# Crystallography News

British Crystallographic Association

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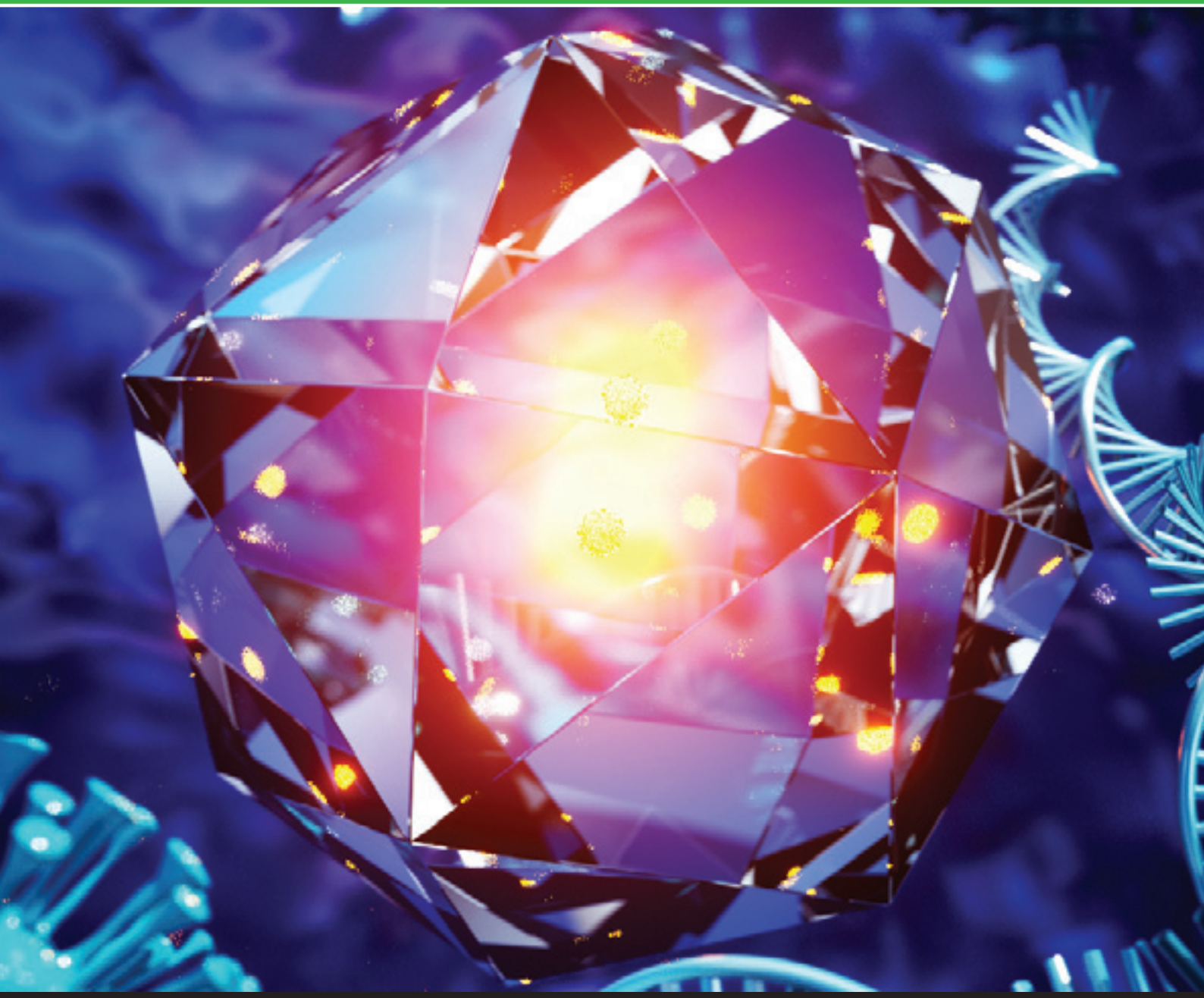

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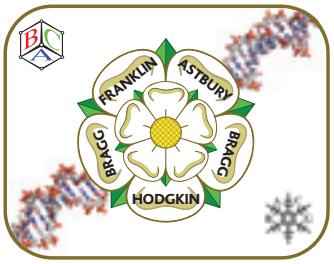


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## *This month's cover:*

*Artist's conception of nanodiamonds used in fluorescence detection of targets in lateral flow tests (see page 4). Credit: Ella Maru Studio/i-sense, UCL)*


**BCA Administrative Office,**
4 Dragon Road
Harrogate HG1 5DF
Tel: +44 (0)1423 529 333
e-mail: bca@hg3.co.uk

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Please ensure that items for inclusion in the June 2021 issue are sent to the Editor to arrive before 25 April 2021.

