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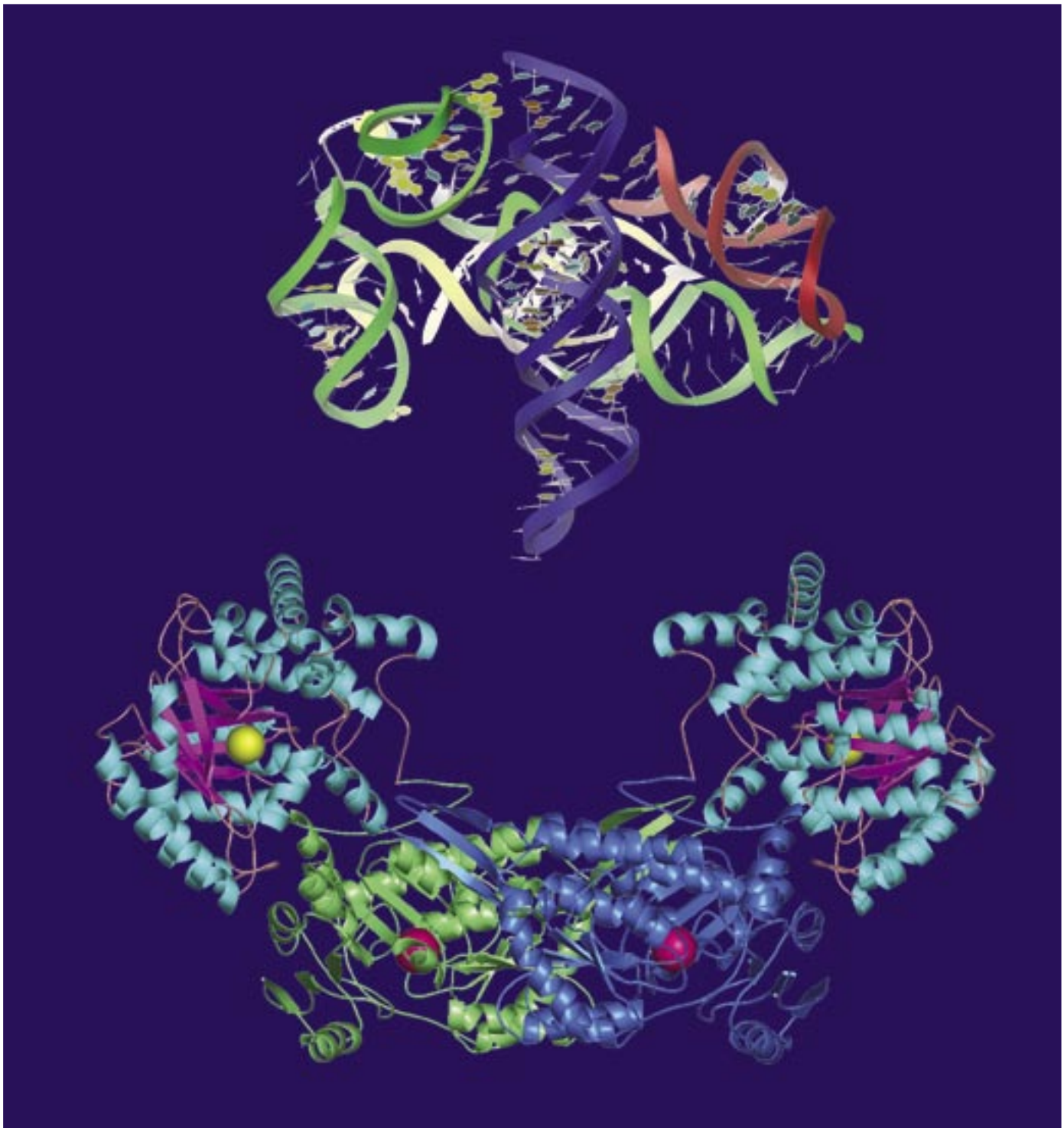

New Structures at the Chicago ACA Meeting

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President's Column

I am delighted to report that by any measure the recent ACA Chicago meeting was an outstanding success. If you missed it, you can read all about it in this Newsletter, pages 34-68. The scientific program was strong, thanks to the efforts of the program chairs, Christer Aakeröy and Marilyn Yoder, as well as the Program Committee members, including Lesa Beamer, Alicia Beatty, Alex Chernov, Brian Patrick, Vivien Yee, Alexandre Yokochi, and Victor Young. The venue functioned smoothly, thanks to the efforts of the local chairs, Bernie Santasiero and Karl Volz, the local committee members, including Sasi Chilukuri, Jill Dombrauckas, Soni Larsen, Melissa May, Andy Mesecar, Kiira Ratia, and Huidong Yu. Many thanks also to Marcia Colquhoun, Patti Coley, and Tammy Colley, who spent many months fielding inquires and compiling all the meeting-related books and schedules, as well as running the registration desk for the entire meeting. Highlights of the meeting included four award symposia, honoring Nguyen-huu Xuong for the Supper Award, Alex McPherson for the Fankuchen Award, Dick Marsh for the Trueblood Award, and Leonard MacGillivray for the Etter Early Career Award. Congratulations are also in order to Alwyn Jones, the winner of the Patterson Award to be given at the 2005 Orlando meeting, the winners of the 2005 Etter Student Lecturer Awards: Mehmet Aslantas, Lincoln Bickford, and Zhanhui Yuan, as well to the students who were feted at the banquet for their outstanding poster presentations at the 2004 meeting (see pages 15-19). Special congratulations to Madeleine Jacobs, who took time out from her busy life, to accept a Public Service Award and who gave an energetic banquet oratory, somehow finding a particularly relevant quote from a Cole Porter song. Even the banquet food was tasty. With 1213 total participants, attendance was the 2nd highest of any meeting. I'm sure ACA members also enjoyed the pleasant weather, the magnificent location on the Chicago river, the superb local dining, and the fine art – with the fantastic city architecture at our doorstep, the opening of Millenium Park, and the special Seurat exhibit at the Chicago Art Institute?

With all the diversions, many attendees missed the ACA business meeting and are unfamiliar with some of the important issues facing our professional organization. So I would like to bring some issues to your attention in this column. One revered tradition of the ACA is the recognition of superior accomplishments of colleagues in the field of crystallography in the form of awards. Please see Lisa Keefe's discussion in her report on Council activities, *pages 10-11,* which also includes news about the formation of a new Industrial SIG, a new dues discount, and new requests for political action. In the recent past, Council has rebuffed requests from several scientific organizations for support and alignment with politically-oriented groups,

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no matter how compelling the argument, until the issue was discussed at a business meeting, because the use of either the ACA name or ACA funds to support these activities smacks of political lobbying. At this business meeting both pros and cons were aired, but the overwhelming sentiment which pervaded the discussion was that the ACA ought to unite with other scientific organizations in efforts to "educate" Congressional leaders about the significance and impact of preserving basic science budgets. Uniting with other scientific organizations essentially means providing partial support for a political lobbyist or a fellowship for training such a person. Are ACA members willing to donate up to $3 each, essentially the price of one cookie at a national meeting? The response at the business meeting was affirmative and so the ACA Council will review all prior requests for support at their next meeting in November. Therefore, if you wish to share your opinion, please do so by emailing one of the council members.

Please see Lisa's discussion of future meeting locations as well, because Council would like to have more feedback from members on this topic. Meeting locations are always discussed at business meetings. At one extreme, some members wish for the old days, when conferences were held on college campuses and were very inexpensive, especially for students. At the other end of the spectrum, some members want to have meetings in interesting locations, with less emphasis on expense. There are merits to these diametrically opposed views, and Council is mindful of them as we attempt to plan scientifically interesting meetings that attract sufficient attendance to support the cost of the meetings – that will break even financially or be revenue neutral. At the business meeting, Council members heard good support for having the 2006 meeting in either Hawaii or in Utah; a decision about the site should be made before this *Newsletter* reaches members. In Hawaii, the hotels are reasonably priced, but the travel expenses are, not surprisingly, higher than other locations. Although regular members may be able to afford Hawaii, will such a location impact the ability of students to travel to the meeting? After all, one focus of the ACA is nurturing younger colleagues. For the Chicago meeting, the ACA Council addressed the issue by increasing the amount of student travel awards by 50%. Council was able to do this because of donations to the student travel fund and because the previous meeting in Covington made a modest profit. From preliminary estimates we expect there will be a small profit from the Chicago meeting as well. Although some of the profits must be prudently put aside to cover the notoriously unprofitable spring meetings, I am hoping that there will be enough funds for extra student travel awards for future meetings. The travel awards may not defer all travel expenses for students, but they certainly lower the costs significantly, so please do inform your students that they should be applying for a Young Scientist Travel Award. The deadline for Orlando meeting applications is December 15th. Even with extra money, there are insufficient funds to support all requests. This past year, Council capped all domestic awards at $599 in order to avoid tax consequences, and Council is likely to do the same next year. If a student is not granted an award one year, the student has a higher priority the next year. Also, keep in mind that students are ineligible to receive a travel award for two years in a row. Council realizes that student travel awards aren't the perfect solution to dictating meeting locations, but I believe it is at least a reasonable compromise between the extremes of opinion. If you disagree, please let me know; I would appreciate alternative suggestions.

Speaking of meetings, the next meeting is at the Walt Disney World Swan Hotel in Orlando. If you are anything like me, the mention of Orlando, conjures up images of Mickey and Minnie Mouse, not good science or adult fare. Thus, I was pleasantly surprised by the site when Council visited last March and I think you will be as well. The Swan is a pleasant hotel which will be filled completely by ACA participants and their families. There was quite a lot of activity around the hotel, including other hotels, dining establishments, nightclubs, and lakeside activities. Please see page 75 for details about the meeting plans. See you in Orlando!

Fran Jurnak

Crystallography Re-examined, a Guest Editorial by former ACA President Abe Clearfield

In 1974 I joined the National Science Foundation as a one year rotator in the Chemistry Division. In that capacity I was present at a meeting where the projected job market for crystallographers was discussed by a group convened by an eminent chemist. At that time automated diffractometers were available but not yet widely distributed. In the hands of a skilled operator a small molecule data set could be gathered and solved in a week. Organics took somewhat longer. Thus, it was broached that technicians could be trained to do the work since it would be routine and so the number of crystallographers required would be greatly reduced. Likewise, cutting edge research would also diminish and less funding would be required in crystallographic research areas. Of course, when the report appeared, crystallographers were outraged. They demanded a second panel meeting to rebut the charges. Again, as an NSF representative I was present at the meeting. The meeting was such that on the whole I would rather have been visiting my dentist. But when the screaming died down, I informed the group, I know not on what authority, that no matter what the area of research NSF always tries to fund the best, most innovative research. So we will accept proposals from crystallographers in all fields of their activities. Thus mollified, the group and the meeting ended on a civil note.

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So how far have we come since then? Certainly the diffractometers have become faster and the software better. Image plate systems appeared on the scene followed by CCD detectors. Low temperature devices have been improved and it has become routine to collect data at near liquid nitrogen temperatures. In 1974 it was a struggle to solve a protein structure. Today the most complex proteins are yielding to faster computers and more accurate data gathering, superior software and improved methodology.

In the early 1980's some crystallographers turned their attention to the solution of crystal structures from powder data. A major difficulty to be overcome was the non-gaussian shapes of the x-ray reflections, making it difficult to derive accurate intensities from the pattern. Many ingenious methods were developed to solve this problem so that Rietveld methods of whole pattern refinement could be applied. Excellent software for every aspect of such powder studies are now available. At first it was thought that only data obtained using synchrotrons could be used. However, with the improvement in resolution and accuracy of in-house powder units and intensity enhancements by optical methods and rotating anodes, high quality data is available at many individual laboratories. Still, for difficult structures, high flux synchrotrons and neutron sources can be used separately or in tandem to supply the required data. Organic structures are beginning to yield to direct space techniques. Who would have thought in 1974 that even protein problems could be investigated by powder x-ray methods?

The emergence of electron crystallography is another salutary development. Crystals of less than one micron in size are sufficient to yield data for structure solution. This technique also has the advantage that the electron beam can be focused. The diffracted beam, after passing through the crystal, may be refocused to form an image that is in essence a hologram that carries all the phase information. Holograms recorded along suitable zone axes supply the amplitudes and phases from which the structure can be obtained. Electron crystallography along with transmission electron microscopy (TEM) have provided detailed information from zeolites never before accessible. Even mesoporous materials that provide less than 30 reflections are yielding to a combination of EC and TEM (*Chem. Commun.* 907-16, 2004).

Finally, I recommend the article ***Beyond crystallography: the study of disorder, nanocrystallinity and crystallographically challenged materials with pair distribution functions*** (*Chem. Commun.* 749-760, 2004). Data gathered at the Argonne Advanced Photon Source (APS) out to high values of Q space allows details about short range order in poorly crystalline and amorphous materials to be unraveled. No presumption of periodicity is required to apply the atomic pair distribution function (PDF). In theory, PDF analysis of x-ray and neutron scattering data can be used to address problems outside the power of traditional crystallography.

So what is the message being conveyed here? After 50 years of chemical crystallography I am still amazed at the complexity of nature's materials and the ingenuity required to understand their structure and function. There will never be a time when we can sit back and say we know enough. Every generation of scientists will have new challenges to meet that will require the full expenditure of their intellect and talent in order to prevail. Shalom,

Abe Clearfield

Robert Newnham Receives Franklin Medal

The 2004 **Benjamin Franklin Medal in Electrical Engineering** was awarded to Robert E. Newnham, The Pennsylvania State U., for his invention of multiphase piezoelectric transducers and their spatial architecture. Robert Newnham has had a long and distinguished career encompassing crystallography, piezoelectric composites, and electronic ceramics. In the late 1970's he invented the composite piezoelectric transducer that has revolutionized fields of engineering such as underwater acoustics, medical ultrasound, and wireless communications.

He received a B.S. from Hartwick College, an M.S. from Colorado State, and two Ph.D.'s, one in physics in 1956 from Penn. State and the second in crystallography in 1960, from Cambridge. He taught at M.I.T. from 1958 - 1966, then joined the faculty of Penn. State. He has also received the **John Jeppson Medal and Award** from the American Ceramic Society, and the **International Ceramics Prize** from the Academy of Ceramics. He is a fellow of both the American Ceramic Society and Mineralogical Society of America. He is a past president of the ACA and is a member of the Institute for Electrical and Electronic Engineering and the National Academy of Engineering.

McMurdie Award to Winnie Wong-Ng

Winnie Wong-Ng, NIST, Maryland, received the 2004 **McMurdie Award** at the 53rd Annual Denver X-ray Conference in Steamboat Springs, Colorado, on 4 August. This award recognizes her contributions to the computer-aided evaluation of x-ray powder patterns, her work as editor of the Powder Diffraction File™, and her accomplishments toward enhancing the accuracy of powder methods of x-ray crystallography.

The award was established in honor of Howard McMurdie, a long time editor of the ICDD Ceramics Subfile, and is presented every two years for distinguished work which improves the Powder Diffraction File™ a database designed to aid in the identification and characterization of inorganic solids. Previous recipients of this prestigious award include: Gregory P. McCarthy, 2000 and Camden R. Hubbard, 2002.

APS Congressional Science Fellowship

The American Physical Society is currently accepting applications for the 2005-2006 Congressional Science Fellowship Program. Fellows serve one year on the staff of a senator, representative or congressional committee and have the opportunity to lend scientific and technical expertise to public policy issues. Qualifications include a PhD or equivalent in physics or a closely related field, a strong interest in science and technology policy and, ideally, some experience in applying scientific knowledge toward the solution of societal problems. Fellows are required to be U.S. citizens and a Member of the APS. The term of appointment is one year, beginning in Sept. 2005. A stipend of $50,000 is offered in addition to allowances for relocation, etc. Please see **www.aps.org/public_affairs/fellows.html** for detailed information on applications.

Deadline for applications: January 17, 2005

New Art in Crystallography Prize

The Editors are pleased to announce that the *Newsletter*, together with the ACA Council will sponsor a new competition open to all ACA members: **Art in Crystallography.** Entries will be accepted in the form of images emailed to either of the Editors (**conniechidester@earthlink.net** or **flippen@rcsb.rutgers.edu**). Each entry should be accompanied by a paragraph explaining the science and the method of producing the image. We would appreciate receiving a photo of the artist as well, but this is not required. Prizes will consist of a small monetary award and a banquet ticket and waiver of registration fees at the annual meeting. Of course we hope that all the **GLORY** that will be garnered by the winners will be an additional incentive. The winning entries will be posted on the web, and there will also be a display of printed images at the annual ACA Meeting. We will also feature some of the images in the *Newsletter* from time to time. Judging will be by a panel appointed by the Editors; please let us know if you are interested in being a judge.

This has come about partly because of the **Web Watch** column contributed to the spring *Newsletter*. The Communications Committee found an interesting website: the UK Center for Materials Science, which had just sponsored an Art in Science Competition. Their winners are on their website: **www.materials.ac.uk/photocomp/**. One of the winning images was used to illustrate the column and several others were used as space-fillers. We also think crystallographers have a history of interest in art. Occasionally there have been art exhibits at meetings, and in 2000 & 2001, the Small Molecule SIG sponsored an Art with Small Molecules contest; the cover of the fall 2000 *Newsletter* featured the winners.

So, please send us your images by email at any time. If we have enough entries soon enough we might even be able to conclude the first competition in time for the spring ACA Meeting.

AIP State Department Science Fellowships

This Fellowship represents an opportunity for scientists to make a unique contribution to U.S. foreign policy. At least one Fellow annually will be chosen to spend a year working in a bureau of the State Department, providing scientific and technical expertise to the Department while becoming directly involved in the foreign policy process. Fellows are required to be U.S. citizens and members of at least one of the 10 AIP Member Societies at the time of application. Qualifications include a PhD in physics or closely related field or, in outstanding cases, equivalent research experience. Applicants should possess interest or experience in scientific or technical aspects of foreign policy. Please visit **http://www.aip.org/gov/sdf.html** for details about applications.

Deadline for applications: November 1, 2004

Call for applications for ICDD Scholarships

To encourage promising graduate students to pursue crystallographically oriented research, 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 $2,250. For details, visit: **www.icdd.com/resources/awards/frevel.htm.** Applications must be received by the ICDD by November 1, 2004.

The 2005 ACA Summer Course in Small Molecule Crystallography.

The course will be held June 5-15 (following the ACA Orlando Meeting) on the campus of Indiana U. of Pennsylvania. Lectures and tutorials will emphasize the basics of single crystal and powder x-ray diffraction and structure determination. There will also be tutorials on the use of crystallographic software and data bases. Tuition will be $250 for academic and government attendees ($750 for corporate scientists). Student apartments and two meals each day will be offered for $400. Up to 15 student scholarships will be available. Further details will be posted at **http:/www.hwi.buffalo.edu/ACA/**. Inquiries should go to Charles Lake at: **lake@grove.iup.edu.**

Bryan M. Craven and Charles H. Lake, Co-organizers

An Olympic Contender in our midst.

Daniel Lincoln, a PhD student with Joshua Sakon, University of Arkansas, competed in track and field events in the Summer Olympics as a member of the US Olympic Team. Dan was 1st in the 3000 m steeplechase at the US Qualifying Trials; he was 2001-3 NCAA Steeplechase Champion, 2003 NCAA 10,000 m champion; and is a 12-time NCAA All American. Dan comes from Ruston, LA. He graduated from University of Arkansas in 2003 and that year was named the NCAA Division I National Scholar Athlete of the Year by the United States Track Coaches Association. See the Olympic website: **http://sports.espn.go.com/oly/summer04/athlete?athleteId=6625**.

Young Scientist Travel Award.

Limited funds are available to help students and young scientists attend the 2005 ACA Meeting. Preference will be given to those presenting a paper. Interested parties should submit the application form included in the Call for Papers to ACA Headquarters by **December 15, 2004.** Forms and instructions will also be posted on the ACA website. Applications received after this deadline will be reviewed only if funds remain after the initial review. Applicants who received travel grants in 2004 will NOT be eligible for funding in 2005 and should not apply.

Reminder: Please VOTE!

Please remember to VOTE in ACA Elections! Candidate statements and photos are in the summer ACA Newsletter; The deadline for mailing ballots or electronic voting via the ACA website is November 15th.

Reminder About Visas

Considering the new regulations since 9/11, it is recommended that applications for visas to the US be made AT LEAST NINE MONTHS before they are needed.
The International Visitors Office (IVO) of the National Academies has launched a new website to provide information on visas for visiting scientists and scholars and advice for organizers of international scientific meetings in the United States. Please see: http://www.nationalacademies.org/visas.

Bridging the Sciences Initiative

We are a coalition of more than 120,000 scientists in U.S. basic research societies: the American Association of Pharmaceutical Scientists, the Biophysical Society, the American Physical Society, the American Society of Biochemistry and Molecular Biology, the Protein Society, the American Peptide Society, the American Physiological Society, the International Society for Computational Biology, the American Mathematical Society, PhRMA, Structural Genomix, and the National Center for Biomedical Space Research. We seek new federal dollars to support basic research at the interface between the life sciences and the physical & mathematical sciences.

We think that major scientific opportunities are being missed in the U.S. today. Biomedical research would not be where it is without the physical, mathematical, and computational sciences, and yet tomorrow's breakthroughs in these areas are often too physical to be supported by the life sciences agencies or too biological for the physical science agencies.

Our aim is to institutionalize a commitment to the basic physical and mathematical sciences within the biomedical funding agencies, or a commitment to the biomedical sciences within the federal math and science funding agencies, or both. The institution we seek would meet the following requirements:

(1) It would provide grant funds to researchers, based on competitive investigator-initiated proposals. We envision a broad spectrum of grant types, from small individual-investigator grants, to large research resources resembling the types of grants currently at NIH and NSF. However, we believe that it is important not to over specify the structure of the research effort. Greater innovation often comes from smaller groups, including individuals.

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(2) The funding institution or mechanism should be permanent, with a long-term stable source of funding. Grants would not be entitlements, but would require renewal after a number of years, as is currently done at NIH and NSF. To provide sufficient long-term stability will probably require a director and staff.

(3) The funding organization would focus on research at the interface between the biological sciences, and the physical, chemical, mathematical, and computational sciences. While NIH, NSF, DOE and other agencies currently fund some chemistry and biophysics at this interface, we envision funding for research that more deeply underpins biological research, reaching further "upstream" into the physical sciences.

(4) The granting and review mechanism must be designed to support long-term payoffs. It is crucially important to embrace risk in order to achieve the levels of innovation and the high rewards that can come from research at this interface. We believe that to stimulate the types of breakthroughs that physics and math have historically given to biology through x-ray crystallography, mass spectrometry, NMR, CAT scans, computational biology, single-molecule and other methods, it is necessary to support the kind of research for which the payoff to biology may not be immediately apparent.

(5) To support the best grants requires a review system involving judgments by qualified scientists, most importantly chosen from the physical and mathematical science communities. It is not likely that small changes of existing NIH or NSF peer review mechanisms will be sufficient to support the deepest levels of innovation that we need.

Ken Dill ***dill@maxwell.compbio.ucsf.edu***

IUCr pilots CrossRef Search

The IUCr is one of nine leading publishers to pilot **CrossRef Search**, a search facility that uses the collaborative environment of **CrossRef** combined with **Google** search technologies. Users can search the full text of high-quality peer-reviewed journal articles, conference proceedings, etc. A typical Google search is launched but the result is filtered using participating publishers' standards, with the intent of reducing the noise produced by general web searches. Other publishers taking part in this initiative are ***American Physical Society; Annual Reviews; Association for Computing Machinery; Blackwell Publishing; Institute of Physics Publishing; Nature Publishing Group; Oxford University Press; and John Wiley & Sons***.

The **CrossRef Search** pilot will run through 2004 to gather feedback to fine-tune the program. To use this free service see: **http://journals.iucr.org/services/search.html**.

Call for Warren and Buerger Award Nominations

Nominations are solicited for the **Bertram E. Warren Diffraction Physics Award** and for the **Martin J. Buerger Award** to be presented at the 2006 ACA Annual meeting.

The **Martin J. Buerger Award** recognizes mature scientists who have made contributions of exceptional distinction in areas of interest to the ACA. It has no other restrictions, and does not require that a candidate be an ACA Member. Recent previous winners are James Ibers (2003), Lyle Jensen (2000), Carroll Johnson (1997), Philip Coppens (1994) and Jack Dunitz (1991). Martin Buerger was interested in the physical and chemical properties of minerals and made many contributions to the understanding of plastic deformations, polymorphism, and twinning, but his influence extended well beyond mineralogy. His study of vector sets and interrelations in crystal space and Patterson space was an early effort to use direct methods to solve the phase problem. He designed the precession camera, contributed to the design of early diffractometers, authored 12 books on crystallography, and was a fine teacher held in high esteem by his many students. He helped to organize the IUCr in 1946, was Editor-in-Chief of *Z. Kristallogr*. for many years, played a major role in the production of the 2nd edition of *International Tables*, was President of the ACA predecessors ASXRED in 1943 and CSA in 1945-46, and helped to found the ACA. He was the first recipient of the Fankuchen Award in 1971. Professor Buerger established an x-ray laboratory at M.I.T. in 1934; his years there paralleled those of Bertram Warren. The award was established in his memory in 1983 and the first award was given in 1985. The Buerger Award selection committee is **David Brown (chair), Carol Huber, Alexander McPherson,** and **Jim Ibers**.

The **Bertram E. Warren Award** recognizes an important recent contribution to the physics of solids or liquids using x-ray, neutron, or electron diffraction techniques. Authors of works published within a six year period ending June 30 of the year preceding the award may be nominated. Recent recipients of the Warren Award are: Takeshi Egami (2003), Ian Robinson (2000), David Long Price (1997), Michael Bedzyk (1994) and James Jorgensen (1991). Bertram Warren's early interest in silicates resulted in many *Z.Kristallogr.* publications, often with W.L.Bragg as a co-author. During his distinguished career at M.I.T. (1930 -1976) he was known as a brilliant teacher as well as for his pioneering research and his widely used 1969 text *X-ray Diffraction*. His interests included studies of glass structure and carbon black that were at the beginning of small angle scattering research, and the development of mathematical and experimental techniques to study non-periodic and nearly periodic structure, order-disorder, temperature diffuse scattering (TDS), and cold-work imperfections in metals. He was the second president of ASXRED, a predecessor of ACA. Students and friends of Professor Warren established the award when he retired from full time teaching at M.I.T. in 1967, and the first award was given in 1970. The Warren Award Selection Committee is: **Winnie Wong Ng (chair), Takeshi Egami, Doug Dorset, and John Tse**.

Please submit nominations to the **ACA office in Buffalo** (see page 1 for address) no later than **April 1, 2005**. A nominating letter clearly indicating the accomplishments of the individual and a *c.v.* for the nominee are required; additional supporting letters are encouraged. Award recipients will be announced at the 2005 ACA meeting May 28th – June 2nd, and the awards will be presented at the 2006 ACA meeting

Highlights of Summer Council Meeting

The ACA Council met in July, just prior to and immediately after the annual ACA meeting in Chicago. Also, nearly every day during the meeting, council met with the committees that are so vital to the activities of the ACA. These included the *Newsletter* Editors, the Meeting Planning Committee, the standing committees, the SIGs, and the session organizers for the 2005 meeting. It is during these council meetings that the committees and SIGs report on their activities for the past year, propose their plans for the upcoming year, and present any requests to council. These meetings occur only once a year and because they provide an opportunity for direct communication and dialogue, they are valuable to Council, the committees, and the SIGs.

The 2004 Chicago Meeting was a tremendous success. With a grand total of 1213 participants (including approximately 200 exhibitors), the Chicago meeting was one of the largest ACA meetings ever. At the business meeting, Doug Ohlendorf reported on the financial status of the ACA. The ACA works to organize revenue neutral meetings. At times when there are fewer registrants than anticipated, the meetings may be a financial loss, but when the number of meeting registrants exceeds expectations, the annual meeting can generate a small profit, and this influences the following year's meeting registration fee. The 2003 Northern Kentucky/Cincinnati meeting generated a small profit. The 2004 Chicago meeting may also generate a small profit. This puts the ACA in excellent financial health. The membership dues increase, which was implemented over the past three years, has reached its goal. Thus, there will be no dues increase for 2005. The ACA award funds are supported by member donations. Since the funds for the Pauling Prize and for the Warren Award both would benefit significantly from more donations, Council encourages you to consider donating to either or both of these funds. The Pauling Prize is awarded annually to not more than five of the best student poster presentations at the annual meeting. Each award consists of $200, a complimentary ticket for the banquet at the annual meeting, and a copy of Linus Pauling's *General Chemistry*. The Warren Diffraction Physics Award is described in the Call for Nominations on page 9. Your membership dues invoice lists the awards and provides an opportunity to make donations.

The May 2005 Meeting in Orlando is scheduled over the Memorial Day weekend May 28 – June 2. The meeting will be held at the Walt Disney World Swan Hotel. Given that the ACA has the entire hotel, ACA members will greatly outnumber the tourists, thereby providing an ideal environment for scientific discussions. The latest plans for the meeting, abstract deadline, Transactions Symposium details, awards, etc. are on page 75. There has already been much interest expressed in this meeting, so make your reservations early.

Where would you like to meet? Council routinely meets the challenge of determining the annual meeting site. Potential sites are visited by the meetings committee (S.N.Rao, Judith Flippen-Anderson and Marcia Colquhoun) to determine feasibility. (Rao is very experienced at negotiating contracts with the convention center or hotel.) Several factors influence the Council's decision,

Back, l to r: Ray Davis, David Rose, Doug Ohlendorf, Marcia Colquhoun, Bill Duax, Iris Torriani; in front: Lisa Keefe, Fran Jurnak, and Louis Delbaere.

including the availability of a local chair (a highly valued volunteer), an appropriately sized conference facility (the exhibition hall needs to be 25-30,000 sq. ft.), sufficient session rooms in close proximity to each other and to the exhibition hall, reasonable cost for both the conference facilities and for the lodging, and of course an interesting locale for the time of year.

At the business meeting, the membership was invited to propose meeting sites for council to consider, especially for the meeting scheduled for the summer of 2006. There are already two sites under serious consideration for 2006 (Hawaii and Salt Lake City) and several others still under investigation (including Portland, Denver, Colorado Springs, Baltimore, and sites in Canada). While council would like to reach out beyond the US national borders by having the meeting in Canada or Mexico, there is the very real concern regarding the potential difficulty for non-US citizens to re-enter the US at the conclusion of the meeting. The 2006 meeting site should be decided long before this *Newsletter* reaches you, but where would you like to meet in the future? Please e-mail your suggestions to an ACA council member. Email addresses are given in the spring *Newsletter.*

The new Industrial SIG: the British Crystallographic Association (BCA) has a very active subdivision on Industrial Crystallography that organizes sessions for the annual meeting of the BCA and presents an award to an industrial crystallographer. In an effort to reach out to the industrial members of the ACA and ensure that the ACA meets their needs, Bill Duax invited industrial members to gather at the Chicago meeting and discuss the possibility of forming an Industrial SIG which might organize a session for the 2005 ACA Meeting in Orlando. See the article on the next page for the result - a new Industrial SIG that Council supports enthusiastically.

