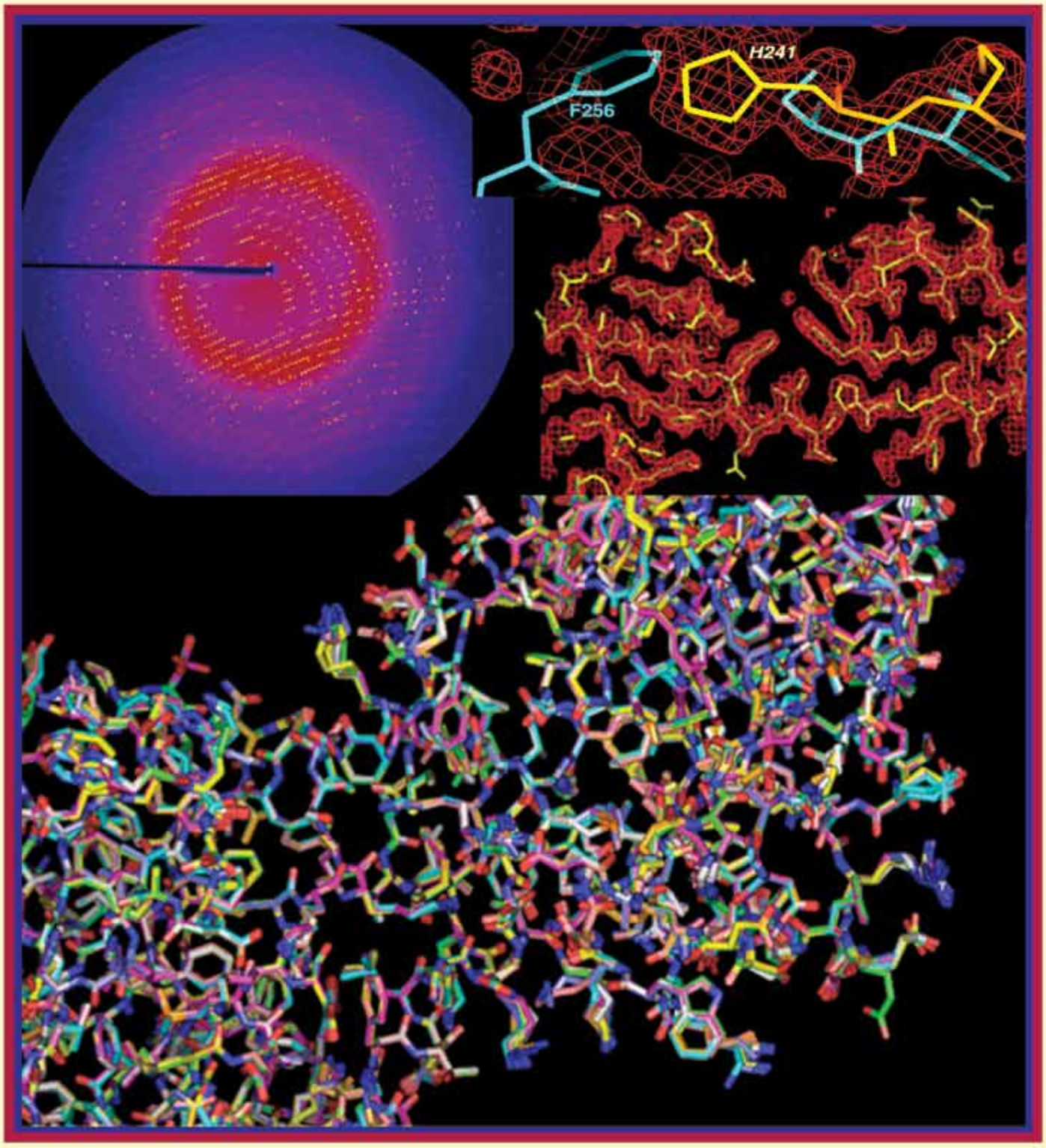
ACA RefleXions

American Crystallographic Association

Number 1
Spring, 2013



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Cover: Tom Terwilliger will receive the Trueblood Award at the Hawaii meeting. See On the Cover, page 15.

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Deadlines for contributions are: February 1 (Spring), May 1 (Summer), August 1 (Fall) and November 1 (Winter)

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Rigaku

It's hard to believe that my year as ACA Vice President passed so quickly yet here I am writing this column as the new ACA President. Council welcomes new members Martha Teeter and Jim Kaduk who will serve as Vice President and Treasurer, respectively. The ACA could not function without the dedicated support of volunteers.

There are three big initiatives for the Council to work on this year.

First, as many of you already know, the ACA has been involved in discussions with the AIP (American Institute of Physics), of which we are a member society, regarding forming a partnership to begin a new open access online only journal. In January the ACA Council voted to move forward and begin the contract negotiations. Through a Board of Managers composed of two ACA representatives and two AIP representatives, we will work together to publish a new journal in the area of Structure, Dynamics, and Kinetics. The AIP, which already provides the global science community with a comprehensive collection of highly cited and peer reviewed scientific information, will be responsible for producing the journal, with the ACA having full editorial control over the content. Council believes that this is an excellent opportunity that will allow the ACA to provide a venue for publishing the diverse areas of structural science in emerging fields at the atomic or near-atomic level which have a time-dependent or kinetic component.

Second, the ACA has begun a strategic planning process that will likely take all of this year. The AIP has graciously offered to let us use some space after our May Council meeting as well as providing a facilitator, Fred Dylla (AIP CEO), who has been guiding the AIP through a similar process. The strategic planning committee is composed of me (chair), Bill Duax, Judy Flippen-Anderson, S. N. Rao, Martha Teeter, George Phillips, and Marcia Colquhoun. We have begun thinking about our mission, and strengths, weaknesses, opportunities, and threats. I will keep you posted concerning our progress. I invite comments or suggestions - please send them by email: ***cheryl.stevens@wku.edu***.

Third, steps have been taken to establish a Latin American Division of the ACA. Including the Canadian Division, this would allow formal participation of all crystallographers in the Western Hemisphere. We hope to have a Latin American representative named to the ACA Council very soon.

I encourage you to get involved. How can you help? This summer's annual ACA meeting is scheduled for July 20-24 in Honolulu, Hawaii. I encourage you to submit abstracts and bring your students. A well attended meeting is more fun and financially good for the ACA. Useful pre-meeting workshops on Biological SAXS, the GSAS-II Crystallographic Analysis System, and the Cambridge Structural Database have also been scheduled. Please take advantage of the opportunity to learn something new. Please volunteer to serve on committees and volunteer ideas for sessions at future ACA meetings. You could also nominate someone for an ACA award. There are never enough nominees for the many awards that we give on a rotating basis.

I'm honored to have the opportunity to serve this year as your president. I am looking forward to an exciting and productive year at the ACA.

Cheryl Stevens

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Errata: The editors regret the omission of a credit in the winter *RefleXions*. On page 16 right column, the photo of Dick Marsh was taken by Rafn Stefansson.

Nominations for 2014

ACA Awards: Nominations for the **Patterson, Wood Science Writing**, and **Etter Early Career** awards are due by May 1, 2013.

ACA Offices and Committees: In the fall of 2013 we will elect a new Vice President and one person to each of the ACA Standing Committees (Continuing Education, Communications, and Data, Standards and Computing). Please send suggestions to the chair of the nominating committee, **Saeed Khan: khan@chem.ucla.edu**. Carrie Wilmot and Tom Koetzle are also nominating committee members. Full details describing the criteria for all ACA awards and offices can be found on the website.

2013 Dues are Due: Please renew promptly and remember to support your favorite ACA Award Funds.

NOTE: It is now possible to renew online.

ACA website: www AmerCrystalAssn.org.

Send all nominations to: Marcia@hwi.buffalo.edu

To sharpen focus on scholarly publishing, the **American Institute of Physics** forms **AIP Publishing LLC**

On February 1, 2013 the AIP announced the formation of AIP Publishing LLC, a wholly owned subsidiary. The purpose of the LLC is to support the scientific and educational mission of the AIP through scholarly publishing activities in the physical and related sciences.

The LLC's board will include experienced publishing experts to enable the publishing group to adapt quickly to changes in the marketplace in which it operates and to plan for the future in a rapidly changing environment. AIP Publishing LLC will focus on expanding its publishing of the best research in the physical sciences to deliver greater value to scientists, students, libraries and other subscribers with an interest in the physical and related sciences.

According to John S. Haynes, CEO of the LLC. "We will also continue to strive to serve physical sciences organizations, including AIP's Member Society publishing partners, and help them to advance their missions."

Since it was formed more than 80 years ago, the AIP has grown in many important ways. It feeds the newswires accurate and interesting science news, introduces students to the larger science community, tracks our community's demographics, education and career trends, and curates history of the physical sciences.

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Photo courtesy of Will Kirk/ Johns Hopkins University

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One of the responsibilities of the Canadian Representative is to publish, at least once per year, the names of the members of the Canadian National Committee for Crystallography. There is a special reason to do so *this* time. Current members are: Jim Britten, Chair, Pam Whitfield, Vice-Chair, Joe Schrag, Secretary, Marie Fraser, Treasurer, Stan Cameron, Lee Groat, Lynne Howell, and, ex-officio, David Rose. The reason this is timely is that several of these people have served for years and are due to cycle off the committee. There were two replacements because of the untimely deaths of Louis Delbaere and Lachlan Cranswick, resulting in the relatively recent additions of Lynne Howell and Lee Groat (who continued on after his term as ACA Canadian Rep expired). However, Stan Cameron and Marie Fraser in particular have contributed many years of service beyond their intended terms. In addition, Jim Britten will soon be due to rotate off the CNCCr. So, we are looking for individuals to fill these slots. We look for broad representation with respect to geography, technical discipline, gender and primary language, though we cannot always achieve this ideal. Please contact a member of the CNCCr if you have any interest in joining. Remember the IUCr Congress is in Montreal in 2014 - a compelling reason to have a strong and active committee to serve as host.

David Rose

On a related topic, the officers of the ACA Canadian Division are Gerald Audette, Chair, and Brian Patrick, Secretary. They would be delighted to hear any input from Canadian ACA members, particularly regarding topics to discuss at the CanDiv meeting in Hawaii; see p 4 for email addresses. Note that the CanDiv is co-sponsoring several scientific sessions at the Hawaii meeting, e.g. 13.01: Struc. Enzymology; 13.03: Comp. Tips & Tricks; 13.06: Cool Struc; & 13.08: Bldg. Research at Undergrad. Institutions. Because Canadians co-chair these sessions, abstracts directed to them stand an excellent chance of being selected for talks. In addition, the Delbaere-Pauling Poster Prize is awarded annually to the top trainee poster from a Canadian laboratory at the meeting.

If, like me, you are looking out the window on a February afternoon of -15°C and a brisk wind, watching snow squalls drop 15cm of snow, you'll be looking forward more than ever to this year's ACA Meeting in Hawaii. I'm just about to submit my abstract. I hope to see you there!

Jim Britten

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Stan Cameron

Lynne Howell

Lee Groat

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Guy Dodson, only 75 at his death, was world-renowned for his research on the three-dimensional structure of biologically important proteins, particularly insulin; for his studies of the mechanism of action of numerous enzymes; and for establishing two first-class centers for the study of proteins, the *York Structural Biology Laboratory* and the structural biology group at NIMR, the National Institute for Medical Research, in northwest London.

From 1967-1976 Guy was in Dorothy Hodgkin's laboratory at Oxford University where he played the leading role in determining the structure of the first polypeptide hormone, insulin, and later related the hormone's chemical and biological properties to its atomic structure. His work on insulin continued following his move to York University in 1976, especially with the use of mutant and chemically modified versions of the hormone designed for analysis of its structure, assembly and action. He also collaborated closely with various pharmaceutical companies that prepared insulins that could be used to improve diabetes therapy.

Guy had strong opinions about the importance of crystal structures to biology, and at York his group focused on enzymes that catalyze chemical reactions. At both Oxford and York, Guy skillfully organized large research groups. Appointed professor at York in 1985, he built up a truly international team including a number of Polish and Russian crystallographers.

In 1993 he was invited by the Medical Research Council to establish x-ray crystallography at NIMR. Again, he was enormously effective with collaborations on enzymes involved in infection by the malaria parasite; on proteins required for the control of RNA metabolism in tuberculosis; and on the structure of the infectious molecules known as prions.

Though he became professor emeritus in 2004, Guy never really retired. His collaborations on research concerning the cellular receptor for insulin and research on the malaria enzymes both yielded outstanding success in the last months of his life.

Guy and his twin brother, Maurice, were born in Palmerston North, his parents having emigrated from Britain to New Zealand a decade earlier. He went to Dilworth school, Auckland, where the senior mathematics and sciences teacher, Donald Gray, encouraged lateral thinking, logical reasoning and intelligent questioning to achieve an understanding of processes, rather than simply memorizing information.

At Auckland University College, Guy obtained his PhD for research using x-ray analysis combined with analytical chemistry. The crystallographic research on large biological molecules in Dorothy Hodgkin's laboratory

Legend for photo: Guy Dodson worked with laboratories in pharmaceutical companies for the preparation of insulins that could improve diabetes treatment.
Photograph by David White

at Oxford, where he went as a postdoctoral research assistant, interested him greatly and he stayed on as a research fellow until Hodgkin's retirement in 1976.