Editor: John Finney
Department of Physics and Astronomy and London Centre for Nanotechnology, University College London, Gower Street, London WC1E 6BT
e-mail: john.finney@ucl.ac.uk

Deputy Editor, Dave Allan
e-mail: dave.allan@diamond.ac.uk



Printed by North Wolds Printers
83 Halifax Way, Pocklington Industrial Estate, Pocklington, York, YO42 1NR
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# From the President

**MY time as BCA President will shortly come to an end and, as I look back, it has been a strange time for all of us. I realise I must have set a new record for the fewest Spring Meetings attended (in person) for a President, just one. My term began at the 2018 Spring Meeting, but I was away in Australia at that time and missed it. I suppose we would now simply arrange a Zoom session, which has become second nature for all of us. Nottingham in 2019 was a great meeting, topped off with a thoroughly enjoyable dinner and ceilidh. I was blissfully unaware that it would be my first and last as President. Things have been very different since the arrival of the SARS-CoV-2 virus in early 2020, when I received an email from my predecessor, Lee Brammer, with the comment "…not what you signed up for as BCA President….". In the event, the BCA has continued to run efficiently using Zoom and email, with sterling support from Council Officers and Members, Group chairs, our Crystallography News editor, the Spring Meeting programme committee, the staff at Hg3 and the membership. The 2020 Leeds Spring Meeting, postponed to 2021, is going ahead (virtually). The BCA remains resilient and vibrant, and the profile of structural studies has been raised by the remarkable successes in vaccine design.**

It has not escaped my notice that my term of office has run concurrently with that of **Donald Trump**, but I trust the handover of power will go more smoothly for the BCA than the USA. This has been an unfortunate era of Fake News and misinformation, and not only in the USA as the reality of the UK Withdrawal Agreement with the EU looks less like the sunlit uplands we were promised. We should be thankful, however, that the UK retains access to the EU Horizon programme and, for the time being, the Marie Curie fellowship programme. Misinformation is not, however, a new phenomenon. The satirist **Jonathan Swift**, probably best known as the author of *Gulliver's Travels*, wrote in 1710:
*"Besides, as the vilest Writer has his Readers, so the greatest Liar has his Believers; and it often happens, that if a Lie be believ'd only for an Hour, it has done its Work, and there is no farther occasion for it. Falsehood flies, and the Truth comes limping after it; so that when Men come to be undeceiv'd, it is too late; the Jest is over, and the Tale has had its Effect…"*
This still sounds familiar today, and Swift's 'Effect' has been turbocharged by social media. As crystallographers we must hold fast to the principle of collecting the best, most reliable data (evidence) possible, and then drawing our conclusions, or developing our hypotheses, as the most likely explanation of those data, in life as in the lab.

One consequence of the Covid-19 pandemic has been a rise in public esteem for science and scientists. Following a period where some of our leaders had "*…had enough of experts…*" they suddenly found themselves in dire need of them. I have written before about the essential contribution of crystallography to the rapid design of Covid vaccines and drug candidates, along with, of course, immunology, virology, cell biology, vaccinology, chemistry and medical practice. Luckily for all of us, research in these areas has been funded, with ups and downs, over the years and this is now paying off. I believe I recall, but I cannot find the quote, that Margaret Thatcher's science minister in the late 1980s, Robert Jackson, once complained of a "*research mountain*" in the UK, meant as a criticism referencing the butter mountain and wine lake surpluses of the European Community. This now appears even more short-sighted than it did then.

Just before Christmas I attended the (virtual) Winter Meeting of the BCA Biological Structures Group (BSG). The afternoon session focused largely on SARS-CoV-2. The virus is encapsulated by a membrane, where the now well-known Spike Protein (SP) is embedded. SP is unstable, and it has two possible structures, one (pre-fusion) in the free virus allowing it to bind to a cell surface, and a second, dramatically different one (post-fusion), that allows fusion of the viral and cell membranes to admit the virus to the cell. It could be thought of as a hair-trigger, spring loaded device, primed to pierce the cell. This general mechanism is common to other human pathogenic enveloped viruses, such as 'flu and Respiratory Syncytial Virus (RSV). **Jason McLellan** (University of Austin at Texas) gave an interesting talk to the BSG (see the report on page 19) describing his work to stabilise SP for use in vaccines. He had worked previously on RSV vaccines, and redesigned the analogous surface protein, using crystallography and mutagenesis, to stabilise its structure for use as the key component. Vaccine design for RSV had been previously unsuccessful, but stabilising the structure was transformative and yielded a workable vaccine. Jason applied these ideas to the SARS-CoV-2 SP, and designed a mutation placing two adjacent proline resides at a critical point in the structure, the 'PP' variant. This stabilises SP in its pre-fusion structure. The PP variant sequence is used in the Pfizer/BioNTech and Moderna vaccines and is key to their success.

I look forward to seeing you all (virtually) at the BCA 2021 Spring Meeting. The 2022 Spring Meeting, however, really will take place in Leeds, unless the SARS-CoV-2 virus has something else up its sleeve. The delayed 25th General Assembly and Congress of the IUCr is due to take place in Prague on 14-22 August. If the Covid-19 situation has improved sufficiently, it will represent a welcome return to some sort of normality. Prague is a beautiful city, and it would be a satisfying sight if it became the venue for a great reunion of crystallographers after 18 months of forced isolation.

When you read this newsletter, voting in the elections for the BCA President, Ordinary Member and Education and Outreach Coordinator will be complete. I hope all members have voted. One only has to look at the USA to see the huge impact elections can have, and the importance of everyone using their vote.