Join the membership: the by-laws of the ACA state that ***the object of this Association shall be to promote the study of the arrangement of the atoms in matter, its causes, its nature and its consequences, and the tools and methods used in such studies.*** ACA members derive benefits from workshops that enhance the hands-on learning experience, from the annual meetings which

provide the forum for presenting scientific achievements, and from the opportunities for professional networking with other members that abound at the meetings. Increasing or at least maintaining the number of members is essential to the success of the organization, so council will continue to strive for innovative ways to accomplish this. At this meeting Council approved a 10% discount in dues for a 3-year or longer regular membership. Council is enthusiastic about offering this incentive and expects our members to embrace this offer. If you choose the multiple year option, please remember that the award funds rely on donations collected at the time of membership renewal. If you so indicate, these donations can continue to be made yearly.

Reaching out beyond our North American borders: Council has been exploring ways to expand the interaction between the ACA and crystallographers from Mexico and from Central and South America. At this meeting a draft policy for country membership was reviewed. The draft is currently being revised by Bill Duax in consultation with Iris Torriani of Brazil (IUCr Representative). The policy proposed offers incentives to students and postdocs as well as to established crystallographers, and offers opportunities for interaction with the ACA at the annual meetings.

New award for software development: Council frequently reviews the various ACA awards and award committees. This summer, Council considered a proposal from Brian Toby that is supported by the Data, Standards, & Computing Committee for an award that would recognize contributions of computer software to the crystallographic community. Acknowledging that to date there are no ACA awards reserved solely for software development, and considering the importance of computer software to the discipline of crystallography, in particular its impact on techniques, and on the pace of structure solution and analysis, Council approved a new award to be given to younger scientists for crystallographic software development which should include a waiver of meeting registration fees. Ray Davis will draft a proposal for the ***Carroll Johnson Award in Computation.***

Taking political action: Fran Jurnak reported on the efforts of the Council of Scientific Society Presidents (CSSP) to sponsor a Fellow to intern with CSSP and lobby for relevant issues (including education, science budget, foreign student visas, and national laboratories and national user facilities such as synchrotrons and neutron facilities). The CSSP has asked for a donation from each member organization. Independently, the Biophysical Society formed the 'Bridging the Sciences' coalition to lobby congress to allocate federal money for supporting research that bridges between the physical/computational and the biological sciences (see article on page 7). ACA council has been asked for a donation for this effort as well. Council will consider these requests at their next meeting. You, as an individual, can be as proactive as you wish to be. The American Institute of Physics, **www.aip.org/gov,** offers tools for scientists as constituents. From their website go to ***Member society policy links*** and then ***American Physical Society*** and access a wealth of information and tools.

Lisa Keefe

New Industrial SIG

A new Special Interest Group was formed at the 2004 meeting to promote the interests of those ACA members who work in commercial environments. The Industrial SIG is intended to represent the entire range of industrial crystallographers, including those engaged in pharmaceutical, chemical, and materials science research, along with equipment and software venders.

The SIG was formed after a number of industrial ACA members responded positively to an e-mail from ACA Executive Officer Bill Duax enquiring about interest in an industry-oriented special interest group. An organizational meeting was held on July 18th at the Chicago ACA meeting. After confirming that the requirements for SIG formation had been met, initial organization of the SIG was discussed, and several ideas for industry oriented session topics at future ACA meetings were generated. Chuck Kissinger agreed to serve as temporary SIG chairman until elections are held. Kevin Parris volunteered to represent the SIG at the program-planning meeting for the 2005 ACA meeting. A session will be sponsored at that meeting by the Industrial SIG with the tentative topic of *High Throughput Crystallography - Crystallization and Imaging*.

If you have questions, comments or ideas concerning the new Industrial SIG, please contact Chuck Kissinger at **crk@stromix.com**.

Chuck Kissinger

Presentation of the Trueblood, Fankuchen, and Supper Awards at their 2004 Symposia

The first **Kenneth N. Trueblood Award**, which recognizes exceptional achievement in computational or chemical crystallography, was presented to Richard E. Marsh, Senior Research Associate, Emeritus, Caltech, at the ACA Annual Meeting. See page 42 for a report on the Trueblood Symposium; Dick's keynote address was *X-ray Diffraction Through the Years: From One Structure per Year to One Structure per Hour*.

ACA President Fran Jurnak presenting Dick with the Trueblood Award. Left, l to r, Ken Hardcastle, Symposium Chair Jenny Glusker, Dick Marsh and Larry Henling. The Dick Marsh T-shirts were done by Larry Henling and Diana St James with assists from Ken Hardcastle, Cora MacBeth, and Barbara Hsu.

The first **Charles Supper Award** was presented to Nguyen-Huu Xuong, Professor of Biology, University of California at San Diego, in the Supper Symposium at the ACA meeting in Chicago. The award recognizes scientists who have made exceptional contributions to crystallographic instrumentation. Excerpts from his delightful keynote address in the Supper Symposium: *Advanced Area Detectors for Protein Crystallography and Electron Microscopy* will be published in either the winter or spring *ACA Newsletter.* A report on the Supper Symposium is on page 40.

At left, Professor Nguyen-Huu Xuong receives the Charles Supper Award presented by ACA President Fran Jurnak..

At left: ACA President Fran Jurnak has just presented the Fankuchen Award to Alex McPherson.

The 2004 **Isidor Fankuchen Memorial Award** was presented to Alexander McPherson in the Fankuchen Award Symposium at the ACA Meeting. The award recognizes the contributions to crystallographic research made by scientists known to be exceptional teachers. Alex was presented with the award by ACA President Fran Jurnak (see photo at left) and he then gave the keynote address for the Fankuchen Symposium: *Where are we going, Where Have We Been*. See the report on the Symposium, page 41.

Note: more complete descriptions of the Trueblood and Supper Awards, and the Award Citations are in the *Winter 2003 ACA Newsletter.* The Fankuchen Award description and the citation for Alex is in the *Fall 2003 ACA Newsletter*.

2004 Etter Award to Leonard MacGillivray

At the 2004 ACA Meeting. the **Margaret C. Etter Early Career Award** was presented to Leonard MacGillivray, Department of Chemistry, University of Iowa by ACA President Fran Jurnak. The award is described in the *Winter 2003 ACA Newsletter*. Leonard's lecture: *Linear Templates: Tools for Constructing Molecules in the Solid State* was presented at the Etter Symposium organized in his honor; the report is on page 37.

Editor's note: see also the report on the Transactions Symposium, page 36. Leonard's presentation in the Crystal Structure Design session was Metal-organic Polygons, Polyhedra, and Extended Frameworks Derived from Molecules Constructed in the Solid State. His ladderane structure was featured on the cover of the Spring 2004 ACA Newsletter.

At right, Joel Harp with Jesse Rowsell. Above, Jesse at the ACA Banquet after he received the prize.

Oxford Poster Prize

The 2004 Oxford Cryosystems Low Temperature Poster Prize was awarded to Jesse Rowsell, University of Michigan, for his elegantly presented poster PPX231: ***Low temperature Investigation of Gas Molecules in a Porous Metal-Organic Framework***. This work employed a helium cryostat to investigate physisorption of gases in a large pore material and revealed the structural details of the binding that occurs at low temperatures. These studies are part of a larger project aimed at producing effective gas storage devices for use in, for instance, hydrogen fuel cells. The selection committee: Joel Harp (chair), Judith Gallucci, Tina Izard, Kathryn Kantardjieff, and Michael Sabat followed previous recommendations (see *Fall 2003 ACA Newsletter*) to focus on posters containing work that specifically dealt with the use of low temperature.

There were many excellent posters including one presented by Teresa De la Mora-Rey from the U. Minnesota, PPX137: ***Catching Catalysis in the Act: Using Single Crystal Kinetics to Trap Methylamine Dehydrogenase Reaction Intermediates***. De la Mora-Rey used a microspectrophotomer to follow the reaction in mounted crystals. Also of special note were entries by Stephan Ginell, APS: PX162: ***Structure of Aldose Reductase-Inhibitor Complexes at Ultra-High Resolution from Helium Cooled Crystals*** and from T. Petrova, CNRS, Illkirch, France, PPX032: ***Comparison of Inhibitor Binding Modes to Aldose Reductase at Subatomic Resolution***. Both posters represent work utilizing low temperature data collection to reduce temperature factors for exciting ultra-high resolution studies.

Joel Harp

Cartoon #79 by Nick D. Kim, Department of Chemistry, University of Waikato, New Zealand To see Nick's other cartoons, visit: http://nearing-zero.net/chem.html.

Pauling Poster Prizes

L to r: Ruchi Anand, Kacey Claborn, Jason Key, Pauling Committee Chair Paula Fitzgerald, Erika Soriano and Shilpa Sambashivan.

It was a pleasure to chair the committee that selected the winners of this year's Pauling Prizes for outstanding student poster presentations. I was particularly taken with how our field has progressed in the fifteen years since I last chaired this committee - the problems that students today are studying are so much more challenging than they were back then, but the tools they have available are also so much more powerful. With so many excellent eligible posters, selecting the winners was a daunting task, and I greatly appreciate the efforts of the Pauling Prize committee: Philip Fanwick, Barbara Golden, Pawel Grochulski, Michael Weiner, John Rose, and Ron Stenkamp. We are pleased to recognize these five posters selected as the 2004 Pauling Prize winners:

Ruchi Anand, Cornell U., PPX270: ***Domain Organization of Salmonella typhimurium Formylglycinamide Ribonucleotide Amidotransferase Revealed by X-ray Crystallography***, Determination of the structure at 1.9 **Å** resolution reveals four domains, with a bound structural ADP molecule and a glutamyl thioester intermediate. The structure suggests that a channel in the N-terminal domain may pass ammonia between two of the other domains.

Kacey Claborn, U. Washintgon, PP180: ***In Search of the Structural Determinants of Optical Activity.*** This work involved a system that allowed imaging of the CD signal of a crystal on a CCD. The optical rotation signal results from the covalent structure of the molecules within the crystal and the chirality of the crystalline matrix. Using this technology it was possible to study and resolve twin domains within the crystals they were studying, and to generate strikingly beautiful pictures.

Marilise A. Hyacinth, U. Virginia, PPX232: ***Structure of Supramolecular Synthons Based on Propargylic Alcohol Derivatives.*** Chiral secondary polyargylic alcohols were used to study the determinants of chiral recognition and discrimination. The interactions between molecules shift dramatically as the composition and chirality of the synthons are varied.

Jason Key, U. of Chicago, PP159: ***Time-resolved Crystallographic Studies of The Heme-based Sensor FixLH.*** Time-resolved studies were combined with static structures to probe signalling in this non-globin heme-binding sensor. These studies revealed the molecular motions that accompany photo-induced release of CO from the heme, and follow the structural relaxation of the protein to the deoxy conformation.

Shilpa Sambashivan, UCLA, PP110: ***Understanding the Structural Basis for Amyloid Fiber Formation of Ribonuclease A.*** Ribonuclease A was used a model system for studying the formation of fibers much like the amyloid fibers that are associated with a number of neurodegenerative diseases. This work uses two aspects of the system-fiber formation of the N-terminal S-peptide and fiber formation by glutamate enriched mutants of the intact enzyme to study the residue interations that lead to fiber formation.

Marilise Hyacinth was not shown in the group photo - here she is with her winning poster.

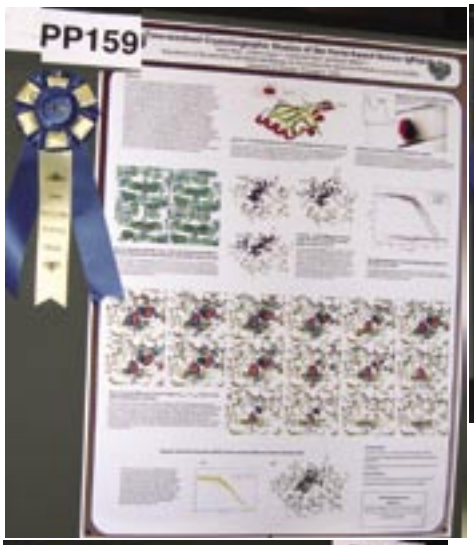
We are also delighted to announce three poster presentations selected for honorable mention.

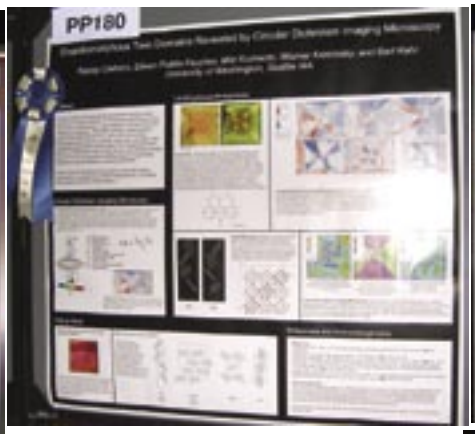
Paul A. Del Rizzo, U. Western Ontario, PP129: ***Structure Determination of the ATP Synthase Peripheral Stalk.*** This study attempts to extend the structural understanding of the role of the b_2 dimerization domain of peripheral stalk. Previous crystallographic studies of the b_2 domain had been in the monomeric state, but now suitably diffracting crystals have been obtained of the more relevant dimeric form.

Brian Dempsey, U. Western Ontario, PP088: ***Unique Zinc Coordination by the C-terminal Domain of SecA.*** Combining EXAFS and NMR techniques, this work showed that the Zn binding site of a SecA peptide is highly unusual. Two of the zinc ligands, C19 and H20, are adjacent in the amino acid sequence, and this sequence proximity results in geometric strain. To achive coordination with the zinc, the His must interact with the zinc with the imidazole ring out of plane.

Erika Soriano, Cornell U., PP133: ***Structural Studies of Pyruvoyl-Dependent Arginine Decarboxylase from Methanococcus jannaschii.*** In this work, two mutants of the enzyme were prepared to test the hypothesis that residues Asn47 and Glu109 were essential to the self-processing activity of the enzyme. Both mutants were crippled enzymatically, as predicted, and crystallographic determination of the strucutres of the enzymes revealed the structure explanations for the loss of activity.

Paula Fitzgerald

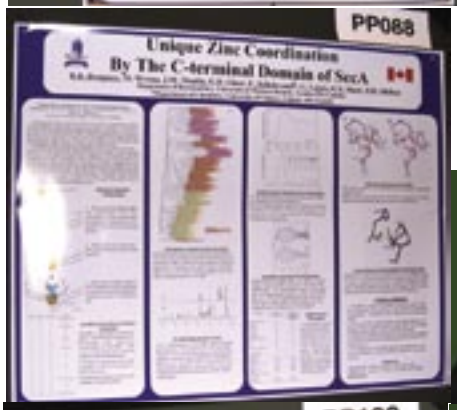


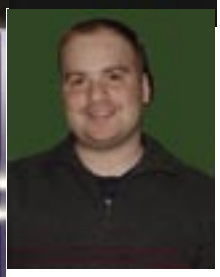


The Pauling Prize winners: ***CW from top left: PP159 by Jason Key; PP180 by Kacey Claborn, PPX270 by Ruchi Anand, PP110 by Shilpa Sambashivan.***

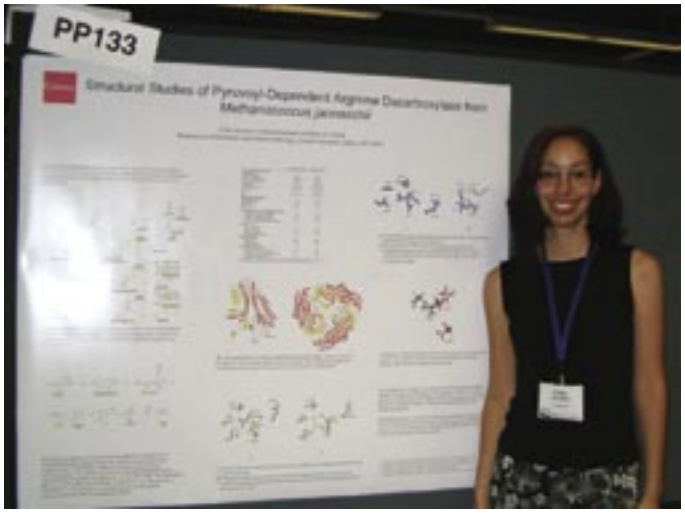
Pauling Honorable Mention winners

At left, PP088 by Brian Dempsey; below, PP129 by Paul Del Rizzo. Brian and Paul were not in the group photo.



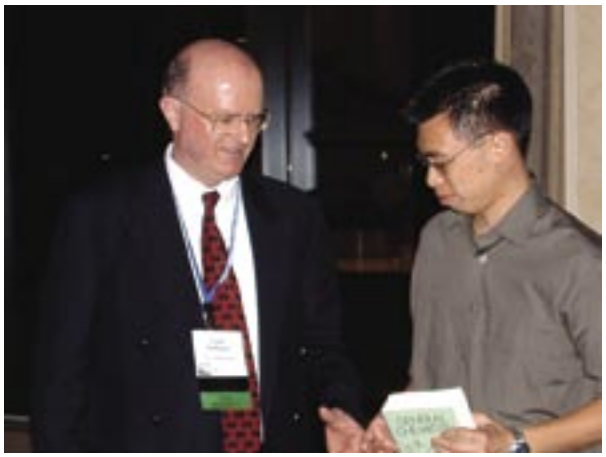


At right, PP133 by Erika Soriano

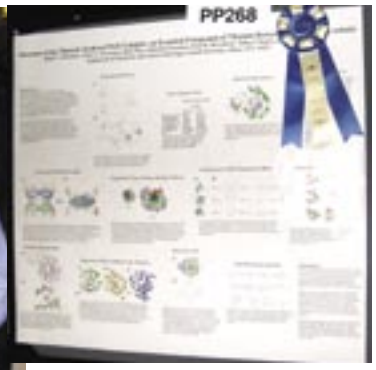


Canadian Pauling Prize

The first **Canadian Pauling Poster Prize** sponsored by the Canadian National Committee of the IUCr was presented to Jeff Lee, The Hospital for Sick Children, Toronto, CA. The Canadian Division was represented on the selection committee by Pawel Grochulski. Jeff's winning poster is PPX047, ***Pico- and Femtomolar Transition State Inhibitor-complexes of MTA/AdoHcy Nucleosidase.***



At right, at the Awards Banquet, ACA Vice President Louis Delbaere presents the Canadian Poster Prize to Jeff Lee.



L to r, ACA Canadian Representative David Rose, IUCr Representative Iris Torriani, IUCr President Bill Duax, and Ethan Settembre. The green hats are to celebrate the newest IUCr journal Acta F.

IUCr Poster Prize

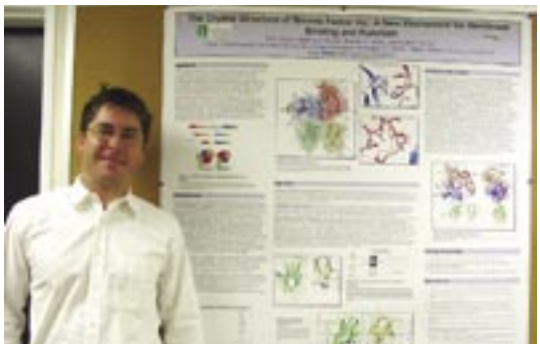
The Executive Committee of the IUCr inaugurated a new series of awards to be presented at meetings of the regional affiliates and national associations. The award consists of either complimentary online access to all IUCr journals for one year or a volume of International Tables or other IUCr publication. Eligibility is the same as that for the Pauling Poster Prize.

At the 2004 ACA meeting, the first IUCr Poster Prize was presented to Ethan Settembre, Cornell Univ., for PP268: ***Structure of the Thiazole Synthase/ThiS Complex, an Essential Component of Thiamin Biosynthesis in Bacillus subtilis.***

RCSB PDB Poster Prize

The Research Collaboratory for Structural Bioinformatics PDB Poster Prize was awarded to Ty Adams, U. of Vermont, for PP068: ***The Crystal Structure of Factor Va: A New Mechanism for Membrane Binding and Function***. The award was *Biochemistry - Vol. I* by Donald and Judith G. Voet and a signed copy of *Introduction to Macromolecular Crystallography* by Alexander McPherson.

Special thanks to the students who participated, and to the judging committee organized by Edward J. Collins: Jung-Ja Kim (Chair), Richard Brennan, Carolyn Brock, John Chrzas, and Nick Sauter.



Ty Adams with PP068

David Blow 1931 - 2004

The determination of the three-dimensional structure of proteins by x-ray crystallography was one of the critical developments in the explosive growth of biological sciences and the associated arrival of modern biotechnology since the 1950's. David Blow was an undergraduate physics student in Cambridge in the early 50's and made fundamental contributions both to the development of the methods used in crystallographic analysis of large biological molecules, and to solving the crystal structures of several key enzymes

After David's graduation he found his way to Max Perutz in the Cavendish and studied crystallographic techniques that he and his mentor hoped would lead to a three dimensional structure of haemoglobin. This was not a popular or fashionable topic at the time. Indeed many doubted that proteins such as hemoglobin even had a unique structure and many conventional crystallographers wondered whether Perutz and Sir Lawrence Bragg (the Cavendish Professor), were wasting their time on frivolous pursuits. However, others saw Perutz as having a far wider appreciation of science than his critics. Indeed he had obtained funding from the Medical Research Council (MRC) and the Rockefeller foundation and was willing to give David a chance as a research student. It soon became apparent that Max Perutz's little MRC unit had more potential than appearances suggested. For instance it housed Francis Crick and Jim Watson who spent their time talking and making the century's most important biological discovery, namely the structure and function of DNA, the genetic basis of inheritance. David benefited greatly from this stimulating environment. It is not surprising that one of the important scientific contributions he made as a graduate student was described in a paper coauthored with Crick[1] which showed how to minimize the effect of experimental errors in the calculation of protein electron density maps.

David married Mavis Sears in 1955 while he was a graduate student. Two years later they left for America where David had been awarded a Fulbright travel grant and enjoyed a post-doctoral position in Alex Rich's laboratory at NIH in Bethesda, close to Washington. Halfway through his stay in the US, Alex moved to MIT in Boston and David moved with him. Alex's laboratory was in many ways an extension of the Cambridge experience for David in that Alex himself had been a frequent visitor to Cambridge and had become interested in the fiber diffraction techniques that had been used for the study of DNA.

It was while David was spending two years in America that I joined Max's unit. During my first year with Max we were able to obtain a low resolution structure of haemoglobin, while John Kendrew obtained a near atomic resolution structure of the related oxygen carrier, myoglobin. The evolutionary significance of these two related structures no doubt contributed greatly to the subsequent award of a Nobel prize jointly to Max and John. Although David missed these exciting times, they formed the basis of our joint work and both of our subsequent careers.

When David returned to Cambridge in 1959 on Max's invitation, he was given desk space in the same small room as I was already sharing with two other visitors. Whenever David or I sat down at our respective desks we invariably bumped into each other. But

David Blow taking an interest in the projects of First Year Physics students Gary Seaborn (at left), and Perry Musty.

Photo courtesy of Nick Jackson, Photography, Blackett lab, Imperial College, London.

we bumped into each other in more than a physical way, for we quickly established a close friendship and intellectual collaboration. I discovered that David had a missionary Methodist background having been educated at the Kingswood School in Bath, which was originally founded by John Wesley. Indeed David's background and my Quaker schooling had much in common. We were also at equivalent stages of our careers, having both spent two years as post-doctoral researchers in American laboratories before returning to England.

In the next five years we wrote a series papers together which were to form the rudiments of much of protein crystallography, the technology that would provide in subsequent years the three dimensional atomic structures of tens of thousands of biological macromolecules. Such information has become essential for drug design by the pharmaceutical industry and is a major unifying topic in modern biology. But in those years that David and I worked closely together we had little idea of the future developments that would take off with exponential growth in the mid 80's.

David Harker[2] had shown that it was necessary to have at least two isomorphous heavy atom derivatives to determine the phases of the native structure factors and the structure determinations of myoglobin and hemoglobin had used six or more difficult to prepare compounds. David (Blow) and I were able to show that one compound could be sufficient to obtain an interpretable map with a single isomorphous replacement (SIR) heavy atom derivative.[3] In the same paper we were able to show that the anomalous dispersion information for the single derivative (SAD) provided considerable additional power, even in the absence of the powerful intensity integration techniques used universally today. At about the same time we pointed out that there are convenient coefficients that can express the relationship between phase angle and phase probability and can be used to correctly combine a variety of phasing information.[4] In this paper we also analyzed the diminishing returns provided by each additional heavy atom derivative. The ideas of this paper were incorporated by Hendrickson and Lattman[5] in their subsequent discussion of the same problem. Perhaps our most important

contribution was the first paper on molecular replacement[6] in which we introduced the concept of non-crystallographic symmetry (NCS) and derived an expression for the rotation function, which we tested on its ability to detect the similarity of the α and β chains of hemoglobin.

It had been David's initiative to study the digestive enzyme, chymotrypsin, which he had learned about from another lifelong colleague, Brian Hartley whom he had met in the 1950s. For a number of years we did this work together, solving many of the technical problems that led to later success.[7] That work came to fruition[8] two years after I left Cambridge for America, when David's group solved the structure of what was then only the third or fourth protein structure and the second enzyme structure to be known. In the world of biology, David is probably best known for his contribution to the discovery of the catalytic ser-his-asp triad mechanism of serine proteases through his work on chymotrypsin. Similar mechanisms have since been found in a vast number of basic biological processes ranging from blood clotting to viral maturation. He was elected Fellow of the Royal Society in 1972, he received the Charles Leopold Meyer Prize of the French National Academy of Sciences in 1979 with (the late) David Phillips, the Israeli Wolf Prize for Chemistry in 1987 and was elected a Foreign Associate of the French Academy of Sciences in 1992.

David left Cambridge in 1977 to set up a biophysics unit at Imperial College in London. Here his research group determined one of the first structures of a tRNA synthatase,[9] an enzyme that translates the three letter code of nucleic acids into one of the 20 amino acids that occur in proteins. He also initiated research on cholesterol oxidase, an enzyme that links steroid structure and chemistry to interactions with protein surfaces, and sucrose isomerase which is an enzyme important in the commercial production of invert sugar. The structures of both were soon solved. David also devoted time to fostering and encouraging research into protein crystallization, a critical but uncertain step in protein crystallographic technology.

With the fame that David accrued on account of his scientific successes came responsibility. In 1991, he was reluctantly persuaded to be head of the Physics Department, a job that no true scientist is likely to enjoy. One of the important services that David gave to British science was to assist in the birth of the British Crystallographic Association of which he was president from 1984 to 1988. Prior to its existence, crystallographers in Britain had been narrowly organized by the Institute of Physics, a hold over from the time when the subject was considered primarily suitable for physicists. In contrast the now buoyant BCA spans physics, chemistry, biology and materials sciences.

In due course David took early retirement, retreating to Devon in 1994, where he and Mavis long had family connections. He paid frequent, often weekly, visits to London writing a book modestly entitled *An Outline of Crystallography for Biologists*. He also wrote scientific reviews and took on numerous voluntary jobs for the benefit of other scientists. Although he was no longer deeply engaged in research, he remained much in demand as a lecturer, especially to give courses on x-ray crystallography. David's scientific contributions and his enthusiasm for the subject gave these lectures authority and popularity. David will be remembered for his unique approach to research, his work on crystallographic methods, his contributions to the understanding of protein structure and enzyme mechanisms and his advice on dealing with the complex issues that arose as structural biology moved from being merely of academic interest to being central to the pharmaceutical industry.

My last letter from David, shortly before his death, ended with "We shall both always remember the wonderful years when we worked together". He is survived by his wife Mavis, his son Julian a biologist at the University of Dundee, his daughter Elizabeth, and their families including five grandchildren as well as many friends the world over.

I thank Guy Dodson of the University of York and Richard Henderson of the MRC Laboratory of Molecular Biology in Cambridge for their help in writing this article.

Michael G. Rossmann

Another version of this obituary was published in *The Guardian*.

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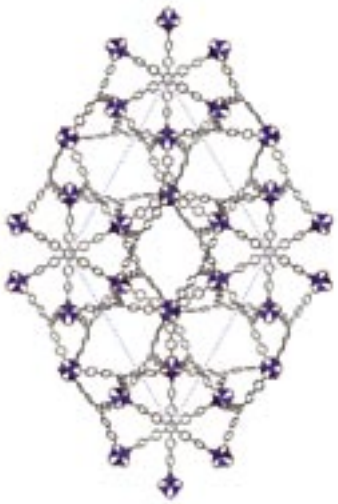

From Omar Yaghi; see page 63.

ACA CORPORATE MEMBERS

Area Detector Systems Corp.
www.adsc-xray.com

Art Robbins Instruments
www.artrobbinsinstruments.com

ATPS Inc.
www.atpsinc.com

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Hannover, Germany

Blake Industries, Inc.
blake4xray@worldnet.att.net

Bruker AXS Systems
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Cambridge Crystallographic
Data Centre
www.ccdc.cam.ac.uk

Charles Supper Company, Inc.
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Corning, Inc.
www.corning.com/lifesciences

Cryo Industries of America, Inc.
www.cryoindustries.com

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Protein Data Bank
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John Maxwell Cowley 1923 - 2004

John M. Cowley, 81, Regents' Professor Emeritus in the Department of Physics and Astronomy at Arizona State University, died suddenly on May 18. Cowley was born Feb. 18, 1923 in Adelaide, Australia. He earned his master's degree from the University of Adelaide in 1945, and his doctoral degree from the M.I.T. in 1949. Cowley was employed by the Commonwealth Scientific and Industrial Research Organization in Melbourne, Australia, from 1945 to 1962, starting his career as assistant research officer and later becoming chief research officer and head of the crystallography section. He began his academic career in 1963 when he was appointed the Chamber of Manufacturers' Professor of Physics at the University of Melbourne.

Cowley joined ASU in 1970, when he was recruited for the university's first endowed chair, the Galvin Professorship in Physics. He founded the electron microscopy facility, which under his leadership came to be recognized as the premier electron microscopy center in the world, and he served as the facility's director from 1983 to 1990. The Center produced many outstanding doctoral students and attracted many leading scientists and post-doctoral researchers from around the world. Cowley's scientific leadership over the years is widely regarded as playing a highly significant role in establishing ASU as a Research I University.