Dorothy's laboratory proved to be a paradise where Guy could receive a thorough grounding in biological perspectives from such scientific leaders as JD Bernal and Don Steiner, and in chemical structure and mechanism from Jack Dunitz and Bob Williams. He also met and, in 1965, married Eleanor MacPherson.

Through Guy's enthusiasm and knowledge of protein structure and Eleanor's mathematical skills they began to accumulate, initially through their research on insulin, scientific achievements that led to their election as fellows of the Royal Society in 1994 and 2003 respectively. Their warmth and inclusiveness was greatly appreciated by generations of students, postdoctorals and visitors.

Guy was active in the local community, notably as the chair of governors of Archbishop Holgate's school. Because he was so charming, he was popular with scientific colleagues from many disciplines and from countries as disparate as India, China and Cuba. He is survived by Eleanor, three sons and a daughter.

from The Guardian article by John Skehel and Keith Wilson, Jan 28th, 2013

Some Reflections about Guy Dodson Written for the York Chemistry Department by Rod Hubbard

In thinking back over the years, it is clear that Guy had a very important effect on the way the Chemistry Department developed. He arrived at York in 1975 / 1976 as Dorothy Hodgkin retired in Oxford. His appointment was an extremely ambitious move by Dick Norman. Guy was not in the same mold as the other members of department – he had essentially no experience of teaching undergraduates – and it showed (I remember his first lecture when I was taking a second year option when he was in transition to York – memorable for all the wrong reasons!). But what he and Eleanor brought to the department was a serious, internationally connected passion for research. Guy's lack of connection with the administrative and teaching remit of the department was difficult for some colleagues to take – but his impact was substantial in establishing (with Eleanor) a truly world leading research presence and activity that gave the department and York a tremendous reputation. He also generated the space and support to allow new, innovative ideas and people to grow. Let us look at some of the impact.

There was not a great deal of research activity beyond graduate students and the odd visiting scientist in York Chemistry in the mid 1970s. Guy and Eleanor brought the first Research Council grants and post-docs, but also an international connection. There were waves of Antipodean, Chinese, Russian and Polish visitors in the 1980s, some of whom stayed. But also, the York lab was on the visiting map for leading international scientists from the US and major European labs. This raised the expectation and level of scientific engagement with the international community, which went on to infect much of the rest of the department. Importantly, Guy provided the space and encouragement to others. This was particularly true for me as I established molecular graphics and

modeling in the early 1980s; Guy was also central in getting my New Blood position in 1983 (though he never did appreciate the difference between Computing Service and Computer Science – my lectureship was a very odd joint Chemistry and Computing Service position!! which didn't last long). Together we had fantastic fun as the Protein Structure Group grew dramatically through the 1980s.

The growth of the lab was due to two major influences: the funding by the Protein Engineering Initiative, which established molecular biology at York, and various large consolidated awards funding the infrastructure; and funding by industrial collaborations. The first of these was the Novo experience. I will never forget walking into a room in Copenhagen with Guy in the mid 1980s and being handed a one page summary of what the people at Novo were proposing as a collaboration. The Novo team walked out and left us to consider - Guy and I looked at the sheet and in stunned silence tried to grasp that they were offering £1M over three years with very little paperwork (that is about £2.5M in today's money). Just an agreement that we would work on some interesting proteins. This money and the continuation over the following decades provided the core flexibility on which the lab depended. But this also led to some amazing discoveries - the structure of the first protein produced by recombinant methods, the insulin work (design of monomeric insulins and structures of crystal preparations designed to give longer acting insulins) and structures of various enzymes (amylase, lipase, cellulose, etc). At this time, the most important pre-requisite for a crystallographic lab was access to pure protein and the samples that arrived from Novo were turned into a series of high profile papers (many in *Nature*). The energy and excitement this developed in the lab, brought many superb postdocs – some of which (e.g. Gideon Davies) stayed. Also, this tradition of working together with industry led to the various large grants I had with GSK, Celltech, Chiroscience, Karobio, Accelrys and so on through to the late 1990s. Looking back, it is amazing how the lab grew and took over much of D block during the 1980s, seemingly without a great deal of fuss, meetings or arguments. It just happened naturally. We also had great fun writing grants. Tony Wilkinson was a postdoc at Harvard when I was a visiting scientist there in the mid-1980s. He wrote to Guy who suggested he talked to me. When I got back to the UK, Guy and I decided one afternoon to write a grant to bring Tony to York as a postdoc. So, we sat down and invented a project to engineer myoglobin so as to change its binding properties. That grant brought Tony to York. On another occasion, when York decided to promote the growth of large, more commercially aware groupings, we had a riotous evening writing a pompous document full of phrases such as 'pioneering posture,' and 'exquisitely poised'. That one didn't get funded (perhaps fortunately).

Traveling with Guy was a total experience. All who went with him to various meetings, conferences, and holidays will have their own stories. One that I remember, but which was probably just 'a day in the life' for Eleanor ocurred at the IUCR meeting in Bordeaux in the hot summer of 1990. Don't forget – this was a time before mobile phones or ubiquitous email. I had been invited to speak at a session on hydrogen bonding and water structure, but before the meeting I was at an IBM meeting in the Swiss Alps. Guy and Eleanor had rented a farmhouse that they *thought* was near Bordeaux - but turned out to be 90 km away in Bergerac. I had arranged to meet Guy at lunchtime on the day of my talk and he said he would bring some food with him. Now, Bordeaux was *full*, no hotel rooms, so I was going to stay with them. Because the farmhouse was a long way from Bordeaux, Guy and Eleanor caught the train from a nearby village in the early morning - but left a student's poster in the station waiting room. I flew into Bordeaux that morning – it was stinking hot (40°C) and the meeting was being held at an out of town campus that was a concrete desert. I arrived at the campus and, quite remarkably, found Guy where he said he would be. He had remembered to bring lunch, but had also invited all the people he had met that morning to join. So, there we were, in this concrete desert with little shade in 40° heat, cowering under a shrub bush, sharing half a crushed baguette and a melted 50g of brie scraped out of Guy's backpack, between about 6 of us. We had to mug passing graduate students with bottles of water to get a drink. I gave my talk (the room was packed, but it was beyond a sauna and I am sure I was hallucinating by the end of it), met up with Eleanor, who said we could travel back together to the farmhouse by train. But I had had enough and caught a taxi to the airport, hired a car, picked up Eleanor and drove her and the student (Xiao Bing) via the station to pick up the poster (she had missed the poster session), back to the farmhouse. We then enjoyed a glorious relaxed evening: a chaotic meal, after which we all - Phil and Carol Evans were there also - ended up in the swimming pool. We stargazed while the Dodson and Evans children were playing football in the orchard. After a few glasses of wine, I collapsed into the bed vacated that morning by Dorothy Hodgkin and so ended an excellent day – for me. But Guy had stayed on for an IUCR committee meeting. Afterwards the *other* committee members dropped Guy and Wayne Hendrickson at about 9 pm on the edge of Bordeaux with no transport or chance of getting back. So, they had a rather rubbish Vietnamese meal and then Guy managed to find one of the only rooms left in Bordeaux - a garret in the eaves of a house with no air conditioning. Guy claimed he watched sweat dribble off his chest during a sleepless night.

Every day was a new day for Guy. He was one who reveled in engaging with people. Martin Karplus described him as 'the really charming New Zealander'. In conversations with Guy you got the full force of his charm and enthusiasm for life and science and felt you were the center of his world.

Roderick Hubbard

Guy Dodson with Dorothy Hodgkin. ***Photo taken by a York staff photographer probably in the early 1980s when Dorothy visited York to work on the big insulin paper.***

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Next Generation Users - Where Are They?

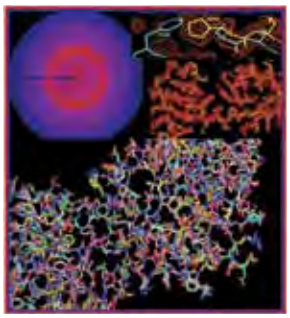
I read with much interest Ross Reynold's *Opinion* column from last year (*ACA RefleXions*, spring, 2012, p 25) musing about the current state of affairs in crystallography. His view of this generation of students, our future practitioners and their world of Ipads, Kindles, Nooks or simply drive space in the "cloud" offers considerable hope. Why, you ask? Simply because, as Ross states, "crystallography really matters" and equally important "… the imagination and creativity,... the perseverance when interest is captured and the curiosity for unknown things still runs strong" with this generation.

Ross and I have at least two things in common. In addition to our affiliation with the ACA, we both serve as faculty at predominantly undergraduate institutions (PUI). Now I don't know if you have looked around lately, but there is not an overabundance of us in the ACA. Certainly this group has experienced steady growth since I became a member many years ago, but still nothing more noticeable than a small tremor. Understandably, the usual line of thought is that PUI resources and expertise are typically insufficient to support or sustain activities involving x-ray crystallography. No equipment or crystallographers = limited ACA participation. While this may have been true many years ago, it is demonstrably not so now. There has been a significant push from the PUI community for undergraduate research. Combine that with changes in funding agency structure and more accessible x-ray hardware/software and the outcome is a stronger presence of crystallography education and research on these campuses.

Why should we (ACA) care? The demographic of our next generation of users is now expanding from post docs and graduate students to an even younger crowd. Recent history strongly hints that there is considerable value in capturing undergraduates and even high school students. It will come as no big surprise that many from our ACA community already reach out to this group. Ask Bill Duax and Carla Slebodnick about what they have been up to the last few summers - organizing opportunities that inspire a host of students to explore the joys and wonders of crystallography. There are many other examples where students engage in crystallography research either through formal classroom activities or focused research. Some are publicized, others operate under the radar. If the potential payback of reaching out to undergraduates or even students at the high school level offers some appeal (it should), then we need to ask ourselves about best practices for effective outreach, training, and support. This demographic presents an assortment of interesting opportunities and challenges that will require attention from our ACA community. How we partner with this group, *i.e.*, nurture, encourage, include, - will not only be critically important to the development of tomorrow's crystallographers, but will directly impact the ACA for years to come.

Not to worry, the ACA and its members have proven to be resilient time and again. Just as we are often uniquely positioned to provide answers to many pressing and highly relevant scientific problems, we are also known to navigate new opportunities successfully. So yes, I think Ross' optimism is well placed. He got it right with his upbeat view of the future of crystallography - a future largely determined by the discoveries and efforts of our current practitioners and undoubtedly dependent on those just finding their stride.

Kraig Wheeler



The **ACA 2013 Trueblood Award** will be given to **Tom Terwilliger** at the Hawaii ACA meeting for, ***...exceptional achievement in computational or chemical crystallography. [He] has made brilliant contributions to the community of crystallographers through his software that permits the near-automatic determination of molecular structures. His deep understanding of chemical crystallography, statistics, and computer codes has enabled him to produce a string of programs that have helped to transform the field of macromolecular structure determination.*** Among his innovations are SOLVE (automated software for finding heavy-atom sites and obtaining electron density maps from MIR and MAD diffraction data) and RESOLVE (automated map improvement by density modification and model-building).

Cover Images. Top left: a false-color diffraction photograph of a *Rhodococcus dehalogenase* (photo by Janet Newman, see ref. **1**); top right: a prime-and-switch electron density map of this dehalogenase calculated from the blue homologous structure; the *R. dehalogenase* structure is shown in yellow (data from **1**; map calculated as described in **2**). Below: electron density and model for *P. aerophilum* translation initiation factor 5a created by SOLVE and RESOLVE (data collected by Tom Peat, see **3**; graphics as described by Alwyn Jones et al, see **5**); bottom is a multiple-model representation of the CD11a I-domain showing multiple conformations compatible with the x-ray data (note that residues in the interior of the protein have mostly unique conformations and many residues on the surface have multiple conformations).The data and starting model are from 1CQP, (see **4**) as described in **6**; figure drawn with ***Pymol*** (see **7**).

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Anton Paar

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In December, the Council for the American Association for the Advancement of Science (AAAS) elected 701 members as Fellows of AAAS. Among the new fellows were five ACA members: **Charles Williams Carter, Anthony A. Kossiakoff, George N. Phillips, Jr., Joel L. Sussman and Leonard Richard MacGillivray**.

Charlie Carter is Professor of Biochemistry & Biophysics at UNC-Chapel Hill. His group uses crystal structures of proteins, bioinformatics, molecular genetics, and various biophysical techniques to better understand the mechanistic basis and historical origins of enzyme catalysis. One challenge the group has undertaken is to study how chemical free energy released by nucleotide triphosphate hydrolysis is converted into protein conformational changes. Charlie is a past-president of ACA.

Anthony Kossiakoff is Professor of Biochemistry and Molecular Biophysics at the University of Chicago. His group is interested in studying, at atomic resolution, the structural and functional properties that define molecular recognition systems that activate and regulate biological properties. In particular they are studying the energetics of hormone-induced receptor activation and regulation of growth hormone and its receptor using x-ray crystallography, site-directed mutagenesis, phage display mutagenesis and biophysical analysis.

George Phillips is Ralph and Dorothy Looney Professor of Biochemistry & Cell Biology, and Professor of Chemistry at Rice. One of the projects his group has underway is directed towards obtaining an atomic description of the basis for binding oxygen and other ligands to heme proteins. The group has determined detailed 3D structures for modified myoglobins and hemoglobins and for other novel heme proteins, such as nitrobindin, a protein they discovered that reversibly binds nitric oxide and is ubiquitous in the animal kingdom. George is Past-President of ACA and still on the ACA Council.

