Crystallography News

British Crystallographic Association

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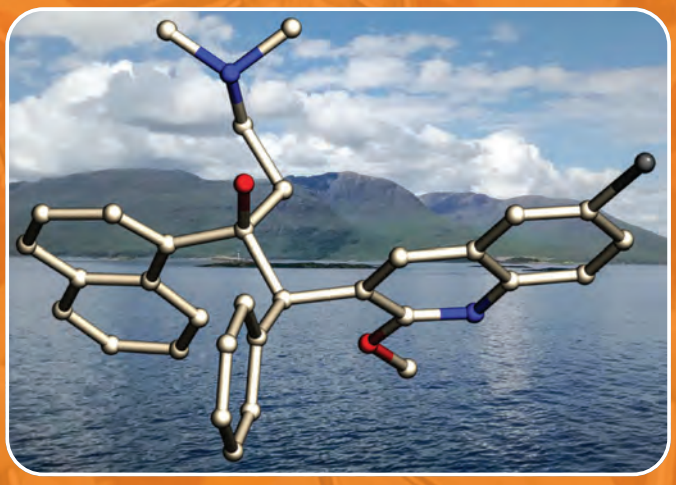

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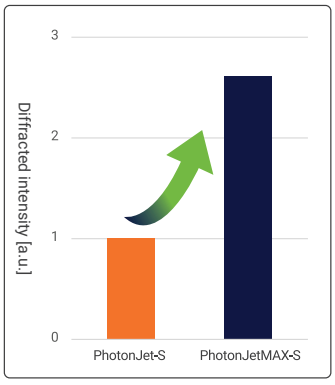

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CRYSTALLOGRAPHY NEWS is published quarterly (March, June, September and December) by the British Crystallographic Association, and printed by BHW Print Group, Malton, North Yorkshire.
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This month's cover:

Learning from and remembering others at recent crystallography meetings.

From the President

DEAR Members, I am writing this not long after returning from the Spring Meeting in Leeds which was a great success, and testament to the dedication and effort of all concerned in the organisation and running (particular thanks are due to Katharina Edkins (Strathclyde), Suzanna Ward (CCDC), the group Programme Representatives and the session organisers), as well as the sponsors who helped make it possible. The programme was a packed schedule of science, networking and industrial engagement which got off to an excellent start with the extremely well attended ESCG event (a great payoff for the hard work of the organisers of this to whom I also extend special thanks). Throughout the meeting it was a delight to see the enthusiasm and energy of the attendees, including interactions with each other and the exhibitor stands during the coffee breaks (the exhibitor passport prize was very well contended!). The high level of engagement from the membership during the AGM was particularly good to see – and I hope that those who could not be present at the Meeting feel free to add their own thoughts through whichever channel they prefer.

I think we would all agree that in many ways the BCA and Spring Meeting follow excellent traditions, but at the same time we should remain open to changes reflecting developments in the practice of crystallography and the modern scientific environment and culture. As an association with just under 500 members we are big enough to have something for everyone, combined with a critical mass to drive issues forward. On the other hand, we are also small enough that the individual can make a big difference, so please do remember that we are always keen to have your input on any aspect of the BCA, be it the Spring Meeting (your Group Representative or **Lewis Owen** as the new Programme Chair are ideal points of contact for this), suggestions for ways to improve how we do things and for new activities or areas to focus on.The Council and Officers are always keen to hear your views, as are the members of the individual Group Committees. I encourage you to (re)familiarise yourself with their details and I will take this opportunity to warmly congratulate **Simon Newstead** (Oxford) on becoming the Chair of the BSG.

As a side note – one thing that not all members may be aware of is that our accounts are open for inspection on the Charity Commission website, so do please go and see how your money is being spent!

I was reading an article recently in Chemistry World about the 11 chemists who have blue plaques in London and noticed that 4 of these are crystallographers – **Dorothy Hodgkin, John Desmond Bernal, Rosalind Franklin and Kathleen Lonsdale** – rather a good showing I think. A visit a couple of months ago to Cambridge gave me the opportunity to see the blue plaque at the Eagle pub which commemorates the discovery of the structure of DNA. After repeated graffiti adding thename of **Rosalind Franklin** to those of Crick and Watson the plaque was updated in 2023 to add recognition of the crystallographic contributions from Franklin and **Maurice Wilkins**, along with other unnamed scientists. On top of the well-deserved individual recognition, I feel it provides a welcome reminder of both the importance of the data underpinning scientific breakthroughs, and the fact that discoveries are rarely down to one or two lone geniuses. Unfortunately I didn't have more time to spend in Cambridge as the Whipple museum has an exhibition with the original graffitied plaque along with some of Franklin's research notes running until September, but I hope some readers might manage to take advantage of this.

To end I would like to draw attention to the obituaries of **George Sheldrick** (Gottingen) and **Alan Mackay** (Birkbeck), sad news of whose passing we have recently received, which appear later on in the issue.

Alex Gibbs
St Andrews

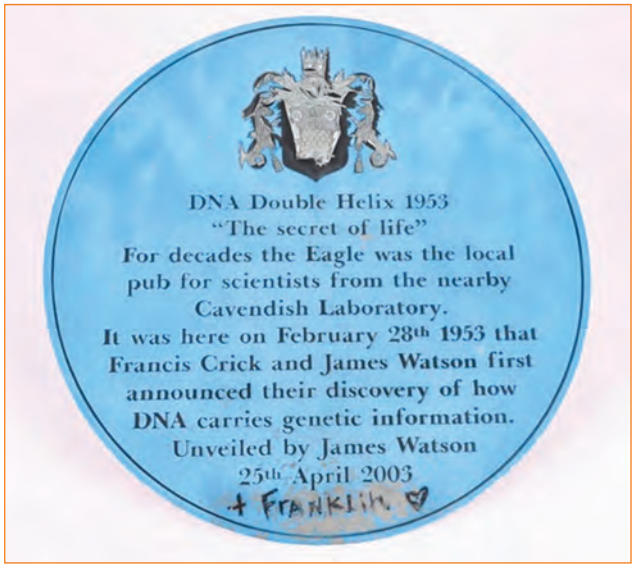

Fig. 1. The original DNA Double Helix plaque (courtesy Cambridge Museums).

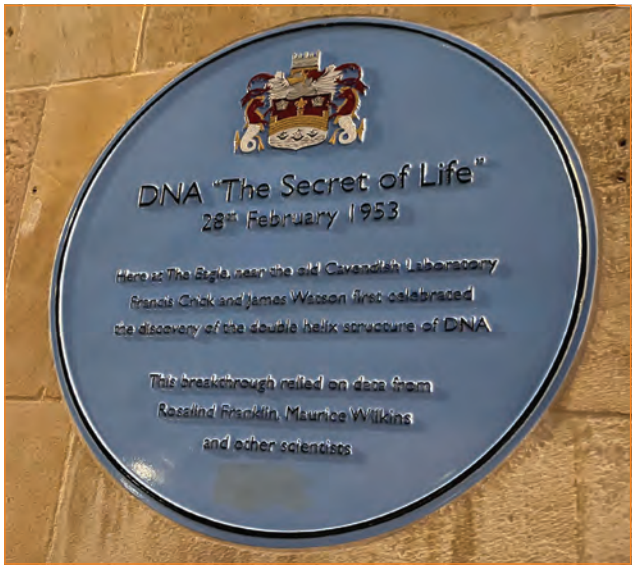

Fig. 2. The new plaque recognising other contributions to the discovery.

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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

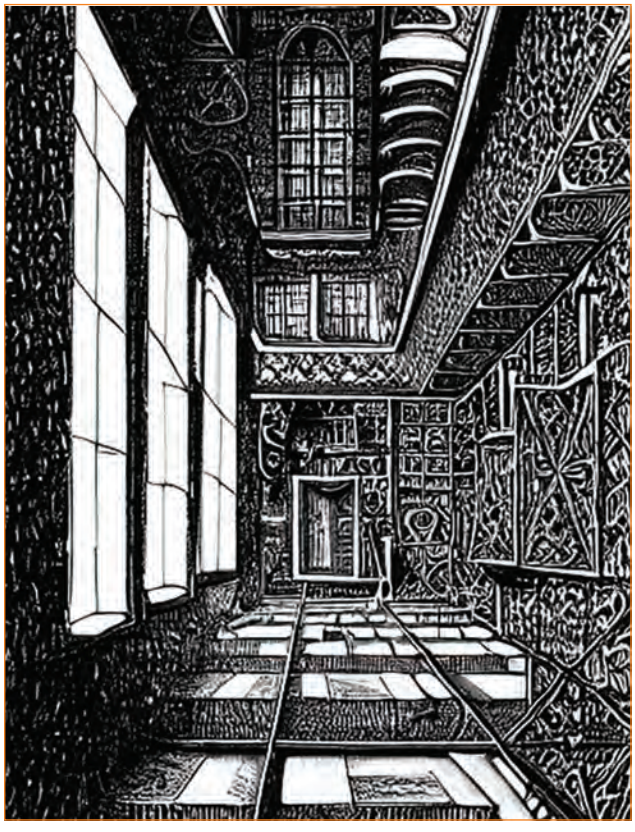
From the Editor

IT is a great pleasure to bring you the June 2025 issue of Crystallography News which features reports on the many excellent sessions at the BCA Spring Meeting in Leeds, including those organised by Physical Crystallography Group (PCG) and the Biological Structures Group (BSG). Due to the constraints of time and space in this issue, reporting of the other sessions will continue in the next Crystallography News. I am extremely grateful to all those who sent me accounts of sessions they attended, especially to the Arnold Beevers bursary fund awardees and I apologise that we have had to defer some until slightly later in the year.

We also report on the CCG Intensive Teaching School which was held in Durham shortly before the Spring Meeting and on the Bruker AXS Symposium which was held on 6th March at the Crick Institute in London. We follow this up with our regular feature on News from the CCDC. Very sadly, it is necessary to bring you two obituaries, firstly for George Sheldrick (Göttingen) and then for Alan Mackay (Birkbeck).

We then have our regular Puzzle Corner and Down Memory Lane sections. In the latter we look at a very interesting and counter-intuitive statistical puzzle which I hope is relevant to crystallographic phasing and other statistical methods that we employ.

Now for something which marks the return of our occasional section on ***Crystallographic Forteana***, unusual phenomena which often challenge the boundaries of scientific thinking, although I am not sure that applies in this case. I thought the following story might amuse members in the light of the equipment which our NMR spectroscopy colleagues use on a daily basis and might even give you some ammunition with which to rib them. The April 2025 edition of the *Fortean Times* (p. 9) reported on an armed police raid at a diagnostic medical imaging facility in Los Angeles. The security services had been alerted to the centre because of its very high electricity usage, leading them to suspect it was being used covertly for cannabis farming. However, during the raid, as an officer burst into one of the clinics, his rifle was wrenched from his hands, flew across the room and became firmly stuck to an MRI scanner's magnet. To retrieve the gun, another officer pushed a sealed emergency power-off button thus evaporating thousands of litres of liquid helium, ultimately damaging the machine due to the loss of superconductivity. The raid is now the subject of legal action by the clinic against the police department, who incidentally found no plants of the Cannabaceae family on site. Whilst that may be odd enough, by a coincidence which is even stranger, we have a little more on medical imaging later on in this issue in the Down Memory Lane section where look briefly at some of the history of X-ray computed axial tomography. We end this issue with some forthcoming meetings which are hopefully of interest to members.



As I mentioned earlier, please note that reporting on the Spring Meeting will continue in the next issue when we hope to resume the series of Corporate Member Profiles!

Jon Cooper
UCL

Erratum

In the Corporate Member Profile for Douglas Instruments in the last issue (172) several co-authors were accidentally omitted from the following reference.

Stubbs, J., Hornsey, T., Hanrahan, N., Esteban, L. B., Bolton, R., Malý, M., Basu, S., Orlans, J., de Sanctis, D., Shim, J. U., Shaw Stewart, P. D., Orville, A. M., Tews, I. and West, J. (2024). Droplet microfluidics for time-resolved serial crystallography. IUCrJ, 11, 237–248. https://doi.org/10.1107/S2052252524001799

I am very grateful to **Patrick Shaw-Stewart** (Douglas Instruments) for pointing that out.

In the same issue, the Down Memory Lane article on June Lindsey entitled "An unsung heroine of the double helix" should have referenced the following obituary in the IUCr Newsletter.

Lindsey, J., Lindsey, R. and MacKenzie, A. (2022). June Lindsey (née Broomhead; 1922–2021). *IUCr Newsletter 30,* https://www.iucr.org/news/newsletter/volume-30/number-1/june-lindsey-nee- broomhead-1922-2021.

I am very grateful to **Mike Glazer** (Oxford) for pointing that out.

There are other interesting articles about June Lindsey online including one in *Chemistry World* and another in the *Ottawa Citizen*.

2025 Spring Meeting Reports

Physical Crystallography Group

The PGC Open Session I was chaired by **Nilanthy Balakrishnan** (Keele) and contained 4 contributed talks, three of which were in person and 1 via Zoom. The session began with a talk by **Patrick Doheny** (Birmingham) who presented a talk entitled "Investigations of ZIF-67 crystallisation mechanisms" which refers to the zeolitic imidazolate framework-67 (ZIF-67). By employing UV-VIS spectroscopy, Patrick showed that the coordination sphere of the solvated Co^{2+} precursor undergoes a transition from octahedral to tetrahedral as the pH of the reaction mixture increases and the ZIF-67 product crystallises. This transition is supported by single-crystal structures of tetrahedral Co^{2+} reaction intermediates isolated from the reaction within specific pH ranges, which show increasing numbers of 2-methylimidazole ligands as the pH is increased. Next, **Geeta Sharma** (Leeds) presented on the subject of the "Effect of rare earth ion substitution on phase decomposition of apatite structure" covering the phase stability and thermal behaviour of rare-earth-doped apatites (doped with cerium, samarium, and holmium ions) over a temperature range of 25°C to 1200°C. Geeta showed the sol-gel synthesis method of rare-earth ion-doped apatite minerals and their phase transition analysis using *in situ* high-temperature powder X-ray diffraction. She used differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA) to study the thermal decomposition behaviour and showed that rare-earth ion doping leads to variations in decomposition behaviour. Notably, cerium and samarium ions were present in multiple oxidation states (Ce^{3+}, Ce^{4+}, Sm^{3+}, Sm^{2+}), whereas holmium existed only in the Ho^{3+} state. Geeta also showed her machine learning model to predict phase stability and decomposition products as a function of temperature. **Daniel Widdowson** (Liverpool) gave the third talk entitled "Crystal Geomap: a visualisation & comparison tool for crystals based on ultra-fast isometry invariants." Daniel introduced the pointwise distance distribution (PDD), a continuous descriptor (isometry invariant) akin to the genetic code of a crystal with no known false positives amongst real organic crystals. Daniel showed that nearly all crystals can be reconstructed from their PDD, and comparisons take only milliseconds. When combined with its centroid, the average minimum distance (AMD), comparisons are fast enough to find all matches in a database of a million structures in a few minutes, a task which would require years for comparison tools such as powder pattern matching or COMPACK. Moreover, Daniel introduced their creation of Crystal Geomap. which allows a user to compare or cluster crystals within the app, which can then be plotted on chosen x and y axes, where all crystals can be viewed together in a space where their coordinates are physically meaningful. **Sarah Dugmore** (Glasgow) gave the final talk entitled "Development of *in situ* Raman scattering and neutron diffraction on SXD" via Zoom. Sarah discussed the technical development and testing of a new sample environment equipment devoted to performing simultaneous *in situ* Raman scattering and neutron diffraction measurements on the single-crystal neutron diffractometer SXD at ISIS Neutron and Muon Facility in Harwell. By employing this technique, Sarah showed that the spin crossover (SCO) complexes are metal-organic compounds that demonstrate chromotropism by the effect of a change in the spin distribution of unpaired electrons in the transition metal atom, which can be induced by temperature change, light irradiation or pressure.