Finally, I will look back with affection to my time as President. I would like to thank again all those who have worked tirelessly to support me, especially my colleagues on Council and at Hg3. I look forward to a return to normality and to seeing you all in person in 2022 at Leeds.

I hope you are all well and wish you the best in these challenging times.

**Simon Phillips**

# BCA Council 2021

## COUNCIL OFFICERS

***President (2021)***
***Prof Simon E V Phillips***
Department of Biochemistry,
University of Oxford,
South Parks Road,
Oxford OX1 3QU
president@crystallography.org.uk

***Vice President (2022)***
***Prof Simon Parsons***
Centre for Science at
Extreme Conditions,
The University of Edinburgh,
Room 2806, Erskine
Williamson Building,
Peter Guthrie Tait Road,
The King's Buildings,
Edinburgh, EH9 3FD
S.Parsons@ed.ac.uk

***Secretary (2022)***
***Dr Alexandra Stanley***
Rigaku Europe
secretary@crystallography.org.uk

***Treasurer (2023)***
***Dr Claire Naylor***
SPT Labtech Ltd
treasurer@crystallography.org.uk

## ORDINARY MEMBERS

***Dr Anna Warren (2022)***
Diamond Light Source,
Harwell Science and
Innovation Campus,
Didcot,
Oxfordshire OX11 0DE
Tel: 01235 778000
anna.warren@diamond.ac.uk

***Dr Cheryl Doherty (2021)***
***Bursary Officer (2019-present)***
GSK
Stevenage
Herts, SG1 2NY
cheryl.x.doherty@gsk.com

***Dr Hazel Sparkes (2020)***
Department of Chemistry,
University of Bristol,
Cantock's Close,
Bristol, BS8 1TS
Tel: 0117 331 8298
hazel.sparkes@bristol.ac.uk

## GROUP REPRESENTATIVES

***Biological Structures***
***Dr Mark Roe***
School of Life Sciences,
University of Sussex,
Falmer,
East Sussex, BN1 9RQ
Tel. 01273 678863 (Office)
Tel. 01273 872896 (X-Ray Lab)
M.Roe@sussex.ac.uk

***Chemical Crystallography***
***Dr Gary Nichol***
University of Edinburgh,
Joseph Black Building,
Edinburgh, EH9 3FJ
Tel: 0131 650 4806
g.s.nichol@ed.ac.uk

***Industrial***
***Dr Helen Blade***
AstraZeneca,
Macclesfield Campus,
Macclesfield,
Cheshire, SK10 2NA
Helen.Blade@astrazeneca.com

***Physical Crystallography***
***Dr Helen Playford***
Building R3, Room 1.22
STFC ISIS Facility,
Rutherford Appleton
Laboratory,
Didcot, OX11 0QX
Tel: 01235 446890
helen.playford@stfc.ac.uk

***Young Crystallographers***
***Dr Tom Roseveare***
D85 (29352),
Department of Chemistry,
The University of Sheffield,
Dainton Building, Brook Hill,
Sheffield, S3 7HF
tom.roseveare@sheffield.ac.uk

## CO-OPTED MEMBERS

***Program Chair (2020)***
***Dr Thomas Edwards***
School of Molecular and
Cellular Biology,
University of Leeds,
Leeds, LS2 9JT
t.a.edwards@leeds.ac.uk

## EDUCATION & OUTREACH

***Prof Simon Coles***
School of Chemistry,
Faculty of Engineering and
Physical Sciences,
University of Southampton.
Southampton, SO17 1BJ
Tel: 023 8059 6721
s.j.coles@soton.ac.uk

## GROUP CHAIRS

***Biological Structures***
***Dr Katherine Brown***
Cavendish Laboratory,
Department of Physics,
University of Cambridge,
J J Thomson Avenue,
Cambridge, CB3 0HE
kb518@cam.ac.uk

***Chemical Crystallography***
***Dr Iain Oswald***
Strathclyde Institute of
Pharmacy and Biomedical
Sciences, Strathclyde
University, Glasgow, G4 0RE
Tel: 0141 548 2157
iain.oswald@strath.ac.uk

***Industrial***
***Dr Helen Blade***
AstraZeneca,
Macclesfield Campus,
Macclesfield,
Cheshire, SK10 2NA
Helen.Blade@astrazeneca.com

***Physical Crystallography***
***Dr Anthony Phillips***
School of Physics and
Astronomy,
Queen Mary, University of
London,
327 Mile End Road,
London, E1 4NS
Tel: 020 7882 3429
a.e.phillips@qmul.ac.uk

***Young Crystallographers***
***Dr Tom Roseveare***
D85 (29352),
Department of Chemistry,
The University of Sheffield,
Dainton Building, Brook Hill,
Sheffield, S3 7HF
tom.roseveare@sheffield.ac.uk

## EX-OFFICIO MEMBERS

***Past President***
***Prof Lee Brammer***
Department of Chemistry,
University of Sheffield,
Sheffield, S3 7HF
Tel: 0114 222 9536
lee.brammer@sheffield.ac.uk