Joel Sussman is Morton and Gladys Pickman Professor of Structural Biology at the Weizmann Institute of Science in Rehovot, Israel. Together with neurobiologist Israel Silman he studies the 3D structure/function of nervous system proteins, such as acetylcholinesterase or AChE, cholinesterase-like adhesion molecules or CLAMs, snake toxins, β-glucosidase, β-secretase & paraoxonase. Their goal is to find new leads for treating neurological disorders, including Alzheimer's disease and autism. They also study intrinsically unstructured proteins and how proteins adapt to extreme environments, e.g. halotolerant proteins.

Leonard MacGillivray, at the University of Iowa, attempts to understand the principles that govern the effects of intermolecular interactions (e.g. hydrogen bonds) on the structure and properties of assemblies of atoms and molecules in the field of supramolecular chemistry. The structure of DNA and the ability of enzymes to catalyze chemical reactions are examples from biochemistry that are regulated by such interactions. His group addresses whether such forces may be used to confront long-standing problems with new perspectives or to design new molecules and materials with unique properties.

Enzyme Molecules as Nanomotors

by Samudra Sengupta, Krishna K. Dey, Hari S. Muddana, Tristan Tabouillot, Michael E. Ibele, Peter J. Butler, and Ayusman Sen, *JACS*, 2013, **135** (4), pp 1406–1414.

Apparently, single molecules of common enzymes can generate enough force to cause movement in specific directions. Peter Butler, Ayusman Sen and colleagues point out that enzymes are the basis of natural biological motors essential to life. To learn whether a single enzyme molecule, the smallest machine that could possibly exist, might be able to generate enough force to cause its own movement in a specific direction, they experimented with two common enzymes, catalase and urease. Catalase protects the body from the harmful effects of hydrogen peroxide formed naturally in the course of life. Urease, found in many plants, converts urea to ammonia and carbon dioxide. They showed that these two enzymes, in the presence of their respective substrates (hydrogen peroxide or urea, acting as fuel), show movement. More significantly, the movement becomes directional through the imposition of a substrate gradient, a form of chemotaxis, the phenomenon that attracts living things toward sources of food. They also show that this movement causes chemically interconnected enzymes to be drawn together; a form of predator-prey behavior at the nanoscale.

From ACS Chemistry for Life, a release by ***newsroom@acs.org*** *on Jan. 30th.*

2013 Ludo Frevel Scholarships

The ICDD Ludo Frevel Crystallography Scholarship Committee has selected 13 recipients for the 2013 scholarships. These recipients were selected on a competitive basis from 69 commendable applications received by the ICDD Scholarship Committee. Three of the recipients are ACA members:
Martin Donakowski presented ***Toward molecular control of early–transition metal oxide fluoride materials***.
Christopher Kane's entry was ***Low packing fraction crystalline cavitands exhibiting molecule-sized cavities***.
Jennifer Urban presented ***Studying self-assembled small molecule hydrogels using x-ray crystallography.***
The ICDD will present each student with a check for $2,500 to assist in the continuation of studies in their selected fields of crystallographic research.

Revolution Hits the Universities

Nothing has more potential to enable us to reimagine higher education than the massive open online course, or MOOC, platforms that are being developed by the likes of Stanford and MIT and companies like Coursera and Udacity. Coursera, co-founded by the Stanford computer scientists Daphne Koller and Andrew Ng, now has 2.4 million students taking 214 courses from 33 universities, including eight international ones. Anant Agarwal, former director of the artificial intelligence lab at MIT, is now president of edX, a non-profit MOOC that MIT and Harvard are jointly building. Since May, 2012, 155,000 students from around the world have taken edX's first course, an MIT intro class on circuits. "That is greater than the total number of MIT alumni in its 150-year history," Agarwal said.

Mitch Duneier, a Princeton sociology professor, wrote an essay in *The Chronicle of Higher Education* last fall about his experience teaching a class through Coursera: soon after commencement in 2012, when the Princeton campus was nearly silent . . . "40,000 students from 113 countries arrived here via the Internet to take a free course in introductory sociology. My opening discussion of C. Wright Mills's classic 1959 book *The Social Imagination*, was a close reading of the text, in which I reviewed a key chapter line by line. I asked students to follow along in their own copies, as I do in the lecture hall. When I give this lecture on the Princeton campus, I usually receive a few penetrating questions. In this case, however, within a few hours of posting the online version, the course forums came alive with hundreds of comments and questions. Several days later there were thousands . . . Within three weeks I had received more feedback on my sociological ideas than I had in a career of teaching, which significantly influenced each of my subsequent lectures and seminars."

Looking to the future of higher education, MIT president, L. Rafael Reif, thinks that traditional on-campus experiences will increasingly be augmented by technology and the internet to enhance classroom and laboratory work and that "alongside that . . . many universities will offer online courses to students anywhere in the world, in which they will earn 'credentials' - certificates that testify that they have done the work and passed all the exams. The process of developing credible credentials that verify that the student has adequately mastered the subject - and did not cheat - and can be counted on by employers is still being perfected by all the MOOCs. But once it is, this phenomenon will really scale."

Imagine how this might change US foreign aid. For relatively little money, the US could rent space in an Egyptian village, install two dozen computers and high-speed satellite internet access, hire a local teacher as a facilitator, and invite in any Egyptian who wanted to take online courses with the best professors in the world, subtitled in Arabic.

Abstracted from Thomas L. Friedman's column in the NY Times, Jan 27th, 2013.

Digital Globes, a New Way to View the World *by Mark Vanhoenacker*

The 6'wide Science on a Sphere was created by NOAA as a tool to teach earth sciences. Photo credit: Chip Clark, Smithsonian Inst.

In the main hall of the hands-on science exhibits at the Cape Town Science Center in South Africa, a lifeless, tattered globe stands under naked fluorescent bulbs, all but ignored by children passing through on school tours.

Across a sunblasted courtyard and up a dingy staircase, another globe - a digital globe - stands in a darkened room. This globe is a shining sphere of light. Children stand awe-struck; adults of a certain age may be reminded of images like Apollo 8's *Earthrise* photograph, while Tolkien fans of all ages will recall the spherical, swirling 'palantír' of Saruman in The *Lord of the Rings* (forged in the days when Middle Earth was still flat).

As the name suggests, a digital globe is a spherically shaped display screen. Digital globes vary in size; a typical model is about 24" across. Unlike your childhood globes, the image on a digital globe can be changed with the touch of a button. Controlled by a keyboard or tablet computer, a digital globe can toggle between familiar, static images, like the world's political boundaries, topography or vegetation. It can animate complex phenomena, like the formation of weather systems, the effect of global warming on wolverine habitats or the annual pulse of sea ice. It can display the surface of the moon, the churning azure cloudscapes of Neptune or the celestial globe - the night sky.

For digital globe engineers, the holy grail remains a spherical computer screen. How to project an image so that it lands equally bright, focused and undistorted on the surface of a sphere? There are various optical solutions; the main distinction between them being whether the image is externally or internally projected. The digital globes that may soon be available outside of museums use internal projectors. Currently these cast an imperfect light upon the world. A small portion of the extreme southern hemisphere (i.e., around the South Pole, if you've chosen to align the earth's axis vertically) is blocked by the projector and base. Brightness, while vastly improved, also remains an issue.

But the biggest obstacle is cost; depending on size and complexity the prices range from $21-$43k. A 24" *Magic Planet* from the market leader, Global Imagination, Santa Clara, CA, ***www.globalimagination.com***, now costs $21k. Prices are falling, however. Mike Foody, the CEO of Global Imagination, says that he hopes to have education-discounted prices down to $2.5k within a year or two. If he succeeds, that would be in the same range as interactive whiteboards.

Not every school has been content to wait. Since 2007, the Mayo High School, Rochester, MN, has used a digital globe in earth science lessons. Lawrence Mascotti, the planetarium director, noted that he regards the globe as a means for teachers to "play" at a student's level, rather than vice versa. He finds the sphere a "more democratic" educational tool than textbooks or computer screens. While some children have difficulty with language-based concepts and mental manipulation, the digital globe works for nearly everyone, Mr. Mascotti says. "It's simple. The mind follows the eye."

Abstracted from NYTimes, Jan 7, 2013. See http://nyti.ms/ZioscA

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Adventures of an Amateur Crystallographer by Marjorie Senechal

I wish I could report that I collected crystals as a child, but I didn't collect anything. A pastime I see now as proto-mathematics was many happy hours spent organizing and reorganizing the buttons in the tin box by my mother's much-used Singer sewing machine. There were dozens of buttons, of many kinds. Some were as large as a quarter, others smaller than a Dutch dubbeltje. Some were painted with flowers or faces. The materials differed too: wood, plastic, metal. I learned there are many ways to classify anything, and every organizing principle is quickly upended.

I entered the University of Chicago without finishing high school but I had no clear idea of what I wanted to study in college. In those days no one expected girls to aim for careers. I enjoyed mathematics. But I didn't know, or think to ask myself, what I enjoyed about it: which areas of math appealed to me and why; what stirred my imagination. After UC, I churned on and earned an MS and PhD in mathematics at the Illinois Institute of Technology.

My first post-PhD job was a one-year appointment (1966-67) in the mathematics department at Smith College, filling in for a woman who took the year off to have a baby. Though I had a two-year old daughter by then and was expecting another child in the spring, I persuaded the department chair to let me teach anyway. The baby would be born during spring vacation, I assured him. And indeed she was. My only problem, as the due date approached, was finding a gripping book to read in the hospital. Serendipity struck: in the science library I came across *Crystals: Their Role in Nature and Science*, by Charles Bunn. All I knew about crystals was that they were pretty. I checked it out and read it with increasing excitement in my few quiet moments the next week. I'd found the answer to my unasked questions. Crystals showed me what drew me to math: geometric forms; patterns, packings and tilings; and elegant puzzles like diffraction diagrams. The woman I'd replaced at Smith decided not to return. Job security gave me respite to think. I felt sure that math and crystallography could be combined in a way that pleased me, but I would have to find it myself.

Just about that time I found an article by the polymathic Arthur Loeb. I went to see him and came home with a box of symmetry workbooks and a bag of plexiglass polyhedra, some empty, others with a plastic ball at their centers. Arthur showed me the astonishing variety of simple crystal structures that can be modeled by fitting these occupied and unoccupied shapes together. He also showed me *Symmetry in Science and Art*, a translation from the Russian of a book his friend V. A. Koptsik had written with the great soviet crystallographer A. V. Shubnikov. This introduced me to color symmetry, which Shubnikov had pioneered; his 1951 *Symmetry and Anti-symmetry of Finite Figures* is a classic of the field. I found that color symmetry meant different things to different authors, and each had hatched his own notation. But on close examination all these different methods were exercises in group-subgroup relations. I wrote a short paper for *Zeitschrift fur Kristallographie* in which I pointed this out and this put me in touch with a wide circle of mathematicians and crystallographers. Colored patterns became my new buttons. I spent hours in Smith's Art Library poring over a massive tome called *The Grammar of Ornament*, one hundred gilt-edged chromo-lithographed plates of ornamental patterns culled from cultures all over the world, and all times. Each plate showed dozens of intricate repeating patterns, a wealth of motifs: yet each pattern belonged to exactly one of seventeen symmetry types. One day a very senior professor of art noticed me browsing on his turf. He asked me (with curiosity, not hostility) what I, a mathematician, was doing there. I explained. "Do you know Dorothy Wrinch?" he asked me. I didn't. "You should," he said. "She is a crystallographer and she has a copy of that book." I went to see Dorothy and explained my new-found interest in crystals. She was, she told me, writing a book on crystal geometry, and I could help her by making models and illustrations. I saw this as an excellent way to fill in my very sketchy background. And so I became her informal, unpaid, post-doc. (We never finished the book.)

Photo of Dorothy Wrinch from the Smith College Sophia Smith Collection

Dorothy never told me she had been the epicenter of a controversy over the structures of proteins; she rarely talked about herself or her life. She taught me the basic notions of symmetry, not from a math text on group theory, but from F. M. Jaeger's *Lectures on the Principle of Symmetry and its Applications in all Natural Sciences*. I learned the importance of making models with my own hands, and studying them from every perspective. Dorothy stressed meaningful naming (hexahedra, not cubes!), exact diagrams, and succinct arguments. She was a demanding taskmaster; no vague or sloppy reasoning escaped her razor mind. More

than any teacher I'd ever had (except my father) she held me to high standards. With two other colleagues I organized a Symmetry Festival in her honor, though she was by then too ill to attend. The proceedings were published as *Patterns of Symmetry*. At that time Dorothy was interested in twinned crystals. They became the driving force of my interest too.

Marjorie with H. S. M. Coxeter, British-born Canadian geometer (about 1985).

I spent my first sabbatical year in Holland with Piet Hartmann and Wiepko Perdok, authors of the Periodic Bond Chain (PBC) theory of crystal growth. I wrote a paper on "The mechanism of certain growth twins of the penetration type" and sent it to Martin Buerger, editor of *Neues Jarbuch für Mineralogie*. Buerger rejected it by return mail, mostly on the grounds that I hadn't quoted any of Buerger's many papers on twinning. And so I learned about turf wars in twin domains. In fact I hadn't read his papers but I quickly did. I added a reference to one of them, the paper was published, and we became friends.

