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Continuing Education Webinar

Protein Crystallography: Getting in on the Ground Floor

Presenter: Dr. Brian Matthews
February 23, 2011
1 PM EST (6:00 GMT)

Brian Matthews, Professor of Physics at the University of Oregon, uses X-ray crystallography, in concert with other techniques, to address some of the fundamental problems in biology: How do proteins spontaneously fold into their biologically active three-dimensional configurations? What determines the stability of these folded proteins? Can stability be improved? How do proteins interact with each other? How do proteins interact with DNA? How do enzymes interact with their substrates and act as catalysts?

Macromolecular Crystallography Training 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.

Crystallization, workflows and data management in CrystalTrak™

Successful use of automation in protein crystallization usually requires standardized workflows that allow for systematic testing of the chemical space. CrystalTrak is a software system that is designed around workflows that have been developed in collaboration with some of the most successful...
CrystalTrak is built around the protein crystallization workflow: Experimental design, liquid dispensing, imaging and optimization.

The core idea is a circular workflow of experimental design, liquid dispensing, imaging and scoring followed by optimization. Each step of the workflow allows users to interact with the automation equipment by either setting parameters or reviewing results. Another important concept of CrystalTrak is that at each step information can be captured for further use. For example, if a crystallization hit is found in a plate, it takes only one mouse click to generate a printable report that contains all information related to the hit, such as screen composition, incubation conditions, and details about the protein sample.

If you want to learn more about CrystalTrak, we would like to point you to a recent series of videos, including an overview, setup of experiments, a discussion on imaging and scoring and demonstration on fine screen optimization.

Request more information on Rigaku CrystalTrak.

**Lab spotlight: Stubbs Lab @ Martin Luther University of Halle - Wittenberg**

The main interests of Professor Milton Stubbs’ lab lie in the field of "rational drug design," where they try to fuse the experimental structural data and thermodynamic measurements of protein-ligand interactions in a computational framework to advance the drug discovery process. Structure determinations of various members of serine proteinases have provided a basis for computer-based drug design within this class of enzymes. In many proteins of interest, however, this course is blocked through a lack of suitable crystals. As a strategy for circumventing such problems, they are investigating the use of surrogate proteins for studying protein-ligand interactions. To test the feasibility of this approach, they have chosen bovine trypsin as a scaffold to reconstruct the ligand binding site of factor Xa.

**Useful links for crystallography**

*Small Angle X-ray Scattering* (eds. Glatter & Kratky) can be freely (and legally) downloaded. The book provides a good basic introduction to SAXS, followed by detailed fundamental theoretical and experimental aspects, as well as methods for data evaluation and description of special experimental techniques. Specific applications, for example biological macromolecules, are covered at the end of the book.

**Selected recent crystallographic papers**


- Alternate states of proteins revealed by detailed energy landscape mapping. Tyka, Michael D.; Keedy, Daniel A.; André, Ingemar; DiMaio, Frank; Song, Yifan; Richardson, David C.; Richardson, Jane S.; Baker, David. *Journal of Molecular Biology*, Jan2011, 405(2): 607-618. [http://dx.doi.org/10.1016/j.jmb.2010.11.008](http://dx.doi.org/10.1016/j.jmb.2010.11.008)


The crystal structure of the ubiquitin-like (UbL) domain of human homologue A of Rad23 (hHR23A) protein. Chen, Yu Wai; Tajima, Toshitaka; Agrawal,
Dr. Dmitri Svergun

Wladek Minor from University of Virginia will give an introduction to structure solution in HKL-3000 alongside hands-on sessions using lab data provided by the attendees. Everybody is invited to bring their own data to take advantage of this exciting opportunity.

Attendance to the EUGM is free of charge, but space is limited.

December Survey Results

What is your most common method for solving protein structures (choose one)?

<table>
<thead>
<tr>
<th>Method</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular replacement</td>
<td>70.8%</td>
</tr>
<tr>
<td>MAD phasing from synchrotron data</td>
<td>4.2%</td>
</tr>
<tr>
<td>SAD phasing from synchrotron data</td>
<td>26.8%</td>
</tr>
<tr>
<td>SAD phasing at home</td>
<td>0.0%</td>
</tr>
<tr>
<td>MIR at home</td>
<td>4.2%</td>
</tr>
</tbody>
</table>

Survey Question of the Month

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

- P2(1)2(1)2(1)
- P2(1)2(1)2
- P2(1)
- R32
- P1
- I4
- Other

Take Survey or cut-and-paste

http://dx.doi.org/10.2210/pdb2wyq/pdb

A generic approach to evaluate how B-cell epitopes are surface-exposed on protein structures. Lollier, Virginie; Denery-Papini, Sandra; Larré, Colette; Tessier, Dominique. Molecular Immunology, Jan2011, 48(4): 577-585.
http://dx.doi.org/10.1016/j.molimm.2010.10.011

