ISSN 1467-2790

CRYSTALLOGRAPHY NEWS

British Crystallographic Association

No.81

June 2002

Agendas for BCA Spring Meerting 2002

The Chatt Lecture, 2002

Educational Models and Crystal Growth in Schools

CCP4 at York

Quarterly




BCA Administrative Office,
Northern Networking Ltd,
1 Tennant Avenue,
College Milton South,
East Kilbride, Glasgow G74 5NA
Scotland, UK
Tel: + 44 1355 244966
Fax: + 44 1355 249959
e-mail:
bca@glasconf.demon.co.uk

NEXT ISSUE OF CRYSTALLOGRAPHY NEWS

CRYSTALLOGRAPHY NEWS is published quarterly (March, June, September and December) by the British Crystallographic Association. Text should preferably be sent as MSword documents (any version - .doc files) or else as .rtf on a PC disk or electronically. Diagrams and figures are most welcome, but, if possible, please send them separately from text as .jpg, .gif, .tif, or .bmp files. Items may include technical articles, news about people (e.g. awards, honours, retirements etc.), reports on past meetings of interest to crystallographers, notices of future meetings, historical reminiscences, letters to the editor, book, hardware or software reviews. Please ensure that items for inclusion in the **September 2002** issue are sent to the Editor to arrive before **19th July 2002**.

BOB GOULD
EDITOR, CRYSTALLOGRAPHY NEWS
33 Charterhall Road
EDINBURGH EH9 3HS
Tel: 0131 667 7230
E-mail: bob@gould.ca

The British Crystallographic Association is a Registered Charity (#284718)

Contents

President's Remarks

The Nottingham Spring Meeting was splendid: excellent science working largely in themes rather than BCA groups, numerous workshops, the Special Interest Groups (SIGs), and the first ever BCA Prize awarded to Professor Bill David from ISIS at the Rutherford-Appeleton Laboratory who gave an excellent talk on neutron powder diffraction. He was introduced by Professor Terry Willis, one of the pioneers of neutron diffraction (and many other things). The Nottingham campus was looking very spring-like, and the sun shone. Living in Scotland, what else can I ask for? We are all very grateful to Sandy Blake and Claire Wilson for their hard work as local organizers, ably assisted as always by the staff at Northern Networking, especially Gill Houston and Euan Woodward. About 250 people attended the meeting which is a quarter of our membership. This is good, but not good enough, and Council has been debating what can be done to increase attendance. We are particularly concerned about macromolecular crystallographers. Not, you understand, because of their crystallography, but because of the wide choices they have as to which conferences to attend; we want a situation where the BCA Spring Meeting is a meeting of choice. To this end, we are going to shorten the meeting to 2-3 days, allow day registration, start on Tuesdays to avoid weekends (a precious resource these days), keep away from school holidays where possible, and work hard to keep costs low. This latter point is difficult. We have always tried hard to do this, but universities are our traditional venue for the Spring Meeting, and they are no longer a cheap option especially when you look in detail at the entire package they offer. (I can see a day when, just like the ACA, hotels become competitive.) This was all discussed at the AGM and gained general approval with caveats about timing.

We are also planning to publish the plenary lectures and associated sessions in a special issue of Crystallography Reviews rather like the Transactions that the ACA produce each year. This is a good deal: Crystallography Reviews gets an up-to-date survey of an important topic in crystallography, and the BCA becomes associated with a high profile, high quality crystallography review journal. We hope to be in a situation to provide cheap copies to the BCA membership.

So, as ever, nothing stays the same, but I think we are moving forward in a positive and exciting way.

I hope to see many of you at the Geneva IUCr meeting.

Chris Gilmore
May 2002

Cover pictures left to right:

The Nottingham team with the VP

Hard at work with CRYSTALS

Poster prize winners

DNA being repaired!

BCA Council Members 2002 - 2003

President (2003)
Prof. Chris J. Gilmore
Department of Chemistry
University of Glasgow
GLASGOW G12 8QQ
tel: 0141 330 3716
chris@chem.gla.ac.uk

Vice President (2004)
Prof. Paul Fewster
Philips Analytical Research Centre
Cross Oak Lane
Redhill RH1 5HA
tel: 01293 815714
paul.fewster@philips.com

Secretary (2004)
Dr. Christine Cardin
University of Reading
Dept of Chemistry
Whiteknights
Reading RG6 6AD
tel: 0118 9318215
c.j.cardin@reading.ac.uk

Treasurer (2003)
Mr. David J. Taylor
35 Birchley Road,
Billinge
WIGAN
Lancs WN5 7QJ
tel: 01744 893108
djtaylor@lineone.net

Ordinary members
Dr Margaret J. Adams (2003)
Lab. of Molecular Biophysics
Rex Richards Building
South Parks Road
OXFORD OX1 3QU
tel: 01865 275391
margaret@biop.ox.ac.uk

Dr Jeremy K. Cockcroft (2003) (Web Master)
School of Crystallography
Birkbeck College
Malet Street
LONDON WC1E 7HX,
tel: 020 7631 6849
cockcroft@img.cryst.bbk.ac.uk

Prof. Paul R. Raithby (2003)
Department of Chemistry,
University of Bath,
Claverton Down
BATH BA2 7AY
tel: (01225) 323183,
p.r.raithby@bath.ac.uk

GROUP REPRESENTATIVES

Biological Structures
Dr. A. Hadfield (2002),
Department of Biochemistry,
University of Bristol
BRISTOL BS8 1TD,
tel: 0117 928 7436,
A.T.Hadfield@brist.ac.uk

Chemical Crystallography
Dr Harry Powell (2002)
MRC Lab. of Molecular Biology
MRC Centre
Hills Road
CAMBRIDGE CB2 2QH
tel: 01223 402423
hrp1000@cus.cam.ac.uk

Industrial
Prof. Christopher S. Frampton
Department of Chemistry
University of Southampton
Highfield
Southampton SO17 1BJ
tel: 02380 594167
chrisf@soton.ac.uk

Physical Crystallography
Dr P.A. Thomas
Department of Physics
University of Warwick
COVENTRY
phrve@csv.warwick.ac.uk

Co-opted Members
Prof. P.Barnes,
Department of Crystallography,
Birkbeck College,
Malet Street,
LONDON, WC1E 7HX
tel: 020 7631 6817
barnes@img.cryst.bbk.ac.uk

Dr C.C.Wilson,
Rutherford Appleton Laboratory,
ISIS Facility,
CHILTON,
Oxon OX11 0QX
tel: 01235 82 1900 ext 5137 or 01235 44 5137,
C.C.Wilson@rl.ac.uk

Ex-officio Members

Editor "Crystallography News"
Dr Robert Gould
33 Charterhall Road
Edinburgh EH9 3HS
Tel: 0131 667 7230
bob@gould.ca

Education Officer
Mrs K.M.Crennell
'Fortran Friends'
P.O.Box 64
Didcot
Oxon OX11 0TH,
tel: 01235 834 357
BCA@ISISE.RL.AC.UK

GROUP CHAIRMEN

Biological Structures Group
Dr. Richard Pauptit
Protein Structure Lab
AstraZeneca,
Mereside,
Alderley Park,
Macclesfield
SK10 4TG,
tel: 01625-516135
richard.pauptit@astrazeneca.com

Chemical Crystallography Group
Prof. Paul R. Raithby
Department of Chemistry
University of Bath
Claverton Down
BATH BA2 7AY
tel: (01225) 323183
p.r.raithby@bath.ac.uk

Industrial Group
Prof. Christopher S. Frampton
Department of Chemistry
University of Southampton
Highfield
Southampton SO17 1BJ
tel: 02380 594167
chrisf@soton.ac.uk

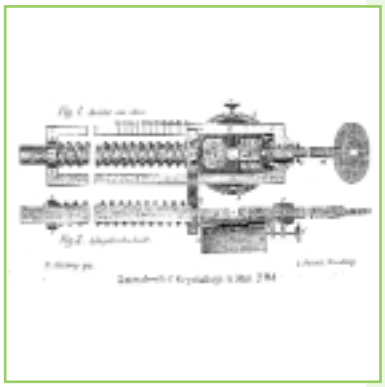
Physical Crystallography Group
Professor J.L. Finney
Department of Physics & Astronomy
University College London,
Gower Street,
LONDON WC1E 6BT
tel: 0171 380 7850
j.finney@ucl.ac.uk

Full committee details on the BCA website - **http://bca.cryst.bbk.ac.uk/BCA/**

Sadly, this issue contains a record number of obituaries, as our community has lost three of our founder members, Helen Megaw, Max Perutz and Charles Taylor, since the last issue. Readers will be also be sorry to hear of the death of Professor Norio Kato, who passed away Friday April 5th. He was one of the founders of X-Ray Dynamical Theory, and a past president of the IUCr.

Most of the rest of the issue is concerned with various aspects of the Spring Meeting in Nottingham. It certainly seemed to be greatly enjoyed by all who were there. Many thanks to all who sent in much material. Among other decisions taken was the final choice of a logo for the BSG, which is shown here:

Shortly before the BCA, I was at the annual meeting of our German counterpart, the Deutsche Gesellschaft für Kristallografie in Kiel. This organisation is almost exactly the same size as we are and has similar numbers at its meetings. It also has difficulty in getting biological crystallographers to its meetings, although they run an almost completely independent programme in the same place. The biologists do insist that all papers are in English, which must deter some members! A talk on the history of Crystallography in Kiel provided more overlap with our meeting, as Kiel was an early centre for studies of the effect of high pressure on crystals. The remarkable apparatus shown in the figure was designed there, and published in 1883.



Our sister publication, the polyglot (Swiss) SGK/SSCr Newsletter has a fine appreciation of Professor Dieter Schwarzenbach of the University of Lausanne, who has recently celebrated his 65th birthday. Few who have attended a European Meeting will not have met this lively man of wide interest in and out of crystallography. They will have no difficulty in recognising the active figure on the bicycle in the cartoon below! We join in wishing Dieter a happy and active retirement.

The September issue will not have many new meetings to report, and will have some book reviews and more items of general interest. It is also an excellent chance to get a letter or other article published – I look forward to hearing from you by 19 July!

Bob Gould
May, 2002

Acknowledgements
BCA Sponsors

The British Crystallographic Association is grateful to Birkbeck College, University of London, who host and manage the server for our Website.

BCA Spring Meeting, 2002

The 2002 Spring Meeting took place from March 25 – 28 on the spacious and elegant campus of the University of Nottingham. Sandy Blake and Claire Wilson, shown in the photograph with their larger-than-life grins, thoroughly deserve to look pleased with the very well-run, friendly and scientifically exciting meeting that they helped us all to have. Great thanks are also due to the rest of the local team and to Northern Networking in its role as the BCA Office. As usual, a huge amount was presented and discussed, and the reports of meetings will flow over into the next issue of Crystallography News.

The working team with the end in sight!

Claire Wilson and Sandy Blake with Paul Fewster at the opening reception

A Very Distinguished Group enjoying the dinner.

Reports on Sessions

An Introduction to Amorphous Materials

Industrial crystallographers often develop something of a blind spot for amorphous materials, even when they are regularly present in the materials routinely handled. We can try to justify a lack of interest by saying that amorphous phases are not crystalline and therefore not the responsibility of the crystallographer. The fact is, of course, that X-ray and neutron scattering can give much useful information about non-crystalline materials but the techniques of data collection and interpretation take us beyond the familiar world of high order.

The session was chaired by Dave Taylor (ICDD) and was, of necessity, a very brief introduction.

John Parker (Sheffield) gave helpful summary of "Measurement, Interpretation and Case Studies", relating much of the tutorial to his interests in glassy materials. The areas covered included: the principles underlying scattering by randomly and non-randomly spaced atoms; problems arising from inelastic scattering and other corrections to experimental data; calculation of the radial distribution function and pair correlation function; termination and convergence errors; the need to use shorter wavelengths than Cu and the benefits of neutrons; modelling and network models for glass. An important reason for the decline in laboratory X-ray scattering studies of amorphous materials lies in the need for short wavelengths to access nearest neighbour information. It seems that the most practical options for reliable results (including the alternative approach of EXAFS) mean starting work at a neutron or synchrotron source.

Geoff Mitchell (Reading) addressed another area with its own set of problems, "Quantification of Crystalline and Amorphous Fractions". Much of the talk was framed around examples from the world of semi-crystalline polymers, but the principles were applicable elsewhere. In principle, crystallinity determination should be simply related to the scattering power of the

crystalline and amorphous phases. However, even the definition of crystallinity is not simple for polymers and really comes down to the distinction between broad and sharp peaks. This was shown to be relatively easy for some materials such as linear polyethylene at low Q, but increasingly difficult at higher Q due to huge numbers of closely-spaced reflections. There are once again practical problems from necessary corrections, including those for inelastic and parasitic scattering and those for geometry. Issues around peak fitting are crucial and a range of techniques has been used, some based on theory that is difficult to put into practice, others on a more pragmatic basis. Establishing the shape of the amorphous component is particularly difficult. Variable temperature measurements and quenching from the melt have been used, but it is important to realise that the amorphous scattering curve can change significantly over a relatively narrow temperature range. Overall, this was a very helpful introduction for many to an area with hidden pitfalls and a useful update for those dabbling in the field over the years.

Amorphous materials continue to grow in technological importance (e.g. pharmaceuticals, polymers, electronics, catalysts). Ignoring them because they are "not crystalline" does seem like burying our heads in the quartz. I will not be surprised if this topic appears again soon.