When I returned to Massachusetts at the end of the year I learned that Dorothy Wrinch had had a stroke; she died a few months later. She had left her papers to the women's history archive at Smith College. Reading her letters, notebooks, and memos I glimpsed the outlines of her remarkable if contentious career. The Wrinch papers comprise some 30 boxes; she appeared to have saved every scrap, flattering and unflattering alike. "They'll never find stuff like that on me!" Martin Buerger exclaimed. (But, writing her biography thirty-five years later, I found the real story in other archives.) I organized a symposium about her papers: *Structure of Matter and Patterns in Science*. There I met Carolyn Cohen and David Harker for the first time. Both became my good friends and encouraged me professionally. Through Harker, I attended meetings of the ACA.

After reading an article by N. N. Sheftal' on tetrahedral penetration twins I wrote to him in Moscow. My year at the Shubnikov Institute for Crystallography, where Sheftal' worked, was invaluable for

Marjorie with N.N.Sheftal', Moscow (1987).

Ravil Galiulin with his wife and daughters, Moscow (1987).

an entirely new perspective on crystal geometry. I began reading papers on mathematical crystallography by B. N. Delone. In Delone I found my real teacher, though I never met him. But on the basis of his papers and through my friendship with Delone's students Ravil Galiulin, N.V. Dolbilin and M.I. Shtogrin, I became and remain his disciple, trying always to emulate his clear and simple approach to crystallographic problems and his informal, lucid writing style. Delone's work has been the starting point for all of mine since then. Not only is his approach simple and elegant, it has turned out to be useful. Quasicrystals show us that sharp diffraction patterns are not the sole province of lattice structures. Evidently "order/disorder" is a spectrum, not a dichotomy. Delone's perspective is a tool for exploring that spectrum.

Soon after I returned to the United States Jose Lima de Faria invited me to write the chapter on the history of geometric crystallography for the *Historical Atlas of Crystallography* he was then preparing. I snatched this chance to repair the gaps in my knowledge and threw myself into the history of science. Reading the original papers to prepare that chapter, I learned the wisdom of the adage "read the masters!" Not only because secondary sources sometimes get things wrong, but because they are necessarily selective. The masters said more than their followers reported. The nuggets left behind were sometimes just the ones I needed. And so I became an amateur historian of science too.

In 1981 I attended the IUCr meeting in Ottawa, my first. One lecture there was crucially important for me, though I didn't know that at the time: Alan Mackay's talk on the optical diffraction pattern produced by a Penrose tiling. Like the patterns in Harburn, Taylor, and Welberry's *Atlas of Optical Transforms*, he'd made a mask, a metal plate punched with tiny holes, and photographed the optical diffraction pattern it produced. But the holes were the vertices of

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Penrose tiles; the diffraction pattern should have been a blur. To the audience's astonishment, despite the apparent disorder of the mask, the diffraction pattern had ten-fold symmetry!

After Ottawa, I had a professional-identity problem on my hands. What was my field? Mathematics? Crystallography? History of Science? And who was I, a teacher in a liberal arts college or a member of the international research community? I decided not to choose, but to juggle instead. Smith College was an ideal setting for this juggling act. I could give courses on topics I wanted to learn, teaching myself along with bright students. There were no textbooks for these courses; I pulled the material together.

In January, 1985, when I arrived in Paris for a conference on mathematical crystallography, a colleague shoved the latest issue of *Physical Reviews Letters* in my face. "Have you seen this?" he shouted. The paper, *A metallic phase with long-range orientational order and with no translational symmetry*, by Shechtman, Blech, Gratias, and Cahn, was astonishing. The diffraction patterns Alan Mackay had manufactured occurred in nature too! The lattice paradigm whose history I had so carefully spelled out at the Hamburg IUCr in August had been toppled. By the time the invited mathematicians, physicists, and crystallographers arrived in Paris for the conference, the program was obsolete.

By a wonderful coincidence, Shechtman, Gratias, and Cahn were in Paris just then. We invited them to join us. The invited lectures were given as planned, but the rest of the time we discussed Penrose tilings and diffraction. Penrose tilings are fascinating objects. They can be studied through several mathematical lenses. First, they are self-similar: they repeat on all scales. Second, they are modular: they can be built by juxtaposing two simple shapes by following prescribed matching rules. And third, they can be obtained from an ordinary periodic cubic lattice by a technique called cut-and-project. Briefly - and I grossly oversimplify here - one takes a high-dimensional lattice, slices it with a plane, and projects the lattice points lying near the plane onto it. If the plane itself contains no lattice points, or only one lattice point, then the projected pattern is nonperiodic. This projected pattern will always have sharp bright diffraction spots. For the Penrose tilings, the lattice in question is cubic, its dimension is five, and the cutting plane is orthogonal to the cube diagonal (1,1,1,1,1). This cutting plane can have exactly one lattice point in it (e.g., if it passes through (0,0,0,0,0)) or none. It can't have more than one. The points of the five-dimensional lattice that are projected onto this plane don't form a lattice in that plane; they are a nonperiodic set. This point set diffracts as Mackay discovered. To get what Shechtman discovered, you do essentially the same thing, except that the high dimensional lattice is six dimensional instead of five, and instead of cutting it with a plane you cut with a three-dimensional subspace. And then you project. This is harder to visualize but the idea is identical. Again, you are guaranteed a nonperiodic pattern whose diffraction pattern shows bright sharp spots.

David and Deborah Harker in 1987 at the Perth IUCr.

I gave a lecture on Penrose tilings at the Perth IUCr meeting in 1987. This led to an invitation from Dan Shechtman to visit the Technion. Members of his own department, the materials science department, didn't understand what his discovery was all about. Would I give a lecture course on crystal symmetry, and teach his colleagues to read the *International Tables*?

Now the field I had hoped to find when I knocked on Dorothy Wrinch's office door was burgeoning, with more conferences in more countries than anyone could possibly attend. I enjoyed my role as go-between, telling crystallographers about developments in mathematics and mathematicians about developments in crystallography. For example, "*Quasicrystals: the view from Les Houches*," which Jean Taylor and I wrote at a quasicrystal conference.

Jean Taylor (left) and Marjorie, Les Houches, France (1989).

The United States was a glaring exception to this international flurry. The influential Linus Pauling's very public disparagement ("there are no quasicrystals, only quasiscientists") discouraged young researchers.

I saw a need for a book on the basics of quasicrystal geometry, one that could supply a common background and vocabulary and introduce readers to Penrose tiles, diffraction geometry, the cut-and-project method, and more. In *Quasicrystals and Geometry* I explained, summarized and synthesized what seemed to me the most important questions that quasicrystals raised for mathematical crystallography and mathematics more generally.

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In October, 2011, when the Nobel Prize in Chemistry was announced, I felt like dancing in the street. "Quasicrystals have fundamentally changed the way chemists think about solid matter," the Nobel Committee said.

After 42 years at Smith, I retired from teaching in 2007 to make time for two big projects. One was to edit *The Mathematical Intelligencer*, an international quarterly then in its 30th year. My other big project was a biography of Dorothy Wrinch. I had given a lecture on her papers soon after her death, and thought I had said all I had to say. Later quite a bit was written about Dorothy, some fiercely pro and more fiercely con, and most of it wrong. Wrong facts, wrong interpretation, and more than a few fictions. The errors propagated: writers who never knew her uncritically adopted the attitudes of people who had and added to the misinformation. Moreover, these writers saw her through the lens of chemistry. But Dorothy had been a trained as a mathematician, had studied logic with Bertrand Russell, and was a disciple of D'Arcy Thompson; *On Growth and Form* was her bible. There was more to her story and I set out to find it. I read letters to and from Bertrand Russell, D'Arcy Thompson, J. D. Bernal, Joseph Needham, Dorothy Hodgkin, Irving Langmuir, Isidor Fankuchen, both Braggs, and many more. Personalities and ambitions and who's right, who's wrong aside, I came to see Dorothy Wrinch's protein model as a lightning rod for a clash of scientific cultures. The clash is the eternal dialogue between truth and beauty, between complexity and simplicity, a dialogue both profound and productive. Indeed, it is an engine of science. And so I called my book *I Died for Beauty: Dorothy Wrinch and the Cultures of Science*. **Editor's note: See the book review of IDFB, p 36.**

Dan Shectman, Budapest (1993). Nobel Prize in Chemistry, 2011.

A crystallography banquet in Moscow in 1987. Marjorie is at left, B. K. Vainshtein, Director of the Shubnikov Institute of Crystallography is at far right and Herbert Hauptman is standing.

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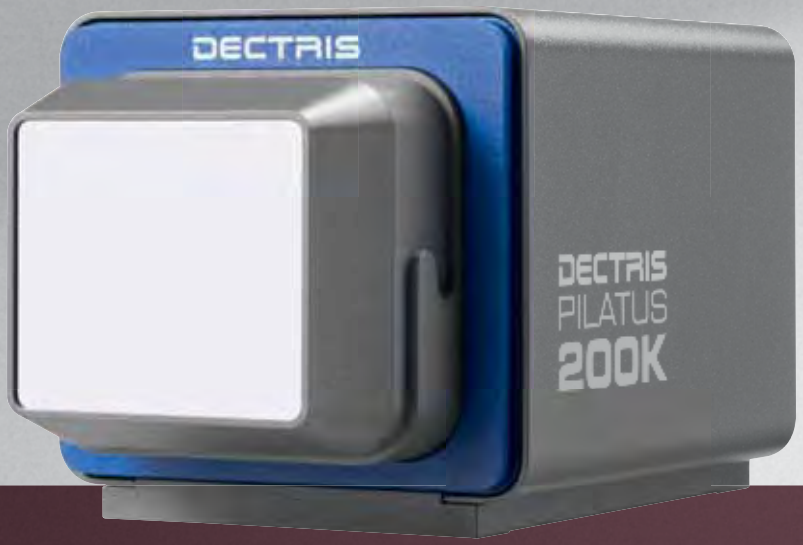

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The Structure of the Telomerase Enzyme

was presented at the 2012 ACA meeting in Boston by **Emmanuel Skordalakes**, Wistar Institure, U. of Pennsylvania, winner of the **2012 Margaret C. Etter Early Career Award**.

The conventional replication machinery of eukaryotic cells is unable to replicate the end of linear chromosomes, a defect that leads to the "end replication problem." Eukaryotic cells have addressed this problem by using a specialized RNA dependent DNA polymerase called telomerase. The core telomerase enzyme consists of a protein subunit (TERT), which contains the active site of the enzyme and an integral RNA component (TERC) that provides the template TERT uses for telomere synthesis during the replication process. Telomere replication allows for the DNA polymerase to replicate the end of chromosomes in full thus assisting the cells in overcoming the end replication problem. Telomeres also serve as a platform that recruits two distinct complexes, the shelterin and CST complex, which serve to protect the ends of chromosomes from exonuclease degradation, chromosome end-to-end fusion events that could lead to genomic instability, senescence or cell death. These complexes also regulate access of telomerase to the telomeric overhang and therefore the length of the telomeres.

The protein subunit of telomerase is largely conserved and consists of 4 or 5 domains depending on the species. The TEN domain at the N-terminal is the least conserved domain of the enzyme (it is absent from species such as insects and worms) and has been shown to bind to telomeric DNA weakly. This weak interaction apparently enhances the ability of the enzyme to add multiple identical repeats of DNA to the ends of chromosomes, a process unique to telomerase, known as *repeat addition processivity* (RPA). The RNA binding domain (TRBD) is universally conserved and is required for TERT-TER assembly and template positioning at the active site of TERT. The reverse transcriptase domain (RT) consists of the *fingers* and *palm* subdomains implicated in nucleic acid and nucleotide binding. The *palm* domain specifically contains the active site of the enzyme formed by three invariant aspartates that form part of motifs A and C. The CTD domain is thought to comprise the DNA binding domain of telomerase and is involved in telomerase elongation complex formation.

Unlike TERT, TERC varies considerably in size and sequence. For example in ciliates TERC is approximately 150-200 nucleotides long, in vertebrates the length is 312-559 and in fungi it is 928-2030. Despite the differences in size and sequence TERC contains conserved motifs such as the *pseudoknot*, the *template boundary element* and the *activation domain* suggesting core mechanistic conservation of telomere replication across distant species.

