Crystallography News

British Crystallographic Association

Issue No. 172 March 2025
ISSI 1467-2790

BSG Winter Meeting and CCP4 Study Weekend

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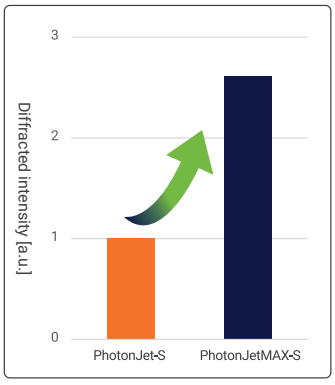

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- Up to 10 free BCA memberships for your employees.
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- Two free non-residential registrations to the annual Spring Meeting.
- Ten complimentary copies of the quarterly Crystallography News.
- Corporate Members will be listed in every Crystallography News and on the BCA website with clickable links to your organisation's website.

Corporate Membership is currently **£850** for one year.

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Benefits of Individual BCA Membership:

- The professional organisation for crystallographers in the UK
- A broad range of meetings organised by the BCA and its subject groups
- Preferential members' rates for such meetings
- Eligibility of students and postdocs for an Arnold Beevers Bursary award
- A copy of Crystallography News every quarter
- Optional E-mail notifications of news items and meeting information
- Influence on the development of crystallography and the BCA

For current rates, and to join, please see **www.crystallography.org.uk/membership/**

Conference Bursaries 2025/26

Bursaries are available for BCA members to attend national/international crystallographic meetings in 2025/26.

Local meetings and virtual meetings (with no travel) are supported. Eligible members may apply every year.

Apply early for in person attendance at international meetings. Successful bursary winners are still eligible.

Further information on the eligibility criteria and the application portal is available here:
https://crystallography.org.uk/prizes/bursaries

Additional carers grants are also available to BCA members at any career stage:
https://industrial.crystallography.org.uk/bursaries-and-awards/

Contents

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Please ensure that items for inclusion in the June 2025 issue are sent to the Editor to arrive before 25 April 2025.

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These details are not divulged to any others without your permission. You may inspect your entry during the Annual Meeting, or otherwise by application to the BCA Administrative Office. We will be happy to amend entries at any time.

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This month's cover:

Scenes from the 2024 BSG Winter Meeting and the 2025 CCP4 study weekend.

From the President

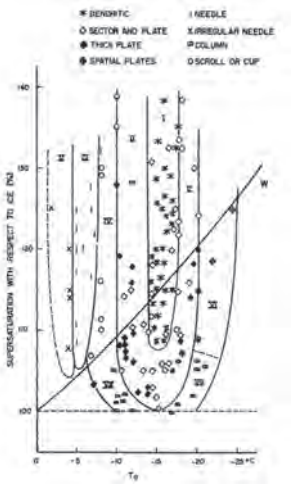
DEAR Members, I hope you have all had a good start to the year. Whilst struggling to get on top of the many uncompleted tasks from the pre-Christmas status of my 'guilt list' it's also equally important to try to make efforts to prevent the new 2025 additions from running away with me too much. One key area of planning is with regard to this year's crystallography conferences and meetings. The most important is of course the Spring Meeting which will take place in Leeds on the 14th-17th April – the Early Bird deadline is the 10th of March so hopefully you will still have time to catch the proverbial worm after you read this. The programme on the website already has invited speakers and it looks to be a fantastic few days of science and socialising (with the traditional Cèilidh taking place as usual!) – many thanks to Katharina Edkins (Programme Chair) and all others involved for their hard work.

As we come up to the Spring Meeting and its chance to catch up across the Association I would particularly like to highlight that **any ideas members have for new activities, communication methods, directions, policies or other developments are always more than welcome** and especially so when we will shortly have a chance to discuss them together, formally and informally, in April. As is always apparent from CN, the Spring Meeting and other activities of the BCA and its groups, the membership is extremely active in the development of the Association so I encourage you to put your minds to this task and bring any ideas to myself, other members of the Council or group officers.

This year's Spring Meeting theme "Learning From Others" is highly relevant to my most recent weekend's activities which have caused me to brush up on my snow crystallography. My 4-year old was lucky to have his first skiing experience this past weekend in the Cairngorms and has been very interested in why some snow is sticky (good for making snowmen), some powdery (not so good) and how large crystals like those pictured below can form. In addition, that fact that snow machines can make artificial snow when the Scottish winter is a bit too warm was also of great interest. The huge variety of snow crystal morphology will not be new to any readers of CN but I was interested to discover that the creator of the first fully systematic characterisation of it, **Ukichiro Nakaya** of Hokkaido University in Japan, was also the first to record creation of an artificial snow crystal. This was created, with his colleagues, using a specially designed convection chamber and a rabbit hair from a fur coat to aid nucleation, on 12th March 1936 and is commemorated in the form of a monument at Hokkaido University. From his careful work on synthetic snow crystals he was able to elucidate the link between growth environment and morphology in the form of the eponymous Nakaya diagram.

I will halt my musings here (recommending you turn to the particularly extensive Down Memory Lane section later this issue for historical treats!) and return myself to my earlier thoughts of warmer months and organisation. Registration for this August's **ECM35, Lviv-Poznań** will be open by the time you read this and planning for next Autumn's **27th IUCr Congress and General Assembly** in Calgary is well underway. For further details please see the section on forthcoming meetings at the end of this issue.

Alex Gibbs
University of St Andrews



Morphology phase diagram from Nakaya's Snow Crystals: Natural and Artificial (Harvard, 1954).

At the time of going to press, we note with great sorrow the passing of Professor George Michael Sheldrick (Göttingen), a giant of the crystallographic computing field. We wish to extend our deepest sympathies to his family, friends and colleagues.

The monument at Hokkaido University to the creation of the first artificial snow crystal. Credit: 禁樹なずな/CC-BY-SA-4.00 Wikipedia.

Snow crystals, Johanngeorgenstadt, Germany.

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Full committee details on the BCA website
www.crystallography.org.uk

From the Editor

WE begin this issue with the detailed programme for the 2025 Spring Meeting in Leeds (14th – 17th April) which is on the theme of "Learning from Others" and is looking very exciting. We follow this with the latest news from the CCDC and the PDBe. Then we have a very interesting corporate member's profile on Douglas Instruments followed by a report on the BSG Winter Meeting. This was held at the LMB-MRC in Cambridge and was organised by Simon Newstead (Oxford) and Andrew Carter (Cambridge). This excellent one-day meeting was entitled "New Advances and Future Directions in Structural Biology." A great account of the 2025 CCP4 Study Weekend by Ben Bax (Cardiff) follows. This year the meeting was on the theme of "Using software, AI and other methods to advance crystallographic models." Members who attended any other meetings held over the Christmas period are most welcome to contribute reports to future issues of Crystallography News.

Very sadly, **Peter Main** (York) passed away in November last year and we have therefore reprinted the excellent obituary which was published in *Acta Crystallographica* by **Eleanor Dodson** (York) and **Kathryn Cowtan** (York). Peter was very well-known in the crystallography sphere for his multi-solution direct methods program MULTAN (Germain, G., Main, P. & Woolfson, M. M. (1970). *Acta Crystallogr. B* **26,** 274-285). In the highly-cited paper entitled "A short history of SHELX" (Sheldrick, G. M. (2008). *Acta Crystallogr. A* **64,** 112-122) the author describes MULTAN as being "the direct-methods program of choice at the time" and how it was the inspiration for the tangent refinement offered by SHELX-76. I was always impressed that Peter went to great lengths to make his theoretical papers as comprehensible as possible, one of my favourites being his comparison of the use of different Fourier map coefficients: "A theoretical comparison of the β, γ' and 2Fo-Fc syntheses" (Main, P. (1979). *Acta Crystallogr. A* **35,** 779-785). That one is a very good read indeed.

Sadly, in February this year we heard about the passing of Jan Drenth in Groningen who was a pioneer in the protein crystallography field and authored a very well-known text book on the subject. We have been able to include an obituary by two members of the Groningen team.

We then have Puzzle Corner which presents a fairly detailed analysis of the tiling patterns which appeared in the last issue. As with the previous puzzles, I am greatly assisted by **John Lisgarten** (London) who provided the photographs and by **Philip Bradfield** (Edinburgh) who provided the answers as well as much interesting material of great educational value.

As members will no-doubt be aware, the CN editor is forever trying to Photoshop himself into the crystallographic history books. Accordingly, this issue features a bumper Down Memory Lane section which starts by covering the development of the television area detector by the instrument designer Uli Arndt in Cambridge and then looks at some fascinating historical items which have resurfaced from Dorothy Hodgkin's laboratory in Oxford. We then look at the life and work of one of the heroines of the discovery of the DNA double helix in Cambridge, June Lindsey (née Broomhead), whom I think has not received appropriate recognition for her contribution, followed by a look at crystallographers in the Darwin family as well as an interesting item from the art world.

In the last issue we spent some time describing the BSG poster prize trophy which is made of Blue John stone mined at Treak Cliff Cavern in Derbyshire. A recent trip to the **Sedgwick Museum of Earth Sciences** in **Cambridge** revealed some very striking Blue John stones in their collection which are shown below. I do hope that members find them as interesting as I did!

Crystallographic forteana will return in a future issue.

Jon Cooper
UCL

Blue John stones in the Sedgwick Museum of Earth Sciences in Cambridge.

BCA Spring Meeting 2025

SESSION DETAILS

ESCG Early Career Satellite Meeting

Monday 14 April 2025

University of Leeds

Early Stage Crystallographers Group (ESCG)

13:00 – 21:00

The ESCG satellite meeting is an opportunity for all early-stage crystallography researchers, from across the BSG, CCG, PCG and IG, to present their work in a supportive and friendly environment, which will be run by fellow early career scientists.

Early-stage crystallographers are invited to share their work in all areas of crystallography—biological, chemical, and physical. This session offers a welcoming space to showcase your research, exchange ideas, and connect with peers in a supportive environment.

13:00 – 13:30

ESCG Opening Plenary:

Rupert Beckett Lecture Theatre, Michael Sadler Building

Session Chair: **Sam Lewis** (Cardiff University / Diamond Light Source)

Speaker: **Mark Warren** (Diamond Light Source)

Title TBC

13:30 – 17:15

ESCG Research Sessions

Contributed talks from the ESCG community

Session 1 Chair: **Rebecca Clulow** (Uppsala University)

Session 2 Chair: **Ben Coulson** (Cardiff University)

Session 3 Chair: **Jake Hill** (University of Leeds)

17:15 – 17:45

ESCG Annual General Meeting

18:30 – 19:00

Flash Poster Presentations

Rupert Beckett Lecture Theatre, Michael Sadler Building

Session Chairs: **Ellie Dempsey** (University of Edinburgh) and **Stephen Brown** (University of Warwick)

Researchers have an opportunity to present an overview of their poster in 30 seconds with one PowerPoint slide.

19:00

Poster Session with Dinner and Wine

21:00

Evening Concludes

BCA 2025 Main Meeting Programme

Tuesday 15 April 2025

09:00 – 09:30

Parkin Lecture

Rupert Beckett Lecture Theatre, Michael Sadler Building

Session Chair: **TBC**

Speaker: **TBC**

09:30 – 10:30

Session 4

Session Chair: **Stephen Brown** (University of Warwick)

10:30 – 11:00

Closing Plenary

Session Chair: **Jake Hill** (University of Leeds)

Speaker: **Jeremiah Tidey** (Warwick / NCS)

Title TBC

MAIN MEETING

Rupert Beckett Lecture Theatre, Michael Sadler Building

11:30 – 12:15

Lonsdale Lecture

Session Chair: **Thomas Hitchings** (University of Kent)

Speaker: **TBC**

Title TBC

13:00 – 13:45

BSG Plenary

Session Chair: **TBC**

Speaker: **Elton Zeqiraj** (University of Leeds)

Unravelling the supramolecular organization of K63-linked ubiquitin chains by JAMM-domain DUBs.

14:00 – 15:30 Parallel Sessions

PCG: Open session I

Session Chair: **Nilanthay Balakrishnan** (Keele University)

BSG: Engineering Biology

Synthetic biology is driving significant development in biotechnology. The ability to harness enzymes from nature and improve or alter their function for biotechnological processes is a powerful prospect. Indeed, de novo protein design is routine, and structural information is key to its success. This session will explore the role of structural biology in synthetic biology/protein design.

Session Chair: **Briony Yorke** (University of Leeds)

Keynote: **Ross Anderson** (University of Bristol)

Totally wired: amping up the de novo design of bioenergetic protein components

CCG/ESCG: Would you publish it?/ Interesting problems in chemical crystallography

Back by popular demand the session 'Would you publish it? Interesting problems in chemical crystallography' is aimed at discussing problematic crystal structures that can be hard to interpret and publish. The session is an open and inclusive environment where constructive comments and feedback are encouraged. Problems might include charge imbalance or other chemical issues, poor resolution or data completeness from X-ray, neutron or electron diffraction, dealing with dynamical effects, complicated disorder, highly restrained models, unexplained residual electron density and other artifacts.

Session Chair: **Toby Blundell** (Durham) and **Sam Lewis** (Cardiff)

Keynote: S**imon Coles** (University of Southampton)

16:15 – 17:45 Parallel Sessions

PCG: Computational Modelling in Crystallography

Session Chair: **Johnathan Skelton** (University of Manchester)

Keynote: **George Darling** (University of Liverpool)

BSG: Open session

This session will cover structural biology as a whole and emerging topic.

Session Chair: **Natalie Tatum** (Newcastle University)

Keynote: **TBC**

CCG: Polymorphism, hydrates and co-crystals

This session delves into the critical role of polymorphism, hydrates, and co-crystals in the design and development of solid-state materials. The diversity in the solid-state is ubiquitous amongst materials hence can impact a number of industries. This behaviour is critical for sectors whose functional materials are flexible and can adopt a number of different packing arrangements. Whether through polymorphic transitions, hydrate formation, or co-crystallization, these different forms can significantly influence the properties of the materials providing extensive parameter space to explore to achieve a positive outcome. In this session, we invite contributions from a wide variety of areas where the properties of materials have been influenced by a change in structure. We look forward to hearing and discussing your research in the area.

Session Chair: **Iain Oswald** (Strathclyde)

Keynote: **Amy Hall** (Durham University)

Are hydrogen bonds really queen in molecular cocrystals?

18:00 – 18:45

PCG Plenary

Rupert Beckett Lecture Theatre, Michael Sadler Building

Session Chair: **Matthew Cliffe** (University of Nottingham)

Speaker: **Robert Palgrave** (UCL)

The Role of AI in Materials Discovery

19:00 – 21:00

Poster Session with Dinner and Wine

Wednesday 16 April 2025

09:00 – 09:45

CCG Plenary

Rupert Beckett Lecture Theatre, Michael Sadler Building

Session Chair: **Hamish Yeung** (University of Birmingham)

Speaker: **Lucia Maini** (Bologna)

Be a crystallographer to investigate the past, the present and the future!

10:15 – 11:45 Parallel Sessions

IG: Amorphous modelling

Session Chair: **Tony Bell** (Sheffield Hallam University) and **Natalie Johnson** (CCDC)

Keynote: **Michael Devlin** (University of Strathclyde)

Title TBC

BSG/CCG: In-situ crystallography

In-situ crystallography, where diffraction data are collected in the vessel where the crystal was grown, is an increasingly exploited tool in macromolecular crystallography. The technique enables the collection diffraction data from fragile or difficult to harvest crystals as well as diffraction at room temperature – in the case of biological molecules these structures can be more physiologically relevant than equivalent structures determined at 100K. As such, there is a dedicated beamline for in-situ crystallography at Diamond Light Source, VMXi, that will be introduced in this session. In this joint session between the CCG and BSG, we will explore the area of 'in-situ crystallography' and how the developments for macromolecular crystallography could be applicable in chemical crystallography.

