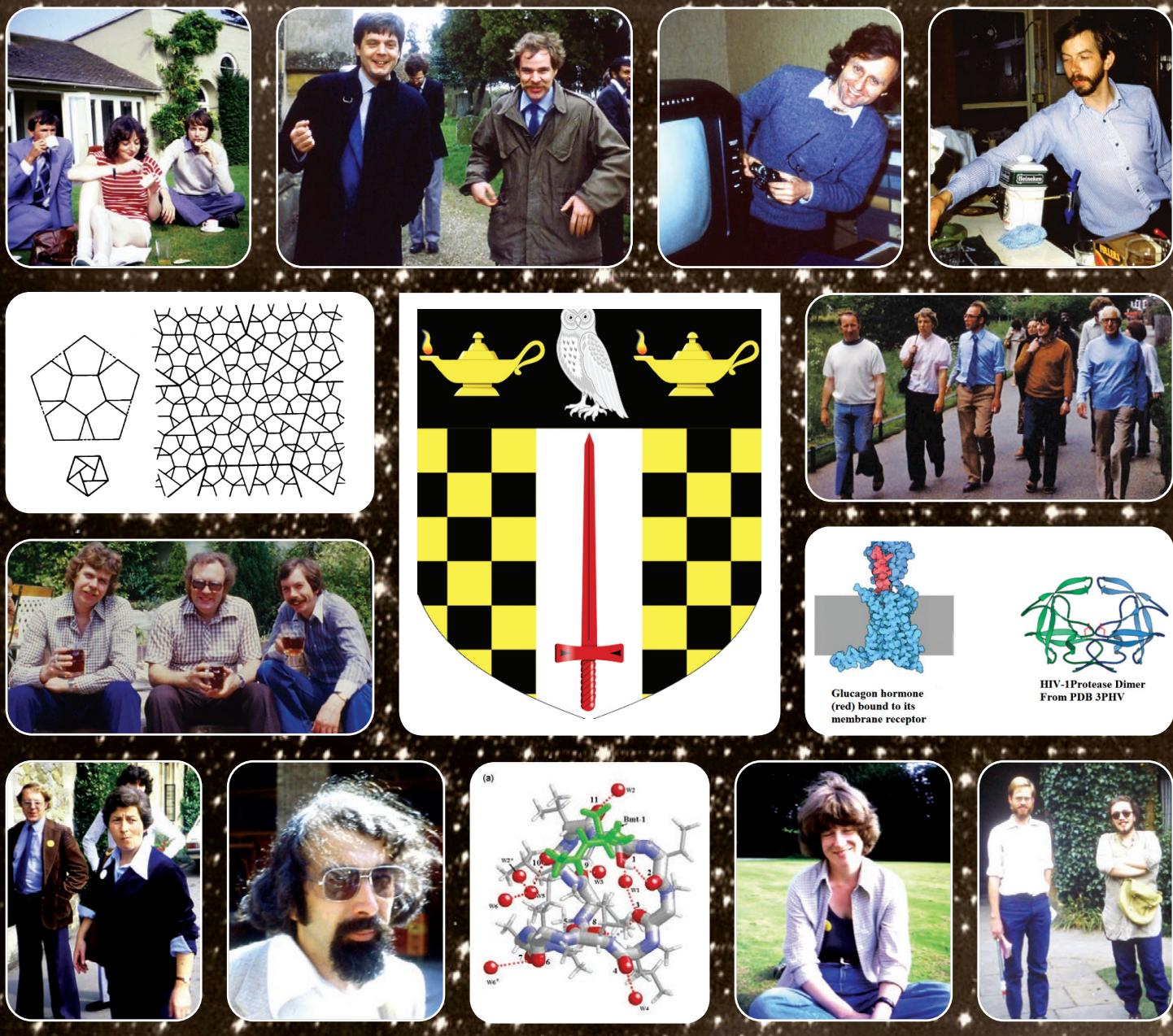


# Crystallography News

## British Crystallographic Association

Issue No. 164 March 2023

ISSI 1467-2790

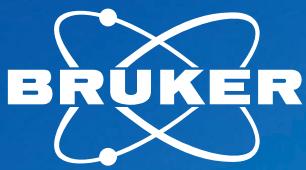


## Crystallography at Birkbeck and BCA Spring Meeting

Spring Meeting 2023	
AGM Minutes	
Obituary	
Crystallography at Birkbeck	

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CRYSTALLIZATION SYSTEMS

# NEWS FROM THE CCDC

## CCDC launches new website

The new CCDC website <https://www.ccdc.cam.ac.uk/> is designed to make information on the CSD data and software more accessible to everybody. It offers a wealth of information about the organization, events and workshops, partnerships, grants, software news and updates, open vacancies, history, mission, and more.

The screenshot shows the CCDC website homepage. At the top is a navigation bar with tabs: Deposit Structures, Access Structures, Contact Us, and My Account. Below the navigation bar is a main content area. On the left, there is a text block: "Join the thousands of scientists using the CSD data and CCDC software to [discover new drugs](#), [improve material stability](#), and [advance structural science](#)". Below this text is a "Read more" button. On the right side of the content area is a large, detailed 3D ball-and-stick model of a complex organic molecule, featuring atoms represented by spheres in various colors (grey, white, red, blue, yellow). The background of the main content area is light grey.

Functional services remain the same. These include Access Structures, Deposit Structures, WebCSD, My Structures, and CSD downloads. Support channels also remain the same: [email support@ccdc.cam.ac.uk](mailto:support@ccdc.cam.ac.uk) for technical help.

### → Latest Blogs

A new article published in the *IUCr Journal* describes how to make more crystal structure data available for the public benefit. Many researchers don't publish their crystal structures in the scientific literature. These unpublished structures are a valuable, untapped, but inaccessible scientific resource. Publishing these structures directly in the Cambridge Structural Database <https://www.ccdc.cam.ac.uk/solutions/about-the-csd/> as *CSD Communications* enables other scientists to find, access, and reuse these previously unpublished data in future research.

Read more at

<https://www.ccdc.cam.ac.uk/discover/blog/sharing-unpublished-crystal-structures-through-csd-communications/>.

### → Upcoming Events

In 2023 we are attending and sponsoring many events worldwide and delivering free virtual workshops and webinars. Visit our events page at <https://www.ccdc.cam.ac.uk/community/events/> for more details on dates and topics.

### → CCDC Webinar: Scaffold hopping for digital drug design – 23rd March

Learn more about the CSD-CrossMiner software, the scaffold hopping component, and how to create feature databases.

Register your place at

<https://register.gotowebinar.com/register/145845147229009421>.

### → New Virtual Workshops series – April and May

Join us in April and May for the new CCDC Virtual Workshops series! They are free online sessions with expert tutors focussed on demonstrating how to use the CSD and the functionality of the CSD Software. You can try the functionality hands-on, ask your questions to our tutors, and take the test to get a certificate. Check our events page

<https://www.ccdc.cam.ac.uk/community/events/> to register.

If you would like to suggest topics for our workshops and webinars in 2023 email us at [hello@ccdc.cam.ac.uk](mailto:hello@ccdc.cam.ac.uk).

### → CCDC Careers

The CCDC is looking for talented individuals to join our team of over 100 staff worldwide. We offer competitive benefits and a supportive, flexible work environment. Don't miss your chance to join this vibrant and friendly organization and help us continue our mission to advance structural science for the public benefit! Check out our open vacancies at <https://www.ccdc.cam.ac.uk/about-us/careers/>.

### → Follow us on Social Media

Want to learn more about CCDC events, blogs, case studies, and software updates? Follow us on

Facebook: <https://www.facebook.com/ccdc.cambridge>,

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CRYSTALLOGRAPHY NEWS is published quarterly (March, June, September and December) by the British Crystallographic Association, and printed by North Wolds, York. Text should preferably be sent electronically as MSWord documents (any version - .docx, .doc, .rtf or .txt files) or else on a PC disk. Diagrams and figures are most welcome, but please send them separately from text as .jpg, .gif, .tif, or .bmp files. Items may include technical articles, news about people (eg awards, honours, retirements etc), reports on past meetings of interest to crystallographers, notices of future meetings, historical reminiscences, letters to the editor, book, hardware or software reviews.

Please ensure that items for inclusion in the June 2023 issue are sent to the Editor to arrive before 25 April 2023.

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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.

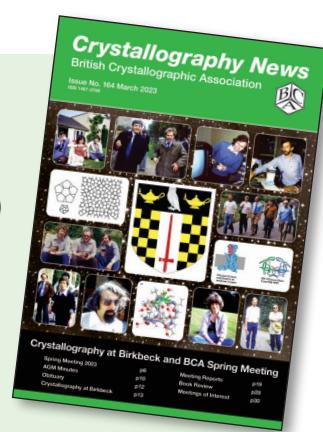
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## This month's cover:

Some Birkbeck Crystallography Department people (credit: John Quinn) and science. The 'wallpaper' is Alan Mackay's optical diffraction pattern of his five-fold space-filling tiling (also shown). Other science images credit: Rex Palmer and the RSC.



# From the President



**IT** is the end of an era for *Crystallography News* – this month's issue marks the completion of John Finney's tenure as Editor. As he steps down, I'd like to thank John for all he has done during his time as editor. He brought his experience and skills to the role and has worked tirelessly to ensure that *CN*

is consistently packed with interesting articles spanning the diverse range of scientific interest of our membership. John also gently made sure that contributors (including this one) met their deadlines. Behind the scenes he worked closely with the designers to ensure that our magazine remains an exceptionally well-presented and professional publication befitting a national scientific association. It has been a pleasure to work with John, and his knowledgeable contributions to BCA Council meetings will be missed.

As one era ends another begins and John's successor hails from the same institution, but with a background in a different branch of crystallography. I would like to extend a warm welcome to **Jon Cooper** from UCL as he takes over as *Crystallography News* Editor and I look forward to working with him over the next few issues.

It is approximately one month until the BCA Spring Meeting in Sheffield (3rd – 6th April 2023). I would like to record my deepest thanks to **Helen Playford** for chairing the scientific programme committee, and to everyone who has worked behind the scenes on the programme committee and at Hg3 organising the meeting. We are spoilt for choice with a diverse range of topics that have been arranged for plenary and parallel sessions. The wide-ranging programme encompasses teaching, software, pharmaceutical science, phase transitions, and dynamics. At the interfaces of crystallography there are sessions planned on complementary methods, crystal growth, XRF and application of computational methods.

If you have an aspiration to organise a scientific session at the 2024 meeting, or if you just want to suggest an idea and hope that someone else organises it, then *right now* is the crucial time to get in touch. As reported last issue, **Peter Moody** and **Hanna Kwon** will be chairing the programme committee, which will begin planning straight after this year's BCA Spring Meeting. They will organise a team of committee members drawn from each subject group of the Association, and you can contact any one of us to volunteer or propose session ideas.

Recently, there has been a great deal of excitement in technology circles following the release of OpenAI's ChatGPT language model, which has caught the public attention with its natural language interpretation of prompts and automatic generation of text. Early reports vary between extremes of utopian tech-hype and doom-laden warnings. The model powers a publicly accessible chatbot <https://chat.openai.com/>. An example prompt and response might go as follows:

Me: Write a paragraph about the history of crystallography.  
*ChatGPT: Crystallography is the scientific study of the structure of crystalline solids, which are substances composed of particles that have an organized and repeating arrangement. This field of science developed in the late 17th century, when René Just Haüy discovered the concept of crystal lattices that form the basis of all crystalline materials. The work of Haüy was followed by the creation of new techniques for the production and*

*analysis of crystals, such as X-ray crystallography and electron diffraction. This led to a greater understanding of the properties of solids, such as their symmetries, as well as the development of new technologies, such as superconductors, semiconductors, and optical fibers. Crystallography has played an important role in the advancement of modern science and technology, allowing us to better understand the atomic and molecular structure of materials.*

The output can be pieced together from online sources and some of the technological leaps are jarring to a crystallographic reader but as a starting text it is quite encouraging. The more impressive aspect is the contextual understanding of requests which is missing in earlier technology and exemplified by "Call me an ambulance" / "You're an ambulance".

When prompted to "write a haiku about calcite" ChatGPT responded:

*White as snow, crystal clear  
Calcite gleams in the light  
Beauty's embrace ever near*

This is a novel composition guided by a natural language input prompt, and demonstrates how the hype has built up. Concern has been expressed because this technology now allows anyone (and perhaps unscrupulous authors – see last column) to rapidly generate plausible sounding essays and arguments on most subjects.

Early adoption of this technology has been enthusiastic in software engineering teams – the language model can also produce working Python, C# and a variety of other popular programming languages. Users can ask the model to write functions or to find bugs in pieces of code. It is here that we can start to understand the capabilities and limitations of the approach. While ChatGPT is capable of producing reams of mostly sensible text and computer code, it is not without small inconsistencies and errors. As a result, the output needs proof-reading and code needs checking and thorough testing. The requirement for end user expertise is not removed at all, but the productivity of an individual may be improved by having a tool which can assemble chunks of code and summarize text rapidly. An essential but little recognized skill of coders is knowing where to find the relevant information to write working code. This new resource is one more tool to master in addition to knowing how to best search Stack Overflow and software manuals.

The impacts for science and crystallography are not clear. The success as a tool for programmers may not transfer well to scientific writing as ChatGPT is not good at including citations, so would not be much use for writing background sections of a paper. I asked for and obtained a syntactically valid CIF file for quartz, but with incorrect cell, coordinates and space group. In time it will become clear which tasks can benefit most from this type of interaction.

The last word goes to ChatGPT, eloquently making an argument about why it might not revolutionize the field of crystallography: *ChatGPT is an AI-driven writing assistant, but it is not designed to revolutionize the field of crystallography. This field requires deep expertise and a high level of technical knowledge, which is not easily acquired or automated. Additionally, the crystallography process requires a combination of both physical and computational techniques, which may be difficult to achieve using AI. Therefore, while ChatGPT can be very helpful in providing expert-level content for many other fields, it is not well-suited for crystallography.*

**Richard Cooper**

# BCA Council 2023

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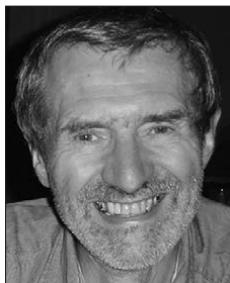


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(The dates in parentheses indicate the end of the term of office).

Full committee details on the BCA website [www.crystallography.org.uk](http://www.crystallography.org.uk)

# From the Editor



**AS** the timing of this, my last issue, coincides with the 200th Anniversary of Birkbeck College, I thought I'd exploit editorial privilege for the last time and make this a bit of a 'Crystallography at Birkbeck' special. Much vanguard crystallography was done there in the group – and ultimately the Crystallography Department – created by Bernal, so it seemed

appropriate to mark the occasion, and recall some of its many alumni who have become household names in the crystallography world for the advances they made in the field (in Bernal's time, think for example Klug, Franklin, Caspar, Finch, Holmes)<sup>1</sup>.

Birkbeck is rather a strange beast in the world of higher education. It started life as a 'Mechanics' Institute' – one of the early institutes set up by an educational movement conceived at the end of the 18th century "as a means of improving the literacy and numeracy of working people and providing them with some basic technical education"<sup>2</sup>. The Mechanics' Institute movement in fact played a vital but often overlooked part in the development of adult education.

George Birkbeck was one of its early lecturers, instituting a series of lectures aimed at mechanics and other tradesmen. In 1823, Birkbeck, together with William Cobbett and others, initiated the London Mechanics' Institute following a meeting at the Crown and Anchor on the Strand (perhaps a highly appropriate location for the founding – the Birkbeck bar continued to provide a stimulus to the science of some of us...). This became a hugely successful and influential educational institution that operated initially for a year from a Presbyterian chapel before taking a lease on a property, Southampton Buildings in Chancery Lane, in 1824. This building housed classrooms, library, reading room and, later, a laboratory. The following year, the Institution purchased the adjacent plot of land and built a lecture hall with seating for over 1,000 people. In 1830, it took a further radical step in becoming one of the first colleges to admit women as students, in advance of Oxford and Cambridge by nearly 40 years. The Institution, which was then renamed the Birkbeck Literary and Scientific Institution, moved to larger premises, Breams Buildings, on Fetter Lane in 1885. It was renamed Birkbeck College in 1907. Becoming part of the University of London in 1920, it fast became the best choice for students who wanted a university education but could not afford to study full-time.



Knowing his politics, I suspect that this tradition was one of the attractions of the College to Bernal (it was for me). Personally, I found teaching there very stimulating. The students were highly motivated – you'd have to be to give up several evenings<sup>3</sup> (6 to 9 p.m.) of your time every week. And in my early days there, it felt a little odd teaching people that were (often very) significantly older than me, and who had a great deal more experience than me of 'real life'. Despite the disruption to

normal family life enforced by the 'unsocial hours' during which we taught (though eased in my case in that my wife-to-be also taught there...), those were good, if challenging times.

So I hope you enjoy reading Rex Palmer's historical account of some of the science and some of the people that inhabited that semi-nocturnal world, as well as the experience of an ex-student of the M.Sc. Course in Crystallography. This course gave a thorough and comprehensive grounding to prospective researchers in crystallography, and there are many researchers from the UK and abroad who have claimed that this was the start of their scientific careers. Though it may be considered to be a grumpy old man's comment, I and others of my then colleagues regret that no course we know of appears to teach students today about the basic principles. In our current 'push-button' world, they no longer seem to have a prominent place – but I'd be delighted if someone can prove me wrong.

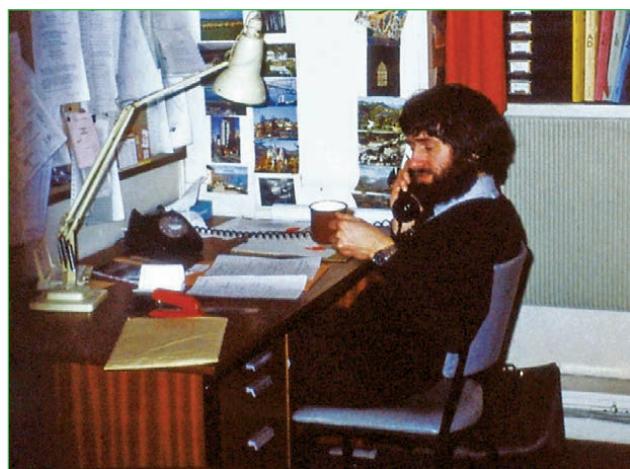
Enough of editorial rant! Elsewhere in this issue you will find further details of the 2023 Spring Meeting in Sheffield, the usual mix of interesting meeting reports, together with another book review.

I hope you enjoy reading this month's offering. And in my final issue it would be remiss of me not to thank all who have contributed pieces in the last three years. I hope the crystallographic community will be at least as helpful to my successor, Jon Cooper, who takes over the reins for the June 2023 issue.