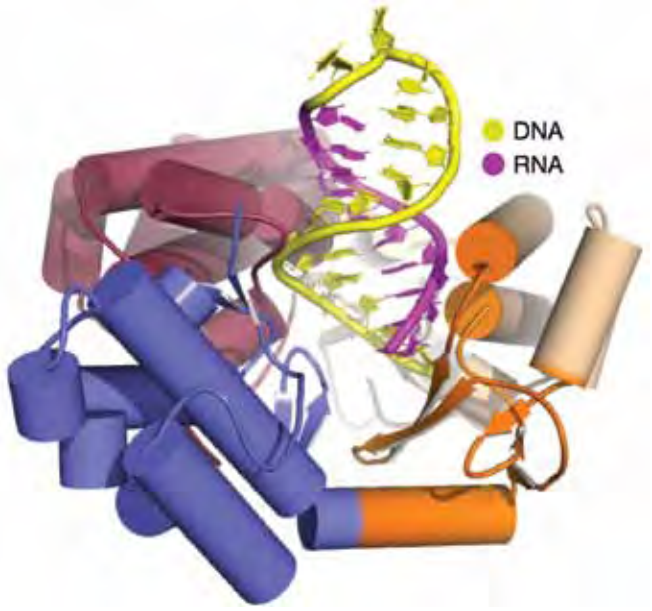
Telomere replication requires that the enzyme gets recruited to telomeres, a process usually mediated by the telomeric capping complexes, sheltering, or CST. Recruitment of telomerase to the telomeres leads to pairing of 4-5 nucleotides of the RNA template with the telomeric overhang. This leaves 4-3 unpaired nucleotides of the RNA template free for replication by telomerase. Once the template has been replicated, the enzyme transiently dissociates from the telomeric overhang only to re-anneal to the 3'-end of the RNA template for another cycle of telomere replication. This process is repeated multiple times, - the number depends on the species -, until the telomeric overhang is long enough to provide the stability and protection required for the ends of chromosomes.

Previous efforts to obtain structural information on telomerase were met with limited success due to the size and complexity of the system. To address this problem we screened TERT genes and constructs from a number of organisms. Our goal was to identify a gene that expressed the protein solubly, in its active form and in sufficient quantities for structural studies. Through this process we identified the *Tribolium castaneum* TERT (*Tc*TERT) as a possible candidate. Following over-expression in *E. coli*, we crystallized the protein and solved the structure to 2.7 Å resolution using x-ray crystallography. The structure revealed 4 distinct domains organized into a closed right-handed polymerase. A search in the PDB database using the Dali server revealed that *Tc*TERT is most similar structurally to the polymerase domain of HIV Reverse Transcriptase (HIV RT) and retroviral RNA polymerases, suggesting an evolutionary link between these families of enzymes.

The TRBD domain, a novel nucleic acid binding fold, is almost all helical and contains two conserved motifs – the CP and T motifs implicated in template boundary element (TBE) binding. A third motif located on the surface of the protein associates with the activation domain (CR4/5) of TER and these interactions provide the stability required for a functional telomerase holoenzyme and promote functional aspects of the enzyme such as RPA, template boundary definition and template positioning at the active site of the enzyme. The *fingers* and the *palm* comprise the RT domain of the enzyme and are most similar structurally to the equivalent fingers and palm domains of HIV RTs. The *fingers* domain contains the CP amd T motifs along with several conserved residues all

of which participate in the formation of the active site of the enzyme. The *palm* domain contains a plethora of motifs implicated in nucleic acid and nucleotide binding. For example, motifs A and C are two short rigid loops located in proximity of each other which contain three invariant aspartates that comprise the active site of the enzyme. The *thumb* domain, like the TRBD, is all helical and contains conserved motifs (thumb helix and loop) that may be involved in telomeric DNA binding and telomerase elongation complex formation.

A close inspection of the TERT ring shows that the motifs implicated in nucleotide and nucleic acid binding are located in the interior cavity of the ring suggesting that this is where the RNA-template and telomeric overhang bind during telomerase elongation complex formation. To better understand the mechanism of telomere elongation, we designed a RNA-DNA hairpin consisting of the putative RNA template of *Tc*TERT and the complementary telomeric DNA, linked together by a stable tetraloop. We designed the hairpin to contain a three-nucleotide RNA overhang for activity tests and structural studies. We showed that *Tc*TERT binds the hairpin with nanomolar binding affinity and that it is able to extend the telomeric overhang by three nucleotides, the length of the RNA template overhang. We then co-crystallized *Tc*TERT with the hairpin, dNTPαS and $MgCl_2$ so that we could trap the enzyme in its catalytic state; subsequently we solved the structure to 2.7 Å resolution using the method of molecular replacement with the substrate free *Tc*TERT coordinates as a model. The map showed clear electron density for the RNA-DNA hairpin in the interior cavity of the TERT ring. Surprisingly there was density for three extra nucleotides at the 3'-end of the DNA substrate suggesting that the active enzyme was able to elongate the DNA template in the crystallization drop. Nucleic acid binding in the interior cavity of the ring induces subtle rigid domain movements leading to a reduction of about 3.5 Å in the diameter of the interior cavity of the ring, a process that most likely facilitates the formation of a tight functional elongation complex. This subtle domain movement observed for TERT was rather surprising because its closest structural homolog HIV RT is known to undergo significant rearrangements of domains: the thumb domain in HIV RT is known to move as much as 30 Å between the nucleic acid free and bound states. The rigidity of the *Tc*TERT ring could be attributed to the *TRBD* domain (which is absent from HIV RTs) and its extensive and conserved interactions with the *thumb* domain. The closed ring configuration of the *Tc*TERT ring most likely prevents it from undergoing significant conformational changes, which in turn suggests that TERT, unlike HIV RT, may have a preformed active site.



Structure of the Tribolium castaneum catalytic subunit of telomerase TERT in complex with the putative RNA template and telomeric DNA. The RNA binding domain (TRBD) showing fingers, palm and thumb domains in blue, orange, wheat and raspberry colors respectively. The DNA and RNA, which are bound in the interior cavity of the TERT ring are shown in yellow and magenta colors respectively.

Telomerase, with the exception of *Paramecium teraurelia*, is a high fidelity enzyme in that it is able to copy the RNA template without errors. The *Tc*TERT - nucleic acid structure revealed that the 5'-end of the RNA template is bound by motifs 2 and B' of the *fingers* and *palm* domains respectively. Contacts involve mostly protein-nucleic acid backbone and solvent mediated interactions. The RNA-protein contacts position the unpaired bases right above the active site of the enzyme where they are solvent accessible for nucleotide binding thus promoting nucleotide selectivity and positioning for telomere elongation.

*Tc*TERT DNA binding is mediated primarily by the *thumb loop* and *thumb helix* of the *thumb* domain. The *thumb* loop adopts to a remarkable degree the geometry of double stranded DNA and makes extensive backbone and solvent mediated interactions with the backbone of the telomeric DNA. The *thumb helix*, which corresponds to helix H of the HIV RTs, docks itself into the minor groove of the RNA-DNA hybrid making extensive interactions with both nucleic acid strands. Contacts between the *thumb* domain and the DNA substrate stabilize the telomerase elongation complex and position the 3'-end nucleotides in proximity to the active site of the enzyme for nucleotide addition through phosphodiester bond formation. Positioning of the 3'-end nucleotide at the active site of the enzyme is further facilitated by motif E, (primer grip region) a short rigid hairpin located on the *palm* domain and close to the interface of the *palm* and *thumb* domains.

To trap the enzyme in its catalytic state, we co-crystallized the protein with a non-hydrolyzable nucleotide dNTPαS and $MgCl_2$. Surprisingly the active site of the enzyme was occupied by the last nucleotide of the telomeric overhang, the one which was extended in the crystallization drop by the active *Tc*TERT. The information provided by the partially occupied active site of the enzyme together with the nucleotide bound structure of HIV RT was used to put together a model of telomerase nucleotide binding. The model shows that the triphosphate moiety is extensively coordinated by the two Mg^{2+} ions of the active site of TERT, the invariant K372 of motif D, which is located beneath the active site of the enzyme, and the conserved K189 and R194 of motifs 1 and 2 of the *fingers* domain. Coordination of the triphosphate moiety by the active site of the enzyme positions the ribose group in a shallow hydrophobic pocket

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formed by Y256 and V342 and located above the three active site aspartates. Ribose - TERT active site binding in turn positions the incoming nucleotide base in proximity to the RNA template for nucleotide selection by means of Watson Crick pairing.

In summary, TERT, the catalytic subunit of telomerase, is structurally similar to the polymerase domain of retroviral reverse transcriptases and viral RNA polymerases, suggesting an evolutionary link between these families of enzymes. TERT, RNA-template usage and DNA binding are similar to that of HIV RTs. Telomerase most likely uses a two metal binding mechanism for catalysis. Nucleotide selectivity is mediated in part by the RNA-template. The interaction of the TRBD with the TBE facilitates template definition and repeat addition processivity. The TEN domain enhances telomerase processivity. *Emmanuel Skordalakes*

Warren Award Lecture: Imaging Interfaces with X-rays by

Paul Fenter, Argonne National Laboratory

It is a great honor to receive the 2012 Bertram Warren Diffraction Award from the ACA. This work was done to understand the structures and reactions at geochemical (solid-liquid) interfaces using interfacial x-ray scattering tools. These systems were simple enough to appear tractable (i.e., single crystal mineral surfaces in contact with aqueous solutions), but were sufficiently complex that traditional approaches for developing structural models were cumbersome. So, it was not apparent to me if the derived results would be truly robust, and these challenges forced us to explore if there were better ways of 'imaging' interfaces more directly.

Solid-liquid interfaces are interesting because atoms at a solid surface are both more reactive and more available for reaction than atoms in the bulk of a solid. Reactions near room temperature therefore tend to occur mostly at interfaces. Interfaces play a critical role in many areas: in natural systems, interfaces influence the cycling of elements on the Earth's surface (due to reactions between minerals and natural waters); interfaces are also critical in the technological world where there is the need to create complex materials with tailored properties (e.g., for better and safer batteries). These areas have a few important characteristics: the materials are complex; the relevant phenomena take place at (buried) liquid-solid interfaces; and the processes are generally poorly understood at the molecular-scale.

In the late 1980's, a grand challenge in interfacial science was to extend our understanding of surfaces into 'realistic' environments, beyond the reach of well-established surface science tools, that were more representative of natural and technological systems. This led me to use synchrotron-based x-ray scattering techniques which have a number of very favorable characteristics: x-rays readily penetrate liquids and solids, can probe structures with Å-scale structural resolution, and have elemental/chemical sensitivities. When I began this work at Argonne, the Advanced Photon Source had just started up and it was clearly a phenomenal and powerful new tool for understanding structures and reactions at geochemical interfaces.

One challenge in using x-ray scattering to understand these complex interfacial systems is the well-known "phase problem". That is, the measured scattering signal is uniquely defined by the structure, but the unknown structure cannot be obtained directly from the measured scattering signals due to the loss of the structure factor phase in the measurement. Consequently, most interfacial structural analyses today resemble more closely the methods used by Bragg, from 100 years ago, than the tools used in modern crystallography (direct methods, MAD phasing, etc.). Typically, a structural model is created with a set of parameters, and these parameters are optimized through least-squares fitting approaches. These model-dependent approaches are not, however, very robust for complex systems. For example, the unknown interfacial structure at geochemical interfaces may consist of 5 or more unit cells of crystalline material below the mineral surface (each unit cell having >50 atoms in some cases), a partially ordered liquid structure extending nanometers above the surface, and adsorbed species (e.g., ions or molecules). Were these systems too complex to be understood uniquely and robustly?

The power of explicit phase information for understanding interfacial systems was long known with the technique of x-ray standing waves, and was an inspiration for much of this work. The recovery of the scattering phase was critical. Once recovered, the phases allow an image of the sample to be obtained by a simple Fourier transformation (as shown schematically in figure 1), transforming these scattering techniques into robust 'imaging' tools. In other words, the solution to the phase problem is also the solution to the complexity problem.

Our work fell in two general areas: 1) imaging interfacial structures on an Angstrom-scale by phase recovery (either through algorithms or by resonant scattering); and 2) the direct imaging of elementary topography and structure with interfacial x-ray microscopy. This work mostly involved the simple case of the specular (i.e., mirror-like) reflection of x-rays by an interface.

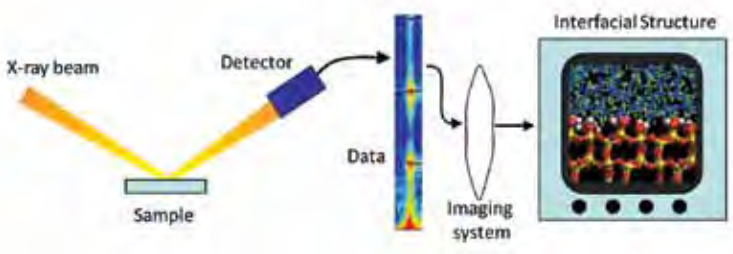


Figure 1: A highly idealized imaging system based on interfacial x-ray scattering: the x-ray beam is reflected from the surface of the sample (left), and the data are in the form of a "crystal truncation rod" (middle). What is needed is an imaging system (e.g., a lens or algorithm) that can create an image of the interface on the display (right) directly from the measured data.

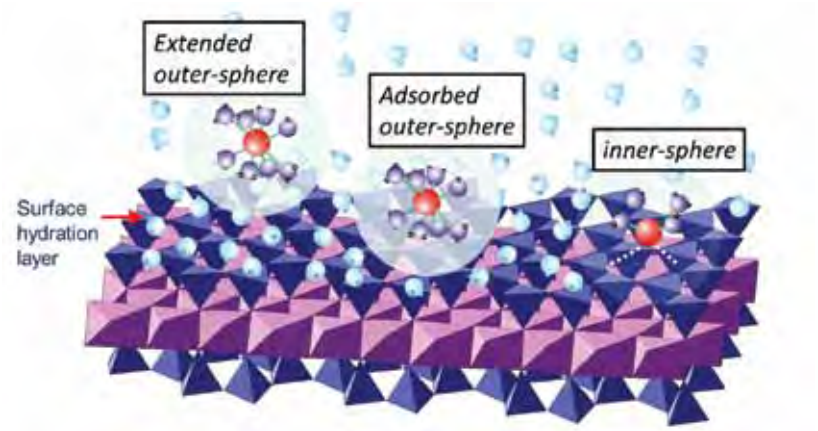


Figure 2: A schematic structure of ions adsorbed at the muscovite-water interface. The model-independent capabilities of resonant scattering were a critical tool for being able to understand these complex structures, revealing for the first time that a single ion can adsorb simultaneously onto this interface in as many as three distinct adsorbed species: inner-sphere, adsorbed outer-sphere and extended outer-sphere species, which have 0, 1 and 2+ water layers separating the ion from the mineral surface. [Adapted from: Lee et al., Langmuir Letters, 26, 16647-16651 (2010)].

