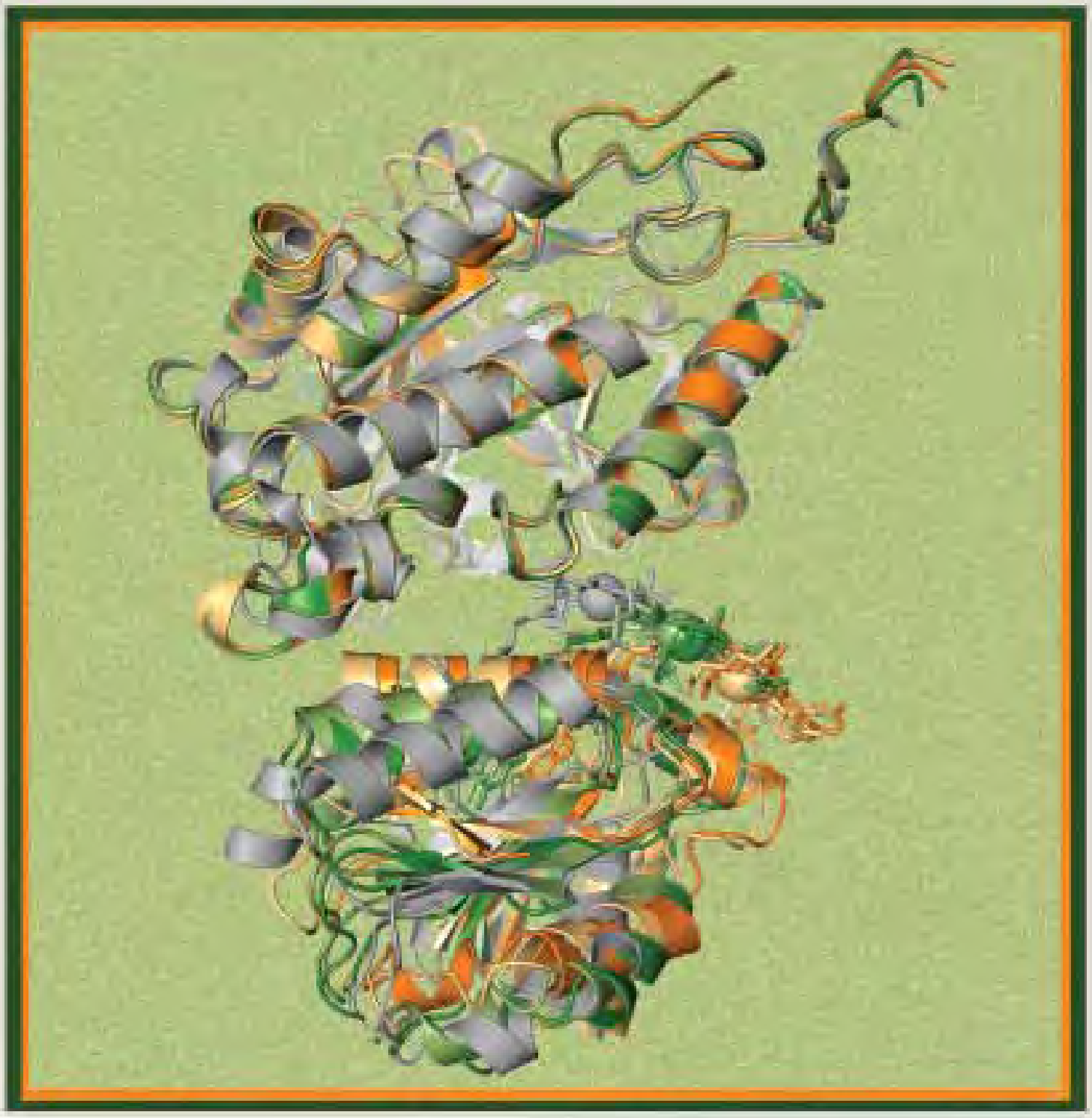
ACA RefleXions

American Crystallographic Association

Number 3
Fall, 2012



Methyl Hand-off Between B Vitamins


NANO ITC

American Crystallographic Association

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ACA HOME PAGE: **www.AmerCrystalAssn.org**

Cover: Depicts the swinging domain motion required for the methyl hand-off between two B vitamins. Image supplied by Yan Kun and Cathy Drennan; see the article on page 3.

Table of Contents













Contributions to ***ACA RefleXions*** may be sent to either of the Editors:

Connie (Chidester) Rajnak
4210 Old Field Trail
Kalamazoo, MI 49008
269-342-1600
conniechidester@earthlink.net

Judith L. Flippen-Anderson
3521 Launcelot Way
Annandale, VA 22003
703-346-2441
ACARefleXions@gmail.com

Please address matters pertaining to advertisements, membership inquiries, or use of the ACA mailing list to:

Marcia J. Colquhoun, Director of Administrative Services
American Crystallographic Association
P.O. Box 96, Ellicott Station
Buffalo, NY 14205
tel: 716-898-8692; fax: 716-898-8695
marcia@hwi.buffalo.edu

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It is with great sadness that we announce the passing on August 25th of Hugo Steinfink. He had been in a Dallas hospital for about 3 weeks following a heart valve replacement. This issue is about to go to press, but we plan to publish a full appreciation of his life in the winter *RefleXions*. Anyone who wishes to contribute memories of Hugo should contact the editors, Judy: acareflexions@gmail.com or Connie: conniechidester@earthlink.net.

ACA *RefleXions* Co-Editors

Judith Flippen-Anderson

3521 Launcelot Way
Annandale, VA 22003
703 560-7436
acareflexions@gmail.com

Connie Rajnak

4210 Old Field Trail
Kalamazoo, MI 49008
269 342 1600
conniechidester@earthlink.net

RefleXions STAFF

Photographer
Peter Müller

Dept of Chemistry
Bldg 2 Rm 325
77 Massachusetts Ave
Cambridge, MA 02139
pmueller@mit.edu

Copy Editor
Jane F. Griffin

Dept of Structural Biology
Hauptman-Woodward MRI
Buffalo 14203
griffin@hwi.buffalo.edu

Historian
Virginia B. Pett

Robert E. Wilson
Prof Emerita
The College of Wooster
1189 Beall Ave,
Wooster, OH 44691-2363
pett@wooster.edu

Art in Crystallography
Edgar F. Meyer

Taos NM 87571
Prof. Emeritus
Texas A&M Univ.
e-meyer@tamu.edu
model_em@yahoo.com
http://molecular-sculpture.com

Books Editor
Joe Ferrara

Rigaku Americas
Corporation
9009 New Trails Dr
The Woodlands
TX 77381
joseph.ferrara@rigaku.com

Puzzle Corner Editor
Frank Fronczek

Chemistry Dept
Lousiana State U
Baton Rouge
LA 70803
ffroncz@lsu.edu

Lots of good things are happening at the ACA! First of all, we had a great meeting in Boston, thanks to all the members who participated and the experienced organizers who set it up. We had over 800 attendees, multiple workshops, and an incredible amount of good science was presented and discussed.

If you were at the ACA meeting in Honolulu in 2006 you need to get your grass skirts out and cleaned up, as we are going back in 2013! Stay tuned for more details. And just to spread things around, 2014 will be in Albuquerque. This will be a spring meeting because of the IUCr meeting in Montreal. We hope our members will avail themselves of both opportunities to share crystallographic results.

Now something really special is happening. Thanks to the efforts of the IUCr and in particular, the Moroccan Crystallographic Association, 2014 has been declared the International Year of Crystallography by the United Nations. This provides us with a wonderful opportunity to tell the world what we do and to celebrate our discipline. Put your thinking caps on, and don't be afraid to boast, or should I say "Bragg" about what crystallography is and what it has done for science. Check out the most recent *IUCr Newsletter* for more information.

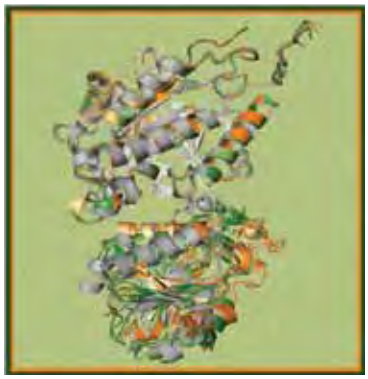
Also on the international front, the ACA is beginning a process to allow for the formation of a Latin American Division similar to the existing Canadian Division. We welcome our neighbors to the south to join in, and who knows, we may have an ACA meeting in the southern hemisphere at some point. I personally think it would be fantastic to have more associations with scientists in Latin America. There is more crystallography going on there than you might think, and even a synchrotron light source in Brazil.

Now back to the local front. The ACA is proposing to publish a new journal in partnership with the American Institute of Physics (AIP). The AIP, of which we are a member society, would be responsible for the production side of the journal while the ACA would maintain full editorial control. The tentative title is *Structure, Dynamics, and Kinetics*, which would capture work on nano-materials, bio-nano-materials, and macromolecules, or really any aspect of structural science at the atomic or near-atomic level with a time-dependent or kinetic component. This might include XFEL or fourth generation synchrotron work, for example, or computational or theoretical work on these systems. Research done by the AIP indicates that this is an area of high interest that does not overlap with existing journals. Given the current publishing climate the journal would be an open access on-line only publication. Council feels that this journal would add value to the membership by providing a venue for the presentation of high quality peer-reviewed results in emerging fields that reflect our broad based international leadership in structural science.

On a final note, the ACA has joined the American Institute of Physics and other societies in writing to President Obama to maintain funding for science, instead of sequestration, i.e. the automatic spending cuts that Congress has set up to take place in January unless there is action to stop it. We know many of our members depend on federal funding for crystallographic research.

That's all for now,

George N. Phillips, Jr.



What's on the Cover

The cover image depicts a swinging domain motion required for methyl transfer between two B vitamins: cobalamin (B12) and folic acid (B9).

Post-World War II, only one vitamin (folic acid) has been deemed worthy of requiring fortification in the US food supply. Folate deficiency impedes the transfer of single carbon methyl units from folate to another vitamin (B12), and is associated with heart disease and serious birth defects. Interestingly, this same transfer reaction is also essential for the ability of certain microorganisms to live on the greenhouse gas carbon dioxide. This image depicts the use of x-ray crystallography to provide the first view of how the methyl transfer occurs from folate, which binds to a TIM barrel protein, to B12, which binds to a Rossmann-like domain (cobalt of B12 shown as large sphere). Dramatic conformational changes are required for the reaction, and a series of structures, capturing enzymatic methyl transfer in the act, reveals the requisite molecular gymnastics of the proteins involved. This work was published in *Nature* (vol 484, pp. 265-269) in April, 2012 and was funded in part by the National Institutes of Health.

The cover image was generated by Yan Kung and Cathy Drennan, HHMI/MIT.

Iolani Palace, Oahu

The only official state residence of royalty in the U.S., Iolani Palace's grounds and galleries are now open to the public as a museum.

Hawaii 2013
American Crystallographic Association

Photo of Patrick courtesy of Richard H. Bromund.

ACA Council Meeting, July 27th 2012

George Phillips announced the 2013 ACA award winners. Richard Dickerson (UCLA) will receive the Isadore Fankuchen Diffraction award; ACA past president Tom Koetzle (Brookhaven National Laboratory) will receive the Richard Bau Neutron Award; Tom Terwilliger (Los Alamos National Laboratory) will receive the Kenneth Trueblood Computational Crystallography award; and Eric Ortland (Emory University School of Medicine) will receive the Etter Early Career award.

George also noted that the ACA has not conducted a full-fledged review of the organization's mission, by-laws, rules, or long-term plans since its inception over sixty years ago. Hence, he is announcing a strategic planning process to carry out such a review. A committee has been formed to this end, consisting of Cheryl Stevens, George Phillips, S. N. Rao, Bill Duax, and Judith Flippen-Anderson. They will get started by interacting with representatives of the American Institute of Physics (AIP) to learn about the process they used for their recent stategic planning initiative.

In the Chief Financial Officer's report, S.N. Rao informed Council that the ACA remains on track towards its goal of having a operating fund of at least one year's office expenses. He also recommended that a separate reserve fund be set up for meeting expenses. Bill Duax and Marcia Colquhoun reported that the number of members who are current in their dues is 1541, which represents a drop relative to previous years; Council is considering how this trend may be reversed.

The 2013 Annual Meeting is scheduled for July 20-24 in Honolulu with room rates not much more than they were in 2006. ACA 2014 will find us back in Albuquerque, New Mexico in the shadow of the Sandia mountains where we will have great conference facilities, reasonable room rates and lots of green chilies. Mark your calendars for both meetings!

The 2012 class of ACA fellows, whose names were announced at the banquet during the Boston meeting, include Donald Caspar, Dick Marsh, Virginia Pett, Jane Richardson, and Thomas Terwilliger.

At the behest of Council, a suggested change in the bylaws was brought forward at the general members' meeting, which would add Latin America to the areas authorized to form a national division. Members in attendance at the business meeting supported the suggested by-law change paving the way for a formal vote by the full membership as part of the balloting in the fall. Finally, Council met with Robert Harington from the publishing division of the AIP, to consider the AIP's proposal for a joint venture to publish an new ACA journal. Details are contained in the President's column.

Patrick Loll

News From Canada

While the Canadian Division does not usually fully sponsor sessions at the ACA Annual Meeting, at recent meetings, we have arranged to co-sponsor a number of sessions, in order to feature Canadian scientists. Co-sponsorship means that normally one of the session co-Chairs will be from a Canadian institution. As the co-Chairs are involved in picking speakers from the submitted abstracts, the intent is that some Canadian content will be featured among the talks. However, this depends on the community submitting high-quality abstracts to the meeting.

At the planning meeting for the Honolulu Conference, the Canadian Division arranged to co-sponsor sessions with the Biomac SIG, Small Molecule SIG, Service SIG, Synchrotron SIG and the session on undergraduate teaching. Keep an eye out for the call for papers and submit your latest results; there is a good chance that your abstract could be chosen for a talk.

There was a small but active Canadian representation at the Boston meeting, including an impressive visibility among the poster and oral presentations. The Louis Delbaere Pauling Poster Prize was awarded to Kevin Leung from Western and, as an additional bonus, the RCSB Poster Prize also went to a Canadian, Sergei Kalynych from McGill.

David Rose

Tuesday September 11, 2012 , Just as we are going to press, we received the sad news that Edie Hauptman, widow of Herb Hauptman, passed away peacefully in bed yesterday.

John Scott Award to Jenny Glusker

On 4th November, 2011 **Jenny Glusker** received **The John Scott Award,** which is given to "the most deserving" men and women whose inventions have contributed in some outstanding way to the "comfort, welfare and happiness" of mankind. The donor, John Scott, was an Edinburgh druggist who in the early 1800s set up a fund calling upon the "Corporation of Philadelphia entrusted with the management of Dr. Franklin's legacy" to bestow upon "ingenious men or women who make useful inventions" a premium not to exceed twenty dollars and a suitably inscribed copper medal. Why Scott chose an American city to administer his bequest is not known, although it is believed he had a longstanding interest in America and appreciated the achievements of Benjamin Franklin. Jenny says the award did indeed include a large copper medal.

Seeking Images from the 1950s

Kevin Lotery is a PhD candidate in the History of Art & Architecture at Harvard. He has been working with exhibition organizers from the Tate and elsewhere on the potential reconstruction of ***Growth and Form,*** an exhibition mounted by British artist Richard Hamilton (1922-2011) in 1951.

One goal of the original exhibition was to bring together some of the most cutting-edge image technologies then available and examine them on aesthetic grounds (electron micrographs, photomicrographs, x-ray diffraction patterns, etc.). Images were gathered from various different scientific disciplines, and some of the most prominent images in the exhibition were from crystallography (often from particular scientists - such as J. W. Jeffery, Kathleen Lonsdale, C. H. Carlisle, L. Heller, I. M. Dawson and V. Vand - or departments that Hamilton visited personally).

Kevin is now in the process of trying to locate repositories of similar images at various universities and institutions in the UK. He is looking, therefore, for high-resolution images or original negatives/prints of images from around this period. Please contact Kevin at +44(0) 75 2823 8040 (UK).

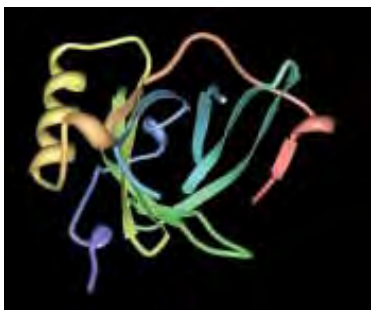
2013 Bau Neutron Diffraction Award to Tom Koetzle

Robert Bau was a teacher and mentor who made major contributions to the development of techniques for single-crystal neutron diffraction. The **Bau Award** will recognize exceptional research achievement in neutron diffraction. The first Bau award will be presented to **Tom Koetzle** at the ACA meeting in Honolulu. Tom has had an exceptional career in neutron diffraction and chemical crystallography. He has played an important role in development and support of neutron diffraction facilities at Brookhaven, Argonne, and Oak Ridge. For over 30 years, Tom collaborated with Bob and members of the Bau research group from USC in a series of groundbreaking studies using neutron diffraction to study metal hydrides and related compounds. Tom also served as director of the PDB for twenty years; he has published more than 200 research papers and mentored a number of postdocs who have gone on to have distinguished careers in structural science.

Errata: The Editors regret the error on page 23 of the summer *RefleXions* which was brought to our attention by Saeed Khan. In the box listing ***Candidates for ACA Offices in 2013***, ***Communications*** should have listed **Graciela Delgado** and **Richard Staples**, and ***Continuing Education*** should have listed **Nick Silvaggi** and **Kraig Wheeler**.

2013 Margaret C. Etter Early Career Award to Eric Ortlund

The **Etter Early Career Award** recognizes outstanding achievement and exceptional potential in crystallographic research demonstrated by a scientist at an early stage of their independent career. **Eric Ortlund**, Emory U School of Medicine, received his PhD in chemistry at the U of South Carolina in 2002 and then did postdoctoral research at both the U of South Carolina and UNC Chapel Hill. From there he went to Emory where he is now an assistant professor in the Department of Biochemistry. Currently his research group uses x-ray crystallography and mass spectrometry coupled with an array of biochemical techniques to study transcriptional signaling at a molecular level. Eric and his colleagues have focused on structural and biochemical studies of human nuclear receptors, which are lipid regulated transcription factors that play central roles in development, cancer, stress and metabolism.



In an early paper (Ortlund et al., Biochemistry (2002) 41, 7030-7037), Eric described the structure of the human complement protein C8gamma at 1.2 Å resolution. PDBID 1IW2 (image created with Simple Viewer).

Below, Peter Müller and Claire Gallou, their daughter Ellen Gesine and new baby Anna Jacqueline Müller who was born just hours after the final meeting of the ACA in Boston and only minutes shy of her due date. Anna checked in on Thursday, August 2nd at 11:08 pm in Concord, MA; height 20 inches and weight 6 pounds, 10 ounces.

Louise Johnson Update

Friends and colleagues of Professor Dame Louise Johnson will be very saddened to learn that she suffered a serious and very incapacitating heart attack with complications in August 2011 and has been in hospital since then. Louise is visited daily by members of her family, and, starting very recently, by a small number of friends. Cards & messages can be sent to Louise c/o Dept of Biochemistry, South Parks Rd, Oxford, OX1 3QU, from where they will be passed on to the family and communicated to Louise.

Digital Artists Take Note

Artist **Julius von Bismarck** won the **2011 First Prix Ars Electronica Collide@CERN** award and has spent the past year in a fully-funded residency at CERN creating new dimensions in the practice of his art because of encounters with the world of science. His work was showcased at this year's Ars Electronica Festival, The Big Picture, 30 August - 3 September.

Last year's open call attracted 395 entries from over 40 countries around the world. This year, artists from all fields are encouraged to apply: experimental sound work and music, architecture and new design, sculpture, generative art and film, social media projects and new design that explores how people relate science and technology are all welcome. The only proviso is that applicants must use digital techniques in the production and/or the development of their proposed project. **The closing date is 26 September 2012** and applicants should submit their entries online, including a short personal testimony video outlining why they want the award. Online submissions should be made at **http://collide.aec.at/** or contact Ars Electronica Press Office: **christopher.sonnleitner@aec.at.**

***RefleXions* Editors Judy & Connie**
are hoping for volunteers
for the position of:
News & Awards Editor
We would also welcome volunteers
for Opinions Column Editor
Please contact either of us.

***Judy:* acareflexions@gmail.com**

***Connie*: conniechidester@earthlink.net**

Judy and Connie are pleased to announce that **Jane F. Griffin**, Principal Research Scientist, Hauptman-Woodward Institute & Assoc. Professor of Structural Biology, SUNY - Buffalo, has joined our volunteer staff as Copy Editor. Jane edited ***all*** the reports in the Boston ACA Meeting section.

International Year of Crystallography

Draft resolution by **Australia, Belgium, Dominican Republic, Luxembourg, Mexico, Morocco and Poland** before the ***United Nations General Assembly***, 15 June, 2012: ***Recalling*** Economic and Social Council resolution 1980/67 of 25 July 1980 on international years and anniversaries and General Assembly resolutions 53/199 of 15 December 1998 and 61/185 of 20 December 2006 on the proclamation of international years; ***Recognizing*** that humankind's understanding of the material nature of our world is grounded, in particular, in our knowledge of crystallography; ***Stressing*** that education about and application of crystallography is critical in addressing challenges such as diseases and environmental problems by providing protein and small molecule structures suited for drug design essential for medicine and public health as well as solutions for plant and soil contamination; ***Considering*** that the impact of crystallography is present everywhere in our daily lives, in modern drug development, nanotechnology and biotechnology, and underpins the development of all new materials from toothpaste to aeroplane components; ***Considering also*** the significance of the scientific achievements of crystallography, as illustrated by twenty-three Nobel Prizes awarded in the area, and that crystallography is still fertile ground for new and promising fundamental research; ***Considering further*** that 2014 marks the centenary of the beginning of modern crystallography and its identification as the most powerful tool for structure determination of matter, Being aware that 2014 provides an opportunity to promote international collaboration as part of the sixty-fifth anniversary of the founding of the International Union of Crystallography; ***Noting*** the broader welcome by the crystallographic community worldwide of the idea of having 2014 designated as the International Year of Crystallography; ***Recognizing*** the leading role of the International Union of Crystallography, an adhering body of the International Council for Science, in coordinating and promoting crystallographic activities at the international, regional and national levels around the world,

1. Decides to proclaim **2014 the International Year of Crystallography**; **2. Invites** the United Nations Educational Scientific and Cultural Organization, mindful of the provisions of the annex to Economic and Social Council resolution 1980/67, to facilitate the implementation of the International Year of Crystallography, in collaboration with Governments, the International Union of Crystallography and its associated organizations throughout the world, relevantorganizations of the United Nations system, the International Council for Science,as well as other relevant non-governmental organizations, also invites the United Nations Educational Scientific and Cultural Organization to keep the General Assembly informed of progress made in this regard, and stresses that the costs of all activities that may arise from the implementation of the present resolution above and beyond activities currently within the mandate of the lead agency should be met-from voluntary contributions, including from the private sector; **3. Encourages** all Member States, the United Nations system and all other actors to take advantage of the Year to promote actions at all levels aimed at increasing awareness among the public of the importance of crystallography and promoting widespread access to new knowledge and to crystallography activities.

Encouraging Research with Implications for ALS

From *Nature* 487, 153 (online, 12 July 2012) doi:10.1038 /487153a: Research published this week offers some hope on both counts, by showing that a lucky few people carry a genetic mutation that naturally prevents them from developing the condition1. The discovery not only confirms the principal suspect that is responsible for Alzheimer's, it also suggests that the disease could be an extreme form of the cognitive decline seen in many older people. The mutation — the first ever found to protect against the disease — lies in a gene that produces amyloid-β precursor protein (APP), which has an unknown role in the brain and has long been suspected to be at the heart of Alzheimer's.

If amyloid-β plaques were confirmed as the cause of Alzheimer's, it would bolster efforts to develop drugs that block their formation in order to treat or prevent the ravaging condition, says **Kári Stefánsson**, chief executive of deCODE Genetics in Reykjavik, Iceland, who led the latest research. He and his team first discovered the mutation by comparing the complete genome sequences of 1,795 Icelanders with their medical histories. The researchers then studied the variant in nearly 400,000 more Scandinavians. The variant is rare, but it has a huge impact on those fortunate enough to inherit even a single copy of it. About 0.5% of Icelanders are carriers, as are 0.2–0.5% of Finns, Swedes and Norwegians. Compared with their countrymen who lack the mutation, Icelanders who carry it are more than five times more likely to reach 85 without being diagnosed with Alzheimer's. They also live longer, with a 50% better chance of celebrating their 85th birthday. The mutation seems to put a brake on the milder mental deterioration that most elderly people experience. Carriers are about 7.5 times more likely than non-carriers to reach the age of 85 without suffering major cognitive decline, such as memory loss. They also perform better on the cognitive tests that are administered thrice yearly to Icelanders who live in nursing homes. Stefánsson and his team discovered that the mutation introduces a single amino-acid alteration to APP. This amino acid is close to the site where an enzyme called β-secretase 1 (BACE1) ordinarily snips APP into smaller amyloid-β chunks — and the alteration is enough to reduce the enzyme's efficiency.

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From Johns Hopkins Current News Releases: July 11, 2012: "Insulating" brain cells appear to play a critical role in brain cell survival and may contribute to neurodegenerative diseases such as ALS. Researchers at Johns Hopkins say they have discovered that the central nervous system's oligodendroglia cells, long believed to simply insulate nerves as they "fire" signals, are unexpectedly also vital to the survival of neurons. Damage to these insulators appears to contribute to brain injury in neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS). The discovery, described online in the journal *Nature*, suggests that a previously unknown - and unexpected - function of these cells is to supply nutrition to the principal brain cells, neurons. This new pathway may prove to be an important and novel therapeutic target for ALS, the researchers say, and potentially other diseases that attack the body's nerve fibers, such as multiple sclerosis.

Jeffrey D. Rothstein, M.D., Ph.D., a professor of neurology and neuroscience at the Johns Hopkins University School of Medicine, and the study's leader, thinks that oligodendroglia insulate axons, like rubber coating around an electrical wire, to speed up the conduction of information. Neurons, the cells responsible for the transfer of information and electrical impulses around the body, work by transferring electrical charges from neuron to neuron. Axons, the wire-like extensions of the neurons, help move the messages from cell to cell, in some cases over many feet. Axonal death is a hallmark of ALS and most other neurodegenerative disorders. Rothstein and his colleagues say the other principal brain cells, the astroglia, were believed to be primarily responsible for providing energy to neurons in the form of glucose, but their experiments show that oligodendroglia are surprisingly crucial in feeding neurons - in the form of less energy-rich lactate, without which neurons and their axons die. Lactate has long been seen as a minor player in this process, but the Johns Hopkins team says it appears to be far more important to nerve cell survival. Moreover, they found that the protein MCT1, the dominant transporter of lactate in the brain, is *only* found in oligodendroglia.

Rothstein says their discovery was rooted in experiments in which scientists, using mice, knocked out the gene that makes the MCT1 protein and saw axons begin to die, even though they were still getting plenty of glucose. Rothstein thinks their findings suggest that oligodendroglia injury - specifically injury to the mechanism that produces MCT1 - may be an important event in the onset and progression of ALS.

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A 1960s-era anti-cancer drug points to treatments for Lou Gehrig's disease. A long-used anti-cancer drug could be a starting point to develop new treatments for the incurable nerve disease known as Lou Gehrig's disease or amyotrophic lateral sclerosis (ALS), scientists report. Their research, showing how the drug prevents clumping of an enzyme linked to ALS, will appear in the *Journal of the American Chemical Society*.

Lucia Banci, **Ivano Bertini** and colleagues explain that ALS causes a progressive loss of muscle control as the nerves that control body movements wither and die. Patients become weak and have difficulty swallowing and breathing, and most die within three to five years of diagnosis. Although some ALS cases are hereditary and run in families, about 90 percent are '*sporadic,*' with the cause unknown. Some research links sporadic ALS to clumping of an antioxidant enzyme called hSOD1. The authors explored whether **cisplatin**, a chemotherapy drug used since the 1960s and that is known to interact with some of the enzyme's amino acids, has any effect on hSOD1 clusters.

They found that in laboratory tests cisplatin binds readily to the enzyme, prevents hSOD1 from aggregating and also dissolves existing bunches. Cisplatin targets sites that can form bonds between hSOD1 after the enzyme loses the atom of copper it normally carries and they note that cisplatin does not prevent the enzyme from performing its normal functions. '***From this work it appears that cisplatin is a promising lead compound for the rational design of ALS treatments,***' the authors say.

2013 American Society for Biochemistry and Molecular Biology Awards

The ASBMB has awarded **Helen M. Berman** the **Delano Award for Computational Biosciences** because she focuses on the structure and interactions of biological macromolecules and the creation of computer resources to enable analysis of proteins and nucleic acids. This award is presented every year to an investigator who develops the most innovative computational tool or application that helps advance the field of molecular life sciences. Helen is Board of Governors Professor of Chemistry at Rutgers, and is a founding member of the worldwide Protein Data Bank (wwPDB) collaboration which supports scientific research and education by providing the Protein Data Bank (PDB) archive. The PDB contains the experimentally determined structures of proteins, nucleic acids, and complex assemblies; information essential to all crystallographers. The Delano award was established by the family, friends and colleagues of Warren L. DeLano; data sharing and accessibility was one of his strongest beliefs.

F. Ulrich Hartl, Max Planck Inst of Biochemistry, who studies the role of molecular chaperones in protein folding and in diseases of aberrant folding & **Arthur L. Horwich,** MD, Sterling Professor of Genetics and Professor of Pediatrics and HHMI Investigator at the Yale School of Medicine, who focuses on chaperonin-mediated protein folding were awarded the **ASBMB Herbert Tabor Research Award**.

Ulrich Hartl and his colleagues have been investigating the mechanisms of protein folding in the cell with the long-term goal to completely understand, at the structural and functional level, how the machinery of molecular chaperones assists in co- and post-translational protein folding. They have been studying the folding pathways in the cytosol of prokaryotes and eukaryotes and hope, ultimately, to understand how protein misfolding causes cytotoxicity and how molecular chaperones act as protective modulators in neurodegenerative disorders such as the polyglutamine diseases and Parkinson's disease.

Arthur Horwich has used genetic, biochemical, and biophysical tools to study the mechanism of action of these ring shaped so-called chaperonin machines that provide essential assistance to protein folding in many cellular compartments. More recently he has focused on neurodegenerative disease as caused by protein misfolding, seeking to understand how misfolded SOD1 enzyme in the cytosol of motor neurons leads to one form of ALS. His lab is modeling mutant SOD1-linked ALS in C.elegans, which paralyze with mutant but not wild-type SOD1, and in mice made transgenic for mutant and wild-type SOD1-YFP that likewise paralyze specifically with mutant transgene. Mutant mice are being analyzed at the level of EM, laser capture of motor neurons for profiling, by ES cell production and motor neuron differentiation, and by genetic modification.

The **Earl and Thressa Stadtman Distinguished Scientist Award** to **Brian K. Kobilka**, Stanford University School of Medicine for his investigation of the structural basis of G-protein–coupled receptor signal transduction. Brian's group studies adrenergic receptors using protein crystallography and biochemical and biophysical tools to determine GPCR structure and to elucidate ligand-induced conformational changes, as well as in vitro and in vivo systems to determine the structural basis for more complex functional properties that are only observed in differentiated cells. For instance, they have used neonatal myocytes from beta1/beta2 adrenergic receptor double knockout mice as a differentiated expression system to study the structural basis for differences in the functional properties of these two receptors. They have developed direct methods to monitor ligand-induced conformational changes in purified beta 2 adrenergic receptor, and recently obtained a high-resolution crystal structure of this receptor.

The **Mildred Cohn Award in Biological Chemistry** to **Jennifer A. Doudna**, University of California, Berkeley, for her studies of RNA-mediated initiation of protein synthesis, RNA–protein complexes involved in targeting proteins for export out of cells and the early steps in gene regulation by RNA interference. Jennifer's lab has three major areas of focus each aimed at understanding the molecular basis for RNA function: catalytic RNA; the function of RNA in the signal recognition particle; and the mechanism of RNA-mediated internal initiation of protein synthesis.

Her group is interested in understanding and comparing catalytic strategies used by RNA to those of protein enzymes, focusing on self-splicing introns and the self-cleaving RNA from hepatitis delta virus (HDV), a human pathogen. They also are investigating RNA-mediated initiation of protein synthesis, focusing on the internal ribosome entry site (IRES) RNA from Hepatitis C virus. Cryo-EM, x-ray crystallography and biochemical experiments are focused on understanding the structure and mechanism of the IRES and its amazing ability to hijack the mammalian ribosome and associated translation factors. The third area of focus in the lab is the signal recognition particle, which contains a highly conserved RNA required for targeting proteins for export out of cells.

Remember to Vote!

Members will be mailed postcards with instructions on how to cast an online ballot. The deadline is November 15th.

ASBMB Awards, cont'd

The **Fritz Lipmann Lectureship** went to **Olke C. Unlenbeck** who focuses on tRNA recognition and relating RNA structure to function. His group prepared a series of derivatives of yeast tRNA Phe which contain single deoxynucleotides and evaluated their ability to bind elongation factor Tu. Of the eight 2' hydroxyl groups predicted by the crystal structure to make contact with the protein, only four have a thermodynamic effect when changed to a deoxynucleotide. They are currently evaluating why the other four do not show an effect. In addition, there is one 2' hydroxyl that affects protein binding by stabilizing the structure of the tRNA in its bound form. This same set of 2' hydroxyl modified tRNAs have revealed that EF-1a, the eukaryotic homologue of EF-Tu, interacts with tRNA in a similar but distinct manner. The group plans to examine the activity of these modified tRNAs with other enzymes that interact with tRNA, including the ribosome.

2012 Anfinsen Award to Barry Honig

The **Christian B. Anfinsen Award**, sponsored by the **Aviv Family Foundation**, recognizes significant technical achievements in the field of protein science. **Barry Honig**, Dept of Biochemistry and Molecular Biophysics, Columbia University and HHMI Investigator, received the 2012 award for his contributions to the understanding of the electrostatic properties of proteins and the development of DelPhi and GRASP, which are among the most widely used programs in structural biology. These and other computational tools from his group have enabled numerous discoveries related to protein molecular recognition, protein-membrane interactions, and protein structural stability. Honig's own recent discoveries related to cell-cell adhesion and sequence-dependent protein-DNA recognition are outstanding examples.

Travel Funds for Students & Postdocs

The IUCr has established a bursary scheme for young scientists attending the annual meetings of the Regional Associates. This is additional to the young scientist support that the IUCr already provides and is aimed at facilitating the attendance of young scientists from the area covered by one Regional Associate at a meeting of a different Regional Associate. The aim is to broaden the knowledge of the awardees and enable them to establish contacts that will be of great help to them in their careers.