***Webmaster***
***Dr Claire Hobday***
University of Edinburgh,
Joseph Black Building,
David Brewster Road,
Edinburgh, EH9 3FJ
Claire.Hobday@ed.ac.uk

***Editor "Crystallography News" Prof John Finney***
Department of Physics
and Astronomy and
London Centre for
Nanotechnology,
University College London,
Gower Street, London,
WC1E 6BT
john.finney@ucl.ac.uk

*(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

**WHILE the start of 2021 was not auspicious for obvious virus- and Brexit-related reasons, we have found some crystallographic highlights that I hope you will cheer you up. The press made a big noise about the ability of AlphaFold in predicting protein structures, so David Jones and Janet Thornton have written for us a clear assessment of what this advance means – both generally and for the crystallographic community specifically. It was also good to see that *Physics World* – the monthly of the Institute of Physics – not only gave its Breakthrough of the Year award to an advance that relies on crystal structure, but half of the ten advances shortlisted for that award are also structure-based (see page 14).**

But there's one further piece of crystallographically-related work that caught my particular attention early this year – and one that is potentially highly relevant in our present difficult situation.

The power of biomolecular crystallography in helping to counter the effects of SARS-CoV-2 has been well demonstrated in recent months. Some of that work has been described in the June and September 2020 issues of *Crystallography News*. However, it's not only the structural biologists who are on the case. The work reported in a recent *Nature* paper[i] implies that non-biological structural work also looks like being able to play a major part in helping to control virus outbreaks.

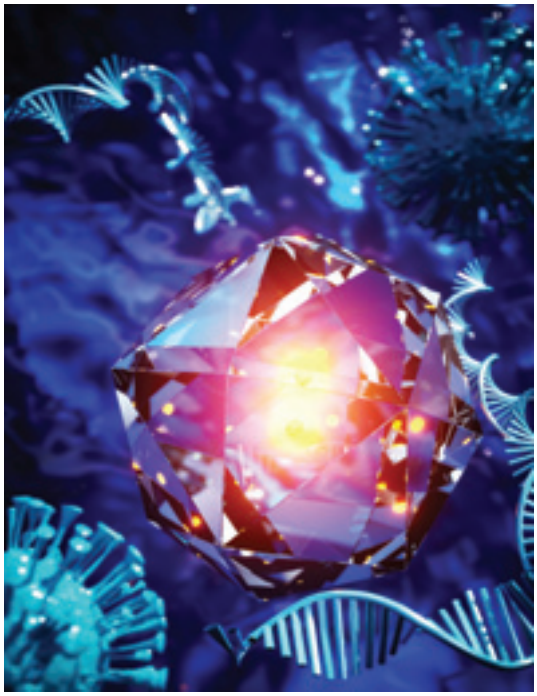
In testing for presence of a virus, *sensitivity* to the presence of the target RNA sequence is crucial. In the 'gold standard' PCR process, this is done by amplifying the amount of the target to facilitate its detection. As we have found from the current problems of getting results from SARS-CoV-2 PCR tests in even 24 hours, the complete process takes time, so in order to decrease the turnround time of a test, *lateral flow test* procedures, which rely on the detection of the target without increasing the amount present, are often used – e.g. in pregnancy testing.

In a normal lateral flow test for a viral particle, antibodies that target it are attached to visual 'tags', usually gold nanoparticles. The target will bind both to the tag and a line on the test strip, resulting in a visible line. In using these as rapid tests for SARS-CoV-2, although false positives are rare, concern has been expressed about false negatives[ii] – these are particularly worrying as they could result in undetected cases circulating in the community.

The false negative problem seems to be one of inadequate sensitivity in detecting the target.

The recent Nature paper tackles this sensitivity problem, not by increasing the amount of target as is done in the PCR test but by increasing the sensitivity of the detection technique. This it does basically by exploiting fluorescence detection, which is inherently more sensitive than light absorption on which the detection success of the gold nanoparticle tag process depends. The fluorescent tags used are nanodiamonds containing nitrogen vacancies, the structure of which causes

*Artist's conception of nanodiamonds used in this work. (Credit: Ella Maru Studio / i-sense, UCL.)*



the nanodiamonds to fluoresce. By manipulating the electron spin of the nitrogen vacancy using an electromagnetic field, the fluorescence intensity can be modulated, and the signal-to-background ratio – and therefore the sensitivity – further increased.

OK. Sounds promising, but how sensitive is this in reality?

In checking this out in lateral flow tests involving biotin, **Miller**, **McKendry** and colleagues found that the nanodiamond test was 100,000 times more sensitive than using the normal gold nanoparticles. For a sample of HIV-1 RNA, they were able to detect just a single molecule after only a 10 minute isothermal amplification step.

More work is needed to make these tests more suitable to primary care settings, but these results seem to me to be impressive. And the author list illustrates something very important: the value of collaborating across disciplinary boundaries. For this work, the authors came from a range of departments: London Centre for Nanotechnology at UCL, the Division of Medicine and the Department of Electronic and Electrical Engineering at UCL, the Advanced Pathogens Diagnostic Unit and the Department of Virology, UCL Hospitals, and The Queen's College, Oxford.