The first area in which we made progress was in the phase recovery of x-ray reflectivity data (the direct analogue of x-ray crystallography as applied to interfaces). As shown by Sayre in 1952, "oversampling" a diffraction pattern allows the phases to be recovered, so that the structure can be defined uniquely based on the measured intensities. Error correction algorithms, developed by the coherent diffraction community, enable this insight by enforcing consistency between the measured amplitudes and unmeasured phases through successive Fourier transforms between the measured intensities and the derived densities while enforcing simple constraints about the sample. Ian Robinson demonstrated the first use of this technique to image interfacial topography in 1997, while Paul Lyman and Dilano Saldin demonstrated the ability to image three-dimensional interfacial structures with Å-scale resolution in 2005. But these algorithms, considered to be robust in three-dimensions, are known to be successively less stable in lower dimensions. Would they be useful for analyzing (one-dimensional) specular reflectivity data to understand molecular-scale structures? Application of these approaches to various mineral-water interfaces, including titania, quartz and alumina, showed that these algorithms could reveal the molecular-scale interfacial water structure, and the results were validated by comparison with the results of model-dependent fitting.

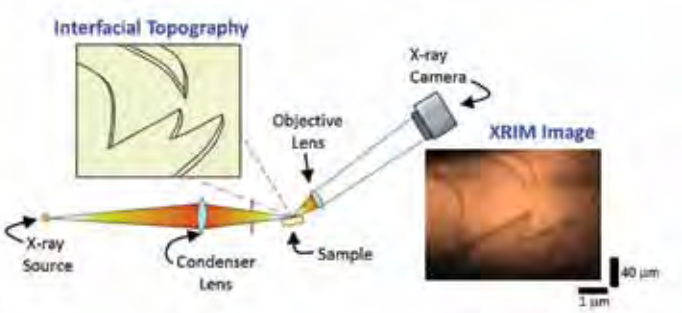
The ability to probe element-specific sub-structures (e.g., adsorbates) is also critical in many areas of interfacial science, especially when the element of interest is found as an impurity. A classic example is the arrangement of solvated ions near a charged liquid-solid interface (the electrical double layer structure). This problem has been known for more than 150 years, but has defied attempts at a full understanding. We decided to use resonant x-ray reflectivity (RAXR) for this problem, where the change in the atomic scattering factors of an element near its absorption edge is used to obtain element-specific contrast (so-called "anomalous" dispersion). Seminal work by Fred Walker and Elliot Specht in 1991 first demonstrated the feasibility of resonant reflectivity, and the subsequent work by Yong Chou and Hoydoo You pioneered the use of resonant scattering as an interface-specific spectroscopic probe (in 1999). The key conceptual advance that we made was the realization that RAXR 'spectra' (i.e., the energy dependent reflectivity near an absorption edge at fixed momentum transfer, Q) could be interpreted simply in the context of the amplitude and phase of the element specific structure, similar to approaches used previously in x-ray standing waves. That is, the shape of the RAXR spectra could be described by a set of universal curves, which consist of admixtures of the real and imaginary parts of the energy dependent dispersion terms, f'(E) and f''(E). This approach allowed the structure factor amplitude and phase of the resonant atom profile to be 'sampled' as a function of Q, and the direct-space ion profile then could be recovered by a simple Fourier transformation. This capability has enabled numerous advances to our understanding of ion adsorption at mineral-water interfaces, in particular the realization that cation adsorption structures at the muscovite-water interface are surprisingly complex with as many as three coexisting species of a single element (figure 2).

The development of an *interfacial* x-ray microscope was another novel development. Again, this work builds on substantial work by others, notably the development of transmission x-ray microscopy. The role of interfacial heterogeneity is central to understanding interfacial reactivity, but x-ray scattering techniques normally rely on probing highly homogeneous interfaces. Could this x-ray imaging technology be used to image interfacial heterogeneity and associated reactivity directly?

This X-ray Reflection Interface Microscope (XRIM) has a design that was similar to that of Hooke's original optical microscope (figure 3). An x-ray "Fresnel zone plate" lens focuses the x-ray beam onto the surface, and a second objective lens images the surface on a CCD camera using the specularly reflected x-ray beam. Specifically, the instrument images the spatial variation of the x-ray reflectivity across the surface. Changes in the local structure

Figure 3: Schematic of the X-ray Reflection Interface Microscopy (XRIM) system. An image of a solid surface is obtained with a focused x-ray beam that is reflected from the surface. The objective lens then images the spatial variation of the reflected x-ray beam on an x-ray camera. The dark lines in the XRIM image are associated with the interfacial topography, in the form of elementary sub-nanometer high steps, as indicated in the schematic (upper left).

[Adapted from: Fenter et al., Journal of Synchrotron Radiation, 15, 558-571 (2008)].



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cont'd from page 29 and topography are encoded in the magnitude of the reflectivity signal. We first used this tool to image the surface topography of the mineral orthoclase, visualizing elementary (0.65 nanometer high) steps on the surface. The XRIM images showed that steps appeared as dark lines, consistent with the general observation that surface roughness (i.e., steps) leads to a reduction in the spatially averaged interfacial scattering signal. This observation, however, led to an unexpected dilemma. It is well-known (in the x-ray microscopy community) that 'pure phase objects' are invisible (i.e., have no contrast) in an ideal microscope. In fact, elementary surface steps that separate equivalently-terminated terraces are an ideal realization of a pure phase object: the surface height changes only the phase of the scattered x-rays and not its magnitude. From this perspective, it was unclear why there was any contrast in these images! Additional studies revealed that the XRIM step contrast derives from the tilting of the x-ray beam reflected from regions near the step with respect to that observed within the flat terrace areas. The dark lines associated with the steps are observed because the reflected beam from these areas is displaced outside of the objective lens aperture, and not because the scattering intensity from these areas is smaller. There is still much to be done in the development of this new capability, and we are continuing to work towards making this, and other phase sensitive approaches, a powerful suite of tools for observing real-time reactions at complex interfaces.

I will conclude by thanking many of the people who have influenced my way of thinking. These include: Toh-Ming Lu with whom I did an undergraduate thesis on diffraction lineshape analysis; Torgny Gustafsson with whom I did my PhD research; Peter Eisenberger, Giacinto Scoles and Keng Liang with whom I learned to use x-rays to probe soft-hard interfaces; Neil Sturchio who introduced me to the world of geochemistry; and Michael Bedzyk at Northwestern who opened my eyes to the importance of phase-sensitivity. There are many others with whom I have had the great pleasure of working, especially current and past members of the Interfacial Processes Group at Argonne, who made numerous contributions to this work. This work would not have been possible without the patient and ongoing support from the Department of Energy's Office of Basic Energy Sciences, and the Geoscience Research Program in particular. Finally, I thank my family for their love and support (and, of course, their patience).

Paul Fenter

Molecules - or a Single-shot AK-47?

Edgar Meyers and his wife, Caterina, on the top of Taos Ski Valley. Edgar says she is the better skier.

In order there is beauty. Having discovered beauty on the atomic scale, we look for ways to share it with others. The world around us is full of functional forms. Increasingly, rapid prototyping is being used to make objects ranging in size and utility from dental implants to jet engine parts - to models of molecules?.

With the celebration of the centennial of x-ray diffraction and the 2014 International Year of Crystallography, the time is ripe to create desk-top models to let the world experience the beauty of molecular complexity, tactually as well as visually - and help the public comprehend the molecular geometry of life-saving drugs or molecular machinery. For example, see at right: a 20cm long model (enlarged 1.4×10^9) of the drug to treat chronic myelogenous leukemia, Tasigna, (PDBID 3CS9), required 51 hours to print on the Ultimaker in my garage shop.

But how, at what price, and when? Some 15 years ago a 3D printer cost about a million dollars. Increasingly, labs or department machine shops are acquiring their own 3D printers (the typical cost is in the $30k-$50k range) - or you can build your own (ca. $2k) from a kit.

Some early 3D printers laminated paper but now two media predominate: extruded plastic and fused polymers. A typical extrusion printer consists of a heated extrusion nozzle with 2D freedom (x,y) above a platform that is displaced (in z) stepwise as the model grows, layer by layer. A 3 mm filament of PLA (polylactic acid) is heated to ca. 200° C and extruded as a 0.4 mm molten fiber.

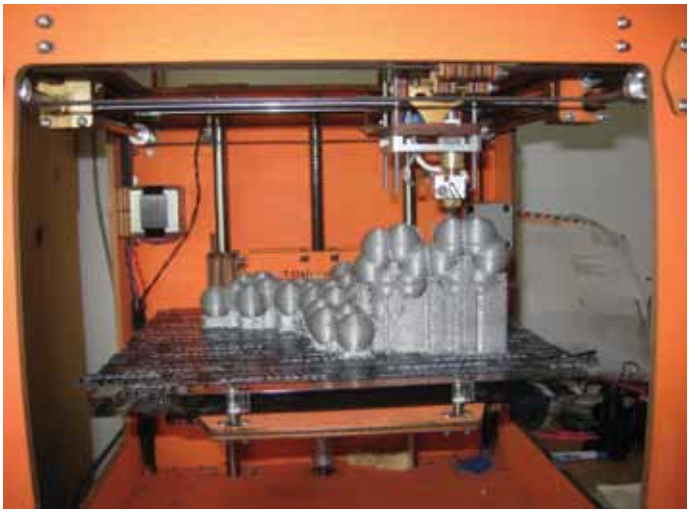
Cellulose, plastic, ceramic, or even metal granules can be coated with a light / heat sensitive polymer to produce spherical particles of a precise size. A laser beam or ink-jet pigment initiates fusion on a monolayer of particles about 0.25 mm in diameter. The platform retracts; the process repeats; and a slowly growing model emerges. Finally, loose unfused particles are dusted away. As with the extruded model, post-processing is necessary to stabilize or finish the model.

3D printers are actually computer-controlled robots, following printing instructions in one of several common formats, for example stereo lithography (.stl), Wavefront (.obj), or virtual reality markup language (.wrl). Whether running a printer in your own lab or sending the file to a production facility, you can generate the instruction file from one of several software

resources. PyMOL, or VMD ***http://www.ks.uiuc.edu/Research/vmd/,*** or open-source animation systems like Blender ***http://www.blender.org*** can produce the file in the desired format. The open-source systems have greater flexibility, but there is an initial uphill learning curve.

As an alternative to having your own printer, several groups provide 3D printing services on an at-cost basis for academic sites using user-supplied descriptor files, for example the Scripps Inst. ***http://models.scripps.edu/*** and 3D Molecular Designs ***www.3dmoleculardesigns.com/***.

George Phillips used PyMOL to generate a descriptor file of the unit cell of one of his structures (see below), which was printed with a Z-corp printer in the departmental shop at the University of Wisconsin; more examples are at ***http://www.molecular-sculpture.com/PDBweb/GP-Rice***. A commercial service can be found at: ***http://www.shapeways.com/create***.



In creating models of macromolecules, judicious manipulation of PDB coordinate sets may be required, removing coordinates of hard-won water molecules, ions, co-factors, etc. to reveal the basic tertiary structures. With larger macromolecules, further editing may be necessary to create a more aesthetic model of backbone atoms, better revealing the molecular scaffold. Likewise, an optimal choice of atomic radii can improve the appearance and structural stability of the model.

An eight cm high model of the porin trimer with the Cα atoms (4 x radii) used in building the molecular scaffold is shown below.

The model required 51 hours to print at a speed of 50mm/sec and consumed about 110m of PLA filament. (***http://www.molecular-sculpture.com/PDBweb/1opf*).**

The extrusion printer has trouble starting the print at the bottom of an atom (sphere), so a software assist (in program CURA, which converts a .stl file to a .gcode file for my Ultimaker printer) builds a scaffold under nascent atoms. An 18 x 14 x 8 cm^3 model of Tasigna (PDBID 3CS9) with 1.5 x atomic radii is shown above.

Istvan Botos alerted me to a service now being offered by Staples in Germany: send them a .obj, .stl, or .wrl file (and some Euros) and they will print your model for you. What could be easier?

Of the three choices, a printing service is clearly the easiest route for a single print. When demand increases, say in a laboratory or university setting, a service facility can maintain the printer and execute many different types of prints. For the individual investigator, an extrusion printer is reasonably affordable. In all cases, patience and skill is required to maintain the printer. Even though it is a challenge to choose descriptive parameters such that the beauty of the molecule is properly expressed, it is well worth the effort and helps fulfill our obligation to demonstrate to the world that crystallography is also an art form.