Session Chair: **Phoebe Allan** (University of Birmingham)

Keynote: **Amy Thompson** (Diamond Light Source)

VMXi: a high-throughput, in-situ crystallography beamline to harness the advantages of multi-crystal strategies

PCG: Complementary techniques

Session Chair: **Evie Ladbrook** (Warwick) and **Karen Johnston** (University of Durham)

Keynote: **TBC**

Title TBC

11:45 – 12:15

CCG Annual General Meeting

BSG Annual General Meeting

PCG Annual General Meeting

13:15 – 14:35

Early Career Prize Lectures

Biological Structures Group Early Career Prize

The BSG will award a prize to someone who has had an impact in the field of Structural Biology (with an emphasis on crystallography) and recently obtained a personal fellowship, a lectureship or equivalent position.

Chemical Crystallography Group Prize for Younger Scientists

The CCG will award a prize to a younger scientist who has performed original research in the field of chemical crystallography or the application of crystallographic information to structural chemistry.

Physical Crystallography Group Early Career Prize

The Physical Crystallography Prize is awarded for the best recently published work by a person in the early stages of their career, working in the field of Physical Crystallography, whose research is expected to make a significant impact in the field.

15:15 – 16:45 Parallel Sessions Workshops

Workshop: Determining a protein crystal structure in 2025 (BSG)

Determining the structure of a protein by X-ray crystallography is a largely automated process today, ever increasingly requiring less manual input. However, difficult cases still require much manual input or decision making. In this workshop we will explore the process of solving a structure in 2025.

Session Chair: **Adam Crawshaw** (Diamond Light Source) and **TBC**

Keynote: TBC

Workshop Outreach (CCG/ESCG/CCDC)

The theme of this workshop is to share ideas and best practice around running crystallography outreach. In addition to the keynote talk from the CCDC, there will be opportunity for small group discussions and activities. The aim is to equip you with resources and knowledge to apply to your own outreach activities.

Session Chairs: **Ellie Dempsey** (Edinburgh) and **Stephen Brown** (Warwick)

Keynote: **Ilaria Gimondi** (CCDC)

Workshop Rietveld refinement (PCG/IG)

The Rietveld crystal structure refinement method was first developed by Hugo Rietveld 60 years ago. It is a method of refining crystal structures from powder diffraction data. An initial structure is used as a starting model and then least squares refinement is used to fit a calculated powder diffraction pattern from this initial structure to the observed data. It was initially developed for neutron powder diffraction data but was then extended to X-ray powder diffraction data. It is now a mature method of refining crystal structures from powder diffraction data, it is also a very useful method for quantitative phase analyses from powder diffraction data collected on multiphase samples.

Session Chair: **Tony Bell** (Sheffield Hallam University) and **Lewis Owen** (University of Sheffield)

Keynote: **Jeremy Cockroft** (UCL)

17:15 – 18:00

Dorothy Hodgkin Prize Lecture: Name

Rupert Beckett Lecture Theatre, Michael Sadler Building

Session Chair: **TBC**

Speaker: *TBC*

Title TBC

18:00 – 19:00

BCA Annual General Meeting

Rupert Beckett Lecture Theatre, Michael Sadler Building

19:30 – 01:00

Conference Dinner & Cèilidh

Thursday 17 April 2025

09:00 – 09:45

IG Plenary

Rupert Beckett Lecture Theatre, Michael Sadler Building

Session Chair: **Natalie Johnson** (CCDC)

Keynote: **John Helliwell** (Manchester)

Adding Open Science to the Modern Discovery and Applications Toolbox in Crystallography

10:15 – 11:45 Parallel Sessions

CCG: Open session

Session Chair: **Tony Keene** (University College Dublin)

Keynote: **TBC**

PCG: Open session II

Session Chair: **Helen Playford** (ISIS Neutron and Muon Source)

Keynote: **TBC**

BSG: Integrative Structural Biology

The accurate characterisation of three-dimensional structures of complex biological macromolecules is essential for understanding their functions. For large, dynamic complexes, the use of one structural biology technique is often insufficient to fully capture their structural properties. This session will highlight the integration of data obtained from multiple analytical methods, showcasing how integrative structural biology approaches enhance our understanding of macromolecular structure, dynamics, and function.

Session Chair: **TBC**

Keynote: **Jaime Blaza** (Leeds)

Using Cryo-EM and symmetry expansion to understand how Rubisco is bound together to accelerate carbon fixation

12:15 – 13:45 Parallel Sessions

CCG/PCG: Coordination polymers and porous materials

Session Chair: **Lauren McHugh** (University of Liverpool)

Keynote: **Valentina Colombo** (University of Milan)

In situ insights into adsorption and catalysis in metal-organic frameworks

PCG: Phase Transitions

Session Chair: **Struan Simpson** (University of Warwick)

Keynote: **Dr Rebecca Scatena** (Diamond Light Source)

BSG: "Mechanisms and disease"

Structural biology plays a pivotal role in advancing our understanding of health challenges. This session will highlight the use of structural biology approaches to unravel the molecular modes of action of protein systems in health and disease, and implications for drug design and therapeutic strategies.

Session Chair: **TBC**

Keynote: **Wyatt Yue** (Newcastle University)

Structural biology at the crossroad of metabolic enzyme disorders and drug discovery

CLOSE OF CONFERENCE

BCA AGM 2024 Minutes

Draft minutes of the 2024 Annual General Meeting of the British Crystallographic Association

University of Leeds, 27th March 2024 at 18:00

The meeting was chaired by the BCA Council President Richard Cooper and notes and an audio recording were taken by the Council Secretary Lauren Hatcher.

Approval of Agenda

The agenda was approved by Gary Nichol and seconded by Claire Hobday.

Apologies for Absence

Apologies were received by the Secretary prior to the meeting from Simon Phillips.

Minutes of the last AGM

The minutes of the 2023 AGM appeared in the Spring 2024 issue of Crystallography News on pages 10-11. They were also disseminated to the membership via email with the agenda to this meeting and are available on the members area of the BCA website. There were no comments or corrections. The minutes of the previous meeting were proposed by Elspeth Garman and seconded by Mark Montgomery.

President's Report

The President's report was presented by Richard Cooper who thanked Hanna Kwon and Peter Moody and the entire Programme Committee, including the YCG satellite organisers, Suzanna Ward, HG3 and the York conferences team for organising the meeting. The President also thanked the sponsors and exhibitors for supporting the Spring meeting (see HG3 report).

The President announced that the 2025 BCA Spring Meeting will be held at the University of Leeds between the 14th and 17th April and the Programme Chair will be Katharina Edkins. Planning will begin with a brief meeting of 2025 Programme Committee members at 08:00 on Thursday March 28th, 2024. There will be another Programme Committee Meeting in late May/early June 2024. The President requested that BCA members please send suggestions for symposia or plenary speakers to their representatives from the BSG, CCG, PCG, IG or ESCG as soon as possible.

Other upcoming crystallographic meetings of note are the ECM 34 (https://www.ecm34.org/ Padova, Italy 26th – 31st August 2024) and the ECM 35 is currently expected to be held in Poznań, Poland and Lviv, Ukraine, in August 2025.

Richard announced that this is the completion of his term as BCA President and thanked all the members of Council for their support, thanking the staff members of HG3 led by Nicola Hardaker for their assistance and conference organisation, and the wider BCA membership for their continued support of the Association.

Claire Hobday will also be stepping down from her role as Webmaster and was thanked by the President for her contributions. Anthony Blue Carter will take over the role of webmaster from this meeting.

There were no questions arising from the President's report.

Secretary's Report

The Secretary's report was presented by Lauren Hatcher.

Following the 2023 AGM, the IUCr and ECA websites were updated with the names of the 2023-24 BCA Council members.

A BCA Council meeting was held on 7th September 2023. This autumn Council meeting was held successfully online via Zoom, as has been done for several years now as this has proved a suitable way to reduce unnecessary travel costs and carbon footprint.

The spring Council meeting was held on 25th March 2024 and offered a hybrid format, again as has been successfully achieved for several years, allowing as many members of Council as possible to attend. Thanks to HG3 for arranging the room and AV facilities for this.

Nominations for 2024 Council elections were received on time, with thanks to the nominating committee for their help in identifying candidates. As there was a single candidate for each of the vacancies (President, Ordinary Member, Bursary Officer, Education and Outreach Coordinator) no elections were held in 2024.

There were no questions arising from the Secretary's report.

HG3 Report

The report was summarised by the President on behalf of HG3. The total number of BCA membership as at 6 April 2024 was 499 (487 in 2023). Corporate Members are as follows: Bruker UK, Cambridge Crystallographic Data Centre, Douglas Instruments Ltd, International Centre for Diffraction Data, Calibre Scientific, Oxford Cryosystems Ltd, Rigaku Europe and Photonic Science and Engineering. The current list of advertisers in Crystallography News for 2024 is Bruker UK, Oxford Cryosystems, Rigaku Europe and Technobis with each appearing in all issues.

Next followed the 2024 Spring Meeting report (as of 2 weeks prior to the meeting). Attendance is 152 delegate registrations, 32 day delegates, 23 invited speakers and 14 exhibitors/sponsors, giving a total number of attendees of 221 compared with 206 attendees in 2023. The exhibitors at the 2024 meeting were Rigaku Europe SE, STOE & Cie GmbH, Anton Paar, Douglas Instruments, Formulatrix Inc, Constant Systems Limited, Oxford Cryosystems, Bruker UK Ltd, CCDC, Malvern Panalytical and Molecular Dimensions. The meeting sponsors were Rigaku Europe, Oxford Cryosystems Ltd and Douglas Instruments. Poster prizes were sponsored by Rigaku Europe and Oxford Cryosystems.

A question was asked about whether HG3 record statistics about gender balance/diversity and it was highlighted that this is a separate standing item in the agenda that would

be discussed later in the meeting. Another question was asked as to how the numbers of attendees in recent years compared to attendance in previous years e.g. in 2018. The President estimated that the number of attendees being around 200 is fairly typical.

Report of the Treasurer to include Presentation of the Accounts for 2023 and the Examining Accountant's Report

The Treasurer's report and Examining Accountants report were presented by the BCA Treasurer Claire Naylor. The Treasurer's report comprised of a review of 2023, the association's income, the 2023 Spring Meeting finances, the association's expenditure and closed with a summary. The reported accounts are for the period of January 1st 2023 to December 31st 2023 and a full break down is included in the BCA annual accounts, available via email or online at the Charity Commission website. The Treasurer summarised that we continue to try and reduce our governance costs and maintain a cautious balanced investment of funds. Investment returns have continued to be smaller than desirable, and we have kept larger sums in cash savings where the increased interest has provided better returns. Please continue to encourage colleagues to join the BCA and to attend meetings as membership is our lifeline – and encourage students to apply for bursaries. The treasurer then thanked HG3, Council members, BCA Group treasurers, Charles Stanley Bank and UHY Hacker Young accountants.

A question regarding the fact the website costs were missing from the accounts was raised and was answered by Richard Cooper: we pay for the website costs every three years so that is why it is not included on the accounts for this year.

The accounts were accepted as presented by Ben Bax and seconded by Simon Coles.

Appointment of Examining Accountant for 2024

The appointment of The Young Co. as the examining accountant for 2024 was proposed by Elspeth Garman and seconded by David Walker.

Update to Statutes and By-laws: Early Stage Crystallographers Group change of name.

Advanced notice of the proposed change of name for the Early Stage Crystallographers Group from its previous name of the Young Crystallographers Group in the BCA Statutes and by-laws was given on 20th February 2024, so as required was more than a month in advance of the AGM.

The change required is outlined below.

Original text of by-law H.2: "2. Ordinary Members of the Association have the right to become members of another Group of the Association without payment of a further subscription. Members of the Association entitled to membership of the **Young Crystallographers Group** have the right to become members of another Joint Group or other Group of the Association without payment of a further subscription; such Ordinary or Student Members shall not be counted in determining any subvention to be paid by the Group to the Association."

Proposed new text of by-law H.2: "2. Ordinary Members of the Association have the right to become members of another Group of the Association without payment of a further subscription. Members of the Association entitled to membership of the **Early Stage Crystallographers Group** have the right to become members of another Joint Group or other Group of the Association without payment of a further subscription; such Ordinary or Student Members shall not be counted in determining any subvention to be paid by the Group to the Association."

A quorum of at least 30 members was required to approve this change and was achieved in the meeting. The update was put to vote by show of hands and the AGM attendees voted unanimously to approve the change. It is noted that Simon Phillips voted in favour by absentia. The change will be made on the website from 28th March 2024.

Elections to Council

New members to Council for 2024 were announced as Alexandra Gibbs (President, 2024 – 2027), Jeremiah Tidey (Ordinary Member, 2024 – 2027) and Education and Outreach Coordinator (Ilaria Gimondi 2024 – 2027).

The 2025 vacancies on Council will be for the positions of Vice President, Secretary and one Ordinary member. All three incumbents are eligible to stand for election for a second three-year term. An email requesting nominations for these positions will be circulated to the membership and the deadline for nominations to be sent to the BCA Secretary will be the 30th September 2024.

Honorary Members

There were no Honorary Memberships awarded this year. New Honorary Life memberships are not necessarily awarded every year and Council can accord Honorary Membership to a maximum of two people in one calendar year. The membership are requested to consider suitable candidates for the upcoming year. Honorary Life Members are chosen for their contributions both to crystallography and to the BCA. Nomination deadline for 2024 Honorary Life Members will be August 31st, 2024. Nominations should be sent to the BCA President along with a short case for support of not more than 400 words. Nominations are considered at the September BCA Council Meeting. Please see http://www.crystallography.org.uk/membership/honorary-members-of-the-british-crystallographic-association/ for more information.

A request was made as to whether there was a list of the current nominating committee. The President noted that there is but there are some positions to be filled and the list could be made available in due course.

Membership, annual subscriptions and subventions

BCA Council recommends no change in membership fees next year. The membership fees for next year will be as follows:

Membership type	*Current rate*	*Fellow membership rate*
Standard	£50	£100
Honorary	£0	£0
Concession (retired/ unemployed/student)	£20	£40
Student 4 year	£60	£120
Overseas	£200	£400

A question was asked about how many people are taking up the opportunity of the Fellowship status. The President reported that this is currently low at 11, but that advertising is being increased. The point was also made that the way the Fellowship option is implemented at renewal is confusing and this information will be fed back to HG3 and acted upon for the 2025 renewal.

Equality, Diversity and Inclusivity report

The BCA Equality, Diversity and Inclusivity (EDI) Policy was adopted in March 2018.

Conference policy

The BCA recognizes the positive impact that a conference speaking opportunity has on an individual's track record and visibility. We also recognize that some sections of the scientific community are often under-represented in conference programmes and that this can affect diversity in the long-term. Our policies are intended to ensure quality and equality.

Speaker invitation policy

The program chairs will ensure the highest quality scientific programme, with speakers that represent the broad diversity of our community. We aim to achieve a speaker and program chair balance that reflects the make-up of our community without bias with regard to gender, sexual orientation, race, religion, geography, disabilities or national origin.

The below EDI report was presented to the AGM. Membership (estimated, 2019) students 50% female, YC (not including students) 45% female and standard members 30% female. In the table below note that the numbers for 2022 and 2023 are rounded to the nearest 5%.

Well done ESCG. Main meeting Plenaries have improved balance this year as do Keynotes. Session chairs and committee – steady. Contributed talks (speakers) – could improve, but approximately reflect our current membership distribution.

The President reported that we are currently unable to report non-binary or other identities in this analysis as we do not collect this information for meeting organisers and speakers. The organisation knows that sex is more complex than simply 'male' and 'female', and gender is more than 'men' and 'women'. There are many people who do not fit into these binary categories, for example non-binary or intersex people. We are also aware that some people's gender identity does not align with the sex they were assigned at birth.

Further information, including the statistics for this meeting, will be available from HG3 in due course and a new EDI area of the website will be set up where this information will be available.