Structural science in the service of mankind. Excellent.

**John Finney**

References:


i. Benjamin S. Miller *et al. Nature*, **587**, 588-593 (2020)
ii. https://blogs.bmj.com/bmj/2021/01/12/covid-19-government-must-urgently-rethink-lateral-flow-test-roll-out/

# Puzzle Corner

**SUDOKU**, which probably helped many over the Christmas holidays, generally features a 9x9 square of squares, and the pattern of the squares filled in with the given numbers usually has a symmetry higher than 1. How many 2-dimensional point groups are possible, and how many different orientations of the symmetry elements are possible for each?

## *Answer to December's puzzle:*

Putting someone in the corner of the room, 9 people can stand in a row along the wall. The next row, $\sqrt{3}$ m from the wall will accommodate 8 people, In the entire hall, 4 rows of 9 and 3 of 8 can be accommodated, making the last row about 12 cm from the wall. Thus we have 60 people in 168 $m^2$ or 2.8 square metres per person. In such an arrangement, considerable care would be needed in arranging entrance and exit!

## BCA Corporate Membership

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# AlphaFold – the end of the protein folding problem or the start of something bigger?

**IN November 2020, a London-based AI company called DeepMind, now part of Google, made the following announcement about the long-standing protein folding problem: "In a major scientific advance, the latest version of our AI system AlphaFold has been recognised as a solution to this grand challenge by the organisers of the biennial Critical Assessment of Protein Structure Prediction (CASP)". This bold claim, if really true, would of course have many implications for both experimental and computational structural biology, so here we try to put these new results in context and try to provide a perspective on the way forward.**

DeepMind addressed this venerable challenge using almost all of our existing knowledge of protein structures, accumulated over 50 years, to train their powerful machine learning algorithms, some of which had already been used in the form of a program called AlphaGo to beat the best human Go players. Their approach is expected to be published along with other papers from the latest CASP experiment (CASP14) in the next few months, so at this stage it is not possible to know exactly why their approach worked so much better than everyone else's. Here we hope to give a balanced overview of what at least we know so far, and try to put the results in the context of experimental structural biology going forward.

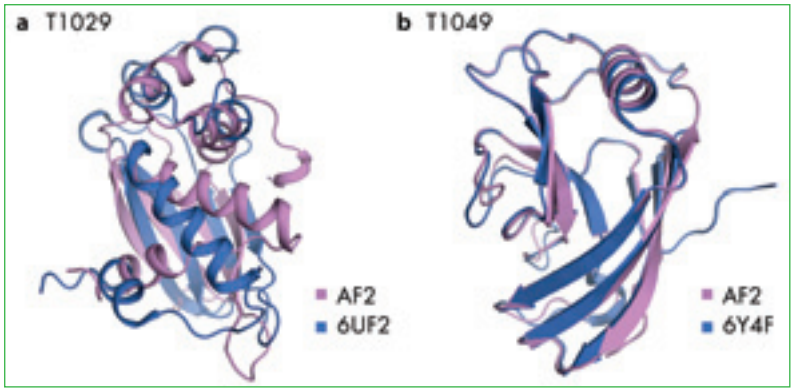


*Figure 1. The 'worst' (a) and 'best' (b) of AlphaFold de novo models. The figures show the superposition of the predicted model and the experimental structure determined later. Target T1029 shows that there can still be issues to resolve in terms of multimeric structures or large conformational changes, but target T1049 shows a more typical case, and how good AlphaFold can be at modelling domains with no available template information.*

## Background

Proteins are the workhorses of molecular biology – doing most of the biochemistry, immunology, structure building and decoding of DNA in all living organisms. These polymers, built as chains of amino acids, have incredible properties, of which perhaps the most important and amazing is that they spontaneously fold into unique 3D structures, which determine their biological functions. Humans have just over 20,000 different proteins, not counting the wider proteome from alternative splicing, each performing a specific role. Currently complete experimental structures (>90% of protein) have been determined for only ~2% of all human proteins, whilst partial structures are available for almost 22% of these proteins. Modelling, based on the structure of a relative from another species, has provided relatively reliable partial models for about 75% of human proteins. For most other organisms the structural coverage is smaller. Having the protein structures contributes to our understanding of how the protein performs its biological function and is essential, for example for drug and vaccine design. Thus, despite efforts from many crystallography laboratories around the world, there are still many, many proteins (the UniProt protein sequence database now holds almost 210 million sequences) for which 3D structures are not available, in some cases because crystallisation proves difficult.

Ever since the first structure of a protein (myoglobin) was solved by **Kendrew** in 1958 and the realisation from **Anfinsen** that simple proteins folded up spontaneously in the right environment, there have been many attempts to predict the three-dimensional structure of a protein from its amino acid sequence. In 1969, the first homology model was built manually in **David Phillips**' lab, using the recently determined lysozyme structure to model the structure of the related alpha-lactalbumin. Most commonly, however, attempts to predict protein structure from sequence have relied on computational methods ranging from simple statistical methods to advanced hardware-based molecular dynamics simulators.

