Crystallography Times
Rigaku

Protein Crystallography Newsletter
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In this issue:

Crystallographers in the News
Max Perutz Prize

The European Crystallographic Association has awarded the seventh Max Perutz Prize to **Prof. Randy J. Read** (Department of Hematology, University of Cambridge, UK) for his contribution to the development and application of advanced statistical approaches to all stages of protein structure solution.

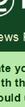
Randy was recognized for his major contribution in the development and application of statistical methods for the calculation of crystallographic Fourier maps, and maximum likelihood methods and their impact on phasing, benefiting many laboratories in the world working with structures of macromolecules. In addition to the development of outstanding crystallographic methods, he has been studying medically relevant proteins, particularly those for which the structure may be useful in the development of new therapies.

Product in the Spotlight

Rigaku's popular Minstrel DT UV

Crystallization Webinar

Nucleation and seeding in protein crystallization



Dr. Allan D'Arcy has given a very successful presentation about microseeding matrix screening (MMS) method on September 4th for Rigaku Crystallization Webinars. 290 scientists registered to the webinar from 22 countries around the world and 180 attended the live presentation. The recorded presentation is now available on the Rigaku Automation website.

Survey of the Month

Rate your level of agreement with the following statement: I would use covalent modification of macromolecules with a fluorescence probe, to detect the binding of individual components in a complex during crystallization, if such a product was available.

- Strongly agree
- Agree
- Neither agree nor disagree
- Disagree
- Strongly disagree

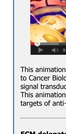
http://www.surveymonkey.com/s/rigaku

Last Month's Survey

Over the last 30 years, which technological advancement has had the largest impact on protein crystallography in the home lab?

Answer Options	%
Multiwire detectors	0.0%
Imaging plate detectors	20.0%
Multi-layer optics	20.0%
Micro-focus generators	12.0%
CCD detectors	8.0%
Hybrid pixel array detectors	0.0%
Software	32.0%
Cryocrystallography	8.0%

Science Video
Introduction to Cancer Biology (Pt. 1): Abnormal Signal Transduction



This animation is the first part of the series "An Introduction to Cancer Biology," and explains the mechanism of abnormal signal transduction resulting in uncontrolled cell proliferation. This animation also provides an overview of the potential targets of anti-cancer therapies.

ECM delegates raise £1376 for Cancer Research UK

As part of the recent ECM, Rigaku wanted to raise money for a chosen charity, Cancer Research UK. Some bright spark (Dr. Mark Benson) came up with the idea to use exercise bikes to cycle the 1376 km straight-line distance required to get us from Warwick, UK to the location of the next ECM in Rovinj, Croatia in 2015. For every kilometer cycled, Rigaku donated £1. Participants received the coveted yellow "Tour de Booth" jersey and the more enthusiastic peddlers battled it out for top spot on our leader board. Prizes were given to those who completed the greatest distances.
>> Read more

Crystallography in the news

September 4, 2013. Computer-designed proteins that can recognize and interact with small biological molecules are now a reality. Scientists have succeeded in creating a protein molecule that can be programmed to unite with three different steroids.

September 5, 2013. While on sabbatical at the Weizmann Institute of Science in 1993, Paul H. Axelsen—currently a professor at the University of Pennsylvania's Perelman School of Medicine—helped figure out how a key enzyme plays a role in communication between certain kinds of nerve cells—the very process that sarin gas interferes with so catastrophically.

September 11, 2013. By taking advantage of the fact that our body proteins and robot arms both move in a similar way, the department of mechanical engineering of the UPV/EHU-University of the Basque Country has developed a program to simulate protein movements.

September 13, 2013. The Royal Swedish Academy of Sciences has awarded the Gregori Aminoff Prize in Crystallography 2014 to Yigong Shi from Tsinghua Univ. in Beijing, China for his "groundbreaking crystallographic studies of proteins and protein complexes that regulate programmed cell death."

September 16, 2013. Stopping short of a merger, the nonprofit Hauptman-Woodward Medical Research Institute is negotiating with the University at Buffalo School of Medicine & Biomedical Sciences to change the way the organization and its scientists are compensated.

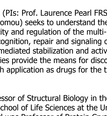
September 20, 2013. Cryo-EM's back-of-the-pack status is changing, thanks in part to technology developed at Berkeley Lab. Using the new generation of direct-conversion electron detector cameras, scientists from the United Kingdom used the method to derive a 4.5 Å resolution image of the yeast ribosome, and did so using only two percent of the data that was necessary for earlier efforts that produced lower-resolution results.

September 23, 2013. Sigma-Aldrich Corporation has announced that SAFC® Commercial, its custom manufacturing services business unit, has engineered additional traits into its CHO2Ni® Platform cell line, increasing the utility of the CHO2Ni® portfolio of products and services. One of the novel cell lines is claimed to be useful for protein crystallography studies, as well as for the expression of biotherapeutics that target mannose receptors.