Message from our new BCA President

The incoming President Alexandra Gibbs introduced herself to the AGM and summarised her background and prior involvement with the BCA and looks forward to her role as President.

AOB

The membership thanked Richard Cooper for his contributions as President.

Meeting closed at 18:39

Lauren Hatcher,
Cardiff

Main meeting year	*2016*	*2017*	*2018*	*2019*	*2021*	*2022*	*2023*
Programme Committee (%)	27	27	27	53	44	55	65
Plenary speakers (%)	25	25	75	29	29	50	40
Keynotes (%)	11	18	28	44	25	30	40
Speakers (%)	31	24	38	38	36	30	35
Chairs (%)	23	42	43	37	36	45	35
YCG Meeting							
Plenary speakers (%)	50	0	50	0	100	50	50
Speakers (%)	62	29	36	50		55	50
Chairs (%)	40	40	33	25	50	15	50

News from the Cambridge Crystallographic Data Centre

CCDC Free Virtual Workshops

Registrations are open for a new series of free virtual workshops – a series of hands-on, guided training sessions, where you learn how to use different components of CSD software. These sessions are open to beginners and more experienced users of the CSD Software.

The format is **90 minutes and Show One, Try One, Explore More:**

Show One: A guided demo of the software by the CCDC tutors.

Try One: Hands-on examples for you to try with CCDC tutors on hand to help.

Explore More: Learning outcomes recap, challenges, and quizzes.

In the upcoming workshops, you will learn how to access and search data using the CSD Python API, understand the intramolecular geometry of the molecules in your structures, and explore and visualize structures in the Cambridge Structural Database (CSD).

Search and Access Structural Chemistry Data With the CSD Python API
11th March – 16:00 (GMT)/ 17:00 (CET)/ 12:00 (ET)

Validate Molecular Conformations With Informatics Software Mogul
25th March – 9:30 (GMT)/ 10:30 (CET)/ 17:30 (CST)

Introduction to Mercury and ConQuest Software To Investigate Crystal Structures With a Focus on Powder Diffraction
8th April – 13:00 (BST)/ 14:00 (CEST)/ 8:00 (EDT)

More CCDC Events in 2025

CMAC Open Days 2025
18th – 20th March, Technology & Innovation Centre, Glasgow, UK

Cambridge Festival 2025
22nd March, Cambridge, UK

4th SCI-RSC Workshop on Computational Tools for Drug Discovery 2025
8th April, Leeds, UK

BCA Spring Meeting 2025
14th – 17th April, Leeds University, UK

ICDD: PPXRD-18 – XRD Training for the Pharmaceutical Scientist
6th – 9th May at the CCDC office in Cambridge, UK

PhD Student Science Day 2025
19th June at the CCDC office in Cambridge, UK

Sign up for the CCDC newsletter to receive inspiring content, the latest data updates and product releases, and event announcements.

New How-to Video: Search and visualize 3D structural data using WebCSD

Watch a step-by-step demonstration of how to search and visualize 3D structural data using WebCSD – the online platform of the Cambridge Structural Database (CSD). You will learn how to draw a substructure query using WebCSD's intuitive sketcher, add 3D parameters with constraints (e.g. distances and angles) and see the tools available for exploring an entry's 3D structure.

Free On-Demand Online Training

Pharmacophore Searching 101 – Introduction to CSD-CrossMiner

The CSD-CrossMiner is software that allows you to build pharmacophore queries and simultaneously mine the Cambridge Structural Database (CSD), the Protein Data Bank (PDB) and your proprietary structural data to quickly identify off-target effects, alternative scaffolds, similar binding sites, interaction motifs, bioisosteres and more.
Start learning today!

Follow us on Social Media

In March, we will release three new 'How-To...' videos on our YouTube channel. Subscribe now to be the first to watch them as soon as they go live.

Want to learn more about CCDC events, blogs, case studies, and software updates? Follow us on LinkedIn, Facebook, Twitter, and Bluesky.

Ana Machado,
CCDC



News from the PDBe

STRUCTURES of many large macromolecular assemblies are now being determined using integrative approaches, wherein information derived from multiple experimental and computational methods is combined to compute their three-dimensional structures. PDB-IHM (formerly PDB-Dev) is a system for archiving and disseminating structures determined using integrative or hybrid methods (IHM), and making them Findable, Accessible, Interoperable, and Reusable (FAIR).

In August 2024, PDB-Dev was unified with the PDB to deliver integrative structures alongside experimental structures in the PDB archive (https://files.wwpdb.org/pub/). With unification, integrative structures are assigned PDB accession codes and Digital Object Identifiers (DOIs), annotated as IHM structures, and can be accessed from the PDB archive, PDB DOI links (e.g., DOI: 10.2210/pdb8zzc/pdb), and the PDB-IHM website. Now part of the PDB infrastructure, PDB-Dev has been rebranded as PDB-IHM, denoting IHM structures archived in the PDB.

Integrative structures can be deposited through the PDB-IHM deposition portal and accessible from the wwPDB OneDep home page. They are processed in parallel to the wwPDB OneDep system. Structures processed by PDB-IHM are released synchronously with PDB structures weekly on Wednesdays at 00:00 UTC.

In the future, the wwPDB partners, including Research Collaboratory for Structural Bioinformatics Protein Data Bank (RCSB PDB) in the United States, Protein Data Bank in Europe (PDBe), and Protein Data Bank Japan (PDBj) will disseminate integrative structures on their respective websites.

We look forward to supporting the structural biology community with depositing integrative structures to PDB-IHM.

Questions or feedback? Contact deposit-help@mail.wwpdb.org or heldesk@pdb-ihm.org.

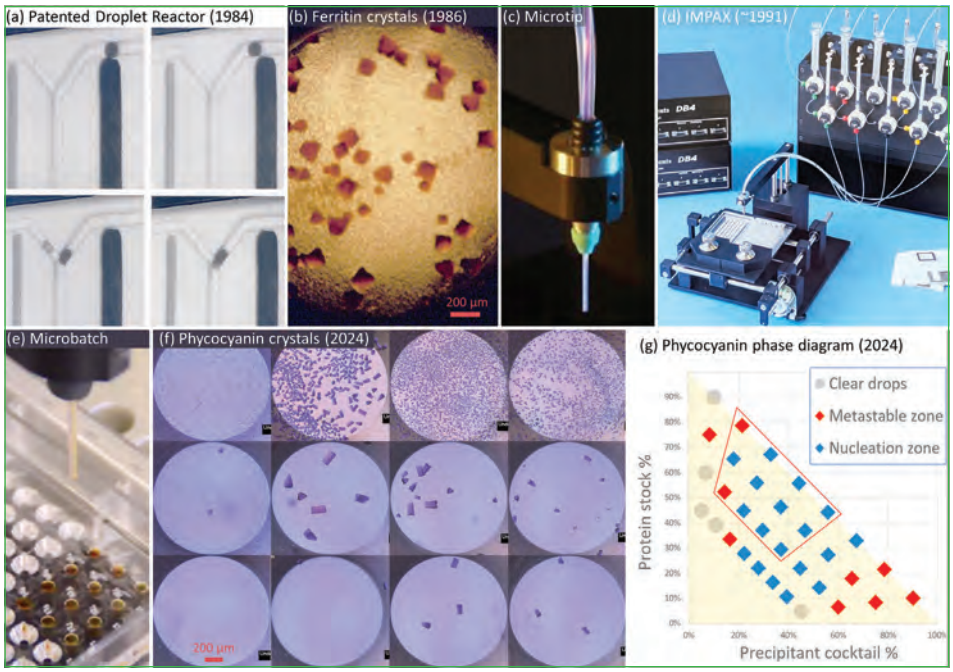
Deborah Harrus,
PDBe – Protein Data Bank in Europe

Corporate member's profile

When innovative crystallization tools come back into fashion: Focus on Douglas Instruments

IN 1985 a young scientist called Patrick Shaw Stewart spent a lot of time in the physics workshop at Imperial College. He was working on his patented liquid handling device – a very early droplet-based "chemical reactor" – what we would now call a microfluidic system, or a lab-on-a-chip [1]. Patrick met a physics student who knew his way around the workshop and could also design electronic circuits; this was Peter Baldock, who later co-founded Douglas Instruments. At that time, Professor David Blow, one of the well-known early UK crystallographers, worked upstairs in the same building. David determined the structure of chymotrypsin and made fundamental contributions in the 1950s and 1960s to the two principal methods of structure determination in protein crystallography – isomorphous replacement and molecular replacement. By the 1980s, David recognized that crystallization was the main bottleneck in protein structure determination, and when he saw Patrick's device he proposed a collaboration. The idea was to develop an automatic system for studying protein phase diagrams in solution. Peter and Patrick knew that automating protein crystallization would be difficult, but they hoped that other UK and international groups would be interested, and they decided to set up a company to work on this, which became Douglas Instruments. They initially focused on Patrick's microbatch method, which uses oil to seal samples [2]. They used this method rather than sealing with glass and grease (the most common method back then), partly because they knew microbatch was very useful for phase diagrams – as it still is!

At first, Patrick and Peter dispensed their crystallization experiments with Patrick's microfluidic device, which moved samples around as droplets in oil [1]. This worked well with coloured water, but when protein samples were used they hit a snag: if a droplet stopped in a channel even for a few seconds the surface became coated with protein, and subsequent droplets would stick and be contaminated. Fortunately, Patrick had worked in the Gatty Marine Biology Laboratory at St Andrews as an undergraduate, and one of the gadgets he used there was a multichannel glass microelectrode, which the Gatty scientists used to impale the brain cells of marine snails. These electrodes were made by melting capillaries and drawing them out, and, by twisting the capillaries, you could arrange that the channels stuck together to form very fine multi-channel electrodes. Glass wasn't practical for protein crystallization – too brittle – but Patrick realized a similar approach could be used with plastic tubing to make multichannel dispensing tips [3], which the company still uses today. The best tubing was not PTFE, but its chemical cousin FEP, which is very inert but can be softened and melted with a hot air gun. Peter and Patrick, with help from Naomi Chayen, designed a simple moving table and arm that held the multichannel tip and dispensed protein and precipitant mixtures into serology plates [4]. The drops were covered with oil to prevent evaporation.



(a) Dispensing and coalescing droplets in oil with Patrick's patented microfluidic Droplet Reactor; (b) crystals of ferritin grown in an under-oil "microbatch" setup using the Droplet Reactor; (c) an FEP multichannel microtip; (d) the IMPAX crystallization robot; (e) a microbatch experiment being set up by a modern Douglas Instruments robot; (f) part of a modern phase diagram experiment showing phycocyanin crystals (grown without seeding); (g) the resulting phase diagram – the metastable points, red, are found by adding a seedstock. The subset of wells shown in (e) are indicated by the red trapezoid.

This was the IMPAX crystallization system, and it was the first "robot" to be designed specifically for protein crystallization. It worked well in David's lab for both screening and making phase diagrams, and David's student Emmanuel Saridakis published several papers showing phase diagrams [5,6]. There were, however, two problems: (1) our experiments normally covered rectangular regions of the phase space, meaning we needed several experiments to cover all the interesting regions. This made it easy to miss important conditions. (2) There was no easy way to find the

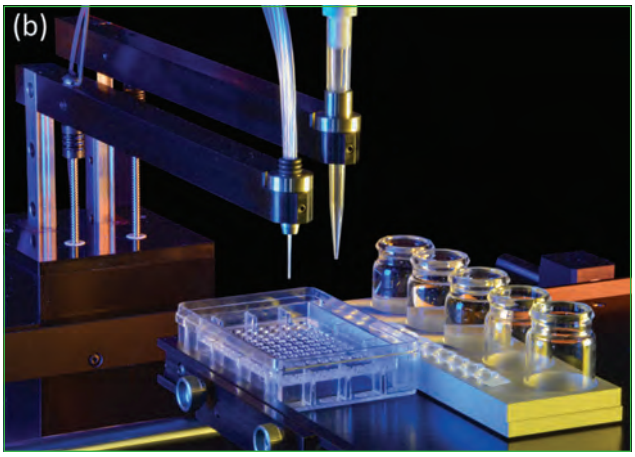
metastable zone, i.e. the region of the phase diagram where crystal nucleation doesn't occur spontaneously, but crystals grow if "seeds" are present. Back then, Emmanuel started at higher concentrations to jump-start nucleation, then subsequently diluted the drops [5], whereas Lesley Haire, another student of David's, worked with temperature if the crystallization system was temperature-sensitive [6].

Since those days Douglas Instruments has introduced many novel crystallization techniques, often in collaboration with our users in the UK, Europe and the USA. Improved experimental design [7] and novel microseeding techniques [8,9] have been particularly fruitful, and phase diagrams became less important – most users could just set up plenty of experiments and rely on chance. But in the last few years phase diagrams have re-emerged as a useful tool for advanced data collection – especially techniques that need very consistent and well-defined samples [10]. Two years ago, we hosted a student in our lab from Southampton University called Jack Stubbs, and we were struck by two realizations: (1) if we turned the experiment through forty-five degrees we could dispense all the points in the yellow triangle shown in panel (g) above in one run – with up to 96 points. (2) We could define the metastable zone simply by repeating the experiment, first without, then with, a seedstock, following Allan D'Arcy's 2007 microseeding protocol [8]. Stefan Kolek, who joined the company in 2009 and is now our third Director, had the great idea of adding seedstock straight into the crystallization cocktail – avoiding having to worry about diluting the other ingredients. The (double) experiment took Jack about 20 minutes to set up with an Oryx8 robot, and allowed him to read off his phase diagram the next morning. The approach can work with almost any protein and allows a very systematic exploration of the crystallization space – helping structural biologists to find the best crystallization conditions for their particular method, whether it's microED, serial data collection (including time-resolved studies), or neutron diffraction.

It's nice to see the work we did in the 1980s finding new applications in a post-Alphafold world!

Douglas Instruments, January 2025

(a) Patrick working on his microfluidic invention, circa 1988. (b) The modern Oryx8 and Oryx4 robots can dispense microbatch-under-oil phase diagrams much more accurately than the original IMPAX robot because drops can be dispensed to the wells "dry" (without oil), then oil is added automatically with the Rainin tip shown on the right.



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BSG Winter Meeting 2024

New Advances and Future Directions in Structural Biology

THE BSG Winter Meeting was held at the MRC-LMB in Cambridge on Friday, December 6th 2024 and was organised by Andrew Carter (MRC-LMB) and Simon Newstead (Oxford). The organisers also chaired the scientific sessions themselves, and things ran so smoothly that at least one of this report's authors failed to notice, or at least note down, who specifically chaired which session, for which that author apologises. The meeting was generously sponsored by the Department of Biochemistry, University of Oxford, Kavli, SPT Labtech, Shimadzu, NanoTemper and iLab Solutions.