The emergence of machine learning has had a large impact in many different scientific fields. In fact, machine learning has been used in structure prediction for almost 30 years, but now extremely powerful machine learning methods, called deep learning, are available as a result of both new algorithm development and also efficient and relatively cheap accelerator hardware. In many ways, the protein folding problem is a perfect arena in which to test machine learning technology – it is complex; the data are well organised, freely available and massive; there are well-tested scoring criteria for success (allowing results-oriented learning); the CASP experiment provides an independent assessment process and there is a large community of people working on it. However, machine learning on such large datasets consumes large amounts of computational resources, especially in the training stages.

The challenge of how to predict protein structure from sequence has engaged many scientists over the years, to the extent that every two years there has been an independent assessment of our current ability to get the right answer – the CASP (Critical Assessment of Techniques for Protein Structure Prediction) meeting. This experiment has been coordinated by **John Moult** (University of Maryland) and colleagues (and funded mainly in the US) since its inception in 1993, and has had a profound influence on the field. Every two years, sequences are made available to the predictors, proposed by crystallography labs worldwide, before the structure is determined or at least before the structure has been submitted

for publication. The predictors deposit their model coordinates and once the experimental structure is determined, the predictions are assessed by independent assessors – usually different experts each year. The results are then presented and discussed at the CASP meeting, and then publications from the most successful groups follow about 9 months later. At the most recent experiment (CASP14), over 200 groups deposited results and 67,976 predictions were assessed for 84 targets. To date, targets in CASP have always been predominantly based on single domains, rather than whole chains, but the definition of domains is done *post hoc*, with predictors not being given any information on the domain boundaries beforehand. Assessment, on the other hand, is solely based on the individual domains. The target domains are divided into categories according to the difficulty of the challenge, initially judged by sequence similarity to any available template structures in the Protein Data Bank (PDB), and later on during final assessment according to structural similarity.

Over the years, CASP has accumulated a wide variety of unique metrics to assess the quality of the predictions, which has without a doubt made the results harder to understand by people outside the immediate CASP community. At first, CASP made use of well-known metrics such as RMSD, where the root mean square deviation of the model from the experimental structure is calculated, either on just Cα atoms (the carbon atoms in the backbone to which the sidechains are attached) or all heavy (non-hydrogen) atoms. One of the issues with RMSD is that it is oversensitive to arguably less important differences in structure e.g. in flexible regions such as in long loops or at the termini. RMSD remains the best measure for relatively close predictions, but for '*de novo*' methods, useful cases where methods had managed to capture at least the correct fold were missed when judged by RMSD alone. Consequently, the CASP organisers developed more forgiving metrics that worked across the range of model quality i.e. from 'correct fold level' to 'close to native structure'. The main metric in CASP has become the GDT score, or more precisely the GDT-TS score (Global Distance Test – Total Score). Briefly, the GDT score is based on the fraction of Cα positions that can be superposed to the experimental structure within a particular distance threshold. Rather than choosing a single threshold, however, GDT-TS makes use of four thresholds (1, 2, 4, 8 Å) and an average is taken. So, if you have a poor model where all the Cα atoms can only be superposed to between 4 and 8 Å, which would be more or less random, you would get a GDT-TS score of just 25%, but if all Cα atoms can be superposed to less than 1 Å then you would get a perfect 100% score. A score of somewhere between 40 and 50 generally indicates that a correct fold has been produced. This means that a model with a GDT-TS score of 100 would at least have all its Cα atoms within 1 Å of the equivalent atoms in the experimental structure, but it doesn't necessarily mean perfect agreement. This is certainly a fairly generous metric compared to things like all-atom coordinate error in crystallography, but nonetheless it provides a good way of comparing both hard *de novo* models and easier homology-based models on the same scale.

## Results

To see both how structure prediction at CASP has evolved over time and what AlphaFold's contribution has been, Figure 2 shows some of the trends. This plot is a simplified version of a plot shown by **John Moult** at the CASP14 meeting. The lines show the mean GDT-TS score performance of the groups in various CASP experiments for targets ranging from easy homology modelling targets to hard *de novo* modelling targets. The lowest line shows the state of play at the very first CASP in 1993. One thing that is apparent is even then it was possible to produce excellent models for the easy targets by homology modelling. This is not really surprising, as sequence alignment alone will get you pretty much the right answer for those targets. This doesn't mean that the side chains are correctly placed, of course, and although not discussed here, this certainly has improved across the years that CASP has been running.