Steve Norval

Crystallography, Drugs and Disease

This session highlighted both the need for novel drug therapy and a wide variety of strategies and techniques for screening for suitable compounds.

Exposure to diseases such as malaria, sleeping sickness and leishmaniasis results in several million human deaths each year as drugs currently prescribed are either themselves highly toxic or of low efficacy. Bill Hunter (University of Dundee) described his search for new anti-parasitic agents through studying the drug resistance of the *trypanosomatidae*. The protozoan enzyme pteridine reductase provides a metabolic bypass, compromising folate antagonists. A short-chain reductase with a Lys-Tyr-Asp catalytic triad and two βαβαβ motifs, it catalyses two reductions in a single active site. The 1.75Å structure of its complex with NADPH and methotrexate (a folate mimic) shows an unusually extensive interaction with NADPH and an exceptionally well ordered active site with a water molecule that may be an active proton donor. Calorimetry and modelling are being used to determine the binding energy of potential inhibitors.

With symptoms described by Virgil as long ago as 25 B.C., anthrax was a prime target of early biologists and with recent concern over undestroyed cultures, is again of considerable interest. Unruffled by a Powerpoint presentation that refused to run, Andrew Pannifer (Syngenta) described work at Leicester University on the structure of Lethal Factor. One of three components of the anthrax toxin, this four-domain protein is "an evolutionary freak". Lacking sequence homology with either, the tertiary structure of domain IV with a HExxH motif at a zinc metalloprotease catalytic site shows strikingly similarity both to thermolysin and to domain I, where the superposed motif becomes YEIGK and is essential for binding the membrane-translocating component. Domain III is a helical bundle apparently formed by repeating elements from domain II, which itself shows unexpected structural homology with the VIP2 domain of a functionally unrelated ADP-ribosylating toxin. Having evolved through gene duplication, mutation and fusion, domains II, III and IV combine to create a deep peptide-binding cleft.

Yuan de Yang (University of Edinburgh) discussed a project to develop novel ligands for human cyclophilin. An isomerase implicated in arthritis, HIV infection and immune rejection, its structure comprises two α-helices and eight β-strands in a collapsed β-barrel. From structural knowledge of the complex of cyclophilin and a commercial compound with a 22mM binding constant, ligands have been designed to increase hydrophobic interaction and hydrogen bonding with the protein. Six of seven synthesized bind in exactly the same mode and with binding constants K_d that can be expressed as a linear

function of buried area and the numbers of hydrogen bonds shorter and longer than 3Å. The seventh ligand does not bind with two methyl groups pointing into the pocket, and perhaps unsurprisingly, its K_d does not fit the same formula.
Richard Pauptit (AstraZeneca, and BSG Chairman) gave a thoughtful and wide-ranging overview of high throughput drug design. Recalling that in the 1980s design was rational and hampered by slow structure determination and limitations of modelling, he credited advances in combinatorial chemistry for leading the move to empirical screening. The current approach is to 'try everything' and rationalise what is successful. There are questions to ask however about the size and diversity of a compound collection, and the quality of assays and analysis. Typically a starting set of a million compounds suffers dramatic attrition at each screen and at best produces two or three leads. Development of robots to deliver samples for 'mix and measure' tests, and of computer programs for structure-based virtual screening, makes it possible in days to find leads that might never have been tried. Seriously impressive as this is, he warned that potency and selectivity are not the only considerations for clinical acceptance.

M. tuberculosis infects a third of humans and is responsible for 2.3 million deaths a year. Drug resistance is a major problem in countries that cannot afford a cocktail of treatments. David Leys (University of Leicester) said sequencing of the mycobacterial genome has revealed a complicated lipid metabolism and twenty P450 enzymes that could be targets for drug design. Two such have been shown to bind azole antifungal drugs with high affinity. The structure of one complex has been determined at 1Å using both medium resolution MIR and high resolution anomalous data, but could not be solved by molecular replacement. The haem is "kinked" by a proline into heterogeneous occupation of two distinct orientations and a bifurcated pathway appears to stage delivery of two protons to reduce its ferric and ferrous-oxy iron. Studies of other azole-bound complexes are unfortunately being hampered by insolubility and extremely slow co-crystallisation.

In the final talk, Ian Tickle (Astex Technology) described development of hardware and software to suit a particular range of well validated targets. Arguing that small fragments with a molecular weight of only 100-200 daltons explore chemical space more efficiently, the Astex project aims to find drugs with affinities for proteases, protein kinases and protein phosphatases that are better than 1mM, a level beyond the range of high throughput screening with target-based assays. As a first stage towards full automation, selected compounds are pooled in sets with similar properties and soaked into native protein crystals. A robot can automate crystal mounting, alignment and data collection at a resolution of 2.8-2.0A, either in house or at a synchrotron. After initial refinement of the protein, the pooled ligand (and solvent molecules) can be located from difference electron density. If a hit is found and a single ligand identified (either manually or by software), an unpooled data set can be collected for proper refinement and evaluation. This method was recently tested and produced 29 hits from 367 data sets.

Sheila Gover

Detectors

The detector session, organised by Peter Moody and chaired by Harry Powell, had a variety of speakers from fields as diverse as astronomy and electron microscopy as well as from crystallography. George Fraser (Leicester) gave an overview of recent developments in electronic imaging detectors for X-ray Astronomy mainly for use in satellites. As well as the better established detector types such as CCDs, he discussed the pros and cons of devices such as microwell proportional counters, microchannel plates, compound semiconductor arrays and cryogenic detectors.

Wasi Faruqi (MRC-LMB, Cambridge) began by discussing the current applications of CCD detectors in X-ray diffraction experiments, and focused on their limitations, particularly their use in indirect mode (i.e. the CCD detects visible light photons emitted from a phosphor irradiated with X-rays), which gives rise to a more significant point spread function

among other problems. He went on to emphasize the potential advantages of using a direct mode detector, for example semiconductor pixel arrays, which do not use an intermediate phosphor. These are characterized by having negligible readout noise and an improvement in spatial resolution, and much faster readout times.

Jules Hendrix (X-ray Research GmbH) began by describing the latest developments in CCD technology by his company, and then described the new solid state detector developed using a selenium photoconductor. The detector is characterized by the large active area (430 mm x 358 mm, containing 7.8 million pixels) direct detection of x-ray photons without an intermediate phosphor, and a negligible point-spread function (well below one pixel). He pointed out that, in spite of using a selenium semiconductor, the detector was still sufficiently sensitive in the Se K absorption region to be of use in anomalous dispersion methods such as SAD and MAD.

Joe Ferrara (Rigaku/MSC) discussed progress in image plate technology and readout methods over the last decade or so and made the case for their continued use. Improvements in phosphors have increased the sensitivity of the devices, and the readout time has been reduced dramatically. For use with a laboratory source, these systems remain competitive against solid state devices.

Roger Durst (Bruker-Nonius) completed the session by introducing a CCD detector using a lens for focussing rather than an optical taper; this has the effect of removing light scattering effects in the fibre optics. Coupling the light image to a backside-thinned CCD (which has higher quantum efficiency than regular CCDs) gives an overall improvement in the overall efficiency compared to conventional devices. He finished his talk with a demonstration of phasing from the anomalous sulphur signal obtained from a laboratory source.

Harry Powell

DNA Recombination and Repair

The session started with a talk from Dale Wigley (Cancer Research UK, Clare Hall) on "Relating Structure to Mechanism in Helicases". He took us through the ATP-dependent translocation of PrcA and RecG – two helicases from different superfamilies – to show the general applicability of the mechanism proposed. The videos were crystal clear!

Daniela Stock (MRC, Cambridge) then proceeded to describe "The crystal structure of Reverse Gyrase: DNA Gymnastics at high temperatures". Quite an exercise it is for this protein to introduce positive supercoiling into the DNA of hyperthermophiles. The mechanism, that requires cooperation of the C- and N-terminal domains, protects the genome from heat denaturation. The C-terminal domain shows high homology to type I topoisomerases.

Speaking of these enzymes… topoisomerase IIβ was shown to bind to Holliday junctions. The next talk explained how yeast Ydc2 resolves the Holliday junction into two separate duplexes. Tracey Barrett (Institute for Cancer Research) solved this first structure of the eukariotic resolvase from *S. pombe* by SAD to 2.3Å, confirming an evolutionary relationship to bacterial RuvC enzymes. A model was proposed for junction binding and cleavage.

So what happens when there is a mismatch? Titia Sixma (Netherlands Cancer Institute) showed how MutS, an asymmetric

DNA Session: from left to right: Titia Sixma, Daniela Stock, Dale Wigley, Peter Moody (Organiser), Mark Odell, Malcolm White, Tracey Barrett.

ATPase from *E.coli* recognises a mismatch. By "reading" the DNA till it finds a possibility to H-bind to a mismatch base, the protein scans and identifies mistakes. It also recognises the greater flexibility of mismatched DNA that can tolerate a higher kink angle. It was suggested that interaction with MutL would play a role in preserving the heterodimer.

After hearing about the recognition of mistakes, it was time to repair them. Malcolm White (Centre for Biomolecular Science, St. Andrews) told us about a DNA-binding and repair enzyme. Alba (Acetylation lowers binding affinity) was isolated from a sample collected in natural acidic, sulphur-rich pools at 80°C. The Sulfolobus solfactaricus protein has a DNA binding affinity controlled by reversible acetylation.

Finally it was time to seal the nicks: "A structural basis for nicked DNA recognition by DNA ligases" was presented by Mark Odell (University of Leicester). He described the structure of the covalent reaction intermediate PBCV-1 DNA ligase-adenylate. Supported by biochemical and mutagenesis studies, a mechanism was proposed for both ATP and NAD-dependent DNA ligase enzymes.

The talks were extremely interesting and integrated, in the sense that each seemed to introduce us to the next. It was a bit like a day in the life of DNA…

Susana Teixeira

Polymorphism and Structural Changes

The first session, chaired by Harry Powell, began with 'A beginner's guide to Polymorphism', in which Chris Frampton (Southampton) began by defining a polymorph as a single crystalline phase, and emphasizing that hydrates and other solvates are not polymorphs. He went on to illustrate one of the major problems in this field, that of the "disappearing polymorph", i.e. a phase which can no longer be found. This often happens when a new phase appears which is more stable than that found previously, and all attempts fail to produce the previous polymorph. The rationale behind this is that the route to the new phase is less favourable kinetically but it may be catalysed by the presence of a pre-existing sample.

He went on to discuss the effect of different polymorphs on the physical properties of the sample in question. These can be examined by standard instrumental analytical methods, e.g. single crystal and powder X-ray diffraction (using variable temperatures and pressure), vibrational spectroscopy, scanning electron microscopy, etc. The stability of different polymorphs can be followed by van't Hoff solubility plots. Different types of polymorphism are distinguished by whether there is one stable and one metastable form (monotropic) or two separate forms which are both stable but, e.g., in different temperature ranges (enantiotropic).

He concluded by pointing out that this is a major problem to the pharmaceutical industry because of changes to bulk density, dissolution rate etc, and gave the example of the disappearing polymorph of paracetamol.

Stephen Tarling (Birkbeck) followed this with an entertaining lecture entitled "Crystallography for the Rich", in which he described his experiences as an expert witness in court cases where disputes have arisen over patent rights and infringements. He began by asking questions such as "Who are the rich?", "How did they become rich?", "What Crystallography do the rich need to know?" and "How can WE get rich?". Within a format which contained several jokes about lawyers (by lawyers), he explained the niceties of devising a good (i.e. defensible) patent and demonstrated the massive economic value of intellectual property to a large pharmaceutical company, where the value of a single compound can be measured in many millions or even billions of dollars.

He outlined one court case which essentially turned on the use and interpretation of the word "essentially" within a patent, and showed how crystallographic analysis, particularly the identification of polymorphs, is now of prime importance in intellectual property disputes involving pharmaceutically-relevant compounds. He also described the methods (which may seem unusual to the lay

observer) used by companies to recruit their expert witnesses, from the initial soundings to final interviews.

Adrian Williams (Bradford) showed that "in situ Monitoring of Drug Form Changes in tablets by Raman Spectroscopy" is often more suitable than trying to follow polymorphism changes by direct crystallographic means. Raman spectroscopy has advantages over the diffraction methods in that it can be used on far smaller samples, and that it can also be used without the concomitant crystal form modifications possible if a sample is recrystallised or milled to provide a sample suitable for powder diffraction work. Raman spectroscopy can be used for analysis of the sample in the form in which it is present in a pharmaceutical preparation. He provided a case history of a pharmaceutical ingredient present both as a crystalline hydrochloride salt and an amorphous free base, and showed that Raman spectra could be used to quantify the proportions of each present in mixtures under differing conditions. This information was then used to optimize the processing conditions and minimize the proportion of free base present.

The second session on Polymorphism and Structural Change was begun by Jim McCabe (AstraZeneca) who talked about rapid throughput screening of salt forms of polymorphic materials. Salt and polymorph selection are important issues in the pharmaceutical industry, the former being employed to improve the physical properties such as crystallinity, melting point, dissolution rate etc. The GADDS X-ray powder diffraction set-up was described, this offering a very high throughput analysis of samples. The GADDS system offers advantages over conventional powder diffraction methods, including the use of small samples, the automated analysis of many samples and rapid collection of data. This makes it ideal for the analysis of samples crystallised in multi-well plates, which was illustrated in the lecture and is ideally suited for characterising the products of salt and polymorph screens. Following this discussion of the hardware, the extensive use of the SNAP-1D pattern matching software was illustrated. This software gives a quick and very reliable means of screening the diffraction patterns of products against known patterns and allows the whole system to be run in an efficient and productive way. The lecture gave a fine overview of the imperatives of such a screening process in an industrial research environment.