Following opening remarks by **Simon Newstead** (Oxford), the first session began with a lecture by **Matteo Allegretti** (MRC-LMB) entitled "The macromolecular architecture of male germ cell nuclei revealed by electron cryo tomography *in vivo*." The speaker outlined the basis of his research on cryo-EM studies of nuclear remodelling in sperm cells and described the structure of spermatozoa, with their well-known tails which are driven by a whole powerhouse of mitochondria. The sperm head consists of a nuclear pocket and a forward facing acrosome which contains the molecular wizardry for docking with and penetrating the female ovum. The speaker described the 110 MDa pores which are known to be involved in Ran-dependent transport across the sperm nuclear membrane. Only the inner ring of the sperm nuclear pore is visible by cryo-EM, in contrast to somatic cells where three layers are visible by this technique. Nuclear pores are critical in regulating gene expression and are connected by septin filaments. They exhibit very low transport activity in spermatozoa where they have a constricted central channel and much reduced scaffolding. The 26S proteasome is present in the acrosome where it is needed to degrade the zona pellucida layer which coats the oocyte. Ion beam milling studies allowed a 7.7 Å resolution structure of the 20S proteasome to be determined showing the proteasome activator protein PA200 binding at the top. The speaker ended by describing nuclear proteasome islands which are present in the protamine DNA but not the acrosome. The next speaker, selected from the submitted poster abstracts, was **Holly Monkhouse** (CIMR) who presented on the subject of "Structural characterisation of a lipid- processing complex." Holly described a system involved in the attachment of glycans to lipid head groups. The speaker explained how the GM2-activator protein (GM2AP) is an essential cofactor in the degradation of ganglioside GM2 to GM3 by β-hexosaminidase A (HexA) in lysosomes. It mediates the interaction between the water-soluble exohydrolase and its membrane-embedded glycolipid substrate at the lipid-water interface. Functional deficiencies in the HexA enzyme result in fatal neurological storage disorders, such as Tay-Sachs disease in which a build-up of GM2 ganglioside occurs. The speaker described how HexA and GM2AP were expressed in mammalian cells for purification by Ni-NTA and SEC. Pull-down studies showed that they interact and a 4.8 Å structure of the complex was determined. Much better crystals were obtained of a catalytically inactive E323 mutant of HexA which allowed the structure to be determined at 2.76 Å resolution and revealed the presence of disordered GM3 – the most common membrane-bound glycosphingolipid in tissues. The main aim of ongoing work is to identify key interacting residues in the complex. The next lecture was given by **Kelly Nguyen** (MRC-LMB) and was on the very interesting subject of "Replenishing the ends: structural mechanisms of human telomerase." The speaker described how human telomeres are located at the tips of the chromosomes and consist of 2 – 100 kb repeats of the short sequence GGTTAG which are replicated by an enzyme known as telomerase. This possesses a reverse transcriptase subunit called TERT. Telomeres become shorter during ageing and are implicated in cell death. In contrast, around 90 % of cancers have upregulated telomerase activity. The enzyme has a remarkable ability to produce multiple copies of the repeat sequence from an internal RNA template. The speaker described an earlier analysis by cryo-EM at 8 Å resolution of the human enzyme which has since been extended to between 3.4 and 3.8 Å resolution, revealing the presence of histones within the telomerase complex. Histones H2A and H2B bind to the telomerase RNA using the same interactions which they use to bind DNA. The resolution was extended with some difficulty due to the enzyme's extreme conformational heterogeneity which meant that only around 1 % of the particles were used in image reconstruction. Mining the remaining 99 % revealed a transient dimer structure in which the linker of the RNA template for the reverse transcriptase (hTR) was resolved for the first time. It was found that hTR knockouts exhibit reduced telomere length and a number of disease-related mutations in telomerase which give rise to premature ageing are now known to affect residues that bind hTR. Next up, the selected poster speaker, **Quentin Smith** (MRC-LMS, Imperial) gave a lecture entitled "Structural basis of negative supercoiling induced CRISPR/Cas9 off-target activity." For the uninitiated CRISPR is an acronym for clustered regularly interspaced short palindromic repeats and, together with the enzyme Cas9, represents a tool for genome editing. Cas9 is a ribonucleoprotein which unzips the DNA double helix and cleaves the backbone at sites guided by its RNA component that can be engineered to make it cut at specific DNA sequences. Negative supercoiling is known to make the enzyme lose specificity. To understand the basis of this effect, structural studies by cryo-EM were undertaken using negatively supercoiled DNA mini-circles which consist of around 100 bp and are about 20 nm in diameter. The structure of Cas9 bound to mini-circular DNA was determined at 3.1 Å resolution revealing that the enzyme's HNH domain moves approximately 14 – 15 Å relative to its position in the presence of linear non-supercoiled DNA. A subsequent 2.6 Å resolution cryo-EM analysis revealed that base mismatches occur in the DNA-RNA complex and the HNH domain (which cleaves one of the DNA strands) gets pulled in, triggering off-target

strand cleavage. The concluding lecture of the morning session was given by **Tracey Gloster** (St Andrews) and was entitled "Structure and function of carbohydrate processing enzymes." Tracy began by outlining some aspects of carbohydrate metabolism such as glycoside hydrolases and sulphatases as well as enzymes which are involved in the breakdown of complex sugars, such as the cell surface heparan sulphate proteoglycans. Particular focus was on the human GlcNAc 6-sulphatase enzyme, the X-ray structure of which was determined initially at 2.7 Å resolution and, following endo H deglycosylation, its resolution was extended to 1.9 Å. Enzymes in this family have a catalytically essential cysteine residue which is converted into a formylglcyine and then hydrated to a diol that becomes sulphated transiently by the substrate during the reaction. Genetic deficiencies of these enzymes cause mucopolysaccharidoses (MPSs), in which incompletely degraded carbohydrates accumulate in the lysosomes. Many of these lysosomal storage disorders are linked with severe neurocognitive deficiencies. Ambitious approaches to discover small molecule 'chaperones' which could stabilise the enzyme and prevent its misfolding were discussed.

Following lunch and posters, **Harry Low** (Imperial) gave a lecture entitled "ESCRT-III-like proteins in bacteria: their role in membrane stress and repair." Harry outlined the bacterial phage shock proteins pspA, LiaH and Vipp1 which are largely α-helical in structure and form large ring assemblies with C14 symmetry. The N-termini of the membrane binding domains hang into the inner lumen of the ring which is then able to bind and deform membranes. These bacterial or plastid proteins are involved in membrane remodelling and repair, and are homologous to the ESCRT-III system in eukaryotes. Vipp1, from the cyanobacterium *Nostoc punctiforme*, was shown by cryo-EM to bind to supported lipid bilayers wherever the surface is 'cracked' or distorted. Videos obtained by atomic force microscopy (AFM) demonstrated that surface binding is followed by a remarkable effect in which the central ring pops out, forming spirals which ultimately allow membrane vesicles to bud off. In these studies, Vipp1 was observed to form planar sheets and helical filaments, as well as the rings, and all of these forms are implicated in mitigating plastid-associated membrane stress. Next up, the selected poster speaker, **Ben Nash** (UEA) presented on the subject of the "Structural basis for extracellular reduction of dimethyl sulphoxide by *Shewanella oneidensis* revealed by cryo-EM." Shewanella are deep sea gram negative bacteria adapted to very low temperatures and extremely high pressures. The speaker began by reviewing the electron transfer complexes which are involved in oxidative phosphorylation and described how gram negative bacteria use c-type cytochromes to effectively push electrons out of the cell. The main shewanella electron transport protein for reduction of extracellular substrates is known as the MtrCAB complex. This is involved in reducing metal ions and detoxifying reactive oxygen species such as hydrogen peroxide. The structure of *Shewanella baltica* MtrCAB was published by the UEA group in Cell in 2020. This revealed a heterotrimeric complex that consists of two multi-haem cytochromes, MtrC and MtrA, and a β-barrel transmembrane protein, MtrB, that surrounds and insulates MtrA. A network of 20 bis-His coordinated haems spans the complex, forming an electron transfer pathway of 185 Å in length. More recently, the DMSO reductase DmsEFAB, which has a molybdopterin cofactor, has been studied by cryo-EM at 3 Å resolution revealing the involvement of 10 c-type haems and an iron-sulphur cluster, in addition to the pterins. Next, the BSG Early Career Prize lecture was given by **Lindsay Baker** (Oxford) and was entitled "Using integrative structural biology to understand how cells respond to their environment." The speaker covered a range of topics including biological membranes and their complexity, as well as the use of bacteria as a model system for studying interactions with the environment. Cryo electron tomography requires ion-beam milling to generate thin samples and such studies have been correlated with light microscopy. *E. coli* cells growing in the exponential phase develop membrane invaginations and, as they enter the stationary phase, the cytoplasm shrinks progressively. Interesting morphologies are observed on treatment of cells with antibiotics. The speaker described the use of DNA origami as a tool for creating labels for specific proteins which are readily visible on the cell surface by EM and fluorescent tags for light microscopy.

Arrival at the entrance hall of the MRC-LMB (Cambridge).

Conference lunch at the 2024 BSG winter meeting.

The speaker concluded by outlining an improved workflow for mass-spectrometric studies of membranes and membrane proteins, avoiding the use of detergents. Last but not least, the final speaker of the meeting was **Helen Cooper** (Birmingham) who spoke on "Native ambient mass spectrometry (NAMS): in situ analysis of proteins and their complexes in tissue." Helen described the NAMS technique which allows proteins to be studied in native-like aqueous, rather than denaturing, solvents in their folded states, along with their preferred quaternary structures and in physiological complexes with other endogenous proteins. The speaker described how sections of tissues can be imaged by continuous flow sampling using the technique of nano-DESI (desorption electrospray ionisation) with a line scan spacing of 200 µm. Helen described studies of the multimeric states and assemblies of various proteins, such as the ridA homotrimer in the kidneys. Also described were studies of brain tissue with particular emphasis on a mouse model of amyotrophic lateral sclerosis, or motor neurone disease. The G93A mouse expresses a superoxide dismutase (SOD) G93A mutant and partly de-metalled enzyme accumulates in the head and neck controlling regions of the brain as well as the central cord of the spine. Helen also described studies of the eye lens aquaporin which is a transmembrane protein involved in fluid transport.

Following the coffee break, a town hall-style discussion was held on "Future directions for structural biology" and was chaired by the organisers. A system for postgraduate training in structural biology and biophysics which would involve centralised teaching of the theory and practice of different techniques for short periods of time, allowing the students to return to their respective groups for their own research, was discussed. Generally this hub-and-spoke training model was accepted as a good proposal by the attendees who then went on to discuss further issues such as the involvement of AI in their research and the value of a town-hall discussion at BSG meetings, amongst many other things.

This was followed by a drinks reception in which poster prizes were awarded to **Abby Lin** (Oxford) for a poster entitled "Structural basis for lipid regulated activity of human CLC7, the lysosomal chloride antiporter" and to **Victoria Cushing** (ICR) for a poster entitled "Structural basis of T-loop-independent recognition and activation of CDKs by the CDK-activating kinase." The organisers, **Andrew Carter** (MRC-LMB) and **Simon Newstead** (Oxford), must be congratulated for delivering such a well-organised, well-attended and scientifically excellent meeting. We also thank the generous sponsors.

Jon Cooper, UCL and **Mark Montgomery**, Syngenta

***Tracy Gloster** (St Andrews) addressing questions from an enthusiastic audience at the 2024 BSG winter meeting.*

Scenes from the poster sessions and reception at the 2024 BSG winter meeting.

Report on the CCP4 Study Weekend 2025

CCP4 Study Weekend, 7th – 9th January 2025, Nottingham

Using software, AI and other methods to advance crystallographic models

Proceedings from the CCP4 2025 study weekend will be published in a special edition of Acta Cryst D. The CCP4 study weekend was preceded by the **Diamond user meeting** – and several published papers on beamlines are referenced below. The day 2 morning session **"What's new in CCP4? "** is also summarised below.

The **Diamond user meeting** preceded the study weekend and started with a talk from **Dave Hall** (DLS), on **"**MX Group Capabilities and News update**"**. There are now seven MX beamlines: I03, I04, I04-1, I23, I24, VMXi [1] and VMXm [2] with unattended data collection (UDC – https://www.diamond.ac.uk/Instruments/Mx/I03/I03-Manual/Unattended-Data-Collections.html) available on I03, I04 and I04-1. I23 is a long wavelength beamline where anomalous data can distinguish chlorine, potassium etc. Access to Diamond is proprietary (paid) or non-proprietary (free – but you must publish results). Samples must be declared before a visit. From December 2027 Diamond will undergo an upgrade to a 4th generation synchrotron, and be shut-down for 18 months. **David Aragao** (DLS) then talked about the "I04 beamline: an update on dose-aware data collection strategies." He recommended using SET TARGET DOSE (in unattended or attended) data collection – 15MGy maximum (for ligands) or 3.33MGy for anomalous data collection [3]. **Mike Hough** (DLS) then continued, talking about "Exploiting automated high throughput room temperature crystallography at VMXi." The system is designed for room temperature *in situ* data collections (rotation limited to 60 degrees per crystal). Multiple crystals are needed per dataset and automated processing is used to obtain a complete dataset [1, 4]. **Allen Orville** (DLS) gave a talk about "The XFEL Hub at Diamond: creating tools for time-resolved crystallography and spectroscopy." Allen is the lead on a proposed UK XFEL project (https://xfel.ac.uk/). Microcrystal slurries are generally used for data collection, and generating enough material for experiments can be challenging. Allen talked about a recent successful trip to the European XFEL (Hamburg), where data collection was matched more optimally to the repetition rate of the XFEL, helping minimize the sample volume needed [5]. **Robin Owen** (DLS) then gave a presentation on "Taking your samples further: opportunities for microfocus and serial MX at I24." I24 is a tuneable microfocus beamline, with variable sample holders – pins, chips etc. to carry out a range of experiments. This includes serial data collection using liquid extrusion or multiple crystals [6] on a chip, with the possibility of using UV-Vis spectroscopy as well as a PORTO laser to carry out light driven reactions [7]. I24 is equipped with a CdTe detector, which allows data collection at higher energies (20 KeV) without the loss of counts (cf older detectors where detector quantum efficiency was lost at high energies). **Gwyndaf Evans** (DLS) spoke on "VMXm and HeXI." HeXI will be for high intensity electron diffraction for crystals between 300 nm and 3 µm in size. 3D electron diffraction should be improved by using the higher energy electrons (up to 1 MeV). The first electrons are planned for summer 2026. VMXm, like I24, is a microfocus beamline but designed to collect data from crystals <10 µm, mounting crystals on cryoEM grids [2]. They recently collected better than 1Å data on virus crystals <5 µm in size. **Taylah Andrews-Clark,** a joint Oxford/Diamond PhD student, then talked about "Investigating the use of cyclic peptides as inhibitors and substrates for the SARS-CoV-2 Main Protease." Using the chip setup at I24 – she looked at a pH jump to initiate reactions (or photocleavage, or diffusible ligands). **Megan Lambert** (DLS) then talked about **"**Room-temperature fragment-based screening at Diamond: towards the optimisation of a high- throughput experiment." Megan is a VMXi post-doc, working closely with the XChem team to optimise room temperature fragment screening on VMXi. **Neeli Katti** (DLS) a software engineer from Diamond spoke about enhancing the Diamond user experience in a talk entitled "Let's polish the Diamond: enhancing user experiences together." Then **Frank von Delft** and **Warren Thompson** (DLS) spoke on **"**Faster, larger, better, XChem: fast-forward fragments for progressing fragment hits" [8]. They discussed four stages in the process: (i) fragment-screen, (ii) fragment-to-hit, (iii) hit-to-lead, (iv) lead optimisation, followed by how to go from fragments to leads in the following three ways: growing, merging and linking. They showed how fragment merging is effective (if one can do 100's). I04-1 will be replaced with K04 in the Diamond-II upgrade. Fragmentation and knitwork are also strategies to aid in merging and design [8]. The session was finished with a Diamond User Committee user survey (on mobile phones) by **David Briggs** (Francis Crick Institute) and **Colin Levy** (Manchester).

This year's CCP4 study weekend was entitled: "**Using software, AI and other methods to advance crystallographic models**" with the talks due to be published in Acta Crystallographica D in 2025. The meeting was organised by **Elke De Sitter** (IBS, France), **Deborah Harrus** (PDBe, UK) and **Dorothee Liebschner** (LBNL, USA). Talk titles (and abstracts) and recordings of the talks are currently available at https://studyweekend.ccp4.ac.uk/programme/.

The main conference started with a keynote lecture by **Yvain Nicolet (**IBS, France) on "Structure-function relationships of metalloproteins and assembly of their metallocofactors." The enzymes discussed contained both Fe_4S_4 and S-Adenosyl methionine (SAM) and catalyse an important variety of reactions. For example, the enzyme HydG has three active sites: one for radical-based tyrosine splitting, another for dehydroglycine splitting and a third for CO production. The day in the lecture theatre was concluded by an enjoyable round table discussion: "Skill mismatch: are we training structural biologists for jobs that won't exist?" led by **Robbie**

Joosten (Netherlands Cancer Institute), with **Tom Davies** (Astex Pharmaceuticals), **Alisia Fadini** (Cambridge), and **Julie Menetrey** (Paris-Saclay). The over-riding feeling was despite the need for improved chemistry and programming skills, structural biology is still a much-needed skill and jobs will continue to exist for well-trained structural biologists. The day's proceedings finished with an informal networking event and poster session.

