Crystallography Times

Protein Crystallography Newsletter Volume 2, No. 3, March 2010

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Continuing Education Webinar Diffraction Image Processing with d*TREK Presenter: Dr. Jim Pflugrath April 22th at 10 AM EDT (14:00 GMT)

This webinar will demonstrate how to use the d*TREK suite of programs to process single crystal X-ray diffraction images from a variety of crystals and detectors. Jim will present first the quick automated method, followed by instructions on finding the X-ray beam center, masking shadows on the detector, refining your goniometer imperfections, scaling the resultant integrated measurements, and determining the crystal space group. He will also cover some advanced d*TREK usage including scripting, ranking of crystals, and processing multiple scans.

Spring Webinar Series Focuses on Software

Note that our continuing webinar program will feature well known expert presenters in a miniseries devoted to commonly used data processing packages.

Crystallography in the news



Rigaku

March 18, 2010. Duke University researchers, led by Prof. David Needham, have devised a method to dry and preserve proteins in a glassified form that seems to retain their molecular properties.

March 11, 2010. Researchers at the University of Minnesota, led by Prof. Carrie Wilmot, have used X-ray crystallography to create a molecular image of a system that moves electrons between proteins in cells.

March 7, 2010. Howard Hughes Medical Institute (HHMI) researchers, led by Stephen C. Harrison, have discovered exactly how one type of New World hemorrhagic fever virus latches onto and infects human cells, offering a much-needed lead toward new treatments.

March 5, 2010. Dr. Mark Ashton at Evotec AG announced that the company has extended its research agreement with Cubist Pharmaceuticals, Inc. to provide fragmentbased drug discovery expertise, including protein crystallography, to profile novel compounds against antibacterial targets.

March 1, 2010. Investigators at the Louisiana State University, led by Prof. Sunyoung Kim, announce a major advance in the understanding of ATP processing based on X-ray crystallographic studies of kinesins.

February 25, 2010. Proteros Fragments and Axikin Pharmaceuticals announced that they have reached "significant milestones" in their drug-discovery collaboration for the discovery and characterization of distinct chemical entities toward a novel therapeutic target for chronic obstructive pulmonary disease.

Custom fine screens on your desktop

The **NEW** Desktop AlchemistTM liquid handling system for protein crystallization optimization is a cost effective laboratory automation tool, allowing complex fine screens to be setup in under 3 minutes, with an entire screen completed in under 25 minutes. From intuitive and easy-to-use software, to industry leading dispense accuracy and precision across all viscosities, the Rigaku Desktop Alchemist delivers reproducible fine screens on your benchtop.

Built upon the industry standard Rigaku AlchemistTM II platform, but with a compact benchtop footprint and lower price, the Desktop Alchemist offers the ability to dispense reagents from ethanol to 100% glycerol with unsurpassed accuracy and precision, ensuring reliable and repeatable results without wasting any expensive additives, detergents or other chemicals. Employing time tested and patented Eppendorf[®] Combitips[®] Plus positive-displacement non-contact dispensers, in conjunction with Rigaku TapperTM technology as part of the unique patented BirdFeederTM assembly, ensures that the correct volume is dispensed—regardless of the density or viscosity of the liquid—down to 1 μ l with a total CV of less than 2%.

Solving the stock solution storage and management problem, the Desktop Alchemist CrystalTrakTM database holds thousands of stock chemicals that can be added or removed from the 26 position deck in a matter of seconds using barcoded BirdFeeder assemblies. Rigaku BirdFeeders then provide one aspirate with multiple dispenses—in a volume range of 1 µl to 10 ml—directly into VDX, Linbro or Nextal plate formats.

Request more information on Desktop Alchemist.



The new Rigaku Desktop Alchemist allows fine screen setups in under 3 minutes.



Dr. Buchanan's group at NIDDK studies transporters embedded in the outer membranes of Gram-negative bacteria, which are surface accessible and therefore have the potential to be good vaccine and/or chemotherapeutic targets against infectious diseases. They also study the membrane associated or soluble protein partners that interact with outer membrane transporters to better understand how these systems function *in vivo*.

Lab spotlight: NIDDK/NIH

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) conducts and supports basic and clinical research on many of the most serious diseases affecting public health. As part of the National Institutes of Health (NIH) and the U.S. Department of Health and Human Services, NIDDK hosts five groups devoted to macromolecular crystallography.

Dr. David Davies' group's interests include HIV integrase and other recombination systems, multienzyme complexes, protein-nucleic acid complexes and innate immune system protein. Dr. Jim Hurley's laboratory is interested in fundamental questions of how the interactions between proteins and membranes determine cell and organelle shape and the evolution of shape over time, how protein-membrane interactions turn on and off the signals that control essential cell processes, and how pathogens such as HIV-1 subvert and co-opt these interactions. Dr. Fred Dyda's group is trying to understand the mechanisms by which genetic information in the form of discrete pieces of DNA moves from one place to another. Dr. Wei Yang's lab is currently working on DNA mismatch repair, translesion DNA synthesis, V(D)J recombination, and various metal ion-dependent enzymes. The focus of Dr. Susan Buchanan's research program is the structure determination of integral membrane proteins by X-ray crystallography and functional analysis of these proteins using biophysical, biochemical, and cell biological techniques.

Useful links for crystallography

SWISS-MODEL is a fully automated protein structure homology-modeling server that features new tools for model and structure quality assessment. The purpose of this server is to make protein modeling accessible to all biochemists and molecular biologists WorldWide.