## John Finney

### References:

1. To be slightly flippant, I remember one comment from a senior Birkbeck academic who shall remain nameless to the effect: "Why are so many of the good crystallographers ex-Birkbeck?". My take on this would be that the Birkbeck group was an excellent training ground, not only for crystallographers, but also for important roles in science policy, industry, and central facility and university management. Such 'moving on' and 'spreading the word' should be seen as a compliment to the group.
2. *Mechanics' Institutes*. Historic England, HEAG187 (2017). <https://historicengland.org.uk/images-books/publications/ih-a-mechanics-institutes/heag187-mechanics-institutes-ih-a/>.
3. Note that in the Birkbeck logo reproduced here, the 'i' is dotted with a moon for good reason!



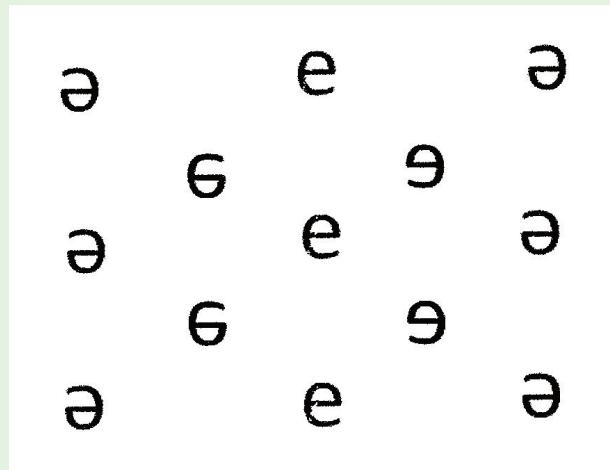
Young (ish) Birkbeck crystallographer hard at work. Credit: John Quinn.



# Puzzle Corner

HERE'S something a little different for this month's puzzle.

The attached is a pattern from a curtain. The problem is to identify any symmetry elements and find the unit cell and plane group.



## Solution to December's puzzle

(substitute bottom line letters with those on the top line):

a b c d e f g h i j k l m n o p q r s t u v w x y z  
f j o g s i q a e p y r c k w x d b l v m t h z u n

The quote, from a talk by Kathleen Lonsdale to sixth formers, was found by our puzzle setter in '*The Christian Life – lived experimentally*', edited by her colleague and notable crystallographer (and also Quaker) Judith Milledge (remembered in the June 2021 *Crystallography News*). Our setter commented that many now will never have known either of those remarkable crystallographers. He also remembers Arnold Beavers (who was another Quaker) once reporting that he had heard one of them asking an overseas visitor to lunch on Christmas Day "so that you could spend Christmas in a typical British home" ... Those of us who knew both Kathleen and Judith will appreciate the above ellipsis '...'.

## BCA Corporate Membership

The BCA values its close ties with commercial companies involved with crystallography. To enhance these contacts, the BCA offers Corporate Membership. Corporate Membership is available on an annual basis and includes the following benefits:



- Up to 10 free BCA memberships for your employees.
- 10% discount on exhibition stands at the annual BCA Spring meeting.
- Two free 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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- Influence on the development of crystallography and the BCA

For current rates, and to join, please see [www.crystallography.org.uk/membership/](http://www.crystallography.org.uk/membership/)

# BCA Spring Meeting 2023



**BCA Spring Meeting**  
**3rd – 6th April 2023**  
**University of Sheffield**

**THE** theme for the 2023 is 'The Year of Learning', with the Programme containing a wide range of pedagogical content interspersed with the more traditional research talks. Details and titles for sessions are given below.

Full details and registration information is at <https://registrations.hg3conferences.co.uk/bca2023>.

## YCG EARLY CAREER SATELLITE MEETING

**Monday 3 April 2023**

### Young Crystallographers Group (YCG)

**13:00 – 21:00**

The YCG 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. It is run by fellow early career scientists.

**13:00 – 13:30**

### YCG Opening Plenary

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

Speaker: **Mark Senn** (*University of Warwick*)

*Symmetry assisted insights into ferroic materials*

**13:30 – 17:15**

### YCG Research Sessions

Contributed talks from the YCG community.

#### Session 1:

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

#### Session 2:

Session Chair: **Josh Morris** (*Cardiff University*)

#### Session 3:

Session Chair: **Alex Campbell** (*University of Edinburgh*)

**17:15 – 17:45**

### YCG Annual General Meeting

**18:30 – 21:00**

### Flash Poster Presentations

Session Chairs: **Phillippa Partridge** (*University of Edinburgh*) & **Julia Gasol Cardona** (*University of Strathclyde*)

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

## Tuesday 4 April 2023

**09:00 – 09:30**

### Parkin Lecture

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

Speaker: **Lewis Owen** (*University of Sheffield*)

**09:30 – 10:30**

### YCG Research Sessions (continued)

#### Session 4:

Session Chair: **Anna Herlihy** (*ISIS Neutron and Muon Source/Diamond Light Source*)

10:30 – 11:00

## Closing Plenary

Session Chair: **Lee Birchall** (*University of Kent*)

Speaker: **Lauren Hatcher** (*Cardiff University*)

*Dynamic X-ray diffraction in photoswitchable materials design*

# MAIN MEETING

11:30 – 12:15

## Lonsdale Lecture

Session Chair: **Anthony Blue Carter** (*Pharmaron*)

Speaker: **Kate Brown** (*University of Cambridge/University of Texas at Austin*)

*From Ångstroms to kilometres and back again: Science at interfaces and the importance of belonging*

13:00 – 13:45

## PCG Plenary

Session Chair: **Lewis Owen** (*University of Sheffield*)

Speaker: **Bo Brummerstedt Iversen** (*Aarhus University*)

*XFEL Crystallography in Materials Science*

14:00 – 15:30

## Parallel Sessions

### CCG/YCG: Crystal Growth

Session Chair: **Jonathan Foster** (*University of Sheffield*)

Keynote: **Katharina Edkins** (*University of Manchester*)

*Making (the right) crystal grow*

Crystallography is nothing without first having a sample to put in a beam. However, this is commonly not a straightforward feat to achieve especially when desired solid forms for study may be challenging to obtain. This session will explore modern approaches to controlling nucleation in order to grow high-quality single crystals and identify new polymorphs.

### PCG/CCG: Software for Data Processing & Analysis

Session Chair: **Dean Keeble** (*Diamond Light Source*)

Keynote: **Jeremy Frey** (*University of Southampton*)

*Will an AI win the Chemistry Nobel Prize?*

Regardless of whether you collect data on a laboratory diffractometer or at a central facility, there's a good chance an experiment performed today will take less time than the same experiment performed a few years ago. This means we're collecting more samples, more complex data, and more data points. Our ability as crystallographers to keep up with these experiments is now entirely dependent on the software tools we use to analyse our data, in many cases without supervision. This session will explore recent developments in processing and analysis software and will consider what we will need to do in the years to come to continue to exploit the ever-accelerating data collections.

### BSG: Complementary Methods for Structural Biology

Session Chair: **Andrew Burnett** (*University of Leeds*)

Keynote: **Henrike Mueller-Werkmeister** (*University of Potsdam*)

*Multiscale time-resolved optical spectroscopies as complementary tool for serial crystallography*

The structural information and functional insight obtained from X-ray crystallography can be enhanced using complementary methods, such as optical and X-ray spectroscopies. These provide insight into a wide range of physical properties otherwise not accessible by crystallography. This session highlights the use of complementary methods in structural biology.

16:15 – 17:45

## Parallel Sessions

### CCG: Databases and Associated Tools

Session Chair: **Andy Maloney** (*CCDC*)

Keynote: **Matthew O. Kitching** (*Durham University*)

*Using Crystallography and Crystallographic Databases for Selective Organic Synthesis*

Crystallographic studies have provided the community with a vast number of high-quality crystallographic data, collated by organizations such as the CCDC, ICDD, and PDB. In addition to the collation and curation of these data, these organizations, alongside other individuals and groups, have provided us with a vast range of digital tools that allow us to readily analyse and extract the data we require from them. This session will highlight some high impact uses of crystal structure databases and associated software/digital tools that have provided us with a great insight into the solid state and structural chemistry.

### PCG: Phase Transitions

Session Chair: **Arianna Minelli** (*University of Oxford*)

Keynote: **Siân Dutton** (*University of Cambridge*)

*Jahn-Teller distortions in NaNiO<sub>2</sub>*

'Phase transitions' are in many ways an old topic that could be considered only part of textbooks. However, a lot of aspects are particularly challenging and there are still many open questions across a host of scientific fields. The aim of this session is to broadly cover these phenomena in a diverse set of systems, from chemistry to biology and from crystals to amorphous. Abstracts are invited from all areas of the community.

### BSG: Dynamic Structures

Session Chair: **Stephen Muench** (*University of Leeds*)

Keynote: **Doryen Bubeck** (*Imperial College London*)

*Controlling MAC pore formation*

Despite the great steps we have made in solving the structures of proteins and protein complexes, we often look at proteins in a 'static' context. This session is about understanding the dynamics of proteins, from different conformational states, how protein complexes are formed and the role of dynamics in function.

18:00 – 18:45

## CCG Plenary

Session Chair: **Michael Probert** (*Newcastle University*)

Speaker: **Kim Jelfs** (*Imperial College London*)

*Exploring Supramolecular Materials with Computation*

19:00 – 21:00

## Poster Session with Dinner and Wine

## Wednesday 5 April 2023

09:00 – 09:45

### IG Plenary

Session Chair: **Helen Blade** (AstraZeneca)

Keynote: **Ahmad Y. Sheikh** (AbbVie)

*From computational solid state chemistry to molecular design – leveraging opportunities in contemporary small molecules drug discovery and development*

10:15 – 11:45

### Parallel Sessions

#### CCG/PCG: Teaching Crystallography

Session Chair: **Emma McCabe** (Durham University)

Keynote: **A. M. Glazer** (University of Oxford)

*Experience in teaching aspects of crystallography to undergraduates*

With the significant advances in instrumentation and software, the practical aspect of using crystallography in research is far more accessible to students and researchers. The talks in this session highlight the ways in which crystallography is taught to students have evolved, as well as the aspects that haven't changed. The session gives an opportunity to present and discuss different approaches to crystallography teaching, and to reflect on strategies that will equip and inspire the next generation of crystallographers.

#### IG: Industrial Crystallography for Pharmaceuticals

Session Chair: **Helen Blade** (AstraZeneca)

Keynote: **Andy Maloney** (CCDC)

*From crystal structures to particle properties: applying informatics approaches to pharmaceutical development and manufacturing challenges*

The use of crystallography within the pharmaceutical industry is applied in a variety of application. This session will cover practical and computational methods using crystallography to aid in drug development, developing control strategies and predictive approaches. Talks from the perspectives of crystallisation, solid form and particles will be welcome.

#### BSG: Science for Better Research

Session Chair: **Sam Horrell** (Diamond Light Source)

Keynote: **Anna Warren** (Diamond Light Source)

*VMXm: A new micro/nanofocus protein crystallography beamline at Diamond*

New experimental methods are driving advances in structural biology, and take as much time and development as the biological questions they help to answer. This session focuses on new experimental methods and techniques that make it easier to answer important biological questions.

11:45 – 12:15

### CCG Annual General Meeting

### PCG Annual General Meeting

### BSG Annual General Meeting

12:45 – 14:00

### 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.

14:00 – 15:15

### Exhibitor Forum

Session Chair: **Tony Bell** (Sheffield Hallam University)

15:15 – 16:45

### Parallel Sessions

#### YCG/PCG/CCG: Central Facilities Panel Discussion

Session Chairs: **Ben Tragheim** (University of Warwick) &

**Natalie Pridmore** (University of Bristol)

A panel session where panellists will each have 10 minutes to present on opportunities and new developments at national facilities. There will be a particular focus on the instrumentation and types of experiments that are possible, and examples of exciting research being carried out because of it. Presentations will be followed by a full panel Q&A session.

#### IG: Industrial XRF

Session Chair: **Tony Bell** (Sheffield Hallam University)

Keynote: **Paul Bingham** (Sheffield Hallam University)

*XRF analysis of feldspars and silicate glass: effects of melting time on fused bead consistency and volatilization*

X-ray Fluorescence (XRF) spectroscopy is a complementary technique to X-ray diffraction (XRD) which is extremely useful in analysis of industrial materials. This session will cover the use of XRF for analysis of industrially relevant materials. Talks will be welcomed on all aspects of XRF work, done with or without the complementary use of XRD.

#### BSG: Science for Better Health and Wellbeing

Session Chair: **Paula Salgrado** (Newcastle University)

Keynote: **Andrea Thorn** (University of Hamburg)

*COVID-19 the pandemic response in structural biology*

Structural biology plays a key role in addressing the mechanisms leading to disease, and the design of new therapeutics and diagnostics. This session will focus on new advances in structural biology that lead to better health.

**17:15 – 18:00**

## **BCA Prize Lecture**

Session Chair: **Richard Cooper** (*University of Oxford*)  
Speaker: **Aurora Cruz Cabeza** (*Durham University*)

*Beyond the bulk: when shall we care about surfaces in molecular crystals?*

**18:00 – 19:00**

## **BCA Annual General Meeting**

**19:30 – 01:00**

## **Conference Dinner & Ceilidh at the Inox**

# **Thursday 6 April 2023**

**09:00 – 09:45**

## **BSG Plenary**

Session Chair: **TBC**  
Speaker: **Simon Newstead** (*University of Oxford*)

*Decoding the role of solute carrier membrane proteins in health and disease*

**10:15 – 11:45**

## **Parallel Sessions**

### **CCG: Powder Diffraction for Chemical Crystallography**

Session Chair: **Iain Oswald** (*University of Strathclyde*)  
Keynote: **Kenneth Harris** (*Cardiff University*)

*Enhancing structure determination from powder diffraction through multi-technique synergy*

This session will focus on the use of powder diffraction for chemical crystallography, particularly where single crystal investigations may falter, for example, via reconstructive phase transformations or *in situ* investigations etc. We welcome contributions that use multiple techniques in conjunction with Powder XRD to elucidate the structure and enhance our understanding of the solid state.

### **PCG: Sustainability**

Session Chair: **Gabriel Perez Garcia** (*ISIS Neutron and Muon Source/Faraday Institution*)  
Keynote: **Xiao Hua** (*University of Lancaster*)

*Application of a big data approach to study lithium-ion battery materials*

The design, development and understanding of materials for improved sustainability requires the use of a variety of techniques and methods across a broad range of length scales. This session will explore sustainability in materials from different approaches, including, but not limited to, structure-property relations, methods for analysis, and novel systems. Abstracts related to the development of new data analysis and processing methodologies to investigate specific phenomena, or the investigation of local structure and its impact on sustainability, are particularly welcomed.

### **BSG: Computational Crystallography**

Session Chair: **Keitaro Yamashita** (*MRC Laboratory of Molecular Biology*)

Keynote: **Elspeth Garman** (*University of Oxford*)

*Dose estimations for a variety of X-ray diffraction and scattering experiments: extensions to RADDSE-3*

Developments in computational methods and software programs underpin structural biology as a field. Further developments help us make full use of experimental data. Computational methods also streamline the pipeline of structure solution (from data collection to refinement and validation). This session will highlight developments in computational approaches to biological structural studies.

**12:15 – 13:45**

## **Parallel Sessions**

### **CCG: Crystal Structure Prediction**

Session Chair: **Louise Price** (*UCL*)  
Keynote: **Lily Hunnisett** (*CCDC*)

*The CCDC Blind Tests: Showcasing the triumphs, challenges, and evolution of Crystal Structure Prediction*

Crystal structure prediction (CSP) is a rapidly advancing field and is one that shows great promise for thorough assessment of the solid form landscape of a molecule of interest. This session aims to highlight the use of CSP in the community, recent advances in the area as well as the current challenges encountered in the field.

### **PCG: Open Session**

Session Chair: **Alex Browne** (*University of St Andrews*)

This open session is a forum for research that falls outside of the targeted topics of other sessions. ‘Physical’ crystallography is interdisciplinary and intersects with many exciting fields. Whether your work is fundamental or applied, theoretical or experimental; whatever your material, whatever your technique, contributions from every corner of the physical crystallography community are welcome.

### **BSG: ‘Difficult Density’ Workshop**

Session Chair: **TBC**  
Keynote: **Tristan Croll** (*Altos Labs*)

## **CLOSE OF CONFERENCE**



# BCA 2022 AGM Minutes

## Draft minutes of the 2022 Annual General Meeting of the British Crystallographic Association University of Leeds 18:00, Wednesday 13th April 2022

### 1) Approval of Agenda

The agenda was approved. Proposer: Simon Parsons, Seconder: Elspeth Garman.

### 2) Apologies for Absence

Apologies were sent to the Secretary from: Morton Moore, Sandy Blake, Hazel Sparkes, Anna Warren, John Finney, Cheryl Doherty, Helen Blade, Chick Wilson and Simon Phillips.

### 3) Minutes of the previous AGM

There were no comments or corrections reported for the minutes of the 2021 AGM and were approved. Proposer: Claire Naylor, Seconder: Simon Parsons.