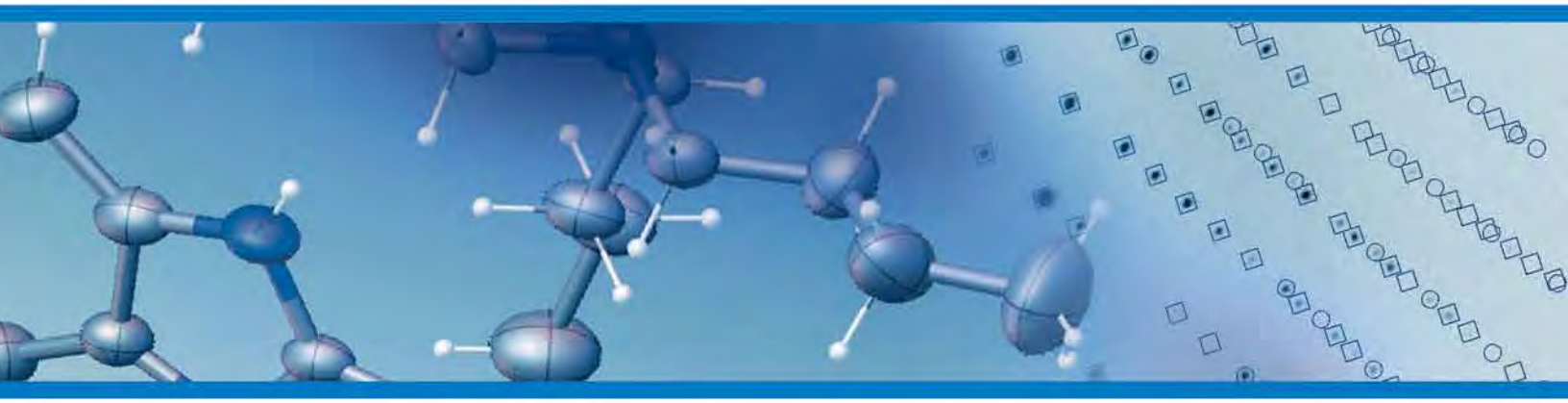
Edgar Meyer

Contributors to this Issue

Gerald Audette, Surajit Banerjee, Richard Bromund, Marcia Colquhoun, Bridget D'Amelio Paul Fenter, Jeanette Ferrara, Joe Ferrara, Frank Fronczek, Jane Griffin, Roderick Hubbard, Tom Koetzle, Jeanette Krause, Patrick Loll, Tyrel McQueen, Edgar Meyer, Peter Müller, Allen Oliver, Brian Patrick, Virginia Pett, George Phillips, David Rose, Marjorie Senechal, Emmanuel Skordalakes, Cheryl Stevens, Tom Terwilliger, Brian Toby, Crystal Towns, Kristina Vitale, Kraig Wheeler, Victor Young.

Teach Structure Determination

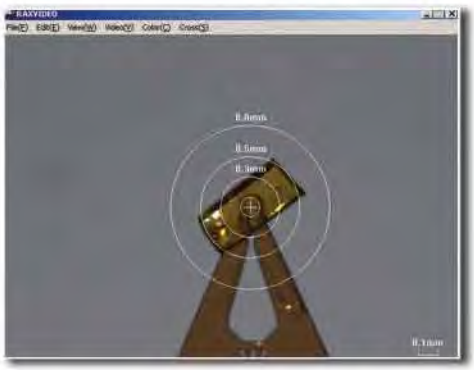
Do-it-yourself CHEMICAL CRYSTALLOGRAPHY



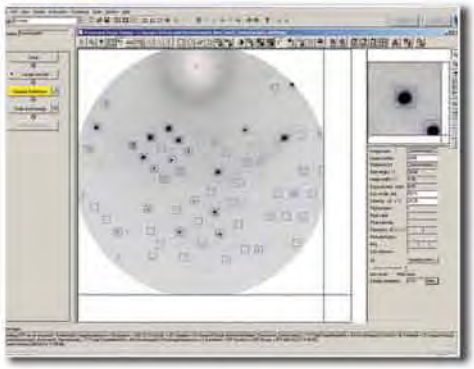
1 Walk up

2 Mount crystal

3 Align crystal



4 Collect data



5 Solve structure

XtaLAB mini™

Rigaku

In 1885 when William Bragg was only 23, he was appointed Sir Thomas Elder Professor of Mathematics and Experimental Physics at the University of Adelaide in South Australia. His son Lawrence was born there and went to college at the University. Because they were the first Adelaideans to win Nobel Prizes, the University was proud to host a symposium, ***Celebrating 100 Years of X-Ray Crystallography***, held December 6th, 2012 in Elder Hall at the University of Adelaide.

Acta Cryst. **A 69**, part 1, (January 2013) was devoted to this symposium. **Anthony Kelly**, U Cambridge, presented a 'worm's-eye view' of Lawrence Bragg's interest in the deformation of metals, a research student's view of life in W. L. Bragg's Cavendish Laboratory from 1950 to 1953. Anthony described the use of the bubble raft' in illustrating the properties of dislocations in crystals.

Anders Liljas, U Lund, gave some background to the Braggs' Nobel Prize. It seems W. L. Bragg would have missed the Nobel Prize if his father had been awarded the prize together with von Laue in 1914. Fortunately, the Nobel Committee for Physics was aware of his contributions and decided to award the prize to W. H. Bragg together with his son in 1915, when they were both nominated.

Thom Mason, ORNL, described the early neutron diffraction experiments performed in 1944 using the first nuclear reactors, referring to 'science in the wings of the Manhattan Project.'

Peter Colman, Walter & Eliza Hall Inst. Med. Research, recollected the early days in drug discovery by means of crystal structure analysis; as an example he used the design of neuraminidase inhibitors which are used to treat influenza.

John Spence, ASU/UC Berkeley, reviewed the history of Bragg's law, his life and his work with particular reference to the development of x-ray and electron microdiffraction, and summarized recent work that applies the hard x-ray free-electron laser to problems in structural biology.

Wayne Hendrickson, Columbia U, presented *The evolution of diffraction methods for solving crystal structures*. The practices for determining the atomic structures in crystals have changed greatly over the century since Lawrence Bragg introduced the trial-and-error method by which he solved structures for rocksalt, iron pyrite and other salts and minerals. Structure determinations for biological macromolecules at first borrowed from the small-molecule tradition, then adopted isomorphous replacement; still newer approaches now dominate, notably anomalous diffraction and molecular replacement.

From Anders Liljas: W. L. Bragg presenting his lecture at the Nobel Jubilee, Uppsala, 1965.

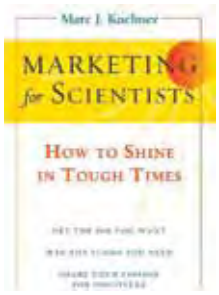
From Peter Colman's files: Max Perutz on the occasion ofhis 80th birthday celebration at the Royal Institution in 1994. L to R: Tony Kossiakoff, Wim Hol, Michael Rossmann, Aaron Klug, Max Perutz, David Blow, Peter Colman, Don Wiley and Wayne Hendrickson.

Colin Humphreys, U Cambridge, discussed the significance of Bragg's second law in electron diffraction with particular emphasis on the differences between x-ray and electron diffraction. He went on to describe recent developments in instrumentation that enable single atoms to be imaged and identified using x-ray analysis within an electron microscope.

Brian Matthews, U Oregon, talked about the early days of macromolecular crystallography emphasizing W. L. Bragg's critical role in encouraging, supporting and establishing the field.

Patience Thomson, the younger daughter of Sir Lawrence Bragg, presented her memories of her father when she was growing up in Adelaide.

From Patience Thomson's tribute to her father: Self portrait by Lawrence Bragg (1965).



Marketing for Scientists: How to Shine in Tough Times by Marc J. Kuchner.

Paperback, Island Press, 2012, ISBN: 978159726994-0, $13.01

I think I saw this book in the reviews section in *Science*. It looked intriguing so I bought a copy. The author is an astrophysicist who also happens to be a published country songwriter. The song writing had been going well enough but publishing the songs wasn't going well, so Kuchner decided he had to learn how to market his music. This book takes the principles he learned marketing his songs in the country music business and applies them to his scientific career, explaining details as he goes.

The book begins by analyzing ***the*** fundamental theorem of marketing: *everything you get from other people comes because you fulfill someone else's needs or desires* and explaining how to apply this theorem to science. Kuchner takes the reader through the process of selling things, for example, one's research project, and describes how to build relationships.

Next Kuchner describes the importance of branding one's research and provides some suggestions about how to do this: *e.g.* getting there first; or in lieu of getting there first, developing a program to be first; also, being the one to name your product or result. He spends some time on developing names and logos.

Kuchner discusses archetype personalities, (there are 12), and gives examples of each. He stresses the importance of *not* being the Orphan archetype.

Then he spends some time defining the consumers of science: colleagues, the scientific community, the general population and the government. All this is important because one's message must be directed appropriately. The next chapters cover the day-to-day business of science: getting funding or a job, writing proposals, generating figures, producing papers, attending conferences, giving talks, and using the internet.

The latter chapters cover interacting with the general public, including journalists as well as the government. Kuchner spends one chapter dealing with how to market science itself, which is becoming a real problem in the US. He closes with a chapter on leadership.

On page 217 all the concepts discussed are neatly summarized. This could be copied and kept in your lab notebook. Kuchner provides numerous references and examples to support his arguments. I liked his argument for selling a blender -- show a margarita.

Joe Ferrara

The Spark of Life by Frances Ashcroft.

Hardcover, W.W. Norton & Co., ISBN-13: 978-0393078039, $17.35

In her newest book, *The Spark of Life*, Oxford professor Frances Ashcroft looks at the role of electricity in the human body. Ashcroft begins by looking at perceptions of electricity's role in the human body in popular culture, and inevitably touches upon the resurrection of Victor Frankenstein's monster in Mary Shelley's eponymous novel. Ashcroft points out that though Shelley's story is obviously one of fiction, Shelley based her idea for the creation of life on research being conducted by her contemporaries. Scientists now know that electrical transmissions in the human body are facilitated by ion channels in cell membranes. Many neurological disorders stem from genetic mutations that lead to alterations in membrane protein structure; the alterations in turn lead to inhibition or altercation in transmission. Ashcroft's research specialty is a particular ion channel, the KATP channel, which is important not only in insulin secretion but in brain function as well. Throughout the book, Ashcroft returns to the KATP channel and its several roles in the body.

She maintains a nice balance between explanations of everyday occurrences, such as why one receives a shock after shuffling across a carpeted floor on a dry, cold day and more technical explanations of neurological phenomena. Perhaps my favorite passage is the one describing the neurotoxins ubiquitous in the animal kingdom. The pufferfish is considered a delicacy in Japan, where it is known as *fugu*. However, if not cooked correctly it can prove fatal to the consumer, because the tetrodotoxin contained in most of the fish's tissues and organs is quite poisonous. Other animals that contain tetrodotoxin, include crabs, starfish, octopi, salamanders, frogs and toads; however, these animals do not actually produce the toxin. A bacterium, *Psuedoalteromonas tetraodonia*, lives in the intestines of these animals and produces the toxin. What makes tetrodotoxin so dangerous is that it blocks the sodium channels in nerves and skeletal muscles, leading to paralysis of the respiratory muscles which usually leads to death. Interestingly, the heart is not affected by tetrodotoxin because it has a different kind of sodium channel that the toxin does not target. There is no antidote to tetrodotoxin and death occurs in less than twenty-four hours, depending on the potency of the dose. The only way to survive is if artificial respiratory support is provided until the body cleanses itself of the toxin, a process that requires several days.

Ashcroft also discusses the role of electricity in human perception; the nervous system is inextricably intertwined with the five senses; *i.e.* taste, touch, sight, smell, and hearing. When the transmission of electrical impulses across cell membranes is impaired, this diminishes the ability of human beings to perceive their surroundings. Ashcroft rounds out her discussion with a look to the future. As far as electrical devices and their interactions with human bodies are concerned, some can be used to kill, but others such as hearing aids can be used to counteract the physical effects of damaged sensory input/output systems.

At times Ashcroft is a bit technical, but overall this book was a good read; definitely enlightening. I recommend it highly.

Jeanette S. Ferrara

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I Died for Beauty: Dorothy Wrinch and the Cultures of Science by Marjorie Senechal.

Hardcover, Oxford Univ. Press, 2012, IBSN 978019973259-3, $27.71

In her new book *I Died for Beauty*, Marjorie Senechal explores the life story of British mathematician Dorothy Wrinch, the first woman to receive a doctor of science degree from Oxford University. Wrinch's accomplishments, much like those of other women in science (i.e. Rosalind Franklin) have often been disregarded by other members of her field. Senechal's study of Wrinch's colorful and sometimes tragic life employs a cast of well-known characters, including but by no means limited to JD Bernal, WH Bragg and his son, WL Bragg, John von Neumann, and Bertrand Russell.

Senechal's work is well-researched and stems from a place of deep personal interest. She knew Dorothy Wrinch, a character who liked to go by "Delta" and signed her personal letters with δ. Senechal details a number of her visits with Wrinch during Wrinch's time as a professor at Smith when Senechal herself was a student. What is genuinely unique about this book is that it is arguably as much a biography of the development of mathematics as a tool in molecular biology and protein crystallography as it is a biography of Wrinch. Senechal explores (albeit in slightly less detail) the relevant life stories of every single one of her characters. She assumes the reader knows nothing about her illustrious cast, and introduces each new character with a hefty tidbit of background information. And if one still has trouble keeping all of these great names straight, she provides a detailed "Cast of Characters" list at the end of the book.