Regulation and structure of YahD, a copper-inducible a/ß serine hydrolase of Lactococcus lactis IL1403. Martinez, Jacobo; Manclí, Stefano; Tauberger, Eva; Weise, Christoph; Saenger, Wolfram; Solioz, Marc. FEBS Microbiology Letters, Jan2011, 314(1): 57-66.
http://dx.doi.org/10.1011/j.femsmi.1974-6968.2010.02144.x

http://dx.doi.org/10.1016/j.jinorgbio.2010.09.007

http://dx.doi.org/10.1007/s10822-010-9397-6

http://dx.doi.org/10.1007/s00775-010-0700-8

http://dx.doi.org/10.1016/j.jmb.2010.10.059

Amyloid fibril recognition with the conformational B10 antibody fragment depends on electrostatic interactions. Haupt, Christian; Morgado, Isabela; Kumar, Senthil T.; Parthier, Christoph; Bereza, Magdalena; Hortschansky, Peter; Stubbs, Milton T.; Horn, Uwe; Fändrich, Marcus. Journal of Molecular Biology, Jan2011, 405(2): 341-348.
http://dx.doi.org/10.1016/j.jmb.2010.11.049

Benchmarking membrane protein detergent stability for improving throughput of high-resolution X-ray structures. Sonoda, Yo; Newstead, Simon; Hu, Nien-Jen; Alquel, Yilmaz; Nî, Emmanuel; Beis, Konstantinos; Yashiro, Shoko; Lee, Chiara; Leung, James; Cameron, Alexander D.; Byrne, Bernadette; Iwata, So; Drew, David. Structure, Jan2011, 19(1): 17-25.
http://dx.doi.org/10.1016/j.str.2010.12.001

http://dx.doi.org/10.1038/nature09640

http://dx.doi.org/10.1021/cg100987g

High-throughput evaluation of the critical micelle concentration of detergents. Jumpertz, Thorsten; Tschapek, Britta; Infed, Nacera; Smits, Sander H.J.; Ernst, Robert; Schnitt, Lutz. Analytical Biochemistry, Jan2011, 408(1): 64-70.
Assisted crystal growing by tempering metastable vapor–liquid fluids.
http://dx.doi.org/10.1016/j.cplett.2010.11.076

Book review:

Galileo Goes to Jail and Other Myths about Science and Religion
edited by Ronald L. Numbers, Harvard University Press, 2009
ISBN: 978-0674033276

I don't know what I was thinking when I picked this book up. It is a set of twenty-five essays on how religion has not negatively impacted science. The fourth myth “That Medieval Islamic Culture Was In hospitable to Science” seemed to have the properties of what I understand to be true so I thought there was promise. Myth 7, “That Giordano Bruno was the First Martyr of Modern Science” just about drove me mad.

The essayist, Jole Shackelford, makes the following arguments that debunk the myth. If you remember, Bruno was a priest who adopted the Copernican view and taught that the earth might not be the only planet with life, among other things. Shackelford suggests that Bruno wasn’t the first scientist martyr because he wasn’t a scientist, that this form of capital punishment was common practice anyway, and finally, that he was a priest and the Church could do what it wanted with him.

The essays give the appearance of being well researched but I felt as if I were reading a skit by a partisan political pundit purporting to provide a fair and balanced viewpoint. Moving onto a more interesting book, in my humble opinion.

The Grand Design
by Stephen Hawking and Leonard Mlodinow, Bantam Books, 2010
ISBN: 978-0553805376

From a technical perspective this book is a relatively easy read. It has lots of good pictures and no math, except a definition of p similar to the Indian legislature's old value. However, don't be fooled, as the philosophical implications are profound. The authors start by introducing the question of why does the universe behave the way it does. Next they pass through history and the development of the laws that we think describe the behavior of the universe: Aristotle's, Newton’s, Einstein’s and Feynman’s theories, to string theory and ultimately M-theory, which is a combination of all the theories necessary to describe the behavior of the universe. The difficulty arises in the concepts of free will and causality.

Do we, as human beings, our brains driven by chemical reactions, which are further described by quantum fluctuations in our brains, have “free will”? Is my typing of this document a series of random probabilities? The other mind bender is the idea that observing an event forces the path of the event to become evident. In other words, observing the present impacts the past. I first came across this concept five years ago in Davies’ Cosmic Jackpot. It still does not sit well.