The second day began with a session entitled **"What's new in CCP4?"** and started with an overview lecture of the same title by **Ville Uski** (UKRI-STFC CCP4). The current version is CCP4 9.0 (Ilkley Moor). New functionality includes: Dials processing via – DUI2, **"**Modelcraft**"** for model building and ConKit (a Contact Prediction ToolKit), also Slice'N Dice, a tool for cutting domains up for molecular replacement. Following this, a talk entitled "What's new in the land of Coot: demo of Moorhen and the newly updated ligand tools" by **Lucrezia Catapano** (UKRI-MRC LMB) covered both Moorhen and Coot 1.1. Coot 1.x is a new version with a re-write of the graphics, allowing one to make good figures, and 'noughties physics' has been reintroduced so that the program behaves like earlier versions from the 2000's. Moorhen is a web version of coot, replacing ccp4mg to produce nice figures (try www.moorhen.org – see also https://moorhen-coot.github.io/wiki/). The current recommendation is to have both coot 0.9 and coot 1.1 installed as not everything has been fully transferred yet. The next lecture was entitled "New approaches for structure refinement in CCP4i2" by **Martin Malý** (UKRI-MRC LMB) who described serial crystallography tasks in CCP4i2. He also spoke about Servalcat having improved twin refinement and how it uses intensities (eliminating the need to do Wilson scaling) – which can improve maps. Servalcat can also refine using cryo-EM SPA (single particle analysis) maps in ccp4i2. **Jools Wills** (UKRI-STFC CCP4) then gave a lecture describing "Linking data sources with CCP4 Cloud: a fully online setup for structure determination." CCP4 cloud requires a web-browser and sits between data collection and the PDB. Datalink is a file storage api which can pull data (raw images) from – XRDA, zenodo, PDBj, etc. and fetch diffraction images from internet depositories. It can also push data to the (CCP4) cloud, managing both data and metadata. The CCP4 Cloud Globus Endpoint allows users to authenticate themselves via an stfc.ac.uk or a globusid.org account. The final talk in this session was entitled "What's new in CCP4 cloud" and was given by **Mario Fando** (UKRI-STFC CCP4) who described new developments in the cloud. There are 19 new tasks – giving 93 tasks in total. There is now an option to change permissions, so there is control over who shares or can see and process data, as well as the addition of a dark theme and custom workflow creator, which are useful. The cloud is looking like a good way to go.

The next session entitled: **"Demystifying the black box – new features and old tricks to use software efficiently"** started with **James Beilsten-Edmands** (DLS) talking about "Approaches to processing and selecting data in multi-crystal collection strategies." Originally data collection was from multiple crystals [9]. However, by the 1990s cryo-cooling had reduced damage about 70-fold and datasets from single crystals became standard. However, there is a move back to collecting partial datasets, with the advent of XFELs [10] and serial crystallography at synchrotrons, requiring many crystals for a dataset. Partial datasets (from several crystals) can be collected and merged using DIALS [11], giving high multiplicity and low dose. DIALS cosym is used to look at different symmetries in data from multiple data collections, and if you plot Rcp (derived from Rd) you can see where X-ray damage causes problems with data [12]. Then **Airlie McCoy** (Cambridge) gave an excellent talk entitled "Solve your structure with MR at warp speed." Phasertng (the next generation) is a new molecular replacement maximum likelihood package that expands and improves on the functionality of Phaser (see https://www.phaser.cimr.cam.ac.uk/). The new software particularly addresses molecular replacement cases that are challenging because there are a large number of parameters of the search space that need to be explored for success, including cases where the crystal contains pseudo-symmetries. New programs/procedures in the package are Picard, Riker, Xtricorder, Changeling and Scotty. The talk included some short Star Trek phaser-themed "mash up" videos for audience entertainment. **Gerard Bricogne** (Global Phasing) then gave an informative talk entitled: "Some considerations on diffraction data quality, diffraction limits and refinement approaches and outcomes." The staraniso server is useful for submitting processing jobs to (http://staraniso.globalphasing.org/). It works well as it understands that not all datasets can be treated with a single resolution cut-off, but instead have different resolutions in different directions (understanding this can lead to an improvement in statistics/structures). For more details, see a discussion of this topic on the CCP4 bulletin board on 17th October 2022 entitled "re: PAIREF, Anisotropy and STARANISO" by Gerard Bricogne.

After lunch the session was: "**Using prior knowledge to improve and validate models.**" **James Holton** (California) talked about how "Untangling models reveals hidden information in structural data" (see the CCP4 Bulletin Board topic entitled "Introducing the UNTANGLE Challenge" on 18 Jan 2024). James believes the future of crystallography includes structures with alternate conformations, dynamics, mechanism, and overlapping states; however, small signals are sometimes a problem. According to Parseval's theorem, the rms error in the electron density map is proportional to the rms error in the (complex) structure factor. If you had an *R*-free less than 3% you could see hydrogens at 3 Å, in a test dataset a 6-sigma peak is observed! Then **Milana Bazayeva** (Cleveland Clinic) talked about "Leveraging large-scale data to refine and validate metalloprotein structures: insights into metal coordination and carboxylate interactions." They use the MetalPDB database to understand trends in metal coordination to carboxylates. They defined a donor atom as a non-hydrogen atom within 3 Å of the metal ion, and there are three types of carboxylate coordination to metal ions: both oxygens (bidentate) or one oxygen (either monodentate syn or monodentate anti). Calcium ions have all three carboxylate types of coordination. The session finished with a joint presentation on: "Reconstructing biological molecules with help from video gamers" by **Robbie Joosten** (Netherlands Cancer Institute) and **Scott Horowitz** (Denver, USA). Scott gave students maps to see how well they could fit a sequence; about 10% of students got a better structure than deposited in the PDB using FOLDIT (https://fold.it/). These models can sometimes be used to improve structures already in the PDB. 83 structures in the PDB-REDO database (https://pdb-redo.eu/) are now based on FOLDIT models; these models have better geometry than the original depositions.

The last session on the second day was "**AI in structural biology I: predicted models and how to use them**." **Eva Smorodina** (Oslo, Norway) talked about "AI for molecular modelling and protein design." A central dogma is that sequence gives structure which gives function and this drives all of the physics-based homology modelling techniques as well as threading and *ab initio* folding. The speaker covered many issues such as protein design, both *de novo* and methods based on known domains, as well as their reliance on scoring and the shift to AI and alphafold 2 which uses multiple sequence alignments. Three useful programs are Alphafold3, Boltz-1 and Chai-1. Alphafold3 seemingly has issues with disordered regions and antibodies giving only a 60 % success rate with antibody-antigen complexes. Chai-1 may be better for antibody complexes but one needs to predict 1000s of models. RoseTTAFold and REdiffusion were also mentioned as valuable methods for protein designers to try. **Oleg Kovalevskiy** (Google Deepmind, UK) talked on "Accelerating biological research using AlphaFold." The AlphaFold3 (AF3) server can model some 5,000 amino acids and can model protein-protein interactions, albeit with a lower success rate in modelling nucleic acids. However, AF3 outperforms AlphaFold-Multimer 2.3 and it can also predict metal-protein interactions [13]. AF3 does multi-sequence alignments and uses tokens: 3 tokens for 3 amino acids or 3 nucleic acids or 13 tokens for a small molecule (one per atom). Timings of 2 – 3 minutes are required for 500 tokens, with 1,000 tokens requiring of the order of 6 – 8 minutes. Oleg recommended using 20 different seeds with AF3, and compared the AF3 server and the github versions (note for non-academics commercial versions must be used). AF3 successfully modelled zinc and calcium binding sites in honeybee vitellogenin and can also model proteins with more complex ligands bound. To use AF3 correctly use the confidence metrics (> 0.8 confidence is good) and including metal ions can improve the quality of scores. The speaker recommended checking the documentation online at the EBI and github, etc. Modelling protein-protein interactions in a dimer bound to another protein, for example, is simply a case of pasting in two identical sequences for the dimeric protein plus the sequence of the other protein. **Clément Bernard** (Paris Saclay) then spoke on "Recent advances and limitations of RNA 3D structure prediction." The speaker described how three methods are available: (i) predicting secondary structure, (ii) using a known 3D structure, and (iii) *ab initio* approaches. Secondary structure prediction for long sequences is often difficult but known tertiary structures enable the use of template based approaches to map sequence onto structures. *Ab initio* methods often involve MD (molecular dynamics) or Monte Carlo simulations followed by energy minimisation and scoring. The speaker described how following on from the success of AF3 in predicting protein structures they are now running CASP (Critical Assessment of Structure Prediction) on more tricky RNA structures [14]. Conclusions: try *ab initio*, template, deep learning and AF3.

Day 3 started with a session entitled: "**AI in structural biology II: other applications**." **Wladek Minor** (Virginia) spoke on "Artificial intelligence in structural biology – the good, the bad and the ugly." The speaker described how the website entitled "Check MyBlob" (https://checkmyblob.bioreproducibility.org/) helps you recognise and validate ligands in X-ray electron density [15]. Wladek has been part of an NIH project on an "Integrated Resource for Reproducibility in Macromolecular Crystallography (IRRMC)" developed as part of the BD2K (Big Data to Knowledge) NIH plan to archive raw data from diffraction experiments. Data curation is sometimes a problem in the PDB (there are 900 Zn atoms with an occupancy 0.0 and 38 Zn atoms occupancy > 1.0). Check my metal now also checks the reported PDB file crystallisation conditions. Then **Piero Gasparotto** (Paul Scherrer Institute / Microsoft Quantum, Switzerland) talked about "Integrating machine learning frameworks in scientific workflows." He divided the talk into two sections: (i) experiments and (ii) simulations. Detectors are improving quickly – for example the JUNGFRAU detector can output more than 2,000 images per second. The speaker then covered serial diffraction experimental work using the TORO Indexer which is a PyTorch-based algorithm specifically written for this technique [16]. The second part of the talk was on simulations and included approaches solving the Schrödinger equation from quantum chemistry models. Pitching wave function methods against molecular dynamics raises 'cost versus accuracy' considerations given that one can still not trust the model, density functional theory (DFT) being more accurate. The last talk in the session was from **Mitchell Miller** (Rice) who talked on "Exploring deep learning approaches to solving the phase problem" [17]. This talk challenged some of the more experimentally minded members of the audience.

After a break there was a session focussing on "**Dynamics**" which began with **Michael Wall** (Los Alamos National Laboratory) speaking on "Molecular-dynamics simulations of protein crystals to enhance conventional modeling and refinement" [18]. MD forcefields, local geometry (distances, angles and dihedrals) and van der Waals forces were covered, as were Coulombic and non-bonded terms. The talk reminded some of Xplor. They are looking at both Bragg and diffuse scattering components, having built supercell models to measure "fractional HKLs" [19]. Then **Sergei Grudinin** (Grenoble-Alpes) talked about "Explaining conformational diversity in protein families through molecular motions and predicting them with unsupervised and supervised learning approaches" [20]. To perform their functions, proteins move and deform – processes that can be modelled by MD which solves Newton's equations of motion for each atom. We can also describe such systems with normal mode analysis (NMA) and an elastic network model. Connecting PCA (positional covariance analysis) with NMA, the speaker talked on exploring conformational variability in protein families using a fully automated computational pipeline called DANCE (Dimensionality Analysis for protein Conformational Exploration). The speaker then considered a range of questions such as whether physiologically relevant, but hitherto unseen conformations, can be correctly predicted. Protein language models ProstTS (sequence + structure) and ESM3 (sequence + structure) were found to be better than ESM2 (only sequences) and NMA. **Virginia Apostolopoulou** (CFEL, Hamburg) followed with a talk entitled 'Mathematically deriving protein flexibility for single protein structures" which entailed understanding how we get from one protein conformation to another to help inform about protein dynamics. She introduced the software RoPE (Representation of Protein Entities [21]) and talked about how this can be used to understand the motion of torsion angles between different structural states using the Vagabond algorithm. A total of 244 structures of haemoglobin were taken from the PDB to understand the changes between the T and R states. The speaker then

looked at γD crystallin, which has 16 structures in PDB. However, it was followed up by asking what could be done if there was a lack of experimental data? The speaker concluded by presenting a kinematic flexibility analysis and showed that these results mapped well with those from the RoPE analysis.

The last session was entitled: "**More ways to characterize your sample**" and began with **Nicolas Caramello** (ESRF) presenting on "Kinetic cryocrystallography vs time-resolved crystallography: when to trap reaction intermediates and when to observe them in real-time." Nicolas spoke about the comparison between time resolved crystallography at the XFEL or the synchrotron, and what can be gained by using each method, including gains in time resolution by using an XFEL. He then also spoke about freeze trapping intermediates which can be a beneficial technique depending on what information one is trying to find during the experiment, with the caveat that it is no longer being carried out at physiological conditions. Following this, **Shumeng Ma** (Yale) spoke about "Placing low-occupancy fragments using the anomalous signal of sulfur and halogen atoms." Shumeng described the use of the anomalous scattering of heavy atoms to identify positions of S, P, Cl, Br and I atoms in a range of fragments. The data were collected at I23 (DLS) at 4.5 keV in vacuum, where the signal for each of these atoms was amplified. She showed some nice examples where it would be difficult to interpret electron density maps traditionally, but with the additional anomalous peaks it was clear which orientation of the fragments should be modelled. **Zoë Fisher** (ESS, Lund) followed with a talk entitled "Joint neutron and X-ray protein crystallography: complementary tools in the detailed analysis of enzyme structures." The speaker started off by introducing the differences between X-ray and neutron structure determination and how hydrogen and deuterium have different scattering cross-sections. Neutron diffraction can be a powerful tool if one is wanting to locate hydrogens clearly in a structure. To do this with neutrons, samples need to be deuterated to get clear maps. Perdeuteration, in which crystals are grown from deuterated material is the most beneficial method, since all hydrogen atoms are replaced by deuterium, whereas if you soak, not 100 % of the hydrogen atoms are replaced. The ESS is currently under construction in Lund with 15 state-of-the-art instruments and the first neutrons will be available later this year. **Ulf Ryde** (Lund) gave the last talk entitled "Improved protein structures by quantum refinement" covering the methods, applications and extensions of quantum chemistry as a refinement technique. DFT (density functional theory) was reported to give a more accurate view of the site of interest but generally it is challenging to run. The speaker described the use of QM/MM (hybrid quantum mechanics/molecular mechanics) as their preferred approach, the MM part being less accurate while quantum chemistry can be done at the active site or specific metal binding sites. Some interesting applications seemed to question the accuracy of some structures in the PDB [22, 23]. This type of refinement can be more accurate if you know what you are doing and understand your chemistry [24].

Ben Bax, Cardiff
Anna Warren, DLS

*Speakers at the 2025 CCP4 study weekend: **Shumeng Ma** (Yale), **Yvain Nicolet** (IBS) and **Airlie McCoy** (Cambridge). Photographs kindly provided by UKRI-STFC and reproduced with permission.*

A panel discussion, the organisers Elke De Zitter (IBS), Dorothee Liebschner (Berkeley) and Deborah Harrus (EBI), the audience and the traditional dance at the 2025 UKRI STFC study weekend. (Photographs: UKRI-STFC).