The PCG session on "Computational modelling in crystallography" was chaired by **Jonathan Skelton** (Manchester). The term "computational modelling", applied to crystallography, encompasses a wide range of topics, and the talks in this session were selected with this in mind. The session began with an invited keynote talk by **George Darling** (Liverpool) on the topic of "Crystal structure prediction and materials discovery for complex inorganic solids." The approach described in the presentation decomposes structures into "modules" that can be used with Monte-Carlo and generative artificial intelligence (AI) techniques to predict the structures of novel chemical compositions. Paired with fast energy evaluation methods, such as machine-learnt interatomic potentials, this forms a practical approach to predicting the structures of complex multicomponent systems. The talk also highlighted some of the limitations of computational predictions, but demonstrated that the pragmatic approach of treating predicted structures as "probes" to guide experiments toward stable compositions can nonetheless be highly successful. The keynote presentation was followed by three contributed talks. **Joseph Arnold** (Birmingham) presented work towards the accelerated discovery of high-entropy alloys (HEAs) with the title of "Exploring the phase composition of high entropy alloys via machine learned interatomic potentials." HEAs are an emerging class of materials for which the major challenge is navigating vast compositional spaces. This talk demonstrated how computational methods, leveraging advances in AI, can guide experiments towards stable compositions with targeted properties. A particular novelty was the use of the Korringa-Kohn-Rostoker (KKR) approach to density-functional theory (DFT) to model partial site occupancy, which can be challenging with "traditional" implementations of DFT. Next, **Lavanya Kumar** (Warsaw) spoke on "Investigating halogen bonding with heavy pnictogen acceptors: a combined experimental and theoretical charge density analysis." The speaker presented work on characterising halogen bonds with pnictogen acceptors using charge-density measurements. Using the quantum theory of atoms in molecules (QTAIM) allowed the electron density at the bond critical points between donor and acceptor atoms to be quantified and correlated to structural and physical properties. In addition to showcasing state-of-the-art crystallographic techniques, comparing QTAIM metrics to DFT calculations was highlighted as an innovative means to assess the accuracy of DFT methods. Finally, **Joseph Flitcroft** (Manchester) spoke on "The effect of co-adsorption of small molecules on CeO_2 nanoparticle morphology." Joseph presented a workflow for using atomistic modelling with periodic DFT to predict the surface

speciation and morphology of CeO_2 (ceria) nanoparticles as a function of environmental conditions. A key finding was that the presence of multiple surface adsorbates can result in both synergistic and competitive interactions, with significant impacts on the surface chemistry and accessible particle morphologies. The session was overall very well attended, indicating that applications of computational modelling, in its various guises, is a worthwhile topic for future meetings.

The joint PCG/ESCG session on "Complementary Techniques" was chaired by **Karen Johnston** (Durham) and **Evie Ladbrook** (Warwick). The session began with a talk entitled "The relationship between functional group orientation and crystal facet behaviours" by **Dave Collins** (Leeds). The speaker presented some very recent developments on the use of angle resolved polarised Raman spectroscopy (ARPRS) to investigate the orientation of functional groups on the crystal faces of paracetamol crystals. Powder diffraction is initially used to identify the orientation of the crystals, then via rotation of the crystals, changes in the intensity of the characteristic vibrational modes can be identified using ARPRS. Combining this with density functional theory calculations, crucial insight into the specific orientation of the functional groups on the crystal facets can be obtained. The effect of humidity on the facets was also investigated, providing useful information regarding the pharmaceutical stability of these materials. **Pedro Nunes** (DLS) followed with a talk entitled "HeXI: The high-energy electron crystallography instrument" highlighting the capabilities of this new instrument currently under construction at DLS. HeXI aims to bridge the gap between electron diffraction and X-ray diffraction, specifically targeting crystals between 300 nm to 3 microns. Utilising a high-energy electron beam (100 kV – MeV), the energy and the beam size will be tuneable to the sample to achieve the best results. An additional benefit of HeXI is that it will be much faster than traditional transmission electron microscopy (TEM), so it has the potential to be used for time resolved studies. HeXI will be an excellent addition and will provide a great complement to beamtime at DLS. The third talk of the session was given by **Kieran Griffiths** (Lancaster) who spoke on "Structural and mechanistic insight into confined photoswitches." Kieran introduced solid-state NMR spectroscopy and demonstrated how it had been integral to his work on photoswitches in the pores of flexible metal-organic frameworks (MOFs). Although single crystal XRD can be utilised to study the framework structure, local structural probes are essential for studying the molecular photoswitches in the pores. Here, solid-state NMR was key in revealing previously unidentified framework dynamics and guest conformations. Under the title of "Spectroscopy and crystallography: hand-in-hand for understanding dynamic framework materials" **Timothy Easun** (Birmingham) ended the session by providing a brief overview of his recent research efforts. The speaker focussed largely on the dynamic behaviour of MOFs using a variety of spectroscopic techniques to identify intermediates from photoswitching that cannot easily be observed using traditional crystallographic methods. For example, it was shown how time-resolved infrared spectroscopy can be used to understand decay on a nanosecond time scale. Tim presented a few case studies that demonstrated how spectroscopic techniques can advance and complement our understanding from crystallography, such as the exploration of ordering of metals in mixed metal complexes or the diffusion of guest molecules from the pores of MOFs into the bulk.

The joint PCG/IG workshop on "Rietveld refinement" was chaired by **Tony Bell** (Sheffield Hallam) and **Lewis Owen** (Sheffield) and began with a keynote lecture entitled "Rietveld refinement: past, present and future" which was given by **Jeremy Cockcroft** (UCL). The speaker gave a historical overview of the development of this well established powder diffraction technique. Structure refinement from powder data was done before Rietveld, but this was only possible for simple cubic structures with no peak overlaps. Hugo Rietveld's classic work of the 1960s, showed how a crystal structure could be refined from powder diffraction data by least squares fitting of a calculated pattern from a suitable starting model to the whole powder pattern. Rietveld refinements were originally used for constant wavelength neutron diffraction. Advances in the Rietveld code were discussed as were the parameters that could be refined by the Rietveld method. The technique has advanced to include X-ray and pulsed neutron diffraction. The speaker brought us up to the present day by discussion of modern Rietveld programs such as GSAS-II and TOPAS. The next lecture was given by **Struan Simpson** (Warwick) and was entitled "Symmetry-informed refinement strategies." Struan brought the Rietveld story up to date by using symmetry mode refinement analyses using ISODISTORT and AMPLIMODES. Tilts and displacements can be applied to starting crystal structures used for Rietveld refinements. Symmetry mode changes for perovskites and Ruddlesden-Popper phases were discussed. A case study on 6H $BaTiO_3$ perovskite was discussed with the distortion parameters refined using TOPAS. Last but not least, the final speaker was **Alex Gibbs** (St. Andrews – ISIS) who spoke on "Key issues in neutron diffraction data analysis." Alex gave an interesting presentation on what is needed to collect good neutron powder diffraction data from pulsed neutron sources (like ISIS). Neutron data collection is very different to that from X-rays. In contrast to the situation for X-rays, oxygen will scatter neutrons more strongly than many elements. Much larger samples are needed and, due to this, care must be taken with multi-temperature scans to ensure that the sample temperature has equilibrated before data collection. Pulsed neutron source Rietveld refinements have different refineable parameters from those used for X-rays, which can affect Rietveld refinement strategies. At the end of the presentation some results from neutron Rietveld refinements were given.

The second PCG Open Session was chaired by **Helen Playford** (STFC) and **Lewis Owen** (Sheffield) and began with **Nilanthy Balakrishnan** (Keele) who opened the session giving a talk about materials for batteries and supercapacitors entitled "Symmetric double-layer capacitor with natural rubber and sodium salt-based solid polymer electrolyte and reduced graphene oxide electrodes." Nilanthy's work is based on exploring interesting sustainable materials choices for battery materials. Working with collaborators from Wayamba University of Sri Lanka they have demonstrated capacitors with promising charging properties made from natural rubber materials. Using an optimised salt ratio, they were able to create a capacitor and test its properties, demonstrating the suitability of these materials for supercapacitor performance. This was followed by **Catriona Crawford** (Warwick) who spoke on "Unravelling t2g Jahn-Teller distortions in fluoride perovskites." Her talk focussed on how by using fluoride perovskites, they are able to explore Jahn-Teller distortions created by specific metal ions. Using a combination of X-ray and neutron experiments, differences in the lengths of the different metal fluorine bonds

could be seen as a function of temperature. Analysis of the distortions using an elegant example of symmetry mode analysis was then able to help describe these transitions and decouple the origin of these effects. The third speaker in the session was **Struan Simpson** (Warwick) whose lecture title was "Structural Goldstone-like mode in hexagonal $BaTiO_3$." Struan had already spoken in the Rietveld session about the method of symmetry mode analysis and now provided an interesting example – exploring the hexagonal polytype of $BaTiO_3$. Using ID11 they were able to obtain 3D-XRD, yielding a strain distribution map for the system identifying a complex microstructure. They were about to show that the primary order parameter, possesses clear Goldstone mode character. Further, preliminary DFT calculations suggest that there may be further examples of this mode character, that have yet to be encountered in this phase space. The final speaker in the session was **Rebecca Clulow** (Uppsala) whose lecture was entitled "Dehydration behaviour and oxygen vacancy formation in compositionally complex $n = 1$ Ruddlesden-Popper perovskites." Rebecca's work explores applying the high entropy principle, originally developed by the alloy community, in functional oxide systems. She presented an exploration of Ruddlesden-Popper materials containing between 5 and 7 mixed ion sites. Using a combination of X-ray diffraction, variable temperature neutron diffraction and thermal analysis, she explored the structure, properties and oxygen vacancy formation within this interesting family of materials.

The joint CCG/PCG session entitled "Coordination polymers and porous materials" was chaired by **Lauren McHugh** (Liverpool) and began with an excellent keynote talk by **Valentina Colombo** (Milan) entitled "Metal-organic frameworks: crystallographic explorations of porosity and functionality." The speaker presented *in situ* insights into adsorption and catalysis in metal–organic frameworks (MOFs). Valentina described how an *in situ* gas cell was employed to activate copper-based MOFs and facilitate CO_2 loading, enabling direct observation of host-guest interactions and adsorption sites. She explained how, using HR-PXRD obtained at the ESRF, the CO_2 adsorption process could be studied in real time – raising the interesting question of whether X-ray data alone could be used to determine gas sorption behaviour. She then explained how PXRD data was used to simulate adsorption isotherms, which showed strong agreement with volumetric isotherms – demonstrating the power of this approach for probing adsorption site behaviour in detail. She then shifted focus to material tuning via ligand modification, specifically in iron MOFs, where a disordered framework suggested by HR-PXRD data was further investigated through comparison with X-ray absorption spectroscopy. The talk concluded by looking at the reversible formation of Cu(I) surface defect sites, highlighting advances in operando characterisation techniques for MOF-based catalysts. Next, we had a very interesting talk entitled "Just add water: exploring phase transformations of a flexible metal – organic framework using *in situ* and *ex situ* powder diffraction analysis" given by **Thomas Roseveare** (Sheffield). Thomas presented his research on phase transformations in the flexible MOF: SHF-61, using both *ex situ* and *in situ* PXRD. He began with a general discussion on how MOFs typically lose long-range order upon exposure to water, before introducing SHF-61 – a dynamic MOF based on an indium metal centre. He explained the framework's solvent-dependent flexibility and then discussed the conversion of SHF-61 into other MOF phases in a mixed water-DMF environment, which was monitored via *ex situ* PXRD, and where the solvent ratio and exposure times proved crucial in directing the nature of the framework conversion. Thomas then showed that the transformations could also be monitored *in situ* using a solvent flow setup at DLS. Shifting focus towards advanced structural analysis techniques, the third talk was given by **Mihails Arhangelskis** (Warsaw) and was entitled "Hirshfeld atom refinement for improved accuracy of MOF crystal structures." The speaker's fascinating presentation turned to the application of the fragmentation Hirshfeld atom refinement method in the quantum-crystallographic refinement of MOFs – using the ZIF-2 framework as an example. Emphasising the capabilities of this approach, Mihails demonstrated that unconstrained refinement of hydrogen atom positions and anisotropic displacement parameters could be achieved using standard laboratory X-ray diffraction data. Notably, he showed that the refined hydrogen positions aligned well with C-H bond lengths typically observed in neutron diffraction experiments and periodic DFT studies. In addition, the work presented, demonstrated a more nuanced understanding of solvent disorder and guest inclusion, offering a more reliable foundation for interpreting host-guest interactions within frameworks. The final talk of the session was delivered by **Ian Williams** (Hong Kong University of Science and Technology) and was entitled "Learning from others: crystallographic adventures in the land of MOFs." Ian's entertaining presentation offered a fascinating overview of his extensive research journey in the field of crystallography, with a particular focus on MOFs. Ian began by reflecting on his early work involving air-sensitive materials, which laid the groundwork for his later transition into the study of porous solids. He detailed his research on aluminophosphates and indium phosphates, before shifting focus to his pioneering contributions to the development of MOFs, including his foundational work on HKUST-1. The talk progressed to other notable frameworks such as the rutile-like $Cu(INA)_2$, and the evolution of linker chemistry from isonicotinate to pyridine-4-oxide in cadmium and calcium-based systems. Ian then discussed pore engineering within $M(INA)_2$ MOFs, followed by the design, synthesis and properties of interwoven structures based on $M(INA)_2$, in planned collaborative work with Sir Anthony Cheetham and the late Sir Fraser Stoddart.