The scheme is run by the IUCr and is the responsibility of the Executive Committee, which will form a sub-committee to select successful applicants.

Rules: 1) Students and post-docs may apply for financial assistance of up to $2,000 towards travel and subsistence expenses to enable them to attend a meeting of a Regional Associate (ACA, Asian Crystallographic Association or European Crystallographic Association) other than the one corresponding to their country of residence/work. Up to five awards will be made for each meeting. **2)** Applications should be sent by e-mail to the Executive Secretary (**execsec@iucr.org**) and include evidence of an accepted abstract for a poster or a talk. An application form may be downloaded from **www.iucr.org/__data/assets/pdf_file/0007/65986/APPLICATION_FORM.pdf. 3)** The application should be accompanied by a CV and a letter of recommendation from an academic supervisor/mentor. **4)** An applicant may receive an award on only one occasion. **5)** For each meeting of a Regional Associate there should be no more than one award for each research group. **6)** An applicant must have (or create) an entry in the **World Database of Crystallographers**. **7)** Awards will not be made in the year of an IUCr Congress. **8)** Applications must reach the Executive Secretary at least three months before the beginning of the meeting.

Ludo Frevel Crystallography Scholarship

To encourage promising graduate students to pursue crystallography-related research, and to honor Ludo Frevel, the International Centre for Diffraction Data (ICDD) has established the **Ludo Frevel Crystallography Scholarship Fund**. Multiple recipients are selected on a competitive basis, each receiving an award of $2,500.

Ludo K. Frevel (1910-2011)

Applications for the year 2013 awards must be received by ICDD no later than 24 October 2012. *Students with a graduation date prior to July 1st, 2013 are not eligible for the 2013 scholarship award.* To qualify the applicant should be a graduate student enrolled in a graduate degree program during the 2013 calendar year, with major interest in crystallography, e.g. crystal structure analysis, crystal morphology, modulated structures, correlation of atomic structure with physical properties, systematic classification of crystal structures, phase identification or materials characterization. The term of the scholarship is one year, but a recipient may apply for an additional year by entering the subsequent year's competition. There are no restrictions on country, race, age or sex. The term of the scholarship is one year.

Visit the ICDD website at: **www.icdd.com/resources/awards/frevel.htm** for complete information on our new on-line application procedure. Contact: **Tess Kozul**, Conference Assistant, International Centre for Diffraction Data, 12 Campus Boulevard, Newtown Square, PA 19073. **kozul@icdd.com; www.icdd.**

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it's what makes us cooler

From the Atlanta Journal-Constitution, June 17, 2012.

The crystallographic world lost another giant when R(obert) A(lan) "Ray" Young, long-time Professor of Physics at Georgia Tech, died earlier this year. He will be remembered both for his scientific results and his contributions to the growth of our science.

Ray was born in St. Cloud MN. After service as an enlisted man in the U.S. Navy and Army Air Corps in World War II, Ray obtained his B.S. and M. S. Degrees in physics at Georgia Tech. He received his Ph.D. in physics from the Polytechnic Institute of Brooklyn in 1959, and spent his academic career as Professor of Physics at Georgia Tech. Ray's main scientific work involved the crystal structures of apatite, $Ca_5(PO_4)_3(OH,F)$, and its derivatives. His high-accuracy crystal structures led to correlations between structure and properties of these phases, and directly to work on tooth enamels. Some of these papers have been cited hundreds of times.

Ray in 1973, the year he was ACA President. From Crystallography in North America.

Most contemporary crystallographers probably know Ray as the author of the very influential IUCr monograph on The Rietveld Method (1993). This widely-cited book is still a good place to learn the method. His work on apatite led directly to his pioneering use of the Rietveld method on X-ray data, as many apatites were not available as single crystals. His DBW(S) family of codes was the first program to be used widely with X-ray data. The distribution of the source code (which made it possible for users to make modifications) helped popularize the Rietveld method. These codes are the basis for at least one commercial package, and are the ancestors of the FullProf suite. The book is his mostly widely-cited publication. Other influential papers include ones on profile shape functions, crystallite size and microstrain distributions, and pushing the limits of the Rietveld method. Ray's scientific work extended to kaolinite and cellulose (to support the paper industry in Georgia), and I have found his contributions to our knowledge of these materials helpful in my own work.

Ray's non-written contributions to crystallography might be even greater than his crystal structures and computer programs. He served as President of the ACA in 1973, and was Treasurer from 1968-1971. He served as Local Chair for the ACA meeting in Atlanta not just once but twice (in 1967 and 1994)! He was Chair of the US National Committee for Crystallography from 1979-1981, and a member from 1969-1981. He served the IUCr as Editor of the Journal of Applied Crystallography from 1970-1978, and was a Co-Editor for three years before that. He was the organizer of the Commission on Powder Diffraction, and served as its first Chair (1987-1993). He served on several other commissions, and on both organizing and program committees for IUCr Congresses. His apatite work led to several positions in the International Association for Dental Research.

Ray probably had his greatest influence as an organizer and teacher in schools of crystallography. These included the Rietveld Summer School at Georgia Tech (through 2003), and schools in Egypt (several), Brazil, Denmark, Pakistan, France, Poland (several), Argentina, and Russia. He spoke fluent French, and that certainly helped his international activities. Ray enhanced the practice of crystallography in the U.S. by serving as Chair of the PRT for the High Resolution Neutron Powder Diffractometer at Brookhaven; he was on the Executive Committee of the X-14 PRT at NSLS; on the Advanced Photon Source Steering Committee (1985-1986); and on NSF panels on "Status and Future of Crystallography" and "Crystallography in Research Institutions".

He was even more active (and had leadership roles) within Georgia Tech (many committees and Sigma Xi) and served the Atlanta community in Planned Parenthood, PTA, Boy Scouts, Atlanta Sister Cities Committee, Atlanta-Toulouse Sister City Committee, l'Alliance Francaise d'Atlanta and his church.

Writing a paper with Ray was an adventure. His professor and editor roles came through strongly, and I was forced to think and express myself accurately and precisely. Although I never saw Ray at the front of a large lecture hall, he was a most effective teacher in smaller settings. His one-on-one interactions with students at the Georgia Tech Rietveld Short Courses were especially productive. In the mid-1990s, Ray shared the vision of Bob Snyder, Cam Hubbard, myself, and others of a comprehensive Powder Diffraction File, applicable to modern analytical problems. His service as Vice Chairman of the ICDD helped make that organization the successful modern database organization that it is today.

Ray's given name was Robert. I never made the mistake of calling him "Bob", and am told that it was not a good idea. Even though we spent lots of time in committees together, I never got around to asking him why he went by RAY. I learned a lot from Ray, and he introduced me to many interesting and helpful people. I will miss him as a gentleman, a scholar, and a friend.

James A. Kaduk

The ICDD Board of Directors in the mid-90s. Ray is in the front row, at right. Photo courtesy of Jim Kaduk.

The **Pauling Poster Prizes,** established to honor Linus Pauling, who was one of the pioneers of American structural research and a very supportive member of the ACA for many years. At each annual meeting the seven best graduate or undergraduate poster presentations receive Pauling awards. Each award consists of $200, a complimentary banquet ticket, and a copy of a Linus Pauling book. The 2012 selection committee members were **Brian Patrick, Katherine Kantardjieff, Alexander Nazarenko, Tobin Sosnick** and **Hilary Jenkins**.

2012 prizes went to: **Nilda Alicea-Velazquez** for **S-01:** ***Structural studies of SHP-1 protein tyrosine phosphatase substrate recognition*** by Nilda Alicea-Velazquez and Titus Boggon.

Nilda Alicea-Velazquez with Poster Chief Ilia Guzei

Yen-Ting Lai for **S-58:** ***Crystal structure of a 16 nm, half-megadalton protein cage designed by fusing symmetric oligomeric domains*** by Yen-Ting Lai, Duilio Cascio and Todd Yeates.

Christopher Boone for **S-23:** ***Kinetic and Structural Characterization of Thermostable Variants of Human Carbonic Anhydrase H*** by Christopher Boone, Zoe Fisher, Shyamasri Biswas, Balasubramanian Venkatakrishnan, Mayyank Aggarwal, Chingkuang Tu, Mavis Agbandje-McKenna, David Silverman & Robert McKenna.

The **Herman R. Branson Pauling Poster Prize** recognizes the contributions of Herman Russell Branson, one of the first African American physicists to make crystallography the focus of his research. The 2012 prize went to **Amber Smith** for **S-15:** ***Investigating the Role of the C-terminal Tail of PLP Synthase*** by Amber Smith & Janet Smith.

The **Muttaiya Sundaralingam Pauling Poster Prize** recognizes the ground-breaking crystallographic research on the stereochemistry of nucleotides and nucleic acids done by Muttaiya Sundaralingam and his colleagues. The 2012 winner is **Tamaria Dewdney** for **S-51:** ***Ligand Modifications to Reduce the Relative Resistance of Multi-drug Resistant HIV-1 Protease*** by Tamaria Dewdney, Yong Wang, Zhi-gang Liu, Samuel Reiter, Joseph Brunzelle, Julia Koyari, & Ladislau Kovari.

The Louis Delbaere Pauling Poster Prize, sponsored by the Canadian Division of the ACA and the Canadian National Committee of the IUCr, is given to the highest ranked graduate or undergraduate poster from a Canadian laboratory. This year the prize went to **Kevin Leung** for **S-35:** ***The Structure of Quinone Reductase 2; Changes Upon Reduction of FAD and Binding of the Anti-malarial Drug Chloroquine*** by Kevin Leung & Brian Shilton.

The IUCr Pauling Poster Prize, sponsored by the International Union of Crystallography, is complimentary online access to all IUCr journals for one year or a complimentary volume of either the *International Tables* or another IUCr publication. It is given to the best poster by an undergraduate or graduate student; the 2012 prize went to **Serah Kimani** for **S-33:** ***Structural Determinants of Substrate Specificity in a Nitrilase Superfamily Smidase*** by Serah Kimani & Trevor Sewell.

RCSB Protein Data Bank Prize

The selection committee members were **Barry Finzel** (chair), **David Rose** and **Patrick Loll**. They decided to award the RCSB Prize to **Sergei Kalynych** for **M-42:** ***Crystallographic Studies of Closely Related Lipopolysaccharide O-antigen Chain Length Regulators*** by Sergei Kalynych, Deqiang Kumar, Sonali Dhindwal & Dipak Paul.

The committee also gave an **Honorable Mention** to **Rebecca Goldstein** for **M-35:** ***A Possible Mechanism for the Regulation of the PI-PLC from S. aureus*** by Rebecca Goldstein, Jiongjia Cheng and Mary Roberts.

The 2012 Crystal Engineering Prize went to **Bo Wang** for **S-56:** ***Cooperative Guest-Host-Guest Recognition in Ferroelastic and Ferroelectric Calixarenes*** by Bo Wang, Matthew Peterson, Shane Nichols, Eric Cha and Mark Hollingsworth.

This award is sponsored by *CrystEngComm*, which is published by the Royal Society of Chemistry. It is given to the best student, graduate or undergraduate poster in the area of crystal engineering supramolecular chemistry. **Victor Young** chaired the selection committee, on which **Louise Dawe** also served.

The ***2012 Journal of Chemical Crystallography Prize*** went to **Steffen Bernard**. Steffen and his co-authors David Akey, Shengying Li, David Sherman and Janet Smith won this award for their research efforts to further understand the role of the sugar O-methyltransferase, MycF, in the biosynthesis of mycinamicin macrolide antibiotics. MycF is a S-adenosyl-L-methionine (SAM) and metal dependent methyltransferase and is responsible for the 3´ hydroxyl methylation of small molecule substrates. The authors have determined several structures of MycF in complex with S-adenosyl homocysteine, Mg^{2+} and the substrate mycinamicin III.

A challenge to data processing and structure determination was the presence of crystals of the same protein-substrate complex with different space groups and identical unit cell constants. This crystallographic anomaly occurred because a translation of layers within the crystal altered symmetry operators while maintaining the unit cell composition. The structures revealed non-specific enzyme-substrate contacts suggesting significant promiscuity in MycF substrate binding. The authors also found that an active site, conserved aspartic acid (Asp 191) is most likely the catalytic base of the enzyme. The activity of this aspartate appears to be directly regulated by a magnesium ion, which is involved in substrate binding and the stabilization of the hydroxylate intermediate. The work presented in poster **M-29:** ***Insights Into the Substrate Specificity and Mechanism of the Macrolide Sugar O-methyltransferase, MycF*** provides significant new insights into natural mechanisms used by this family of enzymes to modify small molecules for stabilization and cell wall permeability.

Jennifer Wierman received an honorable mention for **M-70:** ***A New Technique for Reducing Background Scattering in High Pressure Cryocooling.***

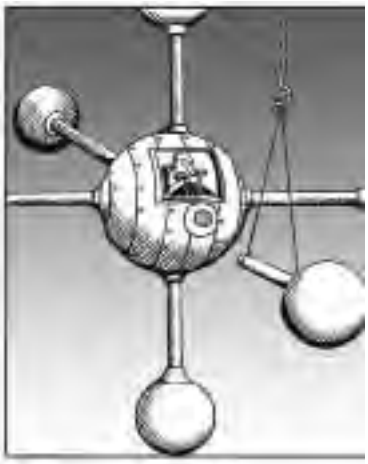
Emmanuel Skordalakes (chair) & Kristin Kirschbaum

The ***2012 Oxford Cryosystems Low Temperature Poster Prize*** was awarded to **Yimin Mao** of Brookhaven National Laboratory for his poster **M-62:** ***Preparation of Cryo-Preserved Membrane Samples Using a Slam Freezing Apparatus for X-ray Scattering Measurements***, (co-author LinYang, also at BNL), by the selection committee: **Bill Ojala, Frank Fronczek, Matt Redinbo**, and **David Jeruzalmi**. In a carefully crafted poster and with an enthusiastic in-person presentation, Yimin explained the technique he developed, and the motivation that led him to this approach can often be used for small samples. He noted that that the technique of rapid freezing using liquid cryogens can be used for small samples (such as protein crystals), but can prove challenging to implement in the case of larger samples, particularly biological tissues, due to cooling rates that are insufficiently fast.

To overcome this problem, Yimin and his co-workers developed a specialized slam-freezing apparatus and associated experimental protocols. The technique described in the poster involves the very rapid thrusting of the sample against a liquid-nitrogen cooled copper mirror. Samples prepared in this manner are well suited for examination by grazing incidence x-ray scattering. Yimin's poster received the cash prize awarded by Oxford Cryosystems at the meeting for the best poster describing work in low temperature crystallography.

Bill Ojala, chair

Editor's note: Yimin was so excited to hear his name announced (this was his very first ACA meeting) - that he took the podium mike and told everybody how happy he was. The audience responded warmly and gave him a big round of applause. Louise Dawe is on the right, and Emmanuel Skordalakes and Katherine Kantardjieff are in the background.



The mysterious world of ligand substitution

From the Nearing Zero website: nearingzero.net/res.html.

2012 ACA Meeting - Boston, MA, July 28th - August 1st

The meeting began with workshops on **Modeling and Refinement of Nanoparticle Structures from Diffraction Data**, **Crystallography - World of Wonders**, **Refmac and Coot**, and **Structure Refinement and Disorder Modeling with OLEX2** on Saturday, July 28th. **Eric Mazur**, Harvard, presented **Confessions of a Converted Lecturer** in **SP.01: Innovations in Undergraduate Education** just before **Donald Caspar**'s fine perspective on **The History of Structural Biology**. See **SP.01** and **SP.02** on page 23). Five of the ACA's major awards were presented at this meeting. The **Buerger Award** went to **John Spence**, AZ State U, page 15; the **Warren** to **Paul Fenter**, ANL, page 17, and the **Etter Early Career Award** to **Emmanuel Skordalakes**, Wistar Inst. & U of Virginia, page 17. The **Supper Instrumentation Award** was given to **Ron Hamlin**, ADSC, page 19. This year the ***Transactions Symposium*** in honor of Bruce Foxman, whose birthday happened to coincide with this meeting, was titled **Transformations and Structural Oddities in Molecular Crystals.** Many of his former students attended (see photo on page 23) and gave him a birthday dinner party.

Daniel Nocera was one of the after-dinner speakers at the Award's Banquet on Wednesday evening, August 1st and received the **Elizabeth Wood Award** for bringing science to the attention of a wider audience. See photos of the banquet on page 66. The **Program Chair**, **Peter Müller**, and the **Local Chairs Bruce Foxman** and Bruce Noll all spoke from the podium, as did **Poster Chief Ilia Guzei**, who doled out the poster prizes, see the two pages immediately preceding this. **Tom Koetzle** gave the **Past President**'s address which is usually last, but this year we broke with tradition. The attendees each had a lottery ticket and were called to the podium to choose books from the ACA office archives. Many of us went home with very heavy suitcases!

Clockwise, from top: Timothy Munsie & Sai Venkatesh Pingali; Peter Strickland & S.N. Rao; Bill Duax and Bob Finnegan; In back, L-R: Joseph Yarbrough, Robert McKenna, Dayne West. In front, L to R.: Mayank Aggarwal, Katherine Sippel, Natalia Diaz Torres, Bhargav Kondeti (partially hidden) and Melissa Pinard.

AW.01: Buerger Award Lecture

John Spence, Regent's Professor of Physics at Arizona State University and LBNL, received the **Buerger Award** from **George Phillips**. The Buerger Award is given to recognize mature scientists who have made contributions of exceptional distinction in areas of interest to the ACA. John spoke on *The Future of Diffraction Physics in Crystallography*, suggesting that, because of advances in instrumentation, crystallography is far from mature, and much remains to be done. As examples he described two unexpected discoveries of the last decade - *lensless imaging*, pioneered in Janos Kirz's group, and the *diffract-before-destroy* approach to outrunning radiation damage, first suggested by Solem and demonstrated at **Flash** (which used to be the Tesla Test Facility or TTF) in 2006.

Spence began his scientific career as a solid state physicist and an electron microscopist in the groups of P. Hirsch and later J.M. Cowley, then moved into biophysics in 2004 with the publication of a paper on serial crystallography. His discussions with Joe Stohr at SLAC regarding the Linac Coherent Light Source (LCLS) also contributed to that 2004 move. After briefly reviewing Martin Buerger's work, he went on to discuss his own earlier work: the *Alchemi* electron channeling method and other topics from his texts on atomic-resolution electron microscopy, -and his work with J. Zuo and M. O'Keeffe on the measurement of bond charges between atoms in crystals using the convergent beam electron diffraction method. He also talked about his work with Zuo and O'Keefe on extension of the charge-flipping method to powder x-ray diffraction for phasing and resolving ring overlaps. Finally he reported the newest results from femtosecond diffraction experiments at an XFEL. In lensless imaging, using oversampled diffraction data, electron density maps from single particles can now be reconstructed by iterative methods. As examples he mentioned the atomic resolution electron diffraction images obtained by Zuo for a single nanotube; work with Chapman, Barty, Shapiro and Marchesini on imaging, using x-rays, nano-sized gold balls on a 3D pyramid at 10nm resolution; and snapshot XFEL imaging of individual viruses led by the Hadju group.

The large group of collaborators at the LCLS in Stanford has in the last two years published several milestone papers using the *diffract-and-destroy* method of serial femtosecond crystallography (SFX). Femtosecond pulses of x-rays, brief enough to outrun the resolution limiting effects of damage, are generated in a micron sized beam from high energy electron bunches with frequency 120 Hz and about 1012 hard x-ray photons per pulse. In the SFX method a constantly refreshed supply of protein nanocrystals flows across the beam in random orientations. By using short pulses *instead* of freezing, data can be collected at room temperature from the many proteins which fail to grow crystals large enough for conventional macromolecular x-ray crystallography. Instrumentation for the delivery of these has been developed by the ASU group (Doak, Weierstall, Fromme, Spence) over the last 6 years. The Monte-Carlo method for merging data from size-varying nanocrystals was described in the dissertation of one of Spence's students, Rick Kirian. This software has since been developed and made available by Tom White in the DESY group. SFX milestones include the achievement of atomic resolution, and the first new biology elucidated by images of a drug target.

John, at left, accepting the award from ACA President George Phillips.

Spence concluded his talk with a review of the rich opportunities for new experiments in time-resolved structural biology at XFELS, including pump-probe experiments on Fromme's Photosystem I using the liquid jet injector, new solutions to the phase problem using the *shape transforms* in nanoxtal data, and snap-shot biochemical dynamics, using correlated fluctuations in two-dimensional fast WAX patterns. All these will be explored at a **Royal Society Workshop on Biology with XFELS** organized by John together with Henry Chapman in October 2013.

Marius Schmidt

13.01: Emerging Sources: Theory and Practice 1

This session covered cutting edge science at existing research facilities and the newest developments in theory and practice at emerging sources such as the free electron laser for hard x-rays (XFEL) at the LCLS.

John Tainer, Scripps Institute, concentrated on small and wide angle x-ray scattering (SAXS/WAXS) techniques. He introduced the **BioISIS** data base as a resource for macromolecular SAXS. Time-resolved SAXS with millisecond and microsecond time-resolution will become routine at emerging next generation x-ray sources such as the LCLS.

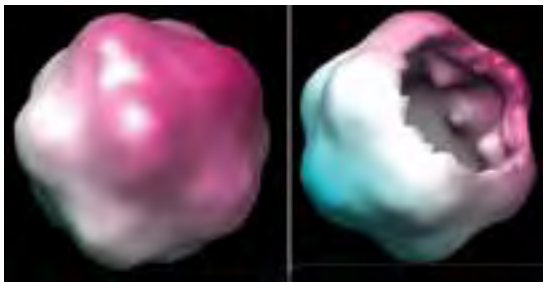
Friedrich Schotte, staff scientist at the NIH, talked about picosecond time-resolved crystallographic experiments performed with P. Anfinrud and others at a synchrotron. His movie, derived from photoflash experiments on carbonmonoxy-myoglobin with picosecond time resolution, showed the detailed succession of structural changes shortly after the carbon-monoxide was flashed away from the heme-iron position. He also showed his newest time-resolved crystallographic results on photoactive yellow protein where two early intermediates complete the photocycle on the picosecond and fast nanosecond time scales.

Peter Schwander, U Wisconsin-Milwaukee, is one of the major developers of embedding diffraction data into low dimensional manifolds. Manifold-embedding has the potential to orient diffraction patterns in 3D at photon counts to be expected from x-ray diffraction

cont'd, next page

13.01, cont'd: experiments on single molecules at the XFEL. More important, he demonstrated how manifold embedding allows one to study structural heterogeneity, and thus removes the need for identical molecules. The talk referred primarily to cryo-electron microscopy, a technique currently used to intensively investigate heterogeneity. He showed that manifold embedding faithfully separates unlike particles at the experimental signal-to-noise ratio of cryo-EM.

In back, L to R: Henrik Lemke, Marius Schmidt, Yun-Xing Wang. In front: John Tainer, Dilano Saldin, Friedrich Schotte, Marc Messerschmidt, Peter Schwander.

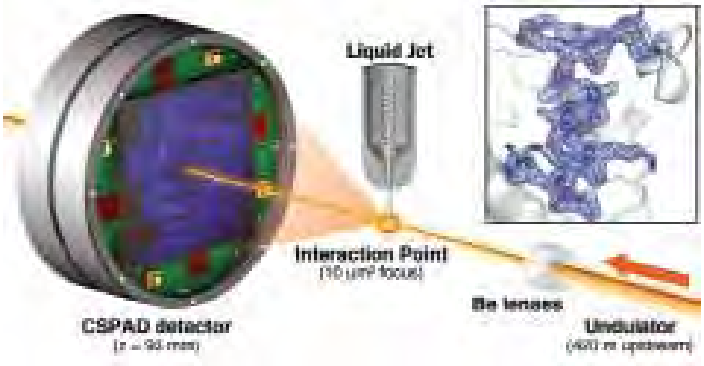


Dilano Saldin, U Wisconsin-Milwaukee, is known for new algorithms in x-ray diffraction theory. He demonstrated how to determine the structure of icosahedral and helical viruses from diffraction patterns of random orientation without the use of crystals. This is achieved by averaging the angular correlations of a large number of diffraction patterns from an ensemble of identical objects. Such diffraction patterns could be obtained using the ultra-short x-ray pulses available at the XFEL.

3D images of the icosahedral satellite tobacco mosaic virus (STNV) reconstructed from simulated diffraction patterns from random orientations of the virus as expected from proposed "diffraction-before-destruction" experiments with an X-ray Free Electron Laser (XFEL). The image at left shows a computational slice through the image, revealing the hollow character of the protein capsid whose atomic coordinates from the Protein Data Bank were assumed in the simulations of the diffraction patterns. D K. Saldin et al., Optics Express 19, 17318-17335 (2011).

Pietro Musumeci, UCLA, highlighted the UCLA **Pegasus** project, which provides a source of relativistic electrons for ultrafast, time-resolved electron diffraction experiments. Since the scattering cross section of matter with electrons is several orders of magnitude larger than that of x-rays, electrons are an attractive alternative. With relativistic electrons the space charge forces are greatly reduced due to relativistic space dilation, and more electrons can be packed into ultrashort pulses. With these, one can study structure and dynamics of matter with high spatial and temporal resolution. The time-resolved melting of gold particles was given as an example.

Uwe Weierstall, Arizona State U, mainly concentrated on the injector technology used to perform recent experiments at the LCLS. He introduced serial nanocrystallography by outlining some of the advantages: nanocrystals are readily obtainable before macroscopic crystals can be grown, they allow dynamic processes to be followed, and they are small enough that they scatter intensity between the Bragg positions, which *can* be used to solve the phase problem. The small crystals are injected into the beam by a liquid jet whose diameter and velocity can be controlled by a surrounding gas stream. Uwe described experiments performed by a large international collaboration on nano sized crystals of lysozyme and membrane proteins such as photosystem I.

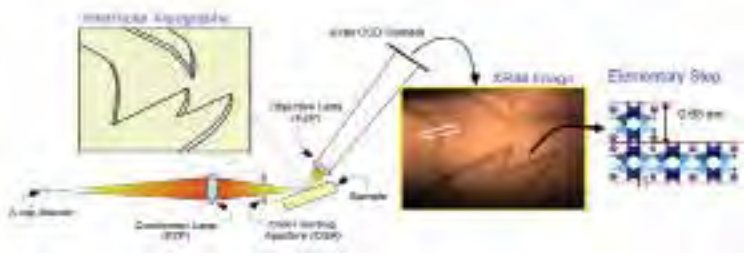


Henrik Lemke and **Marc Messerschmidt** reported the newest developments at their beamlines, XPP and CXI, respectively, at the LCLS. Henrik showed the ins and outs of pump-probe experiments with femtosecond time resolution using the spatially, temporally and spectrally fluctuating x-ray beam at the LCLS. Marc presented the beamline design necessary for the serial femtosecond nanocrystallographic experiments that were recently conducted at the CXI beamline.

Marius Schmidt and Yun-Xing Wang

AW.02: Warren Award to Paul Fenter

Paul Fenter, a Senior Physicist in the Chemical Sciences & Engineering Division at ANL, described his research on liquid-solid interfaces, and explained why they are central to a wide range of energy-related systems and processes critical to modern society. Liquid-solid interfaces are buried beneath a liquid layer that is opaque to surface sensitive structural tools, so Paul and his colleagues developed phase-sensitive x-ray based scattering techniques to effectively image structures and processes at liquid-solid interfaces. He cited three examples: imaging of the vertical (i.e., laterally averaged) interfacial structure of mineral-water interfaces utilizing phase recovery algorithms on x-ray reflectivity data; imaging element-specific ion distributions at charged interfaces through phase-sensitive resonant x-ray reflectivity; and direct imaging of sub-nm high lateral topography and lateral structural variations using x-ray reflection interface microscopy.



The x-ray reflection interface microscope (XRIM) images elementary topography on a solid surface through the use of phase-contrast. The dark lines on the XRIM image correspond to 0.65 nm high steps, whose structure is shown (right).

Paul graduated (magna cum laude) in 1984 with a BS in physics from Rensselaer Polytechnic Institute and obtained his PhD from U Pennsylvania in 1990. He did a post-doc at Princeton and stayed on as a staff member in their Materials Institute until 1997 when he moved to Argonne. He is shown at right receiving the **Warren Award** from ACA President George Philips. The B.E. Warren award is given *to recognize an important recent contribution to the physics of solids or liquids using x-ray, neutron or electron diffraction techniques*.

Connie Rajnak

George Phillips on the right, presenting the Warren Award to Fenter.

AW.03: Etter Early Career Lecture

The **2012 Margaret C. Etter Early Career Award** was presented to **Emmanuel Skordalakes**, Wistar Inst., U of Pennsylvania, - for his elucidation of the structure of the telomerase enzyme. Telomerase is a specialized RNA-dependent DNA polymerase that extends the ends of chromosomes to promote genome stability and is commonly overexpressed in human cancers and other age associated disorders. Emmanuel presented several high-resolution structures of telomerase, alone and in complex with cognate RNA and DNA substrates. He and colleagues in his lab tested various hypotheses about telomerase function, regulation and replication with a series of experiments that were inspired by the structures. Taken together, Emmanuel's findings represent a profound contribution to the structural biology of telomerase. The stage has been set for the design of better therapeutics for treating diseases associated with aberrant telomerase activity.

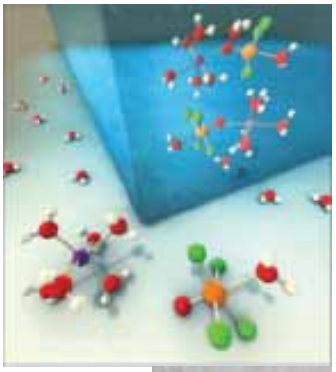
Eric Montemayor

Emmanuel Skordalakes, at left, accepting the Etter Early Career Award from Eric Montemayor.

AW.03 L to R: Angeline Lyon, Gilbert Huang, George Lountos, Joseph Liberman, Eric Montemayor, Martin Donakowski, Bhupinder Sandhu, Hamilton Napolitano, Yulia Sevryugina, Qi Jiang, Xiaofei Jia.

12.01: Etter Early Career Award Symposium

Martin Donakowski, who is currently a graduate student in Kenneth R. Poeppelmeier's group at Northwestern, reported a methodology for designing polar inorganic noncentrosymmetric (NCS) solids with interesting physical properties. By using Λ-shaped basic building units composed of $[Cu(H_2O)_5]^{2+}$ cations and $[VOF_4(H_2O)]^{2-}$ anions, Martin demonstrated a successful design of an NCS structure which crystallizes in the polar space group $Pna2_1$.



The first noncentrosymmetric carbonless molecular crystal, $CuVOF_4(H_2O)_7$ Donakowski, M. D., Gautier, R., Yeon, J., Moore, D. T., Nino, J. C., Halasymani, P. S., Poeppelmeier, K. R. JACS, 2012, 134, 7679.

Bhupinder Sandhu, currently an undergraduate student with Tatiana V. Timofeeva at New Mexico Highlands U, presented her structural studies of co-crystals and salts formed from substituted piperidones or pyridines and a range of dicarboxylic acids.

Gilbert Huang, a graduate student in Choel Kim's group at Baylor College of Medicine, reported how cyclic GMP-dependent protein kinases (PKGs) recognize slight structural differences between the cyclic nucleotides cGMP and cAMP, in order to coordinate different physiological responses to these different signaling molecules. As part of this study, Gilbert solved structures of the carboxy terminal cyclic nucleotide binding domain (CNBD) of human PKG1 bound to either cGMP or cAMP, as well as the structure of CNBD-B in the absence of bound nucleotide. **Angeline Lyon** is a postdoctoral fellow in John Tesmer's group at the Life Sciences Institute of the U of Michigan. Her structural work has helped explain how phospholipase Cβ (PLCβ) is activated in response to extracellular stimuli through specific interaction with the heterotrimeric G protein Gαq. Her structures of PLCβ illuminated not only the structure of the enzyme in its basal state, but also in complex with Gαq, thereby revealing the allosteric mechanism by which PLCβ is activated by Gαq. The structures defined a functional role for PLCβ's unique C-terminal regulatory domain.

The YSSIG **Etter Student Lecturer prize** was awarded to **Joseph Liberman**, U Rochester, in recognition of his outstanding work in elucidating the structure and function of the $preQ_1$ riboswitch.

Yulia Sevryugina presenting the Etter Student Lecturer Prize to Joseph Liberman. Eric Montemayor is on the right.

Riboswitches are RNA-based sensors that are capable of modulating gene expression in response to cellular levels of various metabolites. Joseph not only presented the crystal structure of the $preQ_1$ riboswitch, but also explained how the RNA was initially crystallized and how the phase problem was solved by single-wavelength anomalous diffraction methods.

The integration of biological relevance with technical protocol was an excellent format for a session presented and attended by the young scientist community. The **Etter Early Career Symposium** received generous financial support from Bruker, Art Robbins Instruments, LPS, Emerald Biosystems and Jim Pflugrath that provided funds for a number of travel awards for young scientists presenting their work in this session.

Eric Montemayor & Yulia Sevryugina

AW.04: Supper Instrumentation Award

Ron Hamlin, Area Detector Systems Corporation, was honored with the **Charles Supper Instrumentation Award** for his work in advancing the development of x-ray area detectors. His talk *2-D X-ray detectors -- What do we really want and how can we build it?* covered the development of x-ray detectors from film (used in the early 1900s) to the modern pixel array detectors used today. He began with how he first became interested in x-ray area detectors while at UCSD and how his PhD project, working with Nguyen-Huu Xuong, led to the construction of the first multiwire area detector - which later became a national resource. Ron then highlighted important developments in detector technology: the optical film scanners, the single point scintillation counters used in diffractometers, image intensified television cameras, 2-dimensional gas-filled detectors, image plate detectors, CCD detectors and pixel array detectors. The pros and cons of each of the detectors were discussed as well as the characteristics of the "ideal" x-ray detector that Ron and others have long strived to achieve. Ron also told about the ups and downs he faced as a small business owner striving over the years to keep pace with rapidly developing technology. The talk was very interesting and educational; it was an inspiring story about how the simple interest of a scientist/entrepreneur 30 years ago ultimately had an enormous impact on science.

Ron Hamlin on the left accepting the Charles Supper Award from ACA President George Phillips.

John Rose

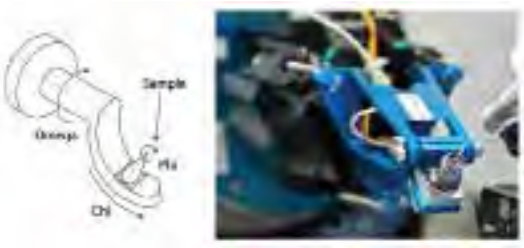
11.01: Advanced Hardware and Applications

11.01 L to R: Malcolm Capel, John Rose, Howard Robinson, Michael Blum, Aina Cohen, Christian Brönnimann, Sandro Waltersperger, David Schuller. (Ron Hamlin not pictured.)