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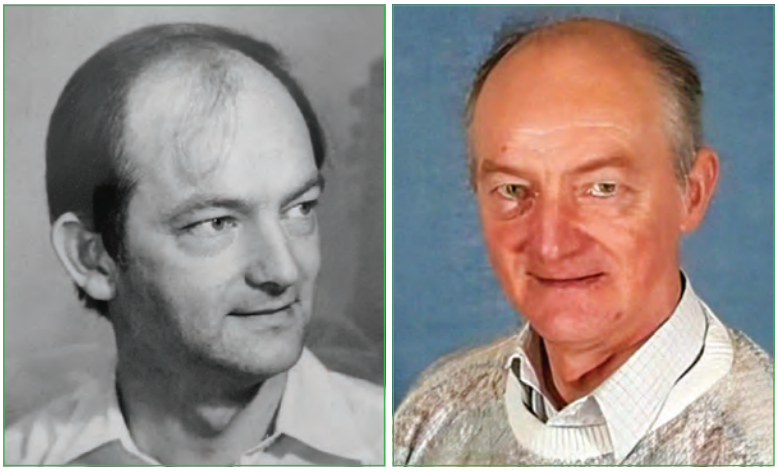
Obituary for Peter Main (1939-2024)

PETER Main, who died on 3rd November 2024, was an innovative scientist and a brilliant teacher. Since the 1960s, Peter had helped transform our knowledge of chemistry and biochemistry, by providing computer software which revolutionized chemical crystallography. He later worked on density modification algorithms which helped solve many protein structures, as well as inspiring others to push these methods further.



Peter Main (1939–2024)

He was an outstanding teacher, always lucid and clear when explaining tricky crystallographic phenomena, and many of us who also worked in the field are deeply indebted to him for this.

Peter was born in the small Northumbrian village of Newbiggin-by-the-Sea, an idyllic spot on the Northumbrian coast. (This maybe helps explain the delight he felt when he could escape into the countryside.) However, he was destined for academia. He studied Physics at the University of Manchester Institute of Science and Technology, and proceeded to do a PhD with Michael Woolfson, a theoretical crystallographer who had made important contributions to the principles underlying phase estimation for structure-factor observations, already labelled as 'direct methods for phase determination.'

Peter's thesis covered more classical crystallographic material; he solved a 16-atom structure by Patterson methods and programmed various calculations, first in a language called Autocode, but later in the much more flexible Fortran language which would dominate early scientific software development.

After his graduation he spent time as a postdoc in Purdue, Indiana, USA, working with Michael Rossmann. Michael had helped develop mathematical methods to use the information present due to non-crystallographic symmetry in protein crystallography, and already saw that this could help refine phases for highly symmetric molecules such as viruses once it could be precisely described. Peter contributed to solving this problem, both by developing the theory and programming the required software.

By 1967, Michael Woolfson had been appointed as Professor of Theoretical Physics at the newly established University of York. He invited his former graduate student, Peter, to join the department as a lecturer, apparently without needing to consult human resources or anyone else!

There followed a period of great creativity, culminating in 1971 with the release of the program MULTAN. MULTAN implemented a 'direct methods' procedure – assign phases to three reflections to define the crystal origin, select a few of the largest reflections and assign them random phases, then generate new phases for more reflections using the 'tangent formula.' The results were ranked by a range of figures of merit; the most promising sets were used to calculate maps, and if these showed a structure which made chemical sense, the trial was deemed to be a success.

For the next decade MULTAN was used to solve most small non-centrosymmetric structures worldwide. It was (and is) a prime example of good programming technique. The program was modular, meaning that, for instance, if a more sensitive figure of merit was discovered, it was simple to add it or replace existing ones. The crystallographic library routines were well designed, well documented and rigorously tested, functional for all space groups, and reusable in other applications. The results were clearly presented and for portability the programming language used was the most basic Fortran.

By 1971, York was recognized as one of the most active centres of direct methods development. Michael and Peter organized a number of very influential direct methods schools. The first, sponsored by NATO, gave a broad overview of the theory and methods of structure determination, and stimulated many students who went on to become leading crystallographic theoreticians themselves (Fig. 1). It was followed by many others – in Erice (1974), York (1975), Erice (1978) and York (1980).

Peter's lectures on direct methods were always beautifully organized. Whenever possible he was asked to open a session – he could make complex ideas seem comprehensible and set the context for new innovations.

During the 1980s, protein crystallographers were realising that although the limited data and poor initial phase estimates obtained for proteins could not yield images that showed individual atoms, their maps did possess other features, such as solvent boundaries, which provided information to improve the phase estimates (Wang, 1985). Michael and his Chinese colleagues were exploring these ideas, and by the late 1980s Peter and his research students Kam J. Zhang and K. Cowtan were providing software applying sophisticated

Fig. 1. The 1971 NATO School official photograph. Typically, given Peter's modesty, he cannot be identified here. Included in the front row are M. M. Woolfson, P. P. Ewald, D. Rogers, D. Viterbo and P. Beurskens. A. L. Spek is two rows behind the lady in the middle of the front row. W. Duax is behind Rogers.

density modifications in real space to perform direct-methods style phase improvement. The programs were distributed with the CCP4 (Collaborative Computing Project Number 4) suite of programs (Winn *et al*., 2011; Agirre *et al*., 2023) and widely used (Main, 1990a, 1990b; Zhang & Main 1990a, 1990b). This led to fruitful collaborations between the physicists and the structural biologists based in York Structural Biology Laboratory (YSBL). SERC funded a collaborative project to assist the links, and the two groups worked closely together over the next decades.

Physics Review magazine was first conceived in May 1990. Several staff at York were particularly excited by the possibilities and submitted a proposal outlining a range of possible approaches to the design, content and overall philosophy of the new magazine. This proposal was successful and led to the establishment of a multidisciplinary editorial board based at York, whose joint efforts led to the first issue being circulated to schools in September of 1991. It was to be 'pitched at the middle-ability 16- to 17-year-old physics student, who has a reasonable grasp of physics at GCSE level, is in the process of getting to grips with some A-level or equivalent material and whose main interest is not necessarily in pure physics.' Over the next 24 years Peter submitted 125 articles to the magazine, on subjects ranging from surfing to music.

Peter expressed his love of the outdoors through cycling. He once told me (EJD) that he always cycled with a packed lunch because he did not like to leave his bicycle alone while he went into a cafe! In 1990, after a heart bypass operation a year earlier, he cycled the 1038 miles from Lands End to John O'Groats to raise money for a coronary support group. He was also a keen walker; in 1981 five members of the Physics Department bought Goose Howe, a cottage in the Lake District, and Peter had spent a week there just before he died.

He was passionate about music too, playing the church organ and Northumbrian small pipes. After his retirement the one place you could be sure to find him was at the keyboard in Heslington Church. Both enthusiasms informed his teaching – he taught undergraduates about the physics of music, and published articles in Physics Review about the physics of cycling.

To sum up, Peter was a rock – always patient, always well informed, always willing to support his students and collaborators, modest to a fault and self-effacing, but always there when needed. We are all lucky to have had such a friend.

Eleanor Dodson and
Kathryn Cowtan, York

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Obituary for Jan Drenth (1925-2025)

WE all know what proteins are. But what do proteins look like at the smallest level? That is the question which Emeritus Professor of Structural Chemistry, Jan Drenth at Groningen in The Netherlands worked on throughout his career. Very sadly, Drenth died on February 11, 2025, just 9 days before his 100th birthday.

Proteins play a role in all kinds of processes in nature, also in our own bodies. Muscle fibres are made up of the protein myosin and our digestion can only function thanks to enzymes that break down food into useful building materials. If proteins do not function properly, it can lead to serious diseases, from hemophilia to Alzheimer's.

To understand how proteins work, you must know their three-dimensional structure in detail, up to the level of the atoms from which they are built. Those atoms determine what the 3D structure of proteins look like and these structures are of great importance for the (correct) function of these molecules. Jan Drenth was at the helm of this kind of structural research from the beginning.

After studying chemistry in Groningen (cum laude completed in 1952) his PhD research followed and that was aimed at unraveling the structure of proteins with a technique called X-ray diffraction. For this work he had to grow crystals of a protein after which he could calculate the protein structure on the basis of the scattering of X-rays.

The technology was still young when Drenth threw himself into this. His PhD research yielded an overall picture of the molecule, but about ten years later it turned out to be possible to zoom in right up to the level of atoms. In 1968, Drenth published a highly detailed structure of the protein-splitting enzyme papain from the pawpaw plant *Carica papaya*. At the time this was the third enzyme worldwide whose structure had been unraveled at atomic level and put the Groningen group on the world structural biology map.

Drenth worked, with the exception of a year as a postdoc in the US, his entire career in Groningen. There he laid the foundations for the structural biology field. In the 1980s, he (together with Wim Hol, George Robillard, Erni van Bruggen and Herman Berendsen) received millions for new equipment, giving structural biology research in Groningen a huge boost.

With a series of PhD students, he managed to determine the structures of numerous other proteins. He enjoyed being in the lab together with PhD students, who later started working in other places on this kind of research. On the funeral advertisement that appeared on 13 February are the names of no less than fourteen former PhD students of Drenth who are still working in science.

The knowledge about the relationship between structure and function can be used to engineer enzymes, for example, so that they can catalyse reactions for the chemical industry in a more sustainable way. With these techniques it is also possible to detect the cause of diseases and then to develop new medicines.

Jan Drenth retired in 1990, but was then present at the lab almost daily for at least another fifteen years. He did experiments aimed at understanding the way in which proteins crystallise and this yielded a publication in 1998 that is frequently quoted. Drenth also wrote a highly acclaimed textbook on the techniques of structural determination that appeared in 1994. The book entitled 'Principles of Protein X-ray Crystallography' (Springer-Verlag) was regularly updated until 2007. In the meantime, the field has developed further, but the information from his textbook still forms the basis of new developments in structure determination.

Drenth is described by those who worked and collaborated with him as a prominent but very modest scholar. He would probably find an extensive memoriam nonsense, yet he earned huge respect as a founder of a field in which the present day Faculty of Science and Engineering is still leading.

Bert Poolman and **Bauke Dijkstra**,
Groningen

Jan Drenth, Groningen (1925-2025) (photograph c/o LinkedIn).

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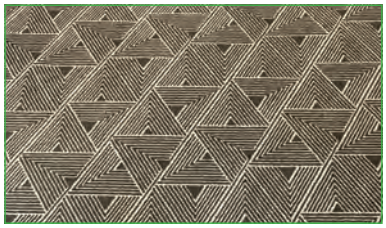
Puzzle Corner

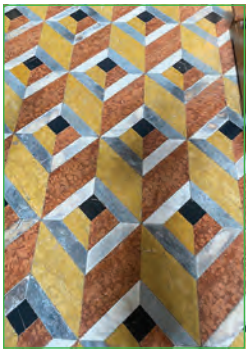
LAST month we had six floor patterns, all from John Lisgarten (London), for members to identify, wherever possible, the plane group symmetry.

(a)

(b)



(c)



(e)

(d)

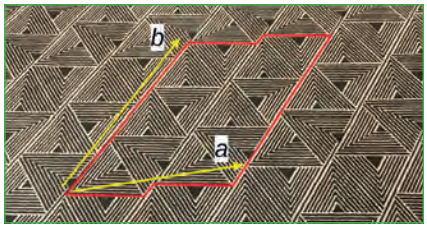
(f)

Philip Bradfield (Edinburgh) has provided an excellent set of answers as below.

(a) *The motif has no symmetry itself and there is no "pairing" so it must be p1 despite the "accidental" orthorhombic (rectangular) "lattice."* I believe Philip is absolutely right on that. I have outlined one of the motifs below in case it helps anyone. It is quite hard to see the effect of perspective in the picture due to the lack of symmetry in the pattern but I think the photographer must have spotted the main axes as they are aligned quite well with the horizontal and vertical directions, or maybe they are aligned with the walls of the room, or the bar (sorry John)!

Philip recommends chapters 2, 7 and 8 of "Symmetry in Science and Art" by A. V. Shubnikov and V. A. Koptsik (Plenum, 1974) and also "Brian Sanderson's Pattern Recognition Algorithm" about which members may find out more by searching the internet using that exact phrase! Basically it is a flow-diagram to work through when trying to identify plane group symmetry. As an added bonus for members, we have included a copy as an appendix to this article, with permission of mathematicians **Dror Bar-Natan** (Toronto) and **Brian Sanderson** (Warwick).

(b) For this one Philip gives us *p6mm ie* of high symmetry, and that seems to be absolutely spot-on, too. The question of the micro – structure of the mosaic/ tessera is a difficult one. They certainly have no internal symmetry but they seem to have a vague starfish pattern which is repeated in different orientations in the different hexagons. However I think Philip is right to simply treat these motifs as "blank."

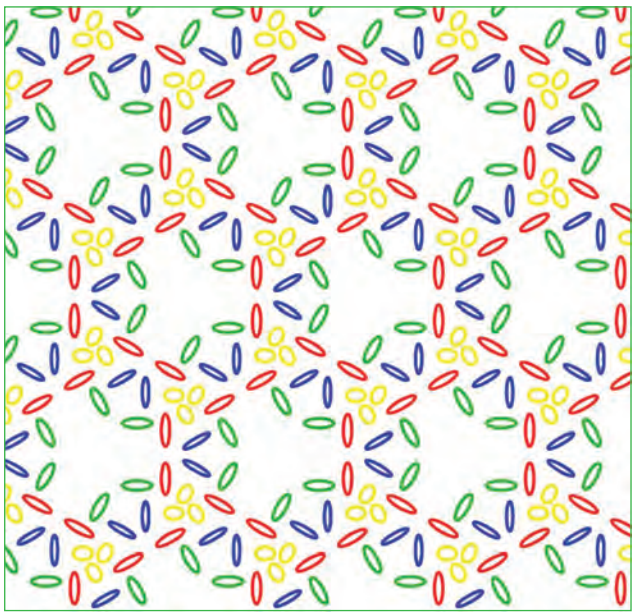


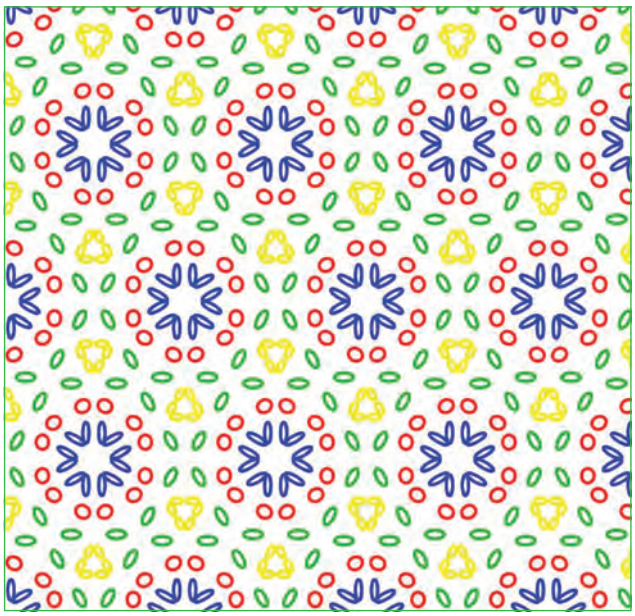
(c) We agree that this one is *p*1 despite being made up of equilateral triangles which give it a vaguely trigonal appearance. The *p*1 lattice vectors are shown in yellow in the figure below and the unit cell contents as the red polyhedron.

(d) Philip's answer of *p4mm* is definitely correct for this one. This is plane group number 11 in the International Tables for Crystallography Vol. A (or Vol. 1 for the earlier issues; IUCr, Chester) and doubles more simply as just *p4m*.

(e) Philip rightly points out that this design is very art deco. Taken at face value, the pattern seems to be rectangular *p*1 but if we simplify it by treating the brown tiles as being the same as the yellow ones, we have both centring and vertical mirror lines which gives us plane group *cm* (number 5 in the International Tables). In "An Introduction to Crystallography" by F. C. Phillips (1974, 4th edition, Oliver and Boyd, Edinburgh) this plane group is called *cl*, due to the author regarding each mirror as being a *line*, or *cg* where the glide lines are half way between the mirror lines. Philip also mentions that if we treat brown as being antisymmetric (*m'*, *g'*) to yellow, we have the plane group *cg'*. Philip claims to have ignored colour symmetry aspects, something which is covered in the book "Colored symmetry" by A. V. Shubnikov and N. V. Belov (Pergamon, 1964).