The PCG component of the BCA Spring Meeting closed this year with the "Phase Transitions" session which was chaired by **Struan Simpson** (Warwick). As in previous years, this session was very well attended which demonstrates that this theme continues to prove popular with attendees. The talks covered a diverse range of phase transition phenomena in several prominent research themes, including molecular perovskites, Li-ion batteries, negative thermal expansion, and ferroelectrics. This diversity reflects the fundamental importance of phase transition phenomena to many materials of topical interest. The keynote lecture was delivered by **Rebecca Scatena** (DLS) and was entitled "Pressure- induced orbital reordering phase transitions." Rebecca discussed several aspects of pressure-induced orbital-ordering transitions in molecular ABX_3 perovskite-based systems containing different molecular cations on the *A* site, Jahn-Teller cations on the *B* site and molecular species on the *X* site. Rebecca highlighted several interesting features of these materials, particularly the unconventional tilt modes which are inaccessible in conventional inorganic counterparts. She showed through high-pressure single-crystal diffraction measurements how these unconventional tilts can be coupled to orbital ordering transitions, enabling

an unusual switching of the orbital ordering configuration upon the application of pressure. This was accompanied by detailed symmetry-mode analysis of the refined structures, which proved to be a recurring theme of interest throughout the entire meeting. Next, **Farheen Sayed** (Cambridge) presented a lecture on "Structural evolution of Mn-based cathodes under extreme conditions" in which she discussed her attempts to identify the interphase products which form between interfacial coatings and cathode materials in Li-ion batteries. Attaining this understanding is typically difficult as the electrochemical degradation products are usually buried deep within the interface. Farheen presented an alternative means to identify these products through the use of spark plasma sintering (SPS) to synthesise cathode materials of the form LiM_2O_4 (M = Mn, Ni) and search for the possible degradation products in this compositional space. Detailed characterisation efforts involving the use of X-ray diffraction, SEM/EDX, XAS, Raman spectroscopy and solid-state NMR allowed for several possible structural transformations from the spinel structure to be identified. These transformations can be considered in terms of transitions across the compositional phase diagram, thus providing vital information for the appropriate processing conditions for coating cathode materials. This work also nicely illustrated the benefits of complementary techniques to conventional crystallographic methods such as X-ray diffraction, so this work also tied nicely into the Complementary Techniques session held on Wednesday. **Eliza Dempsey** (Edinburgh) then presented on "Understanding the phase transitions and thermal expansion of niobium oxyfluoride through phonons and total scattering." The speaker discussed the role of lattice dynamics and local structure in negative thermal expansion behaviour in niobium oxyfluoride materials. This talk gave an excellent overview of several important topics in physical crystallography such as phonons and rigid-unit modes, and how these phenomena can be tuned in niobium oxyfluorides through modifying the fluorine content. Eliza presented compelling evidence to show that while the average crystallographic structure can be considered as cubic, local structural investigations revealed the additional presence of rhombohedral-like distortions due to a combination of the second-order Jahn-Teller effect from the Nb^{5+} cations and octahedral tilts of the NbO_4F_2 units. This represents powerful mechanistic insight into the mechanism of negative thermal expansion in these materials, informing future design strategies within this compositional space. Finally, the session closed with **Sam Thompson** (Durham) who spoke on "Pseudo-symmetry in the Cambridge Structural Database and its application to ferroelectric discovery." Sam's work concerns the use of an innovative symmetry-assisted search algorithm against structural entries in the Cambridge Structural Database as a means to identify new examples of molecular ferroelectrics. This approach revolves around the use of a modified version of the FINDSYM program to search for higher-symmetry versions of known polar materials, thus identifying promising target systems which may exhibit ferroelectric behaviour. Sam also described the use of a method to scrutinise the positive hits generated by his search algorithm based on the calculation of root-mean-squared deviations of the atomic positions, giving a useful structural metric to discriminate the list of candidates in terms of those most likely to display ferroelectricity.

Overall, this final session of the BCA Spring Meeting 2025 provided a fitting conclusion to an outstanding conference.

Nilanthy Balakrishnan (Keele), **Tony Bell** (Sheffield Hallam), **Karen Johnston** (Durham), **Evie Ladbrook** (Warwick), **Lauren McHugh** (Liverpool), **Lewis Owen** (Sheffield), **Struan Simpson** (Warwick) and **Jonathan Skelton** (Manchester).

*The first PCG Open Session: **Daniel Widdowson** (Liverpool), **Geeta Sharma** (Leeds), **Nilanthy Balakrishnan** (Keele, chair) and **Patrick Doheny** (Birmingham).*

*The PCG session on "Computational modelling in crystallography" with **Joseph Flitcroft** (Manchester), **Jonathan Skelton** (Manchester, chair), **George Darling** (Liverpool), **Lavanya Kumar** (Warsaw) and **Joseph Arnold** (Birmingham).*

*The joint PCG/ESCG session on "Complementary Techniques" with **Karen Johnston** (Durham, chair), **Dave Collins** (Leeds), **Pedro Nunes** (DLS), **Evie Ladbrook** (Warwick, chair) and **Timothy Easun** (Birmingham) and **Kieran Griffiths** (Lancaster).*

*The Rietveld refinement workshop: **Jeremy Cockcroft** (UCL), **Struan Simpson** (Warwick), **Anthony Bell** (Sheffield Hallam, chair) and **Alex Gibbs** (St Andrews).*

*The PCG "Phase Transitions" session: **Sam Thompson** (Durham), **Eliza Dempsey** (Edinburgh), **Struan Simpson** (Warwick, chair), **Rebecca Scatena** (DLS) and **Farheen Sayed** (Cambridge).*

*The second PCG Open Session: **Catriona Crawford** (Warwick), **Struan Simpson** (Warwick), **Rebecca Clulow** (Uppsala), **Lewis Owen** (Sheffield) and **Nilanthy Balakrishnan** (Keele).*

*The joint CCG/PCG session on "Coordination polymers and porous materials" with **Ian Williams** (Hong Kong UST), **Thomas Roseveare** (Sheffield), **Mihails Arhangelskis** (Warsaw), **Valentina Colombo** (Milan) and **Lauren McHugh** (Liverpool, chair).*

Biological Structures Group

This year the BSG Plenary lecture was given by **Elton Zeqiraj** (Leeds) whose title was "Unravelling the supramolecular organization of K63-linked ubiquitin chains by JAMM-domain DUBs." Elton was introduced to the audience by the session chair **Charlie Scarff** (Leeds). The speaker outlined the ubiquitin signalling system to attendees, covering ubiquitin ligases (E1, E2, E3) and the de-ubiquitinases, or DUB's for short. The DUB known as BRCC36 is a zinc-dependent metalloprotease which regulates DNA damage and repair, and inhibition of this DUB might prove to be an effective way of treating inflammation and cancer. BRISC (BRCC36 isopeptidase complex) and ARISC (Abraxas1-regulated isopeptidase complex) are key JAMM-domain DUBs involved in cell signalling. BRISC regulates type I interferon signalling by cleaving K63-linked ubiquitin from interferon receptors, while ARISC safeguards genome stability via the BRCA1-A complex. The speaker described a high-throughput screen for BRISC inhibitors in which the main hit of interest actually proved to be a contaminant from the synthesis. Elton described his group's detective work to identify not only an inhibitor, but the structure of that inhibitor when the contents did not match the label – a cautionary tale for all drug discoverers. Through cryo-electron microscopy and crystallography, Elton demonstrated the molecular glue mechanism to exclude ubiquitin through a dimer of the BRISC complex, as well as the linear and cyclic K63-linked structures for which DUBs show specificity. Cryo-EM studies established that this compound inhibits BRISC by inducing dimer formation (651 kDa rather than 329 kDa) rather than binding at the active site. The binding site for this compound has been corroborated by mutagenesis experiments and it has been shown to reduce interferon signalling in cell-based assays. The speaker went on to present a truly impressive set of cryo-EM structures of BRISC and ARISC bound to multiple K63-linked ubiquitin chains, some adopting circular rather than a linear conformations.

The first talk of the BSG "Open Session", which was chaired by **Natalie Tatum** (Newcastle), was a keynote lecture from **Ross Anderson** (Bristol) on protein design entitled "Totally wired: amping up the de novo design of bioenergetic protein components." Using heme-binding four-helical

bundles, Ross showed us how machine-learning methods of sequence optimisation (via MPNN) can deliver soluble, crystallisable, modular protein wires geared towards the development of photovoltaic systems. This was followed by two talks from submitted abstracts. From **Ryan Lithgo** (DLS) whose title was "Crystallographic fragment screen of enterovirus A71 2A protease identifies new opportunities for the development of broad-spectrum anti-enterovirals" we saw a streamlined pipeline of fragment-based drug discovery. From over 3000 fragment-bound structures, a nanomolar inhibitor of the protease has been developed. The ASAP Discovery platform is an open science initiative which publishes protocols and results in near-real time. Closing the session, **Edward Snell** (UB-Hauptman-Woodward Institute) gave a lecture entitled "Validating metal identities in 100 metalloprotein models with particle induced X-ray emission and X-ray fluorescence spectroscopy." Ed described his team's work on validating the identity of metals modelled in the PDB, of which only 14 % agree well with the diffraction data. The CCP4 program EDSTATS was particularly useful in assessing the mismatch between metal ion and density. Through X-ray fluorescence spectroscopy, it is possible to quickly and confidently identify the metal content of even old, dehydrated protein samples to give structural biologists more confidence prior to the crystallisation experiment. However Ed also noted that 48% of the time, the metal ion was replaced by crystallisation buffer component ions – something to watch out for and which an X-ray fluorescence scan at the beamline would catch. This prompted a discussion on how this could be automatically implemented after any data collection and flagged to the end-user.

The BSG networking session was chaired by **Briony Yorke** (Leeds) and took the form of a pub quiz, partially facilitated by Microsoft Copilot's idea of a crystallography quiz. It is fair to say that AI is not coming for the publican's jobs, or ours just yet. More successful in terms of head-scratching was the picture round – aerial shots of synchrotrons around the world! The scores between the three teams were close, and but for some more time on Google Earth could have been full houses!

The joint BSG/CCG session entitled "*In situ* crystallography" was chaired by **Phoebe Allan** (Birmingham) and began with a lecture by **Amy Thompson** (DLS) on the subject of "VMXi: a high-throughput, *in situ* crystallography beamline to harness the advantages of multi-crystal strategies." The speaker described how the VMXi beam line allows high-throughput data collection for both small molecule and macromolecular studies. However, *in situ* work at room temperature does not permit a full 360° rotation range of the sample and this demands high redundancy data collections, typically from 100 crystals. Whilst the merging statistics might not be competitive with conventional data collection strategies, cluster analysis of the resulting data using DIALS can give better results revealing new features in the electron density. The ChiMP software (crystal hits in my plates) allows data from up to 100 microcrystals to be collected per drop. Amy then described some of the nuances of cluster analysis which led them to use the OPTICS (ordering points to identify the clustering structure) algorithm. Amy also mentioned the VMXm beamline at DLS which allows small molecule work to be undertaken using cryo-EM grids *in vacuo* and can yield data to 0.85 Å resolution. The speaker concluded by mentioning the considerable time saving aspect of *in situ* data collection since it obviates the need for crystal mounting. The next lecture was given by **Manuel Fernandes** (Johannesburg) who spoke on "Crystallographic Insights into Solid-State Diels–Alder Reactions." The speaker described the principles of the Diels-Alder reaction in which a diene reacts with an electrophilic 'dienophile.' For this reaction to occur in the crystal, both groups must be in sufficiently close contact with one another (the Schmidt criterion). The speaker described studies of the reaction between bis(N-cyclobutylimino)-1,4- dithiin and the dienophile 9-bromoanthracene which occurs in co-crystals of these compounds. Coating the crystals in epoxy glue allowed structures to be solved for intermediates and products of this reaction. A similar analysis using 9-vinylanthracene was reported. The next lecture was given by **Ross Angel** (Padova) and was entitled "Crystal Palace: new program for parametric crystal structure analysis." The speaker described how the Crystal Palace software is designed to enable comparison of multiple small molecule structures such as those obtained as a function of time or pressure, by concatenating the respective cif files and analysing equivalent atoms. The speaker mentioned that one of the problems is that estimated standard uncertainties can only be obtained from the full refinement matrix but this information is not stored in the cif file by convention. Ross then spoke on how Crystal Palace overcomes this problem by calculating the symmetry-induced covariance for all of the estimated standard uncertainties. Last but by no means least, the concluding lecture in this session was given by **Alexandra Longcake** (Newcastle) and was entitled "Development of a high throughput *in situ* X-ray diffraction workflow in-house using the Rigaku XtalCheck system." The speaker described the use of encapsulated nanodroplet crystallisation (EnaCt) which is a plate-based approach for organic and inorganic molecules in which crystal screening is undertaken using oils to control the evaporation of solvent. Typically 10 mg of compound allows 300 conditions to be screened. In collaboration with SWISSCI a new 96 well solvent- and X-ray-friendly glass plate has been developed which is only 100 µm thick allowing *in situ* crystal screening. Preventing the fragile plate from breaking while the plastic sheet is peeled off it involved imaginative development of plastic bracing and requires the application of a vacuum to the other side of the glass. The speaker described a number of case studies which have relied on this system for polymorph screening which is now offered as part of the UK National Crystallography Service (NCS).

This was followed by a session dedicated to early career prize lectures and exhibitor talks which was chaired by **Alex Gibbs** (St Andrews). The first presentation was by **Simon Tanley** (Calibre Scientific) who described the RAMP lipid screen for identifying specific lipids which stabilise membrane proteins and facilitate their crystallisation. The speaker covered nano-DSF (differential scanning fluorimetry) and nanodisc reconstitution as well as checking the stability of the lipids over time, and mentioned that Calibre Scientific are developing an oil kit. The next presentation was by **Nick Simmons** (Oxford Cryosystems) who described how the company had been in business for 40 years with 3000 systems having been delivered to customers around the world. The speaker outlined the range of open and closed cryosystems that they manufacture and described the recent release of a wide-nozzle cryostream (9 mm versus 7 mm) which increases the volume of gas cooled to the set temperature by 2.5 fold and allows for working with larger samples e.g. in neutron experiments. The next presentation

was by **Gustavo Santiso-Quinones** (ELDICO Scientific AG) who described their commercial ED-1 electron diffraction system system which includes an LaB6 source operating at 160 kV, a Dectris Quadpro detector and a sample transfer compartment which allows for cryo-cooling. A large phi rotation is possible during data collection with conventional samples (-100° to +100°) and a range of -40° to +40° with chip-mounted specimens. **Michael Broom** (Malvern Panalytical) then outlined some of their recent acquisitions in the material science field including the metrology company Freiberg Instruments along with SciAps and Micromeritics, before outlining some of their X-ray fluorescence systems. The final exhibitor presentation was given by **John Kollath** (STOE) who began with the company's emphasis on quality control and their provision of a 10 year product guarantee. John described the STADIVARI X-ray diffraction system for single crystals and powders which allows both cryo- and high pressure work. Improved data processing is provided by the INTEGRATE3D package. Instrumentation for powder work can incorporate a furnace for high temperature studies, an *in situ* reaction chamber and a recently developed coin cell battery holder for full charge-discharge studies of electrode materials.