Yaling Wang (Merck) continued the industrial theme to the session with a lecture on the polymorphic behaviour of an NK1 receptor antagonist. In a complex phase diagram, it was found that transformations tended to occur between the pairs of polymorphs I↔III and II↔IV, but that the thermodynamics of the transition between members of these pairs were rather more complicated. Indeed, an interesting phase transformation route was identified from a more stable polymorph (Form I) to a less stable polymorph (Form II) at room temperature. Various techniques were used to examine and characterise these transformations including differential scanning calorimetry (DSC), thermogravimetric analysis (TGA), X-ray powder diffraction (XRPD), solid-state NMR spectroscopy (SSNMR) and solubility. The talk emphasised the subtlety of the phase diagram, and stressed again the importance of understanding this fully in order to be confident of preparing the correct polymorphic form for proposed use.

Mike Hursthouse (Southampton) then gave a talk on the highly polymorphic sulfonamide systems, in which he showed that not only have new polymorphs regularly been identified, but that salt and mixed crystal systems have also been studied extensively. The characterisation of these structures by single crystal X-ray diffraction allows hydrogen bonding patterns to be identified, categorised and compared, shedding light on how the structures are held together and giving clues about the differences between the polymorphic forms. Mike then went on to talk about the opportunities being provided by combinatorial structural chemistry, and the opportunities and challenges presented by the need to automate many parts of the process, from crystallisation to data collection, reduction, analysis and publication. It is

clear that fast-throughput systems in single crystal diffraction will be developing rapidly in the next few years and crystallographic information exchange must evolve to meet the needs of these developments.

The session was closed with a talk on the use of combined crystallographic and spectroscopic methods in examining new phases of simple molecular compounds, given by Colin Pulham (Edinburgh). Colin showed that apparently simple molecular compounds can undergo many phase transitions and adopt different packing motifs, induced for example by temperature and/or pressure, and the presence of solvent molecules (another recurring theme throughout the session). He showed the complementary use of Raman and other spectroscopies, along with crystallography, in studying the effect of pressure on molecular halides such as BBr_3, $SnCl_4$ and $PbCl_4$, Raman spectroscopy being particularly powerful in identifying phase changes. In addition the effects of solvation on the structures of materials such as paracetamol and acetamide have been investigation by recrystallising these materials under different conditions.

Overall, the three sessions showed the diversity of interest on this topic, and emphasised that the understanding of the relationship between different polymorphic forms can be challenging. The sessions also showed that developing an understanding of structure-property relationships and phase transformations from one crystal form to another requires a broad range of physical characterisation techniques in addition to crystallographic methods.

Harry Powell, Sandy Blake & Chick Wilson

Powder Diffraction Surgery

"Powder diffraction" means different things to different people. This session was a follow-up from the Rietveld refinement workshop and that set the starting point for the discussion. Jeremy Cockcroft was in the chair and his first task, with a little coaxing, was to assemble a 'panel' to field the questions: John Evans, Robin Shirley, Lachlan Cranswick and Bill David eventually succumbed and took their places at the front.

The discussion started with the optimum experimental conditions for 'H' positions by neutron diffraction with deuteration. Bill David advocated medium resolution and huge count rates, but it was claimed that the job could be done better by single crystal X-ray diffraction. The optimum solution could depend on whether the atomic positions or electron density maps were sought.

The capabilities of national powder diffraction facilities and access to them were obviously close to the hearts of many academic practitioners. The need for both powder and single crystal facilities at Diamond was keenly felt. The ISIS GEM facility was producing "immense" data rates, but what do you do with a thousand patterns a day? Meanwhile, about one case in three was getting beam time at most facilities via peer review.

Variable count-rate data collection has long been advocated for Rietveld studies. This is no problem where users write or influence the software, but it would require fundamental modifications to the data formats used by commercial laboratory systems. The best that could be achieved by those collecting data for Rietveld refinement on such systems was to combine multiple scans over different ranges or boost high angle count rates with programmable slits. It was suggested that the more sophisticated data collection strategies could also help more traditional XRPD applications, such as phase identification. This might just be the route to galvanising manufacturers into action. However, there could be a mountain of software rewrites, particularly to take account of errors with variable count rates.

One thing leads to another, and the lack of publicly available software for merging data sets was bemoaned. It was pointed out that this was the kind of routine that many users would write in a few lines of code. Sadly, it seems that few scientists are now taught programming, so spreadsheets might be more realistic for many.

A straw poll showed that Rietveld refinement was being used in industry, sometimes just for the simpler tasks of lattice parameter refinement or phase quantification. In these cases there was no need for the full Rietveld procedures and it was important to choose the parameters for refinement carefully. This led to discussions of the statistical problems associated with background removal and the merits of Pawley and LeBail fitting procedures. The applicability of Rietveld to thin films was raised, but there seem to be problems with line shapes.

The session ended with a few evergreen topics. The Powder Diffraction File is becoming more sophisticated in its database guise and expanding enormously with incorporation of patterns from the inorganic and Cambridge databases. Rather than publish large numbers of full powder patterns, ICCD was incorporating the ability to simulate patterns for different experimental configurations. Optimising diffractometer slits for individual experiments is obviously the right thing to do, unless you work in a laboratory with lots of hands-on users and the chaos that might ensue. A small side step from this topic led to the tribulations of variable slits, particularly when they stick in one position. We can all understand the embarrassment of having such difficulties identified after the data has left the lab!

This was a wide ranging session that took a little time to get going but eventually got many of the audience involved, covering a range of relevant topics and producing interesting answers. There is clearly an important place for regular open discussions of this type, but the huge range of interests amongst powder diffractionists inevitably results in fewer topics that grab everyone's attention.

Steve Norval

Rietveld Refinement

Following on from the very successful Workshop (Introduction to the Principles and Practice of Rietveld Refinement), held as a satellite meeting immediately prior for the Spring Meeting, the Rietveld Refinement session on the last morning aimed at covering some of the latest developments in using the technique. The session was aimed at emphasising new ways of using Rietveld refinement, on its own or in combination with other techniques, as powder diffraction tackles increasingly complex problems.

The session was opened by John Evans (Durham) with a talk on the use of multi-temperature powder diffraction coupled with a parametric approach to Rietveld refinement in the investigation of structural trends in negative thermal expansion (NTE) materials. These materials, with the fascinating property of reducing unit cell volume as the temperature increases, also show other interesting properties such as ionic migration and a range of phase transitions. The applications of the parametric method were illustrated in a series of studies of the NTE material $ZrMo_2O_8$ and related phases, and in addition to uncovering the fascinating solid state chemistry going on in these, John covered improved methods of data analysis to allow extraction of the maximum information from these studies.

Jon Wright (ESRF) was next up with a talk which showed how Rietveld methods are being applied to very large crystal structures - in this case protein structures. The aim of this work is to investigate whether powder diffraction and Rietveld refinement might be a viable alternative to single crystal diffraction for studying macromolecular structures which are totally resistant to growth as single crystals. The problem of peak overlap and consequent reduction in the available data, can to some extent be overcome by the extensive use of stereochemical constraints in the Rietveld refinements. In addition the idea of anisotropic thermal expansion is also being exploited to mitigate the effects of the severe peak overlap present in these systems. The analyses are carried out on relatively low resolution data, but some promising results have been obtained, including the observation of first-order phase transitions in the protein myoglobin at both 245 and 265 K.

The problem of refinement for

structures of materials with highly mobile ions was the subject of the talk by Steve Hull (ISIS). Focusing on superionic materials, Steve showed that the information available from conventional Rietveld refinements of only the Bragg intensities gave only part of the story. In systems with ionic mobility or other forms of disorder, it is important to look at the whole diffraction pattern and gain information from the diffuse background as well as the Bragg peaks. This is especially important as the presence of this type of disorder means that few Bragg peaks can be observed. In addition to the analysis of diffuse scattering, Steve presented several other methods of enhancing the extraction of information from such disordered diffraction patterns. These include MaxEnt Fourier difference maps, Molecular Dynamics simulations and the use of Bond Valence difference techniques. By combining numerical techniques with those in which chemical sense is imposed on possible models describing the diffraction pattern, reliable and detailed information can be extracted, and this was illustrated in a series of superionic compounds.

The session concluded with an overview of the impact and current status of powder diffraction and Rietveld techniques by Jeremy Cockcroft (Birkbeck). By selecting out some of the highest profile recent publications in the field, Jeremy showed not only the wide range of science being undertaken using these methods, but also the quality of much of the science being produced. This provided an ideal context for a discussion of the current proposal for a high resolution powder diffraction beamline at Diamond (Beamline H), and the status of that proposal was summarised along with an initial specification of the beamline.

A lively discussion session followed in which the importance of this beamline to the community was stressed, in the context of some of the exciting and novel science being produced in the powder diffraction field using Rietveld methods.

Chick Wilson

Thin Films

This workshop is one of a series of specialist tutorials, run by the Industrial Group, to introduce new users to different X-ray techniques.

Glancing Incidence X-Ray Analysis (GIXA) is used to determine the thickness, density and interface roughness and of one or more layers on samples, which are optically flat. Typical examples are anti-reflective coatings applied to glass and also structures used in the electronics industry, i.e. multi-layers on magnetic disks.

When a thin layer, (or layers) are irradiated by an X-ray beam which is incident at a low angle (the scan range is typically, 0 to 3° 2θ) an interference pattern is produced. The X-rays are reflected from the interfaces, between the various layers and also the interface between the layers and the substrate.

The interference pattern is a function of the thickness, roughness and density of the layers. This information can be extracted from the pattern by fitting a simulated profile based on estimated, starting values. The method is applicable to layers, which are either crystalline or amorphous.

Professor Paul Fewster of Philips Analytical Research started the session off by describing the physics behind the simulation. He described how the properties of thickness, roughness and density influence the shape of the pattern. His talk was very well illustrated with some inventive Power-Point graphics showing the propagation of the wave front through the layers. Paul expanded his argument to include the determination of in-plane crystallite size and lateral correlation.

Christoph Schug, of IBM Materials Laboratory, Mainz, Germany described the practical considerations for GIXA measurements.

Firstly, Christoph described the attributes of the ideal sample, both the substrate and the layers: A flat, smooth substrate with an RMS roughness of <10Å which has a sufficient difference in refractive index from the layers(s). For example, use a Ge wafer when studying silicon

based layers as their refractive indices are sufficiently different.

The various experimental configurations were then compared and contrasted. Christoph described his favorite,

- A parabolic, multi-layer mirror for the primary optics which removes the K-ß and provides plenty of intensity
- A beam knife, to limit the irradiated area at such small 2θ and ω angles
- Copper foil attenuator to protect the detector from the primary beam

Next the care needed with sample alignment was emphasized and data collection strategies needed to ensure a good fit to the simulated profile. Christoph then gave tips to ensure an accurate fit between the measured and simulated data.

The talk was illustrated with examples, from a simple NiO layer sputtered on a silicon substrate, to complex examples of the layers on magnetic media.

Sadly, we didn't really have enough time to do justice to such an extensive and useful technique, which is quite removed from the more common, powder diffraction methods. However, both speakers made an excellent job, providing a stimulating introduction to a fascinating subject.

Judith Shackleton,
Manchester Materials Science Centre.

Report of the Education SIG

On Monday 25th March 2002 there was a short discussion on Crystallographic education which began with brief reports of existing activities of the BCA Groups and the Education Officer.

Sandy Blake (Nottingham) told us about the ***Intensive Courses in X-Ray Structural Analysis*** organised by the CCG, (Chemical Crystallography Group). These grew out of an idea first discussed in 1985 by Michael Woolfson, David Watkin and Judith Howard who thought there was a need for theoretical and practical education in crystallography for graduates and young scientists. The first course was held in 1987; they are residential, last about a week and run every two years, in Aston until 1995 and in Trevelyan College, Durham, since then. The teaching staff are present for the whole week, and unpaid. There are 4 or 5 lecturers, about 10 tutors and between 70 and 80 students, mostly from Britain but foreign students are admitted if they have funding and space permits. Sponsorship for the course has been provided by the EPSRC, the IUCr and industry. Lectures are usually followed by a tutorial and then a break. The tutorial groups are a key element of the course with students and tutors staying in the same group throughout the course. Although the students work hard there is a strong social element, usually mixed with science (a bar quiz, an expert panel or a ceilidh). Many friendships begin, even a marriage or two, the strong international element chimes with the aims of the IUCr. Students (and others) learn how crystallography is done elsewhere. The next course is to be held ***7th-14th April 2003***, details will be found on the CCG pages of the BCA website.