(f) This is another case of *p4mm*. Sadly the motif was not very clear due to the camera being some distance away, but with some paparazzi image enhancement techniques, I think there can be no doubt about the intended symmetry of this carpet pattern.

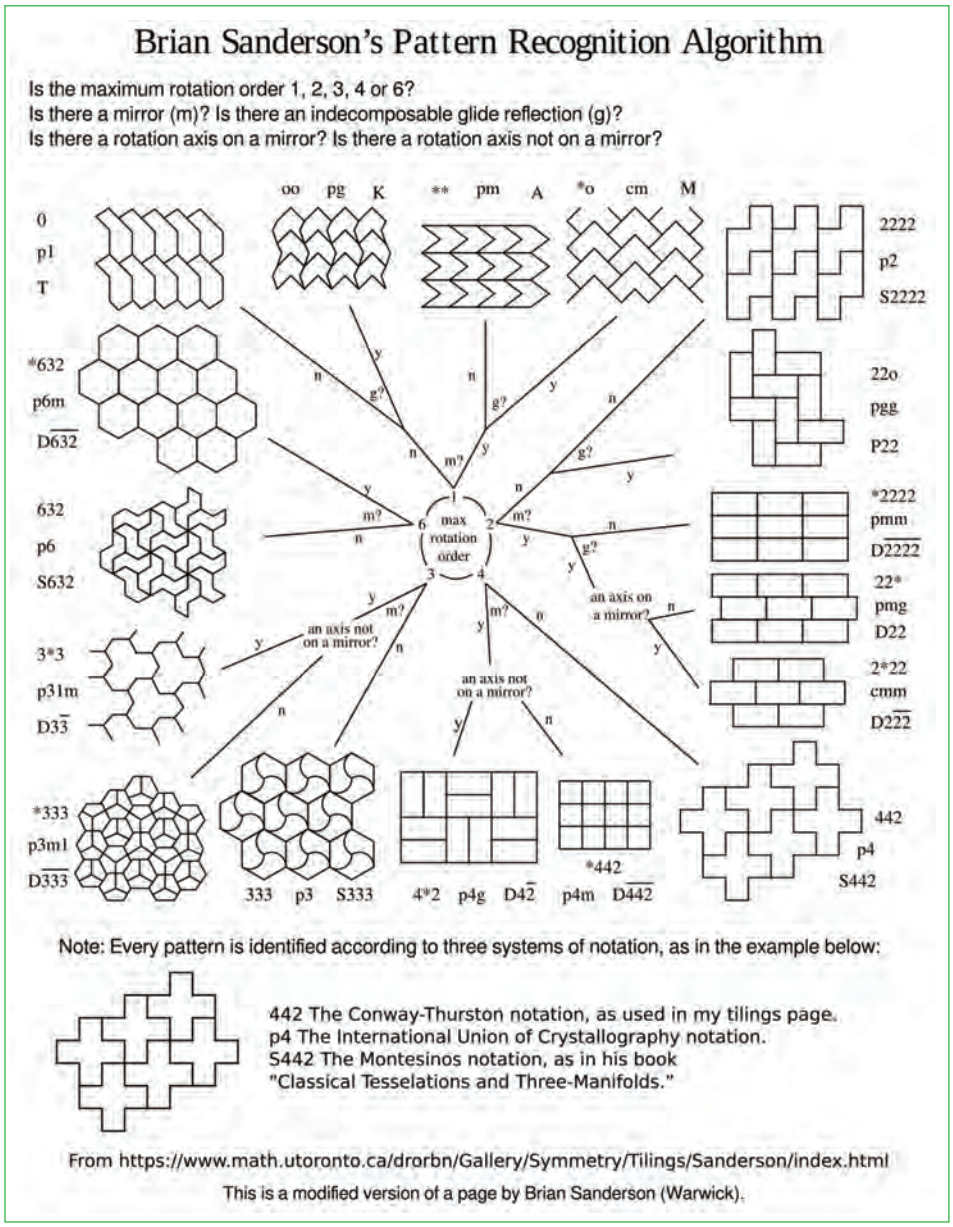




For this issue we have two new synthetic tiling patterns of high symmetry drawn by the editor using the excellent online Wallpaper Symmetry Generator by **David Eck** (Hobart and William Smith, US) for members to identify their plane groups.

Appendix

Brian Sanderson's pattern recognition algorithm. This flow diagram, where one starts in the centre and works outwards, assists in determination of plane groups. The figure is reproduced with permission of **Dror Bar-Natan** (Toronto) and **Brian Sanderson** (Warwick), with minor adaptations.



Down memory lane

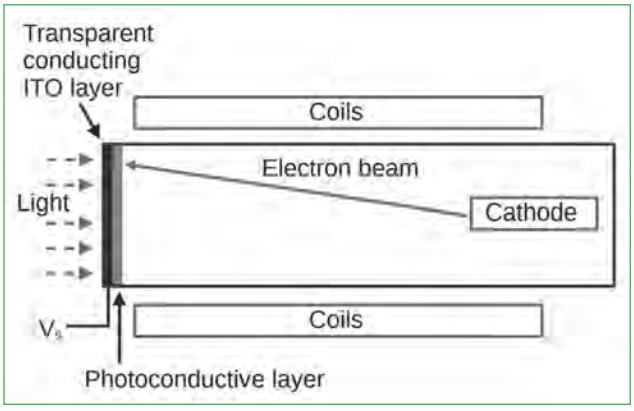
The television detector

THE renowned X-ray instrument designer, Uli W. Arndt at the Cambridge LMB-MRC (1924-2006), spent many years looking at the potential use of the television camera as an X-ray area detector. He is well-known for having developed the Arndt-Wonacott oscillation camera which was used extensively for protein data collection during the 1970's and 80's, at both home and synchrotron sources [1]. However, as a detector, film suffers from limited dynamic range and high background due to chemical fog, not to mention the need to process and digitise the photographs, which were quite labour-intensive processes.

The first published reference to Arndt's work in this field is in his book "Single Crystal Diffractometry" which was co-authored with B. T. M. Willis and published in 1966. The book includes a diagram and a paragraph briefly describing their system [2] but we have to wait a few more years until further details of the system were published [3, 4]. Incidentally, the first of these two papers included an oscillation image of haemoglobin recorded in 20 seconds which would have required at least as many minutes exposure by conventional X-ray film methods. As with indirect charge-coupled device (CCD) detectors in use today, the X-ray diffraction spots were converted to light by use of a phosphor screen made of zinc sulphide. However, whilst the CCD chips of today are sensitive enough to record the scintillations directly, or indeed the X-rays themselves, the television cameras of the 1960's were not, and this required the use of an image intensifier – something we will look at in more detail later.

Leaving the details of Arndt's work aside for the moment, it is interesting to look at how television actually worked in the 1960's. Back then a household television set was basically a cathode ray tube in which vertical and horizontal coils, driven by electronic wizardry, deflected the beam from an electron gun (cathode) so that it flipped across a fluorescent screen at the visible end of a vacuum tube, in the familiar raster scan. The intensity of the electron beam at each point in the scan was governed by the transmitted analogue signal and this gave us the picture, usually in black-and-white, at least in the UK in those days. Incidentally, the household television set was very good at producing X-rays and as a result the tubes were made of glass doped with strongly absorbing elements such as lead and strontium to protect the viewer. Not relevant to X-ray work, but colour television sets worked by having 3 electron guns, one for each primary colour (red, green and blue), and their beams fell on a regular pattern of three phosphor types (again one for each primary colour) on the viewing screen and each phosphor dot glowed its respective colour with the right intensity at the right time [5].

Of course, all broadcasting relies ultimately on the recording camera. According to Wikipedia (the free encyclopedia) the television cameras of the 1960's fell into several classes and all relied on broadly similar principles, the most common being the *vidicon* camera and this is indeed the camera which Arndt preferred for early X-ray applications. In many ways the camera is the reverse of an old-fashioned television set, having a cathode which generates a narrow electron beam and coils to make the beam scan the glass faceplate in a raster fashion. The vidicon camera relies on a photoconductive surface onto which light from the scene is focussed. A photoconductor is a material which is normally an insulator but becomes conductive when light shines on it. The photoconductive layer of the vidicon thus records a 'resistive image' of the scene [6]. One side of the photoconductor is coated with a transparent conducting layer made from indium tin oxide, known as the ITO layer, and this is given a positive voltage by the signal electrode. As the electron beam scans the other side of the photoconductive layer, it brings that side to the potential of the cathode i.e. negative. Light falling on the photoconductor, at the point where the electron beam happens to be, allows current to flow from the ITO layer into the photoconductive layer. The current flowing into the ITO layer via the signal electrode to maintain its positive voltage is thus related to the light intensity of that part of the scene. Since we know where the electron beam is at each point in the scan, the corresponding signal current effectively tells us the light intensity at that point in the image. Whilst all of this seems very neat, do remember that this was state-of-the-art technology in the birth year of the editor when valves were still far more commonplace than transistors in electronic devices and integrated circuits were only just coming onto the scene.



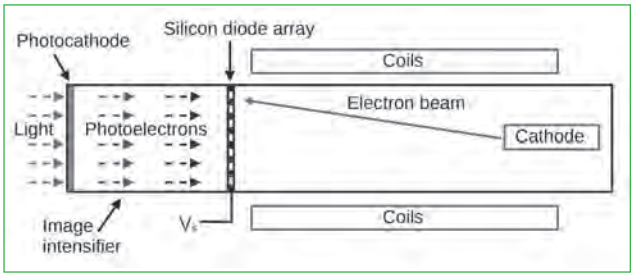
The basic principles of the vidicon television camera, as described in the text.

The vidicon camera was one of many systems developed over the first few decades of the 20th century, details of which may be found on Wikipedia and elsewhere. In the 1970's [4,7], Arndt reports using an *isocon* camera, which is basically an *orthicon* camera, the design of which actually predates the vidicon by about 25 years and is a good bit more complicated, so the details are left for interested members to follow up in their own time. The isocon had the advantage of much lower background noise and could be run in an integrating mode with exposure times of several

minutes, much like film or the imaging plate, by cooling the camera to around – 10 °C. Despite Arndt's digression into isocon cameras, a team developing a similar system at Princeton remained loyal to the vidicon [8]. Like the US team, Arndt's final design [9-11] used a silicon intensifier target or SIT camera which is basically a vidicon with an image intensifier section between the photocathode and the target. The photocathode converts the optical image into electrons which are accelerated towards a silicon diode array target from which the image is read. The current flowing into the array as each diode is hit by the scanning electron beam is proportional to the light intensity at that point.

Regardless of the camera type employed, simply having a phosphor screen in front of a television camera was found not to yield useful data since the signal needs substantial amplification. Overcoming this problem required the use of a device invented for night-vision, namely the image intensifier. However, since these devices work at the level of electrons by accelerating them across a large potential difference, the image intensifier has to have a phosphor screen at both ends. At the end facing the crystal, a phosphor screen converts the X-rays to photons which pass into a photocathode, usually through a fibre-optic coupling. The photocathode converts the light image of the diffraction pattern into electrons, as we described for the SIT tube above. These electrons are accelerated across the potential difference of the image intensifier and then impinge on another phosphor screen. Here they are converted back to a visible image of the diffraction pattern which is strong enough to be recorded by the television camera. The image intensifier usually has to be coupled to the television camera by a fibre optic device.

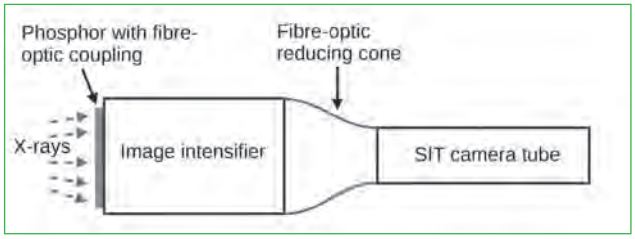
Thus by 1982 the preferred setup was the SIT camera tube with a gadolinium oxysulphide (Gd_2O_2S) X-ray phosphor fibre-optically coupled to the front of a Varian image intensifier. The majority of light from a single scintillation in the phosphor is imaged within one 100 µm x 100 µm pixel of the television frame. Calibration of the detector was required to correct for the spatial distortion of the image and the non-linearity of the



A schematic diagram of the SIT vidicon camera with its built-in electrostatic image intensifier.

intensity response. The computer controlled the gain of the image intensifier and the camera. Since the output phosphor of the Varian image intensifier had an area about twice that of the SIT camera aperture, a reducing fibre-optic cone was needed to couple these two parts of the instrument. A later design, the DEP detector, utilised a Delft Instruments image intensifier with an output aperture exactly matching the SIT camera and this dispensed with the need for the fibre optic coupling cone [12].

The output from these old-fashioned TV cameras was analogue, so computer storage and processing of the diffraction data required analogue-to-digital conversion. The system required a dedicated digital store or dynamic shift register since computers available in the 1970's and 80's could not handle the data rate from the camera, which scanned the image every 40 msec. This store had a capacity of 512 x 512 x 18 bits which was of the order of a gigabyte.



A schematic of the FAST detector showing the fibre optic couplings.

The Enraf-Nonius engineer Harry Dekker installing an upgraded FAST system in the refurbished X-ray laboratory at Birkbeck around 1990. The detector itself is open on the left with the CAD4 goniometer roughly central and the rotating anode of the Elliott GX21 source on the right. This photograph is reproduced with permission from the Birkbeck Image Collections. The instrument is now in the Science Museum Collection.

All areas of the store were kept cleared except those regions where reflections were expected to occur based on the predicted positions of diffraction spots. In order to predict the spot positions during data collection, the orientation matrix of the crystal had to be determined by auto-indexing prior to the main run, however the crystal orientation and lattice parameters could then be refined continuously during data collection for improved accuracy of the spot integration.

Arndt continued to develop the television detector in Cambridge and the system was commercialised in the mid 1980's by Enraf-Nonius as the FAST system under license to the MRC. Data collection using the FAST involved rotating the crystal slowly about the vertical ω axis of the goniometer with each exposure corresponding to a 0.1° rotation; essentially the rotation method [1]. Although the active area of the detector was actually quite small (62.4 mm height x 46.8 mm width), the minimum crystal-to-detector distance was only 35mm and it could be swung out (± 45 °) on θ to maximise the resolution of the dataset in the horizontal plane. When collecting data with the detector tilted in this way, the missing reflections above or below it, along with the blind region or cusp close to the rotation axis, could be collected by reorienting the crystal using the Enraf-Nonius CAD4 kappa goniometer which was controlled by a microVAX computer. The relatively small size and finite resolution of the detector meant that the incident beam had to be quite finely collimated.

According to Arndt's autobiography [13], in 1981 whilst en route to a summer school in Kyoto he visited the Fuji factory. Here he was shown the prototype X-ray sensitive imaging plate but he admits, with astonishing frankness, that he would not have been a very successful industrial spy as the significance of this invention, which was to revolutionise data collection around 10 years later, did not, at that stage, click with him.

According to **Frank van Meurs** (formerly of Enraf-Nonius) the first FAST system was delivered in 1983, after 5 years of R&D effort. The original electronics had been designed to be controlled through a Q-bus interface [14] – technology which became obsolete quickly during the FAST life cycle. In addition, one of the daughter companies of Delft Instruments (DI) had supplied a test night vision system to Jordan, which finally surfaced during the autumn of 1990 in Iraq (during the first Gulf War). In common with many of the world's top high-tech engineering companies entangled in similar conflicts of interest, this led to an embargo by the US government on their business, including that of Enraf-Nonius. Fortunately the embargo was ended a year later, after payment of considerable penalties. Sadly however, in spite of selling about 50 FAST systems, the project turned out not to be a commercial success, no doubt also due to very strong competition from multiwire detector systems such as Xentronics [15] and ADSC (1984-1992, ~80 units) [16- 18], which gained popularity from around 1985. Nevertheless, the FAST sparked much collaboration on development of the software for the project which was known as the Munich Area Detector System, or MADNES for short [13,19]. I remember several of the Birkbeck staff regularly attending MADNES user meetings in Delft in the late 1980s.