Daren Fearon (DLS) then gave the BSG early career prize lecture entitled "High throughput fragment screening and structural enablement" following an eloquent introduction from the session chair, **Katherine Brown** (Cambridge), who summarised Daren's career starting from undergraduate studies in Glasgow and a PhD at ICR followed by post-doctoral work in Southampton and at Evotec, prior to moving to the XChem facility at DLS. The speaker explained how fragment-based drug discovery works best with compounds of molecular weight lower than about 300 Daltons with mM to µM affinity for the target. The high sensitivity of the method drives hit-to-lead progression and lead optimisation. The speaker summarised the steps involved from automated crystal ranking and fragment dispensing through to the crystal shifter which aids the manual freezing step and finally the fully automatic data collection and processing. In some cases the method relies on crystal seeding and other techniques for finding the right crystal form, the SARS-CoV-2 Nsp3 macrodomain being an example of this. The XChem facility has allowed the collection of no less than a quarter of a million datasets for some 300 academic groups, allowing 30-50 thousand ligand structures to be determined and has facilitated over 150 industrial projects. The speaker described how the recent pandemic led to the Covid Moonshot project with numerous potential drug targets being screened and to further NIH funding (AVIDD) being awarded for screening other viruses such as Dengue and Zika in the event of future pandemics. Typically progression of fragment hits involves synthetically merging and mixing them followed by further screening of the products. A routine XChem screen would involve 500 – 1000 fragments but the team is actively developing ways to make these screens bigger and faster, in addition to applying machine learning to fragment progression.

The next BSG session was actually more of a workshop entitled "Determining a protein crystal structure in 2025" and was both chaired and presented by **Adam Crawshaw** (DLS) whose keynote lecture was entitled "Where is protein crystallography going in 2025?" Macromolecular crystallography is a tool within a wide set of structural biology techniques that allow biologists to answer complex biological questions. On the basis that crystals can be generated of a protein of interest, determining the molecular structure using MX is now usually a very straightforward process. This has been enabled by the incredible technological developments at synchrotrons from hardware through to software, including data processing, model building and model validation. Beamlines can collect high quality diffraction data without an operator, let alone an experienced 'crystallographer' and models can be built automatically from the data within a matter of minutes of the diffraction being measured. This leads to the question of what does solving a structure look like today? What expertise is now required by the biologist? Where will future methods developers come from?

The session chair took a look at what it actually means to be a structural biologist and what this means for the future of crystallography. Adam also raised the question of how 'techniques scientists' can best help the 'question scientists' before opening the session to comments from the audience of around 20 or so attendees via an interactive questionnaire or Mentimeter (https://www.menti.com/) which allows speakers to survey audience interests and interpretations. This led to a lively discussion with the BSG attendees using the interactive presentation that allowed them to submit their answers to questions such as 'I identify as a _____' or 'the term structural biologist means to me.' The answers to these questions were surprisingly varied, even in a small group. It was very clear from the discussion that MX is now just a tool within a greater integrative structural biology approach and that central facilities such as Diamond need to better reflect this through their access routes, training and engagement. This also reflects how the BCA-BSG must engage with the wider community in the future. While a philosophical session, these discussions are important for the 'technique scientists' such as beamline scientists to gauge how they can improve access to the tools that they maintain and develop and further the ability of important questions to be answered by question-driven scientists.

With the majority of users working remotely and taking advantage of automated pipelines, the amount of face-to-face contact with the user community has shrunk considerably, which arguably will create challenges in training the next generation and thus future research into methods development. Subjects discussed included what matters most in a project, be it the science question, the methods used or the accessibility of the method. Wide-ranging issues such as the future of crystallography along with more technically oriented questions such as the importance of active monitoring of data quality were discussed. Overall this was a very interesting session that provided a very nice lead-up to the Dorothy Hodgkin lecture which, this year, had a strong biological emphasis.

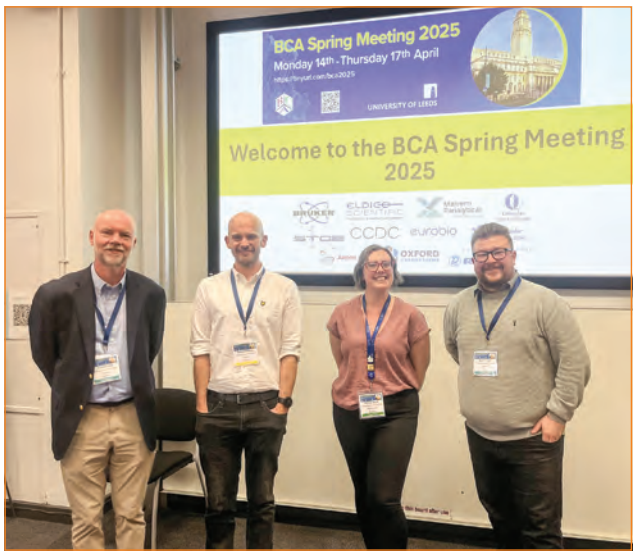
The Dorothy Hodgkin Prize lecture was chaired by **Alex Gibbs** (St Andrews) and was given by **Martin Noble** (Newcastle) whose presentation was entitled "Advancing therapeutic discovery using MX." Alex presented a mini-biography of Martin who then began his lecture by emphasising how the influence of the Nobel laureate Dorothy Hodgkin, after whom this annual lecture is named, extended well beyond the field of crystallography. The speaker described work on the new anticancer drugs rubraca and erdafitinib in collaboration with Astex before moving on to describe some novel concepts in fragment-based

drug discovery which led to development of the FragLites library. These are hydrogen-bond donor compounds which contain heavy atoms to aid determining the orientation of planar groups in the resulting electron density and are now included in the XChem screen at DLS. Martin mentioned how a FragLites screen against a cyclin-dependent kinase (CDK) revealed multiple active site hits as well as others in allosteric sites. Martin then described studies of the bromodomain proteins BRD4 and ATAD, both of which were tested for druggability with the FragLites library. Since BRD4 yielded considerably more hits, it was chosen for further work, including studies involving DNA-encoded libraries (DELS) in which the separate components of a combined chemical entity are identified by molecular barcodes in a covalently attached DNA sequence. When fragment mixtures are used in screening, DNA amplification can be used to identify the fragment which binds to the protein. The speaker emphasised how CDK's consist of a catalytic subunit associated with a cyclin subunit and how one needs to achieve specificity in targetting these enzymes which are all very similar, especially in the active site. The aim of his work is therefore to target sites which only occur in specific CDKs. The FragLites library has proved to be invaluable in identifying sites which partner proteins of the CDK cyclin interactome bind to, suggesting that these sites may be suitable to achieve the required specificity. Mutations of amino acids in one such site confirmed that it was a good candidate for further structure-based drug discovery work.

The final BSG session on "Integrative Structural Biology" was chaired by **Martina Foglizzo** (Leeds) who introduced the first keynote speaker **Jamie Blaza** (York) whose title was "Using cryo-EM and symmetry expansion to understand how Rubisco is bound together to accelerate carbon fixation." The speaker began by introducing the rubisco enzyme to the audience, emphasising that it is relatively slow at catalysing carbon fixation and suffers from a side reaction known as photorespiration. The speaker mentioned how plants have various evolved various micro-compartments and adaptations to allow them to concentrate CO_2 to boost carbon fixation e.g. the pyrenoids found in algal chloroplasts which are 200 nm phase-separated organelles that lack a surrounding membrane. Phase-separation of rubisco in the pyrenoid requires various linker proteins which are poorly conserved. The speaker reported an impressive cryo-EM structure analysis of *Chlorella sorokiniana* rubisco with the linker protein bound to it. Jamie also described how the linker can phase-separate rubisco from higher plants suggesting that engineering pyrenoids in agricultural plants may be a viable route for improving yields. Next up, **Rupesh Chikhale** (CCDC) spoke on "Generative AI and classical modelling methods for the discovery of novel anti-TB molecules." Rupesh began by introducing the tuberculosis field and the well-known problem of drug resistance with this pathogen. The speaker mentioned how only 5 new drugs against TB have been approved since 2000 and some of these are re-purposed drugs. The flavoenzyme DprE1 plays an essential role in cell wall biosynthesis in *M. tuberculosis*, is a promising drug target and a number of crystal structures of it are available in the PDB. The speaker described how, in collaboration with Biovia, a cloud-based molecular modelling platform and docking with GOLD from the CCDC were being used for generative design of new compounds. Progressing from fragments to drug-like molecules is achieved in around 25 iterations and potential compounds are assessed by a desirability score. The next lecture was by **Zihao Wang** (Leeds) who spoke on "Stoichiometry and functional study of human cardiac small heat-shock proteins." The small human cardiac heat-shock proteins (sHSP's) HSPB7 and HSPB8 were investigated and surprisingly were found to be monomeric. The structure of the complex HPB7 forms with heart filamin C was determined revealing how it helps to prevent filamin C from cross-linking the actin cytoskeleton. The latter is known to occur in developmental diseases of the heart arising from the absence of HSPB7 and mutations of HSPB8 are associated with motor neurone disease. Phosphorylation of HSPB7 regulates its association with filamin C. Last but not least, the final speaker in this session was **Wyatt Yue** (Newcastle) who spoke on the subject of "Structural biology at the crossroad of metabolic enzyme disorders and drug discovery." The speaker began by introducing the biochemistry of the universal methyl group donor S-adenosyl methionine (SAM) as the second most commonly used cofactor after ATP. SAM homeostasis is tightly controlled, no doubt due to its multiple roles as a cofactor, as well as being an activator and inhibitor of various reactions. For example the PLP-dependent human enzyme cystathione-β-synthase is activated by SAM and possesses a regulatory Bateman domain, a functional unit which is associated with adenosine binding, in this case SAM. Mutations in the enzyme are known to cause the hereditary disease homocystinuria which is associated with aggregation and misfolding of the enzyme. The speaker showed some impressive cryo-EM reconstructions demonstrating how the enzyme adopts a filamentous zigzag shape which is modulated by the binding of the activator, SAM, thereby exposing the catalytic domains to the substrate. Fluorescence microscopy suggests that similar filaments exist *in vivo*.

Jon Cooper (UCL), **Adam Crawshaw** (DLS), **Mark Montgomery** (Syngenta) and **Natalie Tatum** (Newcastle)

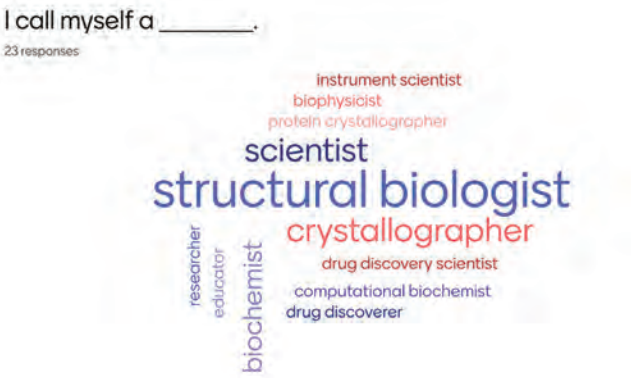
***Daren Fearon** (DLS) receiving the BSG Early Career Prize from **Katherine Brown** (Cambridge).*

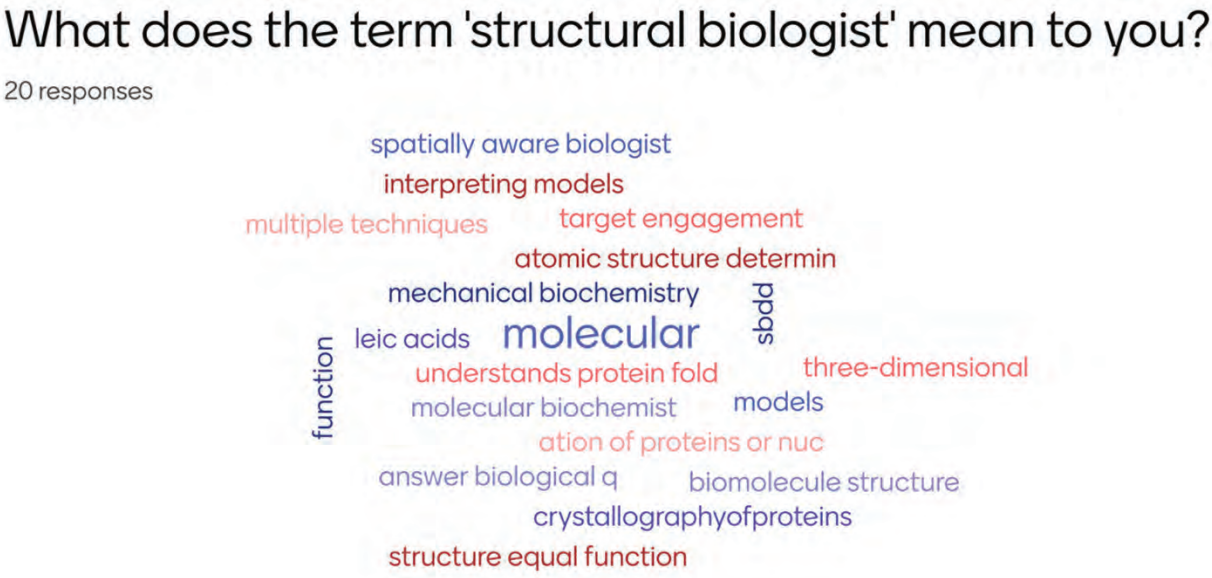


Presenters of the BSG "Open Session" ***Edward Snell*** *(UB-Hauptman-Woodward Institute) and* ***Ross Anderson*** *(Bristol) with session chair* ***Natalie Tatum*** *(Newcastle) and* ***Ryan Lithgo*** *(DLS).*

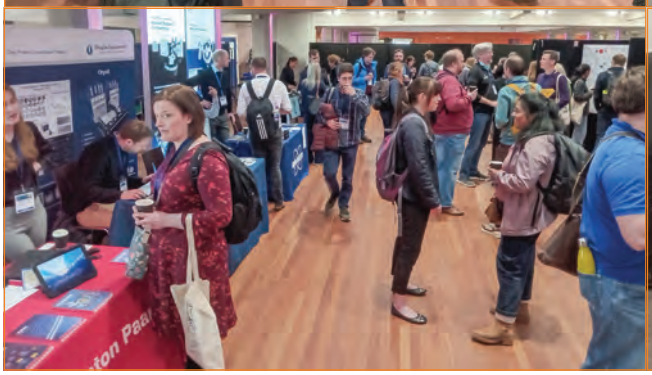
Chair and keynote lecturer in the BSG session on "Determining a protein crystal structure in 2025" ***Adam Crawshaw*** *(DLS). Attendees were spurred on to consider "Where is protein crystallography going in 2025?" amongst many other things, and answers keyed into phones were displayed interactively via a Mentimeter, shown below.*

Speakers in the "Integrative Structural Biology" session: ***Wyatt Yue*** *(Newcastle),* ***Jamie Blaza*** *(York) and* ***Rupesh Chikhale*** *(CCDC) with session chair* ***Martina Foglizzo*** *(Leeds).*





Other Spring Meeting Photos



20th BCA/CCG Intensive Teaching School in X-ray Structure Analysis

THE 20th BCA/CCG Intensive Teaching School in X-ray Structure Analysis was held at the Mount Oswald Hub, Durham from the 29th March – 6th April 2025. The school was once again heavily oversubscribed, due to the school's national and international reputation for providing a good basis in crystallography. This year we welcomed almost 80 students from universities in the UK, Finland, Ireland, Italy, Japan, Poland, Singapore, Slovenia, Sweden, UAE and USA. The variety of nationalities, academic backgrounds and crystallographic experience created a fantastic environment for both learning and meeting new people, with many students and staff commenting on the positive and friendly atmosphere.