September 24, 2013. A revolutionary method for probing molecular structure unravels as authors concede problems with X-ray technique for hard-to-crystallize molecules. The method uses "crystalline sponges" to hold molecules in the regular order needed to perform X-ray crystallography.

Product spotlight: Minstrel's asymmetric lighting

Rigaku's line of Hi-Res Minstrel imaging systems delivers outstanding performance in a variety of different configurations to suit any workflow. Continuing to expand upon this superior image quality and performance, we are excited to announce Asymmetric Lighting as a new feature shared by all new Minstrel systems.



High-contrast protein crystal identification symmetric lighting (left) as compared to asymmetric lighting (right)

Only Rigaku Automation offers a unique and patented LED programmable light source that delivers asymmetric lighting patterns, taking crystal illumination to the next level. Asymmetric lighting delivers the ability to change contrast on the sample, rotate asymmetry 120° and shine light from right to left, making crystal features more pronounced.

With this feature, one can better illuminate tough protein crystals that form in and around edges of a drop. This is the ideal solution for difficult-to-image crystals with very little depth, or 2D-like crystal formations and LCP drops.

Ask for more information about asymmetric lighting and ways to improve your lab's imaging capabilities.

Lab in the spotlight: Pearl laboratory

The Pearl Laboratory CR-UK
DNA Repair Enzymes Research Group
University of Sussex

The research in The Pearl Laboratory (PIs: Prof. Laurence Pearl FRS, Dr. Antony Oliver and Dr. Chris Prodromou) seeks to understand the structural basis for assembly, specificity and regulation of the multi-protein complexes involved in the recognition, repair and signaling of DNA damage, and in the chaperone-mediated stabilization and activation of cellular signaling pathways. These basic studies provide the means for discovery and development of novel small-molecule inhibitors with application as drugs for the treatment of cancer and other diseases.

Professor Laurence Pearl FRS is Professor of Structural Biology in the Genome Damage and Stability Centre, and heads the School of Life Sciences at the University of Sussex. For the previous 10 years, Professor Pearl was Professor of Protein Crystallography at the Institute of Cancer Research in London, where he was also Chairman of the Section of Structural Biology and a member of the Board of Trustees. His laboratory studies the structural biology of DNA repair, signal transduction (the process by which a cell converts one kind of signal or stimulus into another) and molecular "chaperones."

Useful links: History of protein crystallography

In the special 90th anniversary issue, Chemical and Engineering News (C&EN) has published a comprehensive history of protein crystallography (Sept. 9, 2013: Vol. 91, No. 36, p. 44-49): Understanding The Workings Of Life. Pinpointing three-dimensional arrangements of proteins has been crucial for understanding the chemistry of living cells, by Sarah Everts.

Selected recent crystallographic papers

Structural insights into the interaction of IL-33 with its receptors. Xi Liu; Hammel, Michal; Yanfeng He; Tainer, John A.; U-Ser Jeng; Linqi Zhang; Shuying Wang; Xinquan Wang. *Proceedings of the National Academy of Sciences of the United States of America.* 9/10/2013, Vol. 110 Issue 37, p14918-14923. 6p.
http://dx.doi.org/10.1073/pnas.1308651110.

Structural Determinants of Oligomerization of Δ1-Pyrroline-5-Carboxylate Dehydrogenase: Identification of a Hexamerization Hot Spot. Luo, Min; Singh, Ranjan K.; Tanner, John J. *Journal of Molecular Biology.* Sep2013, Vol. 425 Issue 17, p3106-3120. 15p.
http://dx.doi.org/10.1016/j.jmb.2013.05.027.

Hydrogen atoms in protein structures: high-resolution X-ray diffraction structure of the DFFase. Full Text Available By: Elias, Mikael; Liebschner, Dorothee; Koepke, Jurgen; Lecomte, Claude; Guillot, Benoit; Jelsch, Christian; Chabriere, Eric. *BMC Research Notes.* 2013, Vol. 6 Issue 1, p1-7. 7p. http://dx.doi.org/10.1186/1756-0500-6-308.

Iterative projection algorithms in protein crystallography. I. Theory. Millane, Rick P.; Lo, Victor L. *Acta Crystallographica: Section A.* Sep2013, Vol. 69 Issue 5, p517-527. 11p.
http://dx.doi.org/10.1107/S0108767313015249.

The hepatitis B virus preS1 domain hijacks host trafficking proteins by motif mimicry. Jürgens, Maike C; Vörös, Judit; Rauturaeu, Gilles J P; Shepherd, Dale A; Pye, Valerie E; Muldoon, Jimmy; Johnson, Christopher M; Ashcroft, Alison E; Freund, Stefan M V; Ferguson, Neil. *Nature Chemical Biology.* Sep2013, Vol. 9 Issue 9, p540-547. 8p. 2 Color Photographs, 1 Diagram, 3 Graphs. http://dx.doi.org/10.1038/nchembio.1294.