The session, sponsored by the Synchrotron SIG, focused on recent advances in x-ray area detector technology, robotics and automated data collection applied to synchrotron-based structural biology, and how these advances are being incorporated at beamlines in the US and elsewhere.

Howard Robinson, NSLS, reported on the Qmx data collection system developed at NSLS and how it could be used to center the crystal in the beam using both loop centering and a diffraction-based grid search. The automated system is asynchronous in that the crystal can be centered and screened for diffraction quality and then be removed from the goniometer to await data collection at a later time. This allows the user to analyze the diffraction characteristics of the crystal to determine the optimum data collection strategy. The asynchronous system also allows for the interleaving of the screening and data collection processes from multiple users for more efficient beam time usage.

Sandro Waltersperger, Swiss Light Source, described the PRIGo multi-axis goniometer recently installed on beamline X06DA. PRIGo was developed as an alternative to the kappa goniometer or Eulerian cradle and addresses many of the limitations common to multi-axis goniometers. The goniometer enables one to collect diffraction data around several crystal axes, which is beneficial for MAD/SAD experiments since it allows for the capture of Bijvoet pairs on the same image. The PRIGo also facilitates sample reorienta-



From Meitian Wang, Session 13.14: A novel multi-axis goniometer PRIGo installed at macromolecular crystallography beamline X06DA at the Swiss Light Source. Used for sample re-orientation in macromolecular crystallography, PRIGo (Parallel Robotics Inspired Goniometer) is a novel and compact goniometer which emulates an arc. It consists of the usual ω rotation performed by an Aerotech stage, followed by four linear stages working synchronously to allow the three translations (X,Y,Z), the χ rotation (0-90°), and finally the ϕ rotation (0-360°) around the sample holder axis. Spheres of confusion of <1 µm, <7 µm and <10 µm were obtained for ω, χ and ϕ, respectively. PRIGo has been developed at Paul Scherrer Institut and installed at beamline X06DA at the Swiss Light Source. It has been in use since January 2012.

tion to align a long cell axis for better diffraction spot separation or the selection of the optimal part of the crystal. Several successful S-SAD studies using the PRIGo goniometer and a PILATUS 2M detector on X06DA were presented.

David Schuller, CHESS, gave an update on the installation and commissioning of the second generation Berkeley Automounter (BAM-2) at MacCHESS on beamline A-1. Unlike the previous BAM-1 design common at many beamlines that incorporates a pneumatic actuator and a translation/rotation table, the BAM-2 uses a fixed dewar capable of holding nine pucks and a 3-axis cartesian robot. Other improvements include a force/torque sensor for the gripper. The system accepts both Uni-pucks and older ALS style pucks. Schuller is currently working on speeding up calibration and increasing reliability through improved use of the force/torque sensor. The BAM-2 is in the last stage of commissioning and users are invited to try it out.

Aina Cohen, SSRL, conducted a live demo of a remote access *in situ* UV-visible absorption spectroscopy system to monitor metal oxidation states within protein crystals. This system will be installed on SSRL BL9-2 and BL11-1 in their next experimental runs. She then described features of BL12-2, the new undulator station optimized for micro-beam applications, and strategies to optimize its use with challenging systems. BL12-2 employs a locally designed precision air-bearing microdiffractometer with a measured sphere of confusion of ± 0.6 μm, and an inline sample camera capable of resolving objects as small as 1 μm. The beamline uses mirror pitch feedback and temperature control of the optical and hutch components to achieve excellent beam positional stability (0.3 μm RMS drift over 1 hr). BL12-2 also hosts a Stanford Automounting System and a PILATUS 6M pixel array detector making the beamline ideal for fast crystal screening and shutterless data collection.

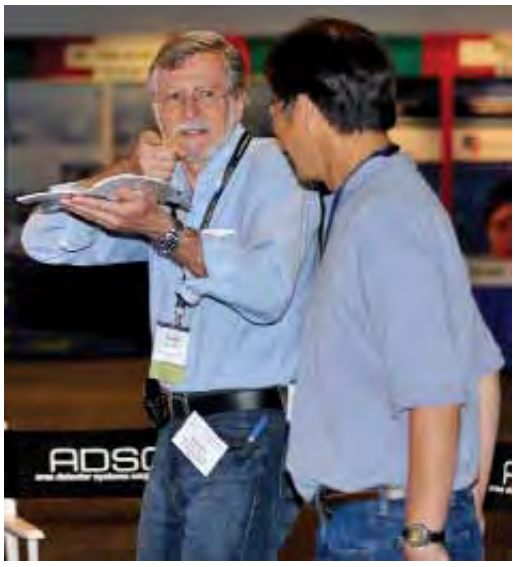
Christian Brönnimann, Dectris Ltd, updated the audience on several developments related to their PILATUS photon-counting detector. These improvements are aimed at optimizing data quality for data collected with ultra-soft x-rays, and enhancement of detection efficiency for hard x-ray applications. They have a new PILATUS3 detector series with improved count rates, readout speeds and global stability; the PILATUS3 ASIC for example. PILATUS modules have been successfully tested under vacuum at energies ranging from 1.75 to 10 keV for SAXS and soft x-ray MX crystallography applications. Thicker silicon sensors (450 and 1000 μm) which have increased detection efficiency for hard x-rays have also been developed and tested. The new PILATUS3 ASIC is capable of count rates of up to 10^7 photons/sec/pixel and has a readout time of less than one millisecond.

Malcolm Capel, NE-CAT/Cornell U, reported on the PILATUS 6MF pixel array detector recently installed on NE-CAT's undulator beamline 24-IDC. The detector's 20 bit dynamic range allows for the optimal collection of high- and low-resolution data on the same image without overloads. The detector's zero read noise, 2.3 millisecond readout speed allows for efficient "shutterless" fine-slice data collection, increasing signal to noise. NE-CAT has developed methodologies to exploit the unique properties of the 6MF including vector scanning, where the crystal is scanned across the beam during data collection. Vector scanning can be used to moderate radiation damage effects on data quality by continually placing fresh crystals into the beam, making more efficient use of samples larger than the beam. Now crystals in opaque cryomedia can be located and the best diffracting crystal domains can be identified. Malcolm also presented an interesting S-SAD study using the 6MF with 12 keV x-rays.

Michael Blum, Rayonix LLC, described a new generation of detectors that Rayonix is developing based on Split Frame Transfer CCDs. The new detectors have a one-millisecond inter-frame dead time and offer frame rates as high as 140Hz. The speed of the new detector will allow for shutterless fine slice ($\theta < 0.5°$) data collections; it is similar to pixel array detectors, but also supports traditional wide slice data collection ($\theta \geq 0.5°$) if desired. Highly parallelized readout from each chip yields excellent noise levels at full speed. A low read noise mode, supporting a dynamic range of 18-bits, is software selectable. An advantage of the CCD based design is that the fiber optic tapers can be shaped to provide optimal detection surfaces for WAXS detectors. The first of these new fast CCD systems will be put into operation at the APS during the summer/fall of 2012.

John Rose, SER-CAT / U of Georgia, presented in John Chrzas' stead their plans for integrating the fast Rayonix MX300HS detector into the SER-CAT undulator beamline 22ID. SER-CAT (Southeast Regional Collaborative Access Team) is a consortium of 23 institutions and serves a user community of over 100 user groups scattered over 13 states. It is unique in that more than 90% of the data is collected remotely. To support the new 10 Hz detector, which will be installed in early 2013, SER-CAT has made upgrades to its sample mounting robotics, network infrastructure, data storage and on-site computing. To handle the 3 - 6 fold increase in sample throughput, the Berkeley Automounter on 22ID is being modified to host two Dewars, each holding 15 pucks, providing a total capacity of 430 crystals. The new detector will be supported by a 100 TB Panasas data storage system running on a 10 GB backbone and a Scyld Beowolf OS based computing cluster capable of 1.1 Tflops for data processing.

Ron Hamlin, Area Detector Systems Corporation, described a new type of pixel array detector called the Dual Mode Pixel Array Detector (DMPAD) that ADSC is developing which addresses the problem of coincidence loss common to PAD detectors at



Ron Hamlin at the ADSC booth, demonstrating (!) for a client.

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Session 11.01 cont'd: high-count rates. The DMPAD has pixels that can be individually programed via the software interface to operate in either (1) the high-flux charge ramp counting mode or (2) the simple x-ray pulse counting mode similar to that used by the PILATUS detectors. While the DMPAD's one microsecond data capture provides nearly ideal support for '*shutterless data collection,*' the DMPAD also offers the ability to map the counting method to detector pixels. This mapping can be exploited to simultaneously measure the bright low-order reflections without dead time loss or saturation effects (dynamic range 107 photons/sec/pixel) using high flux charge ramp counting mode, and also, in x-ray pulse counting mode, the weaker high-resolution reflections.

In addition to the oral presentations, several posters were associated with the session. **Doletha Szebenyi**, CHESS, presented poster **M-81:** *Advances in Pressure Cryocooling at MacCHESS*, describing high pressure cryocooling. In **T-70:** *Automated gradient making for protein crystal optimization,* **Joby Jenkins**, TTP Labtech Ltd, reported on a new low cost automated gradient maker designed to rapidly generate screening or optimization crystallization plates. **Timothy Allison**, Labcyte Inc, reported in poster **T-66:** *Nanoliter scale high-throughput protein crystallography screening with the Echo® liquid handler.* The Echo liquid handler can transfer nanoliter quantities of reagents including even viscous and osmotic fluids. **Ana Gonzalez**, SSRL, presented **T-68:** *Advanced Automation at SSRL with AutoDrug*. She discussed details of the *'AutoDrug'* pipeline developed at SSRL for automated data collection and molecular replacement.

John P. Rose & John Chrzas

Great Events in Chemistry

1867: Kekule, moments before his brilliant insight into the structure of benzene.

Courtesy of Nick D. Kim.

See website at nearingzero.net/res.html.

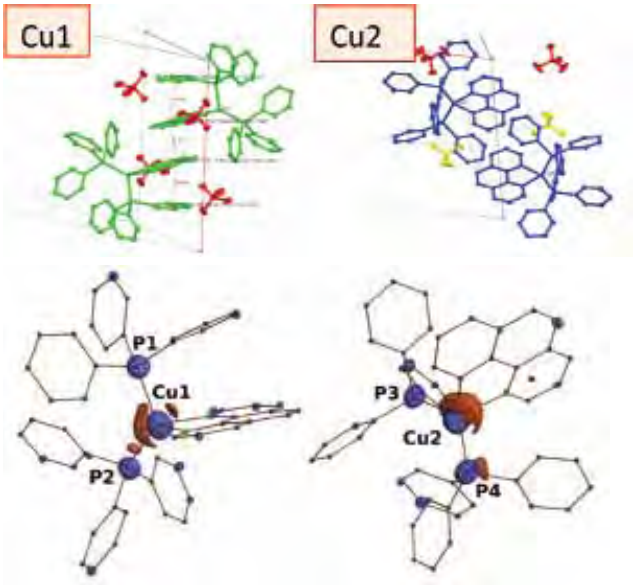
TR.01:Transformations and Structural Oddities in Molecular Crystals: In Honor of Bruce M. Foxman

In the ***Transactions Symposium*** that celebrated **Bruce Foxman** and his extensive contributions to the field of crystallography, a diverse collection of topics ranging from crystal transformations, supramolecular assemblies and synthesis, polymorphism, and function and reactivity of engineered materials were presented by friends, colleagues, and former students. In addition to exceptional scientific research, many personal anecdotes were shared that highlighted Bruce's longstanding friendships and impact on the careers of those in our community.

Looking beyond the structural norms of crystal packing and inspecting the outliers can often provide critical views of crystal formation. **David Watkin**, Cambridge U, discussed his recent systematic studies to understand Z' > 1 structures and their consequence for decoding crystal cohesion.

Carol Brock, U Kentucky, showed how optimizing hydrogen bonds within structures and using enantiomerically / diasteriomerically pure compounds can assist the formation of crystal structures with multiple molecules in the asymmetric unit.

Philip Coppens, SUNY Buffalo, detailed the method of dynamic photocrystallography and its recent use in exploring linkage isomerism as well as its application to stereoselective transformations for structures with Z' = 2.



From Philip Coppens: Top: Cu1 and Cu2 show the difference in packing of two independent molecules in crystals of a Cu(I) phenanthroline complex. Bottom: Time-resolved photodifference map showing that the structural changes on photoinduced electron transfer to the microseconds lifetime excited state are different. Red: positive. Blue: negative. Isosurfaces ± 0.25 e/Å3. (J. Phys. Chem. A, 116, 3359-3365 (2012), and Acta Cryst. A67, 319-326 (2011).

The theme of enantiocontrolled solid-state reactions was continued by **Kraig Wheeler**, Eastern Illinois U. His group has designed J-shaped molecules that form robust supramolecular dimers which readily undergo photodimerizations via single crystal-single crystal processes, often with quantitative conversions.

Joel Bernstein, NYU Abu Dabi, provided an engaging discussion of several well-known structural oddities in the history of crystallography. He spoke about Reginald W. James - the physicist appointed to Shackleton's famed 1914 Antarctic expedition who later acquired a reputation as an authority in the newly developing field of crystallography. Joel's account of James gave new meaning to 'small world' by describing important connections between this seminal scientist and many modern day practitioners.

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TR.01 L to R: Bruce Foxman, David Watkin, Graciela Diaz de Delgado, Kraig Wheeler, Roger Bishop, Magali Hickey, Richard Adams, Menahem Kaftory, Larry Falvello, Carolyn Brock, Michael Ward.

TR.01, cont'd Bruce's interest and reputed curiosity about solid-state reactions provided a central topic for many talks.

Manehem Kaftory, Technion-IIT, showed, in studies of a class of pyridines, that UV illumination of solid samples results in photodimerization so that the reactants undergo molecular flips. Varying the temperature of this transformation gave important insights about the kinetics and Ea of this process. **Miguel Garcia-Garibay**, UCLA, explained his group's general strategies for engineering reactions in crystals and went on to illustrate several remarkable examples of photodenitrogenation of diazo compounds, nitrenes, and azoalkanes, and also the photodecarbonylation of crystalline ketones.

Victor Young, U Minnesota, described an ionic salt that exhibits enantiotropic phase transitions. The system starts from a non-twinned crystal structure and progresses to lower symmetry accompanied by twinning and an order-disorder transition. The complex transition profile was followed with the help of DSC and x-ray data to give an intriguing example of coupled phase transitions.

Bart Kahr, NYU, told remarkable stories related to his recent adventures with common molecular crystals that grow helically with twisted lattice planes. Bart's description of the optical properties and twisting mechanisms he observed offered elegant insights about crystal morphologies. **Jennifer Swift**, Georgetown U, continued the discussion of crystal growth by describing the impact of growth conditions and dye additives on the formation of uric acid crystals.

Örn Almarsson, Alkermes, addressed the importance of crystal structure analysis and data mining as central assessment tools for pharma R&D. Örn's well chosen examples illustrated the link between structural knowledge and progress in pharmaceutical science.

Magali Hickey, also at Alkermes, discussed key factors for optimizing pharmaceutical material performance, the impact of chemical changes on crystal structure and physico-chemical properties, and the use of extant crystallographic data to understand solid-state reactivity in pure drug substance as well as in formulations.

Mark Hollingsworth, Kansas State U, showed that urea, when co-crystallized with alkanes / alkanones / alkanediones, generates ferroelastic domain switching materials that display a range of crystallographic challenges such as twinning, phase transitions, and commensurate / incommensurate phases. **Matt Peterson**, Amgen, also talked about the structural chemistry of urea inclusion compounds. By introducing an α,ω-disubstituted hexane guest, $Cl(CH_2)_6CN$, he showed how crystal formation creates stacked loops of ureas that form undulating channels. By comparing this system to a bromo derivative and evaluating the site occupancies, space group determination could be effectively untangled from disordered components.

Larry Falvello, U Zaragoza, provided an engaging discussion of his work on the complexes from metal-citrate building blocks. These form a variety of cubane topologies that show solid-state reactivity.

The talk on iridium- and osmium-gold carbonyl clusters by **Rick Adams,** U South Carolina, brought attention to the complexities of CO labile systems via crystallography and well placed DFT calculations.

Arnie Rheingold, UCSD, showed that in mixed-valence iron acetates of composition $[Fe_3O(OAc)_6(L)_3S$, the rates of intramolecular electron exchange vary greatly. By assessing these systems crystallographically, Arnie concluded that local symmetry plays an important role in this phenomenon - and that it is controlled by the selection of solvent.

Graciela Diaz de Delgado, U de Los Andes, described interesting structural features displayed by metal carboxylates prepared from various component ratios and various crystal growth techniques.

Roger Bishop, U New South Wales, addressed supramolecular synthesis with his discussion of the structural preferences of molecular tweezers and the inverse relationship between clathrate formation and packing prediction.

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TR.01, Bruce Foxman and former students. L to R, in front: Mike Vela, Roxana Schlam, Magali Hickey, Graciela Diaz de Delgado, Bruce Foxman, Judy Sennet, Carlye Booth, Josh Chen and Mark Turnbull. In back: Mike Moloney, Harry Mazurek, Kraig Wheeler and Robert Sandor.

Michael Ward, NYU, offered an enlightening discussion of robust assemblies generated from his guanidinium organosulfonate building blocks, concluding with some remarkable systems that display frameworks ranging from soft matter microstructures mimics to *Archimedean* polyhedra. **Kenneth Harris**, Cardiff U, described an alternative method for assessing the modes of supramolecular assembly, i.e., using solid-state NMR to carry out *in situ* studies of crystallization, allowing the evolution of polymorphic forms to be monitored as a function of time.

Graciela Diaz de Delgado, Magali Hickey, and Kraig Wheeler

SP.01 Innovations in Undergraduate Education

This year's meeting included an opening lecture preceding the Saturday night reception. Attendees were treated to ***Confessions of a Converted Lecturer***, the exciting educational ideas of Eric Mazur, Balkanski Professor of Physics and Applied Physics at Harvard University and Area Dean of Applied Physics. In addition to his stellar work in optical physics, Eric is interested in education, science policy, outreach, and the public perception of science. He began with the story of his apparent (but false) success as a popular lecturer in traditional undergraduate physics courses at Harvard based upon the usual measures such as course evaluation scores. He asked the audience a series of probing questions early in the lecture designed to remind us that we did not learn from *lectures*, but rather in some framework *after* class such as discussions with fellow students or self-study. Mazur's alternative approach posits that the true hallmark of learning is when the learner can take a concept from one context and transfer it to another. Mazur advocates *peer* instruction that capitalizes on the idea that the student knows the difficulty in understanding a concept better than the instructor. In the peer instruction environment the students have opportunities to think through concepts presented by the instructor during the lecture by informally discussing the concepts among themselves. The students are able to assess their understanding of the ideas presented and the instructor has access to this information. Eric's compelling lecture was delivered with humor, clarity and great enthusiasm. During the presentation there was very lively discussion and this continued afterward at the opening reception. For those seeking further information on Eric's teaching innovations, please refer to his web page at **http://mazur.harvard.edu**.

Bruce Foxman, Bruce Noll & David Rose

SP.02: The History of Structural Biology

At the recent ACA meeting in Boston, Don Caspar gave his perspective on the origins of structural biology. He covered pretty much the whole cast of characters and their roles, starting with when it was first recognized that DNA and proteins had defined structures - what basic structures they adopt, and how these initial discoveries came to pass. X-rays, of course, played a major role in the untangling of the first goofy models of DNA. Also, Don corrected misconceptions and clearly explained the connection between the structure of alpha helices and the fiber patterns taken by Astbury. The scientific process he described was beautifully interleaved with human components, including rivalries and personal anecdotes. Don supported his talk with photographs of the players and an image of a letter from Linus Pauling. The lecture was recorded and the ACA Council is working on a way to make it available for any one to see.

George Phillips

L to R: Thomas Edwards, Surajit Banerjee, Ruslan Sanishvili, Ward Smith, John Hunt, Catherine Cormier, Margaret Gabanyi. Below, Adam Godzik

1.01: Protein Structure Initiative: More Tools for the Home Lab

This session highlighted the tools developed by the NIGMS ***Protein Structure Initiative*** to improve the efficiency of macromolecular structure determination. These tools are available to all. **Maggie Gabanyi**, Rutgers, began the session with a description of the ***Structural Biology KnowledgeBase***. The SBKB is a central Web portal for access to advances in structural biology and structural genomics including linking protein sequences, three-dimensional structures and models to biological function. The SBKB contains information about protocols, materials and technologies related to macromolecular structure and function, including more tools for the home lab. **Thomas Edwards**, Emerald Bio, described the use of iodide soaks for in-house *de novo* SAD phasing. Sixteen of 17 attempts were successful. **Ruslan Sanishvili**, ANL, described recent developments at the GM/CA@APS beamlines at the Advanced Photon Source at ANL, including remote data collection and rapid crystal rastering to locate well-ordered regions on a crystal. Data collection can be set up to move along a predetermined path on the crystal.

Catherine Cormier, Arizona State U, presented an update on the **PSI: Biology-Materials Repository**. This repository is a resource for storing protein expression plasmids. It has stored and distributed more than 160,000 plasmids and includes all protein expression plasmids from the PSI. Investigators are able to search for and order plasmids, and receive them under a simplified institution-wide materials transfer agreement.

Adam Godzik, Sanford-Burnham Med Res Inst, spoke about his experiences data mining the crystallization database from the PSI. He emphasized that the database includes failed experiments as well as successful trials. This allows him to mine statistical information about the frequency with which a related sequence has been successfully crystallized.

John Hunt, Columbia U, described the crystallization problem from a different perspective, examining surface "epitopes" of proteins that have formed a lattice and engineering these epitopes into proteins that are difficult to crystalize. He successfully crystallized 3 of the 4 difficult proteins that he had 'engineered'.

In the final two talks of the session, **Surajit Banerjee**, NE-CAT, Cornell, asked the question *When to do a MAD experiment?* and **Seiki Baba**, Spring8, Japan, described the use of polyvinyl alcohol (PVA) as a cryoprotectant to allow rapid humidity control for improved data collection from crystals sensitive to low humidity and standard cryoprotectants.

Ward Smith

The student AV crew: L to R, Attila Foruchi, David Shin, Alena Carlson, Martina Green, Maria Cassidy, Flor De la Cruz and Emma Kohse.

L to R: Zachary Wood, Eric Montemayor, Karen Allen, Nicholas Silvaggi, Adrian Goldman, Hideki Aihara, Rebecca Page, Xiaojing Yang.

1.02: Structural Approaches to Enzyme Mechanisms

Speakers in this session discussed macromolecular x-ray crystal structures of enzymes complexed to substrates, products, trapped intermediates and transition-state analogues as a "lens" to see enzymes in action. **Catherine Drennan**, a Howard Hughes Medical Institute Investigator at MIT, began the session, describing the visualization of a methyl *hand* between B vitamins. Methylation chemistry is vital for cellular functions, from transcriptional regulation in humans to the ability of acetogens to live on CO_2. Drennan's talk described the long-awaited x-ray crystal structure of the protein components required for the methyl transfer from folic acid (vitamin B9) to vitamin B12, a reaction necessary for maintaining pools of methyl donor S-adenosylmethionine as well for acetogenesis. Her structure, (see cover illustration and *On the Cover* article, page 3), revealed the large conformational changes within the enzyme complex required for the methyl transfer between these B vitamins; motions that appear to be promoted by folate binding. In conjunction with the crystal structure determination, spectroscopic data in the crystalline state demonstrate enzymatic turnover that requires extraordinary movements within a crystal lattice.

Cathy had to leave early, and so was not in the group photo.

Hideki Aihara, Uof MN, discussed the eukaryotic DNA repair enzyme TDP2 (5'-tyrosyl DNA phosphodiesterase), an enzyme that plays a critical role in cellular resistance to topoisomeraseII - induced DNA damage, and a potential drug target for chemotherapy. The structure of TDP2 and the mechanism of its substrate recognition have been elusive. The Aihara laboratory determined the crystal structures of full-length TDP2 in the presence and absence of a 5'-phosphotyrosyl DNA substrate. The structure shows that the active site of TDP2 is similar to that of the endonuclease APE-1 that takes double-stranded DNA as a substrate. However, TDP2 has a narrow groove that selectively accommodates the 5'-terminus of a single-stranded DNA, a novel mode of DNA binding. Curiously, the flexible N-terminal segment of TDP2 can bind in the DNA binding groove of TDP2, with the Glu and Asp side chains occupying the binding sites for DNA backbone phosphates. The observed molecular mimicry might provide a mechanism for auto-regulation of TDP2 activity or a platform for protein-protein interactions in TDP2 signaling.

Rebecca Page, Brown U, presented work aimed at understanding at a structural level how ser/thr phosphatases (PSP) achieve specificity in the cell. The reason is that even though more than 420 genes in the human genome encode for serine/threonine kinases, accounting for 98.2% of all phosphorylation events, less than 40 genes encode for PSPs. During the last decades, pioneering studies have shown that the activities of most PSPs are tightly regulated by their interaction with hundreds of targeting and inhibitor proteins to form PSP holoenzymes. Rebecca described her most recent structures; PP1:targeting and CN:inhibitory protein complexes, which revealed a novel mechanism by which these PSP interacting proteins direct PSP activity - namely, through steric inhibition of substrate sites. Here the targeting and inhibitory proteins do not bind and occlude the active site, but instead bind the PSPs in grooves that are required by substrates for binding. As a consequence, the substrates cannot bind and are not dephosphorylated. Taken together, her studies are providing essential molecular insights into PSP regulation, providing a new model of how PSP regulatory and inhibitory proteins direct PSP activity *in vivo*.

Eric Montemayor, UT Health Science Center at San Antonio, reported the latest results on the intron debranching enzyme (Dbr1) that he and others in his laboratory have found. Montemayor described the first structures of Dbr1 in complex with several RNA compounds that mimic the branchpoint structure in lariat RNA. The structures demonstrate how the catalytic machinery is compatible with the 2', 5'-phosphodiester linkage as opposed to the more abundant 3',5' -phosphodiester linkage. A combination of cell-based functional assays, *in vitro* activity assays, inductively coupled plasma mass spectrometry and x-ray anomalous diffraction methods were used to support a new proposal for the mechanism of Dbr1. In this mechanism a dinuclear metal-binding center alternates between single and double metal ion configurations. The findings provide a framework for understanding the role of Dbr1 in retrotransposon and retrovirus replication, and point to potential evolutionary relationships between retrotransposons, retroviruses and pre-mRNA splicing.

Xiaojing Yang, U of Chicago, explained the use of temperature as a surrogate for time in the trapping of reaction intermediates in phytochromes. Phytochromes and bacteriophytochromes (BphPs) convert a light signal into a biological signal via reversible photoconversion between red-absorbing (Pr) and far- red-absorbing (Pfr) states. To establish the molecular mechanism of photoconversion, Xiaojing utilized temperature-scan cryocrystallography on photoactive crystals of *P. aeruginosa* BphP (PaBphP). By applying a *trap-pump-trap-probe* strategy at variable pump temperatures, they followed the progression of photoreaction initiated in the crystalline state. Temperature mimics time: the higher the pump temperature, the greater the structural relaxation and the further the reaction proceeds. Light-induced difference electron densities at 10 temperatures between 100K and 180K were analyzed, from which three cryo-trapped intermediate structures in the Pfr-to-Pr photoreaction were delineated.

Zachary Wood, U of Georgia, showed that the disproportionately large conformational change in a protein is caused by a small allosteric effector. Wood's work has shown that the allosteric inhibitor UDP-α-D-xylose binds

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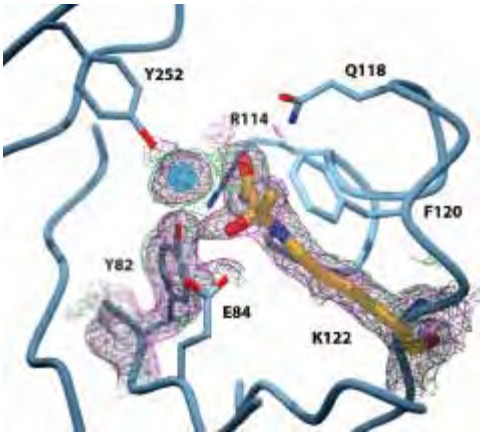
1.02 cont'd to the active site of human UDP-α-D-glucose-6-dehydrogenase (hUGDH), and that the absence of the hydroxymethyl converts an active, 32 symmetry hexamer into an inactive, U-shaped complex. His new work supports an evolutionary model in which catalytic efficiency is sacrificed to select for unstable hexameric complexes. Combining biochemical and sedimentation velocity studies with a new x-ray crystal structure, the Wood laboratory is now equipped to show that apo-hUGDH represents a tipping point between the active and inactive states. Apparently nature selected for a conformation that is suboptimal for catalysis in order that the small chemical difference between the allosteric inhibitor and the substrate can more easily leverage the conformational switch.

Adrian Goldman, U of Helsinki, presented a just-published (Kellosalo et al, *Science*, **337**, pp 473-476, July 27, 2012) structure of the first sodium-pumping inorganic pyrophosphatase, an integral membrane protein from the hyperthermophile *T.maritima* (TmPPase). This structure, and the homologous Mung Bean proton-pumping pyrophosphatase published recently in *Nature* are the first examples of this protein fold family. TmPPase has 16 transmembrane helices, and all of these extend up to 20 Å above the membrane surface on the cytoplasmic side. An inner ring of six helices form the hydrolytic centre (20 Å above the membrane surface), coupling the channel to the gate (just below the membrane), and the exit channel. Based on a series of structures, he presented a *binding change* model of catalysis.

Nicholas Silvaggi, U of Wisconsin-Milwaukee, described the research being done in his laboratory: bioinformatic analysis of enzymes in the acetoacetate decarboxylase-like superfamily (ADCSF), which has led to the identification of families having active site architectures distinct from the prototypical decarboxylases. The image below shows the structural and kinetics investigations of two enzymes from family V of the ADCSF.



The structure of the carbinolamine intermediate in a Schiff base formation of Sbi_00515 with pyruvate. The 2\|Fo\|-\|Fc\| (magenta mesh) and simulated annealing composite omit electron density maps both show clear tetrahedral character at the α-carbon of pyruvate, consistent with the carbinolamine.

Members of this family are not decarboxylases, but rather represent a new fold for type I (Schiff base-dependent) aldolase activity. This finding has begun to answer persistent questions regarding the role of MppR in the biosynthesis of the anti-MRSA antibiotic mannopeptimycin.

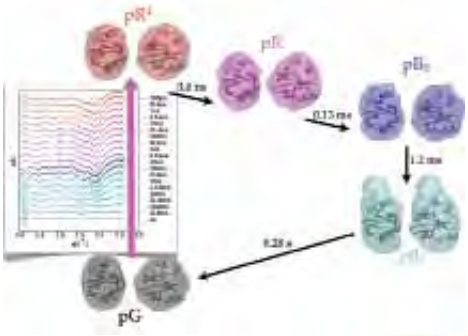
Karen N. Allen

1.03 In back L to R: Savvas Savvides, David Jeruzalmi, Sean Froese, Brandt Eichman, William Royer, Zachary Wood. In front L to R: Cynthia Stauffacher, Flora Meilleur, Celia Goulding, Philip Anfinrud. Liang Tang, who was not present for the group photo, is at right.

1.03: Structural Enzymology - Biology

This session included talks on innovative structural approaches for addressing dynamic problems as well as recent progress on existing biological problems.

Philip Anfinrud, NIH, emphasized the power of ultrafast time-resolved SAXS/WAXS technology to observe real-time protein conformational changes in solution over 10 decades of time.



Time-resolved SAXS/WAXS differences acquired over 10 decades of time after photoactivation of PYP with a blue laser pulse. The protein surface envelopes associated with each state in the PYP photocycle, determined using GASBOR, show that the pB0 to pB1 transition leads to the signaling state.

Using photoactive yellow protein (PYP) as a model system, Phil was able to 'see' the changes in both protein size and shape as PYP undergoes a photoactivated signaling-state transition. This transition was shown to involve a large amplitude global scale structural change that cannot be accommodated in protein crystals. The kinetics associated with this transition indicate that its triggering event correlates with a structure change unveiled by time-resolved Laue crystallography studies of PYP, in which the chromophore transitions from a red-shifted to a blue-shifted spectroscopic intermediate. A water molecule penetrates into the interior of the protein where it forms hydrogen bonds with Tyr42 and Glu46 and temporarily blocks the ground state recovery of PYP. The ability to track large amplitude structural changes in solution via time-resolved SAXS/WAXS is proving to be a powerful complement to time-resolved Laue diffraction studies.

Savvas Savvides, Ghent U, has used a combination of biophysical and crystallographic approaches to tease out the mechanism by which the viral decoy receptor BARF-1 from the Epstein-Barr virus hijacks our immune system. Savvas' work reveals an unexpected allosteric inactivation of the human hematopoietic cytokine CSF-1 by BARF-1. Viral BARF-1 binds CSF-1 at an epitope far from that of the cognate human receptor and locks CSF-1 into a conformation that is unable to bind and signal via the cognate receptor. The result is a beautiful multivalent BARF-1 complex with three neutralized CSF-1 molecules.

Ribbon representation of the BARF1:hCSF-1 complex. Hexameric BARF1 binds three hCSF-1 dimers. The oligo-mannose type glycan structures are shown in stick and surface representation. Adapted from Elegheert et al. (2012) Nature Structural & Molecular Biology (doi 10.1038/nsmb.2367).

Celia Goulding, U Cal Irvine, introduced the contact dependent growth inhibition (CDI) systems of gram-negative bacteria. CDI occurs when the C-terminal tail of CdiA, CdiA-CT, a toxic protein, is translocated into a target cell to inhibit growth. Related bacteria express immunity proteins (CdiI) that neutralize the CdiA-CT proteins. Celia presented crystal structures of two different CdiA-CT / CdiI complexes. These structures show that the CdiA-CT toxins are structurally similar, despite very low sequence conservation. However, one is a tRNase and the other a Zn^{2+}-dependent DNase. In contrast, the CdiI's are

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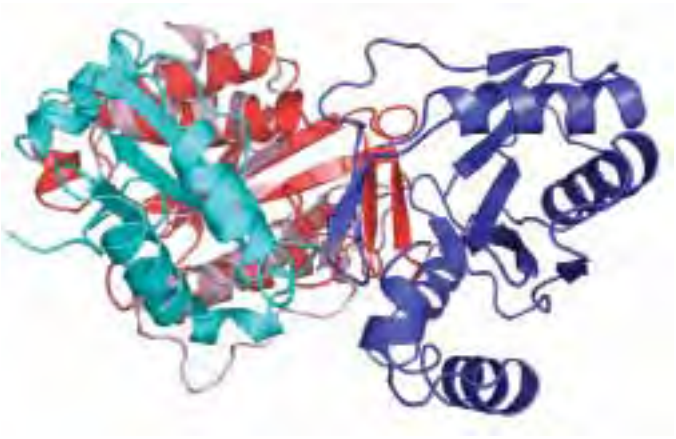
1.03 cont'd nonhomologous structures, showing that the immunity factors have distinct origins in evolution. Furthermore, the CdiI's bind to distinct locations on the molecular surface of its cognate CdiA-CT. Finally, some CdiA-CT toxins require activation by binding to metabolic protein from the target cell. Celia presented the first structure of CdiA-CT bound to its metabolic activator, CysK.