### 4) President's Report

The President, Richard Cooper, started his report with the sad news that a number of BCA members had passed away over the last year, as listed in Crystallography News. A moments silence was held by the meeting in respect for these colleagues. Richard then thanked Iain Oswald (2022 Spring meeting Programme Chair), Simon Parsons (Vice President) and all members of the Programme Committee, including the YCG Satellite organisers, for their hard work in preparing this meeting. He also thanked HG3 and the Leeds University conference team for organising the meeting and for their flexibility in allowing us to reschedule this meeting as a result of the pandemic restrictions in place in 2020 – 2021. Richard also thanked the sponsors and exhibitors for their support, and for the poster prizes this year, which were sponsored by the ACA, AIPP, Crystal Growth and Design, CrystEngComm, Calibre Scientific, Indicatrix, IUCr, Oxford Cryosystems, PDB, Rigaku Europe SE, the Royal Society of Chemistry, Stoe and Cie GmbH and Technobis Crystallization Systems. The 2023 Spring Meeting will be held at the University of Sheffield on 3rd – 7th April. Helen Playford (PCG) has agreed to be Programme Chair for that meeting and her email was shared along with a request for feedback relating to this meeting and ideas for 2023. Please send any session ideas to your group representatives. At the 2023 Spring Meeting we will be awarding the BCA Prize Lecture. Please send your nominations to the President ([president@crystallography.org.uk](mailto:president@crystallography.org.uk)). Other upcoming meetings of note included the 2022 ECM in Versailles, Paris, and the 2023 IUCr in Melbourne. Anyone attending these meeting who is able to prepare a short report and photos for Crystallography News, please send these to John Finney for publication. The BCA Council has recently approved a statement of support for Ukraine which is available on the BCA website. Richard also thanked the BCA Council and BCA Officers, Simon Parsons, Alex Stanley and Claire Naylor, for their input and enthusiasm

this year, Crystallography News Editor John Finney, Nicola Hardaker and all of the team at HG3, and all of the BCA members for their continued support of the Association as we return to in-person meetings. Richard also passed on a report from Education and Outreach Coordinator Christine Beavers, who is currently undertaking an assessment and reorganization of the BCA Outreach materials, and continues to oversee Outreach projects funded by the RSC to produce educational videos. Christine also requests that the Groups let her know when group Outreach officers change so she can update her records. Finally, Richard then introduced a proposal for initial discussion, that we introduce a new Fellowship membership category of the BCA. Fellowship members would require at least 5 years of continuous BCA membership of any type, and will attract a higher annual membership (twice the current annual cost of a Standard membership) that will be used to support the activities of the Association, although they would not hold any additional privileges over any other BCA member. Feedback was requested from the meeting. Elspeth Garman agreed that this would be a good idea. A point was raised that the RSC have a similar fellowship category but in the case that a fellowship member is working for example, part-time, that they do make a reduction of their fellowship dues. This is something that the BCA could also consider. Hamish Yeung asked where the decision for a 5-year membership requirement came from: Richard replied that this was chosen to show a level of commitment to the Association. Mike Probert asked if there would be any requirements for maintaining a Fellowship member status: this idea was discussed by Council but it was decided that we didn't want to have a committee/criteria to judge suitability as this can reduce inclusivity as criteria may not also reflect different career paths and backgrounds. It was also noted that career breaks etc. should be taken into account in the requirements for continuous membership. The comments will be considered by the Council in the drawing up of proposed changes to the Statutes for consideration at the 2023 AGM.

### 5) Secretary's Report

Virtual BCA Council and BCA Officers meetings have proved successful and we plan to continue this format post pandemic to reduce the cost of travel expenses and time commitments. Nominations for Council elections were received in good time and many thanks to the Nominating Committee for their assistance and cooperation.

### 6) HG3 Report

Total BCA membership as of 11th April 2022 was 494. This is an increase of 5 members on last years' total. Corporate Members are: Bruker UK, CCDC, Douglas

Instruments Ltd, ICDD, Molecular Dimensions Ltd, Oxford Cryosystems, Malvern Panalytical, Rigaku Europe SE and Scientific and Medical Products Ltd. Advertisers for Crystallography News are: Bruker UK, Oxford Cryosystems, Rigaku Europe ES and Malvern Panalytical. 2022 Spring Meeting: 162 delegates registered at the start of the meeting, plus 23 invited speakers and 16 exhibitors, totalling to 201 attendees. These figures do not take into account a small number of speakers who have had to cancel and/or present virtually at the last minute due to Covid. The numbers are in reasonable alignment with pre-pandemic in-person attendance levels. Sponsors lists, including poster prize sponsors, were covered in the President's report.

## 7) Treasurer's Report, including Presentation of the Accounts for 2020 and the Examining Accountant's Report

Claire Naylor presented her report and the Accounts to the meeting. Full copies of the Accounts will be available on the website by emailing Claire or on the Charity Commission website. Income fluctuations between 2019 and 2021 can be entirely attributed to the holding, or not holding, of in-person Spring Meetings during the pandemic. Otherwise, the finances are largely stable. It is expected that the projected 2022 accounts will be returning towards pre-pandemic levels again. Claire highlighted the issues that the last three Spring Meetings held (2018/2019/2021) have all made losses, and the additional losses for the cancelled 2020 meeting were paid for by liquidating some assets, which has since been recovered through the recovery of our investments post-pandemic. This is something we should be keeping under review and may lead to an increase in membership fees. Governance costs are kept as low as possible and are fairly consistent: this is being aided by making use of virtual meeting options where possible which has significantly reduced travel claims for Council and other committee meetings. Major expenses during the year: subscriptions to international bodies (IUCr and ECA) is one of our largest outgoings, annual conference costs and Crystallography News, although Crystallography News also brings in more income than its expenditure, *i.e.* it is profitable. Elspeth Garman noted a small error in the spreadsheet: total income should be total expenditure in one column and Claire will amend the accounts accordingly. Expenditure is a little higher at this stage than previous years due to some expected spending on Outreach video projects. In summary: we continue to try and reduce our governance costs, our investments have recovered from the losses in 2020 which enabled us to pay for the loss made for the cancelled 2020 Spring Meeting, and our main income is from participation. Claire thanked the members for getting involved with the Association, and thanked Hg3 (Nicola and Moira, who retired this year) for preparing their accounts, other Council members and the Group Treasurers, and Charles Stanley bank and UHY Hacker Young who prepare the formal accounts each year. Questions from members: John Hellier commented on the rising rate of inflation and asked about the consequences for BCA finances: Claire noted that this will be covered in the next section and there are some plans to try and protect the finances from inflation, but agreed that this is a risk that must be considered. It was also commented that the hospitality costs continue to rise and this continues to be a contributory factor to the losses made from Spring Meetings. Mike Probert asked whether all of the BCA's investments

are being held in ethically-managed funds: Claire reported that she has a meeting scheduled with the investment bank the next day and this issue will be discussed.

The accounts were accepted. Proposer: Helen Duncan, Seconder: Simon Parsons.

## 8) Appointment of Examining Accountant for 2021

UHY Hacker Young were approved to continue as the examining Accountant. Proposer: Iain Oswald, Seconder: Mike Probert.

## 9) Elections to Council

The newly elected members of BCA Council in 2022 were: Vice Chair: Suzanna Ward, Secretary: Lauren Hatcher, Ordinary Member: Lucy Saunders. Richard Cooper also thanked outgoing members of Council: Simon Parsons as Vice Chair and Alex Stanley as Secretary.

Vacancies for Council in 2023 are Treasurer and one Ordinary Member. Nominations can be made directly to the President or Officers or may be proposed via the Nominating Committee. Richard thanked retiring members of the Nominating Committee: Chick Wilson and Lee Brammer.

## 10) Honorary Members

Congratulations to Professor Paul Raithby and Professor Chick Wilson, who were both made Honorary Members of the BCA this year. The nomination deadline for Honorary Members for next year is 31st August 2022 and nominations can be made directly to the President. Please look on the website for instructions for how to nominate a member.

## 11) Membership, annual subscriptions and subventions

Claire Naylor discussed that membership fees will need to be increased to help us to keep pace with rising costs and help to keep the registration for the Spring Meeting lower. It was proposed that standard member subscription be raised from £40 a year to £50 a year, with the other subscription fees also raised in proportion to this. Mike Probert noted that continuing to raise the student membership subscription could become an issue in future, as Ph.D. student stipends were not being increased in-line with inflation. It was also noted that the student fee would be higher than the RSC. It was therefore proposed that we keep the student fee at the same level as 2022 – Proposer: Anthony Carter, Seconder: Kate Brown. Some discussion was also had around the fees for the proposed Fellowship category, which will be considered when creating the changes to the Statutes for this membership category.

Breakdowns of current member levels in each of the groups will be reported in Crystallography News.

## 12) Future bid for IUCr in the UK

The last UK-based IUCr meeting was held in Glasgow in 1999, and trends put an IUCr meeting in Europe approximately every nine years. The next Europe-based meeting will be in 2029 in Berlin, Germany. Hosts who will bid for the 2038 meeting need to begin the planning stage now, and Council propose that we begin this process. Richard noted that we should perhaps consider bringing in other organisations, e.g. the BACG, to bolster the diversity of the scientific content, and also that we need regional support from the ECA. Richard has provisionally contacted the ECA about a potential bid and they

confirmed they are not opposed to the idea at this early stage. Richard/Council proposed that the BCA should develop a bid to host a future IUCr in the UK and that we should begin to research potential venues etc. John Helliwell commented that he supports the forward thinking of the Council on this idea. Lee Brammer seconded this and made the point that 40 years since the previous time the UK hosted the IUCr would be a long enough gap, considering we are a prominent member of the global community. Claire Wilson noted that in the typical IUCr cycle decisions on host countries are typically made six years in advance of the meeting. Mike Probert and Richard also commented that there is no drawback to beginning to plan a bid now. Alex Stanley and Elspeth Garman commented that another advantage to planning early is that often a losing bid for one year is then successful for the next meeting, and so we should keep in mind that this is another potential strategy. John Helliwell noted that in the past decisions (e.g. ECM-2013) have been influenced by significant anniversaries for crystallography events, and so if there was a case to be made for an anniversary of an important discovery linked to 2038 then this should be considered – for example, discussion was had that the first X-ray photograph of DNA was made in the UK in 1938 by one of Astbury's Ph.D. students.

The proposal was put to a vote (show of hands) and was universally accepted (48 in favour and 0 against).

### 13) Equality, Diversity and Inclusivity report

Policies from 2018 were shown during the Meeting, which primarily cover the appointment of speakers and Chairs at

the Spring Meeting. ED&I monitoring numbers were presented for the past few Spring Meetings, but Richard noted that in its current form our monitoring process has not enabled us to collect information on non-binary genders so this information is currently missing from the analysis to date. For the 2022 Spring Meeting, the Plenary speakers have a good gender balance, but there was low female representation for Keynote speakers. The session chairs and Plenary speakers have improved on gender balance from previous years, but submitted speakers did not quite reflect the overall gender balance of the whole membership and so this should be improved upon in future. Lucy Saunders asked if we collect gender balance based on names where members do not chose to disclose their gender during registration. Richard confirmed this was done, but it was discussed that we could collect more robust ED&I information if we changed the registration process, e.g. include an optional ED&I monitoring questionnaire. Richard cautioned that this needs to be done correctly however, as it will involve collecting sensitive personal information.

### 14) AOB

Simon Parsons asked for confirmation of PCG Programme Chairs for the 2023 Spring Meeting. Claire Naylor invited the new Vice Chair and Secretary to attend a meeting with the investment bank the next day, if possible. Elspeth Garman thanked Alex Stanley (outgoing Secretary) and Simon Parsons (outgoing Vice Chair) for all their hard work on Council.

The meeting was closed at 18:57.

## Obituary

### Chris G. DeAlwis 1964-2022



Credit: CWRU.

Chris DeAlwis was a post-graduate research student in the Laboratory of Molecular Biology in Birkbeck's Crystallography Department from 1989 to 1993. He had completed an M.Sc. in Crystallography part-time while working at Kingston University where he had been awarded a B.Sc. (Hons) in Applied Science. His Ph.D. studies, supervised by Tom Blundell, initially

concerned the analysis of aspartic proteinase inhibitor complexes; this work was highly successful. He went on to the more challenging analysis of the structure of mouse submaxillary renin – an enzyme which plays an important role in hypertension. This was a great piece of work which was published in *Nature* (357, 466, 1992) and set his scientific career on a stellar trajectory.

Chris moved to Chicago as a research associate with Keith Moffatt, and then as a research scientist to Abbott Laboratory, Illinois. During three years with Elias Lolis at the Yale School of Medicine, he undertook successful structural studies of chemokine-receptor interactions. Following on from his truly outstanding work at Yale, Chris became Assistant Professor in Biochemistry and Cellular Molecular Biology at the University of Tennessee, Knoxville (UTK) in 1999 and Associate Professor there in 2005. He was then recruited by the Department of Pharmacology in the School of Medicine, Case Western

Reserve University (CWRU). His research focussed on the structure-function and regulation of ribonucleotide reductase by small molecule effectors and its protein inhibitor, Sml1 – this continues to be a highly productive field of cancer research. He also had a great interest in pathogenic amyloid forming proteins and in the investigation of enzyme catalytic mechanisms, dynamics and solvent structure using neutron and ultra-high resolution X-ray diffraction. This work has helped unravel the mechanistic steps in the reaction catalysed by dihydrofolate reductase, a housekeeping enzyme involved in thymine biosynthesis and a classical drug target. At both UTK and CWRU, Chris trained numerous students and postdoctoral scientists – many have gone on to be productive researchers in industry and academia, as well as in medicine and clinical research.

In the three to four years that I (JC) worked alongside Chris at Birkbeck, I found him to be a highly capable, amicable and generous colleague and we maintained a degree of informal contact in the intervening years, partly through our joint interest in neutron diffraction, although I regret that the last time we met was around 20 years ago. I was shocked to hear that he had passed away unexpectedly while visiting his family in England last Summer. I also did not know that Chris had lost his sight several years ago and was supported in his work by his wife Martha. A number of wonderful tributes to Chris can be found online.

**Jon Cooper (UCL), Brad Bennett (Samford University) and Elias Fernandez (UTK)**

# Crystallography at Birkbeck

**BIRKBECK** College celebrates its 200th Anniversary this year. As it was where much crystallographic development took place – and was the location of the first Department of Crystallography – it seemed appropriate to mark the occasion. So we are publishing here a personal account by Rex Palmer – apart from Alan Mackay, the longest surviving member there from earlier days – his personal account of some of people and some of the crystallographic work done in the College over the past eight or so decades since Bernal took over the Chair in Physics there from Patrick Blackett.

This is a shortened version of a longer article by Rex that will be made available on the BCA website at <http://www.crystallography.org.uk/news/2023/01/24/crystallography-at-birkbeck.html>. You might also like to refer to the articles in the Bernal special issue (*Crystallography News*, September 2021), where Christine Slingsby, Paul Barnes and John Finney respectively discuss more of the biological, materials and liquids work that came out of the Department in the Bernal era.

**John Finney**  
UCL

## CRYSTALLOGRAPHY AT BIRKBECK COLLEGE

### Some of the people and some of their science

Crystallography came to Birkbeck when **J. D. Bernal** took over the chair in physics from Patrick Blackett in 1938. With his appointment he brought with him a wealth of knowledge and experience of crystallographic studies of a huge in-depth range of materials from water, metals, proteins and viruses. Much of his pre-Birkbeck history and scientific achievements are discussed in the September 2021 *Crystallography News*.



Fig. 1: The Birkbeck lab. from 1948 to 1966.

After World War II (again see the above *Crystallography News*), he established Birkbeck's Biomolecular Research Laboratory in two war-damaged Georgian houses in Torrington Square (figure 1). This would be a multidisciplinary department that would seek to investigate the structure and function of proteins using all the available physical techniques, including not only X-ray crystallography (where he envisaged making developments in X-ray tubes and instrumentation suitable for both large unit cell systems such as viruses and also liquids), but also the newly invented electron microscope. His plans also included

inorganic work relevant to the building industry, with special emphasis on understanding the shrinkage of cements. So his initial team was made up of **Harry Carlisle** from Oxford<sup>1</sup> to head the section on proteins and viruses, **Helen Megaw** to lead the cement work, **Werner Ehrenberg** to develop new apparatus (especially fine focus, high intensity X-ray tubes), and **Donald Booth** to develop the application of computing to crystallography. When **Helen Megaw** left in 1946 for Girton, she was succeeded by **Jim Jeffery**, who acquired **Alan Mackay** as a part-time Ph.D. student to work on the structure of calcium phosphate.



Fig. 2: The early team at Birkbeck.  
L-R: back row: Sam Levine (a mathematician interested in colloids), Jim Jeffery, John Hirsch (experienced in instrumentation), Geoffrey Pitt (Ph.D. student of Harry Carlisle), Helen Scouloudi (also worked in Harry's team); bottom row: Anita Rimel (Bernal's longtime secretary), Werner Ehrenberg, Bernal, Helen Megaw, Harry Carlisle. Credit: IUCr, Creative commons.

This founding team (figure 2) grew over the years to be a major influence in the development of crystallography, and led to the establishment (after many bureaucratic battles) of a full Department of Crystallography in 1964. Among those joining the team **Aaron Klug**, who worked shortly on Ribonuclease before turning to viruses, in which pioneering work he was joined by **Rosalind Franklin**. Klug took the virus work to Cambridge before publishing any of the results in the name of Birkbeck College. Other names that played major roles in the

early decades include **Don Caspar**, **Isidor Fankuchen**, **John Finch** and **Ken Holmes**. Again, see the above-mentioned *Crystallography News* for a fuller account of this and other biology-related work.

Bernal's Guthrie Lecture 1947 concentrated on proteins as the basis of life, but it was Perutz, still at Cambridge, who picked up Linus Pauling's leads. In the early 1960s, Bernal returned to the subject of the origin of life, analysing meteorites for evidence of complex molecules, and to the topic of the structure of liquids, which he talked about in his Bakerian Lecture in 1962<sup>2</sup>.

### The M.Sc. in Crystallography

In the early years the only taught course was the M.Sc. in Crystallography. This was a highly intensive course for both part-time and full-time students. It gave a thorough and comprehensive grounding to prospective researchers in the field of X-ray crystallography. Part-timers attended lectures from 6 to 9p.m. five days a week for two years and had practicals on Saturdays (!). Full time students were usually supported by grant-giving bodies and covered the lecture courses and practicals by attending special sessions put on for them by members of staff during the day. This was for many years an outstanding course and was held in esteem by many science departments world-wide – many researchers from the UK and abroad have claimed that this was the start of their scientific careers. About 10 to 15 students per year graduated and many continued studying in the Department for part-time or full-time Ph.D. degrees. One of its external examiners was Kathleen Lonsdale of nearby UCL (who also taught on the course). Another was Arnold Beevers, famous for his part in inventing the computational aid Beevers-Lipson Strips. I remember one day in 1964 meeting someone by chance at the Pasadena Institute of Technology in California who asked me where I was from. I told him I was from Birkbeck College to which to my amazement and joy he immediately responded: "I know...the M.Sc. in Crystallography".

### A new building!

In 1952 a new Birkbeck College building was opened in Malet Street. However, the Crystallography Research Laboratories remained in the two Georgian houses in the adjacent Torrington Square. The Computer Section was also in one of these houses (actually in a static water tank about 60 feet long that had been used in the war for fire fighting!). The M.Sc. lectures and practicals were held in another house at 32 Torrington Square. Eventually, in the later 1960s, new lecture theatres and laboratories for both student courses and research were opened in the new building, with Bernal now Head of an independent Department of Crystallography.

The research in the Department was very wide-ranging, covering single crystal analysis of both small organic and inorganic molecules, proteins and viruses. The work continued, with Harry Carlisle leading the groups working on both small organic and protein crystals; Jim Jeffery oversaw the work on inorganic structure analysis and powders; Aaron Klug joining in 1953 to lead the group studying virus structure – by this time Bernal's interest in liquid structure had taken over most of his research time. Other members of staff included Alan Mackay, whose interests developed to focus on generalized crystallography and electron microscopy (see below), and **Graham Bullen** whose interest was in organic crystal structures.

