Crystallography Times

Rigaku

Protein Crystallography Newsletter
Volume 3, No. 2, February 2011

In this issue:

Continuing Education Webinar
Protein Crystallography:
Coot model-building software

Presenter: Dr. Paul Emsley
Date to Be Determined

Paul Emsley is a memenber of The Protein Crystallography Group at the University of Glasgow.

Biological SAXS Workshop
Tuesday, April 12, 2011
Chapel Hill, North Carolina

Rigaku and the University of North Carolina will co-sponsor a workshop on Small Angle X-ray Scattering (SAXS) instrumentation, measurements, techniques, and data analysis methods applied to biological samples. Please contact Judy Bryan or registerto learn how Small Angle X-ray Scattering (SAXS) can contribute to your research.

Macromolecular Crystallography 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.

Crystallography in the news

January 24, 2011. A coder named Bosco Ho has put together an impressive cloud-based three-dimensional protein and DNA renderer which runs in the browser, without any plugins, using HTML5. It's called Jolecule, and due to its HTML5 construction, it'll only work in modern browsers like Chrome and Safari, though you'll be mostly fine if you're on Firefox.

Janurary 31, 2011. To unravel their structures, Harry Quiney and Keith Nugent of the University of Melbourne used X-ray Free-Electron Lasers (XFEL) to produce such a bright light that it is possible to see the X-rays bouncing off a single molecule. A conceptual breakthrough, their work has cleared an important obstacle to achieving the goal of trying to view the structure of a single molecule.

February 1, 2011. Drug maker Pfizer is to close its research and development (R&D) facility in Sandwich Kent, which employs 2,400 people. The closure of the Kent facility is part of Pfizer's reorganization of its research and development across the world. Pfizer Sandwich develops drugs for a range of disorders, such as allergies and infectious diseases including HIV.

February 10, 2011. X-ray optics specialist from La Trobe University, Dr Andrew Peele, has been appointed the new head of science at the Australian Synchrotron. In an exclusive interview with Australian Life Scientist, Peele talks about how the synchrotron aims to work with life scientists to produce world class research.

February 17, 2011. Chemists at the Technische Universitaet Muenchen (TUM) and the Karlsruhe Institute of Technology (KIT) introduced a new method for molecular structure analysis. The team of Professor Burkhard Luy from KIT and Junior Professor Stefan F. Kirsch from the TUM has now shown for the first time that certain NMR parameters, the so-called residual dipolar couplings (RDCs), can make a significant contribution towards determining structure when traditional methods fail.

Product spotlight: BioSAXS-1000 Kratky Camera

Introducing the BioSAXS-1000, a new SAXS camera based on a patented two-dimensional Kratky geometry, which produces significantly higher flux at the sample and no need for desmearing. Designed to fit on an open port of a rotating anode generator, or as a standalone system with a micro-focus sealed tube X-ray port, the small size and high flux performance make it the perfect instrument for incorporating SAXS into the workflow of your lab.

Information derived from a SAXS experiment performed on a protein in solution has been shown to be useful for predicting crystallizability, as well as in modeling after structure determination. And, in the absence of a successful crystallography experiment, the SAXS experiment can at a minimum provide information about the oligomeric state and shape of the molecule or complex.

Request more information on Rigaku BioSAXS-1000.

Lab spotlight: Douglas C. Rees Lab @ CalTech

Rigaku BioSAXS-1000

Douglas C. Rees Lab - A Howard Hughes Medical Institute Research Laboratory in the Division of Chemistry at the California Institute of Technology.

Funny Science Link
Scientists at Baylor College of Medicine parody Lady Gaga's 'Bad Romance'

We are the Hui Zheng lab at BCM and study Alzheimer's Disease.

The research interests of the Rees group (a Howard Hughes Medical Institute Research Laboratory in the Division of Chemistry at the California Institute of Technology) emphasize the general area of structural bioenergetics, using crystallographic and functional approaches to characterize water-soluble and membrane proteins participating in various energy transduction pathways. Studies of metalloproteins containing complex cofactors with either molybdenum or tungsten have defined the unusual structures of the FeMo-cofactor of nitrogenase and the more widespread Mo-cofactor that participate in basic reactions of the biological nitrogen and sulfur cycles. Studies of integral membrane proteins have emphasized energy transduction processes associated with photosynthetic and respiratory processes, mechanosensation, and of ABC transporter systems that mediate nutrient uptake into bacteria.