Jeremy Cockcroft, (Birkbeck College, London) spoke on behalf of the Industrial Group for whom he has given short introductory and refresher courses during BCA Annual meetings and the Physical Crystallography Group (PCG). He described the ***Internet Crystallographic Teaching courses*** run by Birkbeck College, students learn most of their work in their own time via the Internet. This is a natural extension of the work of Birkbeck College which runs many part time and evening course for students in full time employment. The first Internet Course was in protein crystallography run for biological scientists. A newer one is the ***Powder Diffraction*** course for Physical Scientists. This is a one year part-time Distance Learning Course at MSc level, students gain an Advanced Certificate which forms about 50% of the work for an MSc. There are 2 terms of taught material and a one term computer based project. The first term teaches the Basics of crystallography, instrumentation, diffraction and symmetry. The second term is concerned with Data Collection,

Analysis and publication, including how to prepare pages for reports using the language of the World Wide Web, HTML. The students assessment is made up of 20% Coursework in HTML, 30% project and 50% the examination paper. The Course is not free.

The Biological Structures Group also run residential 'Summer Schools' covering all aspects of protein structure determination using X-ray crystallography. These are aimed at graduate students in their first or second year of Ph.D study. They are run annually in September, one year in Bristol, the next in St.Andrews mainly for students in the North of the UK.

Kate Crennell then spoke about her work in trying to encourage young children to play with crystallographic toys, in the hope that as adults they may become crystallographers. This has been described in past issues of 'Crystallography News'. This was followed by a general discussion, during which it emerged that although we all thought that crystallography was being squeezed out of undergraduate courses no one had any statistics so the education officer agreed to survey the membership via the newsletter, mount a survey form on the BCA website and to attempt an email survey of UK academic institutions. The form is printed here and is available on the BCA website in electronic form at http://bca,cryst.bbk.ac.uk/BCA/ed/survey/.

Educational news snippets

CD-ROMS for Secondary Schools from the IoP
The Institute of Physics (IoP) newsletter for April 2002, 'Physics World' carried an article on what the Institute is doing to tackle the shortage of specialist physics teachers in secondary schools in the age range 11-14 year olds. The IoP is planning to develop a set of between 10 and 12 CD-ROMS to cover the physics components for each UK science curriculum. Each CD-ROM will have a "physics story" discussing key aspects of specific topics supported by video clips, ideas for innovative practical exercises, computer simulations, downloadable worksheets, references to further reading and a section on common misconceptions. For more information, contact the education manager by email: catherine.wilson@iop.org. I have suggested one of these CD-ROMS should be about crystallography and its relevance to today's technological world.

Model Kit supplier website address change:
Since publication of the March issue of 'Crystallography News' with a review of this model kit I have been notified of a changed web address. The complete address is now:

Astro-logix Design,
32 Elmore Road, Horfield,
Bristol, BS7 9SD
tel: +44 (0)117 9046768
email: info@astro-logix.com
website http://www.astro-logix.com

When contacting this supplier please mention that you saw the review in 'Crystallography News'.

Winners of model kits
Thanks to the generosity of Cochranes of Oxford (http://www.cochranes.co.uk) who supplied model kits for delegates to try at the 'Education Poster' at the Annual meeting in Nottingham, I had 3 'Orbit system' kits to give away, one of 'Lattices' and two of 'Biochemistry'. I decided the simplest way to do this was to have a Prize Draw, the winners were David Watkin, University of Oxford, David Russell, University of Leicester and Nicola Farley, University of Nottingham.

Kate Crennell, April 2002

Congratulations to Judith Howard, past President of the BCA (and lots of other things too!) who was elected FRS on 13 May as we went to press. The official citation from the Royal Society follows:

Professor Judith Ann Kathleen Howard (née Duckworth) CBE, Professor of Chemistry, University of Durham. Professor Howard is elected as a General Candidate first because of her pioneering developments in X-ray and neutron crystallography, which have encompassed organic, organometallic and inorganic compounds, and secondly because of her major contribution to the wider chemical and crystallographic community in terms of education and public understanding.

Survey of UK undergraduate crystallographic courses

An understanding of basic crystallography is essential to many disciplines, such as condensed matter physics, chemistry, materials, geology etc. The British Crystallographic Association (BCA) is trying to find out how much introductory crystallography is taught as part of undergraduate science and engineering courses, whether the course is taught by a specialist crystallographer and whether additional educational materials are needed for the students or lecturers.

Please help us by completing the survey below:

Your Institution: _____

Your Department: _____

Year when Undergraduate Course is given: 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

Name of Course: _____

Duration of Course: _____

Number of hours in that course taken up by introductory crystallography: _____

Degree is awarded on completion of the undergradute studies: _____
(e.g. Hons B.Sc Materials Science)

Name of Lecturer: _____

Lecturer's main interest: _____
(e.g. crystallographer, materials scientist, inorganic chemist, etc.)

Is crystallography essential to this course? _____

Your Comments *(e.g what might the BCA do to help teach crystallography better?)*

Please return this survey either by post to:
Kate Crennell, BCA Education officer, P.O.Box 64, Didcot, Oxon OX11 0TH
or by email to: BCA@isise.rl.ac.uk

CRYSTALS Workshop

A CRYSTALS workshop, run by Richard Cooper and David Watkin was held at the BCA Spring Meeting at Nottingham University. There were 20 PC's available for use and exactly 20 people attended.

In the first session of the morning, Richard gave a quick talk and demonstration of a structure refinement and analysis using CRYSTALS, which was immediately followed by a hands-on example structure for everyone to refine.

CRYSTALS has been developed to make 'DIY' crystallographic structure determination a realistic prospect for non-crystallographers, by guiding the analysis and spotting problems as they arise. Recent developments to the tools for analysing data during the refinement were highlighted. Plots of I and $\sigma(I)$, merging-R and systematic absence violations give users the chance to spot problems with their data before they even solve the structure. Later, plots of residuals, weighting schemes and F_O against F_C, prove to be very useful for spotting trends such as extinction and outliers in the data.

After looking at this routine structure, participants were invited to solve and refine a poor-quality data set again using the guided mode of the program, but making use of some graphical analyses to spot and correct for problems in the data.

Before coffee there was an interactive space group quiz designed to highlight teaching possibilities within CRYSTALS. Simon Parsons and Andy Parkin were the quickest to identify ten space groups from a list of their systematic absences and were rewarded with a seasonal chocolate prize!

The beginning of the second session focused on tools for crystallographic model manipulation. Tasks ranged from organising a structure to have a consistent numbering scheme, to locating and applying an origin shift to a structure whilst changing to a higher symmetry space group.

The rest of the session was spent looking at twinning. There was a brief talk of the common warning signs of twinning and the use of the ROTAX algorithm (Parsons and Gould, Edinburgh) for identifying possible twin laws. Everyone solved a twinned data set using a Patterson map, refined the structure, found and applied a twin law and then refined the structure to completion. The use of ROTAX and the addition of a graphical interface make these steps very straight-forward within CRYSTALS to the extent that this could perhaps be described as a 'routine twin'.

Finally, everyone took part in another interactive competition, this time "Who wants to be a crystallographer?" including *50/50*, *ask the audience* and *phone a friend* options. Claire Wilson won the prize and the prestige of being an *expert crystallographer*, by getting to a million points in the shortest time.

CRYSTALS is free for academic and not-for-profit institutions from http://www.xtl.ox.ac.uk/crystals.html. We hope participants recommend CRYSTALS to new crystallographers as an ideal way to get started. As always, we gained a number of useful ideas from new users at the workshop about how the system could be improved, and we are grateful to everyone who participated.

We must record our special thanks to local organisers Dr Sandy Blake and Dr Claire Wilson for arranging the workshop and use of facilities.

Richard Cooper

The CCDC/CCG Prize for Younger Scientists

The CCDC/CCG Prize for 2002 was awarded to 2002 Dave Allan (Department of Physics and Astronomy, University of Edinburgh), who presented his prize lecture with the title: "High-pressure structural studies of low melting point small-molecule systems".

Dr Allan stated at the beginning of his lecture than he would indicate the significance of high pressure techniques for small-molecules systems, explain the experimental techniques involved and give examples of his recent

work, particularly those involving alcohols and diols.

He explained how extreme conditions, for example of temperature or pressure, could be used to test theories. Understanding a system under ambient conditions is of necessity a limited understanding which can be increased by altering the experimental conditions. Pressure plays a key role not only in condensed matter physics, material and geoplanetary science but also in less obvious areas such as pharmaceutical processing. High pressure can lead to structural phase transitions and different transport and electrical properties. For example, some metals including barium and gallium undergo dramatic structural changes under pressure.

Molecular systems under pressure have not been studied so extensively. They show a range of interaction types including primary covalent bonding, hydrogen bonding and pi-pi contacts: pressure can convert secondary interactions into covalent bonds. There are important applications to pharmaceutical and food processing where the effect of applying pressure must be known by experiment or prediction.

The key piece of apparatus is the diamond anvil cell which can generate pressures well in excess of 10,000 atmospheres and can be used for both diffraction and spectroscopic experiments. The pressure is measured by laser irradiation of a tiny crystal of ruby within the cell. The sample size is limited to about 100 x 100

Dave Allan receives the Prize from CCG Chairman Paul Raithby

x 50 microns, depending on the pressure, and there are limitations and problems due to diffraction from the various materials used to construct the cell: most seriously only a fraction of the total volume of reciprocal space is accessible. For liquid samples the technique involves loading them then applying pressure to obtain a polycrystalline sample. A hot-air gun is used to melt most of the crystallites and the remainder are then allowed to grow: this is repeated until a single crystal remains.

Monoalcohols can form various structures but the behaviour of ethanol is very different from that of methanol. The former crystallises well but the latter has extensive problems, not the least being the difficulty in distinguishing one end of the molecule from the other, a problem that was resolved by quantum mechanical calculation to reveal a structure dominated by the formation of pseudo hexagonal packing arrangement. Methanol has more ring strain than ethanol and a wide range of O---H...O angles which favours vitrification. The high-pressure form of ethanol exhibits disorder with both trans and gauche conformers present. Propanol does not crystallise, cyclobutanol forms three-fold hydrogen-bonded chains at low temperature and chains of molecules at high pressure. At low temperature, phenol forms helical three-fold hydrogen-bonded chains, while at high pressure the chains are two-fold. *t*-Butanol has a three-fold hydrogen-bonded structure; hexamers with short Me...Me contacts form at 8 kbar.

Dave has extended his studies to diols: at 150 K ethanediol adopts a gauche conformation and a 3-D framework, while at high pressure it is trans and forms hydrogen-bonded chains; propanediol at low temperature is gauche with a framework structure, while at high pressure it forms layers with the trans and gauche conformers segregated into layers.

To round off his lecture, he described the surprisingly complex structures adopted by acetone. At high pressure it adopts a layer structure but at low temperature a complicated orthorhombic phase is seen. Together, these phases manage to display all three types of known interaction between carbonyl groups.

The lecture was an excellent exposition of the application of high pressures to molecular systems, an area of study that will certainly gain in importance in the future.

Sandy Blake

Philips Prize Lecture 2002

The Philips Physical Crystallography Prize is awarded every year by the Physical Crystallography Group for the best recently published work by a relatively young person in the field of Physical Crystallography. This year's winner, Dr Daniel T. Bowron, works in the area of liquid structures. This field has developed quite dramatically in recent years, enabling us to look at detailed structures in the absence of a regular lattice – we are now able to perform 'liquid state crystallography'. Exploitation of these techniques, as Daniel's Prize Lecture showed, is throwing new light on such old – and very central – problems such as the hydrophobic interaction.

Daniel's lecture – entitled "structural studies of liquid systems: short and intermediate range order and the hydrophobic effect" – began by outlining the conventional wisdom of the hydrophobic interaction, which has been current since the classic paper of Frank and Evans [*J. Chem. Phys* **13**, 507, 1945]. Thermodynamic measurements on the dissolution of nonpolar molecules in water show a negative entropy of mixing. The normal interpretation of this is that it is the water of hydration that is ordering in some way, so that when two nonpolar molecules come together in water, this ordered water is released to the bulk solvent, giving rise to an increase in entropy of the system. Hence, we are told, the hydrophobic interaction that is thought to be central to much of chemistry and biology – for example in self-assembly processes or protein association and folding. But where is the experimental evidence?

The standard view of the water ordering is that it forms a structure similar to the clathrate cages found in the gas hydrate structures that inconveniently can block gas extraction and transport pipes (see figure 1). In a direct test of this view, Daniel showed how EXAFS measurements made on station BM29 at the ESRF could be used to extract the hydration structure surrounding a nonpolar atom – in this case Krypton – in both the solution just above melting and in the crystal just below. Comparing the Krypton-centred radial distribution functions for the two cases (figure 2) showed that the hydration in the two states is clearly different. Moreover, as we vary the temperature across that at which there is a solubility minimum – which is thought to relate to a maximum in the water ordering – the observed structural changes with temperature remains monotonic. Another problem for the standard model.

So where do we look for the source of the ordering?

The second part of Daniel's talk focussed on the exploitation of H/D substitution using neutron scattering. He showed how selective deuteration of both water and methyl hydrogens in *t*-butanol – water solutions, which thermodynamics suggests are controlled by hydrophobic interactions, could lead to full structural information on the solution when the Empirical Potential Structure Refinement technique [Soper, *Chem. Phys* 202, 295, 1996] is used. Comparing the partial radial distribution functions (rdfs) for the central carbons of the *t*-butanol (TBA) molecules – which showed how the solute molecules are arranged on average round one another – significant differences were seen on going from 25 to 65C. Interestingly, the partial rdf that gives information on the hydration structure (sitting on the central carbon and looking at the distribution of water oxygens) showed little change in going from 25 to 65C, when an increase in ordering might be expected from the standard model as the hydrophobic interaction is enhanced on raising the temperature. Similarly, little change was seen in the water structure itself.