As a result of feedback from students and staff over the years the format of the biennial course has evolved. It currently consists of a mixture of lectures and tutorials designed to help students improve their understanding of the lecture material. As the name suggests, the course is intensive with a full timetable across the 7 days providing the students with the opportunity to gain a good theoretical understanding of various aspects of crystallography from a single crystal perspective. Beginning with an introductory lecture shortly after arrival on Saturday evening, the lectures given by Professor Richard Cooper; Dr Andrew Bond; Dr Lukas Palatinus; Dr Mark Senn and Dr Helena Shepherd covered maths; symmetry; International Tables; data collection; Fourier synthesis; Patterson methods; direct methods; charge flipping; superspace; parametrisation; least squares; refinement; twinning and derivation of results. An introduction to databases was also given by Dr Natalie Johnson and the use of synchrotron, neutron and 3D ED facilities were highlighted by Dr Ben Coulson, Dr Amber Thompson and Dr Jeremiah Tidey, respectively.

Attendees were assigned to a tutor group, consisting of one tutor and up to eight students, and worked together throughout the week to tackle a series of problems related to the lecture material. This year we welcomed new tutors, Dr Ben Coulson, Dr Tom Fellows and Dr Georgia Orton and welcomed back Dr Andrew Cairns, Dr Samantha Chong, Dr Natalie Johnson, Dr Carsten Lenczyk, Dr Matic Lozinsek, Dr Natalie Pridmore (as a floating tutor), Dr Amber Thompson and Dr Jeremiah Tidey. This year, the lectures and tutorials were held in the Mount Oswald Hub which enabled easy switching between formal lectures and tutorial work, with minimal disruption. The accommodation and evening meals were provided in Collingwood College, which is around a 10-minute walk away, and lunch was in Van Mildert College, which is halfway between the two. This provided a chance for some fresh air and brief exercise during the day and fortunately, the weather was pleasant all week.

As is traditional at the school, apart from the maths lecture on the first day, the evening activities are designed to be more relaxed and provide an opportunity for the students to mix with each other through a combination of educational and fun activities. On the Sunday evening, Richard Cooper ran a successful bar quiz, while Tuesday evening's panel question session was a chance for the students to learn more about the lecturers and also ask more general crystallography questions, which included a discussion of if/how AI could be beneficial to the field.

This year's student presentations, on the Friday evening, were organised by Dr Jeremiah Tidey and Dr Samantha Chong. Each of the tutor groups put together a five-minute presentation on a crystallographic topic, drawn from a hat earlier in the week, and performed it in a style that was also chosen at random. This year, this included crystal growth as a sports commentary, space groups described in TV adverts and structure solution explained in the style of a children's TV show. As with previous years, the scientific quality, thematic accuracy and entertainment value of each presentation was assessed by our elite panel of judges, the lecturers, who were extremely impressed by all the entries.

The conference dinner, held in Collingwood College, on the Saturday evening provided the chance to thank everyone who had contributed to the success of this year's school including the local staff, organisers, lecturers, tutors and students. The positive attitude and hard work of the staff and students alike helped to create a very friendly school. After this year's school, Professor Judith Howard is stepping down from her role as a local organiser, which she has been doing since the first school 38 years ago. We would like to thank her for her role in starting the school and keeping it going all these years. Her drive, enthusiasm and encouragement have enabled the course to run and helped maintain its high standards.

Following on from the school an optional hands-on Olex2 workshop was held on the Sunday, run by Dr Horst Puschmann and Dr Oleg Dolomanov. This was well received by the over 50 registered participants, with a range of experience with the software, who had the opportunity to use Olex2 to apply concepts that they had learnt on the course to both test structures and their own data.

Finally, I would like to say thank you to all the sponsors of this year's school: IUCr, ECA, CCG, BCA-IG, Bruker, Rigaku, CCDC, NCS, CrystEngComm, Journal of Materials Chemistry C and RSC Advances. Without the financial support from these organisations, we would not have been able to help as many students attend the school, or run it so successfully, and we are extremely grateful for their continued support.

Natalie Pridmore, Bristol, local organiser

Attendees of the 20th BCA/CCG Intensive Teaching School in X-ray Structure Analysis held in Durham.

Bruker AXS Symposium on Diffraction Methods in Drug Discovery and Development

4th March 2025, Francis Crick Research Institute, London

THE meeting began with an introduction by Vernon Smith (Bruker) who reminded attendees of the recent sad passing of Prof George Sheldrick (Gottingen) who had a pivotal influence on the field and collaborated extensively with Bruker on software development for something like 40 years. Vernon then described some of the processes in which X-ray crystallography plays a major role in the flow diagram of drug discovery, such as target validation and lead discovery. One emphasis of the meeting was the role which in-house equipment can play in these processes. Indeed, attendees who arrived early were treated to an excellent tour of the X-ray laboratory where Andrew Purkiss (Crick) demonstrated the in-house Bruker D8 VENTURE METALJET system. This has a liquid anode made from a gallium-rich alloy, the melting temperature of which is around 30 degrees. Its emission wavelength of 1.34 Å is conveniently between the copper and molybdenum Kα lines of traditional X-ray sources. Similar systems have been installed in laboratories globally for single crystal applications and it was demonstrated how small crystals routinely synthesised as part of the synthetic process at Pharmaron could be directly used to quickly determine crystal structures on a D8 VENTURE system equipped with a microfocus air-cooled X-ray source. Vernon described several recent acquisitions by Bruker including the Swiss company ChemSpeed which focusses on lab automation and Nion who develop state-of-the-art electron microscopy systems with a range of new features allowing, for example, single molecule spectroscopy to be undertaken.

The first lecture was given by **Chun-wa Chung** (GSK) and was entitled "Synergising protein and small molecule diffraction sciences in drug discovery." The speaker began by outlining the steps of drug discovery from target identification and validation, through to screening and the discovery of hits. The hit-to-lead process and the optimisation of lead compounds was covered next as was the preclinical and clinical work followed by essential review processes. Biological crystallography can play a key role in this process as can chemical crystallography in terms of solid form screening, analysis of polymorphs, solvates, salts and counterions in pharmaceutical preparations. Chun-wa then described the very interesting development of the novel fluoroquinolone antibiotic gepotidacin which targets DNA topoisomerase, a DNA unwinding enzyme. Topoisomerase catalyses three processes namely cleavage of double-stranded DNA, swapping over of the strands and then repair of the covalent phosphodiester backbone. The speaker emphasised that each of these processes can be targetted by inhibitors, e.g. moxifloxacin blocks re-ligation and prefers double strand cleaved DNA whereas gepotidacin binds singly cleaved DNA complexes, acting on both topoisomerase and DNA gyrase. Another gyrase inhibitor based on thiophene has no preference for double or single strand cleavages. These compounds represent the first new class of orally-active antibiotic in over 20 years. The speaker then outlined the many important developments in diffraction methods over the last 20 years and mentioned the current popularity of Diamond Light Source (DLS) for biological crystallography in contrast to small molecule work where in-house data collection still plays a major role. Macromolecular crystallography at GSK benefits from shared access to in-house chemical crystallography equipment. The speaker mentioned how her group collaborates extensively with Newcastle for crystallisation studies and with the GSK Stevenage team for access to a Glacios 200 keV electron microscope. The speaker also mentioned current developments in electron diffraction, although this technique has some catching-up to do in terms of cost-effectiveness. Her group has an *in situ* system for in-plate screening and polymorph analysis and the speaker emphasised the importance of automated and unattended data collection, particularly at synchrotron sources.

The next speaker was **Neil Rzechorzek** (Crick) who gave a lecture entitled "DNPH1: the catalytic mechanism of a human nucleotide pool sanitiser." Neil gave the audience an introduction to DNA damage with a focus on strand breaks, explaining how single-strand breaks are mainly dealt with by the poly [ADP-ribose] polymerase (PARP) repair pathway and double-stranded breaks by homologous recombination, such as via the BRCA pathway, or non-homologous repair. Once the PARP enzyme detects a single strand break, it begins the synthesis of a poly ADP-ribose chain which acts as a signal for the other DNA-repairing enzymes. The speaker mentioned that if one inhibits the single-strand break repair pathway then cells die due to overload of the BRCA pathway, although with time the cells develop resistance to PARP inhibitors. The speaker described a programme of knockout studies undertaken to identify mutants with increased sensitivity or resistance to PARP inhibitors. Knockouts of the DNPH1 gene which encodes a 2'-deoxynucleoside 5'-phosphate N-hydrolase were found to be very sensitive, suggesting that DNPH1 inhibitors may enhance and prolong the effects of PARP inhibitors. The enzyme targets hydroxymethyl-dUMP (hmdUMP) as a substrate, removing the hydroxymethyl-U base by the action of a catalytic triad involving Tyr 24, Asp 80 and Glu 104. This results in the formation of a glycosyl enzyme intermediate bound to Glu 104. The normal role of the enzyme is in degrading hmdUMP, thus preventing its aberrant incorporation into genomic DNA. Crystallisation of an inactive E104Q mutant with substrate bound allowed structure determination at high resolution revealing a dimeric

Rossmann fold protein with its active sites at the dimer interface [1]. The side chain of His 56 was observed to hydrogen-bond the base and, intriguingly, mutation of the neighbouring amino acid (Glu 55) was found to be sufficiently harmful to activity to allow co-crystallisation of the E55Q mutant with the substrate trapped as a glycosyl enzyme intermediate bound covalently to Glu 104. Numerous mutants were engineered and studied by enzyme kinetics suggesting that Glu 55 functions by activating a water molecule to hydrolyse the covalent intermediate. The aim of the project is to discover new DNPH1 inhibitors with success in this area being reported already by another group who have developed transition state analogues. In-house fragment screening studies by the Crick team are in progress.

Next up was **Jennifer Miles** (Leeds) whose lecture was entitled "Design and characterisation of de novo binders." Jennifer described the normally tightly regulated mitotic kinase: aurora-A which is over-expressed in cancers. Inhibiting members of the kinome specifically presents certain problems, not least due to the sheer number of kinases (>500) encoded by the human genome. Since Aurora-A prevents the proto-oncogene protein N-myc from being degraded there is interest in developing inhibitors that would prevent N-myc from binding. Structurally, Aurora-A has two lobes, N- and C- terminal, the latter having a specific loop region which is known to bind activator proteins. In silico screening using the AI-based RFdiffusion algorithm [2] with the X-ray structure of the Aurora-A-N-myc complex was used to discover novel polypeptides capable of preventing N-myc from binding. Some 2000 designs were generated and were analysed for sequence conservation. Several of these were chosen for co-expression with Aurora-A and it was fascinating to hear that co-crystals were obtained, one of which (DBL5) diffracted to 1.8 Å resolution while another, DBS2 diffracted to 2.5 Å. Ultimately structures were obtained for 9 of these AI-designed mini-proteins and the best was found to have a high binding affinity for Aurora-A with a K_d of less than 1 nM. Further design work based on these findings is in progress with the aim of targetting different Aurora proteins and assessing the efficacy of these mini-binder proteins in cells.

The concluding speaker of the first session was **Arnaud Baslé** (Newcastle) whose lecture was entitled "Accelerating drug discovery with a Bruker D8 VENTURE METALJET." Given the large amount of structural biology ongoing in Newcastle, the speaker emphasised the importance of an in-house source for providing fast feedback to chemists and for training purposes. The speaker explained how the Newcastle Research Investment Fund supported the purchase of a gallium METALJET source with a PHOTON III charge-integrating pixel array detector (20 x 14 cm). The generator and optics provide a flux at the sample within a couple of orders of magnitude of that available at Diamond, allowing 1.6 Å data to be collected within about 6 minutes and exposure times of 1 sec / 0.5° crystal rotation to be used. The system is ideal for fragment screening studies – a typical run of 113 samples generated 40 ligand structures with resolutions varying from 2.2 to 1.7 Å resolution. The speaker recommended use of the FragLites library [3] which contains halogenated aromatic compounds, allowing anomalous scattering to be used to resolve their bound orientations unambiguously. Arnaud described the screening facility in Newcastle which is similar to the XChem laboratory at DLS with robots, imagers, acoustic fragment dispensing and a crystal shifter for cryo-mounting the samples. In another impressive study, a total of 1256 crystals were soaked and 102 hits were generated, thus demonstrating, at least to this very impressed attendee, the efficiency of the Newcastle setup! The speaker also mentioned how BBSRC funding had recently been secured for cryo-EM in a partnership of northern universities.

After the tea and coffee break, during which the posters were perused by attendees, the second session was chaired by **Anastasya Shilova** (Bruker) and began with an excellent lecture by **Marianne Schimpl** (AstraZeneca) entitled "The discovery of AZD5305: A PARP1-DNA trapper selective for PARP1 over PARP2 and other PARPs." The speaker began by introducing the PARP family and phylogeny as well as the process of poly ADP-ribosylation which members of this polymerase family catalyse in response to DNA damage. Interestingly, the enzyme poly ADP-ribosylates itself in a process referred to as autoparylation. PARP inhibitors are known to trap PARP on single-strand breaks in DNA and selectively kill cancer cells. Whilst a number of PARP inhibitors are in therapeutic use, such as olaparib, talazoparib, niraparib and rucaparib which have been approved for the treatment of certain ovarian, breast, prostate and pancreatic cancers, they target both PARP1 and PARP2. The speaker explained that since one only needs to inhibit PARP1, there is interest in developing inhibitors with greater selectivity for PARP1 and thus fewer side effects and lower overall toxicity. Screening and other studies led them to focus on tricyclic compounds and further work gave the candidate drug AZD5305 or saruparib which is currently in clinical trials and has demonstrated promising action on brain tumours.

