. *Process Biochemistry*, Oct2011, Vol. 46 Issue 10, p1963-1972. <http://dx.doi.org/10.1016/j.procbio.2011.07.005>

Exploiting Protein Engineering and Crystal Polymorphism for Successful X-ray Structure Determination. Luc Bonnefond, Pascale Schellenberger, Jérôme Basquin, Gérard Demangeat, Christophe Ritzenthaler, Robert Chênevert, Christian Balg, Magali Frugier, Joëlle Rudinger-Thirion, Richard Giegé, Bernard Lorber, and Claude Sauter. *Crystal Growth & Design*, Oct2011, Vol. 11 Issue 10, p4334-4343. <http://dx.doi.org/10.1021/cg101468p>



<http://www.youtube.com/watch?v=dnAUixbXAXg>

Science Video

I'm a Scientist - The film



<http://www.youtube.com/watch?v=OzkN1KNK7e4>

September Survey Results

I participate in the following social networks:

Google+	23.1%
Facebook	61.5%
LinkedIn	53.8%
Twitter	7.7%
No, I'm anti-social	26.9%

Survey Question of the Month

Small Molecule Receptor Protein Tyrosine Phosphatase γ (RPTPy) Ligands That Inhibit Phosphatase Activity via Perturbation of the Tryptophan-Proline-Aspartate (WPD) Loop. Sheriff, Steven; Beno, Brett R.; Zhai, Weixu; Kostich, Walter A.; McDonnell, Patricia A.; Kish, Kevin; Goldfarb, Valentina; Gao, Mian; Kiefer, Susan E.; Yanchunas, Joseph; Huang, Yanling; Shi, Shuhao; Zhu, Shirong; Dzierba, Carolyn; Bronson, Joanne; Macor, John E.; Appiah, Kingsley K.; Westphal, Ryan S.; O'Connell, Jonathan; Gerritz, Samuel W. *Journal of Medicinal Chemistry*, Oct2011, Vol. 54 Issue 19, p6548-6562. <http://dx.doi.org/10.1021/jm2003766>

Construction and Crystal Structure of Recombinant STNV Capsids. Lane, Stephen W.; Dennis, Caitriona A.; Lane, Claire L.; Trinh, Chi H.; Rizkallah, Pierre J.; Stockley, Peter G.; Phillips, Simon E.V. *Journal of Molecular Biology*, Oct2011, Vol. 413 Issue 1, p41-50. <http://dx.doi.org/10.1016/j.jmb.2011.07.062>

Crystal Structures of an O-Like Blue Form and an Anion-Free Yellow Form of *pharaonis* Halorhodopsin. Kanada, Soun; Takeguchi, Yuu; Murakami, Midori; Ihara, Kunio; Kouyama, Tsutomu. *Journal of Molecular Biology*, Oct2011, Vol. 413 Issue 1, p162-176. <http://dx.doi.org/10.1016/j.jmb.2011.08.021>

Comparison of a molecular dynamics model with the X-ray structure of the N370S acid- β -glucosidase mutant that causes Gaucher disease. Offman, Marc N.; Krol, Marcin; Rost, Burkhard; Silman, Israel; Sussman, Joel L.; Futerman, Anthony H. *PEDS: Protein Engineering, Design & Selection*, Oct2011, Vol. 24 Issue 10, p773-775. <http://dx.doi.org/10.1093/protein/gzr032>

Crystal Structures of *Candida albicans* Dihydrofolate Reductase Bound to Propargyl-Linked Antifolates Reveal the Flexibility of Active Site Loop Residues Critical for Ligand Potency and Selectivity. Paulsen, Janet L.; Bendel, Stephen D.; Anderson, Amy C. *Chemical Biology & Drug Design*, Oct2011, Vol. 78 Issue 4, p505-512. <http://dx.doi.org/10.1111/j.1747-0285.2011.01169.x>

Structural anatomy of telomere OB proteins. Horvath, Martin P. *Critical Reviews in Biochemistry & Molecular Biology*, Oct2011, Vol. 46 Issue 5, p409-435. <http://dx.doi.org/10.3109/10409238.2011.609295>

PS1-110 The role of the human DEAD-box protein DDX3 in type I interferon induction. By: Gu, Lili; Oda, Shun-ichiro; Fullam, Anthony; Brennan, Ruth; Bowie, Andrew; Khan, Amir; Schröder, Martina. *Cytokine*, Oct2011, Vol. 56 Issue 1, p45-45. <http://dx.doi.org/10.1016/j.cyto.2011.07.143>

Book review:

The Hidden Reality: Parallel Universes and the Deep Laws of the Cosmos
by Brian Greene, 2011, ISBN-13: 978-0307265630

My wife has been asking me to explain string theory. I had been putting it off until I caught her watching a rerun of *The Big Bang Theory* in which the character Sheldon Cooper heckles the real Brian Greene at a sitcom-style book reading for *The Hidden Reality*. I had listened to an interview with the author on *Science Friday* a few months back and I already had the book. Now I figured I'd better read it.