Useful links for crystallography

Phyre Homology/analogY Recognition Engine - Phyre is a free for academics service for predicting the 3-dimensional structure of a protein amino acid sequence.

The R Project for Statistical Computing - R is a free software environment for statistical computing and graphics. It compiles and runs on a wide variety of UNIX platforms, Windows and MacOS.

Selected recent crystallographic papers

Specimen preparation for electron diffraction of thin crystals. Wang, Huaibin; Downing, Kenneth H. *Micron*, Feb2011, Vol. 42 Issue 2, p132-140.
DOI: http://dx.doi.org/10.1016/j.micron.2010.05.003

Electron cryomicroscopy of membrane proteins: Specimen preparation for two-dimensional crystals and single particles. Schmidt-Krey, Ingeborg; Rubinstein, John L. *Micron*, Feb2011, Vol. 42 Issue 2, p107-116.
DOI: http://dx.doi.org/10.1016/j.micron.2010.07.004

A tool for the qualitative comparison of membrane-embedded and detergent-solubilized membrane protein structures in projection. Jeckelmann, Jean-Marc; Palacin, Manuel; Fotiadis, Dimitrios. *Journal of Structural Biology*, Feb2011, Vol. 173 Issue 2, p375-381.
DOI: http://dx.doi.org/10.1016/j.jsb.2010.09.005

Femtosecond X-ray protein nanocrystallography. Chapman, Henry N.; Fromme, Petra; Barty, Anton; White, Thomas A.; Kirian, Richard A.; Aquila, Andrew; Hunter, Mark S.; Schulz, Joachim; DePonte, Daniel P.; Weierstall, Uwe; Doak, R. Bruce; Maia, Filipe R. N. C.; Martin, Andrew V.; Schlichting, Ilme; Lomb, Lukas; Coppola, Nicola; Shoeman, Robert L.; Epp, Sascha W.; Hartmann, Robert; Rolles, Daniel; et al. *Nature*, 2/3/2011: 470(7332), p73-77. DOI: http://dx.doi.org/10.1038/nature09750

Structural overview of the bacterial injectisome. Worrall, Liam J; Lameignere, Emilie; Strynadka, Natalie CJ. *Current Opinion in Microbiology*, Feb2011, Vol. 14 Issue 1, p3-8.
DOI: http://dx.doi.org/10.1016/j.mib.2010.10.009

Functional and structural analyses of N-acylsulfonamide-linked dinucleoside inhibitors of RNase A. Thiyagarajan, Nethaji; Smith, Bryan D.; Raines, Ronald T.; Acharya, K. Ravi. *FEBS Journal*, Feb2011, Vol. 278 Issue 3, p541-549.
DOI: http://dx.doi.org/10.1111/j.1742-4658.2010.07976.x

Gold nanoparticles: Grown in a crystal. Vekilov, Peter G. Nature Nanotechnology, Feb2011, Vol. 6 Issue 2, p82-83, 2p, 1 *Diagram*;
DOI: http://dx.doi.org/10.1038/nnano.2011.9

Glycine amide shielding on the aromatic surfaces of lysozyme: Implication for suppression of protein aggregation. Ito, Len; Shiraki, Kentaro; Makino, Masatomo; Hasegawa, Kazuya; Kumasaka, Takashi. *Febs Letters*, Feb2011, Vol. 585 Issue 3, p555-560.
DOI: http://dx.doi.org/10.1016/j.febslet.2011.01.008

January Survey Results

Some space groups are more “fun” than others. Which space group is your favorite (choose one)?

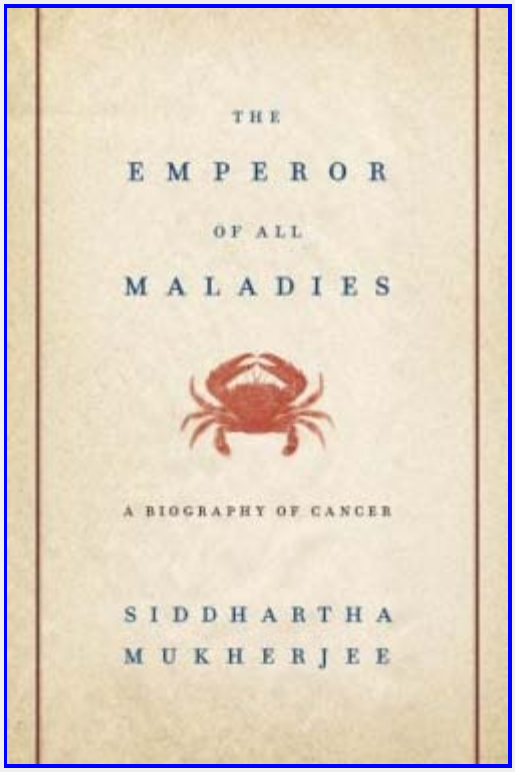
Space Group	Response
R32	30%
P2(1)2(1)2(1)	20%
P2(1)2(1)2	15%
P1	10%
I4	10%
i222	5%
P6(1)	5%
P6(5)22	5%