### Some of the people and their work

**Harry Carlisle** succeeded Bernal as Head of Department in the early 1970s, having interests in the X-ray analysis of both small organic molecules and the much larger molecular weight proteins, concentrating the latter on the medium sized protein Bovine Pancreatic Ribonuclease A. This was extracted from pancreases purchased from a local slaughter house by Ph.D. student **Michael Rosemeyer** who also grew the crystals and prepared heavy atom derivatives. Michael later became Professor of Biochemistry at UCL. As mentioned earlier, Harry Carlisle's small molecule analysis experience had started when he worked with Dorothy Crowfoot (later Hodgkin) on the structure of cholesteryl iodide<sup>1</sup>. Some 50 or so years later the original crystals were found in a phial in the Department in unblemished state and were subjected to a modern high resolution analysis<sup>3</sup>.

Harry's interest in protein crystallography was no doubt also born during his time with Dorothy. He opted to study the protein Ribonuclease because it was fairly small for a protein. For the collection of RNaseA X-ray intensity data, Harry designed a unique 6 cm radius Weissenberg Camera which was built by **Len Stevens** in the Departmental workshop. Many thousands of X-ray intensities were measured by eye estimation by Harry, a process which had a somewhat detrimental effect on his eyesight. Another group headed by Dave Harker in Buffalo was also working on this protein, and I gave a talk in 1964 on our state of progress on Ribonuclease to members of Harker's lab. and other American protein crystallographers.

By the mid 1960s more sophisticated methods were being developed for measuring X-ray intensity data from both large and small molecule crystals. The early linear diffractometer of Hilger and Watts (Y190/A328) designed by Arndt and Phillips was manually operated. The later 4-circle instrument (Y290) was controlled by a PDP-8 minicomputer. The Enraf-Nonius CAD4 diffractometer is characterised by a kappa goniometer. It had therefore become much faster to measure the data, and with greater accuracy, to solve crystal structures. The breakthrough with respect to Ribonuclease came in 1967 with the publication of a low resolution structure, and Harry's group worked on ribonuclease until his retirement. Ribonuclease work continued after Harry's retirement resulting in several publications<sup>4</sup>.

**Jim Jeffery** was Head of the Materials Research team until his retirement. His work in the Department initially focussed on cement-related systems: why cement sets was a pressing industrial problem after World War II, a time when there was a lot of reconstruction work taking place. Bernal thought that "the properties of hydrated cements are closely related to those of many biological gels and are strongly influenced by the same long range forces". Jim's work expanded to a wider range of inorganic materials such as corrosion products in power station boilers and phase separation in, and the crystallisation of, glasses – of contemporary importance in the manufacture of glass ceramics. He was also enthusiastically concerned with instrument development (the Department for many years made its own arcs in its workshop) and experimental methodology, on which he published a book, *Methods in X-ray Crystallography*, in 1971. He was awarded a personal chair in recognition of his many achievements.

Though **Alan Mackay** began his time at Birkbeck in the late 1940s as part of Jim Jeffery's cement-centred group, his interests soon broadened, publishing more broadly than might be expected of a 'normal' crystallographer. It was not only Istvan Hargittai who considered him "one of the rare generalists of our time"<sup>5</sup>. He contributed to the development of the science of structures generally, and was a major driver in developing

Bernal's concept of 'Generalised Crystallography'. Like Bernal who thought that local five-fold symmetry might be relevant to the structure of liquids, much of Alan's focus has been on systems that so-called 'classical crystallography' rejected – for example an icosahedral packing of equal spheres that became known as the Mackay icosahedron, which according to one Chinese researcher "made tremendous impact on particle, cluster, inter-metallics, and quasicrystal researchers"<sup>6</sup>. And it's perhaps in relation to quasicrystals that Alan might be mainly remembered for. Having designed a regular non-periodic two-dimensional structure from regular pentagons (see cover) that was different from the Penrose tiling – and simulated its diffraction pattern – he predicted<sup>7</sup> the possibility of what were to be called 'quasicrystals' three years before their experimental discovery by Dan Schechtman. Though missing out on the Nobel Prize given for quasicrystals, Alan was belatedly elected a Fellow of the Royal Society in 1988.

## Expansion

There was a significant expansion of academic staff in the 1960s/early 1970s.

**Rex Palmer** joined the Department as a Lecturer in 1964, following his Ph.D. on Ribonuclease under Harry Carlisle in 1962, and a year each as a Research Fellow at the University of Illinois and Caltech. His research interests were wide, covering X-ray – and some neutron – crystallography of proteins (Ribonucleases, Ribosome Inactivating Proteins and Lectins); Steroids, Anticonvulsants, Antimalarials, Oligomycins, Cyclosporins, DNA Intercalators, Neuromuscular Blockers, Sugars, Sodium Channel Blockers and other drug molecules. An example of his work is an original method for determining the heavy atom positions in a protein derivative<sup>8</sup>. He also worked on the molecular modelling of the binding of drugs and substrates to proteins. Since retiring in 2001 as Emeritus Reader, he has maintained a research group which has published on a regular basis on various aspects of biomolecular structure and function using X-ray and neutron diffraction, molecular dynamics and model building, with more than 60 papers to date with ex- (student and research fellow) members of Birkbeck. With Mark Ladd, he has authored two books: *Structure Determination by X-ray (and later Neutron) Crystallography and Direct Methods in Crystallography*. Rex was a major contributor to the M.Sc. Crystallography course, for many years being the admissions tutor. He was also secretary of the London University Committee governing this course whose chairman for many years was David Blow.

**Beatrice Gorinsky** (née Woolhouse) came to Birkbeck in the early 1960s to study for the M.Sc. Crystallography degree. Subsequently she registered with Harry Carlisle as a Ph.D. student working on the Ribonuclease project, after which she was awarded a Lectureship in the Department. She continued to be a key worker on the Ribonuclease project and also worked in the team with Peter Lindley (see below) on the structure of Serum Transferrin. Both of these projects were highly successful, the work on Transferrin being a highly innovative project on a biologically very important protein.

**David Moss** joined the Department in the late 1960s as a Lecturer in electron microscopy. His research interests ranged from molecular biology and protein crystallography to bioinformatics, with special reference to symmetry and statistics. He led Birkbeck's efforts in the ImmunoGrid collaborative project to build and deploy a virtual human immune system using computer simulation. The system aims to mimic immune responses to help design treatments for cancer and chronic infections, which it is hoped will assist in understanding

autoimmune diseases such as rheumatoid arthritis, celiac disease, allergies and leukemia relapse. In the latter case, he worked to develop immunotherapies where donor T cells can be used to kill residual leukemia cells.

David was perhaps ahead of his time in introducing internet-based education in 1995, working part-time to run these courses, (even if it meant giving tutorials in the middle of the night to catch students on both sides of the Pacific Rim – Birkbeck being one of the first universities to use the internet for teaching). One of his achievements in his 'retirement job' as a part-time Senior Research Fellow has been to provide the first detailed description of the alpha toxin in certain bacteria and explain how it disrupts the signalling function of cells. The alarming prospect of the use of such toxins in bioterrorism gives this work a strong contemporary importance. His computing expertise has been crucial in research developments in the area of bioinformatics, and the use of computer databases and algorithms to enhance biological research, especially in the area of genetics.

**Peter Lindley** joined the department in 1967. He started work at Birkbeck in the cement area and small molecule crystallography. He established a small molecule service for chemists and biologists which was used by many chemists in the UK and Europe. He played a major role in the Department's fight back against an attempt to close it in the early 1970s, and as part of the internal reorganisation agreed by the staff that followed, he changed tack from small to large biological molecules, working on structures of proteins such as Serum Transferrin, Human Serum Ceruloplasmin, Cupredoxin, Lactoferrin and (with Christine Slingsby – see below)  $\gamma$ -crystallin II. His persistence against great odds in sorting out problems with the water supply system in the basement was instrumental in keeping the lab. operational!

**John Finney** arrived in the Department in 1965 as Bernal's Research Assistant to work on his structural model of liquids with a most imaginative Experimental Officer **Ian Cherry**. Following his (part-time) Ph.D. in 1968 he joined the staff as a Lecturer. With the departure of **Shirley King** from Bernal's Liquid Group (Shirley had worked on adapting Bernal's model of simple liquids to the structure of water), he expanded his interests to water in all its forms, especially its role in biological processes. Here, he teamed up with the protein crystallographic expertise in the Department to examine the detailed structure of disordered water in proteins and other biomolecules – both by X-ray and neutron structure determination and, with Julia Goodfellow (see below) the early application of computer simulation to these complex systems. With great support from Dorothy Hodgkin, he and Ph.D. students **Hugh Savage** and **John Bouquiere**, in collaboration with Peter Lindley (see above), produced a very high resolution neutron structure of the disordered water in Vitamin B12 coenzyme that led to Hugh, on a late night train back home to Littlehampton, determining a set of repulsive regularities that appeared to control not only the observed solvent structure, but also the organisation of water in hydrates and ices<sup>9</sup>.

Concentrating on exploiting neutrons for their ability to clearly see hydrogens, his group discovered and solved the structures of new phases of both crystalline and amorphous ices. He also began to explore isotope substitution in aqueous solutions of chemically and biologically important molecules, work which expanded when, following a period of leave at the UK's pulsed neutron source ISIS as Head of Neutron Science and ISIS Chief Scientist, he moved on in 1993 to the Quain Chair of Physics down the road at UCL.

In the late 1960s, there was a major scientific controversy when a well-respected Soviet scientist, Boris Deraguin,

reckoned he had discovered a new and denser form of water which many thought might be a polymer of water – hence the name ‘polywater’. Having heard a lecture by Derjaguin while a postdoc. in Cambridge, **Paul Barnes** wrote to Bernal asking if he could join the group to work on this. He duly did – see his article in the September 2021 *Crystallography News* for how this work proceeded. Being taken onto the academic staff, he inherited Jim Jeffery’s materials-focussed group. Exploiting X-ray and neutron diffraction and electron microscopy, he and his group did extensive structural work on materials such as zeolites, ceramics, cements<sup>10</sup>, hydrates (particularly those with an industrial application), bulk rock analysis, drug polymorphism, rubber-based materials and micro-mechanical structures. With respect to his recognition in cement studies, he drew together a multinational team of authors in a book *Structure and Performance of Cements* that highlights the latest global advances in the field of cement technology. The Materials Group was strengthened by the arrival in 1994 of **Jeremy Cockcroft** from the ILL. In addition to his research, Jeremy, assisted by **Huub Dreissen**, was a central force in establishing courses in long-distance learning in the Department.

**Christine Slingsby** joined the Department in the early 1970s from the Nuffield Laboratory of Ophthalmology, University of Oxford. Her research concerned the various proteins found in the eye lens, their structures and how they denatured with age to form cataracts, and the role of related small heat shock proteins in neuromuscular systems, ageing and disease. She developed methods for the extraction, purification and crystallization of these proteins, and proceeded to develop a very successful, and as testified by her publication record, very extensive programme of research on crystallins and related proteins, including determining their structures and relating this to the formation of cataracts in old age. Her research has led to the routine treatment of cataracts, and many of us have been successfully treated by surgeons who are extremely aware of the huge influence of Christine on their work.

A comprehensive review of the eye-lens crystallin story can be found in reference 11.

## The Blundell era and beyond

The arrival of **Tom Blundell** in 1976, becoming Head of Department in 1978, signalled major developments in the structural biology research in the Department.

With research interests in elucidating the architecture and function of macromolecules and their multi-component assemblies using methods from biochemistry, protein crystallography, and bioinformatics, he and his team have made major contributions in understanding biological function in many areas (see report on page 26 on the seminar held in his honour in December last year). These include the structural biology of polypeptide hormones, growth factors, receptor activation, signal transduction, and DNA double-strand break repair – subjects important in cancer, tuberculosis, and familial diseases. He has also developed software for protein modelling and understanding the effects of mutations on protein function, leading to new approaches to structure-guided and fragment-based lead discovery. Many of the students and post-docs that worked with him at Birkbeck have gone on to be major players in their own right – examples including **Tim Hubbard** at King’s College London, and **Lawrence Pearl**, who in 2008 followed Tom’s footsteps in being elected FRS. Early on in his time at Birkbeck, he published with Louise Johnson a book on *Protein Crystallography*.

**Janet Thornton**, now Director Emeritus at the European Bioinformatics Institute, joined Birkbeck in 1980. “I was

part-time initially: a wonderful opportunity to spend time with my two children while continuing with my research. Later I understood how lucky I had been and appreciated how much support I’d received at Birkbeck.” Her research focussed on bioinformatics, exploiting computers to study protein sequences and structures; she was one of the first to classify these structures and describe them in terms of their component parts. On being made a Fellow of The Royal Society (one more Birkbeck alumnus to be so recognised), Janet said: “I admire Birkbeck immensely, both for its work in giving people the opportunity to study, but also for its world-class research; the words Birkbeck and crystallography are synonymous”. An example of the internal collaboration across groups within the Department is the development of the program PROCHECK<sup>12</sup>.

**Julia Goodfellow** joined the Liquid Group in the late 1970s to expand its work on the role of water in biomolecular systems, and developed the computer simulation work of the group. Following the departure of John Finney to ISIS and UCL, she developed further her research in a variety of aspects of biomolecular structure, including both the work on protein hydration and stability, and the exploitation of computer simulation in understanding the dynamics and functioning of proteins. Her work and other abilities were recognised in her appointment in 2002 as Chief Executive of the BBSRC, since when she has moved on to other major national administrative roles in science policy and higher education (for example, Vice-Chancellor of the University of Kent).

In the late 1980s, **Bonnie Wallace**, then at Rensselaer Polytechnic, took a sabbatical at Birkbeck to extend her knowledge of Crystallography to add to the techniques she was utilising for the study of membrane proteins. Shortly after her return to the USA she was offered a position in the Department and moved her lab. to the UK in 1991. Her research at Birkbeck has included the structure and function of ion channel and other membrane proteins and the development of methods for circular dichroism spectroscopy, in particular synchrotron radiation circular dichroism spectroscopy where she is regarded as the major figure behind the advancement of this technique.

**Helen Saibil** came to Birkbeck in 1989 as the Bernal Professor of Structural Biology – noting her speciality of electron microscopy and Bernal’s early recognition when setting up the Biomolecular Research Laboratory of the potential of ‘the newly invented electron microscope’ (see Bernal’s comment in paragraph 2 above), occupying the Bernal Chair would seem highly appropriate. She developed the Cryo-EM operation in the Department, with much – though not by any means all – of her research on molecular chaperones and protein misfolding<sup>13</sup>. Helen was also a key figure in the establishment of a cryo-imaging facility at the Diamond Light Source. In 2006 she became yet another Birkbecker to be elected as a Fellow of The Royal Society.

**Jim Pitts** and **Ian Tickle** both came to the Department with Tom Blundell in 1976. Jim completed his Ph.D. on the protein crystallography of avian pancreatic polypeptide. Subsequently appointed to a Lectureship, he continued crystallographic structure/function studies of a number of proteins, including the effects of mutation (of relevance to protein engineering, which was beginning to be seen as a possibility). While Ian also continued to be involved in biomolecular crystallographic projects, he was instrumental in enhancing the Department’s computational capability, in particular the development of computer graphics which was then in its early days. He was also involved in the early days of CCP4 – his report of a day in room 114 makes interesting reading<sup>14</sup>.

## Some concluding remarks

As it was appropriate for a leader with Bernal's social and political convictions to run a Department where everyone was valued for their contributions, it would be amiss not to acknowledge the importance some of the non-academic staff, without whom the Department would not have succeeded as it did. Though there have been many secretarial staff, **Anita Rimel** (Bernal's PA during his whole time at Birkbeck) and **Glenda Dryer** deserve special mention (the latter playing a major supporting and advisory role during the 'battle to save Crystallography' in the early 1970s). Much of the work in the earlier days would not have been possible without the commitment of the Chief Technicians **Stan Lenton** and his successor **Nick Moore** (who also ran the early EM suite), and the superb expertise of the workshop staff led by **Len Stevens**. And without **Derek Coggrave** (who came from Hilger and Watts who made many of the early diffractometers), the staff and the students would have had to take all their data on film...

Finally, if you are interested in reading a little more, there is a report of the meeting celebrating '50 years of biomolecular structure at Birkbeck: Bernal's legacy' on the BCA website at <https://www.crystallography.org.uk/old-bca-website/cnews/1999/mar99/bbk50.html>.

**Rex Palmer**  
Birkbeck College London

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# The Birkbeck M.Sc. in Crystallography; a personal reminiscence

**WHERE** to start. I had just graduated with a degree in geology in the late 1970s at a time when oil and mining companies were cutting back and laying off their staff and jobs were very thin on the ground. And despite my only crystallographic knowledge being short courses on crystal morphology and basic mineral crystal structures, I applied for a job at Philips Research Laboratories as a research technician in the X-ray diffraction laboratory. However, with a degree of luck if not a relevant degree, I was somehow offered the job, in spite of telling one of the interviewers his crystals of quartz that were prominently displayed, were in fact calcite. Armed with a short set of notes on 'how-to' left by my predecessor I rapidly found myself orienting crystals using back-reflection Laue, carrying out Berg-Barrett, Lang and double-crystal topography, and analysis of single-crystal thin-films using single and double-crystal goniometry.

Whilst becoming practically competent, there remained the feeling that to progress further required understanding at a significantly higher level than I had at the time. In the odd times I wasn't working in the laboratory and could be in the office, I had access to a few books on my bookshelf to try and teach myself crystallography. A tatty copy of a book titled '*International Tables for X-ray Crystallography Volume I*' just seemed full of incomprehensible diagrams; Brian Tanner's book '*X-ray Diffraction Topography*' had a formidable chapter on theory

(and full of incomprehensible equations – apologies, Brian), although the chapters on practical techniques were always useful. Helen Megaw's book '*Crystal Structure: A Working Approach*' was much more readable but still contained, what seemed at the time, a large component of jargon.

Somewhat dismayed, but encouraged to persevere by my group leader, the late Ron Pearson, I decided to see if any alternative books were in the laboratory's library (usually my bolt-hole for a mineralogical fix from American Mineralogist). Only one suitable book was on the library shelf, Jim Jeffery's '*Methods of X-ray Crystallography*', which I duly took out to read over lunch. In the introduction, the book described an M.Sc. in Crystallography at a university called Birkbeck College in London, which seemed the ideal course for someone like me, but did it still run? And would Philips give me leave of absence for a year? A further trip to the library to investigate the course, and to my delight, it still ran, and furthermore, it ran in the evenings. Three-four evenings a week over two years part-time, lectures three hours 6-9 p.m., quite a commitment. Providing I was accepted for the course, Ron Pearson would generously find money for the fees, the train fares to London and the occasional day off for home study. I applied for the course and was invited to interview with Rex Palmer. Slightly concerned at my lack of numeracy and background in physics I was expecting a grilling; quite the opposite, a pleasant 15 minute chat and an offer to start the course in the September.