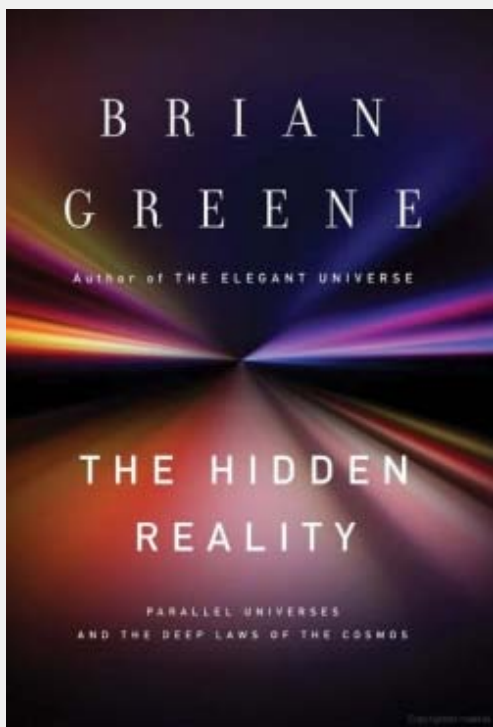
Greene sets the tone with a simple introduction that allows readers to skip ahead at various points. However, unless you really know this stuff, don't — the overview is worthwhile. Greene spends the rest of the book describing in detail the current models for nine possible multiverse theories and the philosophies that might come with them. The first of these multiverses is the Quilted Universe - a multiverse comprised of approximately 10^{500} universes in parallel with ours. In this multiverse, some versions of me are typing this book review and some aren't.

The second multiverse is the Inflationary Multiverse. I came to this section just a few days after the announcement of this year's Nobel Prize in physics to Perlmutter, Schmidt and Reiss for finding experimental evidence of inflation. In this multiverse, inflation causes the popping up of new universes, outside our field of view. In Chapter 4, the author gives us a lesson in string theory. String theory is an attempt to unify all four

Which do you think would be less painful (choose one)?

- ☐ Publishing an incorrect structure and facing the embarrassment of a retraction.
- ☐ Losing out to your intellectually challenged lab mate for a new faculty position at the university of your dreams.
- ☐ Being scooped on a structure that you have spent the last 2 years of your life working on.
- ☐ Stepping on a nail.

Take Survey
or cut-and-paste
http://www.surveymonkey.com/s/Oct_Survey
into your browser.



forces of nature by invoking six extra dimensions that are so small we can't see them. This allows for a description of gravity without the singularities associated with a conventional quantum description. This sets the stage for a description of the Brane and Cyclic Universes in Chapter 5.

In Chapter 6 we learn that Einstein's biggest flop, the cosmological constant, may not have been such bad idea after all since it seems to explain dark energy. This leads the author to the Landscape Universe. Chapter 7 looks at the philosophy of the multiverse and explores the question: If we can't observe them, are they there? Chapter 8 tells the story of the thesis of Everett. Everett asked the questions: What is a measurement, and What is the outcome of a measurement? The answer is that, at the quantum level, the act of measurement creates a new observer, and thusly a new universe. This seems to be a reformulation of the idea that observing an event changes its past. You can imagine that a new universe is generated with each observation.

Chapter 9 looks at the holographic projection of the string theory universe onto a four dimensional universe producing quantum mechanics and general relativity. This one seemed to me to be most comprehensible. Chapter 10 explores the possibilities of a simulated universe (think: *The Matrix*) and the resources required to create it. It also asks question about the nature of sentience and from whence it derives. Also in this chapter is described the Ultimate Multiverse, a multiverse that consists of all universes that can be described by mathematics only.

Looking back, it is clear that the Quantum Multiverse and the Quilted Multiverse are probably manifestations of similar objects. The same might be true of the Brane, Cyclic and Holographic Multiverses. In fact the Ultimate Multiverse might describe/be describing all of them. In the final chapter, the author addresses these questions: which Multiverse is the right one and How would we know? The answers are not known, of course. This is the beauty of science: we can ask questions and search for answers in the data we collect. Like all books of this nature, I come away feeling like a very small and insignificant part of the cosmos.

Joseph D. Ferrara, Ph.D.

Rigaku

Rigaku Corporation
e-mail: rinttyo@rigaku.co.jp
Tel: +[81] 3-3479-0618
FAX: +[81] 3-3479-6112

Rigaku China
e-mail: info@rigaku.com.cn
Tel: +[86] 010-82800840
FAX: +[86] 010-82800864

Rigaku Americas
e-mail: info@Rigaku.com
Tel: (281) 362-2300
FAX: (281) 364-3628

Rigaku Europe
e-mail: info@Rigaku.com
Tel: +[44] 1732 763 367
FAX: +[44] 1732 763 757