The penultimate lecture of the meeting was given by **Jim Spencer** (Bristol) and was entitled "Harnessing X-ray crystallography to elucidate mechanisms of β-lactamase inhibition." The speaker explained how these enzymes which break down β-lactam antibiotics are the main cause of antimicrobial resistance (AMR). Jim mentioned how a recent study reported that 1.3 million deaths worldwide are due directly to AMR and 5 million partially attributable to AMR [4], with Gram negative bacteria being the main threats. The β-lactamase enzymes fall into two classes namely the serine and metallo-β-lactamases (MBLs), the latter having two zinc ions which activate a water molecule to nucleophilically attack the substrate in the same manner as the active site serine of the other class. The speaker explained how structural studies allow the stereochemical configuration of the reaction intermediates and stable endpoints to be determined, possibly allowing β-lactamase inhibitors that form long-lasting complexes with MBLs to be developed [5]. QM/MM simulation studies are being used to determine the activation barriers for the different tautomers of these intermediates. Compounds studied include clavulanic acid and penam sulphones, the latter class being known to experience a mass loss upon binding which was observed by mass-spectrometry but could only be explained by X-ray crystallography which revealed an extra covalent bond being formed. The speaker moved on to bicyclic boronates which should be very good mimics of the transition state. Tricyclic inhibitors in this family were found to have even greater potency and structural studies allowed the stereochemistry of the complexes they form to be resolved. The speaker described time-resolved studies at DLS using chip-mounted crystals from which data are collected by the beam rastering

over the wells. One problem to be overcome with these studies is that of achieving sufficiently fast mixing of the substrate with the mother liquor, although the current setup allows mixing on the 0.1 second timescale. Jim ended by presenting a 'movie' of the reaction mechanism spanning the 0.7 sec to 24 hour timescale and outlined how software developments in serial data processing are likely to yield even greater insights into such processes.

Last but not least, the final lecture of the meeting was presented by **Mladen Vinković** (Astex) and was entitled "Engineering eIF4E to make it suitable for fragment screening." Mladen explained how this eukaryotic translation initiation factor (eIF) is involved in directing the ribosome to the 5' cap of mRNA molecules. It is also involved in mRNA transport from the nucleus prior to translation and is over-expressed in many tumours. Mladen explained the need to engineer the protein to make it suitable for high resolution crystallographic studies and fragment screening by soaking. Mladen described this as making the protein 'pyramid friendly' referring to Astex's proprietary Pyramid Discovery Platform. The starting point for this work was the X-ray structure of the complex that eIF4E forms with an inhibitory binding protein, BP1. Phosphorylation of BP1 *in vivo* is thought to trigger its dissociation from eIF4E, thus activating translation. The Astex team engineered an interesting fusion protein with BP1 joined to eIF4E at the N-terminal end and this expressed very well. Pyramid fragment screening generated hits in the 5'-cap binding site and an adjacent cooperative site which appears to be more druggable than the cap site itself. Accordingly compounds with *in vivo* activity have been developed from these hits [6].

The meeting was wrapped-up by **Vernon Smith** (Bruker) who thanked all of the speakers for giving such excellent presentations, before inviting attendees to the closing wine reception. Other members of the Bruker team in attendance, namely **Anastasya Shilova, Cheryl Haidon** and **Michael Carr** must also be thanked for their considerable efforts in organising such an interesting meeting, not forgetting the Crick team, particularly **Andrew Purkiss** who very kindly demonstrated the METALJET system to visitors.

Jon Cooper, UCL

References

[1] Rzechorzek, N. J., Kunzelmann, S., Purkiss, A. G., Silva Dos Santos, M., MacRae, J. I., Taylor, I. A., Fugger, K. and West, S. C. (2023). Mechanism of substrate hydrolysis by the human nucleotide pool sanitiser DNPH1. *Nature Comm.* **14,** 6809. https://doi.org/10.1038/s41467-023-42544-4

[2] Watson, J. L., Juergens, D., Bennett, N. R., Trippe, B. L., Yim, J., Eisenach, H. E., Ahern, W., Borst, A. J., Ragotte, R. J., Milles, L. F., Wicky, B. I. M., Hanikel, N., Pellock, S. J., Courbet, A., Sheffler, W., Wang, J., Venkatesh, P., Sappington, I., Torres, S. V., Lauko, A., De Bortoli, V., Mathieu, E., Ovchinnikov, S., Barzilay, R., Jaakkola, T. S., DiMaio, F., Baek, M. and Baker, D. (2023). De novo design of protein structure and function with RFdiffusion. *Nature* **620,** 1089–1100. https://doi.org/10.1038/s41586-023-06415-8

[3] Wood, D. J., Lopez-Fernandez, J. D., Knight, L. E., Al-Khawaldeh, I., Gai, C., Lin, S., Martin, M. P., Miller, D. C., Cano, C., Endicott, J. A., Hardcastle, I. R., Noble, M. E. M. and Waring, M. J. (2019). FragLites-minimal, halogenated fragments displaying pharmacophore doublets. An efficient approach to druggability assessment and hit generation. *J. Med. Chem.* **62,** 3741–3752. https://doi.org/10.1021/acs.jmedchem.9b00304

[4] Antimicrobial Resistance Collaborators (2022). Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet* **399,** 629–655. https://doi.org/10.1016/S0140-6736(21)02724-0

[5] Hinchliffe, P., Calvopiña, K., Rabe, P., Mojica, M. F., Schofield, C. J., Dmitrienko, G. I., Bonomo, R. A., Vila, A. J. and Spencer, J. (2023). Interactions of hydrolyzed β-lactams with the L1 metallo-β-lactamase: Crystallography supports stereoselective binding of cephem/carbapenem products. *J. Biol. Chem.* **299,** 104606. https://doi.org/10.1016/j.jbc.2023.104606

[6] Sharp, S. Y., Martella, M., D'Agostino, S., Milton, C. I., Ward, G., Woodhead, A. J., Richardson, C. J., Carr, M. G., Chiarparin, E., Cons, B. D., Coyle, J., East, C. E., Hiscock, S. D., Martinez-Fleites, C., Mortenson, P. N., Palmer, N., Pathuri, P., Powers, M. V., Saalau, S. M., St Denis, J. D., Swabey, K., Vinković, M., Walton, H., Williams, G. and Clarke, P. A. (2024). Integrating fragment-based screening with targeted protein degradation and genetic rescue to explore eIF4E function. *Nature Comm.* **15,** 10037. https://doi.org/10.1038/s41467-024-54356-1

***Chun-wa Chung** (GSK) presenting in the first session of the Bruker AXS Symposium at the Crick Institute (photos: **Cheryl Haidon,** Bruker).*

***Neil Rzechorzek** (Crick) speaking on the discovery of new DNPH1 inhibitors (photo: **Cheryl Haidon,** Bruker).*

***Marianne Schimpl** (AstraZeneca) speaking on an enzyme target for anti-cancer drug discovery (photo: **Cheryl Haidon,** Bruker).*

Other photos

Photos: ***Cheryl Haidon****, Bruker.*

Scenes from the lunch and posters at the Bruker AXS symposium at the Crick.

The Bruker D8 VENTURE METALJET in the X-ray laboratory at the Francis Crick Institute.

News from the CCDC

A huge thank you to all the BCA members who stopped by our stand at the Spring BCA meeting! We appreciated your feedback, questions and engagement – especially in our fun #CSDLeaderboard competition.

Congratulations to Dave Allen for claiming the top spot on the leaderboard and to Wojciech Stawski, this year's well-deserved recipient of the CCDC/CCG Prize!

It was a fantastic week filled with inspiring presentations and impressive posters. We're grateful to be part of such a supportive and engaged community.

Latest Blog

What is stopping MOFs being more widely used?

Professor Omar Yaghi introduced the term "metal-organic framework" (MOF) in the 1990s. MOFs are porous materials made from metal centres and organic ligands, and their structures can be easily modified to achieve desired pore sizes and characteristics. This tunability makes MOFs ideal for various applications, including gas adsorption and separation, energy storage and conversion, catalysis, and sensing. Read more at the CCDC website.

CSD data and software updates

We're excited about what 2025 has in store for users of the Cambridge Structural Database (CSD)! This year's releases bring a host of new features and enhancements to help you get even more from the resource.

Highlights include:

- New data subsets for more targeted exploration.
- Enhanced visualisation of disorder models within the CSD.
- A broader range of data fields to support deeper insights.

Stay up to date with all our latest developments at: ccdc.cam.ac.uk/solutions/whats-new

Meet the team – events in 2025

- 19th June – PhD Student Science Day 2025
- 18-23 July – 75th ACA Annual Meeting
- 25-29 August – European Crystallographic Meeting 2025 (ECM35)
- 4th September – Frontiers of Chemistry Education Panel Webinar

The Cambridge Structural Database (CSD) is celebrating its 60th anniversary this year. To mark this significant occasion, we are hosting numerous events throughout the year, like the Frontiers Panel webinars, inviting our community to celebrate with us, reflect on our past and look toward the future.

Established in 1965, the database includes historical structures dating back to the 1920s. Our global community has been vital to the growth of the database, which now contains over 1.3 million accurate 3D structures, derived from X-ray and neutron diffraction analyses, along with additional curation by the Cambridge Crystallographic Data Centre (CCDC).

Check our events page at the CCDC website for more updates throughout the year!

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- How to use the CSD software and data to inform and advance your research.
- How cheminformatics and structural chemistry can be applied to problems in the discovery and development of new molecules and materials.

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Ana Machado, CCDC

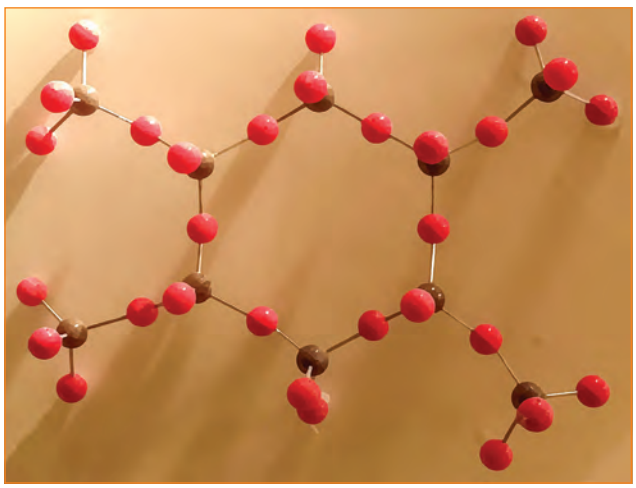
OBITUARY
George Sheldrick (1943-2025)

PROFESSOR George Sheldrick FRS was brought up in Huddersfield where he excelled at grammar school and was awarded a scholarship to study Natural Sciences in Cambridge, specialising in chemistry and later completing a PhD on NMR studies of inorganic hydrides in 1966 [1]. He remained at Cambridge, progressing from demonstrator to lecturer before moving to Göttingen in 1978 to take up a Chair of Inorganic Chemistry.

During the 1960s he began collaborating with the crystallographer Durward Cruickshank (then in Glasgow and later in Manchester) who shared a structure refinement algorithm with him and this ultimately led to George's conversion to crystallographic programming, a speciality in which he excelled [2]. He is best known for having developed the SHELX suite of programs for direct methods and refinement which was and still is pivotal for structure determination by the crystallographic community.

As editor, I remember the first BCA Spring Meeting which I attended in 1986 in York where George gave one of the plenaries. I will also stick my neck out and say that SHELX76 basically solved the phase problem for the vast majority of crystal structures being determined from the mid-1970s onwards. The scale of his achievement is reflected in the impact of his 2008 publication entitled "A short history of SHELX" [3] which, to date, has been cited almost 90,000 times and rocketed the impact factor of Acta Crystallographica A from around 2 to 54 in 2010 [4]. He received a great many prestigious awards and accolades from the structural science community and authored over 800 publications.

From the 90's onwards, George took an increasing interest in macromolecular crystallography and was a frequent contributor to discussions on the CCP4 bulletin board. Many macromolecular crystallographers converted to SHELX around then for both refinement with SHELXL (or SHELXH for 'huge' structures) and for direct methods approaches to locating heavy atoms and anomalous scatterers in MAD and SAD phasing with SHELXC, D and E.



Quoting directly from several members of Reddit crystallography group (r/crystallography): "Very sad news. An absolute giant of science", "Can't even imagine where crystallography would be without his seminal contributions" and "He is immortalised in the crystallography community."

A much more detailed obituary can be found online at the IUCr website [4].

George Sheldrick (1943 – 2025) at the ACA in 2009.
*Photograph by **Peter Mueller (MIT).***

References

[1] Wikipedia, the free online encyclopedia.

[2] Sella, A. (2022). Sheldrick's SHELX. Chemistry World. https://www.chemistryworld.com/opinion/sheldricks-shelx/4015554.article

[3] Sheldrick, G. M. (2008). A short history of SHELX. *Acta Crystallogr. A* **64,** 112-122.

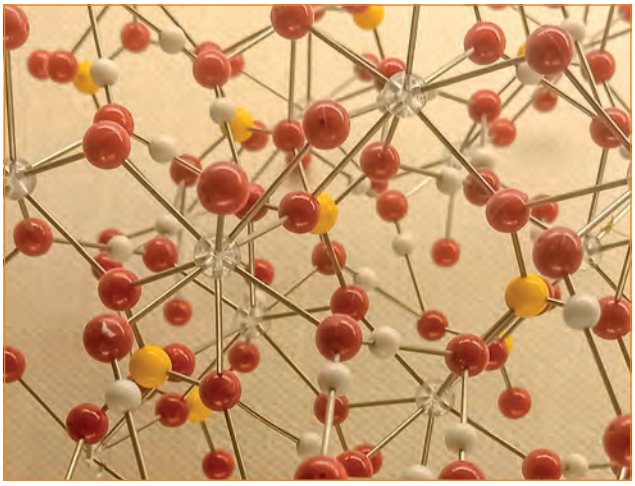
[4] Herbst-Irmer, R. and Usón, I. (2025). George M. Sheldrick (1942-2025). *Acta Crystallogr. A* **81,** in press.

OBITUARY
Alan L Mackay (1926-2025)

IT is with great sorrow that we note the passing of Professor Alan Lindsay Mackay FRS who was Professor Emeritus and Fellow at Birkbeck College London. Alan Mackay was brought up in Wolverhampton and studied as an undergraduate in Cambridge and as a post-graduate with Prof J. D. Bernal at Birkbeck, starting soon after WWII [1]. Bernal was by then well known as a scientist of dazzling intellectual ability, a leading figure in the development of X-ray crystallography and a committed Marxist, as well as someone who contributed greatly to the British war effort.

During his distinguished career, Alan Mackay worked on the structure of materials with a particular interest in icosahedra and five-fold symmetry, which he predicted to occur in quasicrystals in a paper written in Russian in 1981 [2]. Quasicrystals were discovered experimentally a few years later by Dan Shechtman who received the 2011 Nobel Prize for Chemistry. For his contributions to quasicrystals, Alan was awarded the Buckley Prize of the American Physical Society with Dov Levine and Paul Steinhardt in 2010 [1]. Alan described his interest in ordered quasiperiodic structures as generalised crystallography. He also authored a well-known and very useful book on scientific quotations [3].