Survey Question of the Month

Predict the next structural biologist to win a Nobel Prize (it is OK to predict yourself).

Done

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



Nucleation and Crystallization of Lysozyme: Role of Substrate Surface Chemistry and Topography. Delmas, Thomas; Roberts, Michael M.; Heng, Jerry Y. Y. *Journal of Adhesion Science & Technology*, 2011, Vol. 25 Issue 4/5, p357-366.
DOI: http://dx.doi.org/10.1163/016942410X525614

Automated screening of 2D crystallization trials using transmission electron microscopy: A high-throughput tool-chain for sample preparation and microscopic analysis. Coudray, Nicolas; Hermann, Gilles; Caujolle-Bert, Daniel; Karathanou, Argyro; Erne-Brand, Françoise; Buessler, Jean-Luc; Daum, Pamela; Plitzko, Juergen M.; Chami, Mohamed; Mueller, Urs; Kihl, Hubert; Urban, Jean-Philippe; Engel, Andreas; Rémigy, Hervé-W. *Journal of Structural Biology*, Feb2011, Vol. 173 Issue 2, p365-374.
DOI: http://dx.doi.org/10.1016/j.jsb.2010.09.019

Structure of the HIV-1 Full-Length Capsid Protein in a Conformationally Trapped Unassembled State Induced by Small-Molecule Binding. Du, Shoucheng; Betts, Laurie; Yang, Ruifeng; Shi, Haibin; Concel, Jason; Ahn, Jinwoo; Aiken, Christopher; Zhang, Peijun; Yeh, Joanne I. *Journal of Molecular Biology*, Feb2011, Vol. 406 Issue 3, p371-386.
DOI: http://dx.doi.org/10.1016/j.jmb.2010.11.027

Crystal Structures of the Bacterial Solute Receptor AcbH Displaying an Exclusive Substrate Preference for ß-d-Galactopyranose. Licht, Anke; Bulut, Haydar; Scheffel, Frank; Daumke, Oliver; Wehmeier, Udo F.; Saenger, Wolfram; Schneider, Erwin; Vahedi-Faridi, Ardeschir. *Journal of Molecular Biology*, Feb2011, Vol. 406 Issue 1, p92-105.
DOI: http://dx.doi.org/10.1016/j.jmb.2010.11.048

G protein-coupled receptors: Crystallizing how agonists bind. Tse, Man Tsuey. *Nature Reviews Drug Discovery*, Feb2011, Vol. 10 Issue 2, p97-97.
DOI: http://dx.doi.org/10.1038/nrd3379

Kinetic and crystallographic studies of the role of tyrosine 7 in the active site of human carbonic anhydrase II. Mikulski, Rose; Avvaru, Balendu Sankara; Tu, Chingkuang; Case, Nicolette; McKenna, Robert; Silverman, David N. *Archives of Biochemistry & Biophysics*, Feb2011, Vol. 506 Issue 2, p181-187.
DOI: http://dx.doi.org/10.1016/j.abb.2010.12.004

Double Take on Piwi Protein/piRNA Complex Structure. Schwalbe, Harald. *Structure*, Feb2011, Vol. 19 Issue 2, p141-142.
DOI: http://dx.doi.org/10.1016/j.str.2011.01.007

Crystal Structure of SUMO-Modified Proliferating Cell Nuclear Antigen. Freudenthal, Bret D.; Brogie, John E.; Gakhar, Lokesh; Kondratick, Christine M.; Washington, M. Todd. *Journal of Molecular Biology*, Feb2011, Vol. 406 Issue 1, p9-17. DOI: http://dx.doi.org/10.1016/j.jmb.2010.12.015

Book review:

The Emperor of All Maladies: A Biography of Cancer
Siddhartha Mukherjee, Simon & Schuster, 2010
ISBN: 978-1439107959

I am asked where I get ideas for books to review. In this case, I listened to an interview with the author on NPR's Fresh Air. The author said he could not reply to the statement "I'm willing to go on, but before I go on, I need to know what I'm battling." He could not properly answer the question, so he set out to write this book in the summer of 2004. It is a fabulous book. Those of you who know me will understand it when I say this book is one of the hardest I've read in a long time.