One of Senechal's more inventive representations of history involves presenting the multi-decadal "feud" between Nobel Laureate Linus Pauling and Dorothy Wrinch as an opera. Pauling, a chemical engineer by training, saw Wrinch's work, which sought to explain conundrums in chemistry with mathematics, as irrelevant. When Wrinch proposed a simple model for protein architecture similar to a cage, Pauling responded by publishing a list of her "errors" in an effort to push her out of the field of chemistry. Wrinch eventually moved her academic efforts across the pond, continued to insist "beauty is truth" and stood by her model of simplicity. Vindication for her efforts came only partially and too late. Pauling clung to his views on Vitamin C to the end of his career despite mounting evidence to the contrary, which must have seemed like vindication to Dorothy. However it is Pauling, not Wrinch, who figures in most discussions about the history of chemistry.

Senechal does not portray Dorothy Wrinch as a woman wronged by her field of work and by her colleagues in the field, but rather as the story of an important contributor to the field of protein crystallography whose name is often overlooked. Senechal's work is driven by her own passion as a woman in science and her profound respect for Wrinch's contributions and brilliance during a time when most women were homemakers. This book ensures that Wrinch's legacy will not fade, and that her contributions and colorful life will be remembered.

Jeanette S. Ferrara

Editor's note: See the 'Living History' autobiography of Marjorie Senechal, pp 20-23.

Puzzle Corner Editor
Frank Fronczek
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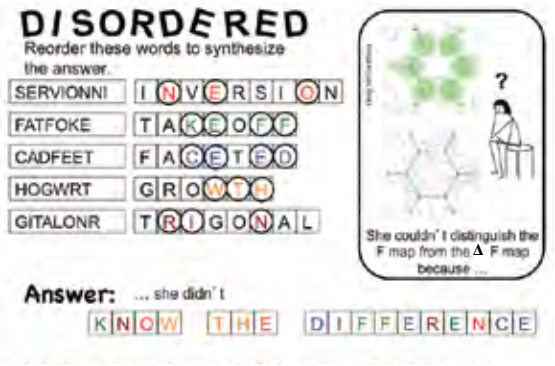
Answer to Winter Disordered ->

In the Winter issue's Crystallography History Puzzle, we asked "What are 'wheaks' and 'relps'? What is 'the Bucessera'? What does 'Vernished' mean? Who was 'A. L. Pon'?"

"A. L. Pon" was Lindo Patterson, who had an especially keen sense of humor. In the early 1950s, *Acta Cryst.* was having financial difficulties, and asked authors to shorten submissions to save on printing costs. Patterson complied by submitting *On the symmetry of the white radiation streaks produced by the Buerger precession camera* in greatly abbreviated form, the fl txt of wch is reprdcd blw. "Relps" are reciprocal lattice points, and "Vernished" is "Verner Schomaker, unpublished", which was a common reference then (see: **www.iucr.org/people/crystallographers/verner-schomaker-1914-1997**). Pon's paper was accepted and then withdrawn, but "Not reprinted from *Acta Crystallographica*" offprints were prepared and were gleefully distributed by Lindo Patterson. The full translation and fuller descriptions of this amusing story can be read in Jenny Glusker's writings, Chapter 1 in *Crystallography in North America*, ACA (1983) or Patterson and Pattersons: *Fifty Years of the Patterson Function*, IUCr (1987), 617-619.



Not reprinted from *Acta Crystallographica*

PRINTED IN DENMARK

On the symmetry of the wheaks produced by the Bucessera. By A. L. Pon, *Senex, Incomparable Philpt., U. A.*

(*Received* 5 *December* 1952)

Recent publications on the reety (some workers prefer the term rekhaning) of diffems of X-tay (Rasset, 1951*a*, *b*; Helliser, 1951; Hoester, 1952*a*, *b*) have suggested the mathiques used in the prone.

It is clear that in all discussions of diffems, the radius of the Ewere can be set at unity.* If then a given relp is associated with monion of a given waugth, then a relve joining this relp with the relor corresponds to the whiess which is necessarily preced with the monion in the X-rube (see any took on the quary). Thus any diffromena praced by the Bucessera possesses planetry about a sylane through the relp, the relor and the diffray.

Refecs

Helliser, N. H. A. (1951). *Intergraphs*, London: Macan.
Hoester, J. A. (1952*a*). *Experientia*, **8**, 297.
Hoester, J. A. (1952*b*). *Acta Cryst.* **5**, 626.
Rasset, G. A. (1951*a*). *Acta Cryst.* **4**, 335.
Rasset, G. A. (1951*b*). *Acta Cryst.* **4**, 431.

* Vernished.

We also asked what all the following words have in common:
BASSET, BULGAR, CARBON, CARNAL, CARPET, CITRUS, DOGSEX, FARMER, MUPPET, POSSUM, SURFER, WASHED.

Answer: *They all follow the conventional Cambridge Structural Database refcode vowel and consonant pattern CVCCVC, and are actual refcodes*. There are many more refcodes which are English words. Two more questions about those in the list above: Only one refers to the chemical name of the compound it represents. Which? Do SURFUR and WASHED contain any water? Also: Are there any refcodes which are palidromic words?

(puzzle adapted from BCA News)

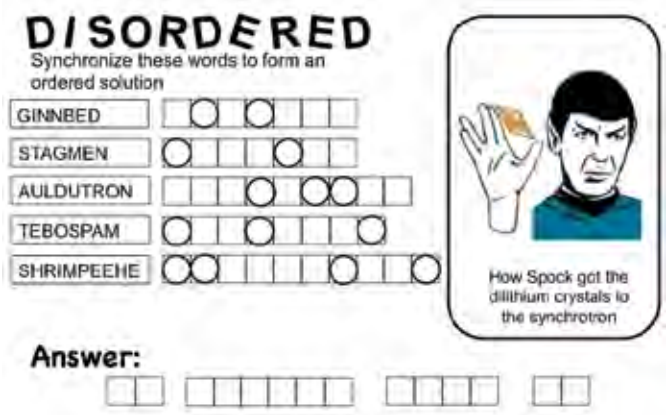
Selections from the Rigaku Crystallography Times, Vol 5, No 1:

Jan. 7, 2013. A research team of scientists from **EMBL** (the European Molecular Biology Laboratory), Grenoble and the **IGBMC** (Institut de Génétique et de Biologie Moléculaire et Cellulaire) in Strasbourg, France have, for the first time, described in molecular detail the architecture of the central scaffold of TFIID: the human protein complex essential for transcription from DNA to mRNA.

Jan.10, 2013. Developments arising from new science techniques at Keele University in the UK, ILL (the Institut Laue-Langevin) which is one of the flagship centers for neutron science, and ESRF (European Synchrotron Radiation Facility), have confirmed the presence of hydronium ions in the protein rubredoxin. These ions, commonly found in comet tails or interstellar space clouds, have been found to be involved in crucial interactions with the protein.

Jan.14, 2013. Using an innovative approach, scientists at **TSRI** (the Scripps Research Institute) have determined the structure of Ltn1, a recently discovered "quality-control" protein that is found in the cells of all plants, fungi and animals.

Jan. 17, 2013. **Joel Ybe**, a senior research scientist in the Department of Molecular and Cellular Biochemistry at **Indiana University**, and colleagues have identified a "topology switch" in the protein clathrin, the function of which may shed light on molecular processes involved in tumor suppression.



New Disordered puzzle

Cartoon courtesy of Nick D. Kim, Univ Waikato, New Zealand.

Hawaii 2013

Logo design by Vanessa Reitz, *vjreitz@prosite.com*

July 20 - July 24, 2013

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Deadlines:

Abstracts: March 31, 2013
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Advance Registration: May 31, 2013
Hotel Reservations: June 18, 2013
Abstracts accepted online only
40% of all talks will be from contributed abstracts

Sheraton Waikiki: city view $183, mountain view $203 + tax
Princess Kaiulani: $143 + tax, students & postdocs only.
Students take note: - use the Room Sharing feature under accommodations on the meeting web site.

The meeting will end on Wednesday, after the Awards Banquet

Submit abstracts - Register - Full call for papers:
www.AmerCrystalAssn.org

Award Symposia

Bau Award in honor of Tom Koetzle
Trueblood Award in honor of Tom Terwilliger
Etter Early Career Award in honor of Eric Ortlund

Tom Koetzle
Robert Bau
Neutron Diffraction Award

Tom Terwilliger
Kenneth Trueblood
Computational Chemistry Award

Photo courtesy of Will Kirk / Johns Hopkins University

Eric Ortlund
Margaret C. Etter
Early Career Award

Program Co-Chairs

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Jeanette Krause
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Poster Chair
Ilia Guzei
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Session Photos
Victor Young
vyoung@umn.edu

Transactions Symposium

Neutron & Synchrotron Sources: Role in Crystallography
Session I - Small Angle Scattering
Session II - Supramolecular Assemblies
Session III - Emerging Characterization Facilities &Tools
Session IV - Chemical Crystallography

Organizers: Richard Gillilan, Greg Hura, Christine Dunham, Eric Montemayor, Antonio dos Santos, Jonathon Hanson, Christine Beavers, Simon Teat

Evening Session: ***Enabling Partnerships for Broader Crystallographic Data Accessibility***

Chairs: Joe Reibenspies, John Rose & John Westbrook

Richard Dickerson

Fankuchen Award Richard is not able to travel to Hawaii to accept the award. However, Alex MacPherson will give a retrospective on his research. Richard will present a Fankuchen lecture at a later date (time and place will be announced on the ACA website).

Videography Team:
Richard Bromund & Virginia Pett

Who Needs to Register: Everyone, (including invited speakers), must submit a registration form with the appropriate fee. Registered participants will receive conference materials and a name badge securing admission to the Opening Reception, the Exhibit Show and scientific sessions at the ACA Registration Desk in the Sheraton Waikiki Hotel.

Obtaining a VISA: Advanced planning is critical. When making plans to travel to the US all foreign travelers should identify whether a VISA is needed. If so, applications should be made 90 days in advance of the travel date. For further information contact the US Department of State: travel.state.gov/visa/visa_1750.html.

Staying Green: The full set of abstracts will be distributed only on CDs. Attendees will not receive a meeting bag so please remember to bring your favorite from an earlier meeting.

As an incentive to stay in the conference hotel, a number of lucky attendees will be selected at random to receive one night's accommodation free!

Financial support: Young scientists can apply for travel support through the ACA and the IUCr. See the ACA website: www.AmerCrystalAssn.org.

Questions: Contact Marcia@hwi.buffalo.edu

Registration fees

Category	Early	Late after May 31
Regular Member	$500	$700
Retired Member	$195	$295
Post doc Member	$250	$350
Student Member	$195	$295
Nonmember*	$700	$950
Post doc Nonmember*	$350	$450
Student Nonmember*	$285	$385
Guest**	$ 65	$ 65

Social events

Opening Mixer	included in reg. fee
Banquet	$70 ($35 students)
YSSIG Event	Free for students & postdocs; $28 for all others

Workshops

WK.01 Biological SAXS - Theory & Practice
Student/Postdoc-$100, Academic-$150, Corporate-$250

WK.02 Introduction to GSAS -II Crystallographic Analysis System
Students-$75, Others $100

WK.03 Getting the Most out of the Cambridge Structural Database
Students-$130, Others $170

Meeting Sponsors

APRIL 2013

7-11 **ACS 245th Mtng & Expo**, New Orleans, LA

MAY 2013

26-29 **4th International Symposium on Diffraction Structural Biology.** Nagoya, Japan. *sbsp.jp/ISDSB2013/homepage/index.html*

JUNE 2013

16-20 **Workshop on Dynamic Structural Photocrystallography in Chemistry and Material Science.** Univ. of NY at Buffalo, SUNY. Organizer: Phillip Coppens *chem9988@buffalo.ed*

2-7 **Gordon Conference: Electron Distribution & Chemical Bonding**, Les Diablerets, Switzerland. *www.grc.org/programs.aspx?year=2013&program=elecdist*

JULY 2013

20-24 **ACA 2013 Honolulu, HI, Sheraton Waikiki.** Program Chairs: **Allen Oliver** *aoliver2@nd.edu* & **Jeanette Krause** *jeanette.krause@uc.edu*

21-25 **ACCGE-19, 19th Amer Conf on Crystal Growth & Epitaxy**; joint with **OMVPE-16, Organometallic Vakpor Phase Epitaxy**. Keystone, CO: *http://crystalgrowth.us/accge19/index.php*

AUGUST 2013

4 - 9 **ICCOSS-XXI** International Conference on the Chemistry of the Organic Solid State, Oxford, UK. *iccoss2013.org*

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

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

MAY 2014

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

AUGUST 2014

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

AUGUST 2015

23-28 **ECM-29**, Rovinj, Croatia; contact Aleksandar Višnjevac *aleksandar.visnjevac@irb.hr; http://www.facebook.com/29thEuropeanCrystallographicMeeting?ref=hl*

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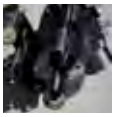

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