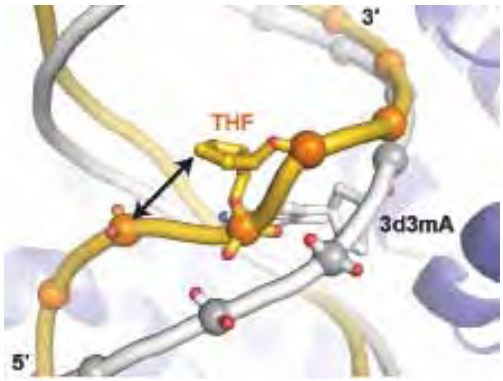
At right, superpostion of CdiA-CT/CdiI protein complexes. The CdiA-CT toxins (red, pink) from two different bacterial species are structurally similar, while the immunity proteins (blue, cyan) are structurally dissimilar and bind to distinct locations on their cognate toxin.

David Jeruzalmi, Harvard, introduced us to the nucleotide excision repair pathway (NER) in bacteria. He focused on the inner workings of the DNA damage sensor from the NER pathway, and how the sensor may identify the presence of UV damage on DNA. His group solved three crystal structures of various components in the pathway, and combined these structures with previously known biochemistry to formulate a new hypothesis about the early steps of NER. The structure of the complete UvrA-UvrB sensor showed that a central UvrA dimer associates with two UvrB monomers to form the tetrameric DNA damage sensor. Current thinking about the mechanism of damage discrimination by NER suggests similarity to the way passengers clear an airport security checkpoint. DNA (native and damaged) is sampled by the open form of UvrA, and sampling involves closing around the DNA to sense its shape. Native DNA passes this airport-style 'pat-down' and is released. However, damaged DNA fails the test, and is shunted to the damage-specific stages of the pathway, which includes the handoff of DNA to UvrB. Damaged DNA is then excised, and this permits the original DNA sequence to be restored via a series of additional factors.

At right, (A) Crystal structures of UvrA show three distinct conformations, and suggest a detailed model for discrimination of damaged DNA from native. (B) schematic for the handoff of damaged DNA to UvrB.

Bill Royer, U Mass Medical School, showed how time-resolved crystallographic analysis has shed light on the cooperative conformational change in the dimeric hemoglobin HbI. Combined with a meta-analysis of 70 structures, Bill and his co-authors revealed the role of water molecules in facilitating the transition between R and T states. The talk culminated with a structure-based *'pliers model'*, which describes how the helices of the different subunits undergo a scissoring motion to facilitate the cooperative transition between states.

Brandt Eichman, Vanderbilt U, demonstrated how alkylated bases are identified for repair. Using a crystal structure of the DNA repair enzyme AlkD in complex with DNA, Brandt revealed that the DNA adopts an unusual conformation that not only exposes alkylated purines, but that also facilitates base excision despite the absence of a direct chemical contact between the enzyme and the labile glycosidic bond.



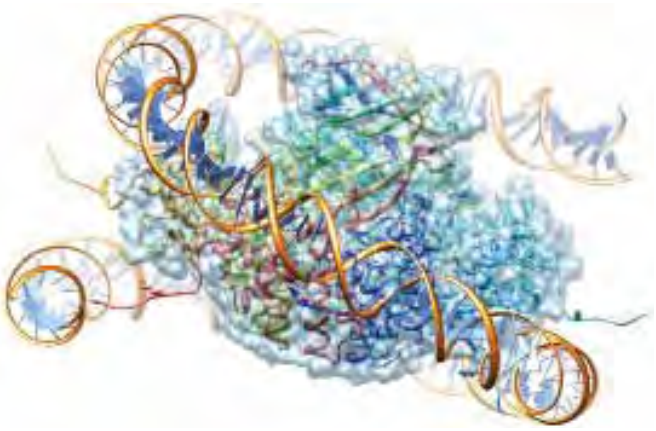
Above, overlay of AlkD bound to DNA containing a tetrahydrofuran (THF) abasic site (gold) and a N3-methyladenine analog (3d3mA, grey). Phosphates are depicted as spheres, and the close proximity of the DNA backbone to the C1α carbon of a basic product is highlighted with an arrow.

This was a nice explanation of how the DNA itself can facilitate catalysis in a DNA repair enzyme.

Flora Meilleur, NC State U, introduced us to IMAGINE, a new high intensity neutron diffraction beam line developed at the High Flux Isotope Reactor (HFIR) at ORNL. This source will begin operations next spring. Flora illustrated the power of neutron diffraction by identifying the hydrogen bonding environment of the E186Q mutation in the enzyme xylose isomerase. This enzyme has a shifted pH optimum, making it interesting to the biofuel community. By mapping the hydrogens, Flora aims to provide a better understanding of the mutant pH activity profile.

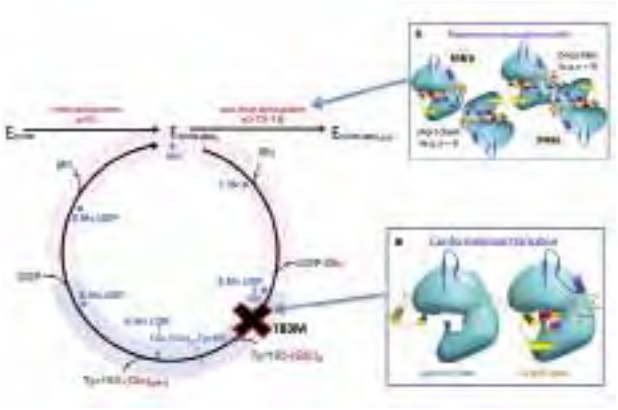
Liang Tang, U Kansas, explained how the bacteriophage Sf6 accomplishes the difficult task of packaging DNA into the viral capsid. The terminase is a large protein complex that pumps DNA through the portal protein channel into the capsid, powered by ATP hydrolysis. The terminase small subunit called gp1 assembles into a ring-like octamer and binds the DNA in nucleosome-like

1.03 cont'd fashion, as a way to selectively pick the viral DNA for packaging. Based on crystallographic evidence,



At right, the structure of the terminase small subunit gp1 suggests a nucleosome-like DNA-binding mode. The ribbon diagrams of the gp1 octamer are shown as rainbow-colored for the eight molecules, superimposed with semi-transparent molecular surface. The DNA in gold.

Below, a schematic illustration of the glucosyl transfer catalyzed by glycogenin during its catalytic cycle. (a) For catalytic function, glycogenin requires a conformation transition between the ground and active states. This is blocked by the T83M GSD -type XV mutation. (b) As the maltosaccharide chains (blue hexagons) attached to the glycogenin dimer lengthen, they switch from intra- to intersubunit threading.

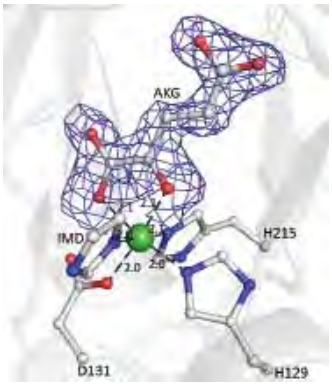


Liang presented the model above showing the gp1:DNA complex acting as a DNA-spooling device to load the capsid.

Sean Froese, Structural Genomics Consortium / U Oxford, described his work on glycogen biosynthesis (see depiction at left). The glycogen core protein, glycogenin, nucleates the synthesis by forming a covalent Tyr-glucose bond. Sean described the conformational changes in the catalytic core of the protein, as well as those of the growing maltosaccharide chain, which are important to the reaction. He also proposed a mechanism for the glycogen storage disorder XV mutation. According to this model, the Thr83Met mutation locks the enzyme in a conformational state that is not catalytically competent to initiate glycogen biosynthesis.

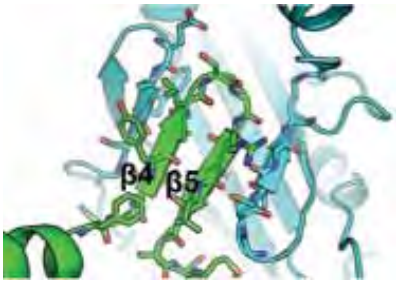
Zachary Wood & Cynthia Stauffacher

Reports on Macromolecular Posters



At left: ORF26 active site showing initial composite omit density (blue mesh) contoured to 1.0 σ from data collected after a 30 minute soak with 2-oxoglutarate. The bound nickel ion is depicted as a green sphere, while residues responsible for metal coordination are shown in ball-and-stick representation. Atoms are colored by type, with gray carbon atoms, red oxygen atoms, and blue nitrogen atoms. The final metal coordination position is occupied by one molecule of imidazole.

Kathryn McCulloch, Vanderbilt University, presented **T-18:** ***Structural Investigation into Orthoester Bond Formation by a Non-heme Iron, α-Ketoglutarate Dependent Oxidase Involved in Everninomicin Biosynthesis***. Orthosomycins are antibiotics that contain a highly unusual orthoester bond between two sugar moieties. Everninomicin (EVN), isolated from *Micromonospora carbonacea*, is an orthosomycin with two orthoester bonds. Of the two possible non-heme iron, α-ketogluatarate dependent oxidases in the EVN biosynthetic pathway that might be responsible for orthoester bond formation, one, ORF26, was solved in complex with α-ketoglutarate. The 1.9 Å structure revealed a large cleft in the active site capable of accepting the bulky EVN precursors and a metal binding site with a coordinated α-ketogluatarate, a result that enabled identification of active site residues and suggested a mechanism for othoester bond formation.



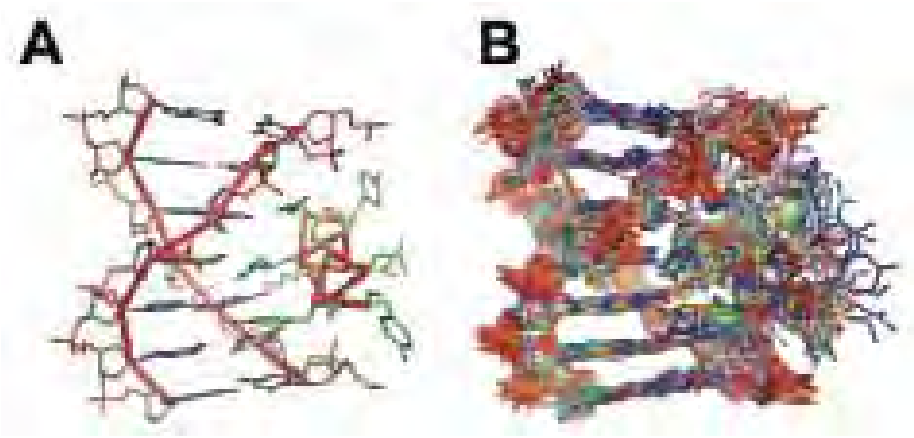
The unique binding interface between E. coli toxin (CdiA-CT, green) and immunity protein (CdiI, cyan) is shown. The CdiA-CT β-hairpin (β-strands 4 and 5) forms an anti-parallel β-sheet with CdiI. The β-hairpin is required for stable complex formation. This interface is distinct from that seen in the B. pseudomallei CdiA-CT/CdiI complex (not depicted).

Robert Morse, UC Irvine, presented **M-13:** ***Structural Analysis of Two Contact-Dependent Growth Inhibiting Complexes***. Gram-negative bacteria can block the growth of neighboring cells by secretion of the toxic C-terminal tail (CT) of a protein called CdiA. They also produce a species specific immunity protein, CdiI, to prevent autoinhibition by CdiA-CT. The crystal structures of *E. coli* and *B. pseudomallei* CdiA-CT / CdiI complexes were determined to 2.35 Å and 2.65 Å, respectively. Comparison of the two complexes revealed unique binding locations of the CdiIs to their CdiA-CT. Despite low sequence identity both of the CdiA-CT proteins display structural homology to known endonucleases, enabling identification of conserved catalytic residues. Activity studies of the CdiA-CT enzymes showed they nicked supercoiled DNA, but for both complexes this activity is neutralized in the presence of their CdiI or by catalytic mutation. These structures aided understanding of the bases of CdiA-CT toxicity, CdiI based immunity, and contact dependent growth inhibition.

Megan Sikowitz

T-79: Barry Finzel and Jeffrey Van Voorst, U Minnesota, described a tool they have developed for mining the PDB for recurring scaffolds involved in intermolecular contacts. They have implemented an algorithm that enables complex substructure searching across a wide selection of macromolecular structures in the PDB. For more details see Finzel *et al*., (2011) *J. Chem. Infor. Modeling* **51** pp 1931-41.

Connie Rajnak

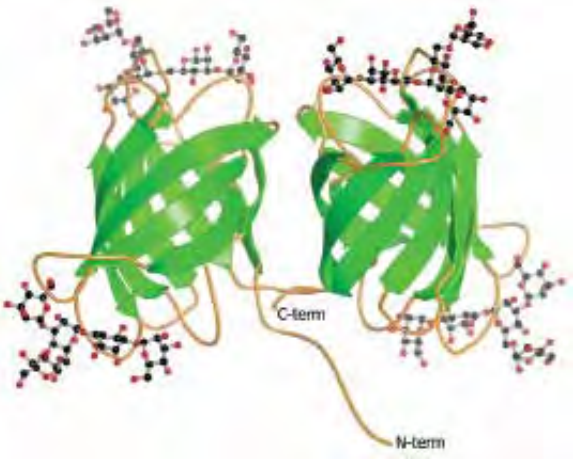


An example of a complex intermolecular substructure query geometry (A) and matching substructures (B).

A target geometry selected from the Ets transcriptional regulator/DNA complex of Batchelor et al., (Science 279:1037-41; 1998) (PDB-1awc) provided the target geometry of CA atoms (peptide) and C1' atoms (nucleotide) of a ternary complex. A search of a distance geometry representation of all protein DNA complexes in the PDB yields 21 excellent matches containing a similar interaction geometry (B).

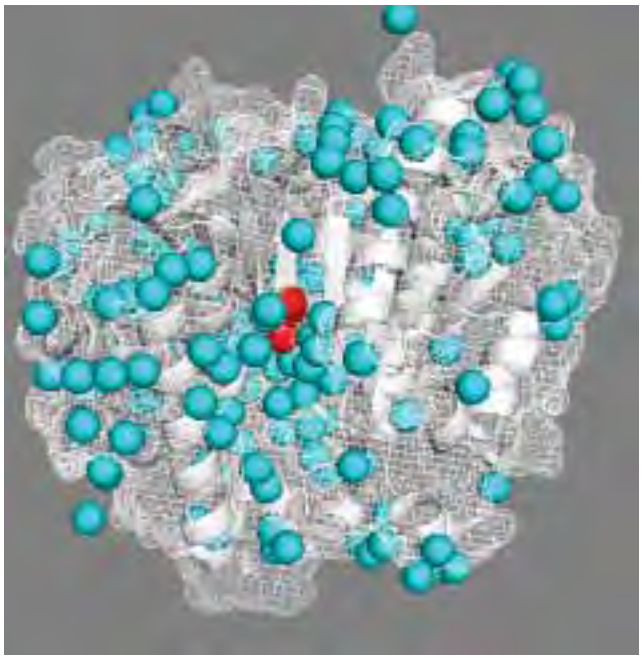
M-59: Carbohydrate Binding Properties, and Anti-HIV Activity of the Proteobacterial Lectin BOA by **Matthew Whitley**, William Furey, and Angela Gronenborn

Burkholderia oklahomensis EO147 agglutinin (BOA) is a 29 kDa member of the OAA family of anti-HIV lectins. Members of the OAA family specifically recognize high-mannose glycans, and by binding to the glycosylated HIV glycoprotein 120 (gp120), they prevent the virus from recognizing and binding to host cells, thereby inhibiting HIV infection. The various OAA family lectins consist of either one or two sugar binding domains, with a single domain being capable of binding two high-mannose glycans. This poster presented the crystal structure of BOA, a double domain, four-sugar-binding-site member of the OAA family, both in the ligand-free state and in complex with the high-mannose glycan 3α,6α-mannopentaose, at resolutions of 2.4 Å and 1.9 Å, respectively. The pentasaccharide 3α,6α-mannopentaose represents the core structure of Man-9, the high-mannose N-linked glycan found in abundance on the silent face of gp120. The structures provide the details of how BOA specifically recognizes high-mannose glycans, in particular mannoses connected by α1-6 linkages. Binding interactions formed between protein and sugar include a strictly conserved tryptophan side chain that packs against the reducing end of the sugar and a series of backbone hydrogen bonds formed between strictly conserved glycine residues and sugar hydroxyl groups. Additionally, the poster presented an NMR characterization of BOA's carbohydrate binding affinity (KD of 20-50 μM) and assayed BOA's anti-HIV infectivity function, yielding a potent IC50 of 12 nM. The combination of structural and functional information presented in this poster will contribute to a greater understanding of an important class of anti-HIV proteins.



Above, monomeric Burkholderia oklahomensis agglutinin (BOA) bound to four molecules of 3α, 6α-mannopentaose. The pentasaccharide ligands represent the core structural unit of Man9, the N-linked glycan frequently found on the silent face of HIV glycoprotein 120 (gp120). The details of the structure presented here reveal how BOA specifically recognizes high-mannose glycans and thus how it potently reduces HIV infectivity by binding to gp120 and preventing it from interacting with target cells in the host.

M-26: *High-pressure-induced Water Penetration and Pressure Adaptation of IPMDH from Deepsea Bacteria* by **Nobuhisa Watanabe**, SPring-8, Takayuki Nagae, Yuki Hamajima, Takashi Kawamura, Leonard Chavas, Ken Niwa, Masashi Hasegawa, & Chiaki Kato.



Observed water molecules for pressure-sensitive IPMDH at 580 MPa. The three newly penetrated water molecules only found at high pressure are shown here as red balls. The side chain of serine 266 of IPMDH contributes to the water penetration, and the one residue has an important relationship between pressure sensitivity of IPMDH.

Watanabe *et al*., presented an analysis of the structural effects of high pressure on the enzyme 3-isopropylmalate dehydrogenase (IMPDH) from the organism *S. oneidensis*. This bacterium exists at normal atmospheric pressure, but homologs of IMPDH are known from organisms that thrive at the high pressures found deep in the ocean (piezophiles). By studying the structural changes that occur in *S. oneidensis* IMPDH at high pressure, the authors hoped to shed light on just which structural features contribute to high pressure tolerance in piezophiles. They found that high pressure induced water penetration into a particular cavity in the dimer interface of the protein, while most of the other cavities decreased in volume. The data were collected using a diamond anvil cell at pressures up to 580 MPa (!) Watenabe *et al* correlated this water penetration with pressure sensitivity and suggested that a serine residue in the cavity, (which is an alanine in the sequence of peizophiles) might have contributed to the observed binding of water. Characterization of the features of proteins that contribute to pressure stability or sensitivity may help facilitate the design of proteins for various industrial processes.

Lesa Beamer

M-01: *Sample loop vibration: Stress testing protein sample mounting loops for rigidity*, by **Randy W. Alkire**, Argonne National Laboratory, F.J. Rotella, & N.E.C. Duke.

The purpose of this study was to determine the relative stiffness of the more common sample mounting loops and to see if they were moving under the influence of the cold-stream. The stress test was to mount a silicon single crystal onto a loop and see how reproducible the data from a single reflection was under data collection conditions. Once relative measures of loop rigidity were determined, lysozyme data was collected and examined for the presence of loop motion. We estimate that smaller loops may be more rigid and larger loops may be under more strain as their surface area increases, though these results are strictly valid only for the 0.2 mm diameter loops we used. Because these results are based on difference measurements, errors due to crystal quality can be neglected. Not every loop that showed motion moved all the time. It is impossible to predict with 100% certainty that a loop will move, only that it is capable of motion. This is because frozen solvent can aid in stiffening the loop as can the crystal itself. *Mitegen Dual Thickness (DT)* loops have the same aperture (10 μm) and body (25 μm) thickness as the *Mitegen Microloop LD*, but only the LD loop showed movement. The difference is likely due to the wicking design present in the DT loop which allows frozen solvent to bridge the thin and thick regions near the aperture.

The loop types highlighted in red above met our criteria for motion on at least one crystal tested. Loop rigidity mainly follows loop thickness. Loops with 10µm thickness are much more likely to move than if they are made from 25µm material. The best performing loop was the *Litholoop* since it showed the least amount of motion in all categories compared to our silicon "no loop" standard. The *Mitegen Mesh* loop was the worst performer. It was made from the thinnest material and had the widest aperture. As a rule wider apertures are more susceptible to motion but it is important to make the connection about thickness. Adding stiffeners, such as epoxy, to a loop prior to mounting a crystal can aid in reducing loop movement if movement is anticipated.

The most relevant parameters in the lysozyme work were changes in linear Rmerge and '*scaling* χ *-squared*' versus '*average intensity*' as output by HKL3000.

Connie Rajnak

Poster M-07: *Structure-Based Evolution of β-Glucuronidase for Antibody-Directed Enzyme Prodrug Therapy* by Sean Dalrymple, Rajendra Jagdhane, David Palmer & David Sanders.

Sean Dalrymple, a postdoc in the lab of David Sanders at the U of Saskatchewan, presented **M-07**, an interesting and ambitious work in progress. If the ultimate goal of his research is realized, chemotherapy will be much more effective and cancer patients will suffer much less from the harmful side-effects of their life-saving medicine. Dalrymple hopes to achieve this by employing antibody-directed enzyme prodrug therapy (ADEPT). In the ADEPT strategy, an anticancer prodrug is paired with the enzyme required for its activation. The activating enzyme is then targeted to the tumor surface via fusion to an antibody specific for a particular cancer cell antigen. The result is that the effects of the cancer drug are isolated within the tumor and healthy cells are largely spared from harmful side effects.

Sean chose β-Glucuronidase (GUS) to serve as the activating enzyme because its high specificity for the carbohydrate portion of its natural substrate allows it to activate almost any drug linked to an aglycone. This strategy of precise drug delivery to the tumor is not without challenges; in this case, because GUS is endogenous to humans, activation of the prodrug within healthy tissues is possible. Also physiological pH is sub-optimal for GUS activity. Dalrymple and his colleagues seek to address these challenges by structurally engineering a mutant GUS that acts on a novel glycan substrate fused to a chemotherapeutic agent and that has maximum catalytic activity at physiological pH. To this end, they designed glycan prodrug precursors that are poor substrates for the native enzyme. Using structural guidance, mutant enzymes have been engineered to restore GUS activity on these novel substrates as well as to shift the pH optimum for catalysis. At present their efforts are focused on obtaining crystal structures of the current generation of mutant GUS enzymes in complex with novel prodrugs that will in turn be used to design even better mutant GUS / novel prodrug pairs that can be used for ADEP Therapy and should improve cancer drug efficacy.

Eric Larson

3.01: General Interest I

The first General Interest Session proved to have presentations that were of interest to all of the crystallographic community - the room was filled to standing room only and overflowed into the corridor. The reason for this, you might ask?

In back, L to R: Allen Oliver, Ethan Merritt, Edwin Pozharski, Bernhard Rupp. In front, L to R: Lee Daniels, Mathias Meyer, Charles Campana.

Two of the first three talks centered on the topic of data fabrication. **Edwin Pozharski**, U Maryland, and **Bernhard Rupp**, Hofkristallamt, provided several examples of structural analyses that were either unintentionally in error or deliberately fabricated from existing data. Clearly, this is of great concern to the crystallographic community. Edwin and Bernhard both demonstrated the signs of what is troubling and inconsistent within published data. It was very clear that a 'good R-factor' does not necessarily mean a 'good structure.' Even incorrect structures can still exhibit reasonable agreements. As a community we need to be vigilant for these problems. Some of this vigilance falls upon reviewers, and some on authors and researchers. The take-home message: it is easier to produce a ***genuine*** crystal structure rather than a modification or fabrication of existing data. Exuberance for the science should be tempered with scientific reasoning.

Ethan Merritt, U Washington, provoked interest by presenting a methodology for TLS (Translation, Libration and Screw) analysis of atomic positions and motion, reminding us that anisotropic displacement parameters can tell us a great deal about the quality of a structure determination. Following the break, **Charles Campana**, Bruker, **Lee Daniels**, Rigaku, and **Mathias Meyer**, Agilent Technologies, discussed the merits of various current hardware and software with regard to data collections for chemical crystallography.

Allen Oliver

BIOLOGY ILLUSTRATED:

The Parasitic Relationship

A *Nearing Zero* cartoon from nearingzero.net/res.html.
Courtesy of Nick D. Kim, U Waikato, New Zealand.

3.02: General Interest II

The second General Interest session consisted of predominantly student speakers.

Christopher Dettmar, Purdue U, discussed particle size analysis and ways to prepare amorphous samples using fluorescence. **Pranoti Navare**, Worcester Polytech, demonstrated how enantioselectivity can be induced on solid surfaces by appending chiral SAMs (self-assembled molecules) to the surface of the substrate. This is of particular interest for the pharmaceuticals industry, since 90% of drugs are chiral. **Chunhua Hu**, NYU, showed how *in situ* crystal-to-crystal transformations of glycine exhibit the complexity of these changes and demonstrate some of the challenges in predicting crystal growth in general.

Allen Oliver at left presenting the Margaret C. Etter Student Lecturer Award to Karim Sutton.

Karim Sutton, U Oxford, UK, and the **Etter Student Lecturer** for the General Interest SIG, demonstrated how a tunable source (synchrotron radiation) can be used to calculate populations of differing oxidation states of an element. This technique could be useful for structures in which doping or partial oxidation of an element as a charge carrier (semi-conductors, super conductors) is present. The reliability of the data was demonstrated by multiple data sets yielding similar results.

Connie Jeffery, U Illinois at Chicago, gave an interesting and provocative talk covering the characterization and organization of proteins that have two distinctly different functions: one within cells and one external to the cell.

In back, L to R: Allen Oliver, Alexander Merriman, Renping Qiao, Christopher Dettmar. In front, L to R: Pranoti Navare, Constance Jeffery, Karim Sutton.

These "moonlighting proteins" are present in many species, and do not always behave with dual activity, drastically increasing the difficulty of assigning them to one category or another.

Michael Matho, La Jolla Inst for Allergy & Immunology, discussed the virus envelope protein D8 and how it may be a source of study for developing vaccines against a number of viruses including small pox, that although eradicated could still pose a threat. **Renping Qiao**, Max Perutz Labs, Austria, continued the membrane protein theme with a discussion on SAS-6 that is implicit in forming centrioles that open channels in the cell membrane and provide rigidity due to their columnar form.

The concluding talk was presented by a high school student, **Alexander Merriman**, Hauptman-Woodward Med Res Inst, whose presentation revolved around the methodology of using conserved amino acid sequences to categorize species and develop a new phylogenic tree.

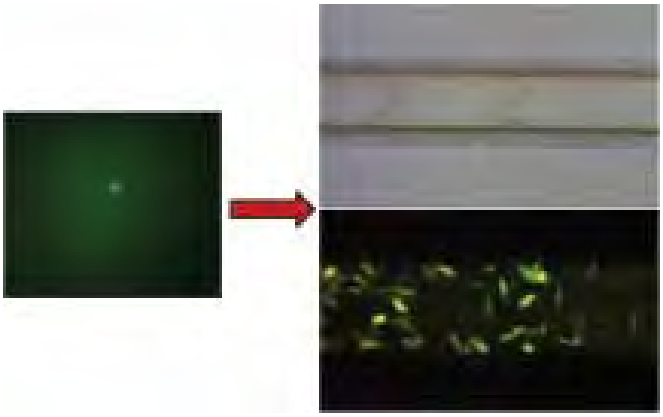
Allen Oliver

Poster M1-7: *Fluorescent Methods for Protein Crystallization Screening* by **Mark Pusey**, **iXpressGenes**.

In **M17**, Pusey presented an interesting diagnostic for crystallization screening of proteins, using a fluorescent tag on a minority (0.25%) of the protein molecules. The example protein crystals were fluorescent (excitation wavelength 530nm; emission 550nm). This diagnostic for salt vs. protein crystals did not require fluorescence in the protein sequence as does a UV microscope. The method requires lysines for modification by the carboxyrhodamine-succinimidyl ester tag. In some otherwise hard-to-interpret aggregates (they looked like goo in white light), the fluorescent tag resulted in bright spots. The bright spots were seen as evidence of pre-crystallinity, and indicated that seeding from the aggregate might yield useable crystals in the next attempt.

The poster also showed evidence that the 0.25% population of tag did not prevent nucleation of crystals. In the Molecular Dimensions booth, iXpressGenes showed its instrumentation made specifically for this fluorescent tagging method.

Dan Anderson



Above, the use of fluorescence to find lead conditions. The protein, an exoribonuclease from the hyperthermophile archaeon Thermococcus thioreducens, showed a 'bright spot' in a well of the screen (left). This condition was subjected to optimization screening using a Microlytic counter diffusion plate, with the results shown on the right side. The top image is white light; the bottom image is fluorescent.

9.01: Functional Nanomaterials

This session brought together researchers who exploit x-ray scattering methods to study structures and properties of nanoscale materials. Grazing-incidence methods (GISAXS, GIWAXS, and GI-XPCS) continue to feature prominently because of their unique ability to measure thin films. Speakers mentioned a wide variety of possible applications for the materials under study, including electronics, piezoelectrics, photo-voltaics, and filtration.

L to R: Alamgir Karim, Detlef Smilgies, Volker Urban, Kevin Yager, Tad Koga.

Alamgir Karim, U of Akron, described a variety of new techniques for controlling the orientation of block-copolymer (BCP) nanoscale morphology. The use of localized but moving hot bands (so-called 'zone annealing') is well-known in metallurgy but has only recently been applied to ordering nanoscale organic systems like block-copolymers. Zone annealing has been shown to enhance ordering kinetics and weakly orient block-copolymer microphases. Karim's group has demonstrated that extremely sharp thermal gradients during zone annealing enables better control of order and orientation. They identified transient reorientation during BCP annealing, which they can 'freeze-in' during the dynamic zone annealing process, while maintaining good order with large grain sizes. This optimized annealing can maintain a vertical orientation for the BCP cylinder phase in films up to 1,000 nm thick. The process was further refined by adding a polymer (PDMS) capping layer to the thin film being zone annealed. This flexible, conformal layer modifies the top-surface interfacial energy, which affects the BCP phase separation causing differing thermal expansion of the PDMS layer, relative to the BCP film and glass substrate, and induces in-plane shearing at the film-PDMS interface. This thermal-gradient-induced shear field, dubbed '*soft-shear*' has a strong influence on the nanoscale morphology of the BCP layer and induces alignment of the BCP layer over the entire macroscopic dimensions of the sample. This unprecedented yet facile ordering was confirmed using AFM images and GISAXS analysis, where an order parameter of 0.99 was computed.

Detlef Smilgies, CHESS, presented a variety of detailed GISAXS and GIWAXS studies of the ordering of thin films, including *in-situ* measurements conducted during the film formation process itself. The assembly of nanoparticles from solution into films (e.g. oleic acid coated PbSe or PbS spheres) was found to be pathway-dependent: the solvent evaporation rate in particular affected assembly of the nanoparticles, which could be tuned continuously between FCC and BCC superlattices. Nanoparticle assembly was also affected by particle shape. Nominally spherical nanoparticles were found to be faceted, and this shape anisotropy drove rearrangement of the superlattice; the particles themselves become oriented within the lattice, as confirmed by WAXS measurements. Studies were also conducted on semiconducting polythiophenes (P3HT). In doctor-blade coating experiments, assembly was affected by shear forces in the drying liquid front. This '*solution shearing*' gave rise to biaxial orienting forces in thin film formation, thus controlling molecular alignment in thin films without any surface modification, applied fields, or post-treatment.

In summary, process history (solvent evaporation, temperature and annealing history, shear, etc.) plays an important role in determining the final nanostructure order; orientation points towards strong kinetic and thus path dependent effects, and roll-to-roll processing is a useful technology in industrial applications of thin film nanomaterials. Detailed *in situ* experiments are needed in order to understand nanostructure formation.

Tad Koga and Kevin G. Yager

In back, L to R: Kwaku Dayie, Xianyang Fang, Osman Bilsel, Michal Hammel, Xiaobing Zuo. In front: Tobin Sosnick, Angela Criswell, Rick Russell, Mark Del Campo.

9.02: Macromolecular Science with Scattering Methods

Solution x-ray scattering has quickly gained popularity and in the past decade has become a major tool for structural biology and biophysics research. This is due, in part, to the development of high flux x-ray sources, large area detectors, and data analysis methods and programs. This session highlighted recent accomplishments in the application of SAXS methods.

Tobin Sosnick, U Chicago, described their research finding that single molecule fluorescence resonance energy transfer (smFRET) and SAXS produce

9.02 cont'd divergent views of the unfolded states at low denaturant concentrations. Specifically, smFRET experiments suggest the chemically unfolded proteins invariably collapse from random coil to more compact dimensions as the denaturant concentration is reduced, while SAXS experiments suggest that such compaction may be rare. The possible cause of this discrepancy was discussed.

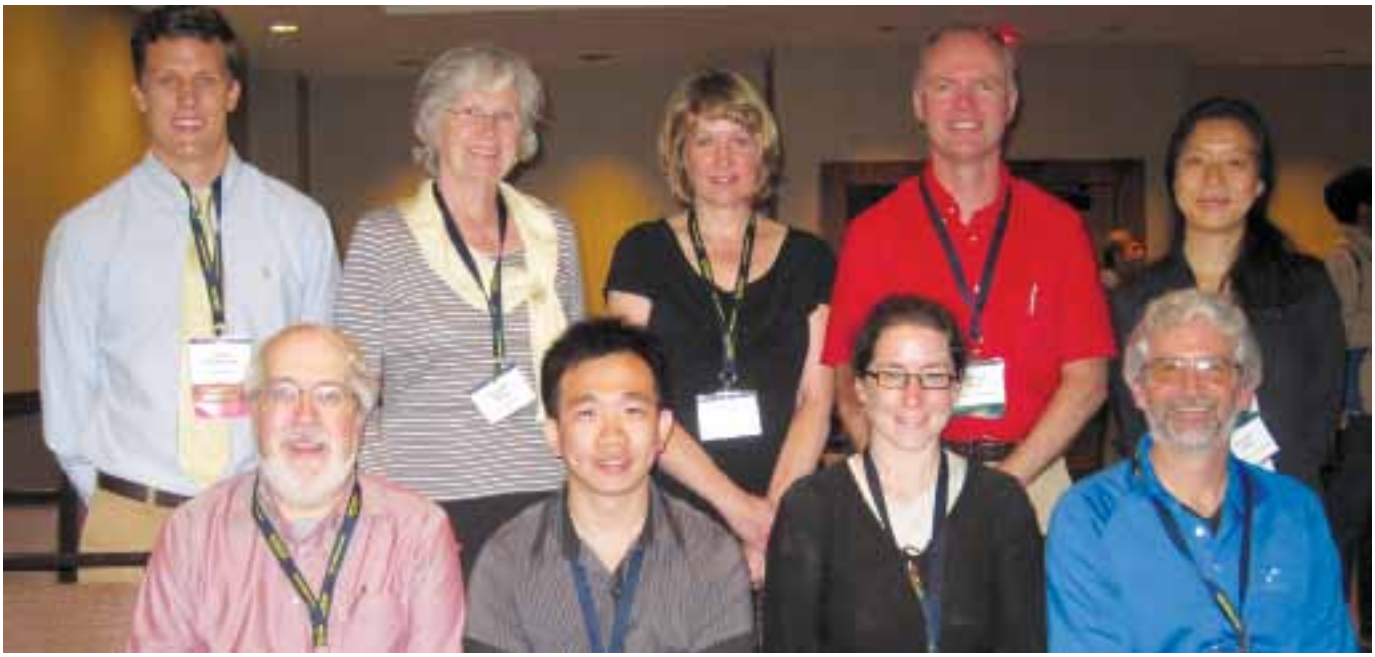
Structural flexibility is often required for biomolecular function, but is difficult to characterize. **Rick Russell**, U Texas-Austin, described his group's study of the interactions between unstructured RNAs and DEAD-box proteins using SAXS. DEAD-box proteins are ATP-dependent chaperones that can unwind short helices in structured RNAs and then refold the kinetically trapped intermediates. Their SAXS studies of DEAD-box proteins CYT-19 and Mss116p showed that the C-terminal tail in the proteins is unstructured and can undergo a large (~100 Å) amplitude conformational change. This flexible, positively charged tail interacts non-specifically with nucleic acid, tethers the protein to the structured RNA, and directs the chaperone protein toward helical unwinding.