An excellent biography of Alan Mackay by **Istvan Hargittai** (Budapest) has been published in Structural Chemistry [4] and can be found on the Springer Nature website. A detailed obituary by the same author has also been published by the IUCr.



Alan is sorely missed by those who knew him and we extend our deepest sympathies to his family and friends.

References

[1] Wikipedia, the free encyclopedia.

[2] Mackay, A. L. (1981). De Nive Quinquangula. *Krystallografiya,* **26,** 910-919.

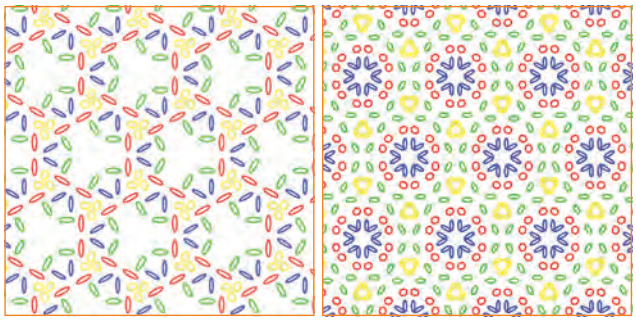
[3] Mackay, A. L. (1991). A dictionary of scientific quotations. Taylor & Francis, ISBN 978-0750301060.

[4] Hargittai, I. (2025). Remembering Alan L. Mackay (1926-2025) – a scientists' scientist in the footsteps of Lucretius. *Struct. Chem.* https://doi.org/10.1007/s11224-025-02486-7.

Alan Lindsay Mackay, photographed at Birkbeck in 1962 and, as the editor remembers him, in 1989. The first image is reproduced with permission of the Birkbeck Image Collections and the second is from a Department of Crystallography photograph taken by Freddie Elliot.

Puzzle Corner

IN the last issue we had two patterns for members to try to identify their plane groups.



Philip Bradfield (Edinburgh) has replied stating that the first pattern is *p*31*m* and the second *p*6*mm*. For this puzzle, I know that these are the absolutely correct answers mainly because I cheated. These are exactly the plane groups which I entered into the Wallpaper Symmetry Generator website by **David Eck** (Hobart and William Smith, US). I also note that *p*6*mm* is shortened to *p*6*m* in my copy of the International Tables Volume I (IUCr 1969).

Philip mentions that both of these plane groups have glide planes that are generated implicitly and that it would be worth discussing why the first one is *p*31*m* rather than *p*3*m*1. There is a difference of 30° in orientation of the mirror lines in these two plane groups and interested readers are referred to pages 247 to 248 of "An Introduction to Crystallography" by F. C. Phillips (1974, 4th edition, Oliver and Boyd, Edinburgh). It seems that there are two ways that one can add mirror lines to the unit rhombus, either perpendicular to its sides (*p*3*m*1) or parallel with them (*p*31*m*). Fig. 443 of the book shows it nicely.

Philip also recommends a study of M. C. Escher's tessellation work entitled "M. C. Escher – Visions of Symmetry" by Doris Schattschneider (Thames and Hudson, 2004) and her "Kaleidocycles" book of folding models (Taschen, 1977; 1987) as well as C. H. MacGillavry's "Symmetry Aspects of M. C. Escher's periodic drawings" (IUCr 1976). All very rewarding!

For this issue we have several more patterns, again very kindly provided by **John Lisgarten** (London), for members to identify their plane groups.

(a)

(b)

(c)

(d)

(e)

Monty Hall Magic

THE Monty Hall problem is a very compulsive mathematical conundrum which was conceived in a letter by Steve Selvin (Berkeley) to The American Statistician in 1975 [1] and was based loosely on a US TV show called "Let's make a deal." The programme was hosted by the popular and philanthropic television presenter Monty Hall, who incidentally graduated in chemistry and zoology before switching to broadcasting.

The most common incarnation of the game is not quite as Selvin penned it in his original letter – these things are always coloured by many re-tellings, but the current version is the same in principle. The usual scenario is for the game contestant to be presented with three closed doors. Behind one of the doors is the prize e.g. a luxury motor car (call it a grand tourer) and behind each of the other two doors is a goat. The following assumes that the contestant wishes to win the grand tourer rather than a goat, but if the latter should be the case (indeed the carbon footprint, running costs, tax, insurance and depreciation would be considerably lower), there is useful advice to be found below for achieving either of the possible outcomes! The general setup of the game with the doors open is shown in Fig. 1(a) although the contestant would, of course, only see it with all of the doors closed, as in Fig. 1(b).

Monty starts by inviting the contestant to pick one of the closed doors (numbered 1 to 3), essentially at random as all three are identical and give no clue as to what is behind them. When the contestant has chosen a door (say 1), Monty opens one of the other doors (e.g. 3) to reveal a goat and invites the contestant to either stick with the door they have chosen (in this case 1) or to switch to the other available door (in this case 2). This situation is shown in Fig. 1(c) which presents the essential quandary of the game, where the player knows that 3 is a goat and has to decide between doors 1 or 2 to win the grand tourer.

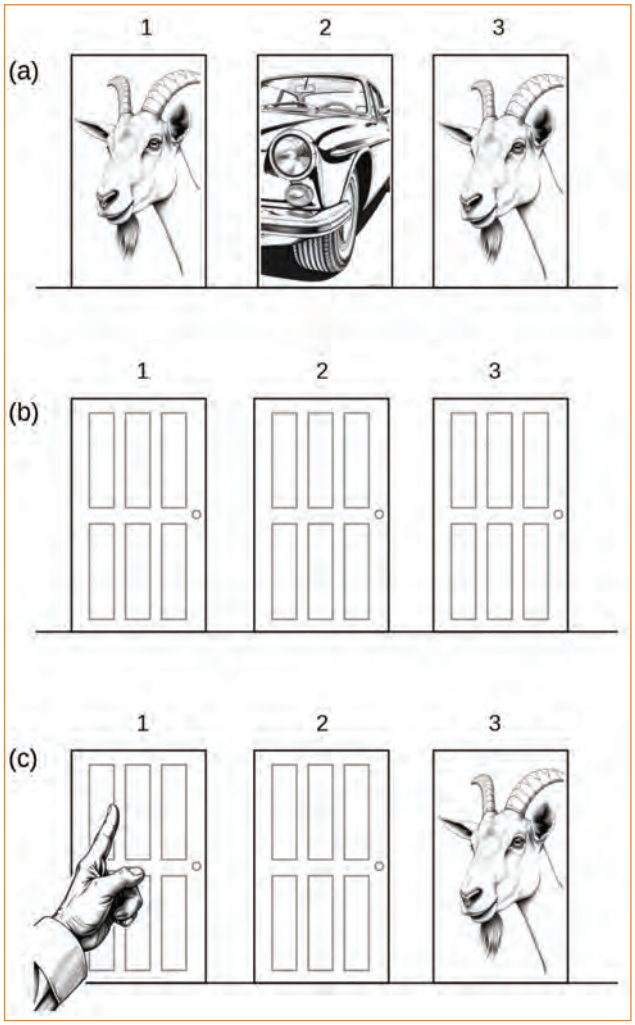


Fig. 1. The general setup of the Monty Hall game. (a) Shows that the prize (grand tourer) is behind door 2 and the goats are behind doors 1 and 3, on this occasion. (b) The player only sees 3 closed doors and has to make a first guess. (c) In this case they have chosen door 1 and Monty has opened door 3 to reveal one of the goats. After seeing where one of the goats is, the player has to decide whether to stick with door 1 or switch to door 2.

One's instinct at this point is that the contestant has a 50:50 chance of winning regardless of whether they stay with the same door or switch to the other. However, astonishingly, if they do switch doors their probability of success is twice what it is if they stay with the same door. It almost seems like magic and a great many people struggle ***very*** hard to believe it, including the editor who was first introduced to the problem a few years ago in an online maths course.

Just to go over some of this again, unlike the contestant, Monty has prior knowledge i.e. he knows which door the prize is behind. Hence, when the contestant has chosen their first door, Monty must, of course, not then open the door to the prize! Even Monty's well-known benevolence does not extend to giving the game away at this point! Neither must he open the door which the contestant has

already chosen since that will, of course, reveal whether their first choice was right or wrong. Instead, he will only open one of the doors which he knows has a goat behind. He then invites the contestant to either stick with their original choice of door or switch to the other door, either of which might have the prize behind it. As said above, one's chance of winning the grand tourer is doubled by switching doors at this point. But how on earth can that be?

I have split my explanation up into bullet points to help my pea-sized brain understand each step in the logic, as far as it can. Start by imagining you are the contestant.

- When you guess which door hides the prize, you have a ⅓ chance of getting it right first time.
- If you happen to have chosen the right door and you stick with that door when Monty shows you one of the goats, you will win.
- In the situation where your first choice was correct, if you regrettably decide to change doors, you will, of course, lose. It's that grim!
- Thus, if you always stick with the door you originally chose, you will win ⅓ of the times you play. It is exactly as if Monty is not there and you are just choosing one door out of three, never changing your mind based on Monty's actions.
- However, think about your first choice of door again. The chance of picking the wrong door at this stage is, of course, considerably higher, being ⅔ rather than ⅓.
- So accept your first choice is probably wrong, or indeed assume it is wrong.
- If your first choice is wrong ***and*** you decide to change doors, then you simply have to win because Monty will show you which one of the other two doors you should not choose.
- If you are always going to change doors, Monty narrows down your choice to only one door which you can switch to.
- Put another way, if your first choice was wrong (that's our assumption now), the door he does not open has to be the winning choice.
- So if you always change doors, you will win ⅔ of the time.
- By switching doors, you swap your ⅔ chance of losing for a ⅔ chance of winning!
- Monty has helped us and raised our chance of winning from ⅓ to ⅔, providing that we switch doors. It's very a clever trick, right?

To help me understand some of this when I first heard about it around 5 years ago, I wrote an emulator script and found that it does reproduce the exact behaviour as explained above. Indeed that was about the only way of convincing me it was correct. Returning to the same script 5 years later, thinking it might be of interest to readers of this article, I then thought otherwise and decided to rewrite it from scratch (Fig. 2) and again found that the Monty Hall effect is definitely a real one.

I apologise if it is not immediately obvious why this is relevant to crystallography, but given the importance of statistics and probability in solving the phase problem, both in direct methods and in the maximum likelihood approaches used by the macromolecular and other communities, it probably is more important than I actually know. It gets mentioned quite often in the context of Bayes' theorem too, but I am leaving it up to our expert membership to let me know more.

Anyway, as this is a historical section, let us look back to some more of the events after Selvin first posed the problem and the answer back in 1975. His proposal generated

```
math.randomseed(os.clock()*100000000000)
stickwins,changewins,stickloses,changeloses=0,0,0,0
for j=1,100000 do
    car=math.random(1,3)    -- The prize door which Monty mustn't open.
    guess=math.random(1,3) -- Player's first guess.
    player_sticks=false  doors_monty_can_open={}
    for n=1,3 do if n~=car and n~=guess then table.insert(doors_monty_can_open,n) end end  -- Doors Monty can open.
        if #doors_monty_can_open==1 then  -- Get a door Monty can open.
           door_monty_opens=doors_monty_can_open[1]
        else door_monty_opens=doors_monty_can_open[math.random(1,2)]
        end
    for n=1,3 do if n~=door_monty_opens and n~=guess then change_door=n end end  -- Door the player can change to.
    players_choice=math.random(1,2)  -- Player chooses at random whether to stick or change.
    if players_choice==1 then door=guess player_sticks=true else door=change_door player_sticks=false end
    if door==car then -- It's a winner
        if player_sticks==true then stickwins=stickwins+1
        else changewins=changewins+1
        end
    else  -- It's a goat
        if player_sticks==true then stickloses=stickloses+1
        else changeloses=changeloses+1
        end
    end
end
print("Stick wins:",stickwins,"Change wins:",changewins,"Stick loses:",stickloses,"Change loses:",changeloses)
```

Fig. 2. The editor's Monty Hall emulator script written in lua which simulates a player choosing whether to stick with the same door or switch entirely at random. Changing the large number (100,000) on line 3 allows the game to be run as many times as desired. Changing doors definitely doubles the number of times you win the car. The code can be found online here: https://pastecode.io/s/to53pyc4 and many other Monty Hall simulators and visualisers are available online.

several letters claiming that he was incorrect [2]. Clearly the editor is not alone in struggling to understand this conundrum. A few years down the line in 1990, the same problem was publicised to a much greater degree in the popular US magazine Parade by Marilyn vos Savant, who also rightly maintained that switching doors doubles your chance of winning [3]. Quoting exactly from Wikipedia (the free online encyclopedia) "After the problem appeared in Parade, approximately 10,000 readers, including nearly 1,000 with PhDs, wrote to the magazine, most of them calling Savant wrong" (editor feeling reassured at this point). Wikipedia also reports that Savant "has the highest recorded intelligence quotient (IQ) in the Guinness Book of Records, a competitive category the publication has since retired." Savant remains amongst the highest scoring contenders of today, although I gather it is now called psychometric testing, in some contexts anyway. Hence, I am definitely not one to pit their wits against Savant's exceptional ability or cast any doubt on her conclusions. Indeed in subsequent published correspondence, it seems that she baited and outed a fair number of expert statistical trolls who were determined to prove that she was wrong, whilst humble school teachers who actually played the game with their classes confirmed that she was absolutely correct.

More reassurance for the editor is provided by a Scientific American article last year in which a psychologist is reported as saying that getting the Monty Hall puzzle wrong indicates that you have a "perfectly normal functioning human brain" [4].

If you ever get to play "Let's make a deal" then switching doors should be your go to choice!

References

[1] Selvin, S. (1975). A problem in probability. *American Statistician* **29,** 67-71. doi:10.1080/00031305.1975.10479121

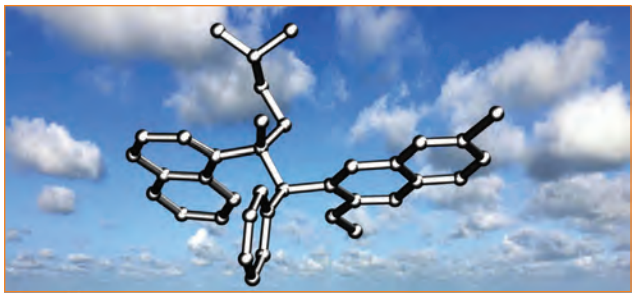
[2] Selvin, S. (1975). On the Monty Hall problem. *American Statistician* **29,** 134.

[3] vos Savant, M. (1990). "Ask Marilyn" column in Parade magazine, (9 September 1990) p. 16.

[4] Parshall, A. (2024). See why everyone gets the Monty Hall puzzle wrong. *Scientific American*, Digital Issues, August 2024.

Artwork is mostly by the Surreal Graphics Generator at deepai.org.