Despite being pleased to have been accepted on the course, nagging doubts on whether a geology degree was a sufficient foundation remained.

During the summer, I left Philips to join the G.E.C. Hirst Research Centre in North Wembley. Two of my new colleagues were former Crystallography M.Sc. students. One, Colin Dineen, used to reminisce about being taught dynamical theory on the course by Kathleen Lonsdale, who assumed the then-recent review by Batterman and Cole was to be her starting point (!). With this information, the doubts increased at least five-fold...

October came and seven students, two full-time, five part-time, awaited our first lecture in diffraction theory from John Finney. In the short time we had to chat before the lecture started, I found we had only one physicist, a couple of chemists, one an Open University graduate, and surprisingly, a dentist; maybe a geology degree wasn't too bad a background after all. I never knew whether John tailored his course to the background of the average student, but over the course of the term his careful teaching took us all from ignorance to understanding the theory to be well placed for subsequent lectures on single crystal instrumentation. Rex Palmer taught a course on crystallographic symmetry throughout the whole of the first year. From introductory point groups through two terms of detailed analysis of space group symmetry via the previously incomprehensible International Tables, this course is the one that set me on the road to structural crystallography. Much of the teaching was based around Belov's classic, but often opaque paper '*A Classroom Method for the Derivation of the 230 Space Groups*'. Rex worked tirelessly to make this work clear and gave confidence to reset space groups in non-standard settings (the years before International Tables Volumes A and A1) or with non-standard origins. This course has proved invaluable for me in subsequent experimental studies of structural phase transitions where retaining standard settings in a sequence of transitions makes little sense when what is important is symmetry lowering from a high symmetry phase. Peter Lindley lectured on a course on single crystal instrumentation taking us on from John's theory course. From simple Laue cameras, via rotation, Weissenberg to precession geometry, Peter somehow retained the geometries in his head and reproduced them on a blackboard. The course was augmented by lectures on molecular geometry requiring us to frequently orthogonalize coordinates from non-Cartesian unit cells and then perform bond length angle and torsion angle calculations using a calculator. Peter was responsible for running the first year practicals based around his instrumentation lectures, and so we learned how to use rotation, equi-inclination Weissenberg and precession cameras. On practical evenings, one of us was sent off to one of the many Indian sweet shops near Euston Station to bring back bags of samosas and pakoras. These were put into one of the film driers to keep warm whilst we worked and snacked and the basement laboratory smelled like a takeaway (yes, eating in the lab.).

First year exams came and went, but the commitment of three-four evenings a week of three hour lectures was demanding and reduced the part-timers to only three entering the second year. This year was comprised mainly of short courses in specific areas of crystallography, supported by a significant number of guest lectures. Graham Fisher of Marconi-Elliott gave a short course on dynamical theory, fortunately not requiring any reading of, let alone understanding of Batterman and Cole. Like John's course earlier, Graham took great care to make the theory followable and understandable and allowed me to re-read Brian Tanner's book on X-ray topography with understanding. Paul Barnes was tasked with

the introduction to powder diffraction methods which I had just begun to use at G.E.C., so his course was timely and useful. John Finney gave a further course on scattering theory, this time firmly based on Fourier transforms and convolution theory. His course was supported by a number of lectures on transmission electron microscopy given by the remarkable polymath Alan Mackay. We never knew for sure, but Alan always gave the impression that he decided on what he had chosen to lecture on or to demonstrate the moment he walked into the lecture theatre and not before. The lectures were always interesting, left field and certainly quickly took me out of my comfort zone; maybe the spirit of Lonsdale lived on in Alan. From epitaxial oxides grown on copper thin films to crystalline phases in pearl nail polish, you never quite knew quite what to expect.

The final term started with one more part-timer sadly dropping out leaving just two full-timers and two part-timers to take the final exams. My final year project to image growth sector boundaries in a sector-fluorescent gypsum single crystal using the department's Lang camera was a 100% failure, and with reflection (no pun intended), hardly surprising given the mosaicity of the specimen kindly donated by The Natural History Museum. Written exams were taken with only the viva to be survived. Watson Fuller was the external examiner and Peter and John the internal examiners. Watson gave me the easiest of rides as an examiner, I passed, and my time at Birkbeck finished. However, in 2003 I returned when the College awarded me a D.Sc. for published work in structural crystallography of minerals and mineral isotopes.

Changing jobs a few years after finishing the M.Sc. I managed to persuade my then-current employer B.P. to allow three of my younger colleagues to do the course, and in the final years that the course ran I too joined the visiting lecturers. The course gave me the foundation and confidence to leave industry and join the ISIS Facility of the Rutherford Appleton Laboratory, joining Bill David's Crystallography Group and working with Richard Ibberson on HRPD. From there I have managed to make a return of sorts to my first scientific love of structural mineralogy.

It is without doubt the hardest that I have ever worked in an educational environment, and without the course, I don't know where I would have ended up. It was really hard work to put in nine hours in the day job, two hours travelling and three hours lectures, four times a week, but it was truly worth it. So at great risk of sounding gushing, thank you Rex, John, Peter, Alan and Paul. I owed you at the time and still owe you now.

#### Kevin S. Knight



# Meeting Reports

## The Braggs and their Contribution to X-ray Crystallography

The Institute of Physics, London, October 3, 2022

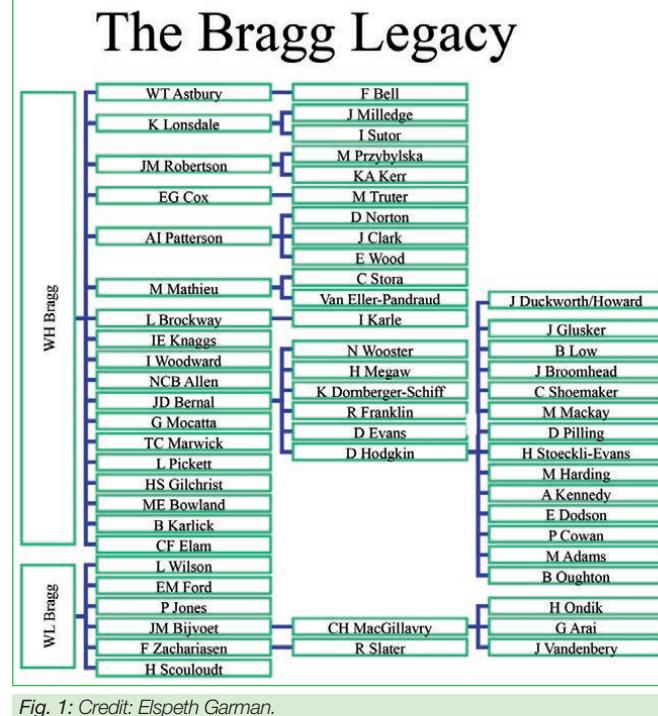
**BEING** the 100th Anniversary of the International Union of Pure and Applied Physics (IUPAP), the History of Physics Group of the Institute of Physics held a half day meeting celebrating the work and legacy of the Braggs. As they were instrumental in the start of crystallography, as well as influencing and supporting the careers of many subsequent eminent crystallographers, I thought I should attend – albeit regrettably online.

In his keynote talk entitled 'What have the Braggs done for us' (perhaps Mike's a Monty Python fan?), **Mike Glazer** (University of Oxford) took us on a fascinating journey that demonstrated how work done over a hundred years ago has had an enormous impact on science. W.H. Bragg's 1912 paper, hot on the heels of von Laue, Friedrich and Kipping's work in Munich that first launched X-rays at a crystal, changed the world of science by starting X-ray crystallography. Commenting that the artistic natures of both W.H. Bragg the father (WHB) and W.L. Bragg the son (WLB) likely played a role in their development of crystallography (and showing some interesting examples of their drawing), Mike summarised the education and early days of WHB – who actually took a maths degree and reckoned he didn't know much physics!

Noting Wilhelm Röntgen's discovery of X-rays, WHB decided to build his own X-ray setup to carry out research in general on the then new and poorly understood phenomenon. At the time, there was disagreement about whether X-rays were particles or waves – WHB being one who supported the particle option<sup>1</sup>. So soon after becoming aware of the Munich work, WHB tried to show that those results could be explained by considering X-rays as particles – but failed. It fell to his son WLB – who had a helpful background in optics – that if crystals contained regular arrays of atoms (not a concept that was universally accepted), there must be planes of them. Further noting that the observed spots were slightly elliptical, and became more elliptical as the sample to detector distance was increased, he proposed that there must be some sort of reflection process involved. Hence his simple formula – of which Mike showed an image of it written down in WLB's 1912 notebook. So, at age 22, WLB had begun the modern field of X-ray crystallography.

Moving on, Mike stressed that WHB's construction of an ionisation spectrometer<sup>2</sup> was an important breakthrough – with it he could now measure intensities. So this was certainly one of the really important things that the Braggs have done for us – this instrument was essentially the precursor to the modern X-ray diffractometer.

1913 saw the first crystal structure, solved by WLB, of NaCl.<sup>3</sup> The structure was highly controversial at the time as chemists were expecting to see individual NaCl molecules. And there was negative reaction from some chemists to physicists muscling in on chemistry (with one in a *Nature* article saying this was 'not chemical cricket').



Mike concluded his really interesting talk with examples of the Braggs' legacy in terms of their scientific 'children' and 'grandchildren' (see figure 1 for some of them). Amongst other crystallographic 'descendents', Dorothy Hodgkin and her B<sub>12</sub> and penicillin work was mentioned (Mike showed a tabloid newspaper article with the headline "Nobel Prize for British wife!"), as was that of Max Perutz and John Kendrew on myoglobin and haemoglobin who worked with WLB when he was in the Cavendish in Cambridge, as well as the DNA work of Watson, Crick, Franklin and Wilkins. During WLB's term as Director of The Royal Institution (1954 – 1966), not only was the first enzyme (lysozyme) structure solved by David Phillips's team, but he also initiated the RI series of lectures for schoolchildren. To demonstrate how he loved – and was good at – teaching children about science, Mike showed a fascinating

1. In fact, even after the wave nature was accepted, it has been rumoured that on Mondays, Wednesdays and Fridays, X-rays were to be considered as waves, while on Tuesdays, Thursdays and Saturdays they should be thought of as streams of flying energy quanta or corpuscles. As Mike observed, this was an interesting take on wave-particle duality!
2. Or to give credit where it's due, it was built by his lab. tech. C.H. Jenkinson.
3. Steve Curry in his later talk quoted WLB as saying it was "on rather indirect and slender evidence that I assigned the structure!"

video clip of one of his RI lectures. A video that was also interesting in having shots of a 14 year old Mike Glazer in the audience – looking really involved in the ‘show’.

Mike’s talked underlined very effectively the seminal importance of the Braggs to the transformation in structural science in the last hundred years and more. The Braggs really did a great deal for us!

**Helena Shepherd**’s (University of Kent) talk on crystallography in the chemical sciences focussed on four areas: structure and function in chemistry; structures of molecules; crystal packing and its effects on properties; dynamic processes in the solid state. After commenting that 33 Nobel prizes have been awarded relating to crystallography, the 56 laureates included 37 chemists. Giving examples varying from diamond/graphite to penicillin, she illustrated how an understanding of structure is a prerequisite to understanding physical and chemical properties. Helena followed this up by exploring the influence of molecular shape and molecular chemistry on how molecules of various kinds can pack together to fill space, and how that can vary, resulting in polymorphs which could have different properties. Commenting that a patent, for example for a drug, requires a crystal structure – a molecular structure is not sufficient – she gave an interesting example of the antiviral HIV/AIDS drug Ritonavir.

Moving on to crystal engineering, examples were given of how co-crystallisation can be used to control properties – with one of the examples being particularly explosive! Noting that it was set up by Olga Kennard – who was inspired by J.D. Bernal who himself spent an early part of his scientific career at WHB’s Royal Institution – Helena gave a good plug for the Cambridge Crystallographic Data Centre (CCDC), noting also its role in education. The latter part of her talk focussed on dynamical processes in the solid state, with examples of chemical reactions and phase transitions, and their potential applications in e.g. sensors. Finally, she touched on *in situ* work such as photochemistry and variable temperature and pressure, and touched on the problems of structure prediction.

In summary, Helena’s talk illustrated well how crystallography has been fundamental to the development of chemistry over the last hundred years, and how intermolecular interactions can be exploited to engineer materials, with the potential of designing materials with specific properties.

After making some interesting comments<sup>4</sup> relating to the very early work of the Braggs, **Stephen Curry**’s (Imperial College London) talk ‘From Bragg to Biology – how X-ray crystallography opened up the molecular secrets of life’ traced the work on large molecules of the Braggs and their protégés, building up to those of biological interest. WHB realised that Fourier transforms were the key to interpreting X-ray photographs<sup>5</sup> of crystals containing larger molecules (early examples included diopside in 1929 and calcium magnesium silicate). Whereas 41 atoms was the limit in 1941, Stephen told us that Dorothy Hodgkin’s solution of the structure of the 181 atom vitamin B<sub>12</sub> in 1954 was helped by the use of computer time bought in the U.S. He went on to mention William Astbury, who, with J.D. Bernal, was at WHB’s RI in the 1920s, developed X-ray diffraction of fibrous proteins in Leeds in the 1930s, while

Bernal and Hodgkin made the critical observation on pepsin crystals<sup>6</sup> that they needed to be hydrated to give a good diffraction pattern. This latter work demonstrated that even such large molecules can take up a regular arrangement, and hence their structures could be tackled by X-ray diffraction.

Stephen presented us with other milestones passed on the way to the very large molecules whose structures can be solved today by X-ray diffraction. Perutz and the first structure of a protein – myoglobin – in 1957 (for which the phase problem had to be solved). Astbury’s X-ray pattern of DNA in 1938 – he showed a picture of it which looked very much like Rosalind Franklin’s famous photo 51. Peter Pauling’s role in the Franklin/Wilkins/Crick/Watson story. The haemoglobin structure in 1962, in which each of the four chains looked like myoglobin. And of course the 1965 solution at WLB’s RI of the first structure of an enzyme, lysozyme. Stephen concluded this part of his talk with the 2011 structure of the ribosome which contains tens of thousands of atoms, and underlined how structural studies on biomolecules have given insights into biological mechanisms. The progress from the structure of NaCl in 1912 to that of ATPase in 2013 was nicely illustrated by his image on the publicity web page for the meeting (see figure 2).

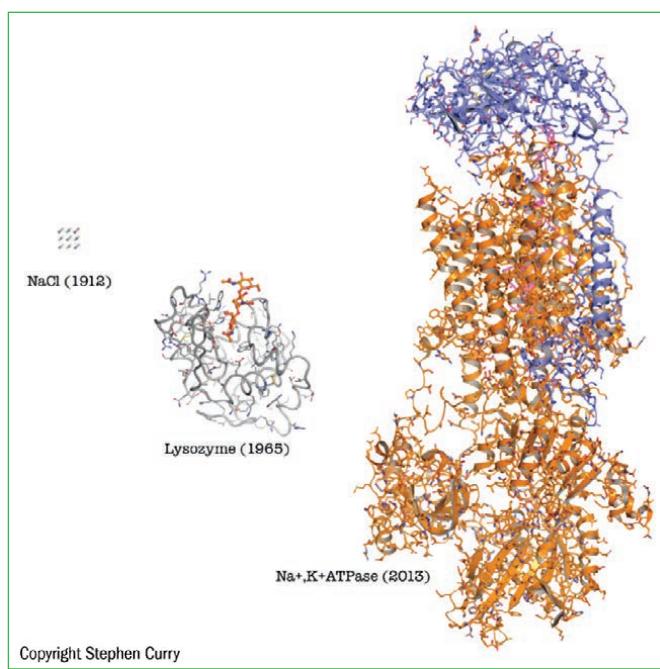


Fig. 2: Credit: Stephen Curry, Imperial College.

Stephen ended his talk by asking two questions. First, as the advances that have been made in the technique mean Cryo-EM can now resolve features at the 2 Å level, will that technique replace X-ray crystallography? Secondly, is AlphaFold2 the end of protein crystallography? My response to the second question would be to refer to the article in last September’s *Crystallography News* by David Jones and Janet Thornton.

What would the Braggs have made of all these developments that have been built on their shoulders? Stephen liked to think they would have been delighted.

4. One of these related the story that WLB hit on his eponymous equation while walking along the Cam – and that his father found its simplicity somewhat embarrassing!
5. W.H. Bragg. The Bakerian Lecture. *Phil. Trans Roy. Soc. A* **215**, 523 (1915). <https://doi.org/10.1098/rsta.1915.0009>.
6. Curry commented that Bernal kept the original pepsin crystals at Birkbeck, but that these were destroyed when the Birkbeck building was bombed during World War II.

The final talk by **Silvia Capelli**, the Instrument Scientist on the SXD single crystal instrument at the ISIS Neutron and Muon Source, looked at the Bragg legacy from the viewpoint of large scale facilities (LSFs). After covering aspects of the history of X-rays from Becquerel's observation of  $\alpha$ -particles from uranium to Bragg's law (and on the way noting that Marie Curie used X-rays in diagnosing the injuries of wounded soldiers), she discussed how LSFs have opened up the possibilities of exploitation of X-ray (and neutron) diffraction in cases where your own lab. may not have the necessary tools – or a large enough space in which to mount, for example, a jet engine in the sample position!

After showing us a map of where synchrotron and neutron sources are located in Europe, Silvia focussed on the synchrotron and neutron facilities available on the Harwell Science Campus. The advantages of both were summarised, the potential of multi-technique experiments discussed (e.g. Raman, gas adsorption, electric fields etc.), and the possibilities of variable pressure and temperature, and *in situ* and *in*

*operando* experiments, set out. As a couple of examples of joint X-ray/neutron experiments, she discussed the self-assembly of tetramethyl-peperidine in water (with X-rays locating the artificial water channels and neutrons sorting out the water molecule disorder), and why the magnetism of a Prussian Blue analogue was so strong. Finally, she stressed the potential of work at LSFs on dynamical processes in hydrogen storage materials, conducting organic polymers, solar cells and maglev materials.

For oldies like me, it was a particularly enjoyable meeting, taking me back to past helpful discussions with – and support from – several of the scientists who have taken the Bragg legacy forward. And I'd like to think that any crystallographer would have found the meeting both interesting and informative.

With hindsight, Mike Glazer's provocative talk title is surely a rhetorical question.