Yale Morph2 is a morphing server, similar to the Morph Server, but specifically designed for morphing between similar proteins rather than different conformations of the same protein.

FoXS is a new webapp which uses the Debye formula for calculating theoretical SAXS scattering profiles. See how it compares to CRYSOL.

BIOISIS is a resource for the investigation of macromolecular structures by SAXS.

Selected recent crystallographic papers

New tools for membrane protein research. Y. Alguel, J. Leung, S. Singh, R. Rana, L. Civiero, C. Alves, and B. Byrne. *Current Protein and Peptide Science* **11** (2), 156-165 (2010).

Mechanism of substrate recognition and transport by an amino acid antiporter. X. Gao, L. Zhou, X. Jiao, F. Lu, C. Yan, X. Zeng, J. Wang and Y. Shi. *Nature* **463** (7282), 828-832 (2010).

Rigaku Hardware Training Classes

Rigaku holds training sessions at our Texas facility tailored towards the needs of macromolecular crystallographers and their staff. Course format is a series of short lectures on theory followed by hands-on activities with detectors and X-ray generators. Safety is emphasized.

Survey Question: Nobel Prize

Who is the most deserving macromolecular crystallographer to win the next structural biology Nobel Prize?



Click to take survey or cut-and-paste http://www.surveymonkey.com/s/VZBW9FB into your browser.



Active site remodelling accompanies thioester bond formation in the SUMO E1. S.K. Olsen, A.D. Capili, X. Lu, D.S. Tan and C.D. Lima. *Nature* **463** (7283), 906-912 (2010).

Femtosecond protein nanocrystallography—data analysis methods. R.A. Kirian, X. Wang, U. Weierstall, K.E. Schmidt, J.C.H. Spence, M. Hunter, P. Fromme, T. White, H.N. Chapman, and J. Holton. *Optics Express* **18** (6), 5713-5723 (2010).

Hydration Potential of Lysozyme: Protein Dehydration Using a Single Microparticle Technique.D.L. Rickard, P.B. Duncan and D. Needham *Biophysical Journal* **98** (6), 1075-1084 (2010).

Size-Sorting Combined with Improved Nanocapillary Liquid Chromatography-Mass Spectrometry for Identification of Intact Proteins up to 80 kDa. A. Vellaichamy, J.C. Tran, A.D. Catherman, J.E. Lee, J.F. Kellie, S.M.M. Sweet, L. Zamdborg, P.M. Thomas, D.R. Ahlf, K.R. Durbin, G.A. Valaskovic and N.L. Kelleher. *Analytical Chemistry* 82 (4), 1234-1244 (2010).

Application of maximum-entropy maps in the accurate refinement of a putative acylphosphatase using 1.3 Å X-ray diffraction data. E. Nishibori, T. Nakamura, M. Arimoto, S. Aoyagi, H. Ago, M. Miyano, T. Ebisuzaki and M. Sakata. *Acta Crystallographica Section* D **64**, 237-247 (2009).

Book review: The Immortal Life of Henrietta Lacks

by Rebecca Skloot

I had originally planned to review *Membrane Structural Biology with Biochemical and Biophysical Foundations* by Mary Luckey this month. The review is done but it will appear next month. I had seen reviews for The Immortal Life of Henrietta Lacks by Rebecca Skloot from The New Yorker to Nature and even The Houston Chronicle. I decided I would not read the reviews but I did listen to an interview with the author. I decided this book was a big deal and started reading it a couple of weeks ago. I just finished the book and decided to review it this month since its central topic, the immortal cell line, HeLa, has so influenced modern medical science.

The author weaves four stories in an out-of-time sequence that makes the book so interesting. The writing is not technical, but enlightening and current. We first learn about the HeLa cells themselves. We also find the author as a precocious sixteen year old in a college biology class, where she first learns about the HeLa cell line, and her subsequent journey into becoming an investigative reporter.

The next story is that of Henrietta Lacks, the woman from whom the HeLa cell is derived, and her family, particularly her daughter Deborah. The author and Deborah become friends but only after an arduous journey and the diagnosis of hypertension and hyperglycemia in the latter. There are parts of this story that will make you mad: for example the family of Henrietta can't get decent health care even though her cells have done so much for medical science.

The story of HeLa cell line itself is also unveiled for us in the context of the importance of this immortal cell line to both medical science and medical ethics. HeLa cells were used to develop the polio vaccine in the 50s. They were sent into space before humans and subjected to nuclear explosions. They have been used for cancer research, in the hopes of curing cancer, creating mouse/human hybrids and infertility studies. The author suggests that all the HeLa cells produced thus far would the circle the earth three times if laid end to end.

Finally we are given a history of informed consent and an analysis of the current arguments for and against the use of human tissue in research without the patient's knowledge of the disposition of the tissue or the profits that might happen. These issues are raised throughout the book and discussed in detail in the afterword.

In the queue: *Science Is Not a Quiet Life* by Max Perutz and William and Lawrence Bragg, father and son, as well as *The Most Extraordinary Collaboration in Science* by John Jenkin. I welcome any recommendations you might have and look forward to

hearing from you at joseph.ferrara@rigaku.com.



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

Rigaku Europe e-mail: info@Rigaku.com

Tel: +[44] 1732 763 367

Rigaku Corporation e-mail: rinttyo@rigaku.co.jp

Rigaku China

e-mail: info@rigaku.com.cn Tel: +[81] 3-3479-0618 Tel: +[86] 010-82800840

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