Computational Design of a Protein-Based Enzyme Inhibitor. Procko, Erik; Hedman, Rickard; Hamilton, Keith; Seetharaman, Jayaraman; Fleishman, Sarel J.; Su, Min; Aramini, James; Kornhaber, Gregory; Hunt, John F.; Tong, Liang; Montelione, Gaetano T.; Baker, David. *Journal of Molecular Biology.* Sep2013, Vol. 425 Issue 18, p3563-3575. 13p.
http://dx.doi.org/10.1016/j.jmb.2013.06.035.

Three-Dimensional Structure and Biophysical Characterization of *Staphylococcus aureus* Cell Surface Antigen-Manganese Transporter MntC. Gribenko, Alexey; Mosyak, Lidia; Ghosh, Sharmistha; Parris, Kevin; Severson, Kristine; Moran, Justin; Chu, Ling; Li, Sheng; Liu, Tong; Woods, Virgil L.; Jansen, Kathrin U.; Green, Bruce A.; Anderson, Annaliesa S.; Matsuka, Yury V. *Journal of Molecular Biology.* Sep2013, Vol. 425 Issue 18, p3429-3445. 17p. http://dx.doi.org/10.1016/j.jmb.2013.06.033.

Structural Insights into the Interaction of IL-33 with its Receptors. Xi Liu; Hammel, Michal; Yanfeng He; Tainer, John A.; U-Ser Jeng; Linqi Zhang; Shuying Wang; Xinquan Wang. *Proceedings of the National Academy of Sciences of the United States of America.* 9/10/2013, Vol. 110 Issue 37, p14918-14923. 6p.
http://dx.doi.org/10.1073/pnas.1308651110.

Quantification of free ligand conformational preferences by NMR and their relationship to the bioactive conformation. Blundell, Charles D.; Packer, Martin J.; Almond, Andrew. *Bioorganic & Medicinal Chemistry.* Sep2013, Vol. 21 Issue 17, p9976-9987. 12p.
http://dx.doi.org/10.1016/j.bmc.2013.06.056.

SedNMR: On the Edge between Solution and Solid-State NMR. Ivano Bertini; Claudio Luchinat; Giacomo Parigi; Enrico Ravera. *Accounts of Chemical Research.* Sep2013, Vol. 46 Issue 9, p2059-2069. 11p. http://dx.doi.org/10.1021/ar300342f.

Insights into Eph receptor tyrosine kinase activation from crystal structures of the EphA4 ectodomain and its complex with ephrin-A5. Kai Xu; Tzvetkova-Robev, Dorothea; Yan Xu; Goldgur, Yehuda; Yee-Peng Chan; Himanen, Juha P.; Nikolov, Dimitar B. *Proceedings of the National Academy of Sciences of the United States of America.* 9/3/2013, Vol. 110 Issue 36, p14634-14639. 6p. http://dx.doi.org/10.1073/pnas.1311000110.

Book review:

Creation: How Science is Reinventing Itself
by Adam Rutherford Pogue
Penguin Group, NYC, 2013, ISBN 978-1-61723-005-9, 278 pages

I listen to the podcast Science Talk, produced by *Scientific American*, on a more or less monthly basis. In July and August they interviewed Adam Rutherford, author of Creation. Rutherford is an editor of *Nature* and I have heard him speak and have read numerous news articles written by him. The interview intrigued me so I bought a copy of the book.

The title is meant to be provocative, at least in the United States where we still seem to have issues with evolution, let alone creation. The book takes a long look at how modern biology has come to terms with both concepts.

I was a little disappointed, though, as I found a few technical errors; for example, diesel does not come from gasoline and the FAA doesn't care about trips to Mars—not yet, anyway. A few trivial errors like these call into question the correctness of the rest of the book. I can't even argue that these were related to nuances in British and American English—the book was printed in the US. One positive aspect of the book is that it presents information as current as the middle of 2012.

The book is divided into two parts: "The Origin of Life" and "The Future of Life". The titles are self-explanatory. The author takes us through the discovery of the cell, the genetic code, and how the genetic code has allowed scientists to hypothesize when LUCA, the Last Universal Common Ancestor, may have come into being. Rutherford reviews our current understanding of how life may have come into existence at undersea vents, rather than in primordial soups activated by lightning.

The first chapter of the second part, Created Not Begotten, reviews the history of our understanding of DNA, culminating in the creation of Synthia by Craig Venter. Interestingly, we learn of the Easter eggs the team left in the genome, including a misquotation of Feynman. The lesson here is not to believe everything you read on the Internet. The next chapter, Logic in Life, looks at how we might use DNA programs to create cancer treatments and sensors. "Remix and Revolution" discusses the BioBrick project and even touches on the intellectual property issues associated with genes. This book was printed before the Supreme Court handed down the *Association for Molecular Pathology v. Myriad Genetics, Inc.* decision, so it does not reflect the results of this historic case.

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