In 1988, Cowley was among the first group of distinguished faculty bestowed with the title Regents' Professor, an honor reserved for a limited, small fraction of the faculty who have demonstrated exceptional scholarship and outstanding achievements. He officially retired from the university in 1994 but he continued to be highly active. He spent time in his campus office almost every day, including the day of his death.

In January 2003, an international workshop was held on the ASU campus to celebrate Cowley's 80th.

birthday and the 25th anniversary of the Center for High Resolution Electron Microscopy. At the Symposium dinner, Cowley was acclaimed by the attendees, who came from all over the world, for his pioneering contributions in the fields of electron microscopy, diffraction and crystallography. In October 2003, the Center for High Resolution Electron Microscopy was re-named in his honor.

Cowley was an extraordinarily productive scientist with an illustrious career that spanned more than five decades. His ideas, enthusiasm and basic understanding of electron optics and diffraction phenomena provided inspiration and leadership to the entire field of electron microscopy. His monograph ***Diffraction Physics*** is the standard reference in the field. He received the highest awards of the IUCr, the Electron Microscopy Society of America and the ACA, and he was honored by election to Fellowship of the Australian Academy of Science, The Royal Society of London, and the American Physical Society.

John Maxwell Cowley was universally admired by his peers and colleagues as a great scientist with a kind and generous personality who was always supportive. His passing is a grievous loss to the campus microscopy community and the entire field of electron microscopy, which benefited greatly from his guidance and leadership. He is survived by his wife of 52 years, Roberta, two daughters Jillian and Deborah, and two grand-children.

David Smith, ASU

Editor's note: ***In 1976 John Cowley, together with S. Iijima, received the Bertram Eugene Warren Diffraction Physics Award for "High Resolution Electron Microscopy of Crystal Structures." At the 1987 IUCr meeting in Perth, Australia, John Cowley and Alexander Moodie were awarded the First Ewald Prize. From the citation for that award: "A theory of Fourier images led them to the multi-slice formulation of the scattering of an electron wave in its passage through a crystal. This formulation is able to take into account many hundreds of scattered beams, and has become the basis of widely-used computer programs. The theory allows the electron micrographs, obtained with modern high resolution instruments, to be reliably and quantitatively interpreted, and used for the determination of the structures of both perfect crystals and crystals containing defects. Professor Cowley and Dr. Moodie, together and separately, have made many further contributions to theory, methods and results in electron diffraction and microscopy. Their work has often stressed a unified approach to diffraction and microscopy through physical optics. An overview of the whole field may be found in Professor Cowley's book Diffraction Physics (1981).***"

Confessions of a Cowleyphile -An Appreciation*

I had originally begun work in electron diffraction to examine materials that refused to crystallize to sizes suitable for x-ray data collection. Funded by a freshly-minted NIH grant, promising to determine lipid structures with electron diffraction data, it soon became apparent that my thesis advisor's warning might have been correct, and that I was indeed in hot water over my head! Somewhere during a frustrating struggle with incomprehensible physics papers, attempting to understand what was going wrong with my data, I began to write Professor John Cowley to ask him questions about dynamical scattering theory. I had often examined his well-written papers that conveyed concepts even if I could not always follow the mathematics. (I am a chemist, not a physicist.) Since he did not know me, he had no pressing reason to answer my queries, but, faithfully, I received long, patient letters back from him with clarifications so that I eventually learned. Later, I was able to pose questions to him at scientific meetings. He was always courteous and I soon learned that one should listen carefully to every word that he spoke because each was pregnant with meaning. The eventual appearance of his excellent monograph, ***Diffraction Physics***, was also a godsend to me. Once, I asked him about what one should do about determining crystal structures from such data and he encouraged me always to try a kinematical approach first. This was a time when the stated *impossibility* of such an endeavor almost became an article of faith in a weird scientific imitation of a Cold War struggle - it was regarded as madness to determine structures from such data, even (especially!) if the Russians said it was OK. However this formulator of multiple beam dynamical theory had also attempted to solve structures from electron diffraction data and had actually made some progress. A careful reading of Cowley's work in the 1960's revealed that he was one of the few in the West who bothered to read the Russian publications in this field to understand what they were doing with texture diffraction data. (He actually justified some of their assumptions from a more rigorous theoretical framework, and, had other electron diffractionists paid similar attention, perhaps the precession method for electron diffraction would have been invented much earlier.) In short, John Cowley always took the time to listen and to understand, revealing his fundamental respect for fellow researchers, no matter how political boundaries were drawn. He was obviously more interested in finding truth than spouting scientific dogma.

In my career, I have been lucky enough to meet many great crystallographers and diffraction physicists of preceding generations - people who actually began great things - but few, I feel, have been of the intellectual caliber of John Cowley, who was the consummate scholar and innovator of his field. While he did not suffer fools, he was always generous to the honestly inquisitive and always found time to talk with them. I last saw him in 2000 when I gave a lecture in a series to celebrate the 25th anniversary of the Center for Solid State Science at ASU. Although "retired" he was still working on the VG instrument and he joyfully demonstrated to me how he could walk a 5 Å diameter electron beam through the unit cell of a crystal. His life's work touched on many topics of diffraction and microscopy and it was all good.

I am, above all, grateful to John Cowley for his generous advice to a kid from the cornfields of Pennsylvania, and his encouragement and help in later stages as research efforts began to succeed. To this day, my feelings for him would be best described by the German word, *Ehrfurcht*. I am grateful to have broken bread with this master, who, by his kindness and basic humanity, on top of manifold accomplishments, has greatly enriched my life and work.

Doug Dorset

**** I was once called this by Elmar Zeitler when he was at the Fritz-Haber-Institut in Berlin-Dahlem; indeed, it was a correct identification.***

Carl-Ivar Brändén 1934 - 2004

Science lost a valued citizen on April 28 when Carl-Ivar Brändén succumbed to lung cancer following an eighteen-month battle. Brändén was a prominent member of the structural biology community.

Carl grew up in Lappland in northern Sweden, where his father was the teacher in a one-room schoolhouse. His active and free childhood instilled a life-long love of exploration and nature. At the same time he developed a strong desire to expand his horizons beyond the frozen north, and decided that a good education was his ticket to rest of the world. This led him, from age 13 onward, to schooling away from his family and eventually to Uppsala University.

Carl's higher education in science was characterized by an ability to take opportunities where and when he found them and by an intellect that was restless unless challenged with an important problem. He began studying mathematics and physics at Uppsala University, but, bored by the undergraduate physics curriculum and inspired by Linus Pauling's texts, he switched to chemistry. An early and important mentor was Prof. Ingvar Lindqvist, who invited Carl into his lab for PhD studies in chemical crystallography. During his studies with Lindqvist, Carl co-authored a least-squares refinement program for the first Swedish electronic computer and used it to refine the structures of several metal coordination complexes he had solved. Again bored and on the verge of leaving both crystallography and chemistry, Carl was enticed to the new field of protein crystallography by a lecture course in biochemistry. Thus he leapt at a postdoctoral opportunity to develop refinement methods for myoglobin with John Kendrew at the MRC lab in Cambridge, UK, where in 1962 joined the first generation of protein crystallographers. In the company of Max Perutz, John Kendrew, Francis Crick, Fred Sanger, Michael Rossmann, David Blow, Sydney Brenner, Aaron Klug, Lubert Stryer, Richard Henderson and many others, Carl experienced the heady early days of molecular and structural biology and celebrated the Nobel prizes to Crick, Watson and Wilkins and to Perutz and Kendrew.

Carl returned to Sweden in 1963 with great enthusiasm for establishing a new research program in protein crystallography. This was not easy, given the resources then available to young scientists starting careers in new (and expensive!) fields. After nearly a decade of work in difficult conditions, Carl had established a group and solved the structure of the enzyme alcohol dehydrogenase. As for all protein crystal structures at the time, the structure determination was a stunning technical achievement, in which x-rays were produced by sealed-tube generators, diffraction was recorded on photographic film, and diffracted intensities were measured manually. All crystallographers remember the thrill of their first solved structure. I imagine that Carl's thrill upon completing the polypeptide chain trace of alcohol dehydrogenase was many-fold greater than what we experience today, due to the years of hard work and struggle that preceded it. Alcohol dehydrogenase was followed by many other crystal structures from Carl's group, notably ribulose bisphosphate carboxylase and thioredoxin. However, alcohol dehydrogenase stood apart because Carl's interpretation of his new structure led to concepts of fundamental importance to biology.

Carl tackled the alcohol dehydrogenase structure at the same time Michael Rossmann and his group were working on the crystal structure of lactate dehydrogenase. From comparison of low-resolution electron density maps, Carl and Rossmann predicted that these apparently unrelated dehydrogenases use a common fold to bind their common co-factor (NAD). It was another four years before both structures were solved in sufficient detail to prove the hypothesis. This also proved to be one of the great "Aha!" moments of molecular biology, in which new information fundamentally changes our thinking about an important problem. The crystal structures showed that although the dehydrogenases had no obvious sequence similarity, they employed the same architecture to perform the same function. Carl and Rossmann concluded immediately that the dehydrogenases had diverged from a common ancestor, and realized that protein structure is more conserved than amino acid sequence. Their excitement about this discovery fairly leaps from the pages of their 1973 correspondence. Eventually light bulbs went on in heads around the world, and a new era of protein structure analysis was born. This discovery, and others that soon followed, led to the sequence-structure analysis that is enormously important to biology today, and to new scientific directions for Carl at the time.

Given the importance of the dehydrogenase discovery, what other fundamentals may lie hidden in the detail of protein structures? Here was an intellectual challenge that fascinated Carl for the remainder of his life. Here was an important problem in which Carl's clear vision, evident in so many areas of his working life, was especially valuable. And herein lies, arguably, his greatest scientific legacy. Protein molecules are treasure troves of interesting detail, interesting to structuralists but not to most biologists. Carl distilled the essence of the detail and presented a clear summary of the most relevant big-picture items. He is credited with recognizing that the active sites of enzymes occur in common locations on their folds: the "top" of the familiar $(\beta/\alpha)8$ barrel, the commonest enzyme fold, and the topological

crossover point of open, parallel β-sheet folds. His ability to communicate essential structural details to a general audience is most evident in his highly successful text *Introduction to Protein Structure,* co-authored with John Tooze. Each drawing in the text, touched by Carl's own hand, illustrates an important point, stripped of distracting detail. This is exactly what biologists need to apply structural information to biological problems. This interpretation of crystal structures helped turn "protein crystallography" into "structural biology." As the rate of structure determination accelerated and with the advent of protein engineering and genomics, Carl was among the first to understand that protein structure was critical to the progress of basic biology, medicine and agriculture. So convinced was Carl of the importance of structure to biology, that in 1993 he joined Wayne Hendrickson in founding the journal ***Structure***, which has become a premier structural biology forum.

Clear vision was also a hallmark of Carl's work in science administration. As he became a senior member of the Swedish scientific community, Carl felt a special responsibility towards younger scientists. He never forgot the importance to his own advancement of his mentor Ingvar Lindqvist, and took great delight in helping younger scientists he thought were able to contribute in important areas. Help came in the form of positions, laboratories, funding and encouragement. Carl did this through his work with Swedish funding agencies, at the European Molecular Biology Organization and on various national and international advisory groups. The vibrant Swedish structural biology community has many outstanding members who were trained, recruited or promoted by Carl. He worked for several years as a member of the Nobel Committee for Chemistry. Always with an eye to the bigger picture, his many science policy activities consistently advanced good science and scientists. Much of his administrative and policy work was done behind the scenes by quietly but persistently promoting projects and people he felt were beneficial to the advancement of biology. His work at the European Synchrotron Radiation Facility (ESRF) is a good example. Near the end of his career, he spent five years in Grenoble in order to give structural biology a solid foundation at the new European synchrotron. Today the ESRF leads the world in providing experimental facilities for macromolecular crystallography.

Carl, known as Calle to family and friends, had a great love of life, and of bright and lively people. I knew him best during his years at the ESRF, which I believe were typical of his approach to life. While in Grenoble, Calle assuaged his homesickness with frequent outings in the mountains, followed whenever possible by a good meal. Together with his wife Malin Åkerblom, he searched out good art in small places in the South of France. He made a research project of stocking a wine cellar for his return to Sweden. He provided a warm welcome to many interesting visitors to Grenoble. And he continuously supported and advanced the best ideas and the best people in structural biology. I last saw Calle at the Advanced Photon Source less than eight months before his death, and was impressed with his courage in the face of illness, his determination to fight cancer, his will to live and work fully for as long as possible,

Carl-Ivar Brändén at his forest home.

and his peacefulness. He told me how fortunate he felt to have had a long working life without a single boring day, and to have shared his life with his wife, two sons and grandchildren. What a lesson for us all.

We shall miss him, his clear vision, and his love of good science, good living and good people.

Janet L. Smith

This obituary was first published in *Acta Cryst.* D60, 1509-1511.

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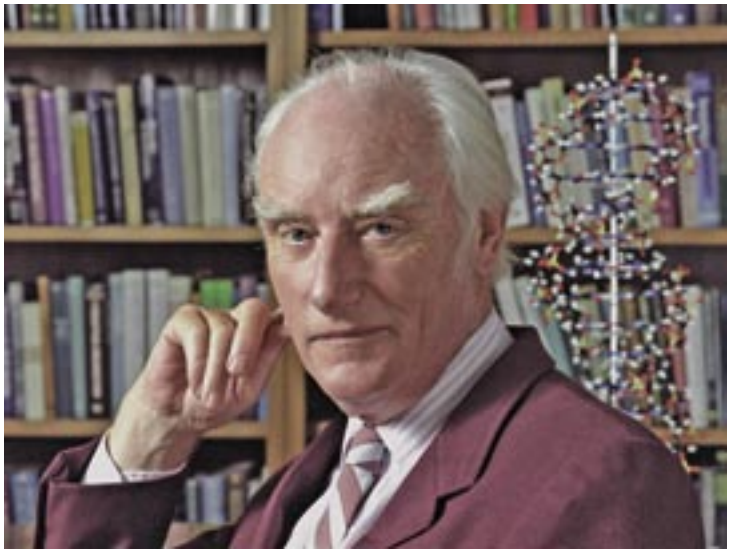
Francis Crick 1916-2004



Francis Harry Compton Crick, who shared the 1962 Nobel Prize in physiology or medicine with James Watson and Maurice Wilkins for discovering the structure of DNA, died July 28th after a long battle with colon cancer. He was 88.

To those who knew him best, it was Crick's insatiable curiosity about life and the creativity of his mind that set up him apart from others. In recent years, he put these qualities to work in an attempt to find the neural correlate of consciousness, a problem he defined as the search for the link between the mind and the brain. Although he was a pathfinder in this young field, he knew that it would take younger minds than his to one day untangle the myriad mysteries of the human brain. When asked what he hoped his future contributions would be, Francis said, "To excite younger people to study the problem of consciousness." Christof Koch, a professor of neuroscience at Caltech and one of Crick's collaborators said "Francis delighted in playing the important role of devil's advocate for several generations of young researchers."

Born in Northampton, England, on June 8, 1916, Francis Crick showed an early curiosity for all things, but for science in particular. To help answer his many questions, his parents Harry Crick and Annie Elizabeth Wilkins bought their young son a Children's Encyclopedia that covered a vast range of topics, from history and music to science. But the subjects that intrigued him the most centered on things like the nature of the galaxy, chemistry and how things were made of atoms. Later, Crick studied physics at University College in London, where he received a bachelor of science degree in 1937. He began studying for his Ph.D., but this work was interrupted by the outbreak of war in 1939. During World War II, he worked as a scientist for the British Admiralty, helping to design magnetic and acoustic mines.

When the war ended, however, Crick found himself less interested in physics and somewhat vague about what he wanted to do with his future. "I still didn't know much about anything so I could go into whatever I wanted," Crick recalled in 1997 during an honors seminar lecture at Rutgers University. "I used what I call the *Gossip Test* to decide what I wanted to do," he said. "The gossip test is simply that whatever you find yourself gossiping about is what you're really interested in. I had found that my two main interests which I discussed the most were what today would be called molecular biology, what I referred to as the borderline between living and the nonliving, and the workings of the brain."

In 1947, Crick turned to studies in biological research at the Strangeways Laboratory in Cambridge, At that time, Crick knew little biology and practically no organic chemistry or crystallography, however he soon went beyond the fundamentals in each of these areas. In 1949, he joined the Medical Research Council (MRC), and in 1951 met James Watson, a young American graduate student. Two years later the two men used their respective knowledge of genetics and x-ray diffraction, along with x-ray images from Rosalind Franklin and Maurice Wilkins, to determine the structure of DNA. Crick and Watson subsequently suggested a general theory for the structure of small viruses. Later, in research with Sydney Brenner, Crick developed ideas about protein synthesis *(the adaptor hypothesis)* and the genetic code.

By 1966, sensing that the foundation for molecular biology was adequately set, Crick turned his attention to embryology. Then, in 1976, he joined the Salk Institute for a sabbatical year away from the MRC. The following year, he left the UK for the Salk Institute in La Jolla, CA, where he pursued his interests in understanding the brain and the nature of consciousness.

In the epilogue of his book ***What Mad Pursuit: A Personal View of Scientific Discovery,*** Crick says that the brain sciences today are reminiscent of the state of molecular biology and embryology in the 1920s and 1930s. "The brain sciences still have a very long way to go," he writes. "But the fascination of the subject and the importance of the answers will inevitably carry it forward. It is essential to understand our brains in some detail if we are to assess correctly our place in this vast and complicated universe we see all around us." A new Center for Computational and Theoretical Biology at the Salk Institute will bear Francis Crick's name.

Aside from more than 130 published papers in his life, Crick also wrote several books including ***Molecules and Men*** (1966), ***Life Itself*** (1981), ***The Astonishing Hypothesis,*** and ***The Scientific Search for the Soul*** (1994). In addition to the Nobel Prize, his honors included the **Lasker Award**, the **Award of Merit** from the Gairdner Foundation, and the **Prix Charles Leopold Meyer** of the French Academy of Sciences. He was a member of the U.S. National Academy of Sciences, the Royal Society, the French Academy of Sciences and the Irish Academy.

Crick is survived by his wife, the artist Odile Speed; two daughters by this marriage, Gabrielle A. Crick and Jacqueline M-T Nichols, both residing in England; a son by a previous marriage, Michael F.C. Crick of Seattle, and six grandchildren. Crick was divorced from his first wife, Ruth Doreen Dodd, in 1947.

Selmer Peterson 1917 - 2004

Selmer W. "Pete" Peterson, a pioneer in neutron crystallography, died at his home in San Jose, California, on June 6, 2004, at age 86. Born in Owatonna, Minnesota, on September 8, 1917, he graduated from St. Olaf College in 1938. His Ph.D. in Chemistry from the University of Maryland in 1942 involved kinetic studies in non-aqueous solvents. It was in Maryland that he met his wife of 62 years, Mary Boggs. After fifteen months of war-related research at the Mellon Institute, he became an Instructor in Chemistry at Louisiana State University, where he remained for three and a half years before moving on to Vanderbilt University.

In 1949 Peterson went to Oak Ridge National Laboratory (ORNL) in Tennessee to work with Henri A. Levy, who introduced him to the principles of diffraction crystallography. He had intended for this to be a one-year sabbatical visit, but he stayed for twelve years. Together he and Levy designed and built a single-axis neutron diffractometer using a beam from the wartime Graphite Reactor. The first material that they studied was potassium hydrogen fluoride, a compound that would prove to have a short, centered, hydrogen bond between two fluoride ions. All neutron diffraction studies that had been done at that time had used powder samples, because it was generally believed that extinction effects would make single-crystal neutron-diffraction studies difficult or impossible. However, when Peterson and Levy found that their powder results were ambiguous, they proceeded with the first single-crystal neutron-diffraction study ever made and determined the structure of this material precisely.

Coherent neutron scattering cross sections were not well known in those early days, so Peterson and Levy experimentally established the values for nitrogen, phosphorus, and vanadium. They systematically studied hydrogen bonded materials, including several phases of ammonium chloride and ammonium bromide. They located the hydrogen atoms in copper chloride dihydrate and showed that there is a short, centered, hydrogen bond in the maleate ion of potassium hydrogen maleate. Some of their work was done in collaboration with visiting scientists. Working with Jurg Waser, they determined the oxygen positions in palladium oxide. With James E. Worsham, they determined the hydrogen positions in urea; and with Stanley H. Simonsen, they located the protons in both the tetragonal phase and the ferroelectric phase of potassium dihydrogen phosphate.

When Harold G. Smith joined the group at ORNL, he and Peterson made the first study of anomalous neutron scattering, from a single crystal of noncentrosymmetric, highly absorbing α-cadmium sulfide. In similar work on cadmium iodide they showed that the Breit-Wigner formula correctly describes the wavelength dependence of anomalous neutron scattering. Perhaps Peterson and Levy are best known for their single-crystal study of heavy ice, which showed conclusively that Pauling's postulated structure with disordered hydrogen bonds is correct. They were later honored for this work by the Antarctic Place-names Commission, who named two islands in ice-bound Crystal Sound after them.

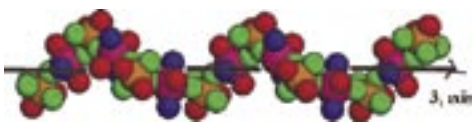
In 1961 he left Oak Ridge to become a Professor of Chemistry at Washington State University. This school was acquiring one of the early university-based nuclear reactors, and Peterson proceeded to construct a neutron diffractometer and to organize a graduate program in x-ray and neutron crystallography.

After six and a half years he moved on to Argonne National Laboratory, joining his former student, Jack M. Williams, in the Chemistry Division. He had hoped to take advantage of the Argonne Advanced Research Reactor, the construction of which had just been started, but shortly after his arrival that project was cancelled. Instead, he designed and built a diffractometer for chemical studies at the existing CP-5 reactor. This equipment was used for determining many structures, including those of several platinum compounds that are one-dimensional electrical conductors.

In the early 1970s he led the development of a single-crystal diffractometer for use at ZING-P', one of the earliest pulsed spallation neutron sources. With this instrument he and his colleagues, Arthur J. Schultz, Raymond G. Teller, and Williams, demonstrated the first successful use of the time-of-flight method to separate the different orders of reflections in a Laue pattern recorded by a two-dimensional area detector. He also designed the instrument for the Intense Pulsed Neutron Source (IPNS), that began operation in 1981.

Retiring to California in 1980, Peterson became an avid gardener specializing in irises. He continued the strenuous physical activities of hiking and tennis. As late as 1992 his U.S. Tennis Association team went to the National Tournaments and won third place. Crystallographers will remember Pete Peterson for his pioneering work in the early days of neutron crystallography at reactor sources and through the early days of pulsed spallation sources. The instrumentation that he helped develop serves as a prototype for the equipment being constructed for advanced neutron sources today.

William R. Busing



From Ken Poeppelmeier; see page 63.

Images from the New Structures session at the 2004 ACA meeting July 17-22

Top image: from **Barbara Golden and Elaine Chase,** Purdue University, West Lafayette, IN: A group I intron from bacteriophage Twort. Group I introns are self-splicing and can catalyze their excision from surrounding exons. This reaction requires a guanosine nucleotide substrate and sufficient magnesium ions to allow the RNA to fold. A 242 nucleotide RNA derived from the Twort orf142-I2 intron was co-crystallized with a 4 -nucleotide RNA that mimics the 5'-exon, providing a view of the architecture and active site of a multi-domain RNA enzyme. This group I intron is organized into 4 domains: P1-P2 (red), P3-P9 (green), P4-P6 (blue) and P7.1-P7.2 (yellow). B.L. Golden and E. Chase, unpublished results.

Bottom image: from **Jack Tanner and Jon Schuermann,** University of Missouri-Columbia, Columbia, MO: Abnormalities in proline metabolism are important in several diseases, including cancer and neuropsychiatric disorders. The enzymes proline dehydrogenase (PRODH) and Δ^1-pyrroline-5-carboxylate dehydrogenase (P5CDH) play important roles in proline metabolism by catalyzing the two-step oxidation of proline to glutamate. In some bacteria, these two enzymes are combined into a single, bifunctional, membrane-associated protein known as PutA (Proline Utilization A). The cover shows a ribbon drawing of the first crystal structure of a PutA protein, which was solved to 2.3 Å resolution by MAD and MIR. The 1000-residue dimeric protein adopts a U-shaped structure measuring 140 Å x 80 Å x 50 Å, in which the PRODH domains (pink/cyan) are far apart from each other in the arms of the U, while the P5CDH domains (blue and green) mediate dimerization in the base of the U. Interestingly, the exit port of the PRODH active site (yellow spheres) faces toward the entry port of the P5CDH active site (red spheres), which suggests that the protein facilitates the 43-Å journey of the PRODH reaction product to the P5CDH active site. J.J. Tanner and J. P. Schuermann, unpublished results.

Editor's note: **see the report on the New Structures session, page 49. Barbara's talk was titled:** ***Crystal Structure of a Self-splicing Group I Intron from Phage Twort;*** **Jack's was:** ***First Structure of a Bi-functional Proline Catabolic Enzyme. Also, please note that there were many new structures presented at this meeting that were reported in other sessions. Among these, the Membrane Protein Structures presentation of the E. Coli ammonium transporter, AmtB, by Robert Stroud, page 51, and Dan Anderson's huge cytoplasmic ribonucleoprotein vault structure in the Difficult Structures session, page 49, are particularly interesting.***

Contributors to this issue:

Christer Aakeröy, Kahlil Abboud, Ty Adams, Paul Adams, Malin Åkerblom, Alberto Albinati, Wayne Anderson, Dan Anderson, Ross Angel, Bob Bau, Lesa Beamer, Alicia Beatty, David Belnap, Joel Bernstein, James Britten, I. David Brown, Susan Buchanan, Bill Busing, Paul Butler, Steve Byrn, Elaine Chase, AbeClearfield, Patti Coley, Ed Collins, Marcia Colquhoun, Patti Coley, Lachlan Cranswick, Bryan Craven, Bob Cudney, Zbigniew Dauter, Roger Davey, Paul Del Rizzo, Louis Delbaere, Brian Dempsey, Jeff Deschamps, George DeTitta, Ken Dill, Doug Dorset, Bill Duax, Dave Duchamp, Al Edwards, Larry Falvello, Daniel Fischer, Paula Fitzgerald, Jenny Glusker, Barbara Golden, Joel Harp, P. John Hart, Chad Haynes, Larry Henling, Tim Herman, Jason Hodges, Andy Howard, Pete Jemian, Frances Jurnak, Katherine Kantardjieff, Lisa Keefe, Chuck Kissinger, Tom Koetzle, Charles Lake, Pat Loll, Gabrielle Long, Robin Macaluso, Emily Maverick, Cory Momany, Jennifer Morris, T.C. Mou, Peter Müller, Gary Newton, Bill Ojala, Arwen Pearson, Ken Poeppelmeier, Joseph Reibenspies, Phoebe Rice, David Rose, Michael Rossmann, Tim Rydel, Ram Samudrala, Meilin Sancho, Bernie Santasiero, Jon Schuermann, Art Schultz, David Smith, Janet Smith, Eddie Snell, Erika Soriano, Steve Sprang, Robyn Stanfield, Bog Stec, Ron Stenkamp, Robert Stroud, Jack Tanner, Jesús Valdés-Martínez, KI Varughese, Carolina Vasquez, Karl Volz, Helen Walden, Mark Whitener, Michael Wiener, James Williamson, Cynthia Wolberger, Winnie Wong-Ng, Omar Yaghi, Wei Yang, Todd Yeates, Marcia Yoder, Alex Yokochi, Victor Young, Jian-Min Zuo.

Special thanks to Victor Young, Dan Anderson, Bill Duax, Gary Newton, Sasi Kiran Chilukuri, Jill Dombrauckas, Soni Larsen, Melissa May, Andy Mesecar, Kiira Ratia, and Huidong Yu for their contributions of photographs.

News from Canada

I'm writing this at the ACA Annual Meeting in Chicago, and am gratified to see a relatively large Canadian contingent (mostly students) from across the country, seemingly larger than in the immediate past. It may be due to the proximity to many parts of Canada or the appeal of Chicago, or even the interest in the excellent scientific program! However, I can't help wondering why the ACA is not more popular among colleagues north of the border. We do not have a formal crystallographic association of our own, and are privileged to have a special status in the ACA, with representation on Council. I have benefitted through the years by meeting and talking with scientists expert in areas of crystallography outside my own, and attending sessions on topics such as crystallographic education, and government funding initiatives. I believe the Canadian Division of the ACA could be a very active body, both by keeping a visible Canadian presence in the ACA, and by mobilizing efforts for outreach, education and representation of our community in Canada. For example, we could have much stronger formal connections with the IUCr Canadian National Committee and the various Canadian organizations that are bridged by crystallography (CSC, CSBMCB, etc).

The ACA (American in the broadest context) is our national crystallographic society. Did you know that 3 of the past 10 ACA Presidents have been Canadian? A common question is, "What do I get for my dues?" The pragmatic answer is that, if you attend the Annual Meeting, your membership is essentially free, since the member registration rate differs from the non-member rate by about the amount of the dues. So the question boils down to, "Why should I go to the meeting?" Sure, you can probably find better places to hear the latest developments in your biology, chemistry or physics discipline. But will those meetings discuss the latest ideas in crystallization strategy, what we have learned from success and (more importantly) failures of high throughput approaches (from expression to structure determination), what radiation damage is doing not only to your data, but to your molecule (and how to minimize these effects), and cutting edge technical advances in the other crystallographic disciplines? How about powder diffraction studies of protein conformational changes? Or small molecule approaches to crystal mounting applicable to macromolecules? Or advances in material sciences that might result in new surfaces to facilitate protein crystal nucleation? These are all topics that were covered at this year's meeting (along with many more, including workshops on MAD/SAD phasing, and synchrotron applications to small-molecule crystallography). Where can you wander the exhibit area and see the latest developments from various vendors side-by-side with representatives from synchrotron beam lines, databases (CSD, PDB), and the authors of the newest software packages (CCP4, etc)? Finally, the ACA has always been an especially friendly organization for young scientists: students, postdocs and starting faculty. There are numerous travel and poster/presentation awards, a very active Young Scientist SIG, and many opportunities to commiserate or just hang out and compare notes with others at your own career stage. Perhaps most important is the chance to make contact with and perhaps to get to know quite well - senior investigators. They might be future employers, or might just give advice or insights. You might even see one or two "let their hair down" at a mixer or local club.

My bottom line is that it is important to have a crystallographic society because our results are only as good as our data, the techniques we use to generate them, and our understanding of those techniques. Learning about the history, theory, and technology behind our method is at least as important as hearing about the latest structures. Meeting the pioneers who have established our method is truly inspiring.