RNAs, as mRNA, rRNA and tRNA, play more important roles in biological processes than previously thought. Understanding the structure-function relationships has been very limited due to the fact that functional RNAs are typically larger than 50 nt, presenting challenges for crystallography and NMR. **Xianyang Fang**, NCI-Frederick, described a SAXS structure of a 230 nt HIV Rev response RNA element (RRE RNA), derived using construct divide-and-conquer and two-step SAXS envelope reconstruction. This RNA element binds to Rev protein to export viral genes from the nucleus to the cytoplasm before splicing, which overwhelms the host's defenses. This SAXS structure revealed that the RRE folds as an asymmetric letter 'A'. The Rev protein binding sites are located in the two arms, about 60 Å apart from one another, and serve as anchoring points for two copies of Rev proteins which then initiate further oligomerization of Rev proteins for viral gene export. **T. Kwaku Dayie**, U. Maryland, described a combined study of SAM-riboswitch RNAs using solution x-ray scattering and NMR techniques. Riboswitches, located in untranslated RNA regions, regulate gene expression through interacting with metabolites. The combined approach revealed that the apo form of the SAM-riboswitch has an extended conformation in which the Shine-Dalgarno sequence is exposed to allow for access and gene expression. In the bound form, the SAM-riboswitch SD-sequence is buried in a pseudo-knot conformation, and gene expression is turned off.

Recent advances in instrumentation, new techniques for SAXS data analysis, and new modeling methods have greatly advanced biomacromolecular research. **Michal Hammel**, LBNL, described their highly automated BioSAXS setup and the services provided at their SIBLYS beamline. He also described FOXS, a program that calculates scattering profiles using the Debye formula, and other SAXS modeling programs developed in the group. **Osman Bilsel**, U Mass, described the collaborative development of the continuous turbulent flow based time-resolved BioSAXS setup with BioCAT at Argonne. The current continuous flow setup at the BioCAT beamline has achieved ~0.26 μs resolution allowing observation of early stages of biomolecular folding processes that would be inaccessible by stopped-flow techniques. **Mark Del Campo**, Rigaku Americas, described a new Rigaku home laboratory SAXS instrument, the BioSAXS-1000. It includes focusing optics and eliminates the need to desmear SAXS data prior to analysis. The BioSAXS-1000 provides usable SAXS data in 5 min -2 hours with reasonable signal-to-noise for typical SAXS concentrations (1-5mg/ml). Currently, no standard exists for establishing the maximum usable q range for SAXS data. Mark advocated using signal-to-noise versus q and illustrated this using SAXS data collected at various exposure times.

During the poster session, **Kevin Pröpper**, Georg August U, presented **M-56**, computational methods for studying protein-DNA interactions. **Cristián Huck-Iriart**, Buenos Aires U, presented **S-44**, results of SAXS research on sodium caseinate (NaCas) micelles and the relevance to understanding NaCas emulsions. **Scott Classen**, LBNL, presented **S-42**, new hardware and software developments at the SIBYLS beamline. **Arne Meyer**, XtalConcepts, presented **M-65**, dynamic light scattering experiments (DLS) to monitor counter-diffusion crystallization experiments in capillaries. **Matt Benning**, Bruker, presented **S-40**, new improvements to home laboratory SAXS instruments.

Xiaobing Zuo & Angela Criswell



In back, L to R: Joseph Yarbrough, Dagmar Ringe, Lesa Beamer, Edward Snell, Nozomi Ando. In front, L to R: David Case, Allan Pang, Arwen Pearson, Allen Orville. Not shown: Agnesa Shala.

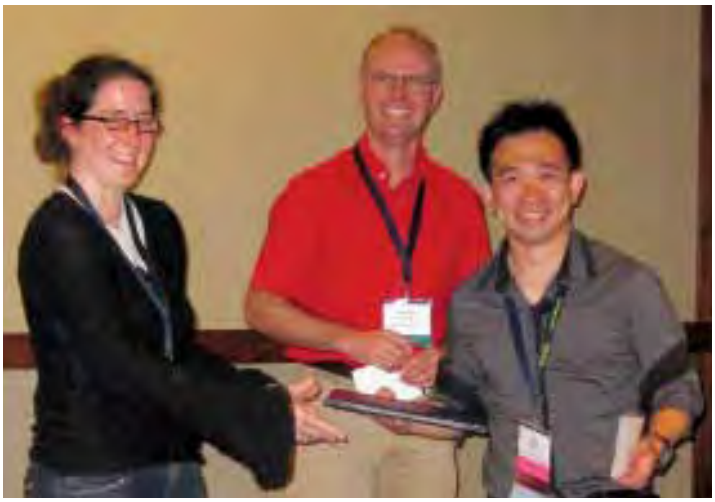
9.05: Complementary Techniques in Structural Biology

David Case, Rutgers U, described results on extending molecular dynamics simulations from individual molecules to crystal lattices for small peptides. The simulations agreed remarkably well with the experimentally observed electron density and showed clear potential to improve solvent modeling within macromolecular structures. **Allen Orville**, BNL, described a high-throughput pipeline being developed to perform biophysical analysis of macromolecules involved in bacterial nitrogen fixation. Allen's talk showed how combining single-crystal spectroscopy, diffraction and x-ray fluorescence was beginning to provide a picture of nitrogen fixation in root nodules. **Joseph Yarbrough**, an undergraduate student at the U of Florida and recipient of an **ACA Travel Award**, discussed the effects of pH on adeno associated virus-8 and how a combination of circular dichroism and differential scanning calorimetry shows that at lower pH one of the three viral capsid proteins begins to unfold and linearize.

Nozomi Ando, MIT, described the allosteric regulation of ribonucleotide reductase (RNR) activity in *E. coli*. Using a combination of small angle x-ray scattering, x-ray crystallography, electron microscopy and analytical ultracentrifugation she showed that RNR existed as a mixture of transient species with distributions modulated by allosteric effectors. Each technique supported evidence from the others and provided unique information, completing the overall picture of structural mechanism.

Dagmar Ringe, Brandeis U, showed how not only active site residues but also those outside the active site control reactivity. She described how structural information was combined with theoretical predictions of perturbed titration curves for individual amino acids in the structure. Ringe went on to discuss insights she had gained about mechaism of action and about the potential for predicting function from structure.

Lesa Beamer, U of Missouri, introduced the use of NMR to put crystallographic information into context and to better understand connections between structure, dynamics and catalysis in phosophohexomutase.



L to R: Arwen Pearson, Eddie Snell and Allan Pang.

Allan Pang, Queen Mary U, **Margaret C. Etter Student Lecturer** awardee and also a recipient of an **IUCr Travel Award**, discussed the multiple techniques he has employed to look at bacterial metabolosome structures. These microcompartments are formed from hexagonal shaped tiles made up of different protein subunits.

Agnesa Shala, York U in Toronto, Canada presented bioinformatic approaches combined with affinity pull down assays and mutagensis to study periplasmic proteins linked to antibiotic resistance in human pathogens. She described the microcrystals produced and directions for the future.

Eddie Snell & Arwen Pearson

10.01 L to R: Larry Falvello, Alberto Albinati, Lawrence Dahl, Mike Hall, Bruce Foxman, Alan Pinkerton, Lee Daniels, Silvia Chiara Capelli, Mark Bowden.

10.01: Important Science from Small Molecule Structures

The speakers in this session had much to say about cluster chemistry, hydrogen storage, topotaxy, displacement parameters, experimental and theoretical electron densities, and reaction mechanisms.

The most traditional and extensively used application of small molecule crystallography is the identification and accurate geometrical characterization of newly synthesized compounds. **Larry Dahl**, U Wisconsin, used structure as a point of departure for addressing complex bonding questions in his family of Pd clusters. He explained the positive stabilizing influence of the Tl(I) 6s25d10 *inert electron pair* in Tl(I)/Pd(0) compounds for which attempts to prepare Au(I)/Pd(0) analogues have not been successful. Larry's clusters are large, and he pointed out that this work would have been impossible without the area detector based diffractometers that arrived on the scene 20 years ago.

Structure is important at the small end of the size scale, as exemplified in the presentation by **Mark Bowden**, Pacific North West National Laboratory, on high hydrogen density materials: the borane adducts beginning with H_3NBH_3, which have greater mass density of hydrogen (~140 g/L) than does liquid H_2 (~70 g/L). A key to using hydrogen stored this way is activation, which means lowering the barrier to dissociation of hydrogen from the complex. A good starting point for more information is *Faraday Discuss*., 2011, **151**, 157-169, (DOI:10.1039/C0FD00015A).

Michael Hall, Texas A&M, brought quantum chemistry in with a discourse on the structural aspects of reaction mechanisms in transition metal complexes. Mike gave an excellent historical introduction to theoretical methods and drew a brief murmur from the audience by describing DFT, (Density Functional Theory), as a free lunch, because the quality of the results obtained from properly used DFT is disproportionate to the relative ease with which the calculations can be done. However, as Mike pointed out, it is possible to get variable results using different functionals. We might infer that inexpert use is to be discouraged. Mike presented, among other examples, the case of a predicted intermediate that was found by DFT, even though it had not yet been experimentally observed.

Alan Pinkerton, U of Toledo, provided a bridge between hard core theory and hard core high-resolution diffraction analysis with a charge density study of croconic acid, 4,5-dihydroxycyclopentenetrione, a high density organic (ρ = 1.912 g/cm^3) which is also ferroelectric at and above room temperature (Horiuchi *et al*., *Nature* **463**, 789-792, doi:10.1038/nature08731). Alan delivered a concise tutorial on charge density analysis when multipole expansion fitting is applied to diffraction data. He went on to explain how the results of charge density analysis explain the close intermolecular interactions in croconic acid. There are two strong hydrogen bonds of ~60 kJ/mol, but in addition the sum of non-covalent non-H-bonding interactions (O...O and O...π) is ~42 kJ/mol, equivalent to two typical hydrogen bonds.

Silvia Capelli, Inst. Laue-Langevin, talked about two non routine state of the art diffraction applications. Normal mode analysis from mean square atomic displacement amplitudes, (Bürgi and Capelli, *Acta Cryst*. (2000) **A56**, 403-412), is used to characterize low frequency, high amplitude vibrations from molecular libration, translation and/or deformation, high frequency intramolecular vibrations and also disorder, provided that anisotropic atomic displacement parameters are available for several temperatures. Analyses based on variable temperature displacement data have a parallel in vibrational spectroscopy, for which the analogous extra information can be obtained through isotopic substitution. Silvia described several examples, including applications to urea and to sucrose, for which the results agree with data from terahertz spectroscopy. Finally, Capelli emphasized the distinguishing characteristics of neutron diffraction; elemental contrast distinct from that of x-ray diffraction, scattering lengths independent of resolution, and hydrogen scattering, so much more powerful than scattering by electrons.

Bruce Foxman, Brandeis U, described thermally induced topotactic reactions since, as he explained, his gamma irradiator is on its ninth half-life. Foxman described the method of establishing the geometrical relationship between different phases oriented under the same conditions e.g. the mother and daughter phases in a transition carried out without removing the crystal from the diffractometer. Bruce uses the *operate group* geometry transformations of the CAD4 program for these analyses.

Alberto Albinati, Lee Daniels, Larry Falvello

10.02 In back, L to R: Allen Oliver, Lorraine Malaspina, Kevin Gagnon, Faye Bowles, Chun-Hsing Chen, James Hall, Xiaoping Wang. In front: Ying-Pin Chen and Elena Forcen-Vazquez.

10.02: Cool Structures

The Cool Structures session, sponsored by the Small Molecule SIG, began with a polymeric theme. **James Hall**, U Reading, UK, introduced a variety of Ru complexes that are able to perform DNA intercalation in a variety of bonding modes. Both Delta and Lambda forms of the complex were found to interact with DNA decamer chains in each of three bonding modes. **Elena Forcen-Vazquez**, U of Zaragoza, Spain, demonstrated the polymeric diversity that copper citrate complexes exhibit: from 1D chains to 3D extended networks. Because of their polymeric nature, these complexes also have properties as single molecule magnets. Elena showed that hydration can affect the polymer formation, resulting in different networks. **Josh Chen**, Indiana U, used cyanostilbene as a precursor to show how large cyclic structures, *cyanostars*, could be readily synthesized. These pentameric complexes introduce cavities suitable for anion uptake and can be tailored to accept different anions. Being pentameric, the cyanostars pose significant crystallographic challenges - five-fold symmetry is impossible! Josh demonstrated how this led to disorder and how this disorder was resolved.

Kevin Gagnon, Texas A&M, presented a series of 1D inorganic-organic hybrid materials made from linear alkylbisphosphonic acids and zinc acetate. The resulting products contain chains with tetrahedral zinc atoms cross-linked by octahedral metal atom forming nanometer-size 1-D tunnels filled with disordered solvent molecules. The hybrid framework shows structural flexibility and the channel shape is sensitive to small variations of zinc site occupancy in the crystal structure. **Lorraine Malaspina**, U Fed Goias, Brazil, discussed her careful analysis of space group symmetry when she analysed the disordered crystal structure of a coumarin ester. The crystal structure of the ester ($C_{14}H_{13}NO_3S$) was solved in both space groups C2/c and $P2_1/c$. The structure solved in the $P2_1/c$ space group has two unique molecules in the asymmetric unit, but exhibits unusually large anisotropic thermal displacement parameters, suggesting that the correct space group is C2/c.

Ying-Pin Chen, Texas A&M, talked about methods for topology control of MOF (Metal Organic Framework) structures. In one case the topology was changed only by changing the molar ratios of the reaction precursors in solution. At a ratio of Zr to TCPP pg 1 / 30, a novel Zr_8-SBU was formed, (TCPP is tetracarboxylatephenylporphyrin). By just doubling the ratio with an excess amount of TCPP ligand used in the reaction, a Zr_6-SBU was obtained instead. Another method from which two MOFs with different Cu-SBUs were synthesized involved changing the solvent combinations. Reaction of Cu(II) with 3,3'-((pyridine-3,5-dicarbonyl) bis(azanediyl)) dibenzoic acid (PDAD) in dry dimethylamine solution yielded a MOF that contained an unusual Cu_4-SBU. However, on addition of several drops of water into the reaction mixture, a paddle-wheel based MOF was formed.

Faye Bowles, UC Davis, discussed studies with C_{60} with regard to various approaches to manipulation and cleavage of metal-metal bonds by reaction of metal-metal bonded carbonyl complexes. It is known that metal-metal bonded carbonyl compounds isomerize in solution, but crystals of their solid-state conformations have not all been identified. It is very revealing to see that C_{60} forms co-with an unbridged dicobalt octacarbonyl and its derivative $Hg[Co(CO)_4]_2$. When a diruthenium carbonyl complex $[CpRu(CO)_2]_2$ was exposed to C_{60}, a new metal-fullerene adduct was formed resulting in cleavage of the metal-metal bond.

All talks were student presentations and were very true to the spirit of what is involved in producing decidedly cool structures.

Allen Oliver & Xiaoping Wang

'Yes of course I'm sure this is the magnetic North Pole. I just wasn't expecting to find a bloody great solenoid. . ."

Courtesy of Nick D. Kim, The University of Waikato, New Zealand. See nearingzero.net/res.html.

L to R: Ovidiu Garlea, Ashfia Huq, Susan Herringer, Simon Parsons, Timothy Munsie, John Greedan, Dimitry Khalyavin.

13.02: Magnetic Materials

Sponsored by Materials, Neutron and Powder SIG, this session featured materials synthesis, molecular magnets studied under pressure and three different families of compounds which have exciting magnetic properties. **John Greedan**, McMaster U, discussed a varied range of short and long range magnetic order that is observed in vacancy ordered / disordered perovskite structures. **Dmitry Khalyavin**, ISIS / Rutherford Appleton Laboratory, introduced the hexagonal lattice system $RBaCo_4O_7$ where a new exchange topology exhibiting geometrical frustration gives rise to varied degrees of spin correlation. **Ovidiu Garlea**, ORNL, described the effect of oxygen doping on the structural and magnetic properties of delafossite compounds. The second half of the session included studies of molecular based magnets under pressure, effects of random exchange in ferromagnetic copper chloride chains and, finally, studies of single crystal holmium titanate.

Ashfia Huq

13.03: Fibril-Forming Pathological Peptides: Prions, Amyloids, and 'Friends'

In back, L to R: Joseph Orgel, Robyn Stanfield, Sankar Naravan Krishna, Wenji Zheng . In front: Christopher Stanley, Gerald Stubbs, William Wan, Hiromi Arai.

The fiber diffraction SIG formally holds sessions in the 'even' years of the ACA's meeting. The SIG has moved to two sessions of much broader interest to the average conference attendees and that are specifically open to presentations from all disciplines within the broader ACA community. The motivation and importance of discussions on prions and amyloids is that these 'generic' structures are the root cause, or at least directly associated with the cause, of numerous systemic and neurological diseases such as Alzheimer's, Parkinson's and Huntington's.

Joseph Orgel, Illinois Inst of Tech, provided a brief overview of pathological fibril forming peptides, their general structure and recent developments in the field to introduce the session.

Christopher Stanley, ORNL, presented a time-resolved neutron scattering study where they were able to follow the aggregation kinetics of huntingtin amyloid precursors. The precursors showed a clear distinction between the wild-type and pathological forms of the protein throughout the data series.

William Wan, Vanderbilt U, talked about structural polymorphism seen within the fungal prionizable element HET-s using fiber diffraction data. William was awarded the **2010 Fiber SIG Etter Young Lecturer Award** for his presentation on structural insights into fungal prion HET-s and has continued that research. When fibrils from this peptide are formed at pH 7.5 they do ***not*** display infectious qualities. However, fibrils formed at pH 2 ***do***. William noted that significant degradation occurs at low pH, which may well account for the different (and infectious) structure of the HET-s fibrils. Not only that, but it appears to be the fibrillar structure itself that is infectious, making the study of independent fragments of the fibrillar structure in isolation less useful to understanding the diseases caused by such entities.

Joseph Orgel & Olga Antipova

L to R: Thomas Weiss, William Heller, Sai Venkatesh Pingali, John Barker, Petra Pernot, Volker Urban, Lin Yang.

13.04: Emerging Sources: Theory and Practice II

The second session in the Emerging Sources series focused on small angle scattering (SAS), a technique that has seen a surge in applications to life sciences in recent years. The session was dedicated to the memory of **Dr. Hiro Tsuruta**, a pioneer of structural biology with synchrotron small angle x-ray scattering, who unexpectedly passed away in 2011. Emerging capabilities and research at leading small angle x-ray and neutron scattering beamlines and supporting facilities that currently exist or are being planned around the world were discussed.

With respect to synchrotron beamlines - **Petra Pernot**, ESRF, described BM29 as a dedicated instrument for protein solution scattering; in recent years solution scattering has seen rapidly growing demands. BM29 is optimized to measure hundreds of protein solution samples quickly without user intervention. **Thomas Weiss**, SSRL, described BM 4-2, the beamline at which Hiro Tsuruta made most of his contributions to the bio-SAXS community. Compared to BM29, this instrument has a wider scientific scope, capable of accommodating static and time-resolved experiments on proteins in solution and lipid membrane structures. **Lin Yang**, NSLS, described the nearly completed LiX beamline as the newest of the x-ray scattering instruments that are dedicated to biological applications. Like 4-2, LiX is a versatile instrument. It offers capabilities that are unique to the bright NSLS-II source, including time-resolved solution scattering using continuous flow cells, scattering-based scanning-probe tissue imaging, and scattering from membrane proteins embedded in single-layered lipid membranes. A common theme in the beamline presentations is the effort to make them more user-friendly by developing more automation and by offering software with which users might already have experience.

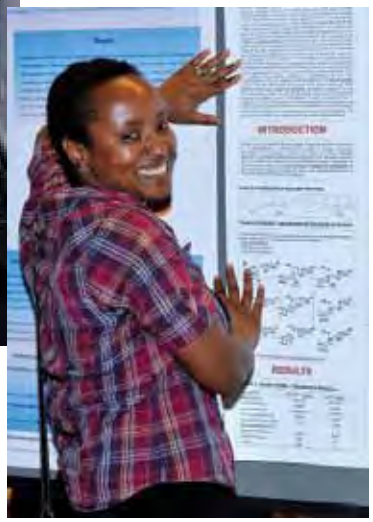
Sai Venkatesh Pingali, ORNL, reported on a new Small-Angle Neutron Scattering (SANS) instrument, the Bio-SANS instrument operated by the Center for Structural Molecular Biology (CSMB) at the High Flux Isotope Reactor of ORNL. This is the only facility in the world specifically dedicated to biological applications of small-angle neutron scattering.

William Heller, ORNL, described the **Extended Q-Range Small-Angle Neutron Scattering** instrument. This is a Time-of-Flight (TOF) SANS instrument located at the Spallation Neutron Source of ORNL. It is a general purpose SANS instrument that possesses a large dynamic measurement range at a single configuration and a high available flux suitable for weakly scattering samples and kinetics studies.

John Barker, NIST, reported on their new very small-angle neutron scattering (vSANS) diffractometer, currently under construction at NIST. It's unique design includes a detector with a 1-mm pixel size, as well as options for multiple confocal beams with focusing lenses at the sample and narrow slit apertures. The instrument will provide, in addition to the usual SANS range, an extended q-range from $q \approx 10^{-4}$ Å^{-1} to 10^{-3} Å^{-1} in a single measurement.

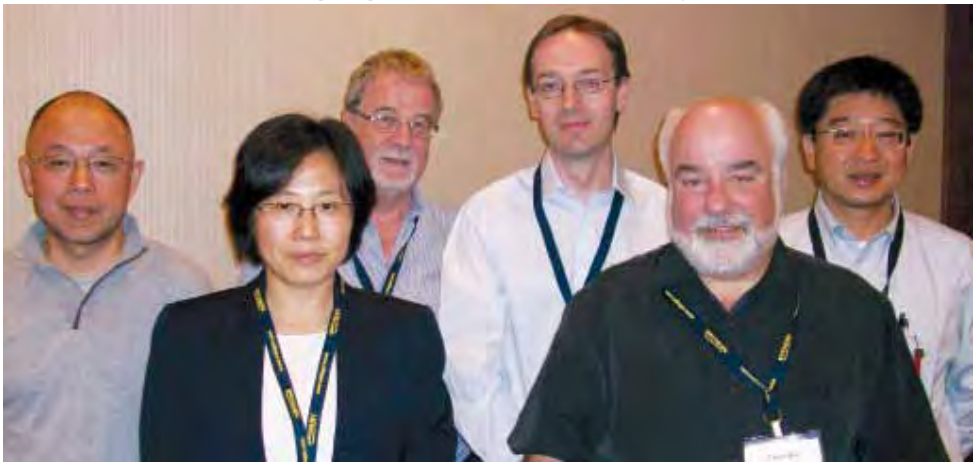
Volker Urban & Lin Yang

At left, Maureen Julian explaining her poster (T-40) to Ying-Pin Chen



At right, Vimbali Chickwana with her poster (T-04).

13.05: Emerging Sources III: Theory and Practice



L to R: Zhong Ren , Wei Kong, Keith Moffat, Jasper van Thor, Timothy Graber, and Masaki Yamamoto.

Timothy Graber and **Zhong Ren**, BioCARS, contrasted the properties of third generation sources such as the APS with those of spectacular, new x-ray free electron (XFEL) sources such as the **Linac Coherent Light Source** at Stanford. Third generation sources offer ready accessibility to users, pink or monochromatic x-rays, high stability, a very high rep rate, and mature beamline instrumentation and experimental design, but cannot come close to XFELs in photons per pulse nor, of course, in the brevity of their x-ray pulses. At third generation sources, pulses are limited to roughly 100 ps FWHM in duration by the characteristics of the RF systems. However, following the lead of Hardrup and colleagues at ESRF, Ren pointed the way to pump-probe experiments which offer a time resolution less than the x-ray pulse length. This is achieved by locating the brief, few ps, pump-laser-pulse within (rather than before) the longer probe x-ray pulse, thus dividing the x-ray pulse into leading and trailing components. Since only the trailing period generates the light-dependent signal, its duration now controls the time resolution, provided the pulse shape is constant and timing jitter is suitably minimized. By systematically tracking the laser pulse across the x-ray pulse, the length of the trailing period is smoothly varied. Ren showed, in initial, time-resolved crystallographic experiments, that this conceptually simple, general approach '*poor man's pulse slicing*' can yield a time resolution <100 ps.

But all such experiments require a carefully-controlled laser pulse to initiate the reaction in the molecules in the crystal, which demands systematic study of the photophysics to achieve maximum yield of the desired species. **Jasper van Thor**, Imperial College London, described such a laser-lab-based study of the photocycle of photoactive yellow protein using fs laser pulses. The yield depends on pulse wavelength, intensity and duration, and on whether or not the pulse is chirped; and, (of course), the sample must not be destroyed. Thus, such studies are an essential adjunct to ultrafast x-ray experiments.

Macromolecular crystallography increasingly focuses on tiny crystals, which requires the design and implementation of purpose-built beamlines that offer a tightly-focused x-ray beam, low x-ray background, the ability to visualize and center tiny crystals, and precision in crystal goniometry to ensure that the crystal remains centered in the beam. **Masaki Yamamoto**, Spring-8, Japan, described a new beamline at Spring-8 that has these characteristics and is proving very effective.

Wei Kong, Oregon State U, described a radically new, laboratory-based approach to structure determination of single proteins. The approach is based on the incorporation of proteins into superfluid helium droplets at 0.38°K without significant unfolding. An elliptically-polarized laser beam is used to orient the droplets, and the electrons are scattered by the now-oriented protein molecules. The goal is to generate a complete, three-dimensional electron scattering pattern from which the structure could be reconstructed. This overall approach has several technically challenging steps, and Kong clearly presented results on successful initial steps in this high risk, high reward project.

Keith Moffat

Crowd scene at a poster session. Below, Lee Daniels.

In back: Winnie Wong-Ng, Hong-Cai Zhou, Karena Chapman, Fernando Uribe-Romo. In front, L to R: Andrey Yakovenko, Christopher Cahill, Debasis Banerjee, Greg Halder.

13.06: Materials for a Sustainable Future

This symposium was a joint collaboration between the Powder Diffraction, Materials, Neutron Scattering, and Small-Angle Scattering SIGs of the ACA, and provided a broad overview of neutron and x-ray scattering studies on materials that address key energy-related problems.

The first session featured a diverse set of talks focusing on molecule-based materials. **Hong-Cai (Joe) Zhou**, Texas A&M U, presented his group's latest work on the design and characterization of highly selective metal-organic frameworks (MOFs) for carbon capture applications. This included a range of lab and synchrotron-based x-ray diffraction techniques that were critical in elucidating the host-guest properties of the materials. Carbon capture in MOFs was also addressed in presentations by **Debasis Banerjee**, Rutgers U, and **Winnie Wong-Ng**, NIST. Studies of materials and properties of relevance to nuclear-energy were also highlighted in presentations by **Christopher Cahill,** George Washington U, on uranium-bearing hybrid materials, and **Karena Chapman,** ANL, on a MOF-based trap for hazardous radiological by-products of nuclear energy production (e.g., molecular I_2). **Fernando Uribe-Romo**, Cornell U, presented several advances on his work with porous covalent organic frameworks (COFs), including the preparation of highly-ordered COF thin films for organic photovoltaic devices.

In back L to R: Natasha Chernova, Jacqueline Cole, Sai Venkatesh Pingali, Greg Halder. In front L to R: Craig Bridges, Michelle Everett, Olaf Borkiewicz, Andrey Yakovenko, Hugh O'Neill, Shishir Chundawat.

Shishir Chundawat, Great Lakes Bioenergy Research Center at Michigan State U, described the advances achieved in understanding the biomass-to-biofuel conversion process, an important approach towards our energy sustainability. He demonstrated that the anhydrous liquid ammonia pretreatment reorganizes the hydrogen bonding network in the crystalline structure, making the pretreated biomass show greatly improved enzymatic deconstruction efficiency.

Hugh O'Neill, ORNL, reported current endeavors in understanding how plants convert solar energy. He specifically discussed his group's recent advances in developing a biohybrid photoconversion system by incorporating natural photosynthetic apparatus with synthetic block copolymers to enable establishing structural design principles of synthetic architectures for solar energy conversion.

Michelle Everett, ORNL, described an approach that provided for a new energy source and carbon sequestration. Her conclusions from neutron powder diffraction studies on seafloor methane hydrate structures suggested that formation of carbon dioxide hydrates was more energetically favorable, leading to the possibility of releasing methane to be used as a new energy source and simultaneously reduce carbon dioxide in the environment.

Jacqueline Cole, U of Cambridge, related their efforts to quantify structure-property relationships of materials for dye-sensitized solar cells using data mining techniques.

The second segment was dedicated to x-ray and neutron scattering studies of battery-related materials. **Natasha Chernova**, Binghamton U / Northeastern Center for Chemical Energy Storage (NECCES), reported on the key atomic-scale processes which govern electrode function in rechargeable batteries, (EFRC). Chernova highlighted the importance of a multi-pronged approach when studying these complex materials, including pair-distribution function (PDF) analysis, x-ray absorption spectroscopy, electron microscopy, Li NMR and magnetic properties. **Olaf Borkiewicz**, ANL / NECCES, presented a detailed examination of the spatial evolution of electrochemical reactions and reaction fronts using *in situ* x-ray PDF analysis. Finally, **Craig Bridges**, ORNL, spoke on neutron powder diffraction studies of disorder and defects in Li-ion cathode materials. ***We thank the following sponsors for their generous support: Bruker AXS, the X-ray Science Division at Argonne National Laboratory, Polycrystallography Inc., and Diffraction Experts.***

Gregory Halder, Sai Venkatesh Pingali & Andrey Yakovenko

13.07: Past Reflections & Future Directions: 100 Years of Diffraction and the 25th Anniversary of the Service Crystallography SIG

L to R: Christine Beavers, Louise Dawe, David Rae, Brian Toby, Curt Haltiwanger, Paul Swepston, Hilary Jenkins, Sue Byram, Jenny Glusker.

This Monday morning session, sponsored by the Service and Small Molecule SIGs, was held in celebration of both the 100th anniversary of x-ray diffraction science, and the 25th anniversary of the Service Crystallography SIG's presence in the ACA. Invited speakers and contributors came from Canada, the U.S. and Australia, and represented national laboratories, industry, and academic institutions. Their talks spanned the history of diffraction experiments, the future of service crystallography, innovations in instrumentation and software and calculations.

Jenny Glusker, Fox Chase Cancer Centre, began the session with her reflections on 100 Years of structure determination. This beautiful talk gave credit to the many scientists who contributed to the evolution of small molecule crystallography, and she included many photos with her history. Jenny gracefully put our science in context for the next generation of crystallographers. There was a near capacity audience for this early morning talk and it was extremely well received. In fact, none of us wanted it to end.

Sue Byram, Bruker AXS, described the ***Evolution of Small Molecule Crystallographic Instrumentation in North America***. Her talk was illustrated with examples of hardware (and software) innovations by many major industrial contributors, and clearly showed the giant steps that have been taken in the more than 100 years of x-ray instrumentation.

Looking to the future, **Brian Toby**, ANL, shared his vision of transformation for service crystallographers. In his view the new advances in diffraction interpretation by software demand that, in order to survive, crystallographers must contribute new ideas and skills to scientists in disciplines that overlap with ours. Brian's outlook was not entirely bleak, -- he presented several practical suggestions for the survival of service crystallography.

13.07 cont'd

Hilary Jenkins, McMaster University, at right, attracted a lot of audience interest with her presentation of exciting new software for viewing data (MAX3D).

Paul Swepston, Rigaku Americas Corp, at left, talked about the collaborations which lead to great science in his *Enabling all Scientists to Utilize Crystallography* presentation.

Discussion during the coffee break, L to R: Tom Koetzle, Richard Staples, James Phillips, and Jenny Glusker.

Further evolutions in dealing with difficult 'small molecules' (which have much in common with macromolecules!) and in methods of refinement were also discussed by **Christine Beavers**, LBNL, and **A. David Rae**, Australian National U, respectively.

At right, Christine Beaver and David Rae.

Louise Dawe & Curt Haltiwanger

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In back L to R: Eric Armstrong, Dirk Zajonc, Douglas Davies, Charles Dann, Graeme Conn. In front L to R: Hua Li, Jason Stagno, Sozanne Solmaz, Sung-il Yoon, Dinesh Yernool.

13.08: Exciting Structures

Jason Stagno, NCI, described the first observation of a truly novel RNA supercoil structure. As in many other nucleic acid-containing crystals, the short double-stranded RNA duplexes used in crystallization form pseudocontinuous helices; uniquely, however, these helices adopt coiled-coil formations that form a yet higher order of structure, a plectonemic RNA supercoil, mediated by the RNA binding protein NusB. This remarkable structure provides novel insights into high-density nucleic acid structures, suggesting, for example, a mechanism by which protein-mediated RNA supercoiling may facilitate the packaging of viral RNA genomes.

Dinesh Yernool, Purdue, presented recent structural studies of a DNA-protein complex from a bacterial two-component signal transduction system. Such signaling circuits afford bacteria the ability to adapt appropriately to changing environments by relaying signals received by sensor histidine kinases to response regulators (RRs) that typically act to alter gene expression. For the first time the structure of a DNA-RR complex was revealed, shedding welcome light on the mechanism by which the phosphorylation signal is communicated, the role of interdomain surfaces in regulation of gene expression, and the basis of the increased affinity of activated RRs for DNA.