Tubercular bells



Bedaquiline drawn using CueMol with a photograph by Maria Erskine (London).

Being cautious that humour and debilitating disease are not things which go together very well, I still think that the former is at least a partial cure for the later. Having just mentioned the Guinness Book of Records, I am reminded of a minor triumph in that sort of arena. If one searches the protein database (rcsb.org) for structures from *Mycobacterium tuberculosis* (the causative agent of TB) and sorts them in ascending order of date, it seems that the first structure of a protein from that organism to be deposited is an iron-dependent superoxide dismutase (Fe-SOD, rcsb-id: 1ids, Fig. 1) which was released at the end of 1994. You might also spot the editor as the first author! That was a nice project with excellent collaborators and I was lucky enough to receive an MRC pilot project grant for one year back in early 90's to complete that structure. That was shortly before the TB structural genomics work began in earnest, and we now have something like over 1,500 structures in the PDB for that microorganism.

Targeting enzymes which have very small substrates (in this case the superoxide radical $O_2^{\cdot-}$) was never going to be easy, although that was long before fragment screening came on the scene and there may be outer parts of the active site which could still be druggable, who knows. I did therefore try to revive some interest in this enzyme as a potential drug target a couple of years or so ago (not least

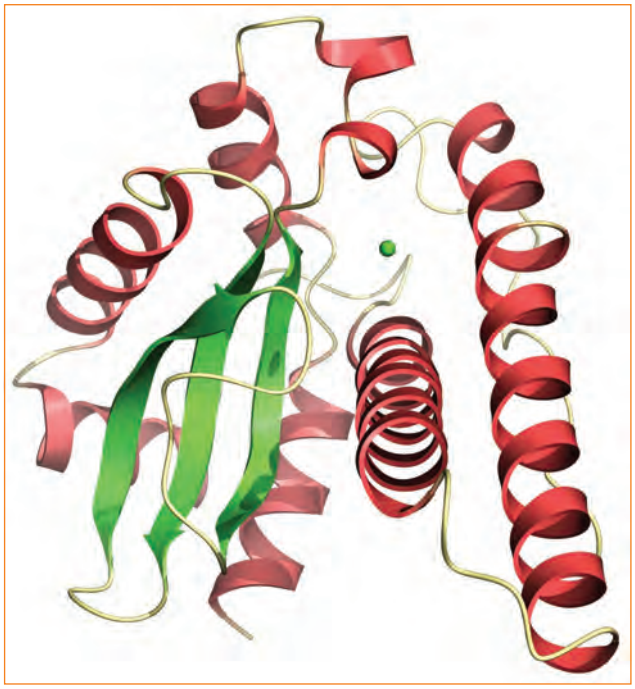


Fig. 1. The iron-dependent superoxide dismutase (RCSB-ID: 1ids) from M. tuberculosis drawn using CueMol.

because it appears to be an essential gene; search for sodA at https://mycobrowser.epfl.ch) but, like most of the editor's best scientific ideas, that one probably only made it as far as someone's spam folder, never to see the light of day again, but there is always scope for improvement in my commitment to these tasks!

The other class of SOD, the Cu/Zn-dependent enzymes, have been targetted in screening studies to identify compounds that enhance their stability and prevent the enzyme from aggregating in motor neurone disease. There is also interest in developing metal-organic frameworks or nanomaterials which catalytically mimic the free-radical scavenging ability of SOD enzymes.

Current antibiotics used to treat TB include rifampicin, rifapentine, isoniazid, pyrazinamide, ethambutol, bedaquiline and delamanid, as well as fluoroquinolones, such as levofloxacin or moxifloxacin [1]. All are given in various combinations with one another and additives to counter their side effects. Isoniazid is a derivative of nicotinamide and inhibits mycolic acid biosynthesis which is needed for the assembly of the mycobacterial cell wall. Ethambutol acts on another enzyme, namely arabinosyl transferase, which is also involved in the biosynthesis of the mycolyl-arabinogalactan-peptidoglycan cell wall, and delaminid acts similarly. Rifampicin and its analogues inhibit bacterial RNA polymerase while bedaquiline acts as an inhibitor of mycobacterial ATP synthase. The fluoroquinolones are inhibitors of DNA gyrase and DNA topoisomerase.

Many of these drugs were simply not around 30 years ago, for example, we had to wait until 2012 for bedaquiline (Fig. 2) to become the first new anti-TB drug of a novel class to be approved by the FDA in something like 40 years. Of course, the newer drugs are more expensive to produce and so they are generally only used if the patient has developed resistance to the older established first-line treatments such as isoniazid, ethambutol and rifampicin.

For anyone interested in TB research, there is a wealth of information at the UCL-TB website.

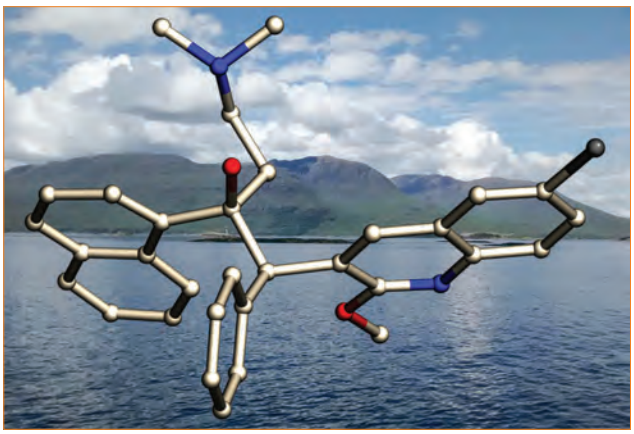


Fig. 2. Back in 2012, bedaquiline became the first novel anti-TB drug to be approved by the FDA in 40 years. The structure shown here is from the Crystallography Open Database (COD) where it has accession number 2022265 [2]. The molecule has been drawn using CueMol (http://www.cuemol.org/en/) and is shown against a background picture of Bernera in the Isle of Lewis by Maria Erskine (London).

References

[1] Wikipedia, the free online encyclopedia.

[2] Okezue, M., Smith, D., Zeller, M., Byrn, S. R., Smith, P., Bogandowich-Knipp, S., Purcell, D. K. and Clase, K. L. (2020). Crystal structures of salts of bedaquiline. *Acta Crystallogr. C* **76,** 1010-1023. https://doi.org/10.1107/S2053229620013455

Computed axial tomography

A late night cat fight saw the editor taking a few trips to the emergency vet in Wimbledon Village. These journeys took me past the site of the Atkinson Morley Hospital which is now a well-to-do housing development. Incidentally Atkinson Morley was a philanthropic hotelier whose very generous donation to UCL allowed the hospital named after him to be built in 1869 [1]. He is buried in Highgate Cemetery and was, at one time, Florence Nightingale's landlord. He owned a large hotel on Trafalgar Square where the South African embassy is now located and his legacy lives on in the Atkinson Morley Wing at St George's Hospital in Tooting. The name of Atkinson Morley is internationally synonymous with specialised neurology, neurosurgery, stroke and rehabilitation, but it is a little known fact that the hospital helped breed at least one Nobel prize-winner in late 1970's in the field of X-ray tomography.

Sir Godfrey Hounsfield FRS was an electronic engineer at EMI who worked on developing the UK's first transistorised computer before shifting to medical imaging in the mid-1960s [2]. He came up with the idea of computationally combining X-ray images obtained during a continuous angular scan in which the source and the detector rotate around the subject. On trying to find a radiologist with whom to collaborate, one of the very few clinicians who thought that he was not completely insane was Dr James Ambrose at the Atkinson Morley who provided a preserved brain with a tumour for analysis. Hounsfield returned with an image showing the tumour and surrounding tissue in unprecedented detail around 5 weeks later. From that point on the two worked together on development of the instrument, with the first patients being scanned at the hospital in 1971. Computed axial tomography (CAT or CT scanning, as it is now known) was born.

Hounsfield received the 1979 Nobel Prize for Physiology and Medicine jointly with Allan Cormack, a physicist, who incidentally had an MSc in Crystallography from Cape Town [1]. Cormack developed the mathematical basis of computed tomography and constructed a similar instrument in the US independently of Hounsfield.

The cat was alright!

Jon Cooper, UCL

References

[1] Wikipedia, the free online encyclopedia.

[2] Pietzsch, J. With a little help from my friends. Nobel Prize Outreach, NobelPrize.org.

Meetings of Interest

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

Assistance from the IUCr website is also gratefully acknowledged.

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

BACG 2025, 54th Annual Conference of the British Association for Crystal Growth, Leeds, 1st-3rd July 2025

Since 1969, the BACG has encouraged scientific and technological communications across national and international platforms, spanning theory and practice of crystal growth, crystallisation and appraisal of crystals. Day one of the annual conference is a student-focussed day. For more details please see: **https://www.bacg.co.uk/**

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The cryoEM revolution in structural biology, Liverpool, 16th July 2025.

The University of Liverpool will be bestowing an Honorary doctorate to Dr Richard Henderson. To mark this, a celebratory symposium entitled "The cryoEM revolution in structural biology' has been organised at the University of Liverpool. This one-day Symposium will bring speakers from the Universities of Leeds, Liverpool, Sheffield, Imperial and Birkbeck as well as from the Crick Institute and Astex Pharmaceuticals. For more details please see: **https://payments.liv.ac.uk/conferences-and-events/events-at-liverpool/institute-of-systems-molecular-and-integrative-biology/cryoem-revolution-in-structural-biology**

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ACA2025, 75th Annual Meeting of the ACA: Structure is forever, Lombard, Illinois, 18th-23rd July 2025.

This milestone event promises to bring together experts, researchers, and enthusiasts from across the globe to celebrate advancements in the field of crystallography. Join us for a week of engaging sessions, cutting-edge scientific presentations, and vibrant networking opportunities in the heart of Lombard. Whether you're a seasoned crystallographer or new to the field, this meeting offers something for everyone – let's come together to explore, learn and shape the future of structural science!

More details can be found here: **https://www.acameeting2025.com**

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

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

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

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

OXFORD CRYOSYSTEMS

OXFORD CRYOSYSTEMS

CRYOSTREAM 1000

Introducing the latest in cryogenic sample cooling

Available in Standard (80K – 400K), Plus or Compact (80-500K) variants, the Cryostream 1000 is a revolutionary edition of the world's leading cryo-cooler. All new electronics and firmware are incorporated into an elegant, compact design with a focus on reliability, simplicity and an enhanced user experience.

For more information, visit our website or contact info@oxcryo.com

KEY FEATURES

- **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.
- **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).
- **Auto Shield Flow:** Automatically optimised shield gas flow rates.
- **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.
- **Eco Mode:** Continual monitoring of the dry-air module eliminates any unnecessary run time, saving energy and reducing maintenance.
- **Improved Pump-out Port Design:** Relocated to the rigid leg and re-designed for ease of use, this eliminates the requirement to remove the coldhead from the cabinet during vacuum regeneration.
- **2 Year Standard Warranty:** All Cryostream 1000 systems ship with a two year warranty.
- **Wide Nozzle Option:** A 146% larger sample area enables large samples analysis and reduces x-ray shadowing for small samples.

SAMPLE COOLING MADE SIMPLE

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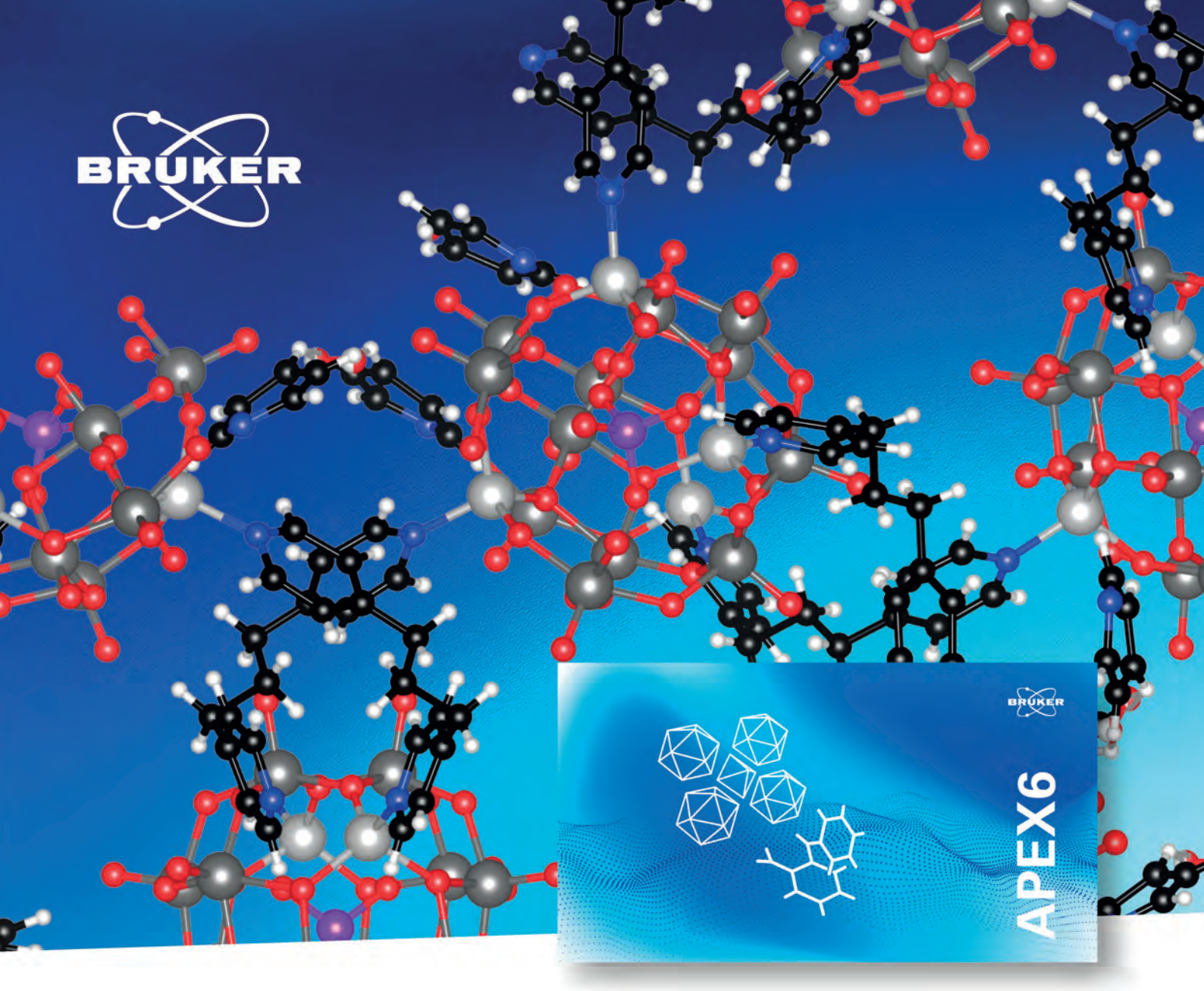

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