David Rose

Crystallography Web Watch

The ACA Communications Committee encourages the entire crystallographic community to participate in the ***Crystallography Web Watch***. Please email the web address and a brief description of any sites that could be informative and/or entertaining to Jeanette Krause: **jeanette.krause@uc.edu.**

Education Sites:

Find tutorials and techniques for x-ray and neutron crystallography at: **chemistry.about.com/od/crystallography/**

Crystallography Course: *Solving a protein structure using MIR techniques*. Available at: **bchs.uh.edu:16080/struct_bio/MIR_course/**

One of the topics that will be sponsored by the Service Crystallography SIG at ACA'05 in Orlando will cover "Effective Presentations and Publication of Results" It is therefore fitting that we revisit this topic. Please see:

Molecular animations: Molscript at: **www.avatar.se/molscript/**

The Moviemol - Molecular Animation Program at: **www.fos.su.se/moviemol.html.**

Effective Presentations - Preparation of effective slides, graphics, etc: **www.research.ucla.edu/era/present/**

Effective Presentations with Visual Aids at: **www.osha.gov/doc/outreachtraining/ htmlfiles/traintec.html.**

Powerpoint tips & guides: www.computertips.com/Microsoftoffice/MsPowerPoint/aheader.htm.

101 Tips for Effective Presentations: http://feh.eng.ohio-state.edu/DesignProject/References/

Wilder Presentations: 10 Steps to Success **- www.wilderpresentations.com/steps/**

ESM Software: Crystal Rendering and Manipulation Software: **www.esm-software.com/crystallography/**

The emphasis on teaching crystallography at the 2004 ACA meeting was remarkable. The **Fankuchen Award** is given to *a scientist who is known to be an exceptional teacher of crystallography,* and **Alex McPherson** fills that bill admirably. The citation for the award in the *Fall 2003 Newsletter* described his many contributions to education; the books he has written; the numerous workshops and conferences he has organized and in which he has taught countless students; the many years he has been an instructor at the Cold Spring Harbor Macromolecular Course; and his participation in outreach programs for high school students and science teachers.

In addition, the ACA meeting also featured a session on **Teaching Advanced Crystallography** organized by **Peter Müller,** a workshop designed for high school teachers and students: **X-rays, Crystals, Molecules and You** organized by **Judy Flippen-Anderson** (Alex was one of the lecturers); Eight posters by high school SMART teams, a booth in the exhibition area by the Milwaukee School of Engineering (MSOE) Center for BioMolecular Modeling, and a poster from MSOE (P249) describing the development of the SMART team program.

When asked to describe the workshop, Judy Flippen-Anderson responded: "Too few of our best and brightest high school students are choosing to major in the physical sciences when they start university life. As crystallographers we need to find ways to share the excitement and wonder that comes from the study of life at the atomic level. At the ACA meeting in Chicago the RCSB PDB and the ACA co-sponsored a workshop for high school students and teachers that used structural databases and crystal growing tips as a means of sharing that excitement. Some of the attendees were involved in the NIH-SEPA (Science Education Partnership Award)-funded SMART Team (Students Modeling a Research Topic) program." Judy first met Tim Herman of MSOE at his (first time) booth at the 2003 ACA Meeting, and the idea for the workshop evolved from that. Kathy Kantardjieff was called upon to help out, and Helen Berman, Director of the RCSB PDB, provided ideas and guidance. The RCSB PDB also funded the workshop, which was very successful (75 participants!) A complete report will be in the winter *Newsletter*.

Tim Herman, Director of the Center for BioMolecular Modeling at MSOE, described the SMART Team program in a column for the *PDB Newsletter*:

"The Center for BioMolecular Modeling (CBM) at the Milwaukee School of Engineering uses rapid prototyping technologies to produce physical models of proteins and other molecular structures based on atomic coordinates obtained from the Protein Data Bank. These physical models are used both by researchers, who find them useful as 'thinking tools' and by students who are just beginning to explore the molecular world.

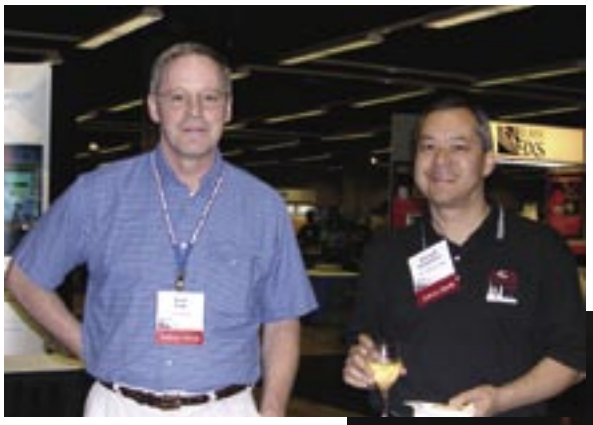
The CBM directs science outreach and professional development programs targeted to both high school science teachers and undergraduate educators. At the high school level, an NIH-funded SEPA allows us to offer a two-week summer course entitled *Genes, Schemes and Molecular Machines*. In this course, teachers are shown how physical and computer-generated models of proteins can be used to make the molecular world real for their students. Using a recently modified version of RasMol (RP-RasMol), teachers are directly involved in the design and construction of the physical models. SMART Teams consist of a high school teacher who has participated in our summer course and a group of 3-5 students who work with a local research lab to produce a physical model of the protein under investigation in the lab. Our first SMART Team, known as ***Team Anthrax***, designed and constructed physical models of the three proteins involved in anthrax pathogenesis in the months immediately following the anthrax attacks in the fall of 2001. Currently, seven SMART Teams are working with researchers in Wisconsin, the RCSB PDB has been directly involved with a SMART Team in The Pingry School, Martinsville,NJ, and other teams have been formed in Ohio, Kansas, and Tennessee. (For information about how to participate in a SMART Team, contact Tim Herman at **herman@msoe.edu.**)

At the undergraduate level, the CBM works with undergraduate educators to explore ways in which physical models can enhance the use of molecular visualization tools. With support from an NSF-CCLI award, the Center plans to launch a Summer Modeling Institute at which undergraduate faculty will have access to our physical modeling technologies to design and produce models that will be used in courses on their local campuses. A Model Lending Library has been created to allow any undergraduate educator to borrow models resulting from this project for use in their classroom. Molecular models for science education, including a DNA Construction Kit, can be obtained from 3D Molecular Designs, a recent spin off of the CBM, **www.3dmoleculardesigns.com."**

Below: Anthony Benz, left, and Michael Ruka, 8th grade students at St. Dominic School, Milwaukee, WI, with their SMART Team poster P256., and, below them, Diane and Tim Herman at the MSOE booth.

At the Awards Banquet

Top, l to r: Lisa Keefe, Bill Stallings, Chris Neilson, Paula Fitzgerald, and Howard Einspahr. Top right: Charlie Carter gazing at Past President Ray Davis' final slide. (If you don't understand Charlie's expression, see the banquet pictures in the fall 2003 Newsletter.) Middle left, Ed Collins and Cory Momany; center, above: Paul Pregosin, Tom Koetzle and Alberto Albinati; center, below: Randy Alkire and Gerard Bricogne; center right above: Sharon and Ray Davis and Herbert and Frances Bernstein; below them: Fran Jurnak presenting the ACA Public Service Award to Madeleine Jacobs. Bottom, l to r: Marcia Colquhoun, Patti Coley and Tammy Colley; Edie and Herb Hauptman at their table talking with Manju Rajeswaran and Sasi Kiran Chilukuri.



Above, Local Chairs Karl Volz on the left, and Bernie Santasiero.

At right, Program Chairs Marilyn Yoder and Christer Aakeröy.

2004 ACA Meeting - Chicago, IL, July 15 - 22

Highlights of the meeting included the presentations of the **Isidor Fankuchen Award** to **Alexander McPherson,** the first **Kenneth N. Trueblood Award** to **Richard E. Marsh,** the first **Charles Supper Award** to **Nguyen-Huu Xuong,** and the symposia organized to honor the award recipients. (See pages 40-43.) **Alicia Beatty** organized the ***Transactions* Symposium** on ***Crystals in Supramolecular Chemistry*** around three topics: ***Crystal Structure Prediction and Polymorphism; Crystal Structure Design;*** and ***Applications of Crystal Design.*** (See page 36.)

In addition, the **Margaret C. Etter Early Career Award** was presented to **Leonard MacGillivray** (see page 37). Meeting participants enjoyed a varied and exciting scientific program, thanks to the dedicated efforts of Program Chairs **Marilyn Yoder** and **Christer Aakeröy**

The **ACA Public Service Award** was presented to **Madeleine Jacobs,** Executive Director and CEO of the ACS, at the Awards Banquet. She thoroughly charmed the audience with her acceptance speech, especially when she recited the Cole Porter song ***Experiment*** which goes, in part: *You all have learned reliance / On the sacred teachings of science, / So I hope, through life, you never will decline / In spite of philistine / Defiance / To do what all good scientists do.*

Experiment. / Make it your motto day and night. / Experiment / And it will lead you to the light. / The apple on the top of the tree / Is never too high to achieve, / So take an example from Eve, / Experiment.

Be curious, / Though interfering friends may frown. / Get furious / At each attempt to hold you down. / If this advice you always employ / The future can offer you infinite joy / And merriment, / Experiment / And you'll see.

Chicago proved to be a terrific venue for the meeting. The Hyatt Regency accomodated us with ease, and the location, with the Chicago river right in front and the brand new Millenium Park in back could hardly have been better. The Mentor/Mentee dinner was a big success. The *Winter ACA Newsletter* will have pictures taken at this event as well as at the lavish parties given by our generous exhibitors. The winter issue will also feature reports on the Workshops and reports from Travel Award recipients.

Our tireless and unflappable Local Chairs **Bernie Santasiero** and **Karl Volz** and their committee made the smooth functioning of the meeting seem effortless. Special thanks from the *Newsletter* Editors to local committee members **Sasi Kiran Chilukuri, Jill Dombrauckas, Soni Larsen, Melissa May, Andy Mesecar, Kiira Ratia,** and **Huidong Yu** for taking photos of speakers at the sessions. We also thank photo contributors **Victor Young, Dan Anderson, Bill Duax, Gary Newton** and **Eddie Snell**.

Below, photos from Dan Anderson of Michigan Avenue scenes. At right, the foodline at the Opening Reception, which was held in the Exhibit Area.

Transactions Symposium TR.01

The 2004 *Transactions* Symposium, ***Crystals in Supramolecular Chemistry*** explored the various aspects of crystal structure prediction and design, crystal growth, and solid state applications of supramolecular chemistry from the perspective of an international coterie of chemists.

Crystal Structure Prediction and Polymorphism: **Sally Price** U. College London spoke first, giving a thoughtful and thought-provoking lecture on where we have been and how far we have come in the prediction of crystal structures. She summarized the results of three blind tests for crystal structure predictions, and provided insight into the problems associated with predicting structures of even simple molecules. **Joel Bernstein,** Ben Gurion U. of the Negev, Israel, followed with a historical perspective on polymorphism, including some rare photos of Kitaigorodskii, (one of which is at left) and gave an often hilarious overview on prevailing attitudes for predicting the structure of polymorphs. **Elna Pidcock,** CCDC, UK, then gave an analysis of crystal packing based on CSD-based statistical analysis, veering away from the lock-and-key model for molecules and demonstrating a box-based approach. **Qi Gao,** BMS, discussed some polymorph and pseudopolymorph screening for drug candidates. Finally, **Ray Davis,** U. Texas, showed how thermal microscopy can be used to identify single and co-crystals before introducing many of us to the concept of *Hirshfeld Diagrams*, which he had recently discovered at the 2004 school in Erice.

Crystal Growth Mechanisms: Bart Kahr, U. of Washington, showed how crystal growth can be tracked by layering of multi-component crystals through sequential crystallization. This led to a discussion of a crystal growth system that explores possibilities for replication of defects. **Jennifer Swift,** Georgetown U., followed with a discussion of uric acid crystal growth, providing a molecule's-eye view of growth rates of this biologically significant solid. The crystal growth theme was continued by **Tayhas Palmore**, Brown U., who discussed growth kinetics and morphology for a hydrogen-bonded coordination complex-based system. **Colin Seaton,** U. Bradford, UK, then showed his modeling of the surfaces of crystals in order to predict the formation of an interface between two crystalline forms. The session concluded with talks by graduate students from the Swift and Kahr groups. Aragose gels and their suitability for chiral separations were discussed by **Rositza Petrova**, Georgetown U., and then **Jason Benedict**, U. Washington, showed how some luminescent probes were used to distinguish between crystal surfaces.

Crystal Structure Design: Wais Hosseini, U. Louis Pasteur, France, assured us that he is not a crystal engineer, while at the same time demonstrating that he can cleverly engineer reproducible networks in crystals through careful synthesis and design. **Christer Aakeröy**, Kansas State U., who may actually be a crystal engineer, discussed the skillful use of synthetically designed asymmetric molecules as hubs for multicomponent super molecules held together by hydrogen bonds of varying strengths. Self-confessed crystal engineer **Lee Brammer**, U. Sheffield, UK, then further enlightened the crowd about intermolecular forces by discussing inorganic halogens and their role in supramolecular assemblies. Putting a different spin on the assembly process, **Jesús Valdés-Martínez**, UNAM, Mexico, described some inorganic-organic hybrid compounds and their potential for π-π interactions. See the image below.

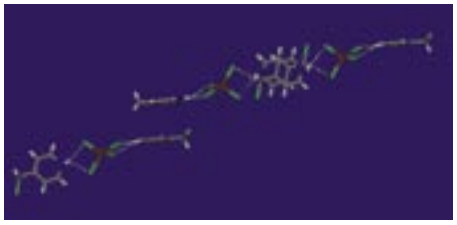


Image received from Jesús Valdés-Martínez.

Crystal Growth Mechanisms: l to r: Jennifer Swift, Jason Benedict, Bart Kahr, Colin Seaton, Rositza Petrova, Tayhas Palmore.

Crystal Structure Design: l to r: Jennifer Swift, Lee Brammer, Christer Aakeröy, Jesús Valdés-Martínez, Jim Wuest.

TR.01, con't.

Jim Wuest, U. Montreal, CA, then demonstrated that careful design and synthesis of organic molecules can lead to single crystals which undergo guest exchange and deformations without loss of crystallinity, and which can also undergo chemical reactions to lead to 3-D covalent structures.

Applications of Crystal Design: Mike Ward, U. Minnesota, demonstrated that hydrogen-bonded guanidinium sulfonate frameworks are capable of selective separation of isomeric organic compounds via crystallization. Although he didn't go so far as to claim that the crystal structures are "predictable," the frameworks are of a predictable type and size, which allows them to serve their useful purpose. Applications of ionic liquids as crystallization solvents were discussed by **Robin Rogers,** U. Alabama, who strongly believes in developing methods for non-traditional crystallization. **Dario Braga,** U. Bologna, Italy, went to the next step by trying to eliminate solvents altogether, as shown in the gas-solid and solid-solid reactions that take place with a "catalytic amount of water." His contribution emphasized the interesting machinations that can take place when one combines inorganic or organometallic complexes that contain peripheral hydrogen-bonding substituents.

As a slight departure, **Joe Lauher,** SUNY, Stony Brook, described subperiodic groups with α- or β-networks, as detailed in *International Tables*, *Volume E*. **Len MacGillivray**, U. Iowa, wrapped up the *Applications* portion of the symposium by showing us that hydrogen bonds and the solid state can be used to position molecules within a prescribed proximity so that stereo-controlled photodimerizations can take place. The progeny of these reactions are further useful as, for example, ligands for coordination polymer assembly.

Acknowledgement and warm thanks to the ACS-PRF Grant # 41054-SE, the RSC journal *CrystEngComm*, the ACS journal *Crystal Growth & Design*, and the *J. of Chem. Cryst.* for their support of the symposium. Further details will be in the *Transactions* volume, to be published online soon.

Alicia Beatty

L to r: Bill Pennington, Leonard Macgillivray, Marilyn Olmstead, Graciela Díaz de Delgado, Bill Ojala, Ekaterina Anokhina, Mark Whitener.

Margaret Etter Early Career Award Symposium AW.01

The **Margaret C. Etter Early Career Award** is presented to scientists who have shown outstanding achievement and exceptional potential at an early stage of their independent career. This year's recipient was **Leonard MacGillivray**, U. of Iowa, whose use of molecular templates to direct the course of [2 + 2] photodimerization in the solid state has allowed the preparation of compounds ranging from *molecular ladders* to intricate metal-organic frameworks. His acceptance lecture described how suitable molecules (such as resorcinol) act like a pair of molecular hands, holding reactant molecules in an orientation particularly suitable for solid-state photoreaction.

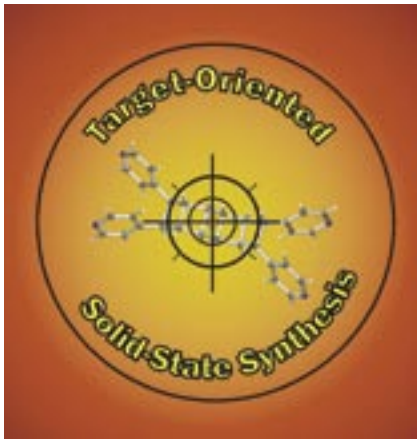


Image from Len MacGillivray.

The subsequent talks strongly reflected the theme of crystal design set by the award lecture, each focusing on a particular design element or strategy. **Bill Pennington** described how halogen bonding, the solid state Lewis acid-base interaction between halogens and nitrogen atoms (such as between an iodine atom and a pyridine nitrogen), can serve as a structural element in crystal design and outlined it's role in some solid-gas reactions. **Xiaoping Wang** described the self-assembly of metal-containing complexes displaying a variety of geometries depending on the strategic choice of polyfunctional organic linkers. The ability of fluorinated tetraphenylporphyrin molecules to form crystalline architectures suitable for the cocrystallization of fullerenes was described by **Marilyn Olmstead**. Carboxylates as design elements were the subject of two lectures. **Mark Whitener** described their use in transition metal complexes intended to serve as model systems for histidine-carboxylate interactions in proteins; one series of structures in this group resembles a reaction coordinate for the interaction of the metal with added ligands. **Graciela Díaz de Delgado** described carboxylate-containing species whose solid-state structures depend on whether they are prepared by hydrothermal methods or at room temperature. **Zhen Huang's** lecture focused on the use of selenium as an alternative to bromine in the derivatization of nucleic acids for phasing purposes. **Ekaterina Anokhina** then described the formation of chiral frameworks in the solid-state structures of nickel aspartates. The extensive array of molecular design elements described in this year's symposium may find creative uses by future winners of the Margaret C. Etter Early Career Award.

Bill Ojala and Mark Whitener

L to r: K.I. Varughese, Gerd Rosenbaum, Andy Howard, Ed Westbrook, Nguyen-Huu Xuong, Ron Hamlin, Frances Jurnak, Christian Broennimann, Vukica Srajer, Jim Pflugrath.

AW.02 The Supper Award Symposium

The symposium began with the presentation of the **2004 Charles Supper Award** to Professor **Nguyen-huu Xuong**, U. California, San Diego, by ACA President Fran Jurnak, who praised Xuong's contributions to area detector development. Xuong was the first recipient of this award, and the symposium was organized to honor him.

Xuong's award lecture was ***Advanced Area Detectors for Protein Crystallography: Confessions of a Reformed Physicist***. His remarks were organized around three confessions. The first was that he had done the right thing -getting into protein crystallography- for the wrong reason. He got into crystallography to use his skills as an instrumentation-intensive physicist in a new realm, both by developing the screenless precession technique for film crystallography and by using drum scanners for reading out film data. He then began an electronic detector development project, applying the multiwire proportional counter (MWPC) technology to crystallography. He and his student, Ron Hamlin, developed electronic readouts for these detectors, and his first system was a success by 1974. Xuong's second confession, in fact, was that the ACA had given the Supper award to the wrong person -it should have been awarded to Ron Hamlin. Xuong's last confession was that he works as a protein crystallographer but dreams of doing cryo-electron microscopy. Xuong described some potential avenues to pursue in developing better cryo-EM detector systems, including an approach involving *active pixel sensors* with epitaxial Si layers. It is likely that a suitable 2kx2k, 10x10 micron detector for cryoEM is achievable. ***Editor's note: A version of Xuong's lecture will be published in the winter or spring ACA Newsletter.***

Ron Hamlin, ADSC Inc., then described the role of two-dimensional position-sensitive detectors in crystallography. Ron described the ways that electronic detector systems address the limitations of film and diffractometry. He discussed the commercialization of the Xuong/Hamlin detectors in 1983 and the gradual adoption of photon-counting detectors in many laboratories. He contrasted MWPCs with image plates and CCDs, which have largely supplanted MWPCs; his own company now markets large-area,fast-readout CCD arrays. Ron described upgrades envisioned for the near future in these CCD systems, including better readouts and altered modes of data collection.

Ed Westbrook, Molecular Biology Consortium, continued the story of CCD and subsequent detector technologies. In 1983 Ed and colleagues at Argonne began developing CCD-based crystallography detectors. Ed's group is continuing to optimize CCD detectors by developing better phosphors, new coupling technologies, and better CCD chips. Lens systems are more feasible now than they were before 1998; they hold the promise of improving optics, spatial resolution, coverage, and maintenance. Ed's *Noir One* lens-coupled detector system has been operating at the ALS since March. Ed described the current research on hybrid CCD/CMOS systems, which could allow much faster readout than CCDs. Ed is also involved in a pixel-array detector project at the ALS.

Christian Broennimann, Swiss Light Source, described his group's pixel array detectors. The requirements for a new detector technology include high DQE, high dynamic range, large size, good spatial resolution, a fast, noise-free readout, no spatial distortion, no dead area, and precise and stable calibrations. He described the 2x1 cm *technological building blocks* of his system and the way that dark current can be obviated through discrimination. The current SLS system employs sixteen 44x78-pixel modules, providing an active area of about 80x35 mm. These can be further multiplexed or *banked* to provide full solid-angle coverage for crystallography. The current system has been used for successful data collection at the SLS. The system is well-suited to fine phi-slicing, or even to continuous, shutterless readout, since the electronics do not add noise.

Jim Pflugrath, Rigaku/MSC, discussed the software requirements for detector data collection. Jim defined the components of the experimental system and how those components' properties interact with detector properties. Jim listed types of crystallographic detectors, and made some specific comparisons between image plates and CCDs -the two prevalent technologies. He contrasted fine-slice and wide-slice approaches to rotation data collection, and explained the advantages and disadvantages of fine-sliced data and the trade-offs between counting statistics and multiplicity. In describing data processing approaches Jim quoted J.S. Rollett: "it is unwise to try to cover unknown systematic errors simply by increasing the estimates of random errors." **Gerd Rosenbaum**, U. Georgia and SER-CAT at APS, discussed the detector requirements for non-single-crystal x-ray diffraction and scattering experiments. Gerd listed the attributes of time-resolved x-ray experiments and the resulting detector requirements, which

Supper Symposium, con't

include low background, fast readout, wide dynamic range, a small point-spread function, and a high DQE. No detector has all those attributes, and the history of this field is filled with various trade-offs. Gerd discussed detectors for solution scattering, and sketched a design for a multi-element detector system employing plastic scintillator fibers read out by an array of photomultipliers. Development of novel detectors for non-single-crystal applications has proceeded slowly because very little money or human resources are available.

Andy Howard, Illinois Tech, discussed area detectors as they are used at synchrotron beamlines. He observed that detectors and synchrotrons, considered separately, offer huge advantages to the crystallographer, but the optimal use of synchrotron data can only be realized if they are collected on a high-quality, fast-readout detector system. Current CCDs cannot cope with the fluence derived from an optimized third-generation beamline, and new technologies will need to be developed. The pixel array detectors discussed by other speakers are the most promising solution to this problem, together with consideration of alternative approaches to data collection, including continuous rotations. All of this will require new software for data acquisition and processing.

The final speaker, **Vukica Srajer**, U. Chicago and BioCARS at APS, discussed experimental requirements for time-resolved crystallography. These experiments enable an understanding of reaction intermediates and mechanisms in the picosecond to microsecond range; for most of this range Laue techniques are required. In many of these experiments a laser initiates the reaction. She pointed out that Laue experiments require wavelength normalization, are more sensitive to sample mosaicity, and produce higher x-ray backgrounds than monochromatic experiments. The user must vary both the angular setting of the crystal and the delay time between the laser pulse and data collection; for irreversible reactions this means mounting many different crystals. Vukica listed the characteristics of an ideal Laue detector system, not all of which are satisified by current systems.

Andy Howard

L to r: Kyle Self, William Somers, George DeTitta, Kim Collins, Alex McPherson, Nadrian Seeman, Frances Jurnak, Bob Cudney, Youngchang Kim.

AW.03 Fankuchen Award Symposium

This year the ACA bestowed the Fankuchen Award on a most worthy recipient, **Alexander McPherson,** U. of California, Irvine. Alex is a leader in the field of macromolecular crystal growth and a superb expositor of science. The session began with the President of the ACA kissing the recipient of the Fankuchen Award. For those of you unaware of the collegial relationship of our president Fran Jurnak and Alex, let's us just say that the President assured all in attendance that she was not a member of the selection committee. **Editor's note: See articles on pp 13 and 32 for more details. Sadly, the digital camera was not quick enough to catch the kiss.**

Alex opened the formal lectures with a tour of where we've been and where we need to go in macromolecular crystallization. Tracing the history of the science from 1840 when Hunefeld crystallized hemoglobin from worm and fish to the modern era when crystallization kits became commercially available in 1991, Alex delighted his audience with his breadth and depth of insight. He made special mention of the contributions of Fankuchen, Crowfoot and Bernal who in 1935 produced the first diffraction patterns from crystals of the protein pepsin. He moved on to the problems that continue to confront us, such as the search for the universal cryosolvent and the development of an understanding of protein crystal annealing processes.

Alex was followed by a number of speakers who touched various aspects of the crystallization experiment, ranging in subject from the most basic, as in **Kim Collins**' fundamental analysis of the Hofmeister series, to the most practical, as in **Kyle Self's** description of the advantages of kinetic control in microfluidic devices. **Youngchang Kim** brought the audience up to date on crystallization results from the MCSG structural genomics consortium while **Bernhard Rupp** waxed eloquent on the analysis of all the data being accumulated by the genomics centers. **Will Somers** spoke of the difference of approach in the pharmaceutical setting -there the emphasis is on the specific problem, where no fruit hangs low. **Ned Seeman**, king of nanotrash (a term coined by Alex during his award lecture) and an old friend of Alex dating back to their shared glory days at MIT, both entertained and edified the audience with his description of the Odyssey of DNA, a molecule of many twists and turns. Those who have not done so should see Ned's cover article in a recent *Scientific American* about the nanotechnological uses of DNA.

An unscheduled speaker rounded out the session. To emphasize the teaching role of Alex, **Bill Furey**, friend and fellow instructor of the Cold Spring Harbor short courses in macromolecular crystallography, took us through a brief history of the highs and lows of Alex's engagement of students during the rigorous course work. Clearly this is a man who enjoys the teaching role, and the Powerpoint slides emphasized the words Alex spoke about the teaching process. The session wrapped up with a warm and sustained round of applause for an individual who has delighted and educated us for many years.

Bob Cudney and George DeTitta

AW.04 Trueblood Award Symposium in Honor of Dick Marsh

The first **Kenneth N. Trueblood Award** was presented to Richard E. Marsh at the Chicago meeting in honor of his exceptional achievements in chemical and computational crystallography (see ACA*Newsletter*, winter 2003). The award was presented by ACA President Fran Jurnak who described Dick's professional career and the great impact he has had as a teacher, researcher, former ACA President and editor of *Acta Crystallographica*. He is well known to us as a "*marsher,*" that is, he shows us when structures are incorrect, in particular when the space group has been wrongly chosen. Speakers in the symposium concentrated on stories of *marshed* structures and on areas of structure determination that would interest Dick.

L to r: Emily Maverick, Sasi Kiran Chilukuri, Hans-Beat Bürgi, Dick Marsh, Joel Bernstein, Jenny Glusker, Larry Dahl, Frank Fronczek, Frank Herbstein, Ton Spek, Carlo Maria Gramaccioli, John Fackler.

In his keynote address **Richard E. Marsh**, Caltech, gave a fascinating talk with examples of crystal structures that deserved *marshing* and explained exactly why this was necessary. The specific problem is often whether or not there is a center of symmetry. Ton Spek pointed out later in the symposium that a survey by Dick Marsh in 1997 of all structures published in space group Cc showed that about 10% of the assignments were wrong, but, he added, a new survey by Dick Marsh in 2004 surprisingly showed that this percentage is still around 10%. Dick queried whether another problem might be that many chirally pure compounds are being refined and reported as racemic mixtures in achiral space groups since many chiral compounds crystallize with approximate centers of symmetry. These observations by Dick provide food for thought in these present days of rapid structure determination.

Frank H. Herbstein, Technion-Israel Institute of Technology, Haifa, Israel, then spoke on *First order enantiotropic solid state phase transitions – from Simon through Ubbelohde to Mnyukh*. He noted in his introduction that his ambition was to *marsh* Marsh, but that the chances of that were like those of winning a lottery. He presented an analysis of enantiotropic phase transitions (involving two different phases of the same compound). He started his talk with description of investigations of the lambda transition in ammonium chloride at 242 K by F. Simon (*Ann. Phys.* **68,** 241, 1922). In the delta (low temperature) phase the ammonium ion is orientationally ordered, while in the gamma phase it is orientationally disordered. The plot of heat capacity as a function of temperature shows a lambda-like shape. Nevertheless the phase transition is first order (Dinichert, 1942). Frank then described the opposing approaches of A. R. Ubbelohde (*J. Appl. Phys.* **7**, 313, 1956) and Yuri Mnyukh (*Fundamentals of Solid State Phase Transformations, Ferromagnetism and Ferroelectricity* 1st Books, 2001). In passing through a phase transition the two co-existing phases could be colloquially compared to a mixture of horses (the low-temperature phase) and donkeys (the high-temperature phase). One important question was whether the intermediate state consisted of horses plus donkeys (a mixture of the two structures) or of mules (a different structure). In the phase transitions of a complex of tetrathiofulvalene and chloranil the intermediate state seems to consist of both species (horses plus donkeys). Recent studies, however, by V. V. Mitkevich *et al*. on hysteresis in the unit-cell dimensions of 4,4'-dichlorobenzophenone (*Acta Cryst*. **B55**, 799, 1999) suggest in this example there is a horses-mules-donkeys sequence.