Interpreting these, and other, partial rdfs in structural terms is not easy. To enable greater structural insight to be obtained, Daniel introduced the concept of the spatial density function (SDF) which shows how the (solute or solvent) molecules surrounding a central (solute or solvent) molecule are arranged around a sphere – i.e. the spherical averaging involved in obtaining the rdfs is removed, revealing details of the geometry of the intermolecular interactions. Using this descriptor, the way in which water is organised around a TBA molecule is essentially the same at 25 and 65C, again confirming the lack of a change in the hydration

structure that the standard model would lead us to expect. When looking at how *t*-butanol molecules are arranged around another *t*-butanol, there were dramatic changes between these two temperatures: whereas at 25C the TBA-TBA contacts are dominated by nonpolar-nonpolar contacts, at 65C there is a shift towards significant intermolecular hydrogen bonding. Thus these results show that an increase in temperature does *not* enhance the hydrophobic interaction as such. Rather it shifts the nature of the solute-solute interaction towards an increased polar-polar character.

Finally, looking at the water structure itself, the SDFs show yet again that the first neighbour environment is affected by neither the presence of TBA at room temperature, nor by an increase in temperature. Yet again, the solvent ordering expected on the basis of the standard model is absent. Interestingly however, if we look at the *second* hydration shell, there *is* evidence of a restriction in the freedom of the water that might perhaps relate to the entropic driving force of the hydrophobic interaction. This restriction is enhanced further at the height 65C temperature – as would be expected if this second shell 'ordering' were indeed related to the hydrophobic driving force.

In conclusion, Daniel stressed that these results show that the structural basis of the hydrophobic effect is more complex than the accepted standard model would lead us to believe. Moreover, when considering amphiphiles – relevant in real cases of e.g. self-assembly or protein folding – the situation is more complex than for purely nonpolar solutes. There is a subtle balance of interactions between solute-solute, solute-solvent, and solvent-solvent interactions that needs to be considered. And the effect of temperature on hydration that is often invoked to explain the enhancement of the hydrophobic interaction as temperature is increased does not hold up to experimental test.

For future work, he underlined the need to move beyond binary systems. The effect of ions on amphiphile interactions in aqueous solutions are important (salting in and salting out), yet the structural basis of these influences are still not understood since they were first formalised by Hofmeister over 100 years ago. Yet the effect of ions is amenable to these experimental techniques. And finally, larger and more complex molecules may be tackled to take us further from simple "model" molecules towards biologically realistic systems.

Daniel's lecture nicely illustrated how our ability to look at detailed structure in the liquid state has developed in a major way in recent years. As crystallographers, we depend usually on the existence of a crystal lattice to enable us to solve structures – remove this regularity and our standard techniques fail. The advances he described have begun to enable us to obtain experimentally full structural characterisations of relatively complex amphiphile solutions that are chemically and biologically relevant. He showed rather beautifully how we are now becoming able to do crystallography in the liquid state. The future should see further advances in helping us to understand interactions in solution, and how they are modulated by the all-important solvent.

John Finney

Further reading. The three papers which were considered in making the award were:
(1) Hydrophobic Hydration and the Formation of a Clathrate Hydrate, *Phys. Rev. Letts* **81** (1998) 4164-4167
(2) X-ray Raman Scattering from the Oxygen K-edge in Liquid and Solid H_2O, *Phys. Rev.* B **62** (2000) R9223-R9227
(3) Temperature dependence of the structure of a 0.06 mole fraction tertiary butanol-water solution, *J. Chem. Phys.* **114** (2001) 6203-6215

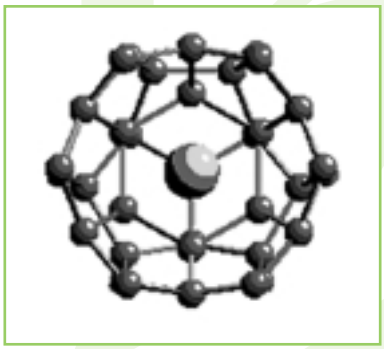


Figure 1. A clathrate cage containing a guest molecule. The one shown here is the large cage of the type II clathrate.

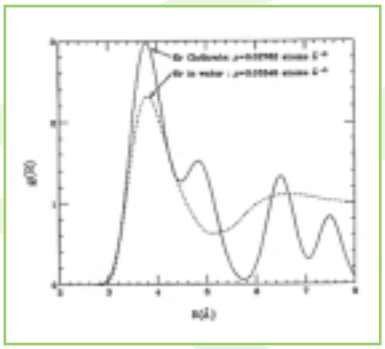


Figure 2. Kr- water oxygen partial radial distribution function for the liquid and solid crystal states, at ~5C and ~110 bars.

Poster Sessions

As is now customary, poster presenters were expected to present a short oral account of their work. The 62 Chemical and Physical posters were completed within 90 minutes, thanks to excellent self control by the presenters, aided by iron-fisted chairing by the three co-chairbeings shown right. The biological session, which sadly had only 7 posters this year was more leisurely! The poster session on Tuesday evening was busy and lively.

The CCG prize was won by James Davidson from the University of Edinburgh for his poster entitled "The Design of Ligands for Metal Surface Engineering" (CP11) . The

Discussion, drinking and nibbling at the poster session

poster presented recent investigations on the search for good corrosion inhibitors for steel. The properties of the surface can be modified depending on the mode of attachment of the inhibiting molecules, whether through primary or secondary bonding or a combination of both. High surface complex stability results when the free energy of the complex is similar to that of the "free" molecule. Enthalpies of solution and surface molecules

Chairbeings Chick Wilson, Ducky Lucky and Bob Gould

were compared and conformational structures investigated using modelling packages.

The BSG prizewinner was James Murray from the University of Oxford for "Investigation of Possible Free-Radical Scavengers in Protein Crystallography" (BP2). This poster dealt with strategies for mitigating secondary damage to crystals by radicals produced by incident X-rays. Localised damage, e.g. to disulfide linkages, can be observed as low as 100 K. Incorporation into crystals of scavengers, including styrene, ascorbic acid or glucose, shows promise as a way of minimising damage.

For the PCG, Neil Parkinson from the University of Durham took the prize for his poster: "The Crystal and Magnetic Structures of Two Double Perovskite structures" (PP1). The perovskites were of the form $Sr_2M(Ru_{1-x}Cu_x)O_6$, where M is Ho or Tb. Partial substitution of Ru by Cu induces superconductivity with $T_c \sim 40$ K. The two systems were chosen because of the large magnetic moments on the Ho and Tb atoms, allowing spin reorientation of the moments to be studied. Some work on the mixed Ho/Tb system was also discussed.

Prizewinners James Davidson, James Murry and Neil Parkinson

The Committees are most grateful to the judges and to the sponsors of the prizes.

The ideal genome show

Article from Simon Pia's Diary, The Scotsman*, 13th March, 2002:*

WHAT do you give the woman with everything? A molecule with her name on it. On her visit to the Biomolecular Research Institute at the University of Edinburgh on Monday, Princess Anne was presented with one.

Our woman behind the bunsen burner explains: "Amino acids are denoted with a single letter and a Beevers model of a sequence of amino acids spelling ANNE, which occurs 20 times in the human genome, was presented to her."

In usual Windsor fashion, she told them she expected one with "the rest of my name next time". Unfortunately, they can't do that, as there is no O protein. But, course, HRH was joking.

By the way, the Beevers model is named after the university's Professor of Crystallography, Arnold Beevers, who died last year at the age of 90 and who up till then was still coming in each day to Kings Buildings. The distinguished professor was once spotted informing an assistant in Jenners that the star on top of their Christmas tree had the wrong number of points.

Helen D. Megaw 1907-2002

Dr. Helen Megaw, born on June 1st 1907, died on February 26th at the age of 94. She was a well-known, highly respected and remarkable member of one of the most important scientific disciplines of the 20th century, namely the field of Crystallography. In her own words, this is "the branch of science concerned with the description of the structure and properties of condensed matter in terms of the spatial relationships of atoms and interatomic forces in an extended array". I should explain that the term 'extended array' means a "crystal" for it is the repeated stacking of molecular units in all directions that distinguishes a crystalline solid from non-crystalline substances like glass.

Helen was born into a distinguished Northern Irish family: her father was a famous judge and Ulster politician. In addition her uncle was a director of the Indian Medical Service, one brother built the Mersey tunnel, the Dartford tunnel, the Victoria line and Battersea power station, another brother was a Justice in the Court of Appeal, and one of her sisters researched diet and health in the 1930's and marriage laws in Uganda in the 1950's. Helen decided on a scientific career, starting first at Queen's University, Belfast before moving to Girton College, at the University of Cambridge, to obtain her BA and PhD. From 1930 to 1934 she was a research student under the great, and some would say 'infamous', J.D. Bernal, along with Dorothy Crowfoot, later Hodgkin. Although she had already become interested in Crystallography while at school, having read Bragg's *X-rays and Crystal Structure*, Bernal was a stimulating influence on her and happily confirmed her interest in crystals. Her choice of Crystallography was a wise one, because it was the one scientific discipline at the time that had already established itself as a place in which both men and women could engage on an equal basis, and she never, or rarely, was aware of any form of discrimination. She began her scientific career in the study of crystals by working on the structure of ice. The naming of an Antarctic island, Megaw Island, in her honour marked this work. If you want to find it, look at 66°55'S, 67°36'W.

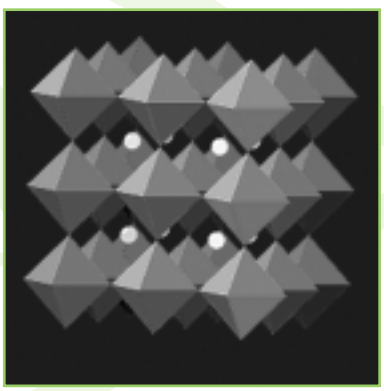
In 1934 Helen spent a year in Vienna and then moved to work briefly under Professor Francis Simon at the Clarendon Laboratory, Oxford. This was followed by two years of school teaching before taking up a position at Philips Lamps Ltd in Mitcham in 1943. It was here that she worked out the crystal structure of a very important industrial material, barium titanate, which is used in capacitors, pressure sensitive devices and in a variety of other electrical and optical applications. This material, which crystallises in the so-called perovskite structure, belonged to the class of materials known as ferroelectrics, originally discovered around1935. This structure is so famous and important that Helen's name is permanently associated with it and with perovskite structures in general. In 1945, she moved back to Birkbeck College London, once again to work with Bernal, and in the following year, she was appointed to a post in the Cavendish Laboratory, Cambridge, where she remained for the rest of her scientific life.

At that time, the Cavendish Laboratory was under the leadership of the great William Lawrence Bragg, and as a result Helen found herself at a place where many important and well-known Crystallographers would pass through. She was there during the exciting double-helix days. However, she remained loyal to her chosen field of mineralogy and inorganic crystals. In 1951, Helen was responsible for providing a number of crystal structure diagrams to the Council of Industrial Design, which were then used in the designs for the textiles used at the Festival of Britain, including in the foyer of the Regatta Restaurant. In 1957, Helen wrote a book entitled simply "Ferroelectricity in Crystals", the first of its kind, and

for many years this became the bible for the fast growing international community of Ferroelectricians. A second book followed years later entitled "Crystal Structures: a Working Approach", a fine text that illustrates well her unique approach to describing the architecture of crystals. In addition to ferroelectrics, by suggestion of W.H. Taylor (WHT), she took up an interest in the crystal structure of feldspars. These complicated materials make up most of the earth's and moon's surface, and are therefore of great significance in earth sciences. The first structure determination had been carried out by WHT before the war, but such is the complexity of this class of materials, there remained a great deal of unknown science to discover.

In 1989, Helen became the first woman to be awarded the prestigious Roebling Medal of the Mineralogical Society of America, and in 2000 at the age of 93 she was awarded an honorary degree at Queen's University, Belfast.

Perhaps, now I can turn to my own involvement with Helen



The crystal structure of perovskite.

Megaw. I first met her in 1969 while at an international conference in Stony Brook, USA. She was looking for a postdoctoral assistant to work on crystal structure changes with temperature in a particular complicated perovskite material. Kathleen Lonsdale, who had been my Ph.D. supervisor in London, had recommended me to her. At the time I was working at the Chemistry Department in Harvard and my interest was in the crystallography of organic compounds. I therefore accepted Helen's offer with some reluctance, because I felt that the subject of inorganic crystals was far too impenetrable for me.

However, I soon discovered that my boss was a remarkable person: formidable in some ways, but also very kind and patient. She had a particularly interesting gift: if you wanted to know what a particular crystal structure looked like from any particular direction, she could somehow turn it around in her mind and then sketch it for you. In the days before computer graphics, this was a very useful trick, especially for a crystallographer, who must somehow always be able to appreciate three-dimensional architecture.

Another personal story shows something of Helen's scientific honesty. In 1972 I wrote a paper on the structures of perovskites, which I thought was rather clever, and sent it for publication. Eventually I received a reply from the Editor with a referee's report of 20 closely written pages of criticism! I was infuriated: how dare a mere referee pull my work apart like that! So, I went to Helen for advice, complaining bitterly about the referee and his attitude. She looked carefully through the comments and agreed that they were indeed over the top. Anyway, she spent hours with me helping me to deal with the comments and eventually the revised paper was sent back. I had to admit that the paper was in fact much better as a result, and subsequently it became one of my most widely quoted pieces of published works. It was a few years later that Helen confided to me that she had been the original referee! The Editor had sent it to her in error and she had pointed this out, but at the same time said that she could be objective nonetheless.