The book follows a general timeline from the first recorded case of breast cancer and mastectomy in Atossa, a Persian princess, to modern day directed therapies. Along the way individual people for which the doctor and his team have provided care are outlined to give the reader examples and to personalize the text.

Mukherjee starts with the diagnosis of a Boston schoolteacher with acute lymphocytic leukemia, ALL, and the start of her treatment. We learn about the ancient descriptions of cancer by Hippocrates and Galen, following

Advance praise for

THE EMPEROR OF ALL MALADIES

"Sid Mukherjee's book is a pleasure to read, if that is the right word. Cancer today is widely regarded as the worst of all the diseases from which one might suffer—if only because it is fast becoming the most common. Dr. Mukherjee explains how this perception came about, how cancer has been regarded across the years, and what is now being done to treat its protean forms. With *The Emperor of All Maladies*, he gives that small fraternity of practicing doctors who cannot just talk about their profession but write about it."
—TONY JUDT, *author of Ponsonar and Ill Fares the Land*

"Siddhartha Mukherjee has done something that should not have been possible: he has managed, at once, to write an authoritative history of cancer for the general reader, while always keeping the experiences of cancer patients in his heart and in his narrative. As once learned and skeptical, entertained and humane, *The Emperor of All Maladies* is that rarest of things—a noble book."
—DAVID RIEFF, *author of Swimming in a Sea of Death*

"*The Emperor of All Maladies* beautifully describes the nature of cancer from a patient's perspective and how basic research has opened the door to understanding this disease."
—BERT VOGELSTEIN, *director, Ludwig Center at Johns Hopkins University*

"A labor of love . . . as comprehensive as possible."
—GEORGE CANELLOS, M.D., *William Rosenberg Professor of Medicine, Harvard Medical School*

"Rarely have the science and poetry of illness been so elegantly braided together as they are in this erudite, engrossing, kind book. Mukherjee's clinical wisdom never erases the personal vulnerability which are its occasion; indeed, he bears with meticulous clarity and profound compassion the beautiful hope buried in cancer's ravages."
—ANDREW SOLOMON, *National Book Award–winning author of The Noonday Demon*

Cancer physician and researcher Siddhartha Mukherjee. Credit: Deborah Feingold

through to the middle ages and eventually the 20th century. Along the way we are introduced to a number of important characters, most notably Sydney Farber and Mary Lasker. It was Farber who first targeted ALL in children with dehydrofolate reductase inhibitors to induce remissions. Farber started with ALL because he wanted a cancer for which outcome and progress are easily measurable via blood count. We learn about the evolution of chemotherapy from short term remission to long term survival with multidrug therapy, radiation and surgery.

We also learn how Mary Lasker helped create the American Cancer Society and helped initiate the founding of the NIH and Nixon's War On Cancer. The author provides a view of the interaction of cancer and the system for providing care for cancer patients. Here we also learn about bone marrow transplants, and how they took so long to move from an experimental technique to standard treatment.

Next the author takes a look at the first cancer epidemic, lung cancer, and its cause, tobacco, as well as the legal wrangling to get cigarette ads off the air, and ends with the reimbursement of states for medical costs. The discovery of *H. pylori*, a cause of stomach cancer, is also described, as well as other preventable cancers.

Readers are provided with more example cases and learn about the genetic basis of cancer using the nuclear estrogen receptor and Tamoxifen in breast cancer as one example and familial retinoblastoma as another.

The author explores the discovery of the HER receptor and development of Herceptin by Genentech. The politics of drug discovery and citizen activism is also elucidated. Finally, he discusses the miracle of Gleevec developed by Ciba-Geigy before the merger with Sandoz.

A final chapter, "Atossa's war," summarizes the book exquisitely. Here the author traces the prognosis of Atossa's disease through the ages from mastectomy to chemotherapy and radiation, to today's directed therapies and a vision for 2050.

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