Hans-Beat Bürgi, U. of Berne, Switzerland, highlighted the importance of the articles by Verner Schomaker and Ken Trueblood on the rigid-body motion of molecules in crystals (*Acta Cryst*. **B24,** 63, 1968) and the correlation of internal torsional motion with overall molecular motion in crystals (*Acta Cryst*. **B54**, 507, 1998). He described a general solution of the problem of correlation between different motions on the basis of data measured at several temperatures. Hans-Beat showed how he had derived information that allows for better models for motion; better distance corrections; the estimation of vibrational frequencies; isotope effects and specific heat; distinguishes motion from disorder; and accounts for the influence of thermal expansion on molecular motion.

Joel Bernstein, Ben-Gurion U. of the Negev, Israel, described crystal engineering as Gerhard Schmidt thought of it, leading to the design and "construction" of crystals, with properties defined in advance. He concentrated his talk on graph-set descriptions of hydrogen bonding patterns, as pioneered by Peggy Etter, and their use in the design of co-crystals composed of a neutral solid and a salt or two different neutral solids. The question was, is it possible to control and direct the formation of a specific desired graph-set pattern (synthon) on crystallization? Some examples of attempts to do this were presented.

Lawrence Dahl gave a talk on metal carbonyl clusters, asking how many metal atoms you can bring together before you get metallic properties. His recent studies have involved homometallic and heterometallic carbonyl clusters with many metal-core atoms consisting of metals (Ni, Pd, Pt, Cu, Ag, or Au) that form direct

metal-metal bonds. These giant-sized metal clusters possess well-defined stoichiometries and precise geometries, and their study provides insight into the onset of metallic character with increasing metal-core size. For example, the structure of a 145-atom palladium cluster has been reported (*Angew. Chem.*, **39**, 4121-4125, 2000). The central Pd atom is surrounded by 12 Pd atoms arranged in the form of an icosahedron. The next shell is 42 Pd atoms, and the third shell contains 60 Pd. Larry also described several other palladium clusters and then some gold clusters. These latter studies, he said, were made possible because John Connally and Richard Nixon took the U. S. off the gold standard in 1971, thus making it practical to do research on gold compounds.

The second session of the Trueblood Award Symposium opened with a talk by **John P. Fackler, Jr.**, Texas A&M, featuring new Au-N compounds. Di-, tri- and tetranuclear complexes are formed with Au(I) and amidinate ligands; dimers may undergo oxidative addition with halogens and halogenated hydrocarbons to form Au(II) complexes with very short Au…Au distances (i.e. 2.475 Å). Some tetranuclear species are luminescent. Calculations indicate that dimers are higher-energy species than related tetranuclear complexes, and the suggestion was made that, while structural theory was ahead of crystallography in the early days, now crystallographic evidence comes in advance of theory to explain it. Aurophilic "bonding" appears to be a relativistic effect.

The physical properties of crystals, such as entropy, specific heat, free energy and vibrational spectra, as calculated by lattice dynamics, were discussed by **Carlo Maria Gramaccioli**, U. of Milan. The calculation of anisotropic thermal parameters, with correlations, for the analysis of thermal motion in the crystal was also presented. Many examples of the successes of lattice-dynamical methods were given. Carlo Maria Gramaccioli, like Trueblood Award recipient Dick Marsh, often finds errors in the literature. For example, the eigenvalues for vibrational frequencies should all be positive, and lattice dynamics is invaluable for checking reported Raman and infrared spectra.

Carroll Johnson was unable to be present. In his place **Abraham Clearfield**, Texas A&M, discussed the influence of solid-state NMR spectra on the solution of the structure of $Cd_3(O_3PC_2H_4CO_2)_2 \cdot 2H_2O$. The powder-diffraction analysis gave a solution in $P2_1/c$, but MAS NMR spectra demonstrated that the molecule must have lower symmetry than that required by this space group. Ultimately the correct molecular structure was found in space group $P2_1$ and reasonable spectral assignments could be made for the $P2_1$ structure. The clues offered by the higher-symmetry analysis, such as rather high R values and a missing O atom, were emphasized.

In a similar vein, **Frank R. Fronczek**, Louisiana State U., spoke of the hazards of using space groups of too-high symmetry, citing several analyses in which the structures were pseudo-centrosymmetric. Such pseudosymmetry should be checked for when the structure contains disorder or when average B values are high compared to the Wilson-plot B. Examples of such inverse-Marsh errors included a chiral compound in P1bar, two diastereomers in a pseudo-centrosymmetric array, and a case in which suspicious H-bonding signaled a C2/c structure that should instead be refined in Cc.

Marshing: Past, Present and Future was the title of the talk by **Ton Spek**, Utrecht U. The cases of incorrect space groups found by Dick Marsh in the published literature are just as numerous in the present as they were in the past, in spite of widespread publicity and better software. The only clear exception is provided by the IUCr journals for which no recent corrections have been reported. Many journals now consign crystallographic details to supplementary material or the CCDC, and many structures are published by chemists in an automated fashion. Much of the deposited material is probably never seen by a crystallographic referee. Ton stressed that spacegroup validation is available free of charge through the web-based IUCr *Checkcif* facility. In addition, academic users can download the relevant software free of charge from **www.cryst.chem.uu.nl/platon** for in-house checking.

Jenny Glusker, Fox Chase Cancer Center, presented results of a survey of metal ions in biological systems based on information from crystallography and theoretical studies. The search mechanisms in the CSD were not found to be helpful for identifying metal ion coordination. Therefore the relative tendencies of metal ions to form bonds with O, N or S, for example, had to be extracted from this database on a structure-by-structure basis. Binding preferences of a wide variety of cations, such as Mg^{2+} and Zn^{2+}, were investigated, and the influence of the lone pair in Pb^{2+} on directional binding was surveyed. Energy calculations were employed to examine the manner in which water molecules surround metal ions (which may cause water to be deprotonated) and the effect of decreasing the inner coordination sphere surrounding Mg^{2+} and Zn^{2+} from 6 to 5 to 4 water molecules. Results were checked with protein structures in the PDB. The objective of these studies is to form a database of the occurrence and biochemical uses of metal ions in protein structures.

Mogul – Rapid Retrieval of Molecular Geometry from the CSD, a knowledge base of molecular geometry, was described by **Gary M. Battle, CSD.** The advantages of Mogul are simple query definition, fast search speed, and accessibility of the results to other applications. The knowledge base is composed of fragments from every CSD entry. The fragments are classified by components. At present, metal ions are not included in the fragments in the Mogul knowledge base. Fragment construction, keys and the search tree were demonstrated, and the statistical methods for evaluating the results of a query were discussed. The underlying methodology and validation work, mentioned by Gary in his talk, is covered in an article submitted to *J. Chem. Inf. Comput. Sci.* by Ian Bruno entitled *Retrieval of crystallographically-derived molecular geometry information.*

We congratulate Trueblood Award recipient Dick Marsh, we thank ACA President Frances Jurnak for her award remarks, the organizers Larry Falvello and Alberto Albinati for a fine program, the twelve excellent speakers for talks that were especially relevant to chemical crystallography, and the large and enthusiastic audience for questions and discussion.

Emily F. Maverick and Jenny P. Glusker

L to r: Rui-Ming Xu, Seth Darst, Cynthia Wolberger, David Bushnell, Richard Brennan, Cory Momany.

1.01: Structural Insights into Transcription

The opening ceremony and Fran Jurnak's welcoming remarks were followed by a well-attended session concerned with various aspects of mRNA transcription, Topics in the six talks ranged from the structure and mechanism of the polymerase enzymes themselves, to the DNA-binding proteins and chromatin-modifying enzymes that control transcription of specific genes.

The session opened with an impressive presentation by **Seth Darst**, Rockefeller U., on the bacterial polymerase enzyme. In a series of structures of the five-subunit *T. aquaticus* core and holoenzyme, he showed how the enzyme binds the DNA template in the active site, the location of the elongating RNA, and the channel that allows nucleotides to enter the active site. A series of structures including the sigma subunit, which binds the core enzyme to form the holoenzyme, nicely explained how sigma aids in bacterial promoter recognition, while at the same time giving rise to non-productive cycles known as abortive initiation through the interference of a linker region with the growing RNA chain. In a separate study of anti-sigma factors, Seth showed how these proteins bind to and sequester the sigma subunit, thereby preventing sigma from associating with the core enzyme.

The next talk by **David Bushnell**, Stanford U., showed how the even larger and more complex eukaryotic RNA polymerase II carries out the same essential steps in transcribing a DNA template. In a remarkable achievement, Dave and his colleagues in Roger Kornberg's laboratory had determined the structure of the 12-subunit core enzyme, which weighs in at 500 kDaltons. Despite the greater complexity of this enzyme, there is striking structural and chemical conservation between the yeast enzyme and its smaller bacterial cousin, including the way in which it binds to the RNA-DNA transcription bubble. The eukaryotic enzyme, though, requires a much larger set of additional polypeptides to bind to a promoter and initiate transcription. The structure of one of these general transcription factors, TFIIB, has now been determined in complex with the core enzyme. This complex suggests how TFIIB might stabilize binding to template DNA and promote formation of the 50-polypeptide transcription initiation complex.

The talks on the transcriptional machinery itself were followed by presentations on the proteins that regulate transcription of specific genes. **Richard Brennan**, Oregon Health Sciences U., presented structures of the proteins involved in carbon catabolite repression. CcpA, a LacI family member, forms a complex with a phosphorylated protein, HpR. This complex binds DNA and either represses or activates transcription. The structures presented of a CcpA-phosphoHpR complex bound to DNA, along with the structure of the CcpA apoprotein, provided insights into how binding to DNA and Hpr modulates CcpA activity.

Cory Momany, U. of Georgia, then presented studies of BenM and CatM, two bacterial transcriptional regulators from the LysR family of DNA-binding proteins that regulate transcription of genes needed for degradation of aromatic compounds. Structural studies were presented that addressed how BenM responds to both benzoate and its catabolite, *cis, cis*-muconate (CCM), while CatM responds only to CCM. Structures of the effector-binding domains bound to these ligands revealed a new class of binding sites in BenM. Differences in the number of anion binding sites of BenM and CatM appear to account for the differential binding of effector molecules.

The regulation of chromatin structure through post-translational modification of histone proteins provides an additional layer of transcription regulation in eukaryotes. **Rui-Ming Xu**, Cold Spring Harbor, described work on the structure of Dot1, a histone methyltransferase that targets a very specific residue, Lysine-79, in histone H3. The structure of human Dot1 bound to its cofactor, S-adenosyl methionine (SAM), showed the enzyme to have a different fold from the SET histone methyltransferases. Interestingly, a large C-terminal domain that is essential for enzymatic activity is disordered in the crystal structure. Nonetheless, it was possible to model how Dot1 binds to a nucleosome and methylates lysine.

The final talk by **Cynthia Wolberger**, Johns Hopkins U. School of Medicine, focused on Sir2 deacetylases, a unique class of enzymes that deacetylate lysine residues in a reaction that consumes NAD^+. Sir2 enzymes were originally identified as histone deacetylases, although various members of the family target transcription factors and other proteins. Intriguingly, high levels of cellular Sir2 activity are associated with lifespan extension. A series of crystal structures were presented that illustrated how an archaeal Sir2 enzyme binds acetylated peptide, NAD^+, as well as the nicotinamide product. Based on these studies a model was presented for the enzymatic mechanism, as well as for how the nicotinamide product serves as a non-competitive inhibitor of the deacetylase reaction.

Cynthia Wolberger

From Dan Anderson: Reflections in "The Bean," a new sculpture in Millenium Park.

L to r: Marco Marino, Holly Heaslet, Christopher Colbert, Maryna Kapustina, David Belnap, Pius Padayatti, Jacqueline Milne, James Williamson.

1.02 Structural Analysis by Hybrid Methods

While all of us recognize that no one technique can do it all, this *not by crystallography alone* session emphasized that fact. The integration of x-ray crystallography with electron microscopy (EM), electron crystallography, Raman crystallography, small angle x-ray scattering (SAXS), molecular dynamics, free-energy simulations, and nuclear magnetic resonance was crucial to the studies presented.

Most studies used x-ray crystallography in conjunction with only one other structural technique, but **Marco Marino**, Biozentrum, U. Basel, Switzerland, has found it helpful to use data from SAXS, NMR, and EM for his work on the very flexible muscle protein titin. One result was the discovery of cadmium ion in titin. Although Marco won the "jack-of-all-trades" award for his use of four structural methods, EM received this year's "most-popular-non-x-ray-technique" prize, as EM also figured prominently in three other reports. **Jacqueline Milne** and **David Belnap**, both from NIH, presented studies where crystal-derived coordinates of proteins were fitted into cryoEM density maps of complexes to give a model of active-site coupling of pyruvate dehydrogenase and to identify conformational epitopes of hepatitis B virus, respectively. **Holly Heaslet**, Scripps, gave a progress report on her work on solving the *E. coli* transhydrogenase complex. Her goal is to merge the previously solved x-ray structures of components with a structure of the complex solved by cryoEM or electron diffraction.

NMR also figured prominently in the session. In addition to Marco's work, **Christopher Colbert**, U.T.SW Med.Ctr., and **James Williamson,** Scripps, find NMR data crucial to their experiments. Christopher studies thiol-disulphide oxidoreductase (TDO). He resorted to an NMR structure of reduced TDO when it resisted crystallization attempts. This structure is being used in conjunction with his x-ray and NMR structures of oxidized TDO to elucidate the enzyme's mechanism. Like two different but complementary people whose individual contributions are essential, James has found x-ray and NMR data very complementary in his work on the yeast ribosomal protein L30. He used both techniques in refinement. In particular, NMR NOEs contributed to the empirical energy function.

Pius Padayatti, Case Western Reserve U., finds that the combination of Raman and x-ray is a powerful way to identify and trap intermediates inside crystals. He used Raman crystallography to track intermediates of beta-lactamases inside the crystal, which then was frozen and the structure solved. He finds this more sensitive than solution Raman analysis. **Maryna Kapustina**, U.North Carolina, elaborated on the way ligand-binding energy is stored in conformational changes and then recovered during catalysis. Her system of study is tryptophanyl-tRNA synthetase. She combines molecular dynamics and free-energy calculations with x-ray data.

David Belnap and James Williamson

1.03 Computational Methods

Seven presentations covered a range of topics with a focus on automation: analysis of diffraction images, substructure determination/phasing, map interpretation, loop building, model parameterization and automated structure solution.

Nick Sauter, Lawrence Berkeley Lab., talked about robust indexing for automated data collection, describing the algorithms behind the lab's *Indexing Toolbox* (LABELIT). Fourier coefficients are used to determine the most likely direct beam position, the determination of the correct lattice basis, and the detection of two-folds for determining crystal symmetry. A comment in the discussion that the latter has been used by small-molecule crystallographers for several years highlighted the need for more interactions between macromolecular and small molecule crystallographers. Finally Nick described how LABELIT is being used in the context of an automated crystal screening system being developed at the ALS in Berkeley. **George Sheldrick**, U. Göttingen, Germany, gave a presentation describing the use of weak anomalous signals for macromolecular phasing. He described the practical use of SHELXD and SHELXE for substructure determination and phasing/density modification, respectively. He gave a concise introduction to the algorithms used in both programs, and pointed out some of the experimental requirements for use of weak signals, in particular the need for redundant data. It can also be important to calculate F_A values for the anomalous substructure when multiple wavelengths are available. George briefly touched upon the possibility of using radiation induced changes in the crystal to obtain experimental phase information.

Bill Furey, VA Med. Ctr, Pittsburgh, described the approaches to automation used in the *BnP* application, which brings together automated substructure determination with the *SnB* program and phasing with PHASES. Bill demonstrated *BnP* during his talk, with the program solving a 10 site MAD structure on his laptop as he was talking. He went through the various aspects of the Java graphical user interface for *BnP*, and showed how the results could be analyzed after the job was finished. After phasing it is possible to automatically launch RESOLVE or ARP/wARP jobs from the *BnP* GUI to perform model building.

Dusan Turk, Jozef Stefan Inst,, Slovenia, presented recent advances in his model building and structure determination program MAIN 2004. He

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1.03 Computational Methods, con't.

described the algorithms used to go from an initial electron density map to secondary structure elements and finally to an atomic model. Residues could be built automatically at a rate that makes model building interactive. A novel skeletonization method is used to generate a trace of the electron density that is then interpreted automatically to locate helices and strands. The trace is then converted into sp3 fragments, from which a polyalanine model is built. Sidechains are built automatically using a dead-end elimination algorithm. Examples were shown using test data and a real 2.8Å MAD map. This new version of MAIN will soon be released. **Henry van den Bedem**, SSRL, described a new approach to automated model completion. In collaboration with computer scientists at Stanford they have developed an automated method for building loops when the end points are known. An inverse kinematic approach is used which can be used to generate many loop conformations that satisfy the fixed end point condition. These loop conformations are scored and then optimized using real space refinement against the observed electron density. Henry showed examples of successful loop building, including a case with two distinct loop conformations in one molecule.

Tom Transue, Nat'l. Inst. Environ. Health Sci., North Carolina, gave a presentation about the geometric restraint values used in macromolecular structure refinement. He compared structures deposited in the PDB with the Engh and Huber parameters determined more than 10 years ago. It was possible to detect some errors in parameterization in existing refinement programs arising from typographical errors. Further analysis of high resolution structures in the PDB indicated that some geometric features are difficult to parameterize with existing methods; for example, changes in the pucker of the proline sidechain are associated with two different populations of bond lengths. It may be possible to address this issue and others in refinement protocols in the future. Finally, **Joe Brunzelle**, Northwestern U. Chicago, shared the knowledge gained from many automated structure solutions using different software packages. He described the Automated Crystallographic System (ACrS) he has built over the last few years. This is able to use many different software packages to analyze crystallographic data. Once deposited in ACrS, programs such as CNS, SOLVE/RESOLVE, SHARP, SHELXD/E, and ARP/wARP are applied to the data in different pathways. Joe described the results obtained and some of the strengths and weaknesses of the software packages. It was very encouraging to hear that it was possible to obtain an 80% complete model for approximately 75% of the data sets.

Paul Adams & Wayne Anderson

L to r: Bertram Canagarajah, Zbigniew Dauter, Vito Calderone, Samita Bilgrami, Dominika Borek, Robbie Reutzel, Dan Anderson, Todd Yeates.

1.04 Difficult Structures

First and second half Chairs **Zbigniew Dauter** and **Todd Yeates** briefly discussed in a (pseudo)mathematical fashion the dependence between the apparent difficulty of solving a crystal structure and the crystallographer's competence, and came up with the conclusion that all presentations of the session were characterized by a high level of both properties. **Bertram Canagarajah**, NIDDK, Bethesda, MD, dealt with the structure of beta2-chimaerin, a multidomain protein displaying a high degree of flexibility, significant nonisomorphism and weak crystal diffraction. The structure was solved by a combination of molecular replacement and SAD phasing. **Vito Calderone**, U. of Siena, Italy, discussed the structure determination of yeast copper thionein, a small protein of 5.6 kDa with eight copper atoms. This structure could not have been solved by molecular replacement or by anomalous diffraction phasing, in spite of the presence of a very strong (perhaps too strong) anomalous scattering signal, above 20% of the diffraction intensities. Eventually the structure was solved from the very highly redundant data set, which proved that it is not the magnitude of the anomalous signal, but its accurate measurement which is most important for a successful structure solution. **Samita Bilgrami**, AIIMS, New Delhi, India, explained how she solved the structure of disintegrin, a potential anticancer agent. The presumed homodimers crystallized in a primitive, but pseudo I-centered cell with half the reflections being very weak. The structure was ingenuously solved first by molecular replacement in the centered cell and then rigid-body fitted in all possible primitive subgroups, leading to only one satisfactory model. Unexpectedly, the structure turned out to contain heterodimers, where a few sequence mutations were responsible for the deviations from the more symmetric centered structure.

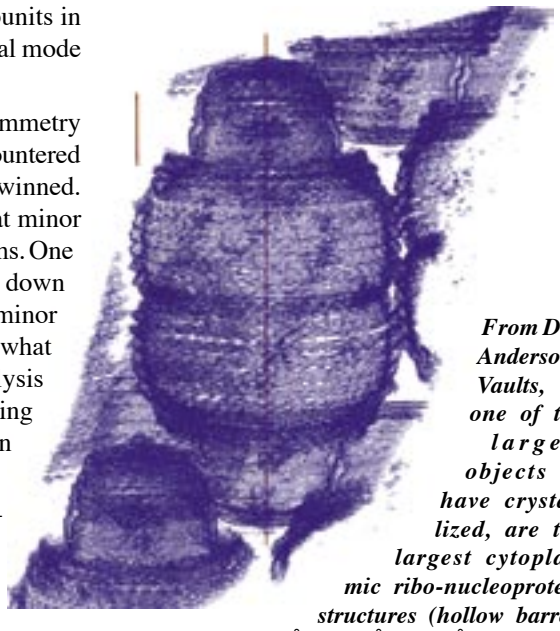
Dominika Borek. U.T. Southwestern, presented the structure determination of the large (a = 230 Å) cubic crystal of the protein yfbU, characterized by a high degree of NCS and pseudosymmetry. The NCS operators were found using a specially written program, and the initial low resolution SAD phases based on 32 Hg sites were extended by NCS and multi-crystal averaging. The protein forms tetrakozamers (24 subunits) with octahedral 432 local symmetry. Two

such complexes sitting on crystallographic 3-fold axes account for 16 subunits in the asymmetric unit. The crystal structure of the complex reveals an unusual mode of domain swapping between protein subunits.

Robbie Reutzel, U. Florida, Gainesville, described a fascinating case of symmetry transitions in crystals of a dimerized form of actin. When difficulties were encountered during refinement, it was discovered that the $P4_3$ crystal was hemihedrally twinned. A comparison to a related crystal form in $P2_12_12_1$ led to the realization that minor molecular rearrangements cause a transition between the distinct crystal forms. One of the crystallographic 2-fold screw axes in the orthorhombic form breaks down to give an NCS symmetry operation, which then promotes twinning. The minor rearrangement simultaneously creates a crystallographic 4-fold screw from what was NCS in the orthorhombic form. The structure determination and analysis was relatively straightforward by molecular replacement once the twinning was identified and taken into account, allowing a structural analysis of an antiparallel actin dimer.

The session was concluded with a talk by **Dan Anderson**, UCLA, describing impressive progress in the crystal structure determination of a 96 subunit, 13 million Dalton vault complex, a highly conserved particle that encapsulates RNA in eukaryotes, but whose specific cellular function is as yet unknown. ***(See image at right.)*** A vault crystal structure, even if approximate, may illuminate its biology, and would facilitate use of vaults as nanocapsules. Careful optimization of crystallization conditions produced diffraction to 8 Å resolution. X-ray data collection details (such as beam focus) had to be tailored to meet the demands of a unit cell exceeding 100 million cubic Å. NCS symmetry averaging, beginning with model phases from electron microsopy studies, has produced an image of a barrel shaped assembly with 48 staves visible in each half of the barrel around its circumference. Even while the vault structure is seen only at moderate resolution, numerous mysteries arise, such as how the architecture of 48 subunits in a ring can be accommodated at the narrow ends of the barrel. Higher resolution data will be required to unlock the mysteries of the vault.

Todd Yeates and Zbigniew Dauter



From Dan Anderson: Vaults, one of the largest objects to have crystallized, are the largest cytoplasmic ribo-nucleoprotein structures (hollow barrels 400Å x 400Å x 720Å); are near-ubiquitous, and yet have unknown function. The figure shows an overall view of vault electron density (about 9Å resolution) in the context of the crystal packing. The asymmetric unit contains half a vault; for this construct, that 's 4.65 megaDaltons. The short red line is a 100Å scale bar, the long red line shows the 48-fold non-crystallographic symmetry axis used for virus-like phasing (the crystal 2-fold is perpendicular to it). The monomer forming the hollow shell of the vault appears to be made from autonomously folded domains.

L to r: Leonard Chavas, Barbara Golden, John Tanner, Helen Walden, Nei-Li Chan, Lesa Beamer, John Hart.

1.05 New Structures

Hailong Zhang, Columbia U., discussed the structural basis for inhibition of the carboxyltransferase (CT) domain of acetyl-CoA carboxylase 1 (ACC1). Because inhibition of this activity shuts down long-chain fatty acid synthesis, ACC1 may be an attractive target for the design of anti-obesity drugs. The structures reveal a dimer of the CT domain both with and without CoA bound to the active site, which is located at the dimer interface. Inhibitors bind at positions that overlap with the CoA binding site or biotin binding site of the enzyme at this interface.

David Cooper, U.Virginia, presented the structure of the N-terminal region of Lis1, which is involved in dynein-mediated motor functions. The N-terminal region contains the LisH dimerization motif that is necessary for function. This motif generates two helices that come together to form what looks like a modified four-helix bundle. In the bundle, hydrophobic residues form the core of the dimerization motif while glutamic acid residues cap the helices. A Phe to Ser mutation found in lissencephaly patients is predicted to affect dimerization.

Barbara Golden, Purdue, presented the structure of a self-splicing RNA molecule from phage Twort. (See cover and page 29.) The structure of this "three domain", 242 nucleotide Group I intron in complex with a 4 nucleotide product-analog RNA has been refined to 3.6 Å resolution. This is a remarkable achievement given the difficulty coaxing this class of molecules to diffract beyond 5 Å. The structure reveals new details of the tertiary interactions that the link the three domains and form the guanosine substrate binding site. **John Tanner**, U.Missouri, described the first structure of the bi-functional proline catabolic enzyme, PutA. (See cover and p 29.) Structure determination of this ~900 residue, multi-domain protein required extensive screening of truncated constructs and homologs from other species. The resulting structure provides new information on how the enzyme links its two enzymatic reactions, which are essential for the recycling of proline in all organisms. The structure also suggests how a mutation found in humans might lead to a loss of function in the enzyme which in turn may lead to schizophrenia.

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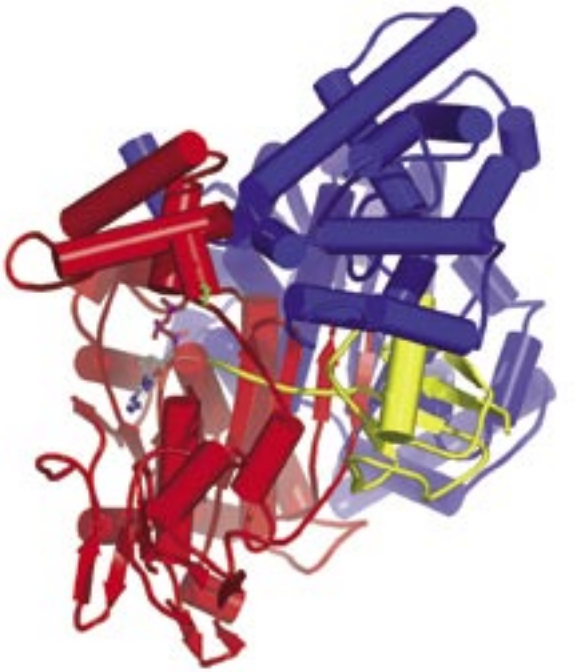
1.05 New Structures, con't

The structure of a ubiquitin-like protein (NEDD8) in complex with a heterodimeric E1 enzyme (APPBP1-UBA3) was reported by **Helen Walden**, St. Jude Children's Hospital. ***(See image, at right)*** This 120 kD ternary complex reveals the basis for E1 selectivity for its cognate ubl. An arginine residue in E1 critical for preventing the misactivation of ubiquitin was also identified. This work adds to the growing structural data on these critical conjugation systems.

Nei-Li Chan, National Chung Hsing U., Taiwan, presented structural data on the DNA-binding C-terminal domains (CTDs) that define the functional differences between topoisomerase IV and gyrase. Although the topoisomerase IV and gyrase CTD structures are both ß-propellers, their topological connectivities are quite different. These structural differences result in a different propeller slope between the two types of CTDs and leads to different curvature of the bound DNA. This is proposed to lead to the different functions of the two proteins.

Leonard Chavas, SBRC, Japan, persevered through technical difficulties with the projector and gave a beautiful talk on the crystal structure of the human cytosolic sialidase Neu2 with and without inhibitors bound. Sialidases have been implicated in several lysosomal storage disorders. Human Neu2 folds into a six-bladed ß-propeller with its active site in a shallow crevice. The two structures reveal large conformational changes illustrating the dynamic nature of substrate recognition.

Lesa Beamer and P. John Hart



From Helen Walden: the structure of the APPBP1-UBA3-NEDD8-ATP complex reveals the basis for selective ubiquitin-like protein activation by an E1. This is a bird's eye view of the enzyme looking down the top at the tail of NEDD8 approaching the ATP sitting in the nucleotide-binding pocket. APPBP1 is in blue, UBA3 in red and NEDD8 in yellow.

Walden H, Podgorski MS, Huang DT, Miller DW, Howard RJ, Minor DL Jr, Holton JM, Schulman BA. Mol Cell. Dec 2003, 12(6):1427-37.

L to r: Bob Stroud, Bryan Berger, Susan Buchanan, Piet Gros, Liliana Sampaleanu, Richard Baxter, Tina Iverson, Bill Clemons, Marianne Schiffer, and Michael Wiener.

1:06 Membrane Protein Structures

This lively session featured eight speakers working on a variety of topics: proteins involved in secretion across inner and outer membranes, bacterial and plant photosynthetic reaction center complexes, and a new bacterial importer. Michael Wiener opened with introductory remarks taken from Stephen White's recent publication on the progress of membrane protein structure determination.[1] Eighteen years after publication of the first high resolution structure of a soluble protein (myoglobin, by John Kendrew), Richard Dickerson estimated that approximately 13,000 structures would be solved by 2001 – a remarkably accurate estimate. Likewise, eighteen years after the first high resolution membrane protein structure was solved (the bacterial photosynthetic reaction center, by Johann Deisenhofer and Hartmut Michel), White's analysis of solved membrane protein structures predicts that the number of membrane protein structures will continue to grow exponentially, exceeding 100 structures in 2005, to about 2,200 structures by the year 2025. At that point, we will need multiple sessions to cover progress in this field!

To begin the session, **Piet Gros** presented the structure of a bacterial autotransporter, NalP. The C-terminal portion of this protein folds into a transmembrane beta barrel, which facilitates secretion of an N-terminal 'passenger' domain across the outer membrane. The structure suggests that the transporter functions as a monomer, since its 12-stranded barrel encompasses a single alpha helix, with the N-terminus exposed at the extracellular surface. A very different type of secretion was discussed by **William Clemons** when he described the elegant structure of a bacterial SecY complex. This heterotrimeric inner membrane protein complex is conserved from bacteria to man, and functions to secrete soluble proteins and to retain alpha helical membrane proteins in the inner (or plasma) membrane by sorting them laterally into the lipid bilayer.