I continued to work with Helen until her retirement in 1972. She retired to her home in Ballycastle to pursue her other interest, gardening. I recall how delighted she was to discover the plant called *Perovskia*, and this quickly made its way into her garden collection. Leaves of Perovskia featured on one of her Christmas cards. Helen's death marks the passing of an era in science. In the words of Professor Robert E. Newnham of Pennsylvania State University: "Along with Kathleen Lonsdale and Dorothy Hodgkin, Helen Megaw is one of the grand old British school of women crystallographers who serve as role models for many of us – men and women alike".

Professor Mike Glazer,
Clarendon Laboratory,
Oxford

Max Perutz 1914 - 2002

By permission, we reproduce here the appreciation first submitted to The Independent *and published on 7 February 2002.*

A young Viennese chemist from a Jewish family, who arrived in Cambridge in 1936 to study under Desmond Bernal, Max Perutz became the leader of the movement which created molecular biology, and the head of the most successful research laboratory in Britain.

Throughout his life, his personal research focused on haemoglobin, a familiar protein molecule whose extraordinary range of properties illuminated every stage of the scientific development leading from spectroscopy and protein chemistry through three-dimensional structure to molecular genetics and medical application.

His achievements followed from a combination of several outstanding qualities, not all intellectual. His irresistible powers of gentle persuasion brought him long-term support from the Cavendish Professor of Physics at Cambridge, Sir Lawrence Bragg, and from the Secretary of the Medical Research Council, Sir Edward Mellanby, setting up a Medical Research Council Unit in 1947 for his work. He communicated ideas with extraordinary clarity and simplicity. Though he retained a strong Austrian accent, his written English was always elegant, compelling and stimulating. He seemed to write with a golden pen. He had a wonderful way of leading research, leaving his staff with the feeling they were free to decide their own way forward, while he created a vision of the long-term goals. And he had uncanny insight into the potential of young researchers seeking to work with him.

By the early 1950s he had drawn together an extraordinary group of people. His senior colleague was John Kendrew, like Max a chemist trained in crystallography, but in personality utterly different. Kendrew was a precise organiser, a gifted computer programmer, a man who knew exactly where he was going and how to get there. His research began by following Max's, but by brilliant organisation it later overtook him (by working on myoglobin, the much smaller brother of haemoglobin). There was also a PhD student with a degree in physics, whose dazzling intellect constantly darted from problem to problem. This man was Francis Crick. A postdoctoral researcher, a 22-year-old whizz kid named Jim Watson, turned up from Chicago.

Only 10 years later, Max Perutz and these three colleagues were all Nobel prizewinners. Max shared the Chemistry prize with Kendrew for their structural analyses of haemoglobin and myoglobin, and in the same year Crick and Watson (with Maurice Wilkins) won the prize for Medicine. But in the early 1950s all these men were unknown, achievements unrecognised, seeking how to use the techniques of physics and chemistry to understand the nature of biological matter.

There were other remarkable people in the group. Hugh Huxley studied with Max using the primitive electron microscopes then in existence. With brilliant insight, they decided Huxley should study muscle, an object ideally matched to the powers of the microscope. In his doctoral thesis in 1954, Hugh Huxley laid out the basic mechanism of muscle contraction. And Max's biochemical assistant, Vernon Ingram, was to discover the precise molecular nature of sickle-cell disease a couple of years later -- a change of one amino-acid in haemoglobin which we now recognise as the consequence of a single mutation.

The group first came to prominence with the achievement of the two young rebels -- Crick and Watson's analysis of DNA in 1953 revealed an exquisite structure whose fascinating implications caught the imagination immediately. Meanwhile Max's own research (and that of Kendrew) had got stuck. The methods of X-ray crystallography had been used to picture the molecular structure of many small molecules, up to the size of penicillin. Perutz and Kendrew wanted to use these

methods on haemoglobin (and its partner in muscle, myoglobin). But the methods that worked for the smaller molecules seemed hopeless for these much larger structures.

While the DNA structure was being worked out, Max had a shattering insight for his own work. If he could attach a heavy atom to a specific site in the haemoglobin molecule, and if it didn't disrupt the structure of the molecule, and if he could make it crystallise in just the same way as ordinary haemoglobin, and if it made changes big enough to measure -- if all these things were true, he could see a way to use the methods of X-ray crystallography to image the haemoglobin molecule. He later wrote:

> *"As I developed my first X-ray photograph of mercury haemoglobin my mood altered between sanguine hopes of immediate success and desperate forebodings of all possible causes of failure. I was jubilant when the diffraction spots appeared in exactly the same position as in the mercury-free protein, but with slightly altered intensity, exactly as I had hoped."*
> *(Perutz, 1992)*

The rest, as they say, is history. Crick and Watson's work led to the discovery of the genetic code, development of molecular genetics, methods to make bacteria produce large quantities of useful proteins such as specific antibodies, towards ways to clone stem cells. The work of Max Perutz led to an understanding of proteins themselves. These are the molecules which DNA specifies. They are also the molecules which control all chemical processes in a living cell and organise its structure. His methods have now been applied to tens of thousands of different proteins, giving clear insights into their mode of action.

In the late 1950s, after Bragg's retirement, Perutz's Unit was based in a small asbestos hut in the car park outside the Cavendish Laboratory in Cambridge. As the research group continued to grow, every empty room and disused shed on the site (including the building which was originally Lord Rutherford's stable) was converted to a laboratory for a different facet of molecular biology. Long before the Nobel Prizes, a report by Perutz convinced the Medical Research Council, then led by Sir Harold Himsworth, to build a large new laboratory for Perutz, Crick, Fred Sanger and others. The new building, known as the Laboratory of Molecular Biology, was completed in 1962 on the new site of Addenbrooke's Hospital, at the edge of Cambridge -- just in time before over-population of the Cavendish site led to any serious dispute.

The Laboratory of Molecular Biology has been an outstanding and continuous success, a breeding-ground for scientific achievement. In addition to the four Nobel Prizes awarded in 1962, which set the laboratory off to a splendid start, it has appeared in the Nobel lists again and again: for the creation of monoclonal antibodies by Cesar Milstein and Georges Köhler with immediate application to medicine, for Aaron Klug's deep analysis of the organisation of nucleic acids in chromatin and other types of nucleic acid structure, John Walker's long study of a beautiful protein (ATP synthase) which acts as a rotary dynamo which stores biochemical energy, and above all Fred Sanger's second Nobel Prize for inventing ways to find the sequence of bases in nucleic acids.

These are only the most visible of the laboratory's successes. Max has left some clues to its achievements:

> *"I persuaded the Medical Research Council to appoint me Chairman of a Governing Board, rather than as Director . . . This arrangement reserved major decisions of scientific policy to the Board, and left their execution to me . . . The Board met only rarely . . . This worked smoothly and left me free to pursue my own research. Seeing the Chairman standing at the laboratory bench or the X-ray tube, rather than sitting at his desk, set a good example and raised morale. The Board never directed the laboratory's research but tried to attract, or to keep, talented young people and gave them a free hand."*
> *(Perutz, 1995)*

He always recognised the importance of new instrumental developments, and maintained large mechanical and electronic workshops, to which research workers had full access, directly passing their enthusiasm to the technical staff. The most characteristic feature was the tearoom, open to all, visited three times a day by most, an important centre for exchange of ideas and scientific news, which was

managed for over 20 years by Max's wife, Gisela.

Meanwhile Max continued his own lifetime study of haemoglobin, "the molecular lung", and showed how concerted structural changes follow from its absorption of oxygen, causing it to be either fully oxygenated or fully reduced, and making it an ideal oxygen transporter. This demonstrated a general principle, since many enzymes and other proteins exploit a similar "allosteric" structural change to switch a process on or off. By collecting abnormal haemoglobins discovered throughout the world, he opened up "molecular pathology", relating a structural abnormality to disease. Long before mutant proteins could be created in the laboratory, he had a large collection of single-site mutants of haemoglobin.

The Medical Research Council had an inflexible rule that when a Director of one of its institutions reached the retirement age, he must not continue to work in the same laboratory. Adroitly, Max announced that he had never been the Director, only a Chairman, and after retirement he would continue to pursue his research as usual. This arrangement, warmly welcomed by the staff, allowed him to continue as he pleased. In retirement he wrote a lot, including book reviews on a wide range of topics from Karl Popper's view of Darwinism, and Fritz Haber's fanatical obsession with poison gases, to the social revolution caused by Carl Djerassi's synthesis of a contraceptive steroid, as well as several books of his own. He continued to travel, to collaborate with scientists from many nations. Above all, he pursued the endless ramifications of his deep understanding of haemoglobin and the many human diseases linked to it. He helped to design a useful drug to deliver oxygen to tumours and to damaged tissues.

In his scientific autobiography *Science is Not a Quiet Life* Max Perutz describes a number of scientific controversies surrounding his work, and how they were resolved. One of these involved a mutant haemoglobin, analysed incorrectly by its Japanese discoverers, suggesting a total conflict with his results. Max and his collaborators identified the mistake:

> *"I worried that if our Japanese colleagues learned of this disproof of their findings, a poor student who blamed himself for their mistake might commit suicide. To avoid such a tragedy, I invited them to publish a joint paper, a gesture which earned me their lifelong friendship."*
> *(Perutz, 1997)*

Max Perutz was a deeply humane man, loved and admired by his colleagues, who combined that gift with exceptional powers of analysis, planning and leadership. His domed forehead suggested a mighty brain, but his small fingers were neat and dextrous. A robust and confident mountaineer, he studied glacier flow early in his career, so as to work in the Alps. A back injury in middle life ended his skiing, but he retained his love of mountains. While his achievements were crowned with many honours, they rode lightly on his shoulders. He refused any honour that would give him a title, and was known, and invariably addressed by colleagues, as "Max". He lived a quiet and unostentatious life, walking from his home to the laboratory almost daily until a few months before his death. His brain remained razor-sharp, he gave thrilling lectures, and his research continued. Within the last year he had made important contributions to the understanding of Huntington's disease, based on ideas of crystal nucleation.

He and his wife, Gisela, who survives him, were devoted to each other and to their two children, Robin and Vivien.

David Blow

Perutz, M.F. (1992) *Protein structure: new approaches to disease and therapy.* Freeman, New York.
Perutz, M.F. (1995) The Medical Research Council Laboratory of Molecular Biology. *Molecular Medicine* **2**, 659-662.
Perytz, M.F. (1997) *Science is not a quiet life. Unravelling the molecular mechanism of haemoglobin.* World Scientific, Singapore.

Max Ferdinand Perutz, molecular biologist: born Vienna 19 May 1914; Director, MRC Unit for Molecular Biology 1947-62; FRS 1954; Reader, Davy Faraday Research Laboratory, Royal Institution 1954-68, Fullerian Professor of Physiology 1973-79; Chairman, MRC Laboratory of Molecular Biology 1962-79; Nobel Prize for Chemistry (jointly) 1962; CBE 1963; Chairman, European Molecular Biology Organisation 1963-69; CH 1975; OM 1988; married 1942 Gisela Peiser (one son, one daughter); died Cambridge 6 February 2002.

Charles Alfred Taylor 1922-2002

Charles Taylor, who was a founder member of the British Crystallography Association, died in Salisbury Hospital on 6th March 2002. A devoted family man, he is survived by his wife Nancy, a daughter, and two sons as well as numerous grandchildren and great grandchildren.

Charles was best known in crystallographic circles for his pioneering work with Henry Lipson on the development of optical diffraction analogue (Optical Transform) methods, first suggested by Sir Lawrence Bragg in 1938. Long before the days of digital computers these methods promised to provide a much quicker alternative to the slow (even with Beevers-Lipson strips) standard procedure of calculating structure factors for trial crystal structures. This work with Lipson was carried out at the University of Manchester Institute of Science and Technology (UMIST) in the years 1948 -1965, first while completing a PhD but subsequently as a Lecturer and later still as a Reader. He obtained his D.Sc. in 1960 for his outstanding work there. During this period he continued to develop the theory and instrumentation for optical analogue methods, including optically prepared Fourier Syntheses, to the point where he was the acknowledged expert in the field. Amongst his achievements were many elegant ways of elucidating the structure of fibres using the optical analogue technique.

During the latter part of this period, however, electronic computers were beginning to make the optical methods redundant for single crystal structure determinations although they continued to be of use for disordered structures and poorly crystalline materials such as polymers. He began at this time, however, to develop other interests, notably in musical acoustics and the perception of sound – subjects for which an understanding of Fourier transforms was equally important – and gained a reputation as an inspirational teacher.

In 1965 he move to South Wales to take up the Chair of Physics at University College Cardiff, together with the Directorship of the Viriamu Jones Laboratory. In this appointment he succeeded another famous crystallographer, A.J.C.Wilson, and the main research interest of the department was also X-ray crystallography. In 1980 he masterminded for the IUCr Commission on Teaching a series of pamphlets designed to "help students with no previous knowledge of X-ray diffraction to understand the general principles and to give some idea of what it can do". He himself wrote the first of these entitled "*A Non-Mathematical Introduction to X-ray Crystallography*". It was during his tenure in Cardiff that I joined Charles's group as a young post-doc. The advent of lasers and the first computer-controlled film-writing devices gave a further boost to the Optical Transform methodology and with funding from Unesco we produced with George Harburn the book entitled "*An Atlas of Optical Transforms*".