Doug Davies, Emerald Bio, described the first structure of an *in vitro* evolved 'SOMAmer' (Slow Off-rate Modified Aptamer) in complex with its protein target. SOMAmers expand the chemical diversity of nucleic acids through incorporation of modified groups such as amino acid-like side chains. This structure revealed that, in contrast to the typically polar nature of unmodified nucleic acid aptamer interactions with their targets, the SOMAmer binds its target protein (a growth factor) largely through shape complementarity and hydrophobic interactions, mimicking the interaction of the target protein with its receptor. This novel structure will help exploit the unique properties of SOMAmers to identify high-affinity ligands for proteins that are recalcitrant to selection using the limited chemical vocabulary of standard nucleic acids.

Sozanne Solmaz, Rockefeller U, described her ambitious work involving the transport channel of the nuclear pore complex. Using structures of complexes of the nucleoporin (nup) interacting domains Nup54·Nup58 and Nup54·Nup62, Sozanne was able to construct a model of the entire transport channel, consisting of 224 copies of the three nups in a stoichiometry of 4:2:1 (Nup62:Nup54:Nup58). The resulting 12.3 MDa complex faithfully adhered to known overall shape and symmetry as determined by electron microscopy. It was also able to account for the remarkable range of pore dynamics necessary for the accommodation of a wide variety of cargo sizes. Certainly, the movie showing the contraction of the channel's ring diameter from ~40 nm to ~20 nm, with a concomitant 150% increase in height from 4 nm to 6 nm, was a highlight.

Hua Li, an HHMI investigator at UT Southwestern Medical Center, presented his most recent advances in the study of the sodium/calcium exchanger (NCX), providing the session with a welcome foray into electrophysiology. Insights gleaned from Li's structure of the outward-facing NCX from *Methanococcus jannaschii* included the elucidation of one Ca^{2+} and three probable Na^{+} binding sites clustered within the center of the protein, as well as a pair of channels where extracellular ions could gain access to these sites. Finally, a model of the as yet unsolved inward-facing *M. jannaschii* NCX was proposed.

The session then switched to a focus on immunology, beginning with innate immunity. **Sung-il Yoon**, Kangwon National U, presented a structure obtained of the N-terminal leucine repeat module of toll-like receptor 5 (TLR5) bound to the D1-D2-D3 domain of *Salmonella flagellin*, thus far the first and only structure of a TLR bound to a protein ligand.

Structural and biochemical analyses established the importance of conformational rearrangement of a protruding loop

13.08, cont'd within TLR5. This change facilitated flagellin accommodation within the binding pocket and resulted in subsequent dimerization of the complex via the receptor's C-terminal tails allowing downstream activation to ensue.

Dirk Zajonc, La Jolla Institute for Allergy and Immunology, focused on glycolipid antigen recognition by type 1 vs type 2 natural killer T (NKT) cells. Zajonc's structure of the CD1d-bound lysosulfatide, in complex with a type 2 NKT T Cell Receptor (TCR) provided a unique vantage point from which to compare various forms of antigen presentation and recognition. Many of the key residues responsible for TCR binding to the CD1d-lysosulfatide complex were shown to be conserved in other known sulfatide-reactive TCR's, suggesting a common structural modality that enables recognition of this class of self-antigens.

Finally, **Charles Dann III**, Indiana U, talked about the potential of novel antifolates to specifically target the human folate receptor (hFR) and thereby carry this well-established class of therapeutics into the next generation of cancer treatments. Dann and his research group solved the first structures of the membrane-anchored protein in its apo form as well as bound to folate and several known antifolates and at both acidic and neutral pH's. Consequently they were well qualified to elucidate the molecular requirements for receptor-ligand interaction while visualizing the pH-dependent conformational changes that occur when hFR undergoes endocytosis. By designing drugs whose sole entry into cells occurs via the hFR endocytic pathway, they hope to circumvent the dose limiting toxicity of traditional antifolates.

Eric Armstrong & Graeme Conn

13.09: Protein and Small Molecule Crystallography at Undergraduate Institutions: Research, Pedagogy and Professional Development

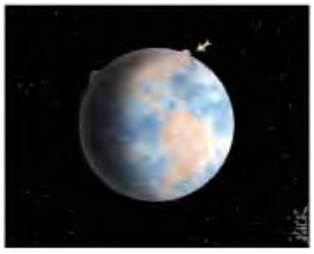
L to R: Douglas Juers, Alexander Norquist, Carla Slebodnick, Roger Rowlett, Kraig Wheeler. At right, Kraig Wheeler speaking in the Transactions Symposium.

Speakers in this half-day session addressed a wide range of topics directed at the practical aspects of building productive x-ray crystallography facilities that serve both undergraduate education and peer-reviewed research programs.

Joe Tanski, Vassar College, (left), described successful strategies for x-ray diffractometer acquisition at a predominantly undergraduate institution. Joe also highlighted a teaching module that exposes undergraduate students to small molecule crystallography including the publication of crystal structure results. **Carla Slebodnick**, Virginia Tech, explained in detail the operational aspects of the summer undergraduate crystallography workshop at VT. Well placed discussions of theory and ample hands-on opportunities with crystals, instruments, and x-ray data serve to energize the participants about science and crystallography. **Roger Rowlett**, Colgate U, focused on strategies for meeting the challenges of building a protein x-ray crystallography capable laboratory, data collection using remote or home sources for student training with protein structure solution, and establishing fruitful research collaborations. **Doug Juers**, Whitman College, also emphasized protein crystallography at undergraduate institutions - both instrument acquisition and several examples of crystallography-focused biochemistry course units and research projects.

Alexander Norquist, Haverford College, described his recent success in cultivating a productive undergraduate research program involving the synthesis and structural properties of chiral vanadium tellurites. His talk also described best practices for including students in the research process and how to succeed without in-house x-ray facilities. **Kraig Wheeler**, Eastern Illinois U, related his journey (strategy, pitfalls, and ultimate success) for NSF-MRI funding.

Roger Rowlett & Kraig Wheeler



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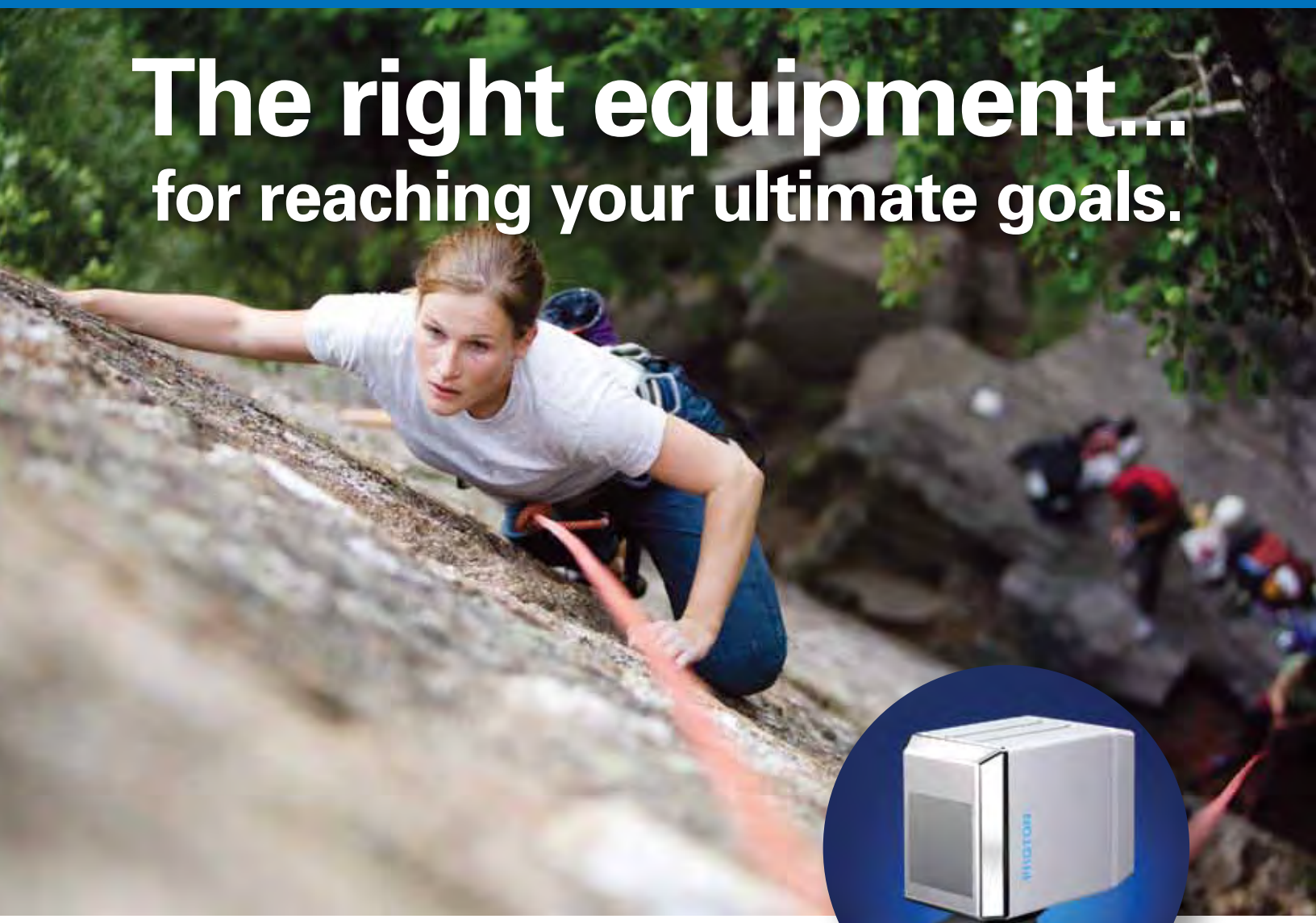

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Crystallography

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In back L to R: Robert Thorne, James Holton, Graeme Winter. In front L to R: Ana Gonzalez, Stephan Ginell, Zou Finfrock, Elspeth Garman, Sandor Brockhauser.

13.10: Radiation Damage

James Holton, BMB/PBD, U C San- Francisco, began by asking the question *Flirting with Radiation Damage: How Much Exposure is Too Much?* and then described the chemistry and physics of radiation damage in macromolecular crystals. Many examples were discussed detailing the consequences of radiation damage, both locally and globally, for x-ray data and the resulting protein structures, also Holton gave guidelines for recognition of radiation damage in data and for obtaining diffraction data such that radiation damage is minimized. The take-home message was that it is a balance between noise and signal but you need adequate signal for good data.

Radiation Damage in Macromolecular Crystallography: Practical Considerations by **Elspeth Garman,** U of Oxford, laid out some considerations about radiation damage from a practical standpoint for an experimenter 'on the ground'. She recommended various measures to optimize the chance of minimizing radiation damage in experiments, including back-soaking non-specifically bound heavier atoms out of crystals to reduce the absorbed dose per incident photon, matching beam size to crystal size, using a '*top-hat*' shaped beam if possible, and making sure the beamline yielded enough information (e.g. photon flux and beam profile on that particular day) -to estimate the dose for your experiment so that you could become 'dose aware' and know what your crystals would tolerate.

Robert Thorne, Cornell U, presented *Time-dependent Global Radiation Damage: Can it be Outrun?* As crystallographers move from solving their first structures to more detailed studies of, for example, conformational substates and allosteric networks essential to mechanism, then data collection using crystals at or near room temperature are essential. Thorne detailed how the solvent-coupled radiation damage processes that give rise to steep increases in radiation sensitivity above ~200°K dictate that data collections above ~200°K should proceed on timescales from microseconds to minutes. Measurements of '*dark progression*' indeed reveal a component of damage that develops over several minutes at 180°K; this component decreases to seconds near room temperature. By collecting data in ~1 µs, using dose rates which approach 1 MGy/s (megagrays per second) and a fast detector, approximately half of radiation damage near room temperature could be outrun. Microfocused beams and faster detectors may reduce room temperature damage per dose to only a few times that at 100°K.

Zou Finfrock, U Washington, presented *Measurement of Mitigation of X-ray Radiation Damage in Macromolecular Crystallography by a Sub-micron Line Focus Beam*. She showed that radiation damage in the irradiated region by sub-μm line focusing is less than 25% of that in the unfocused case with the same x-ray total flux and diffraction signal. For the first time, accurate measurements of both the spatial dependence and penetration depth of photoelectrons excited by 18.6keV x-ray photon energy in a biological material (lysozyme) have been measured; the photoelectron penetration depth is ~ 5±0.5 μm.

Sandor Brockhauser, EMBL-Grenoble, in his talk *Burning Crystals*, also discussed radiation damage and its effect on the collected data, but mainly focused on the practical question of *how to live with this effect as a limiting factor in macromolecular crystallography?* Recently, Sandor and his colleagues have developed a computational model to predict the effect of radiation damage as a function of dose. Their model highlights and links to model parameters all the important experimental conditions and settings. They designed and implemented at ESRF an automated experimental protocol DAWB using their novel software framework. DAWB characterizes a crystal type by calibrating the radiation sensitivity parameters to the other beamline parameters calculated using a set of reference images collected from a sacrificed part of a crystal. The sensitivity parameter gained is then used to optimize subsequent data collections. Crystal shape is also an important consideration for optimization of data collections in case the beam size is much smaller than the size of the crystal. In such cases, off-centered data collection is suggested.

Finally, **Graeme Winter**, Diamond Light Source, talked about *A Novel Statistic for Radiation Damage Analysis?* After reviewing commonly used statistics for characterizing radiation damage in scaling analyses, he introduced a statistic ***Rcp(d)*** which compares, in a pair-wise manner, intensity values measured at different times (this is similar to Kay Diederich's ***Rd***) - -and accumulated up to a dose d, so the data behaves as a function of accumulated dose. He described both SAD and MAD examples,with *no* damage and with *clear* radiation damage, and showed that in these cases using a subset of the measurements gave improved results in phasing. In another example, his statistic made substructure solution possible where previously it was impossible. Finally, he suggested that where the sample lifetime is uncharacterized, measuring high multiplicity data with an attenuated beam, and subsequently analyzing the data using the Rcp(d) statistic - could help cope with radiation damage.

Stephan Ginell and Ana Gonzales

L to R: Rama Sashank Madhurapantula, Barbara Brodsky, Dan Kirschmer, Joseph Orgel, Jeff Deschamps, Olga Antipova, Tom Irving, Li-Kai Liu, Simon Goodson.

13.11 Flesh and Blood: Intact and In Situ Connective Tissue Diffraction Studies of Animals, Plants and Insect Bodies

The Fiber SIG sponsored this session which was topic centered rather than technique centered. Although the topics were chosen with fiber diffraction in mind, the hope was to attract cross-discipline interaction since at an ACA meeting many of these topics are investigated by crystallographers of other persuasions. The session focused on studies of animal, plant and insect connective tissues while they were still principally intact.

Barbara Brodsky, Tufts U, gave an introduction to the history of collagen structure studies. Brodsky began with the very earliest perspectives into its helical symmetry, and then described various studies of collagen packing and fibril forms, noting the different methods used in these studies. Several of the key investigators in the study of collagen and fibrous elements were present in the audience, which helped give the session a feeling of historic significance.

Simon Goodson, Cardiff U, the Fiber SIG's **2012 Etter Student Lecturer Award** winner, presented his work on solving the type I collagen packing structure in the mouse and contrasted the new structure to the rat type I packing structure solved a few years ago. It is not *that* disappointing to solve a structure for the second time only to discover it is essentially the same.... because it confirms both the older and newer work. Having a structure in a model organism specifically designed to study human diabetes is not an inconsiderable achievement.

Dan Kirschner, Boston College, presented ***Novel Molecular Views of Nerve Myelin Using Microbeam X-ray Diffraction (XRD) and Neutron Diffraction (ND)***. Combining x-ray and neutron diffraction of rodent nerve cells to take advantage of the techniques different sensitivity to water, Dan and his colleagues were able to differentiate between CNS and PNS nerves due to the excellent quality of diffraction data recorded. The scans of rodent nerves, which showed clear and recognizable myelin diffraction, were impressive and open the door to many more potentially very useful types of experiments in studies of normal and pathological neurological conditions.

Joseph Orgel & Olga Antipova

Olga Antipova and Joseph Orgel on the left, presenting the 2012 Etter Young Lecturer Award to Simon Goodson.

Con

Index of Advertisers

L to R: Jacqueline Cherfils, Christopher Dettmar, Michel Fodje, Julien Cotelesage, Catherine Lawson, Stephen Tomanicik, Shyamosree Bhattacharya, Filip Van Petegem.

13.12: Complementary Methods

The primary focus of this session was on methods which complement x-ray macromolecular structure information to provide additional biological insight. **Filip Van Petegem**, U British Columbia, Canada, described how electron microscopy reconstruction maps were combined with single-crystal x-ray structural models in order to understand the molecular pathology of malignant hyperthermia and cardiac arrhythmias. Filip presented convincing comparisons between wild-type and mutant ryanodine receptor models revealing that mutations lead to premature and prolonged opening of the calcium channels resulting in abnormal calcium release into the cytoplasm.

Catherine Lawson, Rutgers U, described the EM Databank, a unified data resource for 3D electron microscopy, developed collaboratively between the Research Collaboratory for Structural Bioinformatics at Rutgers U, the European Bioinformatics Institute (PDBe) and the National Center for Macromolecular Imaging (NCMI) at Baylor College of Medicine. Catherine described how the EM Databank provides a one-stop-shop for EM related data, and presented the recent improvements to resources and tools for depositing, accessing and visualizing EM related data.

Stephen Tomanicek, ORNL, described their progress towards determining the x-ray structure of a metallochaperone-like domain of Mercuric reductase (MerA) in an attempt to confirm the orientation of the mercury binding domain to the catalytic core suggested by SAXS and SANS experiments. The MerA structure is made up of a core and two arms each with conserved –SH groups which bind mercury and transfer it to the core for catalysis.

Jacqueline Cherfils, Centre National de la Recherche Scientifique, France, described her work to understand the structure and dynamics of Arf GTPases and their interactions with guanine nucleotide exchange factors. Jacqueline described how Arf GTPases are important regulators of exo- and endocytocis but functional differences between Arf1 and Arf6 were not obvious from static x-ray structures. However using a combination of SAXS, NMR, immune-labelling electron microscopy and tryptophan fluorescence, they gained understanding of the functional differences. The Synchrotron SIG chose **Christopher Dettmar**, Purdue U, to receive the **Etter Student Lecturer Award**. Christopher described the implementation of an instrument for integrating second order nonlinear imaging of chiral crystals (SONICC) and two-photon excited ultraviolet fluorescence imaging (TPE-UVF) with a synchrotron x-ray diffraction beam line. SONICC provides higher contrast imaging than existing UV fluorescence methods for highly ordered materials such as crystals. However, the SONICC method is less effective for high symmetry crystals. By combining SONICC and TPE-UVF, the capabilities for imaging tiny crystals with a high depth of field are significantly improved over existing methods. Christopher detailed the challenges of squeezing, at synchrotron beamlines, the complicated hardware involved into the tiny spaces available and the promising results obtained so far.

Christopher Dettmar, on left, receiving the Etter Student Lecturer Award from Michel Fodje.

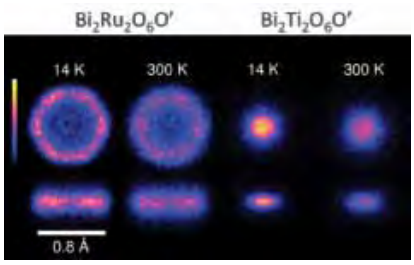
Julien Cotelesage, U Saskatchewan, Canada, described how x-ray absorption spectroscopy can complement x-ray crystallography models. X-ray absorption spectroscopy is capable of providing more accurate bond lengths between metals and their ligands than diffraction experiments, as well as information about the oxidation state of metal ligands that is not available from diffraction experiments. Julien described the efforts to integrate online x-ray absorption spectroscopy and diffraction at the Canadian Light Source macromolecular crystallography beamline 08B1-1. The preliminary results show that spectra obtained from crystals are comparable to those obtained from concentrated samples on a dedicated x-ray absorption spectroscopy beamline.

Shyamosree Bhattacharya, U Wisconsin-Madison, described the structure-guided design of a fluorescent phytochrome. In order to improve the use of phytochromes as biomarkers, their stability, quantum efficiency, size and stability need to be improved. Shyamosree presented results on the x-ray structure determination of wild-type and mutant phytochrome IFP1.4 and described how the information obtained is guiding protein engineering efforts to design a smaller, more compact and more stable fluorescent phytochrome.

Michel Fodje

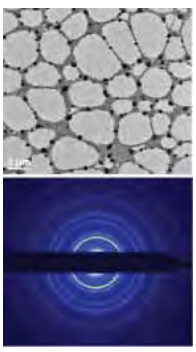
L to R: Branton Campbell, A.M. Abeykoon, Breaunnah Bloomer, Elena Aksel, Daniel Shoemaker, Katharine Page, Mikhail Feygenson, Claire Saunders. (Absent: Co-chair Thomas Proffen)

Daniel Shoemaker, ANL, demonstrated how data-driven reverse Monte Carlo simulations can be effective methods of creating large-box models to capture atomic disorder in a variety of complex materials. Many kinds of experimental data as well as chemical knowledge can be incorporated in this process; it has the unique advantage that separate constraints (PDF, Bragg, bond valence) can be satisfied simultaneously. Careful statistical analysis of the resulting configurations is crucial to understanding the physical meaning of the atomic ordering observed in the model. Among his beautiful examples were complex oxides, crystal growth, and semiconducting chalcogenides. The consequences of lone pair topology and oxygen vacancy in lone-pair pyrochlores is partly conveyed in the figure at right.



Real space maps of static Bi displacements in insulating $Bi_2Ti_2O_6O'$ and metallic $Bi_2Ru_2O_6O'$ are viewed along (top) and normal to (bottom) the O-Bi-O bond. Static disorder in both produces hexagonal ring or disk shapes centered on the ideal position, with striking differences in displacement magnitude. DP Shoemaker, R Seshadri, M Tachibana, and A.L. Hector, 'Incoherent Bi Off-centering in $Bi_2Ti_2O_6O$ and $Bi_2Ru_2O_6O$: Insulator Versus Metal,' Phys. Rev. B. 84, 064117 (2011).

A new capability was introduced by **Milinda Abeykoon**, BNL, who showed that using the pair distribution function (PDF), data of sufficient quality for quantitative analysis of nanoparticle structures can be obtained using a transmission electron microscope (TEM). Abeykoon discussed the methodology for obtaining the 'ePDF' as well as some limitations and opportunities. The ease of data collection and ubiquity of TEMs could make this an important tool in the characterization of nanostructured materials if the barriers to data processing can be overcome. PDF data, like those produced from the gold nanoparticles in the figure, were seen to show promise for quantitative analysis of nanomaterial structures.



(Top) A TEM image of ~100 nm Au nanoparticles. Black dots are the nanoparticles on the grid and the large white areas are the holes in the grid. (Middle) A background subtracted electron diffraction image, collected from the same region of the sample using 200 keV electrons. (Bottom) The 1D electron diffraction pattern obtained by integrating around the diffraction rings. The inset shows a magnified region of the integrated electron diffraction pattern as indicated by the dotted lines. M. Abeykoon, C. D. Malliakas, P. Juhas, E. S. Bozin, M. G. Kanatzidis and S. J. L. Billinge, Quantitative nanostructure characterization using atomic pair distribution functions obtained from laboratory electron microscopes, Z. Kristallogr. 227, 248–256 (2012).

Branton Campbell, Bringham Young U, described fits of local structure models to 3D volumes of single-crystal x-ray diffuse scattering data in relaxor ferroelectrics. He discussed, among other models, Huang-scattering from point defects. Point defects produce long-range distortion fields in the surrounding material, which Campbell explained were, 'much like those that troubled the sleep of the main character in the story of *The Princess and the Pea*'(!) With high-resolution reciprocal space reconstructions and highly-parallel optimization algorithms, good quantitative agreement was achieved.

Mikhail Feygenson, a NOMAD instrument scientist at ORNL, related how PDF analysis can provide quantitative information about the local arrangement of atoms, enabling studies of defects, surface relaxation and local disorder in nanomaterials. He focused on opportunities emerging for researchers at large scale facilities, stressing the complementarity of neutrons and x-rays for nanoparticle research.

Several talks by students followed, beginning with the Neutron Scattering SIG's **Margaret C. Etter Student Lecturer**, **Elena Aksel**, U of Florida, who presented local atomic structure deviations from the average structure of $Na_{0.5}Bi_{0.5}TiO_3$ ferroelectric ceramics. Undergraduate **Breaunnah Bloomer**, LANL / Howard U, demonstrated local structural changes occurring during geopolymerization synthesis, and finally, undergraduate **Claire Saunders**, ORNL / Duquesne U, discussed instrument resolution effects on PDFs.

Katharine Page

L to R: Meitian Wang, Robert Fischetti, Jim Pflugrath, Armin Wagner, Christoph Mueller-Dieckmann, Matthew Benning, B.C. Wang, Manfred Weiss, Naohiro Matsugaki, Wayne Hendrickson, and Zhi-Jie Liu.

13.14: Extended Wavelength X-ray Crystallography

The session, co-sponsored by the Macromolecular SIG and the Synchrotron SIG, focused on the potential and practical aspects of using extended-wavelength x-rays (0.7Å to 3.5Å and above) in structural biology research.

Bi-Cheng Wang, U Georgia/SERCAT/APS, opened his talk with a question on what additional biological/biophysical information can be obtained when SAD or MAD experiments are carried out using x-rays anywhere within 2.5 to 15 keV. He pointed out that the speakers would address this question in four related areas: new beamlines & equipment; sulfur phasing; phosphorous phasing and halide phasing. Wang then presented some recent results from his lab, which showed that using a multiple-data-set (MDS) data collection approach, successful S-SAD phasing could be carried out on a single insulin crystal with reduced radiation dose. He then collected several data sets that spanned the absorption edges of the metals, and showed that the oxidation states of metals/ions in crystals could be monitored using data collected across the Fe absorption edge for crystals of bovine catalase.

Christoph Mueller-Dieckmann, ESRF, described their structural biology group's plans to maximize the success of macromolecular crystallography experiments at ESRF. The plans include the MASSIF sample evaluation and sorting facility as well as upgrades to ID29 to enable data collection using low energy (E = 5 keV, λ = 2.5 Å) x-rays. He then described the work already done: upgrading a harmonic rejection mirror; installing a stepper shutter and extendable vacuum beam paths; and investigating several methods of soft x-ray data collection including cluster analysis.

Naohiro Matsugaki, Photon Factory, described their new beamline dedicated to SAD/MAD experiments that uses wavelengths greater than 2.7 Å to enhance weak anomalous signals. A standing helium path, which can accommodate manual sample exchange, has been developed to reduce the increase in background noise at longer wavelengths. The beamline also offers loopless '*capillary-top-mounting*' to further reduce the background noise. Naohiro then presented some recent sulfur-SAD phasing results using data collected on the beamline including the 2.5Å structure of the 43 kDa protein (glucose isomerase) for which automated model building was able to fit nearly all of the residues.

Jim Pflugrath, Rigaku, USA, reported some interesting results on the use of halide (KI) soaks for SAD phasing. He showed that it generally works to simply mix the halide with a drop of reservoir solution (post-growth) to create a nearly saturated solution of halide, and then swish the crystal through the solution or dilutions of the solution. Jim also showed a video entitled '*Mastering the Halide Swish*' produced by his colleagues Sara Lee & Jennifer Rieger to further illustrate the simplicity of this approach. Finally, he emphasized that with accurate data collection using current in-house equipment the *Halide Swish* approach using potassium iodide does not require highly redundant data for successful SAD phasing.

Matthew Benning, Bruker AXS, began his presentation with the statistics on in-house SAD phased structures in the PDB in terms of year, resolution, and solvent content. He pointed out the importance of data optimization and presented two recent successful results from crystals of moderate diffraction quality using S-SAD phasing. He noted that the accuracy of low-resolution data was important for S-SAD phasing and that although his data sets were low-resolution they had high redundancy. In one case, rapid crystal decay required the use of data from two crystals to solve the S-SAD structure. Matt also reported the successful phasing of a 42 kD protein soaked with $PtCl_4$. In all cases the data were collected using Cu Kα x-rays.

Manfred Weiss, Helmholtz-Zentrum Berlin, opened his talk with answers to the question *Why longer x-ray wavelengths?* followed by a discussion of the associated challenges and problems in using long wavelength x-rays. He mentioned that there are now about 90 novel S-SAD structures in the PDB and that over 50 methodological papers have been published. A survey of S-SAD structures solved in terms of year, wavelength used, number of amino acids per asymmetric unit, and symmetry group was also presented. He gave three examples, i) the lysosomal 66.3 kDA protein by *Lakomek et al, 2009*, ii) the microneme protein SML-2 (amino acid content 6 x 138) by *J.J. Muller et al, 2011*, and iii) the Grh1- the yeast homologue of GRASP55 (100 amino acids) by Haas *et al.*, unpublished. He suggested ways to improve the success of S-SAD phasing, considering crystal mounting, data collection and data processing. Finally Manfred presented a slide that showed that based on the ratio of amino acid content to sulfur atoms more than 96% of all proteins could be possible targets for S-SAD phasing.

cont'd on next page

13.14 cont'd **Armin Wagner**, Diamond Light Source, emphasized that Beamline I23 at the Diamond Light Source will be the first MX beamline optimized for the long-wavelength region (1.5 - 4Å). It will provide a unique tool to fully exploit the potential of experimental phasing from native protein and DNA/RNA crystals. He then described the advantages of using longer wavelengths in terms of wavelength dependent absorption edges and crystal size used for data collection. He showed that the optimal wavelength for S-SAD is about 4.5 Å for 0.05 mm sized crystals and 3.4 Å for 0.1 mm sized crystals. To minimize absorption effects, the complete beamline including sample, goniometer and detector will be operated in a vacuum. An x-ray tomography setup will be integrated into the experimental end station to determine the crystal shape and size for analytical absorption corrections. Sample cooling will be achieved using a conductive path running from a pulse tube cryo-cooler through the kappa goniometer. A large curved detector will allow access to diffraction data up to $2\theta = \pm 90°$.

Meitian Wang, Swiss Light Source, described their progress in improving the signal to noise ratio in S-SAD and P-SAD phasing experiments using the X06DA super-bending magnet beamline which has a double channel-cut monochromator, PRIGo multi-axis goniometer and new PILATUS 2M detector (installed November 2011). The newly development PRIGo goniometer (sphere of confusion < 1 μm) is able to place the best part of the crystal in the beam, align long-crystal axis to avoid overlaps, record Bijvoet pairs on the same image and carry out multi-pass data collection with different crystal orientations to achieve true redundancy. ***(See the photo of a PRIGo in 11.01 report, page19)*** Meitian then presented several successful structure determinations using data collected with the new system including a 14mer RNA structure and the sarcin / ricin loop along with the results from three S-SAD structure determinations where the number of amino acids ranged from 84 to 387.

Zhi-Jie Liu, Institute of Biophysics, Beijing, described two new tools for successful S-SAD phasing. The first tool is a web-based server (**http://159.226.118.93**) located at the Institute of Biophysics in Beijing that provides a quick and easy means of evaluating the readiness of a beamline or other data collection system for successful S-SAD data collections. The user simply logs in and uploads a Zn-free insulin test data set collected on the system being analyzed. The server will then carry out a series of tests and present the user with the outcome of the test. The second tool, X2DF, is an updated version of the SCA2 Structure (parameter space screening) pipeline developed by the SECSG for phasing S-SAD and other data. Zhe-Jie then used the recent structure determination of the 40kD protein DR6 to illustrate the usefulness of X2DF for automated S-SADS structure determination using data collected at Photon Factor Beamlines 17A and 1A, using 2.0Å and 2.7Å x-rays.

Wayne A. Hendrickson, Columbia U, NSLS, reported on the recent work published in *Science* (**V. 336**, 1033-37) on using cluster analysis to merge S-SAD data sets collected from multiple crystals. In each of the five cases presented, 5 to 13 data sets identified from cluster analysis were merged to first yield the anomalous substructure (4 to 52 anomalous scatterers; $Z \leq 20$) and then the experimental protein phases. The structures ranged from 22 to 1200 residues per asymmetric unit with resolutions ranging from 2.8 Å to 2.3 Å. The elemental identities for Ca, Cl, S, P and Mg associated with the structures were confirmed by f'' scattering factor refinement using PHENIX. The procedures used in the analysis are robust and when aided by synchrotron beamlines optimized for low-energy x-ray diffraction measurements will offer truly routine structure determination of generic native macromolecules.

Bi-Cheng Wang and Robert Fischetti

L to R: Antonio dos Santos, Scott Misture, Kamila Wiaderek, Garrett Granroth, Dermot O'Hare, Mario Wriedt, Peter Khalifah. (Xiangquiang Chu is shown in the photo on the next page.)

13.15: In Situ Parametric Studies

Dermot O'Hare, Oxford U, has designed a custom built cell that allows the study of reactions *in-situ*, using energy dispersive and monochromatic x-rays. The cell is infrared heated and was successfully commissioned on beamline I12 at the Diamond Light Source in the UK. The flux growth of $Bi_5Ti_3Fe_{(1-x)}Mn_xO_{15}$ *Aurivillius* phase under different experimental conditions was monitored and it was observed that product formation is preceded by the formation of an intermediate phase.

Mario Wriedt, Texas A&M U, presented details of his study of a copper based metal-organic framework material containing neutral nitrogen-rich moieties. In this system a single reaction led to the formation of three different crystals of different hydration states. The hydration state was changed *in situ* and it was shown to be reversible through the control of the temperature and humidity. In this compound the

13.15 cont'd structure distortions resulting from the change of water content in the structure lead to different magnetic properties.

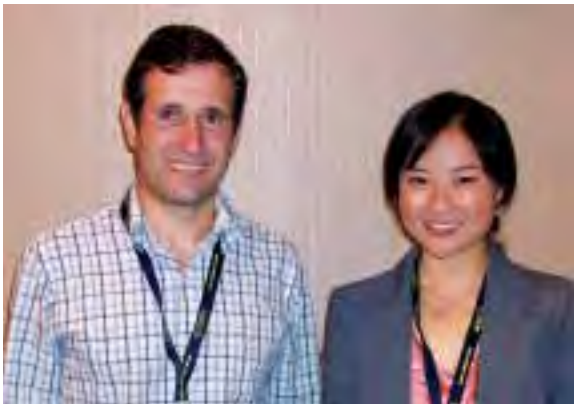
Garrett Granroth, ORNL, described a particularly complex experiment performed at the Sequoia time-of-flight spectrometer at the Spallation Neutron Source. $MnWO_4$ is a multiferroic material with a magnetic phase diagram consisting of at least 6 phases. Previously, little was known about the magnetic structure of the phases that occur in high magnetic fields. The experiment required careful timing of the 30 T magnet to the 60 Hz neutron pulse, and resulted in clarification of the magnetic structure of two of the high field magnetic structures.