Although the first bacterial photosynthetic reaction center structure was solved over 20 years ago, two talks showed that we are still far from complete understanding of the coupled processes of electron and proton transport. **Marianne Schiffer** discussed structures of reaction center mutants defective in proton transport,

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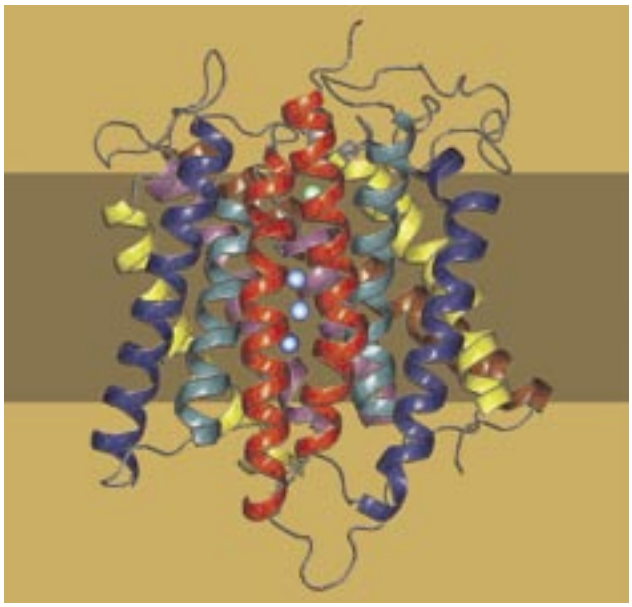
1:06 Membrane Protein Structures, con't

while **Richard Baxter** described time-resolved experiments to look at light-induced structural changes occurring upon transfer of electrons. The analogous complex in plants, photosystem II reaction center, was described at 3.5 Å resolution by Tina Iverson. This very large structure consists of 19 subunits (there are only 3 in most bacterial versions) and in addition to transferring electrons and protons, photosystem II contains an 'oxygen evolving center' consisting of manganese, oxygen, and calcium, which functions to split water into hydrogen and oxygen.

Several speakers discussed the experimental difficulties encountered when solving membrane protein structures, and these practical aspects were enthusiastically received by the audience. **Liliana Sampaleanu** spoke on her attempts to prepare and analyze proteins involved in Type IV pilus biogenesis, while **Bryan Berger** described experiments investigating the role of protein and surfactant interactions in crystallization, using bacteriorhodopsin as a model system. **Tina Iverson** also spoke about the influences of cell growth, protein purity, and removal of protein aggregates on obtaining well ordered membrane protein crystals.

The session ended on a high note with the new 1.3 Å resolution structure of the *E. coli* ammonium transporter, AmtB, presented by **Robert Stroud**, ***(see image)***. This 11-helix monomeric protein contains a hydrophobic lumen, and Stroud suggests that it is likely to function as a channel rather than as a transporter; moreover, he presented evidence that it is ammonia gas (rather than the ammonium ion) that traverses the membrane through the channel lumen. AmtB is the highest resolution membrane protein structure solved to date, and gives us a benchmark for future structures.



From Robert Stroud and Shahram Khademi. The AmtB molecule with two-fold symmetry related helices (M1-M5 and M6-M10) in the same colors. Three ammonia molecules are shown with blue spheres; the green sphere is the ammonium molecule. Science, Sept. 10, 2004.

The progress made in determining membrane protein structures continues to amaze and inspire us. If Stephen White's prediction is correct, the next twenty years will be breathtaking.

Susan Buchanan and Michael Wiener

1. White, S.H. (2004). The progress of membrane protein structure determination. *Prot. Sci.* **13**: 1948-1949.

1.07 Macromolecular Assemblies

The cytochrom bc_1 complex is a multi-subunit membrane protein with molecular mass approaching 500 kDa that shuttles protons across the membrane and couples proton pumping to electron transfer. Although the first crystal structure of bc_1 was determined several years ago, the molecular mechanism of electron transfer remained unknown. **Di Xia** presented a series of crystal structures of bc_1 in different conformations "frozen" by various inhibitors, and these structures beautifully illustrate the pathway of electron transfer through the complex and across the membrane. **Tina Izard** focused on the macromolecular interactions between cells and extracellular matrices (aka focal adhesions) and reported the crystal structures of human vinculin (116kDa) and its activated form, vinculin-talin complex. These structures reveal a spectacular flexibility of the helical bundle assembly in vinculin. To solve the structures of such large, loose and multi-domain proteins remains technically challenging, but the hard work was rewarded with the revelation of signaling mechanism for cell adhesion.

At the end of the session, the spotlight was shifted to protein and nucleic acid interactions. **Alba Guarné** reported the crystal structures and functional analyses of a DNA-binding protein, SeqA, and its complex with DNA. Crystallographic studies reveal that SeqA, even though small (21kDa), contains both a DNA-binding domain and a self-assembly domain. Their structural results led to mutagenic and *in vivo* functional analyses, which confirm that both DNA binding and self assembly are essential for SeqA to regulate initiation of DNA replication in *E. coli*.

See page 62 for the 2nd part of 1.07 report.

Wei Yang

1.08 Structural bioinformatics

A key theme in the structural bioinformatics session was about using structure (both predicted and experimental) to ask and answer questions about evolution. It is generally accepted that knowing structure helps in understanding or deducing function. However, in nature structure is more conserved than sequence or function (*i.e.*, extremely different sequences and functions adopt the same fold), and therefore structure may have greater utility in helping determine evolutionary relationships between proteins. This was explored in several of the talks in this session.

Phil Bourne opened the morning session with a talk on using conserved protein folds within an organism's proteome to determine evolutionary distances and construct phylogentic trees. He was followed by **Bill Duax** who combined information on protein structures and conservation of amino acid sequences in families of ancient proteins to trace the evolution of the genetic code. **Danny Fischer** finished off the morning session with a talk on genomic ORFans - ORFs that show no sequence

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Coffee breaks

At top, l to r: Kevin Battaile. Anne Mulichak and Mike Becker; Hans-Beat Bürgi, Ken Hardcastle, Frank Fronczek, and Larry Henling. 2nd tier, l to r: Andy Howard and B.C. Wang; Jeff Deschamps, Duncan McRee, Judy Flippen-Anderson, and John Norvell. Next tier, l to r: Andy and B.C. with Andy's hat; Paula Fitzgerald and Janet Smith; bottom row, l to r: Bill Duax online; Jenny Glusker, Sheila and Bob Gould.

1.08 Structural Bioinformatics, con't.

similarity to any other protein in the databases. Fischer showed how experimental and computational structural biology are already helping to shed light on the many evolutionary puzzles due to ORFans.

Ling-Hong Hung was the only speaker to focus on *de novo* structure prediction using evolutionary structural information to design better sampling algorithms. Finally, **Jeffrey Roach** used a novel encoding of protein structure to create one-dimensional strings that could be used to compare structures using a variety of sequence comparison methods, which may be capable of detecting novel evolutionary relationships.

Many in the audience commented that it was refreshing to have a bioinformatics session at the ACA meeting. Methods to predict structure may be used to predict and/or understand biological function, and can now, in some cases, be used to help in the experimental structure determination process itself. This section focused on the use of structure to pose and answer questions about biological evolution, guided by sophisticated bioinformatics tools.

Daniel Fischer and Ram Samudrala

Coffee Breaks, con't: ***above, Dick Marsh with Dave Duchamp. Below, l to r: Aude Izaac, George DeTitta, and Stacie Gulde.***

Back, l to r: Ray Jacobson, Al Edwards, George Phillips, Bill Studier, Steve Kent. Front, l to r: Frank Collart, Song Tan.

1.09 Fresh Approaches to Express and Purify Biomolecules

Given the dubious distinction that it was placed in the final time slot of the meeting, attendance was remarkably good, and attendees heard a wide range of methods discussed. **Steve Kent** gave a thoughtful and comprehensive analysis of protein synthesis using chemical methods. He showed many examples of chemically synthesized proteins whose structures were determined by x-ray or NMR, and then explained the advantages and limitations of the synthesis methods used and how they might be applied to other proteins. It was clear that the approach, though rarely used at present, may have widespread applicability. **Bill Studier** then described improvements to the T7 expression systems which he pioneered. He described a new strategy, based on the principle of diauxic growth in *E. coli*, which allows for inducible recombinant protein expression in the absence of a chemical inducer. This so-called *auto-induction* medium is entering widespread use with impressive results.

Frank Collart described his group's preliminary efforts to express membrane proteins and their domains, on a large scale. **Al Edwards** presented an entertaining and thought-provoking talk covering many lessons from his structural genomics efforts, including the use of orthologues to improve success rates of expression, solubility and crystallization, and screening for small molecule interactors to identify potential function and to stabilize enzymes during crystallization. **George Phillips** compared the expression of about 100 plant proteins in wheat-germ cell free extracts and in *E coli*. This is an important study because cell free methods have rarely been compared in a controlled manner with bacterial expression. His team observed a correlation between the levels of protein expression in the two systems, with some differences in the protein expressed at middling levels. This work will be published soon. **Ray Jacobson** then described purifying an essentially native multicomponent complex from the yeast *Saccharomyces cerevisiae* using a version of the TAP tag system in wide use for analysis of protein-protein complexes. Ray was able to purify the megadalton TFIID assembly of transcription proteins to apparent homogeneity. Although the yields are extremely low by most standards, he made a compelling case that the amounts obtained were compatible with new nano-scale crystallization methods.

Al Edwards

L to r: Peter Müller, Robert Gould, Larry Falvello, Michael Sawaya, William Clegg, Jenny Glusker, George Sheldrick.

2.03: Teaching Advanced Crystallography

Peter Müller organized the session in order to emphasize teaching more advanced aspects of crystallography to people who already have some basic crystallographic knowledge. Before a large audience, seven distinguished crystallographers and experienced teachers gave presentations on bringing crystallography to students.

The opening talk was given by **Jenny Glusker**, who shared some of her experiences teaching crystallography to biologists. Among other things, she pointed out the importance of teaching the meaning of resolution, and the relation between resolution and the amount of information about a protein molecule obtainable from a diffraction experiment. Glusker also gave tips about to how to give an overview of crystallography in only four lessons and touched upon other topics like the Patterson function, the phase problem and direct methods, as well as neutron diffraction.

Bernhard Rupp focused on teaching crystallography to bioscientists. He introduced his *Crystallography 101* at: **www-structure.llnl.gov/Xray/101index.html**) and spoke about the importance of carefully teaching the practical aspects and about generating a healthy skepticism towards the results. In addition, Rupp gave several didactical tips about the presentation of crystallography to students, and demonstrated a diffraction experiment with the laser pointer. *Making a MAD experiment seem rational* was the title of **Michael Sawaya's** presentation. Sawaya described how he generally introduces anomalous scattering and the MIR, SIRAS and MAD methods. An image of a child on a swing illustrated his analogy to aid comprehension of the 90° phase shift of the imaginary part of the scattering factor. Using this analogy as a basis, one can generate a two-hour lecture about MAD phasing that actually leads to an understanding of the method.

Turning from biological topics to fields more relevant to the world of chemical crystallography, **Bob Gould** gave a report on the BCA/CCG intensive teaching school in x-ray structure analysis that he co-organized and taught for many years. He described the outline of an intensive course on crystallography and how to actually run such a school.

Bill Clegg talked about the teaching of disorder, twinning and pseudo-symmetry. In his introduction he gave a list of required basics (fundamental diffraction geometry; direct and reciprocal lattices and unit cells; basic crystallographic symmetry; solving, refining and interpreting well-behaved structures) and general recommendations for the teacher (use real examples; use good materials developed by others; build on a firm foundation of basic crystallographic knowledge; be clear about meanings and use the correct terms). This was followed by a number of educational examples of disorders and twins.

Crystallography post-refinement was **Larry Falvello's** topic. Focusing on the analysis of structural results in a chemical or physical context, he reminded the audience to keep crystallography connected to the underlying properties of the system under study. In several examples Falvello showed what can be learned from a crystal structure if the scientist understands the structural model and makes observations open-mindedly.

Finally, **George Sheldrick** discussed useful concepts in teaching structure determination and structural chemistry. He started with a report on the structural inorganic chemistry course he regularly teaches at Göttingen University. In this class Sheldrick combines theory lessons and exercises with practical projects, so that students solve structures and deal with simple crystallographic problems. He also talked about Patterson superposition methods and crystallographic computing. Speaking generally, Sheldrick remarked that the internet is a good source for materials and stressed the importance of always encouraging students to think independently.

Peter Müller

3.01: Interface Between Powder and Single Crystal Diffraction.

This session highlighted the common ground between powder and single crystal diffraction. **Doug Dorset** began with some insights into the role of electron crystallography in the structural determination of microcrystals, powders and fibers. **James Kaduk** revealed that a common cold can lead to scientific discovery, as when he determined the structure of Guaifenesin from powder diffraction data. The study of polymorphs relies on both single crystal and powder diffraction, and **Stephen Boerrigter** presented intriguing work in this area. **Peter Zavalij** introduced us to the solid state bis(oxalato)borate salts and what powder and single-crystal diffraction could teach us about these systems. We were educated by **Akhilesh Tripathi** on ion exchange mechanisms in titanosilicates and how powder and single crystal diffraction provide answers to everyday problems in nuclear cleanup projects. **Rob Grothe** brought us all up to date on the process of structural investigations of aniostropic scattering materials and of how structure elucidation is possible.

We entered the realm of micro diffraction when **Nattamai Bhuvanesh** demonstrated that molecular structures can be solved and refined from µgs of microcrystalline material. **Ralph Tissot** remarked on the versatility of x-rays and how a small concentrated

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beam of x-rays can answer difficult questions posed by the materials scientist. **Alex Yokochi's** talk involved thin films and how the single-crystal diffractometer can be used to examine non-crystallographic problems. **Stephen Guggenheim** demonstrated that the single crystal CCD diffractometer could be used to collect powder data.

L to r: Alex Yokochi,, Joe Reibenspies, Jim Britten, Stephen Boerrigter, Rob Grothe, Stephen Guggenheim, James Kaduk, Ralph Tissot, Nattamai Bhuvanesh, Peter Zavalij, Peter Lee, Akhilesh Tripathi, William Clegg..

The synchrotron is the ideal source for both single-crystal and powder diffraction studies. **Peter Lee** informed us of the new role the synchrotron will play, now and in the future at the ANLS. Finally, **Bill Clegg** showed us the ability of the synchrotron to solve smaller and smaller crystals, and how we may best make use of this resource.

Joseph H. Reibenspies and James F. Britten

Back, l to r: Robert Bau, David Vicic, Doug Ohlendorf, Ian Anderson, Wim Klooster, Bryan Chakoumakos, Michael Heinekey; In front: Brian Toby, Herbert Hauptman, Art Schultz, Alberto Podjarny, Tom Koetzle.

4.01: Frontiers in Single-Crystal Neutron Diffraction

Nearly 100 attendees heard highlights of recent developments in neutron sources, instrumentation, and single-crystal diffraction applications in chemical crystallography, materials science, and structural biology. **Ian Anderson,** Spallation Neutron Source (SNS), opened the session with an overview of the exciting progress at SNS. This included spectacular videos shot at the SNS construction site on Chestnut Ridge in Oak Ridge that featured workers maneuvering massive steel assembles into place. The SNS, which will be the world's most powerful pulsed neutron source, is scheduled to begin operation in 2006. SNS will operate as a user facility, open to scientists and engineers from universities, industry, and government laboratories in the U.S. and abroad. Sixteen instruments (out of the 24 positions available) have been approved and funded, including a state-of-the art single-crystal diffractometer for small-molecule studies, to be named '*Topaz*', a powder diffractometer, a high-pressure diffractometer, a disordered materials diffractometer, and an engineering diffractometer. Planning also is well underway for a macromolecular neutron diffractometer *'MaNDi'*.

Robert Bau, USC, described studies by his group on the structural chemistry of covalently bonded metal cluster hydride complexes. The hydrogen atoms in the interstitial sites and on the surface of discreet molecular clusters serve as models for studying the bonding modes of hydrogen on metal surfaces and in bulk metals. An example is the distorted cubane-like cluster $H_4Co_4Cp^{\#}_4$, where $Cp^{\#}$ is tetramethylethylcyclopentadiene that Bau's group has studied at the Institut Laue Langevin (ILL) in Grenoble using their new *VIVALDI* qausi-Laue diffractometer. At *VIVALDI*, as at other new instruments around the world, neutron data collection times are being reduced significantly. When the *Topaz* instrument at SNS becomes available in 2009, complete neutron data sets on crystals a few tenths of a millimeter on edge will be obtainable in a few hours!

Michael Heinekey described research probing the structures and dynamics of metal dihydrogen and dihydride systems prepared in his laboratory at the U. of Washington. Proton, deuterium, and tritium NMR are invaluable probes for investigating these structures, combined with diffraction. The dihydrogen and dihydride species often are found to be exceedingly floppy with isotope- and temperature-dependent NMR couplings and structures. Without doubt, this flexibility is important for hydrogen activation processes that often take place at metal centers. **David Vicic**, U. Arkansas, rounded out the morning program with a talk describing his group's studies of the organometallic chemistry of nickel. His talk included a description of the investigation of an unusual linear M-H-M bond in a dinuclear nickel complex derived from pulsed neutron time-of-flight Laue diffraction data using the IPNS SCD. Comparisons with related molecules indicate that the M-H-M angle is sensitive to the degree of occupation of a frontier metal-metal antibonding molecular orbital.

Bryan Chakoumakos, Oak Ridge, gave a fascinating account of studies on skutterudites, which are of interest for thermoelectric applications. These are cubic cage structures having the formula $A_{1-x}M_3Pn_{12}$. Here M is a group VIII transition metal

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4.01 Frontiers . . Neutron, con't.

and Pn a pnictogen. The skutterudite cages can be filled to a varying degree by lanthanide, actinide, alkaline earth, or thallium. Neutron diffraction provides accurate atomic displacements for the filling atom, A, as a function of temperature and makes it possible to quantify the disorder and correlate the large amplitude 'rattling' of the filling atoms with the dramatic decrease of the lattice contribution to thermal conductivity. **Calum Chisholm,** Caltech, spoke on proton conductor materials, which can be exploited in a number of applications including hydrogen separation membranes and fuel cells. He described two alkali acid sulfates, and a mixed acid sulfate phosphate. For each material neutron diffraction was essential for a proper complete description of the structure.

A number of contributed papers were showcased. **Wim Klooster**, ANSTO, talked on the new quasi-Laue instrument at the Replacement Research Reactor in Australia, which will be similar to *VIVALDI* at ILL. **Brian Toby**,NIST, described a promising test station installed on the NIST reactor's thermal column. Dysprosium foils, which become activated in the white beam, are used at this station to detect the Laue patterns from single crystals. The last three talks of the session described studies on proteins. **Alberto Podjarny**, Strasbourg, France, described work underway on the *LADI* instrument at ILL on a fully deuterated human aldose reductase. The neutron experiments complement very high resolution synchrotron x-ray studies and reveal additional detail, for example, on the protonation states of active site residues. **Doug Ohlendorf**, U. Minnesota, described preliminary studies on protocatechuate 3,4-dioxygenase using the *PCS* instrument at the Los Alamos pulsed source.

Finally, **Herbert Hauptman**, HWI, Buffalo, described recent successes with direct methods applying a new shake and bake (*SnB*) protocol, to, for example, phase simulated error-free neutron data for hen egg-white lysozyme. The power of neutron *SnB* is dramatically enhanced when using isomorphous data sets where a few protons are replaced by deuteriums. In the poster session, on behalf of the *MaNDi* Instrument Development Team (IDT), **Arthur Schultz** and **P. Thiyagarajan**, IPNS, Argonne, presented details of the SNS instrument's design. *MaNDi* has the potential to make neutron diffraction much more accessible to the structural biology community.

Thomas Koetzle and Arthur Schultz

L to r: Jack Faller, Paul Pregosin, Alberto Albinati, Mike Hall, Juergen Eckert, Bob Scheidt, Larry Falvello, Ilia Guzei.

Session 05.02: Combining Spectroscopy, Calculations, and Crystallography for Solving Chemical Problems.

In this session speakers attempted to show how the combination of theoretical calculations, spectroscopic techniques, x-ray diffraction and neutron inelastic scattering can give a detailed description not only of the structural features of molecules but of their dynamics and chemical and biological reactivity. Complementarity was indeed a common theme.

Antonio Deriu, U. Parma, Italy, described neutron elastic scattering experiments varying thermodynamic parameters such as temperature, pressure and hydration, on a 100ps to 5 ns time scale. Results in starch, for example, reveal the role of fluctuations of hydrogen-bonding networks as driving forces for structural transitions. Dynamics again was the protagonist in **Bob Scheidt's,** (from U. Notre Dame, IN), animated presentation on Nuclear Resonance Vibrational Spectroscopy, a highly accurate synchrotron technique best described as Mössbauer spectroscopy with vibrational side bands.

"Synergy" was the term used by **Juergen Eckert**, LANL, to describe the relationship between neutron scattering and computational methods in the particular context of his talk on sorbates in porous materials. The same term could have been used for the concerted use of x-ray structures and computational methods, specifically density functional theory, as described by **Mike Hall**, Texas A&M, whose clever examples dealt with the separation of electronic, steric, and packing effects in explaining structural features and chemical reactivity. The crystallization process itself can drive the isolation of one or more of a varied set of possible products; this was the theme of **Jack Faller's**, (from Yale), talk on crystallization-induced asymmetric transformations and the chiral organometallic compounds that can result from them.

The interpretation of crystal structures relies on indicators that need to be defined as accurately as possible. **Ilie Guzei**, U. Wisconsin, presented a thorough treatment of the calculation of the solid angles subtended by ligands is a novel means of solving an old descriptive problem in crystal structure analysis. Even the best descriptors arising from crystal structure analysis have a context, and a thought-provoking talk by **Paul Pregosin**, U. of Milan, Italy, in which x-ray crystallography and NMR spectroscopy were described as "two partners separated by a solvent" made it clear that even molecular dimensions are not cut-and-dried concepts. The hydrodynamic radius, measured in solution by NMR, complements "x-ray radii" when one wants to describe the behavior of a compound in a setting other than the crystal.

Larry Falvello and Alberto Albinati

L to r: Vic Young, Bruce Noll, Charles Campana, Michael Sabat, Chris Frampton, Jeff Deschamps, Mark Hollingsworth.

5.03: Non-Routine Refinement of Small Molecules

Problem structures are always interesting to small molecule and service crystallographers. Consolidating papers from both SIGs, with the theme *non-routine refinements*, the topics were: twinning, absolute configuration, incommensurate structures, disorder in space groups with crystallographic mirrors, domain switching in ferroelastic materials, the accurate location of hydrogen atoms, and charge density studies.

Michal Sabat, U.Virginia, detailed the structure solution and difficult refinement of a BINOL compound. BINOLs are chiral compounds that are used extensively to control asymmetric synthesis. The specimen selected for data collection suffered from twinning by merohedry. He showed that this structure could be solved using SHELXD after 96 hours of computing time. After the initial refinement, the important question of the correct absolute configuration was answered. The data for this light-atom structure were collected using a Cu-source, which provided an unambiguous absolute configuration determination.

Charles Campana, Bruker-AXS, described a commensurately modulated carborane compound. This material was first prepared nearly forty years ago, but no structure was ever published. Chuck compared film, serial diffractometer and CCD unit cell indexing attempts all of which led to ambiguous unit cells. He identified which reflections belonged to the subcell and which to the supercell, then used supercell reflections to determine the correct modulation vector and proceeded with data processing of the modulated structure. After the initial solution with SHELX, the structure was expanded to the correct superspace group and refined in JANA2000.

Jeffrey Deschamps, NRL, presented a series of organic structures with inherent molecular mirror symmetry except for the various R-groups. He explored the connection between molecular symmetry and crystallographic symmetry for these compounds, with the idea that there are examples of symmetric molecules that crystallize in space groups with and without mirrors, and, on the other hand, molecules with obvious breaks from mirror symmetry that crystallize in space groups with mirror symmetry, with static disorder across the mirror. He compared his structures using energy calculations from CrystMol. He then surveyed the CCDC for disordered structures with $Z'= 0.5$ and $Z' \neq 0.5$. Interestingly, the result was that common space groups with crystallographic mirrors had an abnormally high percentage of disordered structures.

Mark Hollingsworth, Kansas State U., presented a study of ferroelastic channel inclusion compounds. This class of materials switches domains in response to mechanical stress. The guest species simply reorient in response to the stress applied to the host, causing twinning of the resultant structure. Disorder of the guest species within the channels is an additional complication. Both applied-stress reversibility and memory effects within these ferroelastics were presented. Comparing subcell and supercell refinements, it was clear that these structures can be quite complex.

Bruce Noll, U. Notre Dame, presented various methods for finding hydrogen atoms in x-ray diffraction data. Some hydrogen atoms can be placed accurately in calculated positions based on host atoms, but metal hydrides, bridging hydrogens and some borane hydrogens are examples of hydrogen atoms that cannot be placed accurately by calculations. Three techniques were presented to find hydrogens: brute force, modifying least-squares weighting terms, and omitting higher angle data. Several examples were presented comparing and contrasting the strengths and weaknesses of these methods.

Chris Frampton, Bruker-AXS, presented the multipole refinement of a peri-substituted naphthalene and made comparisons to theoretical DFT density. He challenged us to conduct charge density experiments on laboratory CCD diffractometer instruments. Charge density studies no longer need be thought of as non-routine.

Victor G. Young, Jr

Judy Flippen-Anderson: single-handed photography. (Photo contributed by Eddie Snell).

At the Opening Mixer

Top, l to r: Abe Clearfield, Ton Spek, Victor Young, Ruth Clearfiield; Kathy Kantardjieff, Wilson and Florence Quail. 2nd tier: Fran Jurnak, Charlie Carter, Michael Blum and (just visible) Christine Muchmore; Louis Delbaere; Steve Ginell and Lisa Keefe. Below them, Alice Vrielink and Lesa Beamer; Anders Markvardsen, Shintaro Misaki and Cristina Horcajada. Bottom row: Lee Brammer and Bob Bau; Rick Bott, Ron Stenkamp, Claire O'Neal, and Mae Saldajeno.

6.01: General Interest I

I. David Brown, McMaster U., began with a graph theory-based view of molecular bonds in both inorganic and organic molecules that can predict, within a margin of error, their bond lengths. **Mikhail Antipin**, New Mexico Highlands U., then gave an overview of the electron density distributions in several series of compounds, and implications for bonding in the different systems.

John MacDonald, Worcester Polytechnical Inst., presented work on the preparation of complex crystals, where a crystalline layer of a metal complex is grown on top of a pre-existing seed crystal of a chemically related species.

The second part of the session started with brief presentations by **Frank van Meurs,** Bruker Nonius, on the performance of new multilayer optics and issues related to their design, and **Cheng Yang**, Rigaku MSC, on the advantages of using chromium radiation for structural characterization of biomolecules.

Nick Sahinidis, U. Illinois, Urbana-Champaign, presented a novel approach to solution of the phase problem in centrosymmetric structures, using a combination of renormalization of the phase space variable to yield an integer problem, followed by use of a global optimization algorithm. Applications of similar techniques to non-centrosymmetric structures were also discussed.

The session ended with an overview by **Constance Jeffrey**, U. Illinois, Chicago, on the growing number of so-called "moonlighting proteins," proteins that are found to have multiple functions, and by their moonlighting nature complicate the interpretation of the human genome.

Posters P181 and P184 were particularly relevant to this session. P181 by **Manju Rajeswaran,** Eastman Kodak, identified several new phases of tris(8-hydroxyquinolinium)aluminum, a well known organic electroluminescent phosphor, from differential scanning calorimetry experiments and the structural characterization by powder x-ray diffraction, attesting to the power of this technique. P184 by **Damon Parrish,** Naval Research Lab., described the results of a charge density study of an opioid molecule where the diffraction data were collected in 27 hours using Mo radiation and an R-Axis Rapid diffractometer.

Alex Yokochi

6.02: Cool Structures

A broad range of challenging and intriguing structures, from inorganic salts to biological molecules, were considered *Cool*. **Jeremy Rush,** Kansas State, who received an Etter student lecturer award, began the session with an excellent overview of ferroelasticity and then described his own results on urea inclusion compounds, illustrated with some spectacular optical micrographs of ferroelastic twinning. Emphasis on ferroic materials continued with a description of the high-pressure ferroelectric transition in lead phosphate by **Ross Angel**, Virginia Tech. The phase transition from C2/c to R-3m symmetry that occurs at 1.8 GPa probably involves static disorder. In an exemplary use of crystal engineering to obtain materials with specific properties, **Tatiana Timofeeva**, NM Highlands U., told us how to develop acentric packing of imine derivatives through tailored use of hydrogen bonding schemes. Her student, **Tiffany Kinnibrugh,** then illustrated the challenges of structure and polymorph prediction with her theoretical study of a compound known to crystallize in three polymorphs with three molecular conformations.

Carol Brock, U. Kentucky, discussed an apparently "simpler" molecule, pinacol, which is in fact quite complicated because it exhibits a wide range of structural packing motifs in its hydrates and has three independent molecules occupying three different symmetry sites in the crystalline anhydrous form. Again, this structural complexity is attributed to the large number of groups in the molecule available for H-bonding. Complexity was also a feature of the biological contributions to the session. **Miroslaw Gilski**, U. Texas SW Med. Ctr., described packing complexity in an oligomeric protein assembly consisting of twleve pentamers that crystallizes in the space group I23, while **James Geiger,** Michigan State U., discussed how the structural interactions between the sub-units of the tetramer comprising an enzyme help regulate its biological activity.

Ross Angel

6.03: Advances in Computing Environments for Crystallography

The first talk, by **Russ Miller,** HWI, Buffalo, was about *SnB* (Shake-and-Bake)/*BnP* (protein phasing) software on the Advanced Computational Data Center (ACDC) -Grid. See **www.hwi.buffalo.edu/SnB/** and **www.ccr.buffalo.edu/grid/content/overview.htm**. Russ clearly defined Grid computing and, in particular, what is not Grid computing, providing a breath of fresh air and distinguishing reality from hype and buzzwords. Pointing out that "The Grid" does not exist in the form that is commonly hyped but is currently under development, Russ elaborated on custom administrative tools written at the Center for Computational Research at SUNY-Buffalo in the context of the SUNY/HWI collaboration to make Grid computing practical. Russ then gave a live Internet demonstration of the *SnB*/*BnP* software via a standard web interface, and showed how users can check the status of jobs and quickly evaluate structure solution results. Software for collaborative examination and manipulation of molecular models via the Internet was also displayed. Queried on whether authors of crystallographic software should make their programs Grid-aware, Russ cautioned that until the Grid computing system proves itself, it might be wise not to commit to Grid computing. Beta testers for the new *SnB*/*BnP* for Grid are most welcome and should contact Russ via the above address.