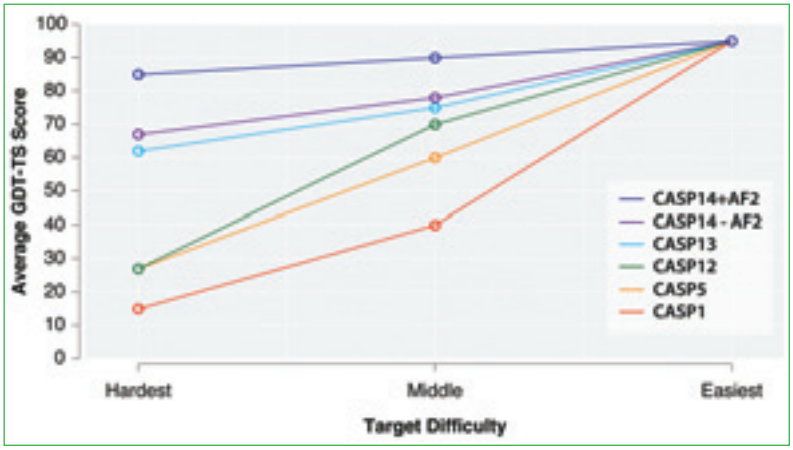


*Figure 2. A comparison of pooled results from CASP experiments since CASP1 held in 1993 to the recent CASP14 held in 2020. Targets are divided into the hardest (de novo targets), middle and easiest (simple homology modelling targets). For CASP14 the results are shown with and without the results from AlphaFold. Data from* ***https://predictioncenter.org/casp14****.*

The first significant progress that took place in CASP was in the middle of the difficulty range. Methods like Hidden Markov approaches to improve sequence alignment, fold recognition to identify distant relatives and fragment assembly methods, to identify fragments of a known fold and stitch them together, had a major impact. This progress more or less stalled between CASP5 and CASP12, however. Also during this time, at least some of the hardest targets remained intractable for all groups until CASP13 in 2018. Two things contributed to this big jump in accuracy. Firstly, with the rapid growth in sequence data banks, amino acid covariation methods had begun to be used in CASP to pick up correlated mutations in multiple sequence alignments. These evolutionary constraints identify amino acids which are close together in the 3D structure and allowed even some hard targets to be modelled accurately. The second development that appeared somewhere between CASP12 and CASP13 is that groups started to make use of deep learning methods to get more accurate information from this evolutionary information. AlphaFold is essentially the pinnacle of both of those advances along with some new ones of its own.

Figure 2 shows the impact that AlphaFold had in CASP14. The top line shows the average performance of all groups in CASP14, and the next line shows the same, but with AlphaFold's models excluded. It's quite clear that AlphaFold alone has produced another step change in our ability to model protein domain folds. It was also very consistent, producing a

model with a GDT score of 90 or more for two thirds of the targets, with a median score of 92.4 for all targets and a median of 87 even for the hardest targets; it also produced the best model for over 90% of the targets. That's remarkable. Of course, it might be tempting to be critical of the fact that AlphaFold never produces a GDT score of exactly 100, and so clearly doesn't reach the accuracy expected of good crystal structures. However, that would be a naïve view. As a good topical example, Figure 3 shows DeepMind's model for ORF8 of SARS-Cov2 compared to Chain A of PDB entry 7jtl, which was the official target structure in CASP14. It's clear that AlphaFold has done a very good job here, with a GDT score of 87, and a Cα RMSD of 1.84 Å. At first sight, it would appear that the model, whilst very good, could have been better. But to put this in context, there is now a second higher resolution crystal structure available for ORF8 with PDB code 7jx6. The resolutions for 7jtl and 7jx6 are 2.04 and 1.61 Å respectively. AlphaFold's model still only has a GDT score of 87 to this new structure, which may not be surprising, but what is surprising is that the maximum GDT score *between the two crystal structures* is also only 87. So, despite the low coordinate error we would expect for structures at this resolution, which conformation is the correct one? Can we call AlphaFold's model incorrect when two independently solved structures of the same small protein do not agree? Now inspection of all these structures clearly shows that the differences in this case come down to the large loop between residues 44 and 68 (visible at the top left of Fig. 3), which is probably flexible and perhaps only adopts a stable conformation when bound to its correct ligand. It's also possible that the loop in the two crystal structures is distorted by different crystal contacts. AlphaFold's model may in fact be a better unbiased estimate of the conformation that the loop adopts in free solution. We don't know.

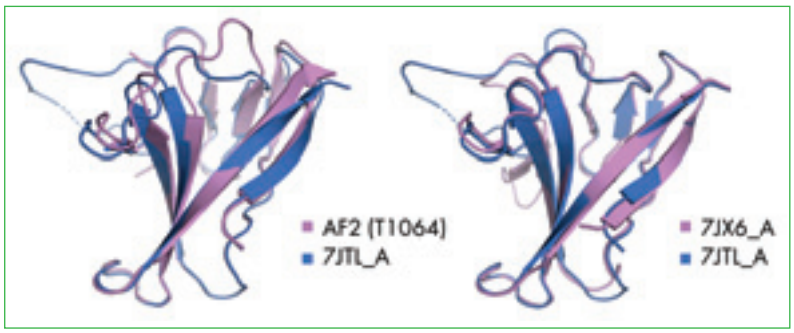


*Figure 3. TAlphaFold's prediction for SARS-Cov-2 ORF8. This is clearly a good model, but there are differences between the model (AF2) and two independently solved crystal structures (PDB structures 7JTL and 7JX6 A chains).*