A total of 209 structures in RCSB PDB cite "Enraf-Nonius FAST" as the "diffraction detector" with the majority being deposited after 1995. I know of many more structures arising from FAST datasets which were deposited well before that date so I suspect the detail with which depositions were annotated improved around then and the number of structures solved using FAST data is thus underestimated by a large amount. In addition, the FAST has also been used extensively to collect single-crystal diffraction data on small and medium sized molecules; for example it was the production engine for the National Crystallography Service (NCS) in the UK during the period 1989-1997. There, in the hands of Mike Hursthouse and Simon Coles, it must have produced at least 4500 structures.

I am very grateful to **Frank van Meurs** and **Jim Pflugrath** for providing much of the information and many references as well as commenting on this article.

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Some historical treasures from Dorothy's lab

Given my very narrow social circle, a chance meeting with John Golding in the first few days of this year turned out to be an interesting one. John is Professor of Applied Psychology at the University of Westminster. Like me he studied biochemistry in Oxford (70 – 73) and then took another degree in Psychology followed by a DPhil in Experimental Psychology in the Department of Zoology building, before finally leaving Oxford in 1982 – the year after I started my Biochemistry degree there. John remembers that sometime in the late 70's he was tasked with setting up a small psychology test library in what was laboratory space occupied by the world- leading crystallographer Dorothy Hodgkin FRS, Britain's only women Nobel Prize winner in the sciences. The biography, "Dorothy Hodgkin: a life" by Georgina Ferry (Granta, London, 1998) mentions that on her retirement in 1977, Dorothy's laboratory space was indeed returned to Experimental Psychology, as was agreed before she even moved in. By then Guy and Eleanor Dodson had moved to York and Dorothy had given them her X-ray equipment which had been funded by her previous work on the structure of insulin.

John recalls Dorothy introducing herself to him and, probably because of his biochemical background, she very kindly offered him a number of items which would have otherwise been disposed of. Thus, to this day, John retains one of Dorothy's hand-contoured electron density maps and a Philips X-ray tube from her laboratory which he has stored very carefully over the intervening years.

The map has "1.9 Å" written in the top left corner and has line a drawn on all the sections at 60 degrees to the horizontal. I would therefore guess that this is for the rhombohedral crystal form of porcine insulin [1, 2]. Can any members shed more light on these fascinating items?

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An unsung heroine of the double helix

In the previous article we mentioned Dorothy Hodgkin FRS who was awarded the Nobel Prize for the structure of vitamin B12 in 1964. One of Dorothy's research assistants on that project was June Lindsey (née Broomhead, 1922-2021) [1] who had previously studied the X-ray crystal structures of purines and pyrimidines, the bases found in DNA, in Cambridge for her PhD. The first of her published works [2] describes the structure of adenine hydrochloride which was determined using Weissenberg photography by visual estimation of the diffraction intensities based on an intensity scale. Given the presence of chloride ions, the structure was solved by heavy atom Patterson methods. A later analysis of the same structure by Bill Cochran [3] using data measured by Geiger counter confirmed June's main findings. Cochran also narrowed down the number of possible canonical forms of this planar molecule by inspecting the bond lengths and electron density distribution as well as locating most of the hydrogen atoms. Another paper by June Lindsey in 1951 who was by then in Oxford, although about to move permanently to Canada, revealed the structure of guanine hydrochloride by similar methods [4].

Extrapolating from the hydrogen bonds found in these small molecule structures to those involved in the AT and GC base pairing which links the strands of the DNA double helix is unimaginably hard, not least due to the presence of chloride ions and water molecules which make hydrogen bonds to the bases. Nevertheless the detailed diagrams of the bond lengths and angles of the A and G bases in June Lindsey's papers were used to make the mechanical models with which Watson and Crick made their incisive discovery in 1953 [5]. The idea of the bases recognising each other

through hydrogen bonding was key to their thinking that one strand of the DNA molecule was the template for synthesis of the other.

Having read The Double Helix by James Watson at least twice, I could not recall a mention of June Lindsey. Indeed after downloading a plain text version of the book from academia.edu and searching it, I cannot find a mention of either her maiden or married names. This is perhaps forgivable given that Lindsey had left Cambridge before Watson arrived but she had worked opposite Crick at the Cavendish for a number of years. In contrast Bill Cochran is mentioned several times as is the chemist, Jerry Donohue, who was an expert on the canonical forms of the bases and was, at one point, found to be in the presence of a 'popsy' when Francis Crick burst into his office, prompting a quick retreat.

Watson does mention building models of DNA which involved the hydrogen bonding patterns that were found in the crystal structure of adenine (June Lindsey's work) with pairs of identical bases coming together about an intervening two-fold axis and connected by two hydrogen bonds. As mentioned above, this was a significant starting point leading to the ingenious idea of A pairing with T and G pairing with C which elegantly explained Chargaff's rules. It is interesting that the first published model of DNA contained only two hydrogen bonds between G and C while we now know that there are in fact three, thereby accounting for the thermostability of GC-rich DNA. June Lindsey's work is also mentioned in a figure legend where it says that the possibility of a third hydrogen bond was "rejected because a crystallographic study of guanine hinted that it would be very weak." Having read the Broomhead paper on guanine [4], I struggle a bit to see Watson's point here, but then I have to accept that today we have the unfair advantage of about 7 decades of structural hindsight. Much better insight into this matter is provided in a 2006 Nature article entitled "The third bond" by Simon Wain-Hobson [6] which mentions June Lindsey's work and attributes the discovery of this extra hydrogen bond between G and C to Pauling and Corey in 1956. All of this reminds me that I have to confess missing out an important hydrogen bond in one of the structures which I solved for my PhD and this was pointed out to me by my external examiner, the late Professor Louise Johnson FRS.

Members are referred to the Wikipedia page for June Lindsey and to several interesting online articles about her life and work.

Thematic images by the Surreal Graphics Generator at deepai.org.

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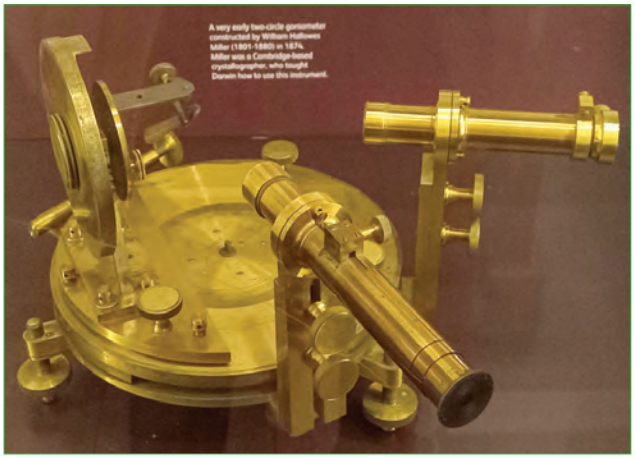
Doing the sights

A trip to the excellent Sedgwick Museum of Earth Sciences in Cambridge turned up an interesting find in the form of this Victorian optical goniometer. Sharp-eyed members may be able to read the caption which says that this instrument was constructed by W. H. Miller (1801-1880) in 1874. The website mineralogy.eu confirms the construction date for Miller's two-circle goniometer. Miller was Professor of Mineralogy in Cambridge from 1832 to 1870 and was the inventor of the well-known Miller indices. The last line or two of the caption also states that Miller taught Darwin how to use ***this*** instrument.



Caption: A very early two-circle goniometer constructed by William Hallowes Miller (1801-1880) in 1874. Miller was a Cambridge-based crystallographer, who taught Darwin how to use this instrument

I should have studied the rest of the exhibit more carefully, but I have a question for members. Does this refer to the famous evolutionary biologist, Charles Robert Darwin (1809-1882) who studied in Cambridge and subsequently communicated extensively with Miller regarding the samples he collected on the Beagle, or to one of his 10 children, at least 4 of whom studied science at Cambridge, one even founding the Cambridge Scientific Instrument Company? My worry is that by 1874, a fair amount of water would have gone under the Bridge of Sighs for both Darwin senior and Miller. My interpretation is that Miller must have taught Darwin to do optical goniometry, but most probably using an ***earlier*** instrument. What do members think?

Regardless of my confusion, there definitely is a strongly expressed crystallography gene in the Darwin family. His grandson Charles Galton Darwin (1887-1962) is well-known for developing the dynamical theory of diffraction and the concept of crystal mosaicity. In turn, his own daughter, Cecily Darwin (1926-2022), studied with Dorothy Hodgkin in Oxford before moving to the US to work with Arthur Patterson at the Fox Chase Cancer Center in Philadelphia.

Finally, we all like a good cut-away diagram – those drawings that help to explain how televisions, cameras, engines and other complicated devices actually work. In many ways crystallography is a tool for giving us cut-away diagrams of things we wish to study such materials, molecules and living systems. This idea is slightly turned on its head by the following photograph which was very kindly sent to me by **Maria Erskine** (London) showing a sculpture by Daniel Arsham at the Moco Museum in Marble Arch, London, entitled "Blue calcite eroded Porsche 911-S." The artist's idea is that when we uncover works of our existence thousands of years into the future, they will have been subjected to erosion and internal crystallisation, which is an interesting thought.

Members can rest assured that this make of car is not within the budget of the Crystallography News editor.

Jon Cooper,
UCL

References

Wikipedia, the free encyclopedia.

Meetings of Interest

Where possible, information on the following meetings has been abstracted from the conference websites, where further details may be obtained.

Assistance from the IUCr website is also gratefully acknowledged.

If you have news of any meetings to add to future lists, please send them to the Editor, **jon.cooper@ucl.ac.uk**.

BCA Spring Meeting 2025, Leeds, 14th-17th April

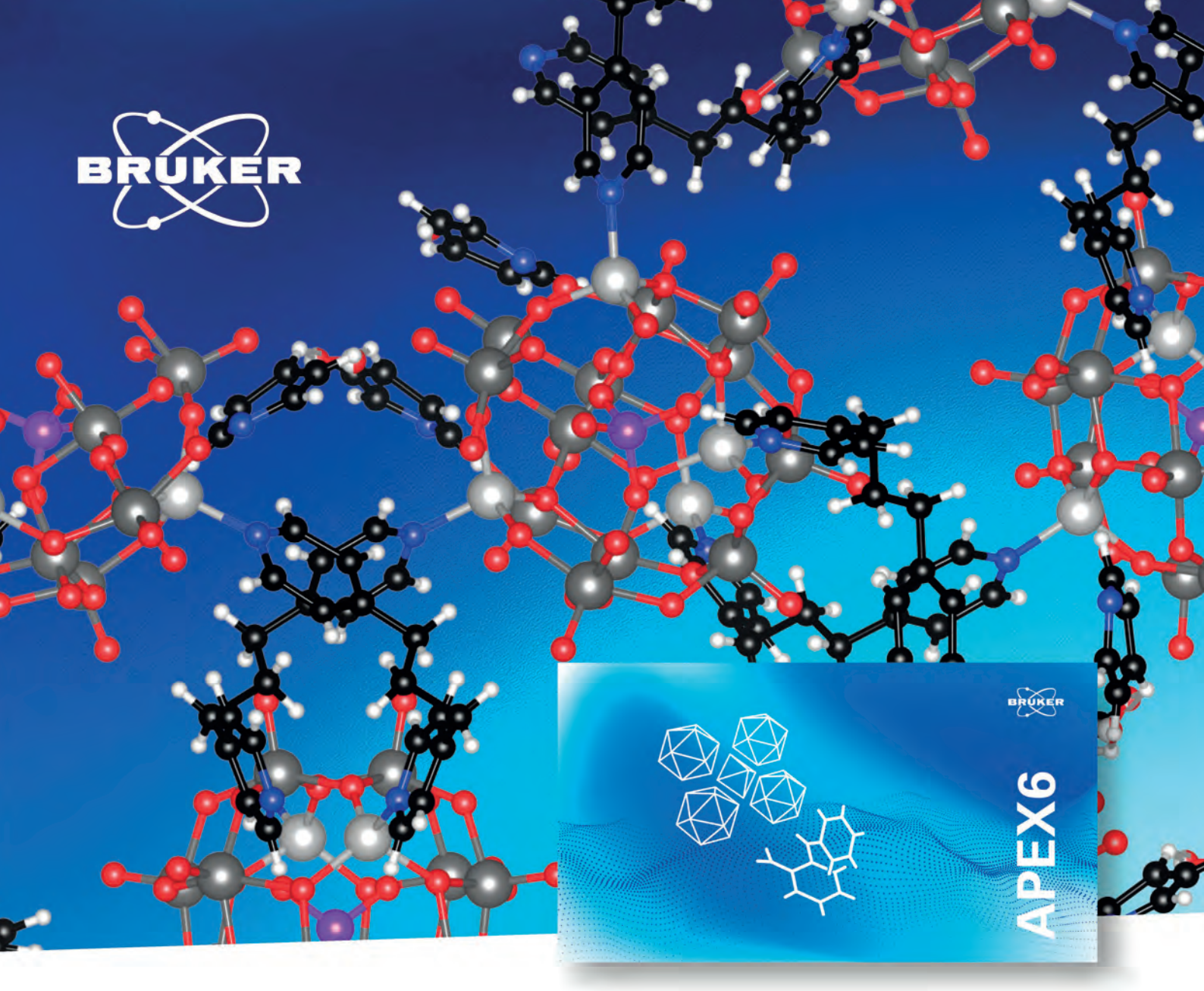
The theme of this year's BCA Spring Meeting is "Learning from Others", which highlights the necessity in the current research environment to interact and collaborate to get the best data or to develop a deeper understanding. The field of crystallography lends itself to multi-disciplinary research, and the Spring Meeting will celebrate this. In addition, we don't only learn from other researchers but from a wide range of stakeholders, no matter whether they are from academia, industry or the general public. To showcase the theme, the subject groups have put together an exciting programme with inclusive and collaborative sessions as well as a number of workshops. We are looking forward to seeing (and learning from) you in Leeds. More details and registration are available at **https://tinyurl.com/bca2025**

Twenty-Seventh Congress and General Assembly of the International Union of Crystallography, Calgary, Canada, 11th-18th August 2026.

IUCr2026 is set to be held in the magnificent city of Calgary, located in the heart of Alberta, Canada, from 11th to 18th August 2026. Calgary, a city renowned for its breathtaking natural beauty and warm hospitality, has been chosen as the host for this remarkable occasion. Nestled amidst stunning landscapes and boasting a rich cultural heritage, this vibrant metropolis promises to provide an unforgettable experience for all attendees. More details and registration are available at **https://www.iucr2026.org/**

ECM 2025, Lviv-Poznan, 25th-29th August 2025

The flagship of ECA activities is the European Crystallographic Meeting (ECM), held every year, except when there is an IUCr Congress. The ECMs are the main meeting point for crystallographers in the ECA area to show their recent research. Microsymposia at ECMs are proposed and organized by ECA SIGs. At the XXV Congress and General Assembly of the International Union of Crystallography in Prague, it was decided that the 35th European Crystallographic Meeting would be held in Lviv, Ukraine, in 2025. Thanks to a collaboration between the Ukrainian Crystallographic Committee and the Polish Crystallographic Association, the conference site will be Poznan, a city in neighbouring Poland. It is a pleasure for us to join our forces in elaborating an attractive scientific program that will show the multiple aspects and broad possibilities of Crystallography. The European Crystallographic Association and the Ukrainian Crystallographic Committee, cordially invite you to ECM35 in Poznan. More details and registration are available at **https://ecm35.ecanews.org**



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