Scott Misture, Alfred U, presented recent research on a series of transition metal oxides with potential applications in fuel cells. In these experiments, a set of high temperature data was collected under controlled atmosphere. The electrochemical activity was also monitored *in situ* and was related to the phases present under experimental conditions, mimicking the operation environment of fuel cells. The *in situ* study of these systems is critical, as frequently they exhibit reversible transformations that might be undetected in recovered samples.

Peter Khalifah, SUNY Stony Brook, presented his group's research on the de-lithiation paths and subsequent degradation of $LiFeBO_3$, a high capacity battery material. The crystal structure was redetermined based on a 4D modulated space group $C2/c$ (1/200)00. It was found that this modulation hindered Li mobility in the structure and that improvement of the performance of $LiFeBO_3$ can be achieved by reducing this modulation. Chemical doping, for example, or by disrupting the long range modulation in the structure in some other way.

Kamila Wiaderek, ANL, used a combination of PDF techniques to study the structure and size of nanoparticles in iron-based battery materials under operational conditions. These experiments were done in a custom made electrochemical cell designed at Sector 11 of the APS. This combination of techniques allowed the study to be done at both nano and meso scales. A ripening of the nanoparticles was observed upon cycling and this may contribute to the performance degradation observed in these materials.

Xiang-Qiang Chu, ORNL, shown below with Session Chair Antonio dos Santos, discussed the use of quasi elastic neutron scattering to study the relaxational dynamics of two proteins - hen egg white lysozyme and an inorganic pyrophosphatase. The slow dynamics of these globular proteins could be adequately modeled by the mode-coupling theory that predicts a logarithmic decay of the relaxation time. Another find was that, while the two proteins have two rather different activity profiles as a function of temperature, the same dynamical model could be applied.



Antonio dos Santos

In back L to R: Glen Spraggon, Todd Green, Nicholas Noimaj, Patrick Shaw Stewart, George Lountos. In front L to R: Eric Ortland, Zygmunt Derewenda, David Waugh, Miki Senda.

13.16: From Constructs to Crystals

Nick Noinaj, NIDDK /NIH, provided the audience with a very thorough introduction to membrane protein expression, purification and crystallization, drawing upon his experiences in the Buchanan lab at NIH. **David Waugh**, NCI, discussed the discovery and practice of using the maltose binding protein as a fusion partner, which has become a staple of protein purification across the globe. **Todd Green**, U Alabama at Birmingham, presented the ins-and-outs of protein and nucleic acid production and crystallization.

Finally, **Zygmunt Derewenda**, U Virginia, gave a provocative presentation on current progress in enhancing the crystallizability of proteins via surface entropy reduction as a way to compromise the '*entropy shield*' that prevents most proteins from crystallizing. Certainly, well placed lysine-to-alanine substitutions have proven to be useful in generating hydrophobic patches that favor nucleation. Derewenda also presented evidence suggesting that replacing bulky hydrophobic residues with alanine may improve protein solubility and stability, thereby enabling many previously intractable biochemical techniques for poorly soluble or unstable proteins to succeed.

Eric Ortlund and George Lountos

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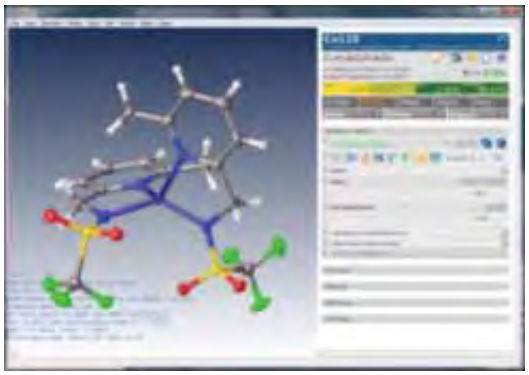
L to R: Xiaoping Wang, Richard Cooper, George Sheldrick, Anthony Spek, Ronan Keegan, Robert Von Dreele, Oleg Dolomanov, Nicholas Sauter.

13.18: Public Domain Software

Anthony Spek, Utrecht U, presented the latest developments of the crystallographic software tools in PLATON, a program package widely used for chemical crystallography and the basis of the IUCr CheckCIF project. Many changes for CIF Validation, SQUEEZE, TwinRotMat and Bijvoet analysis tools were implemented in the new SHELXL-2012. The new CIF will include .res and .hkl from final structure refinements, and implicitly includes information on twinning, constraint & restraint details. In addition to CheckCIF, FCF-Validation has now become a standard part of the IUCr CheckCIF service. A listing file is created with a report on various issues for FCF-Validation, including variance analysis; data set completeness, beamstop reflections and outliers; checks for unresolved twinning (TwinRotMat); checks on the value of the Flack parameter and Hooft y; checks on residual density, including density on atom sites. Molecules of interest often co-crystallize with interstitial solvent molecules in the lattice, but the solvent molecules often fill voids with disorder and are often located on symmetry sites and with partial occupancy. **Refinement of a meaningful disorder model is preferable.** Refinement in case of hopeless solvent disorder can be handled with SQUEEZE which takes the contribution of disordered solvents to the calculated structure factors into account by back-Fourier transformation of density found in the 'solvent accessible volume' outside the ordered part of the structure with the observed Fobs data untouched. The new SHELXL2012 'LIST 8' detwinned .fcf file will now allow the application of SQUEEZE for twins as well. PLATON is available online at **www.cryst.chem.uu.nl/spek/platon/**.

The **General Structure Analysis System** (GSAS), written in Fortran more than 25 years ago, was originally developed to analyze multipattern single crystal and powder diffraction data sets produced at the Los Alamos spallation neutron source (LANSCE). **Robert Von Dreele**, ANL, presented GSAS-II: rewritten in python; available in Windows, Linux and Mac OSX platforms and now loaded with graphics, GUI and mathematical packages such as matplotlib, pyOpenGL, wx, numpy and scipy. It incorporates numpy array routines for highly efficient and fast code execution. Approximately 20,000 lines of python codes in GSAS-II replace 125,000 lines of Fortran in GSAS. Tests show that it takes only ~1 second to complete a charge flipping iteration for 500K reflections/map points. For least-squares, the program uses a modified Levenberg/Marquardt algorithm that is fast and exceedingly robust. GSAS-II now has a modern GUI interface and varieties of visualization tools for single crystal, powder, texture and PDF analysis. A new calibration tool for area detectors has been added in GSAS-II, which can be used as a replacement for the Fit2D program. Currently, GSAS-II handles only monochromatic CW x-ray/neutron data for powder, single crystal and PDF applications. The program has yet to be developed for neutron time-of-flight data, which was a distinctive capability of the original GSAS program. GSAS-II is available online at **https://subversion.xor.aps.anl.gov/trac/pyGSAS**.



The GUI interface for Olex2.

Oleg Dolomanov, OlexSys Ltd. UK, presented the newest version of Olex2, an open source project originated at Durham U that has been developed extensively over the last 6 years. The idea behind Olex2 was to combine different crystallographic packages for small-molecule structure solution and refinement with a single easy-to-use user interface. Olex2 reads standard SHELX ins/res files and uses instructions that are the same or similar to those in the SHELX program. The program also provides its own olex2.solve and olex2.refine programs that resulted from the development of the smtbx (small molecule toolbox), part of the cctbx (computational crystallography toolbox) for structure solution and refinement. The cctbx now is an integral part of Olex2 and Olex2 also incorporates the new developments in smtbx. The *Report* function in Olex2 gives users the choice to upload

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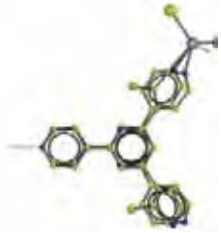
CIFs for direct deposition to the CCDC. The program package is available online at **www.olex2.org**.

George M. Sheldrick, U Goettingen, presented his new SHELXL-2012 program that has been tested by about 100 beta-testers. The SHELX program only gets updated when improvements in theory or hardware make this desirable. The gamma-test release is planned for later this summer with an official release that includes updated versions of XCIF/CIFTAB and templates before the end of 2012. The SHELX program was written in a universally acceptable subset of FORTRAN. It is robust, with stand-alone binaries and zero dependencies. SHELX is an open source program, i.e. when a program has been adequately debugged and described in a peer-reviewed paper the source is made available. Precompiled binaries for Windows, Linux and Macs platforms are available to download. ***It is not recommended for users to recompile.*** SHELXL-2012 includes many new features while remaining upwards compatible with SHELXL-97 and SHELX-76. The .ins and .hkl files for SHELX76 can still be used with SHELXL-2012. SHELX-2012 now uses command line switches to assign memory and CPUs for multi-thread processes. Formerly, only a limited number of atoms could be addressed by a single instruction such as: DELU N_1 > LAST. This problem has now been solved in SHELXL-2012 by simply using more memory. A fix was made for the fact that the SHELXL-97 definition of atom site multiplicity was different from the IUCr definition. The program now deduces the space group name and Hall symbol from the LATT and SYMM instructions for 249 common space group settings. The space group is also written to the .pdb file in a way Coot can understand. SADI without atom names expands all SAME instructions into SADI and writes them to the end of the .res file. This facilitates the modeling of disorder. HTAB without atom names now writes the appropriate EQIV and full HTAB instructions to the end of the .res file so that they can be used in the next refinement job. Non-classical C-H..O hydrogen bonds are also generated. An extended rigid bond restraint can be applied using RIGU, which assumes that the relative motion of two atoms is perpendicular to the bond joining them. Improvements in data collection hardware and software now make it possible to determine absolute structure even when the anomalous scattering is extremely weak. For non-centrosymmetric structures SHELXL-2012 calculates the Flack parameter at the end of the refinement by two different methods and outputs the results to the console (as well as to the .lst and .cif files). The value with the smaller esd is written to the CIF file. MERG 2 is required. The Parsons' method almost always gives better results, because errors that affect both I^+ and I^- equally should cancel. The hkl data and the .res file from final structure refinement are now embedded into the .cif output file with checksums included. This makes it possible to repeat any refinement exactly, and discourages cosmetic editing of the CIF file. Information for SHELX is available at **shelx.uni-ac.gwdg.de/SHELX/**.

CRYSTALS has been developed and maintained in the Chemical Crystallography Laboratory in Oxford since it was launched about 40 years ago. It is an x-ray & neutron crystal structure refinement package widely used in research, teaching and service. **Richard I. Cooper,** Oxford U, presented three new features that have been developed during the last 12 months at various different levels of the CRYSTALS program: parallel computation, asymmetric restraints and tools for modelling disorder. The program now uses OpenMP to upgrade old Fortran code for parallel code execution. By applying asymmetric restraints, the entire shift due to the restraint is applied to one atom. New asymmetric distance, asymmetric Hirshfeld and asymmetric adp similarity restraints give finer control over the types of models which can be investigated. The CRYSTALS command line allows for complex refinement setup. GUI only handles common refinement scenarios. Although treating disorder requires manually appending CRYSTALS instructions, this can be done using the built in CRYSTALS scripting language. The program is available for a Windows platform at **www.xtl.ox.ac.uk/crystals.html**.



Disorder modeling in CRYSTALS.

Ronan Keegan, CCP4, introduced AMPLE, an automated software tool jointly developed by the U of Liverpool and CCP4 for protein structure solution with the employment of *ab initio* protein structure modeling techniques in molecular replacement. Structures of smaller proteins or protein domains can now be reliably predicted for use as search models in cases where no homologous structure is available. AMPLE is designed to make this technique available to users in an automated way that requires only limited computational hardware resources. Initial tests on a set of 296 cases drawn from the PDB showed that the techniques employed in AMPLE can result in solutions for approximately 40% of the targets. A beta release version is included in the latest release of the CCP4 software suite: **www.ccp4.ac.uk**.

Data rates for new pixel array PILATUS and PAD detectors can reach > terabytes/ hour in a typical time-resolved raster scan experiment. New efficient software tools are needed for high -throughput work in data processing as light sources and detectors continue to improve. **Nicholas Sauter**, LBNL, demonstrated a python-based software tool that provides a flexible platform for addressing these issues. The BPCX program incorporates pre-existing modular tools for software management and adopts an open source, BSD-style license to allow distribution of derivative works. Anyone can modify source code & contribute to the official version. The current package contains a python-based image viewer and a still-image data reduction toolbox, cctbx.xfel, capable of handling concurrent event requests with the use of a multiprocessing server. The copyrighted, open-source code is bundled with the CCTBX software project available at **cctbx.so**

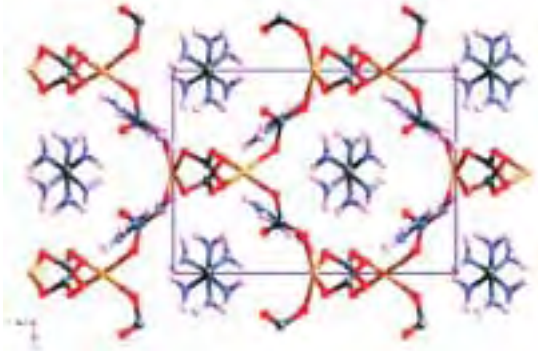
Xiaoping Wang

In back L to R: Emil Bozin, Tiffany Kinnibrugh, Hans-Conrad zur Loye, Andrey Yakovenko. In front L to R: Elinor Spencer, Margot Fabian, Craig Bridges, James Kaduk. (Max Kaganyuk not shown.)

13.19: Functional and Emerging Materials and Technology

This session was intended to highlight new results on materials of current interest, to complement the energy-related materials in session 13.06. The session began by looking at inorganic solids synthesized using high-temperature (fluxes) or hydrothermal (supercritical water) solvents. **Hanno zur Loye**, U South Carolina, showed that metal hydroxides are very effective for the growth of high quality mixed metal oxide single crystals, such as $Sr_5Co_4O_{12}$. A hybrid approach, using a low temperature hydroflux, has been effective for the growth of mixed metal hydroxides, such as $Sr_2Mn(OH)_6$ and many others. **Emil Bozin**, BNL, showed by PDF techniques that Ir^{4+} dimers exist locally at all temperatures in $Cu(Ir_{1-x}Cr_x)_2S_4$, even though long-range order is already lost by $x \sim 0.05$.

Making use of high-pressure single crystal studies, **Elinor Spencer**, Virgina Tech, characterized the 3D metal-organic hybrid material $\{[Cu(CO_3)_2](CH_6N_3)_2\}_n$, and showed that it is about as strong as zeolites.



The high pressure behaviour of the 3D copper carbonate framework $\{[Cu(CO_3)_2](CH_6N_3)_2\}_n$ by Elinor C. Spencer, Nancy L. Ross and Ross J. Angel, J. Mater. Chem., 2012,22, 2074-2080, DOI: 10.1039/C2JM15206A, published online December, 2011.

Tiffany Kinnibrugh, Texas A&M, used powder diffraction techniques to characterize the structural changes on dehydration of several (potentially nanoporous) Zn phosphonate compounds.

Combined x-ray and neutron PDF measurements, as well as reverse Monte Carlo simulations, were used by **Margit Fabian**, LANL, to determine that the glassy networks in MoO_3-Bi_2O_3-WO_3 and MoO_3-Nd_2O_3-MgO(B_2O_3) systems are built up of distorted MoO_4 tetrahedra and mixed WO_3/WO_4 or BO_3/BO_4 structural units.

Andrey Yavenko, right, accepting the Margaret C. Etter Student Lecturer Award from Session Co-chair Craig Bridges.

Finally, **Andrey Yakovenko**, Texas A&M, showed that structure envelope density maps, calculated from 1-10 well-determined structure factors from resolved low-angle peaks can be useful for determining the pore structure and locations of guest molecules in the pores of MOFs. Crystallography is so powerful that '*not much data*' can be useful!

James A. Kaduk & Craig Bridges

Scientists Playing God by Nick D. Kim.

From the Nearing Zero website: nearingzero.net/res.html.

L to R: Robert Stroud, Robert Fischetti, Vadim Cherezov, Eugene Chun, Tommi Kajander, Ehud Landau, Nicholas Noinaj.

13.20: Membrane Proteins: from Start to Finish

Membrane proteins constitute about one third of all proteome, perform a variety of essential cellular functions, and represent important drug targets. By virtue of their nature, however, these proteins are very difficult to work with. This fact was recognized by the NIH and other funding agencies in the US and worldwide, initiating specialized programs to fund large centers and individual group R01/R21 type grants. Such programs provided a tremendous boost in membrane protein research with many exciting breakthroughs in the structural coverage of ion channels, G protein-coupled receptors, transporters and other membrane protein families. Nevertheless, membrane proteins still remain highly challenging objects to study and, thus, the idea was to devote this session to discussions on the experience of working with these difficult targets at all stages, starting from expression through purification and crystallization, to crystallographic data collection.

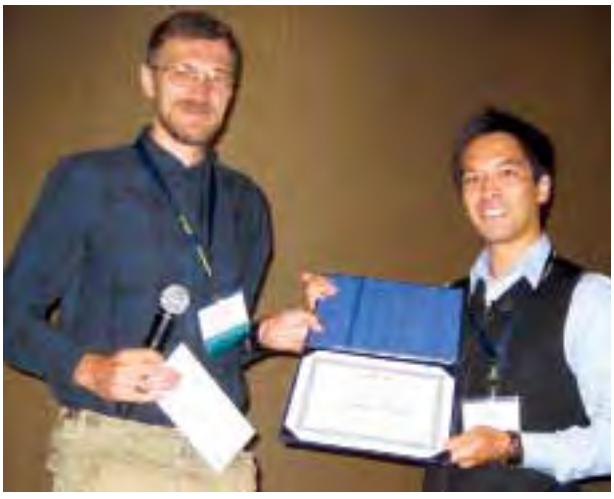
Robert Stroud, UCSF, Membrane Protein Expression Center (MPEC) head, began with a comprehensive overview of different expression systems used at MPEC for production of eukaryotic membrane proteins. The remainder of his talk was focused on the recent structure determination of components of a zinc pump belonging to the heavy metal extrusion class of the resistance-nodulation-cell division (RND) superfamily of membrane proteins.

About 15 years ago **Ehud Landau**, University of Zürich, along with Jürg Rosenbusch from Biozentrum in Basel, introduced a novel concept for crystallization of membrane proteins using a greasy lipidic mesophase known as lipidic cubic phase (LCP). At the time, the reaction from the membrane protein structural community was mixed, with some considering this method to be revolutionizing, and others believing it would be a '*one-trick pony*', suitable only for a specific class of proteins. Time has proven that the LCP crystallization method is more than just viable, it has contributed more than 100 membrane protein structures to the PDB, representing 32 unique proteins from at least 7 different families, including the highly challenging superfamily of G protein-coupled receptors. Landau shared his take on the history of LCP technology development and the most critical breakthroughs and achievements during the last 15 years. His message was that LCP technologies have matured, and while it does take an effort to learn and perfect their usage, those labs that took the plunge have been highly successful, and the perspectives look bright for the newcomers.

Nickolas Noinaj, NIDDK, talked about nits and grits of his work on structural determination of components of a beta-barrel assembly complex. He claimed the key to success was careful selection of protein constructs and crystallization in bicelles.

Along with developments in membrane protein expression, stabilization and crystallization, significant progress has been made during the last few years at synchrotron beamlines, allowing for data collection on ever small crystals of more challenging targets. **Robert Fischetti**, GM/CA CAT at the Advanced Photon Source, described advanced tools such as 5, 10 and 20 μm diameter beam collimators, automatic rastering, vector data collection and other available resources at the 23-ID-D/B beamlines (the beamlines of choice for many recent membrane protein structures). Future upgrades planned include a micro-focused beam with variable 1-20 μm diameter and about a 10 fold increased flux, a new generation PILATUS3 detectors, and a SONICC system for detection and alignment of optically invisible small crystals.

Eugene Chun, Scripps Research Inst, was the BioMac SIG's choice to receive the **2012 Margaret C. Etter Student Lecturer Award** for his work on development



Eugene Chun, at right, accepting the Margaret C. Etter Student Lecturer Award from Session Chair Vadim Cherezov.

of a fusion partners toolchest for stabilization and crystallization of G protein-coupled receptors. Eugene described in detail the procedure used to identify and test a panel of

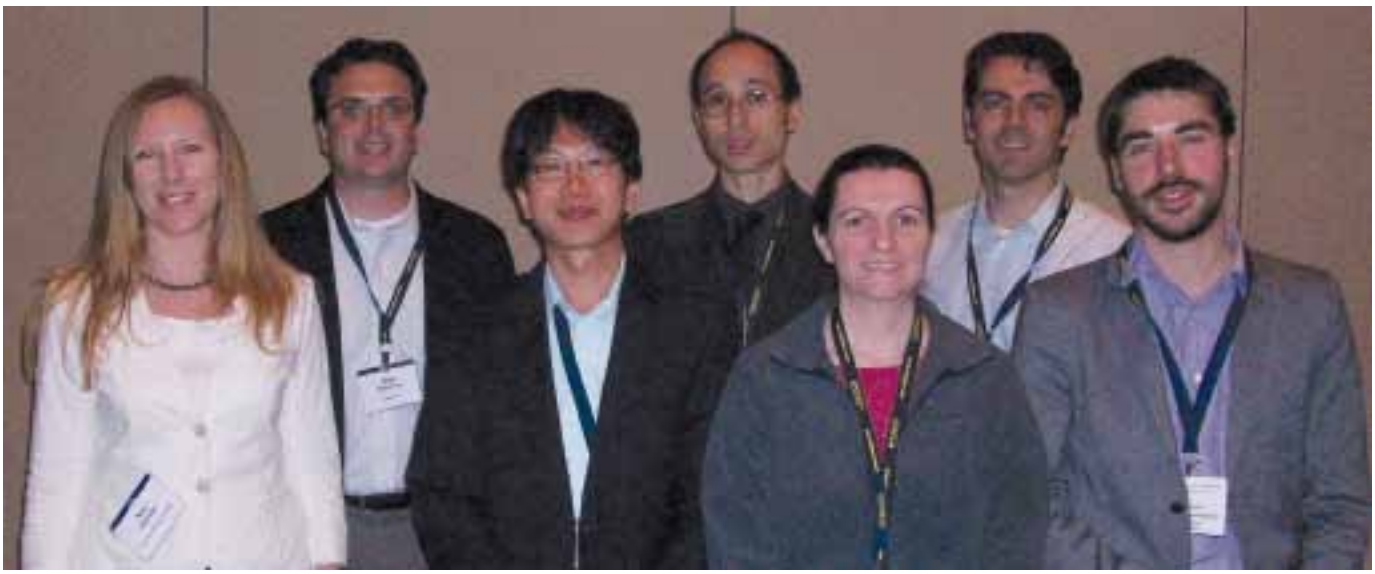
cont'd on next page

13.20 cont'd five soluble fusion partner candidates, out of which a thermostabilized mutant of the apo-cytochrome b562, termed BRIL, proved to be the most successful. When fused to the intracellular loop 3 of the adenosine A2A receptor, BRIL yielded the best structure to date of a GPCR at 1.8 Å, and when fused at the N-terminus, it aided determination of a structure of the nociceptin/orphanin FQ opioid receptor. The method should certainly find broad applications in structural studies of GPCRs and other membrane proteins.

Tommi Kajander, U of Helsinki, described his journey towards the structure determination of Na-pumping pyrophosphatase from *Thermotoga maritima* at 2.6 Å resolution. Phasing was achieved by MIRAS on tungstate and lead derivatives combined with a new Rosetta molecular replacement method developed by the D. Baker group and implemented in PHENIX. Structures solved in a resting state and with a bound product shed light on the catalytic cycle of the sodium pumping mechanism and suggested that the protein has evolved through gene triplication.

The session provided broad coverage of the structural studies of membrane proteins, including reports on the details of the structure determinations of five new membrane proteins. It was supported by contributions from Avanti Polar Lipids and TTP LabTech.

Vadim Cherezov



L to R: Noa Marom, Matthew Peterson, Eugene Cheung, Eric Chan, Magali Hickey, Mark Oliveira, Peter Wood. Patrick Connell left prior to end of session.

13.21: Crystallographic Information in Pharmaceutical Research & Development

With aims of highlighting the importance of crystallographic information and data mining in pharmaceutical development, a wide range of topics, largely focusing on small molecule crystallography, were presented.

Patrick Connelly, Vertex Pharmaceuticals, highlighted several examples where the complement of crystallographic, computational and thermodynamic data impacted the progress of development compounds. **Peter Wood**, CCDC, presented an assessment of isostructurality in pharmaceutical salts, highlighting the real lack of similarity and predictability between crystal structures of most sodium and potassium salts of drug-like molecules.

Changing focus to the use of powder x-ray diffraction, which can quickly assess form changes during dehydration processes, **Eugene Cheung**, Amgen Inc., showed the differences between thermal expansion, dehydration, and form change using variable temperature powder diffraction data. **Noa Marom**, U Texas, Austin, described advances in dispersion correction schemes employed in DFT computations, using case studies on several polymorphic systems.

Eric Chan, Bristol Meyers Squibb, discussed models of the diffuse scattering from single crystals of two aspirin polymorphs, a study that highlighted the power of the diffuse scattering method in comparison to routine analysis of diffraction data. Finally **Mark Oliveira**, Alkermes Inc., described the unique structure of an opioid modulator and a structural and computational analysis of closely related analogs.

Matthew Peterson & Magali Hickey

The Seal of Approval

Courtesy of Nick D. Kim.

From Nearing Zero website: nearingzero.net/res.html.

In back L to R: Stefan Knapp, Gregg Crichlow, Alan Hruza, David Eisenberg. In front L to R: Jaeok Park, Helen Berman, Shraddha Thakkar, Stephen Burley.

13.22: Structure-Guided Drug Discovery

Participants from industry and academe were found both in the audience and on the podium at this session sponsored by the Industrial SIG. **Stefan Knapp**, Oxford U / Structural Genomics Consortium, presented the results of structural and functional studies on targeting of epigenetic effector domains of the bromodomain family. **Helen Berman**, Rutgers U / Research Collaboratory for Structural Bioinformatics / PDB, described recent advances in data management of small molecule ligands, antibiotics and peptide inhibitors in the PDB.

David Eisenberg, UCLA / HHMI, presented promising efforts aimed at discovering small molecule inhibitors of amyloid formation in various neurodegenerative diseases.

Alan Hruza, Merck Res Labs, explained how modest resolution x-ray structures of the aurora kinase catalytic domain informed structure-based design of imidazo [1,2a] pyrazine inhibitors.

Shraddha Thakkar, U of Arkansas Medical School, was chosen by the Industrial SIG to receive a **Margaret C. Etter Student Lecturer Award** for her presentation entitled *Structure based design of anti-methamphetamine single chain antibodies*.

Stephan Burley

Courtesy of Nick D. Kim. Nick is an analytical environmental chemist currently working for the Waikato Regional Council. He is an honorary leturer at the University of Waikato in New Zealand.

From Nearing Zero website: nearingzero.net/res.html.

Stephan Burley presenting the Margaret C. Etter Student Lecturer Award to Shraddha Thakkar.

L to R: Andrew Torelli, Edward Collins, Zbigniew Dauter, James Holton, Raj Rajashankar.

13.23 Data Collection with the Pros

For the second year of the '*Blackboard*' sessions at the ACA meeting, the focus was on best practices for data collection. **Zbigniew Dauter**, NCI / ANL, gave a real-time demonstration of data collection on SER-CAT's ID beam line at ANL. He mounted the crystal, took the shots and discussed his analysis of the crystal quality, best parameters for distance, time per frame, attenuation of the beam, etc.

James Holton, UCSF / BMB / PBD, led a spirited discussion of critical sources of error found in crystallographic data that can make the difference between solvable and intractable data.

Raj Rajashankar, NE-CAT & CCB / Cornell U, discussed how to collect good data using the 6 million detectors that comprise the latest generation of PILATUS x-ray detector arrays. Links to the powerpoint slides and videos of the talks can be found on the ACA website. Click on the '***Jobs/Education***' link at the top of the ACA home page and then click on the '***Blackboard Sessions***' link under the '***A Crystallographer's Resources***' section heading. Next year's Blackboard session will address structural validation.

Andrew Torelli and Ed Collins

L to R: Stacey Smith, Marcus Bond, Elinor Spencer, Mario Bieringer, Patrick Mercier, Branton Campbell, Saurabh Tripathi.

13.24: Phase Transitions in Inorganic Systems

Patrick Mercier, NRC, Canada, presented a systematic analysis of the layer stacking polytypes available within the kaolin system. *Ab initio* DFT calculations of the energy and enthalpy of each polytype make it possible to rationalize the experimental phase sequence observed up to 60 GPa, including the relative rarity or absence of other phases that might otherwise be expected to occur.

Elinor Spencer, Virginia Tech, discussed a high-pressure (diamond anvil cell) single-crystal diffraction study of the mineral petalite ($LiAlSi_4O_{10}$). Two high-pressure phases and their supercells and symmetries were explored in terms of observed superlattice reflections, volume changes and group-subgroup relationships.

Stacey Smith, Brigham Young U, described the formation and subsequent temperature evolution of the structure of La-doped gamma-alumina nanoparticles prepared via a novel solvent-deficient method. The presence of two different types of high temperature surface area loss and the location of the La atoms point to a potential mechanism for the La-stabilization of the gamma phase.

Mario Bieringer, U of Manitoba, presented the structural phase diagram of the $Sc_{1-x}Lu_xVO_3$ perovskite family. The smaller Sc cation results in a disordered bixbyite structure and the larger Lu cation results in a perovskite phase, so the family spans both structure types. High-pressure stabilization of the Sc-rich perovskite phases made it possible to track the physical properties of the family across the boundary between stability and metastability.

Saurabh Tripathi, Central Michigan U, spoke on the structural origin of the ferroelectric polarization of $YMnO_3$, and its evolution with decreasing particle size. A PDF analysis of the local structure vs particle size revealed features that explain the observed trend.

Marcus Bond, SE Missouri State U, explained that due to strong ligand-ligand interactions, $CuBr_4^-$ salts have been generally viewed as incapable of forming the square-planar complex observed in some $CuCl_4^-$ salts. If present, such a square-planar complex transforms to a flattened-tetrahedral geometry at higher temperatures, accompanied by change in color. The square-planar to flattened-tetrahedral transformation has now been observed in 1,2,6-trimethylpyridinium salts of both $CuCl_4^-$ and $CuBr_4^-$.

Branton Campbell

Top, L to R: David Watkin & Sai Venkatesh Pingali; David Rae, Bruce Foxman & Peter Muller. Middle: John Spence & Daniel Nocera at banquet table; George Sheldrick & Bruce Noll; Crystal Town at the banquet. Last row, L to R: Ethan Merritt, Judy Flippen-Anderson, Marcia Colquhoun.

For those of you who might not have noticed, the reviews of *Knocking on Heaven's Door* in the spring 2012 *RefleXions* and of *Packing for Mars* in the summer issue were both written by my daughter Jeanette. I think she did a great job and she will be making guest appearances in this column in the future.

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The Optics of Life: A Biologist's Guide to Light in Nature

by Sönke Johnsen. Paperback, Princeton University Press, 2012, ISBN-13: 978-0691139913, $42.41 (BN.com price)

I saw this book in *Science* a few weeks ago and picked up a copy. The author sets out to describe how light and life interact with each other. Johnsen keeps the number of equations to a minimum and uses Feynman's ***Quantum Electrodynamics*** and ***QED: The Strange Theory of Light and Matter*** as background material to describe various phenomena.

One of the things I really enjoyed were the explanations of how we see and perceive the world around us. I will watch twilight with a new perspective now, see Chapter 3. Since this book is written for biologists there are numerous examples of how living things have evolved to use light in different ways. Here I thought mantis shrimp were just good to eat.

Chapter 1 provides an ***introduction to light*** and the book itself, while Chapter 2 provides a ***description of the units and geometry of light***, and gives a good historical background as well as sage advice about how to avoid mistakes in reporting results.

Chapter 3 covers the ***emission of light from natural sources***, both biological and non-biological.

Chapter 4 provides a good description of the ***absorption of light*** and how it affects measurements under various conditions and also discusses how photoreceptors work.

Chapter 5 does a very good job of covering ***scattering*** while Chapter 6 extends these concepts to ***scattering with interference***.

Fluorescence and phosphorescence are described in Chapter 7. I found Chapter 8 on ***polarization*** interesting because I did not realize that certain animals could detect polarized light, let alone use it.

Chapter 9 covers the ***measurement of light*** and avoiding certain pitfalls. Design of experiments is reviewed in this chapter and worth the read. Chapter 10 delves into the ***particle/wave nature of light*** and even attempts a description of quantum coherence.

Visual Strategies: A Practical Guide to Graphics for Scientists and Engineers, by Felice C. Frankel and Angela H. DePace, Hardcover, Yale University Press, 2012, ISBN-13: 978-0300176445 $22.05 (BN.com price)

I saw a review for this book in *Nature* and picked up a copy for myself. The authors set out to provide a modern guidebook for improving the transmission of scientific information to other scientists and non-scientists. Edward R. Tufte has done this before but this book considers the latest tools of the trade, so should become a companion or even a replacement to Tufte's *Quantitative Display of Information*.

The book is divided into 8 tabbed sections. The tabs are designed to allow you to quickly go to a particular section quickly. The first tab is the ***Overview*** and includes an interview with the authors and Stephan Stagmeister, the designer of the book. The authors introduce three questions that should be asked of every graphic:

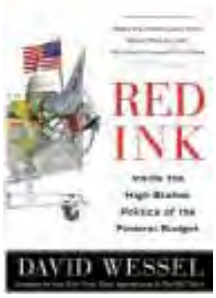
1. Is the graphic explanatory or exploratory?
2. How will the graphic be used?
3. What is the first thing you want the viewer to see?

The authors next describe five steps to designing a graphic: compose, abstract, color, layer and refine. These steps are reviewed for a number of examples provided in the Overview. The next three chapters (tabs) cover the topics ***Form and Structure***, ***Process and Time***, ***Compare and Contrast*** with before and after examples showing how to improve a particular graphic. The ***Form and Structure*** chapter provides two examples relevant to structural biology. All three chapters provide examples for biology, chemistry, physics and medicine.

The next chapter, ***Case Studies***, takes a long look at developing a particular graphic from the ground up by an expert in the field. Jane Richardson provides the example titled, ***Representing Folded Proteins***. The last chapter is titled ***Interactive Graphics*** and describes in detail how to use web based tools to enhance a graphic that would be too hard to make easily understandable only on paper. The structural biology example is ***The Ribosome in Animation*** and was created by Said Sannuga ***http://pubs.acs.org/cen/multimedia/85/ribosome/translation_bacterial.html.*** This example is not really interactive but shows the power of modern tools for describing complex processes.

The penultimate tab is a ***Visual Index*** so one can quickly locate a particular example by its graphic. The final tab is an ***Appendix of References and Resources***.