**John Finney**  
UCL

## Biological Structures Group Winter Meeting 2022 – Dynamic Structural Biology

**COLD** and snowy was the weather on Monday 12th December 2022 but, undeterred, a hardy band of loyal BSG delegates made their way to London's newest and most prestigious medical research establishment, the Francis Crick Institute. While delegates had the option to attend virtually, real-world attendees were accommodated in an excellent three-screen conference room. The laboratory itself is located within a stone's throw of St Pancras International, the station and its surroundings being named after a little-known saint who was martyred at the tender age of 14 by the Roman emperor Diocletian!

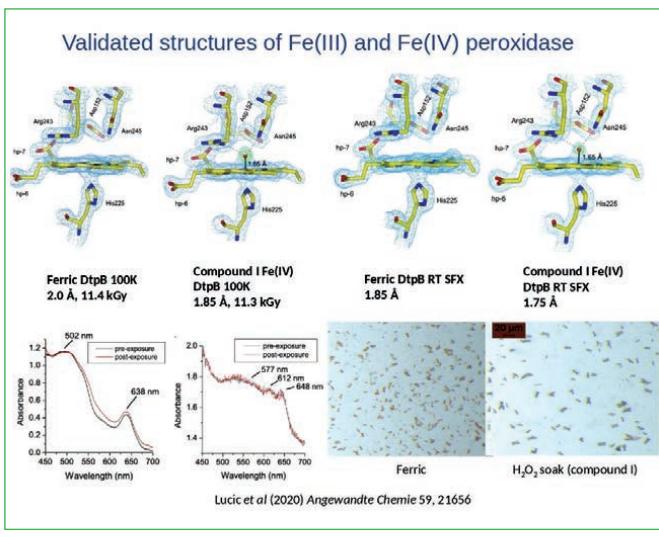


Fig. 1: Speakers at the 2022 BSG winter meeting. From left to right: Isabel Moraes, Radoslav Enchev, Doryen Bubeck, Helen Walden, Mike Hough, Halina Mikolajek, Briony Yorke and Sofia Jaho.

The meeting began with a welcome by **Mike Hough** (Diamond Light Source, DLS) who not only chaired the first session but, also, gallantly stood in for one of the speakers whose train from Bradford was waylaid by the weather, with that talk consequently moved to a later session. The first speaker was **Doryen Bubeck** (Imperial College London) whose presentation was entitled 'CD59: the gate keeper to pore formation'. The speaker described the membrane attack complex (MAC) which is a large pore generated by the complement cascade, primarily to lyse infected host cells and gram-negative bacteria.

The host protein CD59 acts as the last line of defence against the MAC. Accordingly deficiencies in human CD59 give rise to haemolytic anaemia and the related disease PNH syndrome. Tumour cells are also known to overexpress CD59 to protect themselves against attack by the MAC. The CD59 protein works by binding to the complement proteins C8 and C9 via their pore-forming domains and this inhibits their polymerisation which occurs during pore formation. During formation of the MAC, part of C9 undergoes a helix-to-strand transition leading to assembly of the large transmembrane  $\beta$ -sheet pore. CD59 has been shown to bind to the extended strand region of C9 and this prevents pore formation. The speaker reported cryo-EM studies of the complex of C5b8 and CD59 which was assembled into lipid nanodiscs, and subsequent image enhancement by *in silico* purification showed that CD59 also binds to the transmembrane  $\beta$ -hairpin regions of C8. A similar analysis of C5b9-CD59 confirmed that CD59 deflects the pore-forming  $\beta$ -strands and the speaker ended by describing how the MAC localises to cholesterol lipid rafts, with implications for numerous inflammatory disorders. The next lecture was given by **Sofia Jaho** (DLS) and was entitled 'Time resolved crystallography at I24'. The speaker began by outlining the capabilities of the I24 tuneable beamline at DLS which has an energy range of 7 – 23 keV with high flux density, adaptable beam size and a choice of either Pilatus or Eiger detectors. Sofia outlined the advantages of a new generation of cadmium telluride detectors which outperform other types at high energies and are suitable for serial data collection. The beamline has capabilities for room temperature collection of data from crystals mounted on special chips with robotic scanning of up to 25,000 positions, in addition to a viscous extruder for delivering membrane protein crystals grown in the lipidic cubic phase (LCP) into the beam. The beamline also has a PORTO laser with a small beam size for time resolved studies of photocaged compounds and instrumentation for UV-visible microspectroscopy.

The next speaker was **Mike Hough** (DLS) who handed chairmanship of the remainder of this session to **Mark Sanderson** (Kings). The speaker's presentation entitled 'Ambient temperature and serial crystallography to explore the



## Multiplexing with the Hadamard Method

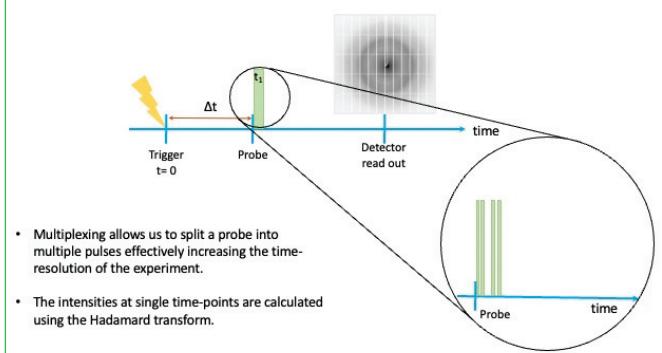


Fig. 4: Briony Yorke described how multiplexing methods such as Hadamard transform time resolved crystallography (HATRX) help to extend the achievable time-resolution using monochromatic synchrotron radiation.

mechanisms of heme enzymes' concerned studies of various dye-metabolising peroxidases (DtpA, DtpAa and DtpB) from *S. lalandeae*. The well-known problem of X-ray induced radiolysis of water which generates photoelectrons that reduce Fe IV and III centres to the II state during data collection was described. Mike described how the Fe IV state of one of these enzymes exists as an oxo-ferryl compound which can be generated by treatment with hydrogen peroxide and is stable for approximately 3 hours. In contrast the Fe III state has a water molecule bound to the iron. The speaker described painstaking studies to confirm the presence of the Fe IV state by microspectroscopy at the beamline and to determine intact structures using XFEL radiation, and how the redox behaviour of different Fe centres is affected by their proximity to solvent channels. Accordingly, studies of a range of mutants confirmed that waters mediate the proton transfers at the active site.

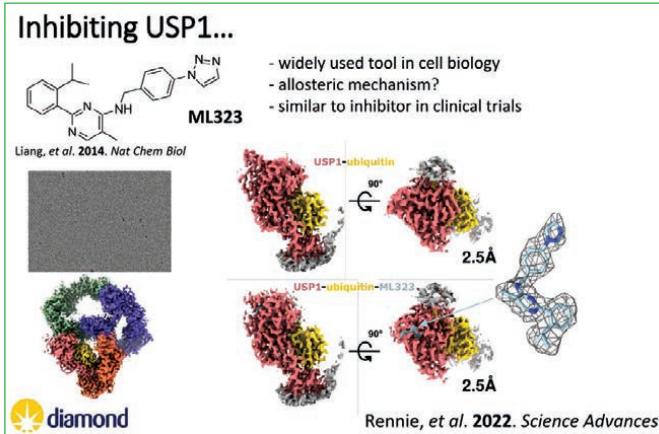


Fig. 3: Helen Walden detailed the allosteric mode of inhibition of ubiquitin-specific protease 1, as revealed by cryo-EM.

Following lunch, the afternoon session, chaired again by **Mark Sanderson** (Kings), began with a lecture by **Helen Walden** (Glasgow) entitled 'Regulation of the Fanconi anaemia pathway by ubiquitin'. Helen described the mono-ubiquitination of the protein FANCD2 which is a key signal in a DNA repair pathway that is defective in Fanconi anaemia. This disease results from a failure to repair interstrand DNA crosslinks – a process which is normally triggered by FANCD2. However, ubiquitination by Ube2T locks FANCD2 and FANCI onto the DNA as an ID2 heterodimer clamp. The speaker described a cryo-EM study

at 3.6 Å resolution of the ID2 clamp with the ubiquitin specific protease USP1 and its activation factor UAF1. Inhibitors of ubiquitination therefore have therapeutic potential. Accordingly, the USP1 inhibitor ML323 was shown by cryo-EM to bind in a hydrophobic pocket displacing two β-strands which perturbs the active site of the enzyme. Next, **Briony Yorke** (University of Bradford) gave a presentation entitled 'Using time-resolved crystallography to investigate the UV damage mechanisms leading to cataract formation'. Briony began by outlining the timescales on which different experimental techniques are effective, ranging from  $10^{-15}$  sec. for XFEL sources to the 10<sup>0</sup> second timescale for conventional synchrotrons. The speaker outlined use of the Hadamard transform for more efficient time-resolved measurements and summarised some prior studies involving photocaged compounds and disulphide bond breakage. Briony then described her work on UV-induced ageing in the eye lens protein γ-crystallin using continuous wave and nano-second pulsed 280 nm radiation. These studies indicated that DTT binds to Cys residues by disulphide bridge formation in a reversible manner and suggested that the biological reductant glutathione may fulfil a similar protective role *in vivo* due to its high physiological concentration (10 mM). The speaker also outlined the possible role of the interesting compound kynurenone which is formed by UV-induced or enzymatic metabolism of tryptophan and suggested that Trp-Cys energy transfer may be involved in redox protection. Briony's talk was followed by a presentation from Douglas Instruments given by **Patrick Shaw Stewart** entitled 'Exploring chemical space for cryo-EM using dynamic light scattering (DLS) and crystal concepts'. Patrick began by outlining the range of stability and solubility additives available for crystal screening and how the successful conditions can be scaled up. The improvement in success rates due to the inclusion of seeding agents in crystal screening was emphasised, as were the benefits of using microbatch crystallisation and diluting seed stocks to obtain larger crystals. Next up, Isabel Moraes (DeepMind) gave a presentation entitled 'New approaches to prepare high-density membrane protein microcrystals in LCP for serial crystallography and fragment screening'. The speaker began by explaining some of the practical difficulties encountered with crystal growth in lipidic cubic phase. Interestingly, crystals can be grown in syringes either for injection of the gel into the beam with serial crystallography or for transfer to fragment libraries prior to data collection. Isabel outlined studies of the membrane protein archaerhodopsin-3 (AR3), the time-resolved data for which were collected at SACLA (Spring-8, Japan) along with studies of drug complexes of the GPCR A<sub>2A</sub>-receptor which were undertaken using XFEL with crystals grown in glass vials.

Following an afternoon coffee break, the final session of the meeting, chaired by **Claire Naylor** (SPT Labtech), began with a lecture by **Halina Mikolajek** (DLS) entitled 'A high-throughput crystallisation facility interacting with the new VMXi beamline at the Diamond Light Source'. This particular beamline is dedicated to room temperature experiments using plates, such as crystallisation screening and routine room temperature structure determination, with rapid data processing from multiple crystals being enabled by recent developments (dials.multiplex) in the XIA2 package. A range of *in situ* crystal growth formats were described including the use of plastic films to achieve lower background scattering. Halina then described several user case studies including a gas binding c-type cytochrome and the SARS CoV-2 macrodomain, before discussing beamline developments to enable time resolved serial crystallography. Presenting remotely, the next speaker, **Paul Miller** (University of Cambridge), gave a lecture entitled 'Using structure to understand how ligands modulate GABA-A receptor function'. Paul described the variable subunit structure of the GABA receptor; the synaptic form consists of two  $\alpha$  subunits, two  $\beta$  subunits and one  $\gamma$  subunit whilst the extra-synaptic form has the composition  $2\alpha 3\beta$ . In response to the agonist GABA, the synaptic version of the receptor flickers open a lot more than the extrasynaptic form, although the latter is the more sensitive of the two. The speaker described how the use of special antibody technology, involving nano- and mega-bodies, was required to increase the number of side views of the nanodiscs which were used in cryo-EM structure determination. A similar study of the complex of the receptor with cobratoxin showed that it binds in the same site as GABA, pushing the agonist-binding residues out of the way. The structure of the complex with zinc showed that this metal ion binds to the His 267 side chain of three subunits in the central channel of the receptor. Paul concluded by offering an explanation for the differing

properties of the two forms of the receptor: for instance, the synaptic form has a markedly more open gate made of hydrophobic residues in the channel. The next speaker was **James Gordon** (Rigaku) who described the range of equipment supplied by this company for X-ray and electron diffraction (ED) including a commercial hybrid ED system combining features of an electron microscope and an area detector, in a manner that would be familiar for X-ray crystallographers. Currently its main use is for small molecule structure analysis using sub-micrometer-size crystals and the instrument even allows electron beam milling of the crystals prior to data collection. The final talk of the meeting given by **Radoslav Enchev** (Francis Crick Institute) was entitled 'Visual biochemistry'. The speaker described systems for microfluidic mixing of samples for electron microscopy and outlined studies of the DNA-RecA complex which is involved in recombination repair of DNA and forms tractable filaments. FRET was used to prepare the samples for cryo-EM. Radoslav concluded by outlining studies of the Cullin-RING ligase, which is involved in ubiquitin signalling, and its regulator CAND1 which accelerates the release of ubiquitinated protein from the ligase.

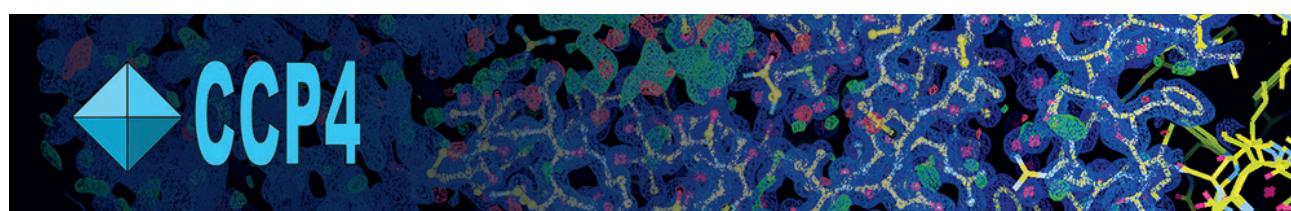
The meeting was closed by **Mark Sanderson** (Kings) who thanked all the speakers, organisers and session chairs for their excellent contributions to the meeting. In addition, the BSG is very grateful to Rigaku Europe SE, Douglas Instruments, Dectris, Molecular Dimensions and SPT Labtech for generously supporting this meeting. The meeting highlighted that things do wriggle inside crystals and a vast amount of biological information can be obtained from dynamic structural biology studies.

**Jon Cooper, UCL**

**Shabir Najmudin, King's College London**

## CCP4 Conference 2023

East Midlands Conference Centre, Nottingham, 4th–6th January 2023



THE conference started with a plenary by **Monserrat Soler-Lopez** (ESRF) on 'Linking Structural Biology data sources to tackle Alzheimers'. Impaired energy metabolism is one of the earliest and most consistent features in Alzheimer's disease (AD). In Alzheimer's, disease-related proteins are more highly connected than random, and network biology could be used to identify new proteins involved in AD. The most promising was ECSIT (a transporter interacting with the mitochondrion). In AD, the brain accumulates complex I sub-assemblies. ECSIT is part of the core sub-assembly (MCIA). A complex of ACAD9 and the ECSIT C-term could be stably formed, but no crystals could be grown. ACAD9 binds Acyl-CoA, but this gets ejected on ECSIT binding. Cryo-EM finally gave structure at low resolution. They could only see a small part of ECSIT, which is sitting in the FAD site. The binding of ECSIT changes ACAD9 from fatty acid metabolism to MCIA complex, which may be relevant to AD.

There was then a round table discussion involving **Gerard Bricogne** (Global Phasing Ltd), **Sameer Velankar** (PDBe), **Loes Kroon-Batenburg** (Utrecht University), **Dave Stuart** (Diamond Light Source DLS), **Jim Naismith** (Rosalind Franklin Institute), **Kristina Djinovic-Carugo** (EMBL Grenoble) and **Annalisa Pastore** (ESRF) on 'Structural biology data sources', mainly discussing what data should be stored or made public.

The first session of Day 2 was started by **Graeme Winter** (DLS) with a title of 'What are Data?' He showed how Darwin's formula can be used to calculate structure factors from intensities and showed how bigger crystals, longer  $\lambda$  and a stronger beam give stronger intensities  $I$  while a bigger unit cell gives weaker ones. The measurement of  $I$  includes some uncertainty, which can be random (counting statistics etc.) or systematic (radiation damage, detector saturation etc.), but high multiplicity can be used to average out random effects. Data should be: nice spots, good separation, low background,

sensible beam centre. **Greta Assman** (Paul Scherrer Institute) then gave 'An educational introduction to the statistics we use to judge and compare data sets'. She started off by defining accuracy and precision and stated that accuracy=precision if there is no systematic error. Thus all variation is due to random error which can be reduced with multiple measurements. She then went to show how CC1/2 and CC\* are better quality indicators than R-factors. The third talk was given by **Kevin Dalton** (Harvard) on 'State-of-the-art scaling and merging'. In diffraction experiments, the primary data are the images from which one needs to predict the spot positions, measure intensities and scale the data to remove as many errors as possible. The good news is that this works really well for standard single-crystal rotation data, but is not as robust for other modalities. They have written a program called careless that uses gradient-based optimisation to optimise all the necessary parameters. The last talk in the session was given by **Richard Gildea** (DLS) on 'Past, present and future challenges of multi-crystal data'. Before cryo-protection, most data collection required multi-crystal datasets. Problems encountered then were: indexing ambiguities, preferential orientation, radiation damage etc., and, due to radiation damage, it was only possible to collect a complete dataset from multiple crystals. The merging techniques used then are now important for time-resolved crystallography. Main challenges are: identification of a consensus symmetry (complicated by indexing ambiguities), non-isomorphism, preferential orientation and radiation damage.