Anders Markvardsen, Rutherford-Appleton Lab., UK, discussed the use of distributed computing to find optimal Hybrid Monte-Carlo (HMC) parameters for structure solution from powder diffraction data. These optimal values can then be applied to structure solution software running on single workstations. Using distributed computing tools to link local workstations, results could be obtained in a couple of weeks that would have taken half a year or more using a single workstation.

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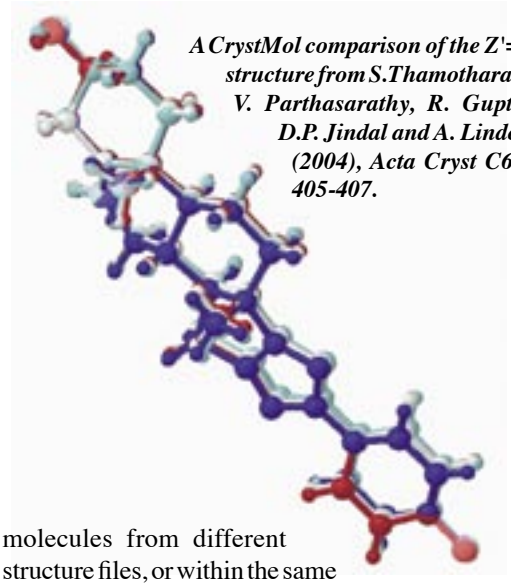
6.03: Advances in Computing, con't.

Showing a healthy disregard for conformity in computing and conference requirements for MS-Windows compliance, **Paul Emsley,** U. York, UK, used his Apple MacOS X laptop to demonstrate the Coot (Crystallographic Object-Oriented Toolkit) model building tools for protein crystallography. Coot is part of the CCP4 Molecular Graphics Project and has some features that resemble those of Frodo, O, Quanta and XtalView's XFIT. Paul's live demonstration showing Coot re-optimizing the incorrect orientation of a residue in real-time drew *ooh's* and *ahh's* from the audience. Coot is freely available in source code form under the GNU GPL License at: **www.ysbl.york.ac.uk/~emsley/coot/,** and compiled binaries for a variety of operating systems (SGI IRIX, Mac OS X, Redhat Linux) are available at: **www.ysbl.york.ac.uk/~emsley/software/binaries/**

Dennis Mikkelson, U. Wisconsin, Stout, introduced a GPL'd user friendly software package for viewing raw neutron Time-of-Flight (TOF) single crystal data, with an indexing option and integration speeds of visualisation of about a second for reconstructed raw image files of reciprocal space collected with multiple detectors. Both manual and computer based indexing options were shown for handling multiple crystallites; and the software can integrate 3D diffraction spots. Various "wizards" to aid in analysis, and an hkl slice viewer are in the latest (1.7.1 alpha 7) build available on the ISAW (Integrated Spectral Analysis Workbench) website: **www.pns.anl.gov/computing/isaw/**. This interactive software offers the TOF single crystal community, as well as x-ray CCD based crystallographers, the opportunity to integrate their raw single crystal data in a highly flexible manner.

Finally, **David Duchamp,** demonstrated the latest feature of CrystMol 2.1, available in Windows and Mac versions, for visually comparing similar molecules from different structure files, or within the same structure where Z' is greater than 1, as well as for comparisons of similar proteins. See **www.crystmol.com/**. This is a very useful feature for comparing polymorphs, or chemically similar structures. Molecules can be compared automatically using a point and click menu, or via the CrystMol scripting system. RMS differences are also listed.



A CrystMol comparison of the Z'=4 structure from S.Thamotharan, V. Parthasarathy, R. Gupta, D.P. Jindal and A. Linden (2004), Acta Cryst C60, 405-407.

Lachlan Cranswick

7.01: Biological Macromolecules: Solution Behavior and its Relation to Crystallization

The battle for well-diffracting crystals of macromolecules is won or lost in solution, before the crystals ever form. This exciting half-day session focused on the solution behavior of macromolecules and how events and behavior in solution can be used to control and/or predict crystallization. **Peter Vekilov**, U. Texas, described thermodynamic studies aimed at assessing the anisotropy of intermolecular interactions, and how such interactions can lead to stable liquid-liquid phase boundaries in macromolecular solutions. **Denis Vivares**, U. Delaware, continued this theme as he described work exploring how crystals nucleate in or around liquid protein droplets. **Sebastian Boutet,** U. Illinois and **Susan Krueger**, NIST, spoke of work in which different scattering methods (coherent x-ray diffraction for Boutet, and small-angle neutron scattering for Krueger) was used to probe the behavior of both pre-crystalline protein and small crystal nuclei. The session ended on a practical note with a talk from **Paul Kenis,** U. Illinois, describing a platform for vapor diffusion crystallization that allows for complete control of equilibration rates and end points.

Pat Loll

7.02: Macromolecular Crystal Quality and X-ray Diffraction

The *American Association of Crystal Growth* sponsored this session. **Zhengwei Hu,** NASA Marshall Space Flight Center, spoke on the use of coherent x-rays to study imperfections in protein crystals. He introduced a wide range of x-ray techniques that have been applied to semiconductors and then pointed out the differences in crystalline properties that make protein crystals much harder to study. Phase contrast techniques were successfully applied to image defect structures in protein crystals, and this technique shows promise as a useful tool to gain insight and optimize the crystallization process.

Vivian Stojanoff, Brookhaven NSLS, followed with at talk describing the application of topographic techniques to macromolecular crystals. Topography uses a fine pixel detector to image a single reflection in great detail, revealing distinct parts of the crystal that contribute to the Bragg peak at any one position. Vivian showed images of clear growth boundaries and different types of dislocations in the crystals. She then introduced reciprocal space mapping, profiling the lattice points in two dimensions Using this in combination with other techniques enables complete characterization of the crystal in terms of its x-ray properties. Topographic techniques are currently being applied to describe crystal growth.

A significant amount of research in applying physical x-ray techniques to biological specimens has been sponsored by national space agencies. **Hiroaki Tanaka,** Japan Space Utilization Promotion Center, Tokyo, gave an elegant description of improving the quality of α-amylase crystals using microgravity. The care and thought taken in this experiment was gratifying with consideration of the most suitable method of growth, modeling

7.02: Macromolecular Crystal Quality ..., con't.

of the process to choose ideal growth conditions and identification of a good cryoprotectant. Diffraction data of α-amylase recorded at SPring-8 improved from 1.12 to 0.89 Å. A poster by Tanaka predicted that improvements from reduced acceleration could be enhanced by using viscous solutions for crystallization such that larger, diffusion dominated depletion zones are formed.

Turning from physical studies to more applied topics, **Jeff Habel,** U. Georgia, described the crystal salvaging efforts of the crystallomics group at the Southeast Collaboratory for Structural Genomics. When screening fails to produce high quality crystals, a variety of methods have proved successful in obtaining diffraction quality crystals and ultimately a structure. Jeff described re-cloning, alternate expression, purification, chemical modification, and crystallization techniques. He focused on several areas: further purification increased diffraction from 3.0 to 2.3Å; the addition of an inhibitor (a small concentration of DMSO) gave much better crystals, and a combination of further purification then methylating the sample went from no crystals to small crystals then, finally, crystals that gave good structural data. For his final example he changed unusable sea urchin formations into nice single crystals by crystallizing in a gel. The salvaging techniques still require a human component but they might be automated in the future.

Any talk that opens with Eleanor Dodson, "xxx" email and spam in the same sentence is sure to get attention. **Angela Criswell,** Rigaku/MSC, gave a talk on ranking crystals from diffraction images. She described how algorithms used to identify spam email and mistakes the software made *i.e.* a "xxx" residue activating the spam filter, were the seed for developing techniques to study the quality diffraction images in the program d*TREK. A test set of many x-ray images were ranked on eleven rules and the results compared to human ranking of the same images - almost every crystallographer visiting Rigaku/MSC was seeing spots before their eyes for a while. Correlation with the human ranking showed that the principal rules defining quality were the number of reflections per resolution shell and the average signal-to-noise in the shell. The automated ranking is proving a useful tool to quantitatively compare experimental and instrumentation parameters. Increasing exposure time improved the ranking as did lower divergence x-ray optics. Pitfalls include anisotropy in the data and variable crystal-to-detector distance, but there are plans to overcome these.

Taking the audience on a ride through many areas of science, food and stock prices, **Keith Brister,** Consortium for Advanced Radiation Sources, U. Chicago, talked about putting crystals under a little pressure. Pressure, it seems, makes bad crystals worse, good crystals bad and occasionally good crystals better. Keith's talk started with an introduction to pressure and Nobel prizes. It was almost lunchtime, so he mentioned oysters and guacamole before turning to egg proteins with a diversion through the ups and downs of the stock market. His high pressure cells were used to hold crystals of cowpea mosaic virus under 2.2 to 3.5 kbar. That difference in pressure resulted in an increase in data resolution from 3.0 to 2.1Å. Misbehaving crystals do better with a little pressure. However, the current pressure cells are more suited for geological samples and seem to require a similar timescale for loading them. Keith is working to make the technique more routine.

Eddie Snell

8.03: Complementary Methods using Synchrotron Radiation

This session, sponsored by the Synchrotron Radiation SIG, began with **Bruce Bunker,** Notre Dame, who spoke about the structure of core-shell and alloyed binary nanoparticles. He used x-ray absorption fine structure spectroscopy (XAFS) along with other techniques to study non-melted core-shell nanoparticles and the time evolution of their structure. XAFS was used as a direct probe of the mixing of Au and Ag in Au/Ag core-shell structures. By combining the XAFS results with time evolution of the nanoparticle from optical measurements and molecular dynamics simulations, he and his collaborators found that the interdiffusion rates are more than four orders of magnitude greater than would be expected from a solid nanoparticle without defects. A model with 5% initial vacancies at the core-shell interface quantitatively explains their results on the Au-Ag nanoparticles. The same techniques were used to explore the structure of Pt-Ag, Pd-Ag, TiO_2-Au, and CdSe nanoparticle systems. In all these cases, both SR-based and non-SR techniques were necessary for a full understanding.

George Srajer, Argonne, spoke next about probing magnetic structures with circularly polarized synchrotron radiation. In his first example, the low-field surface nucleation and evolution of the inhomogeneous magnetic state in strongly coupled Fe/Gd ferromagnetic multilayers was measured using grazing-incidence x-ray magnetic circular dichroism. Experimental data and theoretical calculations unambiguously confirmed the existence of the long-predicted inhomogeneous magnetic state. In the second example, proximity effects in artificially structured cobalt arrays were studied using a photoelectron emission microscope (PEEM). Initial micromagnetics simulations confirmed experimental observations that a single domain state is favored when the elements of the array are separated by a distance less than 250 nm. **David Cookson,** APS, reported on small and wide angle scattering at the ChemMatCARS beamline. He presented a number of examples, including hydrogenated $LaNi_5$ alloys and super-hydrophobic silica/polymer hybrid surfaces, to illustrate the value of using SAXS and WAXS data to understand how structures on different length scales modify, enhance or simply complicate the nature of the component molecules.

Gabrielle Long, Argonne, discussed the development of Ultra SAXS as a complement to small angle scattering analysis. USAXS imaging utilizes the contrast of density variations in a sample to provide information on the shape and three-dimensional arrangement of the scattering objects. She provided examples of imaging the microstructure of a variety of materials, from cavitation in deformed metallic materials to growth of osteoblasts on artificial tissue scaffolds.

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8.03: Complementary Methods, con't.

Lee Makowski, APS, Argonne, discussed the use of wide-angle solution scattering to characterize protein secondary and tertiary structure motifs. A large test set of proteins with known structures were examined and principal component analysis was used to extract relationships between features in the diffraction patterns and alpha helical and beta structure content. Extension of this approach should allow the classification of protein architecture based on solution scattering, even for those proteins that fail to crystallize.

Andrew Stuart, CHESS, presented work on the direct experimental measurement of triplet phases for protein crystals. Using reference beam diffraction, a modification of standard oscillation geometry and an area detector, researchers from Cornell have measured a large number of triplet phase interference profiles for several proteins. He described the work they are doing to automate the data collection and phase determination process.

Gabrielle Long and Wayne Anderson

9.01: Topics for Young Scientists & YS-SIG Meeting)

This meeting marked the 10th anniversary for the YS-SIG and was opened by 2004 Chair **Arwen Pearson,** U. Minnesota. **Matt Clifton,** Purdue U., chaired the session. For the first time, the session had corporate sponsors -special thanks to Nextal, Fluidigm, and Hampton Research. Attendence was large, about 150 people. As expected, most were graduate students and postdocs, but there were also many others. **Joe Ferrara,** Rigaku/MSC, presented a overview of the interview process from the viewpoint of the interviewer, thus providing insight into common misunderstandings the interviewee might have about what to aim for. The needs and concerns of postdocs, with emphasis on proper compensation, benefits, and mentoring were addressed by **Alyson Reed,** Executive Director of the National Postdoc Association (NPA). Alyson's extensive knowledge and experience in scientific policy and development was clearly displayed through an eloquent presentation regarding the mission and activities of the NPA.

ACA President, **Frances Jurnak,** UC Irvine, presented a frank lecture regarding academic faculty job acquisition. She explained what is required from faculty applicants who are seeking an appointment in various academic sectors. The number of first authored, peer reviewed research articles deemed essential for a faculty job search was pegged from 5 to 7. So guys, you'd better get back to work. **Nabeela McMillian,** Marshall, Gerstein and Borun, LLP, spoke about intellectual property and patents, a subject which has been severely underrepresented. Nabeela's former experience as an academic postdoc combined with her expertise as a patent attorney made her the ideal person to explain IP issues. **Jim Kaduk,** BP Chemicals, closed with an honest, insightful, and appropriately humorous presentation on what it really means to be an industrial analytical crystallographer. Once again, the job growth forecast for the analytical crystallographer appears unclear.

YS-SIG Business Meeting: Copies of all the YS-SIG 2004 session presentations will be available from the YS-SIG website as soon as it is up and running. Until then, if you would like a copy of one of the 2004 presentations, please contact Arwen Pearson, **pears079@umn.edu**. Participation in YS-SIG has risen considerably over the past few years and, indeed, the doubling of YSs at the SIG business meeting was good verification of this phenomenon. All present felt that the session was well organized and exceptionally informative. The effectiveness of both the mentor/mentee dinner and the YS mixer was discussed, and while the dinner was dubbed a roaring success, the YS mixer did not live up to expectations. It was decided that next year's mixer will be held off site, most likely at Walt Disney World Downtown. Of course planning next year's YS-SIG session was the top priority. **Chandra Patel,** U. Kentucky, was selected as the session chair for 2005 and **Holly Heaslet,** Scripps, volunteered to serve as the YS-SIG webmaster. Topics for the 2005 half day session were discussed. Nominations for YS-SIG chair-elect 2005 are officially open and should be sent to the 2005 chair, **Chad A. Haynes, cah@caltech.edu,** as soon as possible. Also, the YS-SIG planning committee is in search for YSs in the central Florida region who can help coordinate the planning of social events at WDW. Please contact Chad or Chandra (**cpate2@uky.edu**) to offer your support. Finally, the YS-SIG planning committee would like to encourage the growing enthusiasm and support from the ACA community. By working together, we can continue to build on what is proving to be a model for future membership growth.

Chad Haynes

1.07: Macromolecular Assemblies, con't.

Douglas Freymann, Northwestern U., described the heterodimer formed by the "NG" GTPase domains, Ffh and FtsY, of the bacterial signal recognition particle (SRP) and its receptor. Almost unique among regulatory GTPases, these two molecules serve as GTPase activating proteins for each other, which leads to their disengagement. The heterodimer exists in a "latched" state in which nucleotides bound to both GTPase domains are in direct contact across the pseudosymmetric interface, but with p-loop and catalytic site arginine ill-positioned for catalysis. The complex awaits activation translocon machinery. **Lincoln Bickford**, HHMI, NY, described progress in deciphering the specificity of the CopII coat complex that coordinates the budding of transport vesicles from the endoplasmic reticulum. CopII comprises the Sar1 GTPase and two macromolecular subcomplexes which must specifically recognize SNARE proteins required for docking, and the protein "cargo" that is destined for secretion. Binding and crystallographic studies show that Sec24, a component of one of the two subcomplexes, contains two distinct binding sites for SNARE components, one of which also corresponds to the binding site for protein cargo. Sequential binding events appear to organize the assembly of SNARE/CopII complexes with protein cargo. There are still mysteries to be solved concerning the mechanism by which electron transfer is coupled to proton transport in the Cytochrome bc_1 complex. **Di Xia**, NIH, demonstrated how bc_1 specific inhibitors can be used to trap states of the molecule in which the dynamic iron-sulfur protein component can shuttle electrons from one quinone site to the other.

Steve Sprang

See p. 51 for the first part of the 1.07 report.

10.01 Materials for the 21st Century

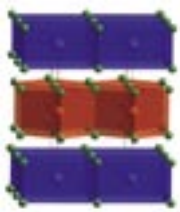
The application of new materials to all aspects of life led to enormous change in the 20th century. Now, at the beginning of the 21st century, the need to develop new materials is even more urgent. The need is global, and the challenge is to make materials and devices inherently more efficient, biodegradable, biocompatible, renewable and nonpolluting. In this session, we covered at least an invigorating few of the current materials research directions.

L to r: Volker Urban, Kenneth Poeppelmeier, Mercouri Kanatzidis, Omar Yaghi, Jason Hodges, James Richardson, Zhanhui Yuan.

P. Thiyagarajan, Argonne, presented the detailed atomic scale structure of variant Aß peptide self-assemblies. The laminar structure and growth mechanism in solution of these fibrils were studied using a combination of techniques including solid-state NMR, SANS, and SAXS, and the insights provided into the role of zinc in fibril nucleation and growth should prove valuable in combating diseases such as Alzheimer's. Thiyaga also presented unique Aß peptide nanotube self-assemblies constructed from coded peptides, in which the peptide sequence offers a unique handle for controlling their dimensions and properties. **Paul Butler,** NIST, presented a large scale structural study of two different clay-PEO polymer systems. Although these nanocomposite systems appear very similar from both macroscopic behavior and underlying morphology of the clay particles, Paul was able to demonstrate, through a series of very careful small angle neutron scattering measurements, that they exhibit quite different structural responses under application of shear flow.

Clay-polymer gel from Paul Butler:

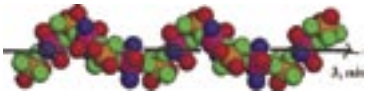
The synthesis of new single crystal heavy fermion intermetallics was discussed by **Robin Macaluso,** Louisiana State U. Following an introduction on heavy fermion and correlated electron materials, the synthesis and intergrowth structure types of the Ln_nMIn_{3n+2} (M = Co, Re) family of intermetallics were discussed. The Ce_nReIn_{3n+2} members are of intense interest since they exhibit coexistence of superconductivity with anti-ferromagnetic ordering. The crystal structures and magnetic and resistivity properties of the $CePdGa_6$, Ce_2PdGa_{10} and Ce_2MGa_{12} (M = Ni, Pd, Pt, Cu, Re) array of heavy fermion intermetallics were introduced as structurally and electronically related to this family,



$CePdGa_6$ from Robin Macaluso.

Trudy Kriven, U. Illinios, Urbana-Champaign presented a fascinating overview of ferroelastic ceramics. These materials display phase transformations with large volume and/or shape change hysteresis, and find application in both transformation toughening and smart ceramics. Using a unique portable compact thermal image furnace at both NSLS and APS, ferroelasticity and ferroelastic transformations *in situ* powder diffraction studies were shown for high temperature $YNbO_4$ and $DyNbO_4$ niobates having scheelite type crystal structures.

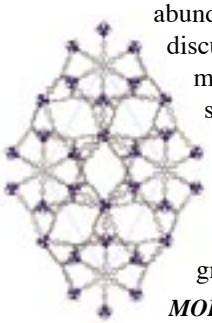
Ken Poeppelmeier, Northwestern U., showed, with many beautiful examples, that by taking advantage of the *cis*- and *trans*-directing properties of polar metal oxide fluoride anions, disorder can be eliminated and noncentrosymmetric crystal structures produced. Noncentrosymmetric solid-state materials are of technological importance since they often display important physical properties such as piezoelectricity, ferroelectricity, and non-linear optical response. Related directing strategies were outlined for one-dimensional chain structures for the production of chiral and chiral-polar materials.



From Ken Poeppelmeier, $Zn(pyz)(H_2O)_2MoO_2F_4$

Mercouri Kanatzidiz, Michigan State U., gave a very interesting and detailed analysis of the complex relationship between crystal and electronic structure in polytelluride compounds with square nets. By applying Peierls distortion to two-dimensional Te square nets, their inherent electronic structure instability was highlighted. Often this instability leads to structural distortion or charge density wave phenomenon and the opening up of a small gap at the fermi surface. Such materials are of interest for their use as thermoelectrics. The modulated crystal structure of $KBa_2Ag_3Te_6$ was shown along with the associated electronic band structure calculations revealing the presence of a small gap. Using an octet electron counting scheme for chemical bonding, the distortions present in the Te net layer were rationalized. This chemical bonding approach was used to help solve a wide series of commensurate and incommensurate superstructures of closely related polytelluride compounds including $K0_{.65}Ag_2Eu_{1.35}Te_4$, $K_{2.5}Ag_{4.5}Ce_2Te_9$ and $CeTe_4$.

A *tour de force* presentation of the synthesis and crystal structures of highly porous metal-organic framework (MOF) solids was given by **Omar Yaghi,** U. of Michigan. Starting from MOF-5 through interpenetrating MOFs and on to the queen-of-MOFs, an abundance of MOF structures were shown with discussion of framework patterns and the development of a reticular synthesis approach. The first step towards developing MOFs as low weight hydrogen storage materials was demonstrated. Aspiring to a very bright future for MOFs, the optimized MOF-177 exhibited an astonishingly high Langmuir surface area of greater than 4500 m^2/g.



MOF-190

Jason Hodges

11.01 & 11.02: USAS Science and Techniques

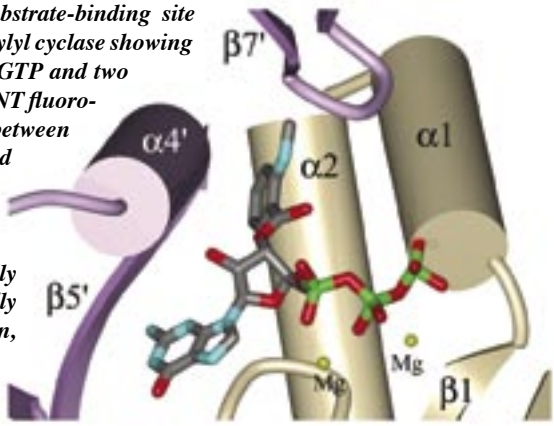
The International Consortium for Ultra Small Angle Scattering (IConUSAS) co-sponsored these sessions. Loosely-defined, USAS experiments access $Q < 0.001$ /Å with comparable Q resolution,usually by Bonse-Hart techniques. Applications presented included the more traditional topics of pores, colloids, gels, and polymers, as well as *in situ* studies of the flame aerosol process (**Greg Beaucage,** U. Cincinnati), provenance determination of marble in ancient sculpture (**Roberto Triolo,** U. Palermo, Italy), microstructural characterization of cheese (**Wim Bouwman,** Delft U. of Tech., The Netherlands), and the structure of lens crystalline proteins in fish eyes (**Amir Mirarefi,** U. Illinois, Urbana-Champaign). The structure factor of dense colloidal suspensions and gels was measured using a 2-D collimated USAXS instrument by **S. Ramakrishnan,** U. Illinois Urbana-Champaign.

Peter Jemian, Purdue U., reported on the status of Bonse-Hart USAS instruments at synchrotron x-ray and neutron sources (both reactor and spallation) with references to papers describing various optimizations and corrections. An alternative to Bonse-Hart optics, SESANS (**Wim Bouwman**) accesses the USAS region by exploiting properties of neutron spin-echo resonance to investigate strongly scattering samples. Applications of the SESANS instrument to colloid science were given. A report of the first experiments of a Bonse-Hart instrument at a time-of-flight neutron source was given by **Kazuya Aizawa,** Neutron Science Research Center, Tokai, Japan. The topics of multiple scattering and collimation correction also provoked lively discussions. USAXS Imaging to Complement USAXS Analysis (**Gabrielle Long,** Argonne) is a promising new x-ray technique for the characterization of materials microstructure.

Pete R. Jemian

Posters with Structure & Function Emphasis

Although posters in this category at ACA always cover a wide range of topics, I did notice a trend towards more structural information that impacts human health. This might reflect my own school of pharmacy bias, but I also think the funding atmosphere and the continuing international emphasis on health might have something to do with it. Three posters highlighting the mammalian (host) side of health caught my eye.



From T.C.Mou: Substrate-binding site of mammalian adenylyl cyclase showing positions of MANT-GTP and two Mg2+ ions. The MANT fluorophore that is bound between β1-α1-α2 of VC1 and β7´-β8´ of IIC2 acts as a wedge to prevent VC1•IIC2 from adopting a fully closed and catalytically active conformation, and results in a novel mechanism of inhibition that provides for isoform-specific selectivity and for potential therapeutic drug development.

P073, Mou *et al.,* U.Texas SW Med. Ctr., reported their structure of the catalytic core of mammalian adenylyl cyclase complexed with MANT-GTP and metal ions. MANTs, a recently discovered class of mAC inhibitors, are highly fluorescent nucleotide analogues. The structure identifies the binding site, which appears to be a new means of inhibiting adenylyl cyclase by blocking the formation of the catalytically competent enzyme. **Goldman** *et al.,* U.Helsinki, Finland, (**P087**) showed their structure of one component of the receptor for glial-derived neurotrophic factor, GDNF family co-receptor alpha1 (GFRα1) domain 3, solved at 1.8 Å. They found a novel fold consisting of a five-helix bundle stabilized by five disulfide bridges. By homology modeling, a more complete model for GFRα1 was generated that could be related to other GFNF-family members. **P091,** by **Kamata** *et al.*, Tsukuba Research Inst, Japan, on the structure of the human glucokinase, identified the glucose binding active sites as well as allosteric regulatory sites. This protein structure may offer new insights into controlling type 2 diabetes mellitus, a disease approaching epidemic proportions in our increasingly overweight population.

Also many posters highlighted the pathogen side of health. **Audette** *et al.,* U.Alberta, Canada, (**P074**) presented the structures at 1.5 and 1.8 Å of several truncated pilins from *Pseudomonas aeruginosa,* a human pathogen that attacks the immunocompromised and is a common source of infections in hospitals. Despite poor sequence homology among the pilins, the pilin receptor-binding loop may use a conserved mechanism involving main-chain interactions. Such a mechanism allows sequence diversity among the pilins while maintaining a conserved binding surface. **Zhang** *et al.,* SBC, Argonne, (**P083**) presented structures of the Sortase B from *S. aureus* and a related sortase from *B. anthracis*. Sortases proteolytically remove the C-terminal signal sequence from proteins directed to the cell wall of the bacteria. These two structures reveal a likely Cys-His-Asp catalytic triad. **Carrell** *et al.,* Washington U., St Louis, (**P082**) solved the structure of nikkomycin synthase, a protein involved in the multi-step synthesis of nikkomycins in *Streptomyces*. Nikkomycins inhibit chitin synthase, one of the cell-wall proteins found in fungi. Chitin synthase has long been viewed as a drug target since humans lack cell walls. Therapeutics targeting the protein could be very selective, with hopefully little side effects. Interestingly, the structures of the Nikkomycin synthase selenomethionyl-derivative used for phasing and the native protein showed substantial differences in the active site. These changes are somewhat surprising considering that native and selenomethionyl derivatives are generally treated as isomorphous. Subtle pH differences may account for the structural variation, but the structures may indicate that the reaction mechanism may involve large conformational changes.

Though we don't always think of bioremediation as a health issue, polychlorinated biphenyl compounds, better known as PCBs, can cause significant health problems. Fortunately microorganisms have enzymes, often locally evolved in response to the environmental pollutants, that can breakdown PCBs. Biphenyl dioxygenase is one such

protein. **Kumar** *et al.,* Purdue U., (**P095**) presented structures of dioxygenases from *C. testosteroni* and *Burkholderia*. These enzymes differ in their substrate interactions and substrate recognitions, suggesting a logical approach to their development as bioremediation tools.

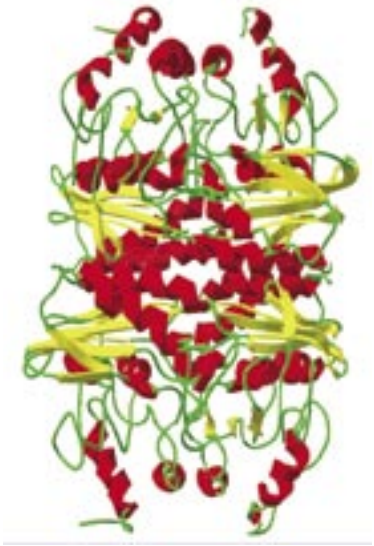
Pallan *et al.,* (P269) on structural studies of TNA/DNA hybrids also caught my eye, although it doesn't fit with the health theme. TNA is a nucleic acid having 3' to 2' linkages and a threofuranose sugar instead of the more familiar 5' to 3' linkages and (deoxy) ribose found in DNA or RNA. TNAs have chemical behaviors similar to DNA and RNA. They can base pair and be recognized by several enzymes that function on nucleic acids. TNAs are hot because they may be the evolutionary precursors of RNA. Hey, evolution could be considered a health issue too- right?