Red Ink: Inside the High-Stakes Politics of the Federal Budget by David Wessel, Hardcover, Crown Publishing Group, 2012, ISBN-13: 9780770436148, $13.30 (BN.com price).



I listened to an interview with the author on Fresh Air and thought this would be a good read. Wessel is economics editor for the Wall Street Journal and author of The New York Times bestseller *In Fed We Trust*. The author gives the reader what I would consider a non-partisan view of the problem the US faces with increasing spending and reduced taxes.

This is a very quick, read only five chapters and a number of illustrative graphics. First Wessel describes how the federal government spends 400 MUSD (million US$) / hour giving numerous examples of where it has been spent and where it being spent.

Wessel then gives us a short history of taxes, budgeting and spending as it pertains to the US government. The author then explores the spending in detail, 21% of the budget goes to Medicare/Medicaid, 20.4% to Social Security, 19.4% to the military, 15.1% benefits besides health, 6.4% to interest (interest is very low right now so will increase soon) and 18% for everything else including NIH, NASA etc.

We are then taught about taxes, who pays them and in what percentage. We also learn how people have avoided paying them. I had never heard of a 1031 swap until today. This is a tax loophole from the 1920's which allows one to exchange pieces of like property and not pay any taxes on the gains. In another example we are reminded of how well Nixon had gamed the system until he was caught after Watergate and forced to pay 495 KUSD in back taxes.

The final part of the book summarizes the problem: we spend more than we take in and if we don't make some hard choices (decrease unemployment, fix health rising care costs, cut defense spending) all the security the military provides will be for naught because there won't be an economy to protect.

Every generation before us has given us a better society in which to live. We owe it to our children to do the same. We have an important election coming up in the US on November 6 and everyone should read this book or least listen to the interview **www.npr.org/2012/07/30/157449392/a-portrait-of-a-country-awash-in-red-ink**. The fact is we can't continue to spend money the way we are and not pay for it – we are going to have to make some sacrifices. Neither party is going to solve the problems alone, so use your vote wisely.

Joseph D. Ferrara

When Alice turned around, the rabbit had drawn a 9 mm Beretta automatic.

'*Curiouser and curiouser,*' said Alice. Courtesy of Nick D. Kim, ***nearingzero.net/res.html.***

Photo courtesy of Goran Bajic

The 45th Course: ***Present and Future Methods for Biomolecular Crystallography***, was held at the **Ettore Majorana Foundation and Centre for Scientific Culture** in Erice. The scientific program organizers were **Vladimir Lunin, Randy Read** and **Sacha Urzhumtsev**, with local organization by **Paola Spadon** and **Annalisa Guerri**. There were 141 participants from 31 countries and there were 56 lectures, including 7 chosen from poster abstracts submitted by participants. In addition, there were 4 software demos and 11 different tutorials (each repeated twice). Ninety posters were presented in two poster sessions, each of which was preceded by short oral presentations. Poster preview sessions (accompanied by a pizza or pasta buffet) provided the opportunity for mingling. As always, the special environment of Erice encouraged interactions between all participants, rewarded this year by the determination of at least three new structures during the school.

Goran Bajic and Randy Read.
Photo courtesy of Marco Mazzorana.

Jane Richardson opened the meeting by reminding everyone that structure validation is a continuous process of quality control that should play a role in every step of structure determination, not just at the end. **Zbyszek Otwinowski** discussed what can go wrong when there are failures in proper validation. Structure determination starts with protein production, and **Stephen Kent** showed how it is possible to synthesize proteins chemically, which opens the door to exciting new approaches such as crystallization from racemic mixtures of the protein and its mirror image. **Todd Yeates** discussed why it turns out to be easier to grow crystals from racemic mixtures, as well as how crystallization can go wrong with pathologies such as twinning and lattice translocation disorders. Growing crystals is particularly difficult for membrane proteins, and **Martin Caffrey** showed how the special properties of lipidic mesophases make them particularly useful, as well as how the resulting crystal structures give important insights into biology.

Collecting good data from a hard-won crystal is not necessarily straightforward. **Sean McSweeney** showed how to find the best crystals, or even the best parts of the best crystals, and how to merge compatible data from multiple crystals. **Kay Diederichs** suggested an approach to answering the perpetual thorny question about how to choose a resolution limit for a data set. **Elspeth Garman** explained why radiation damage limits how much can be collected from one crystal, as well as ways in which the severity of radiation damage might be reduced. Radiation damage depends in large part on the elemental composition of the crystal, and Elspeth also showed how the technique of microPIXE can be used to determine elemental composition for this and other purposes. **Tatiana Petrova** presented some case studies showing the physical consequences of radiation damage on the proteins inside crystals. **Dominika Borek** showed that, to a great extent, careful data processing can ameliorate the effect of radiation damage on the data. Practical aspects of data processing were also addressed in a demo (**Zbyszek Otwinowski**: **HKL3000**) and tutorials (**Kay Diederichs**: **XDS**).

As the Protein Data Bank expands fewer truly novel structures are determined, so the majority can be solved using the molecular replacement method. **Randy Read** showed ways of extending the reach of this method in **Phaser**, including approaches that combine molecular replacement with other phasing methods. **Isabel Usón** presented the *ab initio* **Arcimboldo** procedure, which uses molecular replacement to place small fragments such as helices, which can then be expanded to a complete structure.

More typically, novel structures are solved by experimental phasing methods such as SAD or MAD (reviewed by Zbigniew Dauter), starting from the substructure of anomalous scatterers (SHELXD: Tim Gruene). **Felix Frolow** presented several case studies of structures solved with a weak anomalous signal. **Clemens Vonrhein** outlined how multiple sources of phase information can be combined using the **Global Phasing**

At right: Luxi Li. Below right: Richard Birkinshaw and Nikolaus Gössweiner-Mohr. *Photos courtesy of Marco Mazzorana.*

Above, Sam-Yong Park Photo courtesy of Jan Stransky.

Right, Annalisa Guerri Photo courtesy of Fabio Nicoli.

software. **Vladimir Lunin** showed how reliable phase information can be obtained just from the native structure factor amplitudes, albeit only to low resolution.

Tim Gruene and **Tom Terwilliger** presented different approaches to using a combination of density modification and automated model building to improve the electron density and interpret it as an atomic model. **Tassos Perrakis** showed how automated building methods have been adapted to create the **PDB_REDO** service, which automatically improves the majority of structures submitted to the PDB. Often human abilities are needed to supplement automated building algorithms, and **Paul Emsley** showed how **coot** provides a large number of intuitive tools to interpret electron density manually.

Dancers, L to R: Claudia Minici and Orazio Mistretta; John Irwin. Below, Paola Spadon & Giovanna Scapin

Pavel Afonine described the tools in **phenix.refine** to refine macromolecular structures to give better agreement with the diffraction data at a variety of resolutions, and **Sacha Urzhumtsev** concentrated on the special considerations of interpreting data at both extremes, i.e. very high and very low resolution. Model-building and refinement are particularly difficult at low resolution: **Garib Murshudov** discussed approaches in **Refmac** to dealing with these problems, and **Axel Brunger** explained the **DEN** refinement approach implemented in CNS. **Piet Gros** showed how an ensemble of structures can be refined against the data, gaining insight into atomic movements and structural uncertainty.

Once the structure has been obtained and refined, it is ready to be presented to the world. **Jaime Prilusky** showed how this can be done interactively on the **Proteopedia** website, and he challenged the participants to prepare their own Proteopedia pages during the course.

A number of speakers presented the structural fruits of their research: complement proteins (**Piet Gros**), Z-DNA at 0.55Å resolution (**Zbigniew Dauter**), enzymes mutated in lysosomal storage diseases (**Randy Read**), viral membrane fusion proteins (**Felix Rey**), monoamine oxidase inhibitors (**Andrea Mattevi**), proteins involved in Ca-triggered vesicle fusion (**Axel Brunger**), retropepsin (**Mariusz Jaskolski**), autotaxin (**Tassos Perrakis**), and the eukaryotic ribosome (**Sergey Melnikov**).

Although the course concentrated on single-crystal x-ray diffraction, the horizons were broadened with a number of complementary approaches. **Nobuo Niimura** described how the emergence of new neutron radiation sources is leading to a renaissance of neutron diffraction; by showing the positions of protons and deuterons it nicely complements the information on heavier atoms from x-ray diffraction. **Petra Fromme** showed that X-ray Free Electron Lasers (XFEL) can be used to collect data from nanocrystals, in the instant before the crystal is vaporized. She also showed the insights that can be obtained from the photosystem-1 crystals being used in the XFEL experiments. **Pierre Thibault** showed how objects can be reconstructed from x-ray diffraction without a crystal, using coherent diffraction and nanotomography methods. Similarly, **Tatiana Latychevskaya** showed that diffraction with low-energy electrons can be used for image reconstruction. **Dmitri Svergun** explained how molecular shapes can be determined at a surprising level of detail

At left: Eva Bligt-Linden. Her photo, as well as the photos of dancers, courtesy of Marco Mazzorana.

with the one-dimensional information obtained from small-angle x-ray scattering. Finally, **Frank DiMaio** talked about how the modelling program **Rosetta** can be used in computational enzyme design when experimental data is unavailable, and also how it can leverage small amounts of data by improving models for molecular replacement or by extending the convergence radius of refinement.

A special session commemorated the valuable contributions of three crystallographers who passed away recently: **Lodovico Riva di Sanseverino** (the linchpin of the Erice schools for many years), **Herb Hauptman** (direct methods) and **David Sayre** (direct methods and coherent diffraction imaging). Contributions were made by **Davide Viterbo** (who knew all three), **Paola Spadon**, **Randy Read** and **Pierre Thibault**, who uploaded the first Wikipedia article about David Sayre in front of the audience.

Randy Read

Peter Kwong, receiving the 2012 SERCAT Outstanding Science Award from B.C. Wang.

The annual SER-CAT symposium was created in 2003 and is held each spring at a SER-CAT member institution preceding the official meeting of the SER-CAT Board. It is designed as an opportunity to exchange ideas about research methods and discuss interesting discoveries so that SER-CAT users can get the most productive use of the facility. Symposia have been hosted by the U of Alabama - Birmingham (2004), St. Jude Children's Research Hospital in Memphis, Tennessee (2005), Georgia State U (2006), NCI/NIH (2007), Medical U of South Carolina (2008), the U of Alabama - Huntsville (2009), ORNL (2010), and North Carolina State U (2011). The 2012 symposium was held at the U of Kentucky, on March 6th. Welcoming remarks from the U Kentucky Associate Vice President for Research **Martha Peterson** were followed by a welcome message from the meeting hosts **David Rogers** and **Peter Vander Kooi**.

The morning session, chaired by **Jonathan Wagner** and **Matthew Parker**, both of U Kentucky, began with **Michael Wiener**, U Virginia: *Going for baroque: TonB-dependent outer membrane active transport*. Michael explained that in gram-negative bacteria the outer membrane active transport system has three main components: a porin like outer membrane transport protein, an inner membrane TonB multiprotein complex (which serves as the motor) and the inner membrane itself which provides the protonmotive force that drives active transport. He then presented structural and functional results on both the outer membrane transporter and the inner membrane TonB motor that provide intriguing insights into the mehanism of action of this unique system. **Christopher Davies**, Med. U. of South Carolina, presented *Understanding antibiotic resistance at the structural level*, which focused on antibiotic resistance in *Neisseria gonorrhoeae*, a growing health concern. He then gave an update on mutation studies on the penicillin-binding protein 2 (PBP 2) in terms of kinetics and crystal structure. **Peter Kwong**, Nat'l Inst. of Allergy and Infectious Disease/NIH, was the **SERCAT Outstanding Science Award** winner. Peter presented *HIV-1 vaccine design with HIV-1 Env structures, broadly neutralizing antibodies, and SER-CAT*. Peter heads a group targeting the HIV-1 glycoprotein gp120 as a possible candidate for vaccine design. Knowledge about the interaction of HIV-1 immunogen with antibody is key to this undertaking. Peter and colleagues in his lab have characterized the atomic-level interactions between HIV 1 gp120 and the potent neutralizing antibody PG9. See J.S. McLellan *et al*., *Nature* (2011) **480**: 336-343.

Jason Stagno, NCI, **SER-CAT Young Investigator Award** winner, presented *Structural basis for RNA recognition by NusB and NusE in the initiation of transcription antitermination*. This work involved the crystal structure of a NusB-NusE-dsRNA complex that is important for processive transcription antitermination. The structure revealed a new BoxB dsRNA-binding site consistent with the structural features of the classical lambda antitermination site. The data together with other known antitermination factor interactions suggests a specific model for antitermination complex assembly. See *Nucleic Acids Res*. (2011) **V39**, pp 7803–7815. **Samuel Bouyian**, U. Missouri at Kansas City, reported on *Protein tyrosine phosphatases and contactins in nervous system development*. His group is investigating the biochemical and structural analyses of receptor protein tyrosine phosphatase zeta (PTPRZ) and its homolog receptor protein tyrosine phosphatase gamma (PTPRG). Samuel discussed the crystal structures of the carbonic anhydrase-like domains of PTPRZ and PTPRG in complex with fragments of contactin family members that suggest that PTPRG, PTPRZ and their interactions with contactins may play an important role in the adhesive interactions that underlie the construction of neural networks. **Guoxing Fu**, Georgia State U, talked about *Conformational changes and substrate recognition in Pseudomonas aeruginosa D-arginine dehydrogenase*. He presented the first x-ray crystal structures of arginine dehydrogenase (DADH) at 1.06Å resolution and its complexes with iminoarginine and iminohistidine at 1.30 Å resolution. The crystal structures of the DADH complexes show two distinct ligand binding modes that are consistent with the 1000-fold difference in the kcat/Km values for d-arginine and d-histidine. The binding site plasticity supported by the kinetic data presented suggests that the enzyme has relatively broad substrate specificity, being able to oxidize positively charged and large hydrophobic d-amino acids.

The lunchtime poster session, chaired by **Peter Vander Kooi**, featured a prize for the best poster of the 23 presented. The winner was **Stefan Gajewski**, St. Jude Children's Research Hospital, for *Structural transitions within an intrinsically flexible protein captured at low resolution*.

The afternoon session, chaired by **B.C. Wang**, U Georgia and **David Meekins**, U Kentucky, focused on updates to the APS and SER-CAT facilities and on new methodology. **Denny Mills**, APS, ANL, gave an update on the ongoing $350M APS upgrade, which will continue over the next 5 years. He also told us that the APS has a new director, **Brian Stevenson**, and that **Keith Moffat** has been appointed **Senior Advisor for Life Sciences** at the APS. Also, APS has formed a **Life Sciences Council** to reflect the significant impact that life sciences research has on the facility. **Peixuan Guo**, U Kentucky, presented an interesting talk on the application of nanotechnology to RNA crystallization. Topics included: bottom-up self-assembly; the use of scaffold motifs; ribozyme processing; use of sticky ends and palindrome sequences; formation of unique oligomer complexes; formation of patterned arrays to permute crystallization; methods to control twisting angle and the formation of 1D and 2D sheets. **Bi-Cheng Wang**, SER-CAT & U Georgia, presented *Forward-looking possibilities for x-ray sources having optimized extended wavelength capabilities*, which outlined the opportunities for and community interest in having a dedicated and optimized extended x-ray beamline in the US. B.C. discussed several potential applications including light element-SAD phasing (S-SAD), heavy element-SAD (Xe-SAD/MAD phasing) and the positive identification of bound metals or surface ions based on the wavelength dependency their anomalous scattering profiles exhibit. **John Chrzas**, SER-CAT & U Georgia, focused on recent upgrades to SER-CAT hardware and software. He talked about the delivery status of the new Rayonix MX300HS detector (January 2013); improvements to the SER-CAT network and computing infrastructure (10 GB internet connections, new 1.1 Tflop computer cluster and new100 Tbyte data storage system); a kappa upgrade to the MD2 (currently available upon request), and expanded capacity (430 crystals) of the BAM-S crystal storage dewars. John also demonstrated, via remote access to SER-CAT, two new features of SER-GUI, namely diffraction based crystal centering and helical data collection.

Stefan Gajewski (left) receiving the SERCAT Poster Award from Craig VanderKooi.

In the evening, all were bussed to the Kentucky Horse Park for a dinner reception. Before dinner, guests were invited to wander in the ***Museum of the Horse*** and were given a very informative lecture on Kentucky's prizewinning horses in the ***Hall of Champions***. During dinner the local band ***Love, Peace and Chicken Grease*** entertained guests.

John Rose

Jason Stagno receiving the 2012 SERCAT Young Investigator Award from B.C. Wang.

Participants at the 9th Annual SER-CAT Symposium held at U Kentucky, Lexington, KY.

Contributors to this Issue

Alberto Albinati, Randy Alkire, Karen Allen, Dan Anderson, Philip Anfinrud, Olga Antipova, Lesa Beamer, Craig Bridges, Stephan Burley, Branton Campbell, John Chrzas, Ed Collins, Angela Criswell, Lee Daniels, Louise Dawe, Graciela Diaz de Delgado, Martin Donakowski, Antonio dos Santos, Cathy Drennan, Brandt Eichman, Howard Einspahr, Larry Falvello, Paul Fenter, Michael Fenwick, Joe Ferrara, Barry Finzel, Robert Fischetti, Michel Fodje, Bruce Foxman, Frank Fronczek, Stephan Ginell, Ana Gonzales, Celia Goulding, Jane Griffin, Ilia Guzei, Gregory Halder, Curt Haltiwanger, Ron Hamlin, Magali Hickey, Asfia Huq, Hilary Jenkins, David Jeruzalmi, Jim Kaduk, Katherine Kantardjieff, Saeed Khan, Nick Kim, Kristin Kirschbaum, Tad Koga, Yan Kung, Eric Lawson, Patrick Loll, George Lountos, Kathryn McCulloch, Keith Moffat, Eric Montemayor, Robert Morse, Peter Müller, Alexander Nazarenko, Bruce Noll, Bill Ojala, Allen Oliver, Joseph Orgel, Eric Ortlund, Katherine Page, Rebecca Page, Brian Patrick, Arwen Pearson, George Phillips, Sai Venkatesh Pingali, David Rose, John Rose, Roger Rowlett, Savvas Savvides, Marius Schmidt, Yulia Sevryugina, Megan Sikowitz, Nicholas Silvaggi, Emmanuel Skordalakes, Ward Smith, Eddie Snell, Tobin Sosnick, Elinor Spencer, Cynthia Stauffacher, Liang Tang, Andrew Torelli, Volker Urban, Bi-cheng Wang, Xiaoping Wang, Yun-ying Wang, Nobuhisa Watanabe, Kraig Wheeler, Matthew Whitley, Zachary Wood, Kevin Yager, Andrey Yakovenko, Lin Yang, Xiaojing Yang, Victor Young, Xiaobing Zuo.

*****We especially thank Howard Einspahr for his tips about ASBMB awards, and MOST especially thank our staff photographer Peter Müller, for all the terrific photos in this issue. *****

Fluffy, the '*Galileo of the Lemmings*,' with his stopwatch.
Courtesy of Nick D. Kim, University of Waikato, New Zealand.
See nearingzero.net/res.html.

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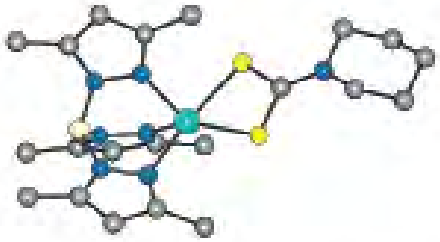
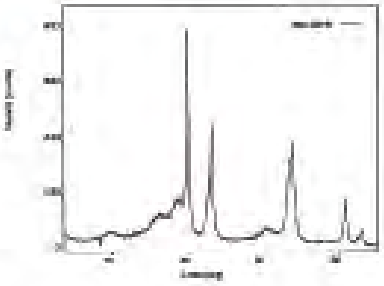


Mid-June 2013



Host Campus: **Northwestern University**, Evanston, IL

Co-organizers: Amy Sarjeant (Northwestern)
Charlotte Stern (Northwestern)
Allen Oliver (Notre Dame)

For information visit: ***acasummercourse.net***

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ACA 2013 July 20 - 24

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Student Hotel Sheraton Princess Kaiulani

Abstract Deadline: March 31, 2013
Student and Young Scientist Travel Grant Applications: March 31, 2013
Advance Registration Deadline: May 31, 2013
Hotel Confirmation Deadline: July 5, 2013

The 2013 Meeting will have a 4-day, 5 concurrent session pattern. The meeting will start with workshops on Saturday, July 20, and scientific sessions on Sunday, July 21; it will end on Wednesday, July 24 after the Awards Banquet.

NOTE: Sheraton hotel rooms will go fast. The conference rates are: Hotel City View: $183 + tax (no resort fee); Mountain View: $203 + tax (no resort fee); Sheraton Princess Kaiulani: $143 + tax (students & postdocs only).

Register online and see *Call for Papers*: *www.AmerCrystAssn.org*
Meeting website: *www.amercrystalassn.org/2013-meeting-homepage*
Exhibits website: *www.amercrystalassn.org/2013-exhibits*

Awards

Tom Koetzle
Senior Chemist, BNL, Retired
Robert Bau Neutron Diffraction Award

Tom Terwilliger, LANL
Bioscience Division,
Kenneth Trueblood Computational ChemistryAward

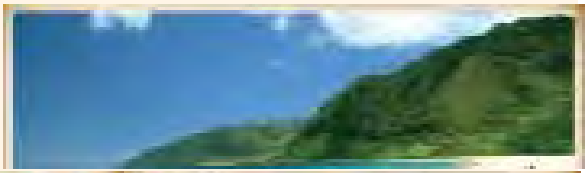
Eric Ortlund, Director of Recruiting for Molecular Systems Pharmacology, Emory School of Medicine
Etter Early Career Award

Richard Dickerson
Professor Emeritus, UCLA
Isadore Fankuchen Diffraction Award

Program Chairs

Allen Oliver
aoliver2@nd.edu

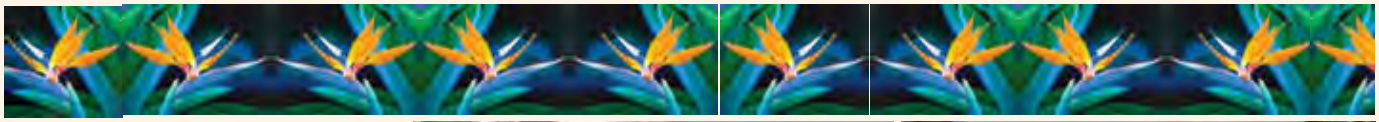
Jeanette A. Krause
jeanette.krause@uc.edu











RefleXions Photographer
Peter Müller
pmueller@mit.edu


The scenic photos are from www.gohawaii.com/oahu/guidebook/gallery, and from RefleXions and ACA Headquarters archives.

Logo design by Vanessa Reitz
vjreitz.prosite.com

Poster Chair
Ilia Guzei
iguzei@chem.wisc.edu

Chief, Session Speaker Photos
Jeff Deschamps
deschamps@nrl.navy.mil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Puzzle Corner Editor, Frank Fronczek ffroncz@lsu.edu.

DISORDERED

Reorder these crystallographic words to find the best FOM

FWOCKYF	WYCKOFF
TACTILE	LATTICE
NAGSUSIA	GAUSSIAN
ZORNTEL	LORENTZ
FONTOSE	FESTOON

Answer: A WULFF NET

Answer to the summer puzzle.

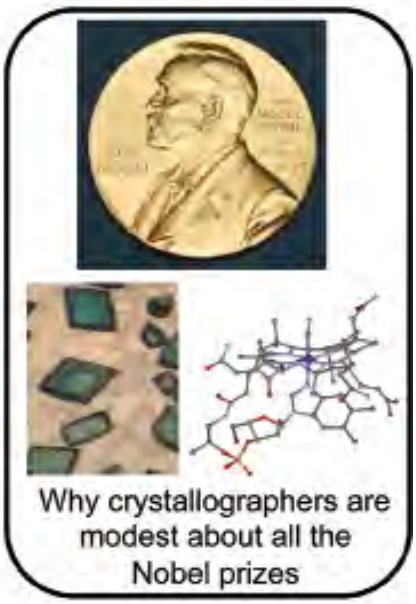
Can anyone identify attendees at the Women's Symposium at the McMaster ACA meeting in 1986??

And the NEW Puzzle is - - -

DISORDERED

Reorder these names to reconstruct the dynamite answer.

BILGEDORE	
TONNERG	
DINGHOK	
RELAK	
PUNTHAMA	
THEMANSCH	



Answer: " " " "

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20-27 **BioCrys2012 - Fundamentals of Modern Methods of Biocrystallography.** Oeiras Portugal. **biocrys2012.itqb.unl.pt**

28-31 **13th European Powder Diffraction Conference** Grenoble France.

NOVEMBER 2012

18-23 **15th International Small-Angle Scattering Conference,** Sydney Convention & Exhibition Centre. **www.sas2012com.** Contact: **ICMS Australasia info@sas2012.com.**

25-3 **MaThCryst Int'l School on Fundamental Crystallography** (ISFC2012). Uberlândia Brazil. **www.crm2.uhp-nancy.fr/mathcryst/uberlandia2012.php.**

26-30 **MRS Fall Meeting.** Boston, MA, USA. **www.mrs.org/fall2012/.**

DECEMBER 2012

2-5 **AsCA'12**, joint meeting with **SCANZ**, Adelaide Convention Centre, Adelaide, Australia. Contact: **crystal2012@sapmea.asn.au**.

6 **The Bragg Symposium**, Elder Hall, University of Adelaide. Celebrating 100 Years of Crystallography. Adelaide Australia. **www.sapmea.asn.au/conventions/crystal2012/bragg.html.**

AUGUST 2013

25-29 **ECM28.** University of Warwick, UK. **http://ecm28.org/.** Contact: Sandy Blake, Chair of ECM28: **a.j.blake@nottingham.ac.uk**. **http://ecm28.org/.**

11-16 **ICCGE-17, 17th Int'l Conf. on Crystal Growth and Epitaxy.** University of Warsaw, Warsaw Poland. **http://science24.com/event/iccge17/**.

JANUARY 2013

18-20 **CUWiP Conference for Undergraduate Women in Physics,** Colorado School of Mines & Denver West Marriott. Contact Ariel Bridgeman at **abridgem@mines.edu**

JULY 2013

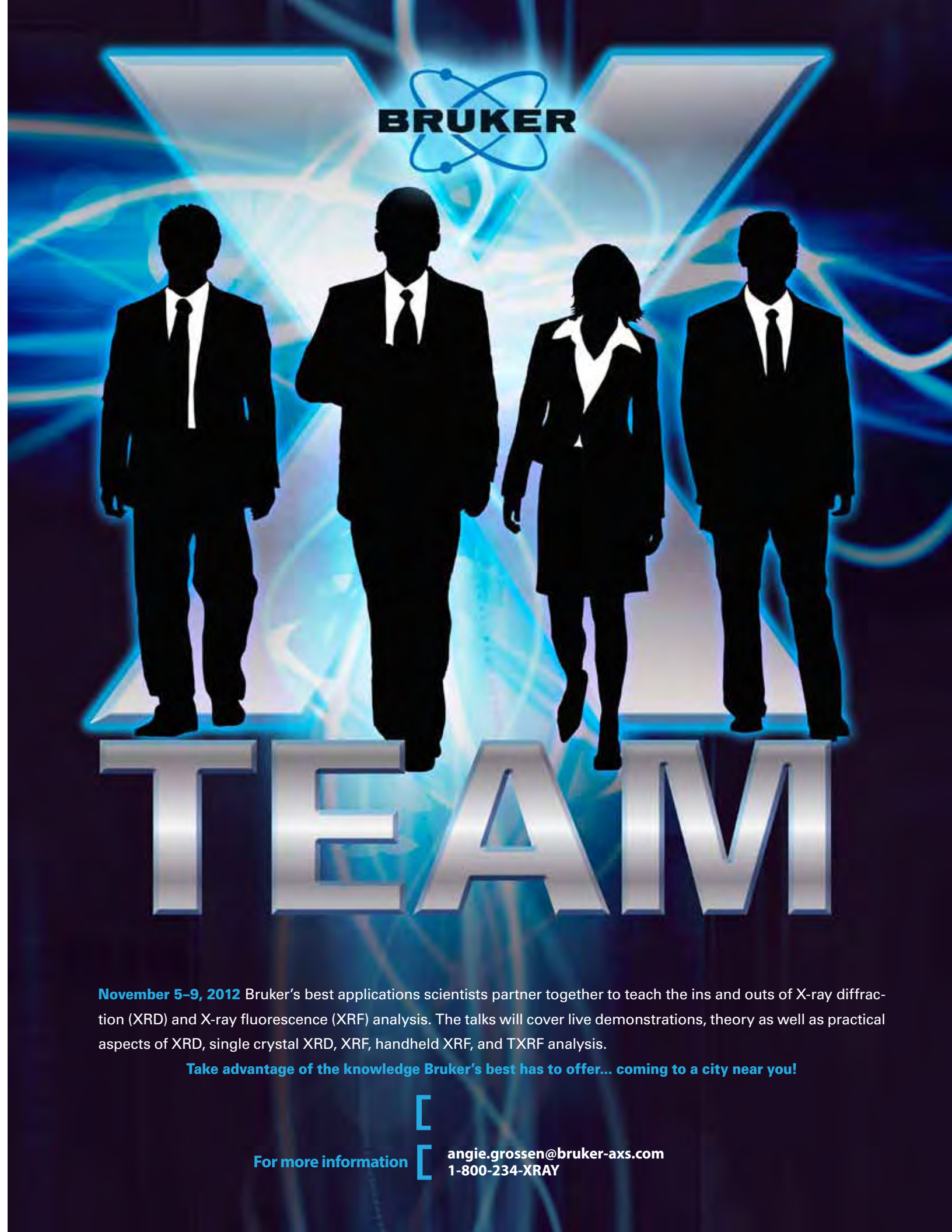
20-24 **ACA 2013 will be back in Hawaii at the Sheraton Waikiki.** Program Chairs Allen Oliver **aoliver2@nd.edu** and Jeannette Krause **jeanette.krause@uc.edu**

MAY 2014

20-24 **ACA 2014 Annual Meeting,** Albuquerque, NM, Albuquerque Convention Center & Hyatt Regency Hotel. Program Chairs: Christine Beavers, & Petrus Zwart. Local Chairs: Zoe Fisher & Kate Page.

AUGUST 2014

5-12 **XXIII Congress and General Assembly of the IUCr,** Montreal, Quebec, Canada. **www.iucr2014.org/.**



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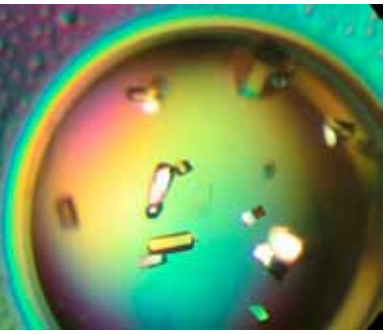
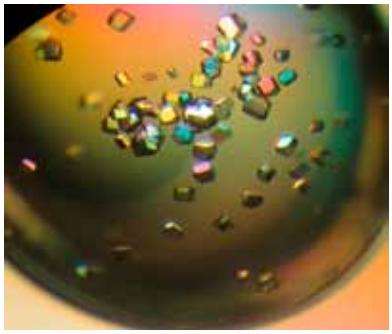
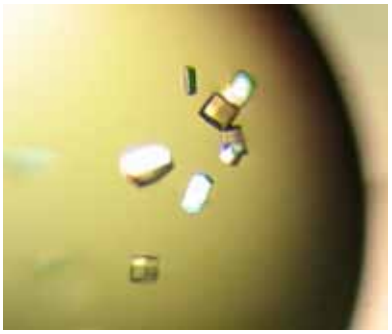
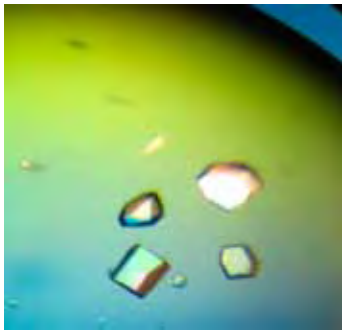

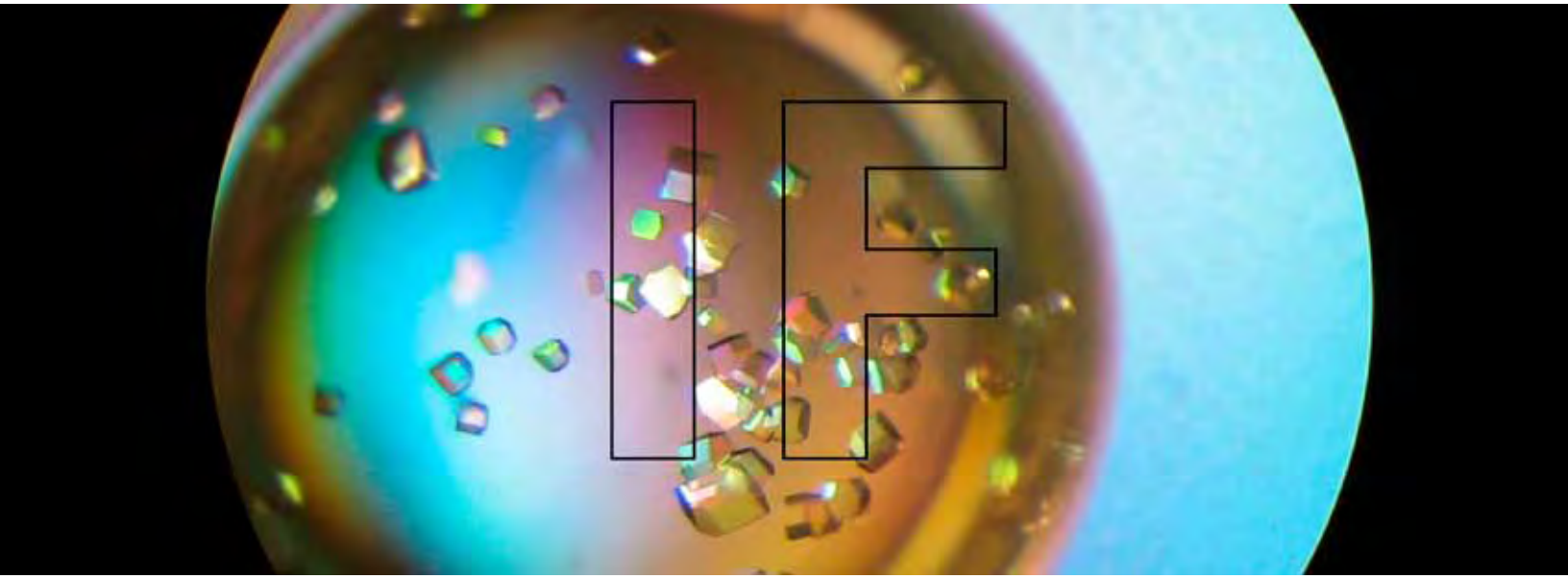

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