The second session opened with **Ralf Flairg** (DLS) on 'Data collection strategies and processing pipelines for the 21st Century'. He started by listing some assumptions: 3/4th generation synchrotron, fast pixel array detectors, cryo-cooled samples and using the rotation method. The stated goals were: to measure all unique reflections, measure good multiplicity, maximise signal and minimise radiation damage. With fast pixel detectors there's no reason not to collect 360° and, if possible, collect more than one orientation (unless there's a specific reason not to – e.g. MAD collection). There is always a need to optimise signal-to-noise, so make use of the strategy programs to improve this (e.g. BEST). Data should be fine sliced ( $\Delta\omega \ll$  mosaicity), often around 0.1°. Match beam to crystal size, use the best part of crystal, match detector distance to the resolution. **Kathryn Shelley** (University of Oxford) then talked on 'Quantifying radiation damage in protein crystal structures'. Only a tiny fraction (0.2%) of X-rays contribute to the diffraction pattern. 1.8% are inelastically scattered, which deposit energy in the crystal and manifests as radiation damage. Specific radiation damage happens in a known order, but it can be difficult to tell whether a side chain is missing due to radiation damage or mobility. She has calculated the metrics  $B_{\text{damage}}$ ,  $B_{\text{net}}$  and  $B_{\text{net-percentile}}$ , all based on B-factors. Often, though, there is a good correlation between the packing density and mobility, so these effects can be separated. Analysis of the Protein Data Bank (PDB) shows that structures with high  $B_{\text{net}}$  and  $B_{\text{net-percentile}}$  have radiation damage. **Maria Garcia** (EMBL Hamburg) then gave a talk entitled 'Be prepared. Good data from good sample preparation'. Poor protein leads to expensive experiments giving poor data. Most important factors are: purity >95%, homogeneity, identity, integrity, batch-to-batch consistency, UV spectrum (for DNA), stability, how active (enzymes) and optimisation of storage conditions. The ESRF has two platforms: one to produce high quality proteins and one to crystallise them. She introduced eSPC, an online data analysis tool for molecular biophysics, which can take in user-generated data (thermal shift, ITC etc.) and indicate how good the protein is. The next talk was given by **Phillippe**

**Carpentier** (ESRF) on how to 'Spice up your diffraction data using high-pressure macromolecular crystallography as ancillary technique'. HPMX (High Pressure Freezing Lab. for Macromolecular Crystallography) is a lab. where proteins can be frozen under a high pressure, pure atmosphere. There are over 1600 structures in the PDB containing gases. There are various applications – noble gases for SAD, mapping internal tunnels, probing the hydrophobic surface etc. For the experiment the crystal is loaded into a loop, placed inside a tube, pressurised with gas and soaked for ~10 minutes, then plunged into liquid N<sub>2</sub> while still under pressure. They can offer He, Ar, Kr, Xe, O<sub>2</sub>, CO<sub>2</sub>, CH<sub>4</sub>, N<sub>2</sub> gases for experiments.

The last session of the day was opened by **Meytal Landau** (EMBL Hamburg) with a talk on 'Microbial and Antimicrobial Amyloids in Infections and Neurodegeneration'. Biofilms are a huge problem for healthcare and amyloids are key to biofilms formation as scaffolds. The initial amyloid structure showed the fibres were so stable because of a cross-β structure. She then started working on bacterial amyloid structures – these can have both microbial and anti-microbial properties. These have amphipathic cross-α-helical structures, which appear critical for cell toxicity. Computational analysis of the sequence found similar anti-microbial peptides. Biophysical methods show that these structures can switch to the cross-β form depending on environmental cues. **Antoine Royant** (IBS, ESRF) then talked on 'From femtoseconds to minutes: TR serial protein crystallography at XFELs and synchrotrons'. Time resolved (TR) crystallography is done at 3rd generation synchrotrons (100K) or 4th generation XFELs (293K). TR analysis requires structure determination of as many reaction intermediates as possible. The intermediates are unstable in time, so one needs to shoot fast (293K) or trap the intermediate (100K). For slow reactions (>100ms) freeze-trap works well, but one can get radiation damage problems in cryo-trapping experiments. He showed an example of bacteriorhodopsin with data collected at synchrotrons and at the XFEL. Next **Arnaud Basle** (Newcastle University) gave a talk entitled 'Capabilities of a modern "home" source'. They have a Bruker D8 Venture MetalJet D2 with SCOUT robot. The Ga (1.34Å) source is the strongest in-house source (3.3e<sup>9</sup> (70μm on sample) versus 3.5e<sup>12</sup> for I04-1). The SCOUT automounter takes 40s to load the sample (7s out of liquid N<sub>2</sub>). Centering can be done manually in a few seconds or automatically in a few minutes. For a typical drug discovery project sample, they can collect a full data set in 6 minutes. The last talk of the day was given by **Hongyi Xu** (Stockholm University) on 'Structure Determination of Macromolecules by MicroED'. 3DED/MicroED has several benefits: electrons interact much more strongly than X-rays, thus smaller crystals can be studied; the interaction is with the e<sup>-</sup> cloud and nuclei, so it is possible to see charge; dynamical refinement can be carried out giving the absolute structure and electrons can be focussed leading to high resolution images. The samples are set up similarly to cryo-EM. Focussed Ion Beam milling can be carried out if the crystals are too large, but often it is easier to de-optimise the crystallisation to get small crystals (usually by seeding techniques). He showed several examples exemplifying the technique.

Day 3 started with a talk by **Derek Mendez** (SLAC, Stanford) on 'ExaFEL – exascale computing for SFX data processing' (Exa = 1 quintillion or 10<sup>18</sup>). The Exascale computing project has several goals, one of which is light source enabled analysis of proteins, molecular structure and design. The AGIPD detector can collect at 3.5kHz (19 million images in 90 minutes). To get 'real-time' understanding of the diffraction they need to process very quickly. Thus, all major sites in the US and EU

are connected by dedicated fibre optic cabling that can run at excess of 400Gb/s, thus enabling sending all data to the exascale supercomputer to process. **Marjan Hadian-Jazi** (WEHI, Melbourne) then showed her program for ‘Robust statistics for serial crystallography data processing’. Statistics help to describe structures in data. She has written a package RobustGaussianFittingLibrary (RGFlib) which can be used to improve data processing. At AGIPD, ~4M images/s are recorded, though only a few thousands of these are hits. Bragg Peak finding must be run on each image to discover the hits – a challenging task with noise, artifacts and outliers. Robust Peak Finder can be used to improve this. She also showed how to use robust statistics to generate masks for the detectors to remove bad/broken pixels. Then **Briony Yorke** (University of Bradford) spoke about ‘Time-resolved crystallography data wrangling’. The shortest timescale at 3rd generation synchrotrons is ~ms. So how can we extend this to shorter timescales without using XFELs? Fast reactions (<ms) need to use laser pulses to initiate the reaction as rapid mixing is diffusion limited. To get to even faster timepoints one needs to reduce the probe pulse width at the same time as increasing signal-to-noise without increasing the length of exposure or increasing the beam flux. This can be done by recording multiple time points in a single image by using the HATRX method. Finally, **Kyle Morris** (DLS) explained ‘The data behind the cryo-EM structure, the microscope behind the data’. At eBIC at Diamond they have 5 Titan Krios, producing ~1M cryo-EM movies per month, equating to petabytes of data. One needs to acquire enough high-quality data to solve a structure – but how do you know when this is achieved? eBIC uses a pipeline to streamline the process of data collection and can initially process data in a few hours to the point where it can be used for structure determination. Having this pipeline also provides lots of feedback of how the microscopes are performing.

After the break **Gloria Borgstahl** (University of Nebraska) spoke about ‘Dealing with Aperiodic Protein Crystal Structures’. The term aperiodic crystals covers quasi crystals, composite and incommensurately modulated crystals. The crystal modulation affects diffraction resulting in a loss of translational symmetry. Data processing can be achieved with the q-vector, using EVAL15, the structure can be solved in (3+1)D superspace and then refined back in 3D space. Gloria showed an example of the Profilin:Actin complex which is normally periodic, but can be made incommensurately modulated. Next was **Clemens Vonrhein** (Global Phasing Ltd) on ‘Analysing beyond your expectations – opportunities for better data and models’. He is trying to set up rules for depositing unmerged raw data to improve data quality. Often the metrics in the PDB are wrong, due to mistakes during uploading of data. If the unmerged data were deposited, these metrics could be easily recalculated if required. He stated that the PDB should move to force deposition of unmerged data. **Andrey Lebedev** (CCP4) gave a talk entitled ‘Things you don’t want to see in your data – and what could be done’. He stated that if your autoprocessing gives different space groups then you probably have problems with your data. He went on to show five examples of problem data that can be fixed with DIALS. The last talk in the session was from **Steve Meisburger** (CHESS) on ‘Observing dynamics in proteins from diffuse scattering’. Diffuse scattering is seen in many protein crystals, but only 15 have been so investigated. He wanted to answer the questions: what is causing the diffuse scattering and how should the data be processed? He chose P1 Lysozyme as test case (high resolution, low mosaicity, large crystals for room temperature) and collected a low dose, high multiplicity dataset. Halos around the Bragg peaks and a more diffuse cloud could be seen. The halos are due to

lattice vibrations of the molecules which can be simulated (GOODVIBES) with three degrees of freedom per molecule. This doesn’t fully explain the diffuse scatter, though, which may be due to residual internal motion.

The last session started with **Sylvain Engilberge** (IBS, Grenoble) and a talk entitled ‘Combining time-resolved techniques to decipher protein dynamics’. In the AlphaFold2 (AF2) era it is very easy to get *in silico* models to get static information. But we require experimental data to get functional and dynamic information. He is combining macromolecular crystallography with *in crystallo* optical spectroscopy to probe redox states or to probe the state of photoactive or fluorescent proteins using two instruments at the ESRF: icOS (100K + RT, fluorescence, Raman, single crystal, ms to hours) and Tr-icOS (same as icOS but dedicated to pump probe experiments). He gave an example of icOS with Phototropin 2. Next **Dan Rigden** (University of Liverpool) spoke about ‘CASP15 and the changing landscape of new generation structure prediction’. He started by stating that the CASP15 categories were quite different from CASP14 due to massive success of AF2. Groups using AF2 and multiple sequence analyses to start the predictions did much better than those not doing so. Free models (no sequence homology) were still difficult to predict (even with AF2). Predictions were also significantly worse for those targets with low  $N_{eff}$  (low template availability). All the targets produced were able to solve the data with molecular replacement, often straightforwardly, though sometimes auto-editing with Slice’N’Dice was essential. Quaternary structure prediction was also much better – mainly due to AF2-Multimer (>90% predicted correctly). Then **Isabel Usón** (IBMB-CSIC, Spain) gave a talk on ‘Prediction-based tools for experiment preparation and post-experiment perspective’. She started by saying that fold predictions have reached an unprecedented accuracy. Now we need to try and translate sequence into function, but this is much more difficult. She introduced Arcimboldo-AIR which parses AF2 output to produce multiple templates for similar models and ranks these with ALEPH and pairwise correlations. Finally, the last talk of the meeting was given by **Anastassis Perrakis** (Netherlands Cancer Institute) on ‘AlphaFill: adding metals, ligands and cofactors in AlphaFold model’. He showed three examples where AF2 provided extra insights into proteins they had been working on, but also showed that there were things missing from these predictions – e.g. cofactors, ligands. Thus, can we transplant ligands/cofactors from PDB models to the AF2 protein models? They have created AlphaFill – which takes the AF2 model, runs blast on PDB-REDO and checks for transplantable compounds, aligns the structures and copies over the compound, following by removal of clashes by energy minimisation.

**Mark Roe**  
University of Sussex



# Cambridge Symposium for Tom Blundell

Thursday 15 December 2022



**DECEMBER 15** was indeed a memorable day for attendees of the symposium held in honour of Professor Sir Tom Blundell FRS, whose distinguished career has led to so many crucial scientific breakthroughs, as well as innumerable researchers entering the structural biology field. The meeting served partly as an inauguration event for his new research group in the Heart and Lung Research Institute at the Papworth Hospital.

The meeting started with a welcome by **Marko Hyvönen** (University of Cambridge) who chaired the first session, beginning with an introduction by the Head of Biochemistry **Eric Miska** (University of Cambridge). The first speaker was **Steve Wood** (University of Portsmouth) whose presentation was entitled 'The early years 1972-1996' and in which he described his experiences in Tom's group, then based at the University of Sussex. By 1975 the group was performing very well with significant research funding and several *Nature* publications. These successes led ultimately to Tom's appointment to the Chair of Crystallography at Birkbeck College London in 1976, where his group was then based for another 20 years. The speaker described how, in addition to biological crystallography, the department at Birkbeck was also heavily involved in material science and electron microscopy. Whilst at Birkbeck, the group had major funding successes for numerous research projects as well as for the procurement of X-ray and computer graphics equipment. Steve described a number of amusing trips for collecting samples on a research vessel during the Fastnet storm of 1979 and at an abattoir, where Tom expressed great concern for the wellbeing of the lowly paid workers. Whilst Tom was officially in charge of the BBSRC at Swindon from 1991 to 1996, he retained a very large and active group at Birkbeck. Steve emphasised Tom's great skill for 'selling science' as well as the importance of the numerous international contacts he made during his pivotal research on insulin with Dorothy Hodgkin. The next speaker was **Alex Wlodawer** (NIH) whose presentation was entitled 'From NGF to HIV protease'. Alex described early studies of nerve growth factor (NGF) in the 1960s in Italy and how he began work on crystallising it as a post-doctoral researcher at Stanford in 1974. Alex spoke briefly of his neutron diffraction work on ribonuclease which was undertaken in the late 1970s prior to

his group moving to the National Cancer Institute at Frederick. The speaker explained that although crystals of NGF were first obtained as early as 1978, the structure evaded solution until 1991 when Tom's team at Birkbeck (including Risto Lapatto, Neil MacDonald, Judith Murray-Rust, amongst others) made a pivotal re-interpretation of heavy atom data and the problem was solved. Alex also described his work on the aspartic proteinase chymosin which was undertaken in collaboration with Tom. Studies of the related enzyme from retroviruses, such as HIV, also dominated their work in the late 1980s, with Tom targeting the recombinant enzyme and Alex a fully synthetic version made by Stephen Kent at Scripps. Alex also spoke of the field-leading journal, *Current Opinion in Structural Biology*, which was launched by Tom and is now edited by him. Next up, **Neil MacDonald** (Crick/Birkbeck) gave a presentation entitled 'PAR-6-dependent control of protein kinase C (PKC) substrate-targeting' beginning with an outline of the mechanistic biology of protein kinases. These are key signalling enzymes involved in many cellular processes such as synapse maturation and cell polarity as well as disease mechanisms and interventions. A number of kinase inhibitors have been developed by Neil's group and are in clinical trials for cancer treatment. The speaker moved on to the PAR family of protein kinases which have been shown to be involved in establishing cell polarity in drosophila. Several protein-protein complexes involved in this pathway have been studied by cryo-EM such as that formed by the lethal giant larval (LGL) protein and PKC, in which the kinase domain of PKC docks with the β-propeller domain on LGL. The next speaker was **R. Sowdhamini** (IBAB, Bangalore) who described her experiences in the Blundell group at Birkbeck from 1991 to 1996 and then in Cambridge where Tom received his knighthood in 1997. Following her move to Bangalore with her husband (the late N. Srinivasan) the speaker continued comparative molecular modelling studies that were initiated in the Blundell group. Her group also works on prediction of transient protein-protein binding interfaces and structural alignment of protein families. The speaker reminded the audience of Tom's significant skill in using two 24 mm slide projectors at once, in days when slides really were physical entities that broke when dropped and could become interminably mixed if you dropped the whole carousel, or even stuck in the projector, rather than mere pages

in a presentation file. The next speaker was **John Overington** (Exscientia) who described his Ph.D. research with Tom in the late 1980s on homology modelling software along with studies of protein evolution and conservation. This phase of John's career was followed by a move to Pfizer and later to a number of bioinformatics companies. John emphasised how one of the challenges of drug discovery is attempting to pre-empt the emergence of drug-resistant mutations and how bioinformatics can assist in designing compounds which minimise the problem. The final speaker in the first morning session was **David Burke** (EMBL-EBI) who described his work with Tom from 1995 onwards on the Tripos-funded development of the Composer package, focusing on fold recognition, loop prediction and side chain modelling. His current research covers mutations in congenital diseases, single nucleotide polymorphisms, variants of the flu virus and using the artificial intelligence (AI) system AlphaFold to predict protein-protein interfaces and disease-causing mutations.

After much-needed coffee, the second morning session, which was chaired by **Dima Chirgadze** (University of Cambridge), began with a presentation by **Frank von Delft** (Diamond Light Source DLS) who outlined his Ph.D. research with Tom from 1997 onwards on the pantothenate biosynthesis pathway. Frank then moved to the SGC in Oxford and then to DLS where his group developed large-scale fragment-based drug screening methods and established the world's first peer-reviewed screening facility for academic groups. Frank also outlined how developments at DLS will considerably speed up the process in the near future. The next speaker was **Mark DePristo** (BigHat Biosciences) who described his work with Tom from 2000-2004 as well as his subsequent work at Harvard with a range of biotechnology and bioinformatics ventures in the immunotherapeutic field. The speaker emphasised that although the cost of sequencing the human genome has reduced by something like a million-fold over the last 20 years, the data from the very fast sequencing methods of today need a lot of computational cleaning up. The following lecture was given by **Juan Fernandez-Recio** (CSIC, Spain) whose lecture was entitled 'From protein docking in Cambridge to the new challenges in protein assembly'. Juan described his move from Scripps to Tom's lab in 2003 and his interest in docking studies, focusing on the impact of mutations on protein-protein interactions and binding energy, as well as drug discovery targeting protein-protein interfaces. The next speaker was **Nick Harmer** (University of Exeter) who described his Ph.D. and post-doctoral work with Tom from 2000 to 2006 on fibroblast growth factor (FGF) receptor complexes by crystallography and mass-spectrometry, in collaboration with Carol Robinson (Cambridge). Nick ended his talk by giving tribute to Tom's contribution across the whole of the university. The final speaker in this session was **Yvonne Edwards** (University of Alabama) who studied with Tom in the early 90s and gave a short but moving tribute to the importance of his advice throughout her career in bioinformatics and molecular genetics.

After lunch, **Luca Pellegrini** (University of Cambridge), who chaired the first afternoon session, introduced **Charlotte Dean** (University of Oxford) whose talk was humorously entitled 'A little bit of science from a recovering Blundell Ph.D. student'. Charlotte outlined the history of research on antibody structure and function as well as describing her own work in the Oxford Protein Informatics Group on setting up databases and servers for predicting and analysing the accuracy of antibody structures. Charlotte emphasised the importance of validation for structural models generated by AI and concluded by outlining some of her recent roles with UKRI as the Covid

Response Director and Deputy Executive Chair of the EPSRC. The next speaker was **Sheena D'Arcy** (University of Texas, Dallas) whose talk was entitled 'A retrospective look at a Ph.D. with Prof Sir Tom Blundell 2004-2008'. Sheena outlined her work on growth factor receptors, DNA repair and drug discovery as well as her more recent involvement in the Critical Assessment of Protein Structure Prediction (CASP) programme and emphasised Tom's very major contribution as career mentor, both for herself and so many other researchers. Next, **Sherine Thomas** (University of Cambridge) gave a presentation entitled: 'Targeting mycobacterial tRNA modification – fragments, fun and so forth' in which she concentrated on proteins from non-tubercular mycobacteria (NTM), in particular TrmD from *M. abscessus*. This is a tRNA methyl transferase that is essential for preventing frameshifts and is being studied by X-ray fragment screening, elaboration and fragment merging, in collaboration with the Cambridge group of the late Chris Abell. Compounds with good antibacterial activity have been generated. The next speaker was **Bridget Bannerman** (University of Cambridge) who described her pivotal role in establishing a number of global health databases on antimicrobial resistance, epidemiology and systems biology of a range of developing world diseases and Covid, as well as clinical outcomes. The following speaker in this session was **Pedro Torres** (University of Rio de Janeiro) who presented virtually on studies of cystic fibrosis mycobacteria and the development of antibiotics targeting cell wall biosynthesis, folic acid metabolism and DNA gyrase. The speaker described how the criteria for a good target are high essentiality, druggability and bioaccessibility along with low mutability and similarity to host proteins. Pedro emphasised that pre-emptive work to discover new drugs and predict new drug targets bioinformatically is becoming ever more crucial and increasingly within our grasp. He described some of his current work on modelling homomeric complexes and reminisced about his work within the Blundell group, as well as Tom's election to the Brazilian Academy of Sciences. He also enthusiastically showed some slides taken by Glaucius Oliva – former president of the Brazilian National Council for Science and Development, himself an ex-Blundell group post-graduate from Birkbeck in the mid-late 80s. The final speaker in this session was **Eddy Arnold** (CABM and Rutgers University) who, presenting remotely, described Tom's many contributions to structural biology as well as the occasion of his meeting with Bill Gates. The speaker also paid tribute to Tom for his pivotal role in establishing the International School of Crystallography in Erice.