Cory Momany

Structure & Function Posters, con't

Posters emphasizing Structure and Function vividly demonstrated the wide variety of biological problems being addressed by ACA members, and showed that crystallography is an essential tool for probing the intimate relationship between function and three-dimensional structure. Several posters were presented by visitors from other countries, adding a much-appreciated international flavor to the ACA meeting. Highlights are:

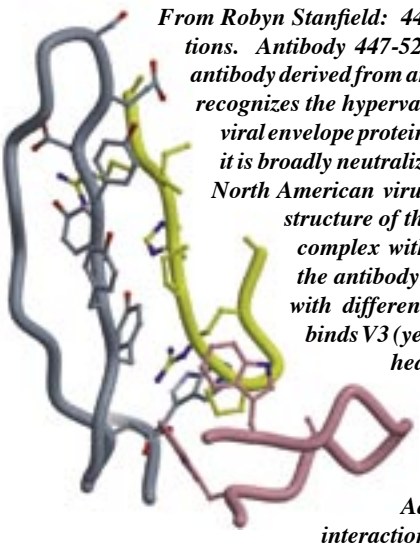
Zoë Fisher (**P033,** U. of Florida) presented structures of mutant carbonic anhydrase II at various pHs. The structures showed how changes in pH alter solvent hydrogen bonding in the active site, and that these changes were correlated to changes in activity. This work emphasized the importance of careful solvent modeling. **Robyn Stanfield** (**P035,** Scripps) presented another in a long list of important Fab structures from Ian Wilson's group at Scripps. This time, they tackled an anti-HIV-1 antibody that recognizes the V3 loop of gp120. The unusual binding mode of a V3 peptide explained the broad specificity of this medically important antibody. ***(See image at right.)***



Bog Stec (**P036**, U. of Texas, El Paso) presented an interesting study of inositol monophosphates with three different metal ions bound (Zn, Mn, Ca). The structures highlighted the important role of metal ions in catalysis. On a more global level, their structural analysis has led to key insights into the evolutionary roots of this family of enzymes. ***(See image at left.)***

From Bog Stec: An inositol monophosphatase from Thermotoga maritime, one of the most active IMPases known. The tetrameric organization of this enzyme is analogous to regulated tetramers of fructose 1,6 bisphosphatases from eukaryotic organisms.

O. Mayans (**P037,** Univ. of Basel, Switzerland) reported the structure of anthranilate phosphoribosyltransferase (AnPRT) in complex with its two substrates, An and PRPP. My favorite part of this work was that the structure showed that the two substrate binding pockets are too far apart to react, so there must be some sort of hinge motion that brings them together. Thus, dynamics plays a critical role in enzyme function. Two groups from the National Tsing Hua University in Taiwan presented very interesting posters focusing on the structural basis of lipid recognition by proteins. **Yuh-Ju Sun** (**P050**) reported three complexes of a lipid transfer protein with fatty acids. The structures suggested that plasticity of the C-terminal loop allows recognition of different fatty acids. Once again we see the important role of dynamics in protein function. **C.-D. Hsiao** (**P056**) presented the structure of cobra cardiotoxin, which induces membrane fusion of vesicles. The 1.9Å structures showed the protein surrounded by several SDS molecules. The bound detergent molecules likely mimic anionic lipids of the membrane. **C.-J. Chen** (**P052**) presented two high resolution ferredoxin structures, corresponding to aerobic and anaerobic forms. The structures were solved using Fe-SAD phasing. The electron density from the 0.9Å aerobic structure was



From Robyn Stanfield: 447-52D binding site interactions. Antibody 447-52D is a human monoclonal antibody derived from an HIV-1 infected patient that recognizes the hypervariable V3 loop on the gp120 viral envelope protein. 447-52D is unusual in that it is broadly neutralizing against many dissimilar North American virus strains. The 2.5Å crystal structure of the antibody Fab fragment in complex with a V3 peptide reveals how the antibody is able to recognize isolates with different V3 sequences. The Fab binds V3 (yellow) primarily with its long, heavy chain CDR3 loop (blue), forming a 3-stranded β sheet, composed of two strands from the Fab and one strand from the peptide. Additional side-chain specific interactions are formed between the Fab light chain (pink) and the conserved GPGR tip of V3. Thus, the antibody achieves high affinity through non-specific main-chain hydrogen bonds to the hypervariable portion of V3, yet retains specificity through side-chain specific interactions with the more conserved V3 tip (Stanfield et al., Structure, 12:193, 2004).

truly stunning. An interesting note: addition of Zn improved the resolution from 1.7 Å to 0.9 Å. Break out the $ZnCl_2$! **D.R. Davies**, U. Washington (**P053**), reported structural studies of tyrosyl-DNA phosphodiesterase. This fascinating DNA repair enzyme cleaves stalled topoisomerase I-DNA complexes by catalyzing hydrolysis of a phosphodiester bond between a tyrosine residue and a DNA 3' phosphate. The enzyme complexed with vanadate, a DNA oligonucleotide, and a tyrosine-containing peptide provided insights into mechanism. The active site included a unique vanadate-glycerol interaction that formed during a 60 second cryosoak. Since vanadate mimics the transition state for SN2

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Structure & Function Posters, con't

hydrolysis of phosphate esters, the vanadate-containing structures are proving to be very useful for examining mechanistic issues, and for developing inhibitors. **Y. Yamada** (**P062**) presented work of a Japanese team from the Structural Biology Research Center in Ibaraki and Kyoto University on gamma-1-adaptin, which is involved in vesicular trafficking between the Golgi and endosomes. Structures of adaptin complexed with two peptides provided insights into how adaptin recruits accessory proteins. Both complexes showed two aromatic side-chains of the peptide buried in cavities lined by basic residues. Curiously, conserved acidic residues of the peptide did not interact with the basic residues forming the cavities. This is an interesting and unusual case of molecular recognition driven by hyhdrophobic interactions. **C.A. Smith,** U. Auckland, New Zealand, (**P063**) presented research on the amide-bond ligase bacterial cell wall enzyme, MurC. The structure was solved from 3-wavelength Se-Met MAD data with very high anomalous completeness. An exceptional aspect of the structure determination was that the program MAID autobuilt the majority of the protein at only 2.6Å resolution. Impressive indeed!

Jack Tanner

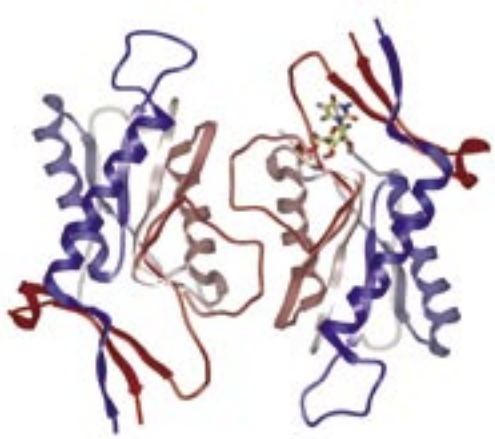
Posters of Pharmaceutical Interest

Macromolecular crystallography has a flourishing partnership with structure-based drug design (SBDD), and many ACA members that are employed in industry and in academia regularly use crystallography to contribute to SBDD initiatives. Why? Because crystallography has had a profound impact on our ability to visualize macromolecular targets for drug design, postulate therapeutic interventions, and optimize drug candidates at a molecular level.

A few posters especially caught my attention. It's worth noting that all of the structures benefited from diffraction data collected at synchrotron x-ray beam lines in the U.S.

Researchers from deCODE Genetics had two interesting posters. In **P060, Bart Staker** presented three ternary complexes of human topo I with a 22mer of dsDNA and diverse anti-cancer compounds. Though the compounds were structurally different, they all bound to the covalent protein-DNA complex using common structural principles. In P161, **Joe Lomino** presented crystal structures of the (*R*)-rolipram inhibitor in complex with phosphodiesterase (PDE) 4D, in both the apo-(free enzyme) and holoenzyme (Mg^{2+}-containing) forms. The motivation for the work was to gain insights that would help design a drug that is specific for PDE4D and has limited interactions with other members of the PDE superfamily. PDE4D is implicated in ischemic stroke.

Two labs from Michigan State U. had noteworthy posters. **Anne Mulichak, P127,** presented crystallographic work from the Garavito lab on two structurally homologous glycosyltransferases (Gtfs). The structures of GtfA and GtfD, which are involved in vancomycin biosynthesis, were solved in ternary complexes with thymine diphosphate and a natural acceptor substrate. What's remarkable is how these two similar enzymes utilize strikingly different binding modes for the same substrate. **P113,** by **Sarah Weaver** in Jim Geiger's lab, revealed the crystal structure of angiostatin, an angiogenesis inhibitor, bound to VEK-30, a peptide from the group A streptococcal surface protein PAM. Angiostatin is an internal fragment of plasminogen, and it contains three of the five kringle structures of the molecule. EntreMed currently has angiostatin in clinical trials with cancer patients, and supplied the angiostatin for this work. The angiostatin-VEK-30 complex is the first example of a multiple kringle containing protein and ligand to be characterized crystallographically. Kringle 3 was disordered in the structure, though augmenting the molecular replacement phasing with phases from a heavy atom derivative did allow the K2-K3 connection to be revealed. This structure shows how angiostatin may bind protein ligands involved in angiogenesis.



From Carolina Vasquez: the Mycobacterium tuberculosis pyrR gene (Rv1379) encodes a protein that regulates expression of pyrimidine nucleotide biosynthesis (pyr) genes). PyrR has been shown to be upregulated during hypoxic stress, characteristic of the environment found in the granuloma harboring Mtb. Because pyrimidine biosynthesis is an essential step in the progression of TB, pyrR is an attractive antitubercular drug target. Shown is the 1.9Å structure of the pyrR dimer with UMP docked in silico to the monomer at the right. Coloring of the polypeptide ribbon trace is blue to red, N- to C- terminus, and coloring of UMP is by atom. Image rendered with ICM-Pro 3.1.02.

Carolina Vasquez, from the Kantardjieff group at Cal State-Fullerton, (some co-authors were from the Terwilliger lab at LANL and the Rupp lab at LLNL) presented **P121,** a visually striking poster on the structure of *M. tuberculosis* pyrR and results of virtual ligand screening studies. Mtb pyrR regulates the expression of genes and operons of pyrimidine nucleotide biosynthesis, a key step in TB progression - making it a plausible drug target for tuberculosis. Virtual screening of uridine nucleotide analogs identified potential drug lead compounds and useful pharmacophores. The group plans to use to these leads to proceed with further SBDD and with solving the structures of promising inhibitor-target complexes.

Tim Rydel

More Macromolecular Posters

The challenge, as always, is to pick which few posters to mention. My favorites are these: **P059,** presented by **Phoebe Rice,** U. Chicago, a fascinating structure of the Rad51 filament. This is the eukaryotic homologue of the eubacterial RecA protein and is involved in the repair of double stranded breaks in DNA. What I found most remarkable here was that, although crystals were only obtained in the presence of DNA, no DNA was visible in the density. The structure itself was very beautiful with long monomer filaments.

From Phoebe Rice: Structure of a filament of the yeast homologous DNA recombinase Rad51. The filament is formed by the packing of two crystallographically independent monomers (blue and green) along a 3(1) screw axis. The ATP-binding site (marked by a sulfate ion, black) lies at the interfaces between protomers. DNA is expected to bind near the filament axis. Figure adapted from: Adam B Conway, Thomas W Lynch, Ying Zhang, Gary S Fortin, Cindy W Fung, Lorraine S Symington & Phoebe A Rice, Crystal structure of a Rad51 filament, Nature Structural & Molecular Biology v11 p791-796, Aug 2004.

P001 by **Ramalakshmi Darbha,** NCI, Maryland, provided an exciting insight into the role of a single loop of an antibody able to neutralize a wide variety of HIV strains through binding to a viral envelope glycoprotein (gp120). The flexible CDR H3 loop adopts 8 distinct conformations in the crystals. This flexibility is proposed to allow the antibody to bind strongly to gp120 from different HIV isolates and prevent HIV entry into cells. Darbha suggests using this loop as a basis for the design of HIV infection inhibitory peptides.

Arwen Pearson

High Resolution & Archaeal Protein Posters

P089, P099 and **P120** were the posters about new high resolution structures that interested me most. **P089** by **J. Deng** *et al*. from Wim Hol's group, U. Washington, presented the high resolution structure of the RNA editing ligase from *Trypanosoma brucei*. The structure showed an adenylation domain of editing ligase in complex with ATP and magnesium. The distinct 3-D architecture of the nucleotidyl transferase pocket provides some unique opportunities for design of specific inhibitors for this class of dangerous pathogens. **P099, G. Minasov** from Wayne Anderson's group at Northwestern, was very interesting. They managed to isolate and crystallize an unknown protein from *Bacillus stearothermophilus*. The protein RBSTP1166 has very few homologs in a very narrow range of species. This is yet another example when the structural genomics studies provided a tentative lead towards the function of an unknown protein. The structure at 1 Å revealed a relatively novel fold that upon a closer inspection can present itself as a new class of lysozome. High quality data allowed for very accurate structure description including locations of hydrogen atoms. The functional studies will answer the mechanistic questions concerning it's enzymatic designation. **B. Zhao** and M. Waterman, Vanderbilt U. Med. School, Nashville (**P120**) presented an exciting study of the structure of a novel Cytochrome P450 from *Streptomyces coelicolor* (CYP158A2). Two structures of this enzyme showed a large conformational change upon substrate binding. The structure showed unique binding modes of substrates and provided insights into the catalytically competent conformations and the modes of inhibitor binding.

Several new archaeal proteins were presented, of which two were especially interesting. **P079** by **R. Dasgupta** from the Hackert group, U. Texas, described two structures of 4-oxalocrotonate tautomersases from *Helicobacter pylori* and *Archaeoglobus fulgidus*. Both structures apparently have a characteristic ß-α-ß fold but with striking differences between them. Both are also quite different from the enzyme from *P. putida*. It was suggested that those structural differences modulate the electrostatic field that is responsible for differences in activity between those enzymes. Finally, **V.A. Weinreb** and **C. Carter,** U. North Carolina, **P141**, studied by a variety of spectroscopic techniques the thermodynamics of conformational changes involved in chemical reactivity of the tryptohanyl-tRNA synthetase (Trp-RS). This study takes an important step toward understanding the coupling of the free-energy changes with conformational states of the protein during their catalytic cycle.

Bog Stec

Synchrotron and Neutron Diffraction Facilities Posters

This relatively new category of posters, started last year, was once again well represented by numerous U.S. and Canadian facilities, and the sessions were well attended.

X-ray Synchrotron Facilities

Allen Oliver and co-workers, **P246,** described a small-molecule beamline dedicated to collecting data on crystals considered too small for conventional laboratory sources. This facility is at Beamline 11.3.1 of the Advanced Light Source (ALS) at Lawrence Berkeley National Lab, and structural analyses have been routinely performed on samples as small as 20 x 20 x 20 microns. **Kevin Battaile, P247,** described a high-throughput protein crystallographic facility developed by a consortium of pharmaceutical companies, IMCA-CAT (Industrial Macromolecular Crystallography Association Collaborative Access Team), located at the APS (Advanced Photon Source) at Argonne National Laboratory. This group has moved to implement robotics on Beamline 17-ID to mount samples, automatically center cryoloops, screen samples and collect data. **Stephen Ginell** and co-workers of ANL presented **P236** on the national user facility run by the ANL Structural Biology Center (SBC) for macromolecular crystallography at the APS. In it, they describe the details of two beamlines operated by the SBC Collaborative Access Team (CAT), 19-ID (an insertion-device beamline) and 19-BM (a bending-magnet beamline) available to the crystallographic research community via a peer-reviewed proposal system. **Ward Smith** and co-workers, also from Argonne, presented **P239** on GM/CA, a new NIH-funded sector for protein crystallography at the APS which will provide two independent undulator beamlines, while **P244** by **Steven Ealick,** Cornell, and co-workers described the Northeastern Collaborative Access Team (NE-CAT), a consortium of scientists organized to develop a structural biology sector at the APS. Their prime focus will be on technically challenging crystallographic projects. NE-CAT facilities are located at APS sectors 8 and 24, and station 8-BM is nearing operational status and has been visited by about two dozen groups during the past year.

P245 by **David Schuller** described MacCHESS, a world-class facility at CHESS, Cornell U., which supports users at one MAD and two monochromatic stations for protein diffraction research. User support staff are on call 24/7 to help with data processing, resolve problems, and provide crystallographic advice. **P209** by **Pawel Grochulski, Louis Delbaere** and co-workers described the 08-ID beamline, the initial phase of the Canadian Macromolecular Crystallography Facility (CMCF) at the Canadian Light Source (CLS), Saskatoon, Canada. The scientific goal of the 08-ID-1 beamline is to study small crystals, and crystals with large unit cells.

Neutron Diffraction Facilities

Art Schultz, Pappannau Thiyagarajan and co-workers, Argonne, presented **P240** on MaNDi (Macromolecular Neutron Diffractometer), a single-crystal instrument being proposed for the new Spallation Neutron Source (SNS), currently under construction at Oak Ridge, Tennessee. Because the SNS, due to be completed in 2006, promises to deliver neutron fluxes between one or two orders more intense than those at existing spallation neutron sources, it is hoped that MaNDi, when funded and built, will be capable of collecting a full hemisphere of Bragg data with a resolution of 1.5 to 2 Å on a protein crystal with a lattice constant up to 150 Å in a few days.

In **P242** by **Volker Urban, Dean Myles** and co-workers, the Center for Structural Molecular Biology (CSMB) at Oak Ridge National Laboratory (ORNL) was described. Two key features of this user facility are: (1) a deuteration lab, designed to provide the user community with improved technologies for the production of deuterated biological macromolecules; and (2) a small-angle neutron scattering instrument (Bio-SANS) dedicated to biological samples. More details of the second facility, the new SANS instrument at the High Flux Isotope Reactor (HFIR) of Oak Ridge, were given in **P241** by **Gary Lynn** of ORNL. A third poster from Oak Ridge, **P243** by **Gregory Smith** and **Bryan Chakoumakos,** gave a more general description of the various facilities at the High Flux Isotope Reactor (HFIR). In particular, a description of a recent major upgrade of this older neutron source was given. This important upgrade, during which bigger beam tubes were installed in the reactor, will greatly enhance the performance of the numerous state-of-the-art instruments that will be available to the user community, such as two diffractometers to be installed in the coming year.

Lachlan Cranswick described in **P248** the neutron powder diffraction facilities at Chalk River in Canada. The poster gave a detailed description of existing capabilities and ancillary stages, as well as future initiatives and intended improvements at this neutron source. In particular, facilities for studying samples at high temperatures (up to 2000°C), a clathrate cell that will handle gaseous pressures up to 20 barg, as well as a hydrogen/deuterium/purge gas-cycling cell for the *in-situ* study of hydrogen storage materials, were described. Neutron-scattering studies of biological membranes were featured in **P237** by **Stephen White,** representing a group at the NIST reactor. The main emphasis of this poster, entitled *Cold Neutrons for Biology and Technology* (CNBT), is the development of advanced neutron scattering instruments devoted to the structural study of these important and complex systems. A new bioengineering partnership, a consortium involving NCNR (NIST Center for Neutron Research), NIH, and six universities, has built a next-generation neutron diffractometer/reflectometer fully dedicated to biological membrane studies. Finally, **P238** by **Benno Schoenborn** was scheduled to be presented describing the PCS (protein crystallographic station) at Los Alamos National Lab (LANL). This instrument, the only one currently available in the U.S. for collecting single-crystal neutron diffraction data on macromolecular samples, has been operating for over a year and has already collected data on at least half a dozen different samples. Unfortunately, the recent "lock down" at LANL prevented the poster from actually being presented.

Bob Bau

Electron Crystallography at Erice, 9-20 June

The 36th Course on Electron Crystallography at the International School of Crystallography was held at Ettore Majorana, the center for scientific culture in Erice, Sicily. The meeting was held simultaneously with the school on polymorphs, solvates, and phase relationships. Participants had the opportunity to attend both schools through several joint sessions, individual lectures and social events. School activities were superbly arranged by the local hosts, led by **Lodovico Riva di Sanseverino** of Bologna. Participants enjoyed both the beauty offered by the ancient mountain town of Erice and the local hospitality. The school was sponsored by the Italian ministry of education and research, the Scicilian regional government, the IUCr and NATO, with corporate contributions from FEI, LEO, DITABIS and GATAN.

The focus of the school was on novel approaches for structure determination of nanosized materials. Electron diffraction is used extensively in materials and biological sciences for structure characterization. The technique complements x-ray and neutron diffraction because of two unique properties of electrons: 1) electrons interact strongly with matter and 2) electrons form very small probes and real space images. The recent rapid progress in nanomaterials has provided further impetus for developing electron nanocrystallography techniques for structure determination of individual nanostructures.

Topics covered included theory of electron diffraction and image formation and simulations, convergent-beam electron diffraction, direct methods, electron crystallographic image processing, electron diffraction refinement, charge density analysis, electron spectroscopy, and powder and gas phase diffraction. The significance of electron techniques was highlighted by the range of materials applications lectures; from oxides to organic molecules and from polymorphs to nanocrystals and nanotubes. The learning experience was further enhanced by hands-on afternoon practice sessions, where students were exposed to a number of simulation and data processing software for electron diffraction.

The school was taught by experts: **A. Avilov** (Institute of Crystallography, Russia), **G. Cox** (Ludwigshafen, Germany), **C.J. Gilmore** (Glasgow, UK), **I. Hargittai** (Budapest, Hungary), **S. Hovmöller** (Stockholm, Sweden), **H. Jiang** (Bejing, China), **J. Jansen** (Delft, Nederland), **C. Kisielowski** (Berkeley, USA), **U. Kolb** (Mainz, Germany), **C. Kübel** (Eindhoven, Netherlands), **J. Làbàr** (Budapest, Hungary), **J. Mayer** (Achen, Germany), **J. P. Morniroli** (Lille, France), **D. Nihtiabova** (Sofia, Bulgaria), **J.C.H. Spence** (Tempe, USA), **O. Terasaki** (Stockholm, Sweden), **M. Tsuji** (Kyoto, Japan), **D. Wang** (Berlin, Germany), **T.E. Weirich** (Achen, Germany), **Xiaodong Zou** (Stockholm, Sweden) and **J.M. Zuo** (Urbana, USA). **Xiaodong Zou** gave an introduction to electron crystallography to the particpants of both schools. The theory of electron diffraction was introduced by **John Spence**.

There were 87 participants. Students came from Europe, the Middle East, Asia and USA, presented their own research, exchanged scientific ideas in the poster sessions and socialized during many occasions. They enjoyed the scenery of Greek temples and the sandy beach while celebrating 30 years of crystallography in Erice. The school was organized by **Janors Làbàr**, **Thomas Weirich**, and **Xiaodong Zou**.

Jian-Min Zuo

In front, l to r: Jacob Jansen, Michael Stepputat, Tatiana Gorelik; behind, from left: Lan-Yun Chang, and Christian Kuebel.

L to r: Maria Bacia, Jean-Paul Morniroli, Olanrewaju Ojo, Giuseppe Nicotra, Xiaodong Zou.

Temple "E" at Selinunte, a Doric temple built in the 5th century BC and dedicated to Hera. This temple was rebuilt in 1960.

Photos were contributed by of Jian-Min Zuo.

Diversity Amidst Similarity- *a multidisciplinary approach to polymorphs, solvates and phase relationships.*

Erice, home of the International Summer School of Crystallography, is indeed a special place. It was hot and sunny and shorts were the order of the day when we arrived; one week later it was cold, windy, raining and we were all looking for our jumpers and coats. Probably a small price to pay for the privilege of spending time here amongst cobbled streets and the world's experts on all aspects of polymorphism. This review is not an exhaustive listing of all the lectures- we didn't go to them all! We found ourselves using the time to discuss life and science- but that's what Erice is about.

Frank Herbstein gave a wise and thoughtful introduction to the school, reminding us of many things from phase diagrams to the nature of transitions; to be precise in our nomenclature and to avoid ill-defined terms like pseudopolymorph. Co-director **Joel Bernstein** challenged the younger members to ask more questions - a copy of his book was the prize for the most verbal. The first day was dominated by thermodynamics and use of thermal methods, aspects that were reinforced through **Griesser's** microscopy workshop and **Henck's** Energy - Temperature problem classes. These workshops were a special feature of the school.

Day 2 was more computational in nature. **Gavezotti** gave another of his deep talks, this time on his new pixel method for lattice energy calculations; **Sally Price** reported on what looked like a disappointing outcome of the 3rd blind test of structure prediction and **Spackman** described the use of Hirshfeld surfaces in polymorph discrimination. The next day brought us some great techniques, XRD, NMR, other spectroscopies and an interesting overview of polymorph analysis by **Dave Bugay**. **Bill David's** exposition on the modern developments in structure solution really put PXRD on the map as an important tool in the modern armory. For our afternoon out, we boarded buses, stopped to pick up lunches in Trapani, and headed out to the ruins of temples and cities at Selinunte and Segesta. We had supper outside, some dancing and then the bus for home.

Nucleation, crystal growth and polymorph control with additives were topics the next day. We heard about the jaded history of ammonium nitrate and HMX (His Majesties Explosive!) from **Brill** and this was followed by a very colourful presentation on crystal chemistry and application of pigments by **Erk** of BASF. The following day was dominated by high-throughput screening with presentations from all the major players - Transform, Aventium and Symyx. **Kruger** talked about the crystal structures of alkylammonium bromides, reminding us that it was he who solved three of the structures of sulphathiazole, possibly one of the world's most worked polymorphic materials. The second of two stimulating poster sessions reviewed many fascinating aspects of the field. The next morning brought talks of experts such as **Ward** and **Schenk** (chocolate) interspersed by short student presentation of which **DeMato's** report of *in situ* monitoring of crystallization and phase transition using synchrotron radiation was an excellent example. Then, in the afternoon another well-earned break with the treasure hunt followed by the 30th Anniversary celebration dinner.

Pharmaceuticals, and patents were featured next. **Steve Byrn** started with an overview of polymorphism in pharmaceuticals. **Howard Levine** and **Jen Swann** provided an excellent overview of patents. Several discussions and debates ensued. **Luigi Nassimbeni** presented a fascinating overview of crystal solvates and their behavior. In discussion, opinions ranged from patent work should not be of major interest to comments that patents are one of the reasons for the technological advances of society and insure that the investment required to commercialize an invention will pay off. Saturday the program involved an eclectic series of interesting talks. **Sophie Clas** gave an excellent description of polymorph studies in the pharmaceutical industry, emphasizing that polymorph research is a continuous process throughout drug development. **Joel Bernstein** gave and excellent overview of the chemical aspects of polymorph patents. **Bill Duax** then provided an entertaining overview of the 28 Nobel prizes awarded to crystallographers. Following an excellent 'ask the experts' session, **Joel Bernstein** concluded, using the interesting case of the drug *Ritonavir* to summarize all that the meeting covered.

Gert Krueger, left, and Leslie Leiserowitz.

Roger Davey on left with Ed Collier.

Many thanks to organizers **Joel Bernstein** and **Ray Davis** for making us all more aware of the substantial importance of polymorphism in our world.

Roger Davey and Steve Byrn

Photos courtesy of Roger Davey and Ed Collier

ACA 2005 May 28 - June 2 Walt Disney World Swan Hotel

Abstract Deadline: December 15, 2004
Advance Registration Deadline: April 15th, 2005
Advance Hotel Registration Deadline: April 18th, 2005

On-line abstract submission instructions, on-line registration and further meeting information will be posted to the ACA 2005 site at: **www.xray.chem.ufl.edu/aca2005/index.htm** or consult the ACA site: **www.hwi.buffalo.edu/ACA/.**

The 2005 ACA meeting will begin with workshops on Saturday, May 28th. Symposia and Sessions will commence Sunday morning, May 29th. Consult the **Call for Papers** for detailed information on workshops and sessions.

At left, Khalil and Ed at the 2004 meeting; above, Thomas Selby.

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Symposia:

Transactions Symposium, New Horizons in Structure-Based Drug Discovery, organized by: Anthony Kossiakoff; speakers: Tom Blundell, Ruben Abagyan, Andrea Cochran, Jim Wells, Patricia Weber, Ben Cravatt, Homme Hellinga, Bob Keenan, and Tony Kossiakoff.

A. Lindo Patterson Award Symposium to honor T. Alwyn Jones, 2005 award recipient.

Etter Early Career Award Symposium organized by Arwen Pearson and Jeanette Krause.

Workshops and organizers:

Macromolecular structure validation, Katherine Kantardjieff, kkantardjieff@exchange.fullerton.edu. & Bernhard Rupp, rupp1@llnl.gov.

Biology on the colloid to nano-scale, T. Narayanan, narayan@esrf.fr; Susan Krueger, Susan.Krueger@nist.gov; & P. Thiyagarajan, thiyaga@anl.gov.

Structure solution and refinement of difficult structures using powder diffraction, Lachlan Cranswick l.m.d.cranswick@dl.ac.uk, & Nattamai Bhuvanesh nbhuv@mail.chem.tamu.edu; website: www.chem.tamu.edu/xray/acawork/acaworkshop.html.

Photos courtesy of webmaster at www.swandolphininfo.com (leftmost), & Orlando/Orange County Convention & Visitors Bureau.

Meeting Calendar

OCTOBER 2004

21-22 **SSRL 31st Annual Users' Meeting**, Stanford, CA. **www-nmr.cabm.rutgers.edu/icsg2004/**

28-30 **Pittsburgh Diffraction Conference**, Pittsbugh, PA. **www.pittdiffsoc.org/PDC_04_initial.htm**

NOVEMBER 2004

16-17 CRSJ 2004 Annual Meeting, Osaka, Japan. **wwwsoc.nii.ac.jp/crsj/index-e.html**

19-26 **Biocrys 2004: Fundamentals of Modern Methods in Biocrystallography** Instituto de Tecnologia Química e Biológica, Oeiras, Portugal. **http://biocrys.itqb.unl.pt/**

17-21 **The 3rd International Conference on Structural Genomics (ICSG 2004)** Washington, DC.

27-2 **International Conference on Neutron Scattering 2005,** Sydney, Australia **www.icns2005.org**

DECEMBER 2004

4-9 **Regional School of Crystallography and Diffraction.** Havana, Cuba **www.cristalografia.net**

JANUARY 2005

17-18 **Protein Crystallography in Drug Discovery.** Dedicated to structural genomics & proteomics. South San Francisco, CA **www.protcrystconf.com**

MAY 2005

19-29 **Evolving Methods in Macromolecular Crystallography,** 37th crystallography course, Erice, Italy. **www.crystalerice.org/futuremeet.htm**

MAY / JUNE 2005

28-2 **American Crystallographic Association Annual Meeting, ACA 2005, Walt Disney World Swan Hotel, Orlando, FL. www.xray.chem.ufl.edu/aca2005/index.htm Local Chairs: Khalil Abboud, abboud@chem.ufl.edu, and Tom Selby, tselby@mail.ucf.edu; Program Chair: Ed Collins, edward_collins@med.unc.edu.**

AUGUST 2005

18-23 **IUCr Computing School** (prior to IUCr Congress in Florence), in Siena, Italy.

23-31 **XX IUCr Congress**, Florence, Italy. **Local Chair:** Paola Paoli, **iucr@iucr2005.it**, **Program Chair,** Carlo Meali, **www.iucr2005.it**

JUNE 2006

9-18 **The Structural Biology of Large Molecular Assemblies**, the 38th crystallographic course at the Ettore Majorana Centre, Erice, Italy. **www.crystalerice.org/futuremeet.htm**

JUNE 2007

7-17 **Engineering of Crystalline Materials Properties: State-of-the-Art in Modeling, Design, and Applications**, the 39th crystallographic course at the Ettore Majorana Centre, Erice, Italy.