While in Cardiff his interest in acoustics and music (he was an accomplished pianist and organist) led him to establish a small research group concerned with the perception of sound. This lead to a collaboration with the Catgut Society of America (which pioneered a new, rational sequence of instruments for the violin family) and thence to the establishment of a system with which the vibrational modes of violins and guitars could be studied by holographic interferometry. He also established a degree course in "*Physics and Music*" that, during a period of rapid expansion of the Hi-Fi industry in Britain, was timely indeed.

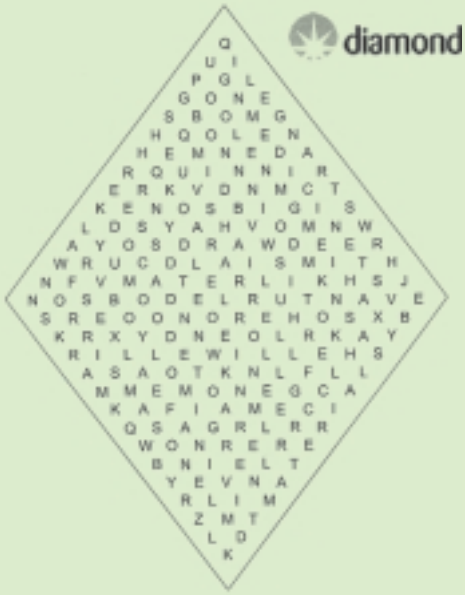
While still at Cardiff Charles was appointed in 1977 as Visiting Professor of Experimental Physics at the Royal Institution and held this position until 1990. He was a great believer in the value of lecture demonstrations and built himself a considerable reputation

for this genre, most notably on the topic of physics and music but also on others such as diffraction, image formation and colour. He became very concerned that science, and physics in particular, was perceived by children as a difficult, uninteresting subject and devoted much effort to arousing interest and encouraging a spirit of enquiry in children right down to those as young as 7 or 8. "*Physics and music*" was the subject for the first (of two) series of televised Christmas Lectures for Children that he was invited to give at the Royal Institution. Overall he gave some 150 lectures to schoolchildren at the RI as well as presenting 8 Friday Evening discourses there. In addition he undertook a number of lecture tours both in the UK and abroad. The Institute of Physics awarded him its Bragg medal for his contribution to Physics Education.

It was on one of his many lecture tours, when he visited Australia in the late 1980's, that I last saw Charles. My most vivid, fond and lasting memory of him is with flowing grey hair crouched in concentration over a carpenter's saw (bent into an 'S'-shape) and convincingly extracting a melody from it using a violin bow. He was an inspiration to me and I am sure to many other young prospective scientists and he will be sadly missed.

Richard Welberry

Puzzle Corner



This month's puzzle is a word search submitted by our indefatigable Education Officer, Kate Crennell. It is a word square, or, to be more precise, a word diamond!

This puzzle is intended to teach you a little about the diamond project. It contains 28 words which follow the usual rules for word squares, letters are in adjacent squares, they run in only one direction which may be forward or backwards, horizontally, vertically or diagonally.

The words are 4 research topics to be studied at 'diamond' and the surnames of 24 people associated with the project, 23 with the 'diamond' project itself, and the last one the surname of the recently appointed CLRC Director for Synchrotron Radiation.

All the names can be found on the Internet, most of them on the diamond' website at **http://www.diamond.ac.uk**

A prize of a £10 book token is offered for the best solution. Entries should be returned to the Editor by 19 July, 2002. A copy of this puzzle will be available on the BCA website after 1 June 2002 at **http://bca.cryst.bbk.ac.uk/BCA/CNews/Comp/Jun02.html**

While you are looking at the diamond website you are invited to contribute to their newly launched discussions group at **http://www.jiscmail.ac.uk/lists/diamond.html**

The discussion area is only available to registered users; help and a registration form can be found via the Discussions page at **http://www.diamond.ac.uk/Activity/ACTIVITY=Discussions**

The winner of the eight-pointed "snowflake" competition was David Blow who submitted by far the best and – let's be honest – the *only* solution I received. It was handed to me on a piece of paper measuring 145x100 mm, and is well worth quoting in full! "The assignment of point group 8mm typifies an error crystallographers learn to avoid, namely ignoring the third dimension in viewing an illustration. The object is plainly cubic. All lines of growth are almost parallel to cube axes. It lacks symmetry because the subsidiary growth directions are rotated by homometric distortion. This piece of paper is too small to write out the distortion tensor."

Indeed – and I expect this one is too. Congratulations, and many thanks, David!

The Editor

CCG and IG Autumn Meetings

The CCG Autumn Meeting 2002, sponsored by Bruker Nonius will be held at King's College London on Wednesday 13 November, with Jon Steed and Jamshed Anwar as the local organisers. The title of the Meeting is "Dealing with difficult data" and so far the following have agreed to speak:

Simon Parsons (Edinburgh):
"Difficult datasets - an overview"
Simon Coles (Southampton):
"Getting good data out of bad crystals"
Simon Teat (Daresbury):
"A bright way of handling difficult data"
David Watkin (Oxford):
"Weak data can still be good data"

There will be the opportunity for short presentations, and anyone wishing to offer one should contact the CCG Deputy Chairman, Sandy Blake (email: A.J.Blake@nottingham.ac.uk). Further details and a registration form will appear in the September issue of Crystallography News, and will also be available on the CCG website: **http://bca.cryst.bbk.ac.uk/BCA/CCG/ccg.html**

The IG Autumn Meeting 2002 is at the Manchester Materials Science Centre on Thursday 7 November. The theme of this meeting is "Sample Preparation" and we are looking for speakers. Do you have any interesting solutions to difficult problems? Have you got some hints and tips, which you would like to pass on? Have you encountered a hideous problem, which the rest of us should avoid? Industrial type problems are particularly welcome.

Do you need some help and advice?

The Autumn Meeting will be rather like a workshop; we would like to base the program on problems and their solutions.

Do you have a story to tell or a problem to solve? Please contact Judith Shackleton at Manchester Materials Science Centre: 0161-200-3581 Judith.Shackleton@man.ac.uk

The BSG Winter Meeting 2002

The BSG Winter Meeting is entitled "Macromolecular Complexes: and will be held at the University of Warwick onn Friday 13th December 2002. Further information will be in the September issue. Meantime, contact Vilmos Fulop. vilmos@globin.bio.warwick.ac.uk

New group committees

Following the AGMs in Nottingham, the membership of the Chemical and Physical groups are as follows:

CCG:

Chair
Professor Paul R. Raithby, University of Bath (2003)
Vice-Chair
Dr Alexander J. Blake, University of Nottingham (2003)
Secretary/Treasurer
Dr Harry Powell, MRC-LMB (2004)
Ordinary Members
Dr Simon J. Coles, University of Southampton (2004)
Dr Richard Cooper, University of Oxford (2005)
Dr Michaele Hardie, University of Leeds (2005)
Dr Georgina M. Rosair, Heriot-Watt University (2005)
Dr Jonathan W. Steed, King's College, University of London (2003)
Dr Simon J. Teat, Daresbury Laboratory (2005)
Co-opted Student Representative
Mr Duncan Tooke, University of Newcastle-upon-Tyne (2003)

PCG:

Chair
Dr P A Thomas (Dept. of Physics, University of Warwick; phrve@csv.warwick.ac.uk)
Vice-Chair
Dr P G Radaelli (ISIS Facility, Rutherford Appleton Laboratory; P.G.Radaelli@rl.ac.uk)
Secretary/Treasurer
Dr J S O Evans (Dept. of Chemistry, University of Durham; john.evans@dur.ac.uk)

Ordinary Members
Dr D R Allan (Dept. of Physics, University of Edinburgh; dra@ph.ed.ac.uk)
Dr J K Cockcroft (Dept. of Crystallography, Birkbeck College; cockcroft@gordon.cryst.bbk.ac.uk)
Dr S P Collins (Synchrotron Radiation Dept., Daresbury Laboratory; S.P.Collins@dl.ac.uk)
Dr J P Goff (Dept. of Physics,. University of Liverpool; jpgoff@liv.ac.uk)
Dr S H Kilcoyne (Dept. of Physics, University of Leeds; S.H.Kilcoyne@leeds.ac.uk)
Dr J C Wasse (Dept. of Physics, University College London; ucapjcw@ucl.ac.uk)

The British Crystallographic Association

Summary of the consolidated BCA accounts for year ended 31 December 2001

The full BCA accounts for 2001 are available on request as an E-mail attached rich text file from the BCA admin office.

Examining Accountant: R A Young, The Young Company, Lakeview Court, Ermine Business Park, Huntingdon PE29 6XR

These are consolidated accounts and include the BCA, BSG, CCG and IG funds.

INCOME:

	31.12.01	31.12.00
Glasgow 1999	32,114	76,000
Annual Conference	59,481	56,635
Meetings of Groups	3,843	3,471
Newsletter	23,797	13,230
Membership subs.	14,380	9,302
Course fees	15,521	-
Grants and sponsorship	19,237	537
Net income from trading	16	63
Donations	1,206	256
Investment income	5,419	4,275
Interest received	2,929	2,980
Sundry Income	277	-
TOTAL INCOME	**178,220**	**166,749**

EXPENSES:

	31.12.01	31.12.00
Direct charitable expenditure (1)	141,918	86,034
Management and administration (2)	18,090	14,983
TOTAL EXPENDITURE	**160,008**	**101,017**

	31.12.01	31.12.00
NET INCOME (EXPENDITURE)	18,212	65,732
Unrealised gains (losses) of investment assets	(2,895)	70
NET MOVEMENT IN FUNDS	**15,317**	**65,802**
Balances brought forward at 1 January 2000	178,903	113,101
Balances carried forward at 31 December 2000	194,220	178,903

ASSETS:

Fixed Assets	**2001**	**2000**
Tangible assets	36	81
Investments	94,385	49,838
	94,421	49,919
Current Assets		
Stocks	3,240	3,264
Debtors	17,556	4,870
Short term deposits	78,923	100,630
Cash at bank and in hand	17,640	30,028
	117,359	138,792
LIABILITIES: amounts falling due within one year	15,793	7,480
LIABILITIES: amounts falling due after more than one year	1,767	2,328
NET ASSETS	**194,220**	**178,903**

INCOME FUNDS

	2001	2000
Restricted funds (3)	62,782	38,327
Unrestricted funds (BCA)	131,438	140,576

BCA CASH FLOW STATEMENT FOR YEAR ENDED 31 DECEMBER 2001

	2001	2000
Net cash inflow (outflow) from operating activities	13,347	76,964
Investment expenditure	(47,442)	-
Increase (decrease) in cash and cash equivalents	(34,095)	76,964
Cash and cash equivalents at 1 January 2001	130,658	53,694
Cash and cash equivalents at 31 December 2001	96,563	130,658

NOTES TO THE ACCOUNTS:

1. DIRECT CHARITABLE EXPENDITURE

	31.12.01	31.12.00
Previous year conference	548	-
Subscription to International bodies	1,925	1,175
Annual Conference	59,052	61,883
Meetings of Groups	1,330	2,056
Newsletters	20,247	10,516
Colour supplement	-	5,212
Course fees and accommodation	29,962	1,000
Grants and sponsorship	2,050	1,000
Prizes	160	1,413
IUCr Congress	25,000	-
Awards and bursaries		
- Chemical	-	25
- Arnold Beevers Bursary Fund	1,400	1,520
- Industrial Group	244	234
	141,918	86,034

2. MANAGEMENT AND ADMINISTRATION

General expenses		
- Depreciation	45	135
- Administration fee	13,094	8,812
- Accounting fee	2,115	1,527
- Insurance	192	175
- Bank and security charges	154	116
- Other	684	364
- Special Interest Group administration	700	649
- Transfer of Physical Group fund	-	180
	16,984	11,958
Council Expenses		
- Council	377	317
- Officers	447	883
- Administration expenses	282	459
- Printing, stationery and postage	-	893
- Telephone	-	523
	1,106	3,025
Total	**18,090**	**14,983**

3. Restricted Funds

	Biological Structure Group	Industrial Group	Chemical Group	CCG Teaching School	Dorothy Hodgkin Prize	Arnold Beevers Bursary Fund	Totals 2001	Totals 2000
Balances at 1.1.00	16,026	8,158	1,596	6,526	7,005	-		
Balances at 1.1.01	17,393	6,453	2,024	6,578	5,879	-	38,327	39,491
Donations	-	-	-	-	30	1,156	1,186	256
Interest received	247	50	41	244	211	-	793	894
Transfers	-	-	-	-	-	20,000	20,000	1,240
Net income (expenditure)	(584)	847	367	3,246	-	-	3,876	(621)
Bursaries awarded	-	-	-	-	-	(1,400)	(1,400)	(1,520)
Dorothy Hodgkin Prize	-	-	-	-	-	-	-	(1,413)
Balances at 31.12.01	17,056	7,350	2,432	10,068	6,120	19,756	62,782	38,327

Treasurer's Report - 2001 Accounts

The 2001 accounts see some major changes to the Associations funds. In April the BCA gratefully received £32,114 from Crystal Congress 99 when the company was wound up. The money came with a wish that £25,000 be offered to the next IUCr congress for use in providing bursaries. To accommodate this request £25,000 was transferred to IUCr Congress in December with the proviso that the funds would be returned to the BCA from meeting profits to support bursaries at future congresses.