After coffee, **Dima Chirgadze** (University of Cambridge), whose talk was entitled 'From photons to electrons' was the first speaker in the ultimate session of the meeting, which was chaired by **Ben Luisi** (University of Cambridge). Dima began by describing the establishment of Tom's laboratory in Cambridge in 1996 when he and Ben effectively combined their research groups. The speaker moved on to some of the history of X-ray data collection, emphasising how the CCD detector was a major improvement on the image plate and allowed in-house phasing by sulphur SAD, so long as the protein contained at least one sulphur per 25 amino acids. The group acquired significant funding for cryo-electron microscopy in 2016 and this allowed one structure, which took 7 years to solve by X-ray methods, to be solved in 7 weeks by EM. Further recent developments allow the same structure to be solved routinely in 3 hours. Next, **Amanda Chaplin** (University of Leicester) gave an interesting presentation entitled 'The journey of non-homologous end-joining', describing how DNA repair is important in cancer and ageing, with a double-stranded breach of the molecule being the most harmful. Cryo-EM has

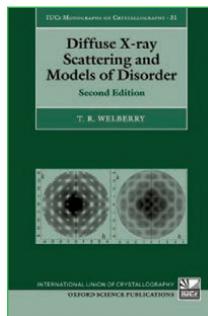
been used to study the role of the protein Ku in directing DNA-dependent protein kinase (DNA-PK) to the sites of damage, where DNA-PK phosphorylates itself and other proteins involved in repairing the DNA, forming a 1.66 MDa super-complex which has been studied extensively by EM. Finally, the pièce de résistance was the closing lecture given by **Tom Blundell** (University of Cambridge) entitled: 'Six decades of science and its applications'. Tom began by outlining his current research portfolio which includes cancer targets, diabetes, mycobacteria and Covid. He emphasised how recent years have seen two revolutions in structural biology – EM and AI – and how emerging drug resistance has become an important growth field. Tom described the key roles played by Dorothy Hodgkin and her Ph.D. supervisor John Desmond Bernal in the very early stages of protein crystallography with their realisation that keeping the crystal hydrated in a glass capillary tube was essential to preserve its ability to diffract. In 1967 Tom began working on insulin with Dorothy in Oxford and the structure was published in *Nature* in 1969. During his time in Oxford, Tom was heavily involved in local politics. He moved to Sussex in 1973 where his group had a number of landmark successes leading to his appointment as the Chair of Crystallography at Birkbeck in 1976. His research in those days included experimental studies of polypeptide hormones, eye-lens proteins and enzymes, including renin and HIV protease, as well as theoretical homology modelling. His move to Cambridge in 1996 led to further work on mycobacteria

involved in leprosy and cystic fibrosis, along with breast and urothelial cancer targets and multiprotein cell-regulatory systems. In addition, he maintains a strong interest in theoretical studies of protein modelling, stability and interactions. With Harren Jhoti and Chris Abell, Tom established the highly successful drug discovery company, Astex Pharmaceuticals, in 1999, which pioneered the use of X-rays for fragment-based drug discovery. Tom concluded his talk by emphasising the important role that diversity has played throughout his career and mentioned that he is currently writing a book on race, gender and ageism. We look forward to this and his future contributions in the next decades.

The scientific sessions were then followed by a superb champagne reception and dinner in the stunning refectory of St John's College, during which **Harren Jhoti** (Astex Pharmaceuticals) gave a moving tribute to Tom's truly outstanding achievements. **Marko Hyvönen**, **Ben Luisi**, **Luca Pellegrini** and **Dima Chirgadze** (all University of Cambridge) must be congratulated for organising such an excellent meeting, and the Cambridge University Biochemistry Department, Astex Pharmaceuticals, Exscientia and Cambridge Crystallographic Data Centre must be thanked for their generous sponsorship of the event.

**Jon Cooper, UCL**  
**Shabir Najmudin, King's College London**

## Book Review



### Diffuse X-ray Scattering and Models of Disorder

**T. R. Welberry**

International Union of Crystallography Monographs on Crystallography No. 31 Second Edition.  
 Oxford: IUCr / Oxford University Press, 2022. Pp. xx + 400.  
 ISBN: 9780198862482.

**DIFFUSE** scattering methods have risen to prominence as the method of choice for interrogating the structures of non-trivially disordered crystalline materials. Although the field has a long and rich history, its importance is now increasingly recognised by the mainstream in solid-state chemistry, materials, and condensed-matter physics. There remain relatively few texts devoted to the measurement and interpretation of diffuse scattering, and Welberry's *Diffuse X-ray Scattering and Models of Disorder* has been compulsory reading for newcomers to the field since its initial publication in 2004. At that time, the advent of area detectors and readily-accessible computing power was transforming both the ease with which diffuse scattering might be measured and also the ability to calculate diffuse scattering patterns from candidate models of disorder. The eighteen years that have passed since have seen equally transformative developments, such that a new edition of the text is more than warranted.

Determining the structures of disordered materials is not (yet) a linear process of collecting diffuse scattering data then extracting

a microscopic model of disorder in some automated or deterministic approach. It is rather a convergent exercise of measuring data, on the one hand, and developing and testing candidate models for consistency with experiment, on the other hand. It is this convergent approach — and its implication that practitioners in the field must be versed in both measurement and simulation — that informed the structure of Welberry's original text. That structure is preserved in this new edition. Part I focuses on the experimental requirements and approaches for measuring high-quality diffuse X-ray scattering; Part II covers a range of simple but important models of disorder; and the remainder (now split into Parts III and IV) leads the reader through a variety of examples of using the latter to interpret the former, drawn mostly from the author's published work.

Almost nothing has been dropped from the first edition. The experimental section has been updated to include discussion of single photon-counting hybrid pixel detectors, and the original coverage of diffuse neutron scattering measurements — which focussed on the SXD instrument at ISIS — has been expanded to cover the CORELLI instrument at SNS. Both aspects feed directly into what is probably the single most important addition to the text in this new edition: namely, the coverage of 3D-PDF (and 3D-DPDF) methods in the very final chapter. The new tranche of examples, collated in Part IV, form the bulk of the additional material in this second edition. They serve primarily to introduce a variety of developments in the modelling of diffuse scattering that have emerged since 2004. The text now covers calculation of diffuse scattering from molecular dynamics simulations, the use of *ab initio* calculations to determine interatomic potentials, coarse-grained effective interaction models, and also a new empirical refinement strategy developed relatively recently by the author.

Researchers interested in the technical considerations of measuring diffuse X-ray scattering will benefit enormously from the lucid and authoritative summary provided in Part I. Here, the reader is introduced to the various pros and cons of many different scattering geometries, sources and detectors now routinely available to experimentalists in the field. Particularly valuable is the discussion of experimental artefacts that, to the uninitiated, might easily be misinterpreted as diffuse scattering. Inelastic scattering is covered briefly in the context of neutron studies, and this leads into discussion of separating elastic and inelastic contributions to the diffuse scattering function with CORELLI. This capability is elegantly illustrated by Welberry's own measurements on a single-crystal of benzil – an historically important example in the field of diffuse scattering: the richly beautiful diffuse features first measured by Kathleen Lonsdale (Welberry's Ph.D. supervisor, as it happens) all but disappear as soon as the inelastic scattering contribution is removed. The implicit caveat is obvious: distinguishing static and dynamic disorder may be crucial to the physics of a given system, but distinguishing the two cases can require carefully chosen diffuse scattering experiments.

The use of electron diffraction to measure diffuse scattering patterns is covered only very briefly, and is included only really because of its relevance to some examples in Part III. Despite the many valid limitations of electron diffraction flagged by the author, the field is currently evolving very quickly in terms of technical advances that permit quantitative measurement of diffuse scattering intensities. A key driver is the prospect of measuring single-crystal data from polycrystalline specimens – potentially opening up the advantages of 3D-(D)PDF methods to a much wider range of materials. Though the field is still maturing, it would not be surprising if this section were to be substantially longer in a future, third, edition of the text.

Part II covers a range of Ising and growth models for describing disorder in one, two, and three dimensions. The emphasis throughout is one of developing an intuitive understanding of the link between model parameters and the form of the diffuse scattering to which they give rise. This section is illustrated with a number of real-space/reciprocal-space pair examples that are reminiscent of Welberry's landmark *Atlas of Optical Transforms*, and which are similarly useful in developing a qualitative understanding of how one might interpret directly the various structured features present in a diffuse scattering image. The examples drawn are nearly all abstract – Welberry mostly waits until Part III to relate these to physical systems.

A particularly valuable aspect of this section is its elegant demonstration of counter-intuitive aspects of diffuse scattering. One is the point that Bragg and diffuse scattering functions can have different point symmetries for the same system. Another is the reminder that diffuse scattering is insensitive to three-body and higher-order correlations – a point conveyed most starkly in a series of examples of real-space configurations that give rise to identical diffuse scattering functions.

The bulk of the text comprises summaries of experimental studies of real disordered systems – these summaries span the nearly 300 pages of both Parts III and IV. A recurring narrative is one of measuring diffuse scattering data, then inferring a likely disorder model by direct interpretation of the diffuse features, and finally varying the model parameters (either manually or automatically) until the best match to experiment can be obtained from the corresponding calculated diffuse scattering function. The examples draw on a wide variety of systems – from minerals to pharmaceuticals, and from inclusion compounds to relaxor ferroelectrics. By consequence they

also reflect a wide variety of physical origins of disorder: compositional, orientational, displacive, conformational, and combinations thereof. This breadth is ultimately a strength of the text, because it is effective in conveying the universal importance of diffuse scattering analysis across the structural sciences. But it requires of the reader a scientific nimbleness as one progresses from example to example. Most readers will likely focus on the specific subset of most direct relevance to their own research interests, and this part of the book can probably be read effectively in this manner.

Quite understandably, the various case studies are drawn primarily from Welberry's own work, and so focus on his particular approach to analysing and interpreting diffuse scattering. In this context, a strength of this second edition is that it includes a number of analysis methods that were impractical when the original text was first published, but which are now being used relatively routinely in the broader community. Molecular dynamics simulations are an obvious example, illustrated here with the ever-topical cases of relaxor ferroelectrics and barium titanate. The link to *ab initio* calculations is made via model-fitting rather than explicitly considering *ab initio* molecular dynamics simulations, or thermal diffuse scattering calculation from DFT-derived phonon dispersion relations – no doubt these would also be aspects that might feature in a future edition.

For readers already familiar with the first edition of Welberry's text, probably the most intriguing addition is his discussion of pair distribution functions (PDFs) – both one- and three-dimensional. With respect to the conventional one-dimensional PDF, Welberry's emphasis is on its (in)sensitivity to meaningfully different disorder models – briefly focusing on the specific case of defect cluster arrangements in wüstite. Experts in powder PDF methods might flinch at one or two nuances of the discussion here, but no-one would argue with the excitement conveyed in the summary of 3D-(Δ)PDF methods that follows. This final section of the text begins with a series of elegant reciprocal-space/real-space pair examples based on the work of Thomas Weber and Arkadiy Simonov. These illustrations demonstrate the relationship between diffuse scattering and difference PDFs, conveying the different signatures of occupational, displacive, and mixed disorder. The effectiveness of the 3D-ΔPDF approach is then demonstrated through the example of  $\text{Na}_{0.45}\text{V}_2\text{O}_5$ , a sodium-ion intercalation compound and an excellent case study – because its 3D-ΔPDF is particularly straightforward to interpret directly.

*Diffuse X-ray Scattering and Models of Disorder* remains essential reading for anyone interested in diffuse scattering methods – novice and expert alike. For the novice, there is the helpful background one needs to enter the field, and the advantage of learning from the experience of one of the field's true pioneers. For the expert, the text is rich with nuggets of profound insight into the structures of disordered systems and the relationship between disorder and the scattering function.

**A. L. Goodwin**  
University of Oxford

# Meetings of interest

WITH a little less concern about the virus, the conference scene seems to have been strongly revitalised, with a lot of new meetings being organised – so you might well find something new and interesting in this list. Most meetings are in-person ones, though some remain online or hybrid. Further information may be obtained from the websites given. Assistance from the IUCr website is 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](mailto:jon.cooper@ucl.ac.uk).

## 3rd Apr 2023 - 5th Apr 2023

Faraday Joint Interest Group (session on Neutron Scattering)  
Sheffield, U.K.

<https://www.rsc.org/events/detail/73818/>

## 12th Apr 2023 - 14th Apr 2023

Harnessing Non-covalent Interactions for Synthesis and  
Catalysis (Faraday Discussion)  
York, U.K.

<https://www.rsc.org/events/detail/48165/>

## 16th Apr 2023 - 21st Apr 2023

Experimental Advances in Macromolecular Crystallography  
Dubrovnik, Croatia.  
<https://htcc5.org/>

## 19th Apr 2023 - 21st Apr 2023

Neutron and Muon Science User Meeting (NMSUM) 2023  
Warwick, U.K.  
<https://www.isis.stfc.ac.uk/Pages/NMSUM2023.aspx>

## 12th Jun 2023 - 16th Jun 2023

Summer School on Mathematical Crystallography  
Nancy, France.  
<http://www.crystallography.fr/mathcryst/nancy2023.php>

## 18th Jun 2023 - 24th Jun 2023

8th European Crystallography School  
Berlin, Germany.

<https://ecs8.ecanews.org>

## 3rd Jul 2023 - 6th Jul 2023

16th International Conference on Materials Chemistry  
Dublin, Ireland.

<https://www.rsc.org/events/detail/72840/>

## 7th Jul 2023 - 11th Jul 2023

73rd ACA Annual Meeting  
Baltimore, MD, U.S.A.

<https://www.amercrystalassn.org/future-meetings>

## 23rd Jul 2023 - 29th Jul 2023

18th International Summer School on Crystal Growth  
Parma, Italy.

<https://isscg-18.unipr.it/index.php>

## 30th Jul 2023 - 4th Aug 2023

20th International Conference on Crystal Growth and Epitaxy  
Naples, Italy.

<https://www.iccge20.org/>



## Conference Bursaries 2023

Bursaries are available for BCA members to attend national/international crystallographic meetings in 2023.

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 local/virtual meeting 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/>

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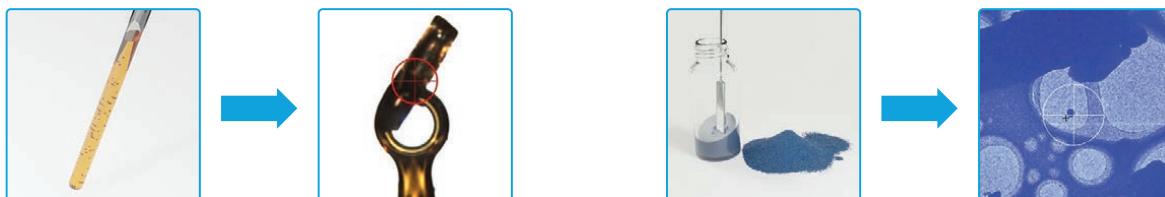


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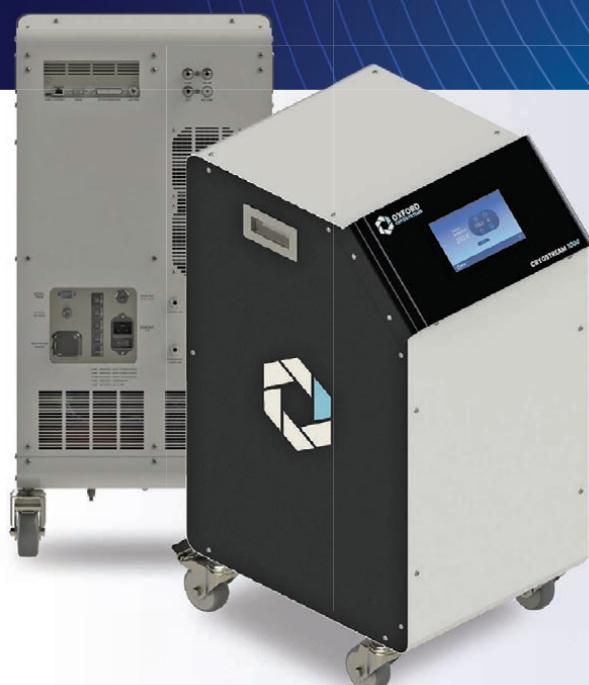
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## KEY FEATURES

**X-ray Transparent Nozzle:** An optional attachment for the coldhead nozzle, the X-ray transparent extension is made from a durable and low-temperature compatible material that minimises shadowing on the X-ray detector, increasing the amount of useful diffraction data collected without compromising cooling performance. This can either reduce the duration of experiments or improve the signal-to-noise ratio and overall data quality.

**LED Status Indicator:** The coldhead now provides the user with immediate visual feedback on the Cryostream's operational status without the need to refer to the control screen.

**Gas Supply Module:** Combines the Nitrogen pump, dry-air supply and touch screen controller into a single, compact and portable enclosure that reduces cabling, simplifies installation and improves the user experience.

**Remote Annealing:** Controlled and programmable interruption of the gas flow over the sample for annealing without physical manipulation (also available via an open network protocol).

**Intelligent Diagnostics:** An integrated real-time clock now tracks the use of the system, notifying the user of upcoming service requirements, helping to eliminate unscheduled downtime.

**2 Year Standard Warranty:** All Cryostream 1000 systems ship with a two year warranty as standard.

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