The 2001 AGM approved an investment strategy to increase our longer term investments by £50,000 split between Convertible Preference Shares or Bonds and UK Income Growth Investment Trusts. This underpins our established fixed interest investments in gilts which started to mature this year with £8000 of 11.5% Treasury 2001/2004 repaid. In October Council agreed to follow the advice of Charles Stanley and reinvest £5000 in John Laing 6.4% convertible Preference Shares. These new investments contribute dividends of almost £1500 to this year's account.

Council agreed in April to make changes to the bursary fund. The fund has been renamed the Arnold Beevers Bursary Fund and re-established by transferring £20,000 of the Glasgow Congress surplus. Seven applications for Arnold Beevers Bursaries were made this year and all received a £200 award. The total award of £1,400 is a little down on last year. Through the year other meetings and good works have received total sponsorship of £2050. These include the schools crystal growing competition, Neutron summer school, archiving of crystallography records and the Chatt Lecture.

The Reading Spring Meeting gave bursary funding of £2000 to benefit 40 students with the meeting making a small surplus.

The Newsletter made a surplus of £4,112 this year. The new format has been well received by members and advertisers. Increased production costs totalling £19,685 have been offset by increased advertising revenue.

This year has seen the introduction of corporate membership with a range of benefits for an annual fee of £600.00. Nine companies have taken up corporate membership in the first year to provide a new income stream. The current corporate members are shown on the start page of the BCA web site. Membership income has increased by £5,000.

Administration costs are higher this year with the first full year of our contract with Northern Networking impacting on the figures.

Donations totalling £1,206 were received up from £256 last year due in most part to the great respect in which Arnold Beevers was held by our community. Many of our members have now signed Gift Aid declarations and a refund of £668.32 from the Inland Revenue was claimed on behalf of 183 members. Council agreed to allocate this and future Gift Aid refunds to the Arnold Beevers Bursary Fund.

Meetings of interest

Further information may be obtained from the website given. If you have news of any meetings to add to list please send them to the BCA Web Master cockcroft@img.cryst.bbk.ac.uk or to the Editor, bob@gould.ca

June 17 - 22 2002
VI International School and Symposium on Synchrotron Radiation in Natural Science - ISSRNS2002, Ustron-Jaszowiec, Poland.
[http://info.ifpan.edu.pl/ISSRNS2002.html]

June 18 - 19 2002
CHESS User Meeting 2002. Ithaca, NY, USA.
[http://www.chess.cornell.edu/Meetings/default.html]

June 19 - 21, 2002
11th Annual Fibre Diffraction and Non Crystalline Diffraction Meeting, Keele University, Staffordshire.
[http//www.ccp13.ac.uk]

June 23 - 27, 2002
American Conference on Neutron Scattering, Knoxville, TN, USA , sponsored by the Neutron Scattering Society of America (NSSA) and the Spallation Neutron Source High Flux Isotope Reactor User Group (SHUG). Deadline for abstract submission: March 25, 2002 [http://www.sns.gov/acns]

June 24 - 26, 2002
Time-Resolved Chemistry: From Structure to Function, Manchester.
[http://www.rsc.org/pdf/confs/faradisc/fara122/pdf]

June 27 - 30 2002
11th Slovenian-Croatian Crystallographic Meeting, Bohinj, Slovenia.
[http://www.uni-lj.si/~fn01leban/slkr11/]

June 29 - July 3 2002
Gordon Research Conference On Correlated Electron Systems,Colby College, Waterville ME, USA
[http://www.grc.org]

July 4 - 6 2002
XIII Symposium of the Spanish Group of Crystallography (GEC) Oviedo-Asturias, Spain
[http://www11.uniovi.es/gec/13simposio/main.html]

July 14 - 19, 2002.
International Conference on the Physics and Chemistry of Ice , Newfoundland, Canada
[http://www.housing.mun.ca/conf/pci/]

July 15 - 19 2002
XIV Russian Synchrotron Radiation Conference - SR-2002. Novosibirsk, Russia.
[http://ssrc.inp.nsk.su/english/load.pl?right=conference.html].

July 29 - August 2, 2002.
Denver X-ray Conference, Denver, USA
[http://www.dxicdd.com/02/]

July 29 - August 2, 2002
Seventh International Conference on X-ray Microscopy, Grenoble, France.
[http://www.esrf.fr/conferences/XRM2002/index.html].

July 31 - August 2, 2002
Exploring Modern Computational Chemistry , University of Nottingham. Organised in association with the Royal Society of Chemistry Theoretical Chemistry Group.
[http://www.nottingham.ac.uk/chemistry/emc2]

August 1 - 3 2002
Crystal Chemistry of New Materials and Soft Matter Studied by Synchrotron and Neutron Diffraction - IUCr-2002 Satellite Meeting, Grenoble, France.
[http://www.ill.fr/dif/iucr/].

August 4 - 6, 2002
Neutron and Synchrotron X-Ray Scattering in Condensed-Matter Research, Villingen, Switzerland
[http://www.psi.ch/sls/NSCmr2002]

August 6 - 15, 2002
IUCr XIX - XIX Congress and General Assembly of the International of Crystallography, Geneva, Switzerland
[http://www.kenes.com/iucr/ also at http://www.unige.ch/crystal/ahdf/geneva02.html]

August 10 - 17 2002
1st PSI Summer School on Condensed Matter Research, Lyceum Alpinum, Zuoz, Switzerland
[http://psw100.psi.ch/www_sls_hn/zuoz_cmr2002/]

August 19 - 23 2002
LINAC 2002, Gyeongju, Korea
[http://linac2002.postech.ac.kr/].

August 25 - 29, 2002
SAS 2002, XII International Conference on Small Angle Scattering, VENICE, Italy with some satellite meetings
[http://www.isf.unian.it/isf/SAS/Home-SAS.html]

August 28 - September 6 2002
Synchrotron Radiation Summer School., Chester and Daresbury, UK.
[http://srs.dl.ac.uk/Meetings/chester2000/front%20page.html].

September 4 - 6, 2002
Synchrotron Radiation in Polymer Science II, European Physical Society Conference on Macromolecular Physics, Sheffield.
[http://www.polymercentre.org.uk/srps/]

September 11-13, 2002
Advances In Thin Film Characterization By X-Rays, Genova, Italy
[http://www.ing.unitn.it/~maud/esqui/esqui.html].

September 12, 2002
Industrial Aspects of Crystallisation from Solution: Nucleation and Polymorphism: SYMPOCRIST, Marseille, France [http://www.crmc2.univ-mrs.fr/confs/sympocrist/]

September 16 - 27 2002
6th Laboratory Course Neutron Scattering, Juelich, Germany [http://www.neutronscattering.de/labcoure.html]

September 23 - 27, 2002
Analyse Structurale par Diffraction des Rayons X. Sturctures absolues, macles, incommensurables, Toulouse, France [http://www.lcc-toulouse.fr/congres/ecole_rx_2002/index.html]

October 10 - 12 2002
2002 ALS Users' Meeting. Berkeley, CA, USA [http://www-als.lbl.gov/als/usermtg/].

October 11 2002
35th Annual SRC Users Meeting. Stoughton, WI, USA. [http://www.src.wisc.edu/].

early December 2002
The 2nd symposium on Pharmaceutical Powder X-ray Diffraction, PPXRD-2, Philadelphia, PA, USA [http://www.icdd.com/ppxrd/default.html]

April 14 - 17, 2003
BCA Annual Meeting, York University. Last day is Maundy Thursday

August 2005
XX Congress of the International Union of Crystallography, FLORENCE, Italy [Carlo Mealli, email: mealli@fi.cnr.it]

New Honorary Members

The concept of honorary life membership for distinguished crystallographers was first instituted in 1998, and incorporated into the BCA Statutes in 2000. Initially the BCA President chose the names, more recently, they have been suggested by members of the BCA Council and voted on at Council meetings.

New ones in 2002 are:

Jane Brown - for her work with neutrons at the ILL particularly on magnetism

Bill David - this year's lecturer of the 'BCA Prize Lecture in honour of Terry Willis' who spoke on 'Decades of neutrons' and his work on the development of neutron high resolution powder diffraction.

Andrew Lang - for his work on topography; he won the Hughes medal of the Royal Society in 1997.

Michael Woolfson - for his seminal work on Direct Methods. He will be awarded the very prestigious Ewald Prize of the IUCr at the Geneva meeting this summer.

The complete list in April 2002 (in alphabetical order of surname is):

- Jane Brown
- Bill Cochran
- Bill David
- Bob Evans
- Bruce Forsyth
- Ron Jenkins
- Aaron Klug
- Andrew Lang
- John E. Walker
- Terry Willis

Since the latest members honoured are physicists, the BCA Council has asked Representatives of other Groups (BSG, CCG, IG) to collect further names from members for consideration at the next BCA Council meeting in September 2002.

Please send your nominations to your Group Representative, contact details can be found in the front of this newsletter. Our Constitution limits the number of Honorary members to 20.

For the benefit of younger members who may not be familiar with the achievements of these distinguished crystallographers I am compiling Web pages for the BCA website. There is a list of people associated with British crystallography on the page: http://bca.cryst.bbk.ac.uk/BCA/obits/names.html

Please look at the information there for our Honorary members and send comments or further information to me.

Kate Crennell,
BCA Education Officer.
email: BCA@isise.rl.ac.uk.

Corporate Members

Anachem Ltd

Astex Technology

Bede Scientific Instruments Ltd

Bruker/Nonius

Cambridge Crystallographic Data Centre

Hampton Research

International Centre for Diffraction Data

Oxford Cryosystems

Oxford Diffraction

Philips Analytical

Rigaku MSC

BCA Corporate Membership

The BCA values its close ties with commercial companies involved with crystallography. To enhance these contacts, the BCA is pleased to announce that they are now offering Corporate Membership.

Corporate Membership is available on an annual basis running from 1 January to 31 December and includes the following benefits:

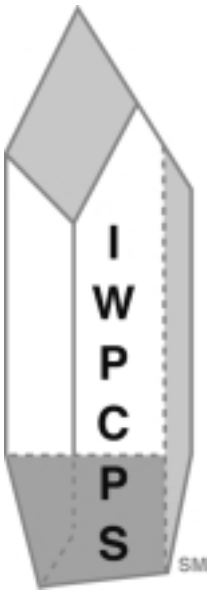
- Up to 10 free BCA memberships for your employees.
- A 10% discount on exhibition stands at the annual Spring Meeting.
- Free insert in the annual Spring Meeting delegate bag.
- Two free full registrations to the annual Spring Meeting.
- Ten complimentary copies of the quarterly BCA Newsletter.
- Corporate Members will be listed in every BCA Newsletter and on the BCA Web Site with links to your corporate site.

The cost of this membership is £600.00 per annum

To apply for Corporate Membership, or if you have any enquiries, please contact:

BCA Administrative Office
Northern Networking Ltd
1 Tennant Avenue
College Milton South
East Kilbride G74 5NA

Phone 01355 244966
Fax 01355 249959
e-mail bca@glasconf.demon.co.uk



Third International Workshop on Physical Characterization of Pharmaceutical Solids[SM]

IWPCPS[SM]-3 www.**assa***international*.com June 9 - 14, 2002

Leading professionals will present current industry information and explore analytical approaches to characterizing a solid. Workshop participants learn how these approaches can complement each other and be utilized individually or in concert to solve real problems. This is the third year for IWPCPS[SM] and is the only workshop of its nature worldwide. Brand new session topics are geared to keep attendees at the leading edge of solid-state chemistry.

The Preliminary Workshop Topics* include:

A Modern Pharmaceutical Solids State Laboratory
Solid State NMR Applications
Amorphous Content - Determination And Characterization
Morphology And Surface Characterization
Characterization And Control Of Dissolution & Bioavailability
Expert Systems For Formulation Design(Informatics ñ Particle Engineering)
Novel Technologies for Assessing Bulk Physical Properties
Polymorphs and Solvates
Special XRD Applications
Modern Thermal Analysis Applications
Drug Product Characterization
Supercritical Fluids (Particle Design)
Regulatory Patent Issues
Screening and On-Line Technologies

Keynote lectures* are given by recognized experts including representatives of:

Aventis Pharma, France
Boehringer Ingelheim Pharmaceuticals, Inc., USA
Bruker-AXS, Germany
CRIT Pharma, France
GlaxoSmithkline, UK and USA
Merck&Co, USA
Monash University of Melbourne, Australia
Purdue Pharma, USA
Toho University, Japan
University of Bradford, UK
University of Minnesota, USA
AstraZeneca, Sweden and UK
Boehringer-Ingelheim, Germany
CCDC, UK
DuPont Pharma, USA
Hecus M. Braun, Austria
Merck Frost, Canada
Pfizer, UK
Threlfall Associates, UK
University of Belfast, Ireland
University of Leeds, UK
UMIST, UK

Find more information about the workshop, scheduled speakers and abstract submission as well as online registration at **www.assa*international*.com** or contact us at **workshops@assa*international*.com**.

Tel: +1-203-312-0682 or +1-610-942-0261; Fax: +1-203-312-0722 or +1-610-942-0983 **Topics and lectures subject to change.*