One very interesting result in CASP14 was that for three or four structures, which the crystallographers were struggling to solve, the AlphaFold models were sufficiently accurate to produce a molecular replacement solution. One such protein was target T1100 (Archaeal Transmembrane Receptor Af1503), provided by one of the CASP14 assessors **(Andrei Lupas** (MPI Tűbingen)). This protein had been sitting "in a drawer" since 2010 with native diffraction data available at 3.5 Å, but despite there being a reasonable template available in the PDB, no phasing model had ever succeeded in producing a solution. The submitted AlphaFold models, however, produced a clear hit and allowed the structure to be determined. This case is interesting because whilst the domain folds of target T1100 were not in doubt, and many groups produced quite reasonable models, the details of the model clearly were important. As one of the assessors, **Nick Grishin** (University of Texas), joked, what AlphaFold got right in this case that nobody else did, were the details. This is evident by the fact that the all-atom RMSD for DeepMind's best model for the complete chain was 2.0 Å, compared to 4.7 Å for the next best group, which is even more impressive when you realize that T1100 is a homodimer and AlphaFold only submitted a single chain model.

## How did DeepMind win CASP?

Obviously, the full details of how AlphaFold works must wait until the paper is published. Other than the CASP results themselves, all we have to go on at the moment is a short presentation at the meeting and some press material. However, even from this limited material, the basics are obvious. In terms of machine learning, AlphaFold uses an attention-based neural network approach. This basically means that the neural networks learn which bits of the data should be focussed on at different stages of prediction. This can be a very powerful approach, but one that requires a lot of computing power. Despite that, however, in other areas, such as automated language translation, attention-based methods produce excellent results. The use of attention, whilst no doubt important, may not be the main conceptual advance. The true secret as to how AlphaFold made such a big jump ahead of the field is more likely down to an even more powerful high-level concept, and one that might radically change the way we do scientific computing in the future.

What DeepMind did that separated them from the pack was that they took the whole CASP prediction process, and numerically optimized the whole thing. This approach is commonly known as differentiable programming, and in this specific application is called *end-to-end protein structure prediction.* Basically, the whole process of competing in CASP was captured in a single neural network system, from extracting contact and distance information from the sequence alignments, through the steps of producing an approximate fold (which is where most of us in CASP stop) and finally through to the very difficult process of refining that approximate fold into an accurate all-atom model. All the way to calculating a final RMSD for all of the models generated, in fact. Each of these steps is usually treated as a separate part of the CASP experiment, but here it was implemented in the form of a set of linked neural networks, which made *the whole process fully differentiable*. In other words, they simply did gradient descent on the whole CASP experiment and were able to come up with an unbeatable system by simply training the system to win CASP. They built a modelling system that had the *theoretical* capability of predicting protein structure at high levels of accuracy, if the optimum parameter settings could be found, and then they basically let the system evolve until it reached the highest level of accuracy. Simple it might sound, and others have proposed more limited approaches along similar lines, but getting all of that to work is still a hugely impressive engineering feat. However, even beyond the engineering challenge, the sheer amount of parameter searching that would have been needed would have been way beyond the computational resources available to most researchers, certainly the vast majority working in academia.

## Limitations of AlphaFold

Without a doubt, AlphaFold's results in CASP14 were remarkably good and certainly represent a major step forward in the field of protein modelling. Nevertheless, the approach likely still has some limitations. To be fair, we can't really say for

sure what limitations it has, because CASP is a very limited experiment. It has to be borne in mind that CASP only looks at a relatively small sample of test proteins. These proteins are selected not because they cover a wide range of problem cases, but simply because they happen to be being solved during the CASP experiment timeline. Given the time constraints, results do not sample important classes of proteins sufficiently to say whether or not AlphaFold is likely to work on that class of protein. Based on current evidence, we simply do not know whether it can handle multimeric structures well or protein-protein complexes at all; it (probably) does not address ligand binding, either small molecules or biological polymers (such as with DNA/RNA/sugars or lipids); and finally, it seems to require very large amounts of computing power to produce its models.

Another fundamental limitation that perhaps has not been emphasized enough is that AlphaFold is dependent on having a reasonably good multiple sequence alignment as input. There is no evidence that (unlike real proteins) it can fold up a single amino acid sequence, but rather that, like other methods before it, it is still exploiting evolutionary information for its predictions. From a purely practical perspective, especially given the rate at which genome sequencing is taking place, this may not be so important, but there will always be niche proteins for which only one or maybe several related sequences can be found. Then there is the problem of modelling the effects of mutations on protein structures, where AlphaFold may or may not produce the same answer as it does for the wild type protein.

A final point to note is that, whilst CASP predictors are invited to submit four models additional to their main model, AlphaFold's best model was not always its top-ranked model, so it is far from omniscient. For all these reasons, therefore, it's simply not possible to say how close AlphaFold is to "solving protein folding". Winning CASP, even by a large margin, has only ever been a necessary but not sufficient condition for anyone to make such a claim. It might be close to a complete practical solution, or a thousand miles away; we just don't know. Far more extensive testing by the research community will be needed before we know for sure how close to that point we really are.

The issue of computational power requirements remains something of a fly in the ointment, also. Although it's usual for large neural networks to require a lot of computational power to train, once trained we normally expect predictions (inference) to be very quick. AlphaFold requires a fairly large amount of computation even to make predictions. Far less than needed to train it, admittedly, but still a lot. We were told that predictions took anywhere from hours on 5 TPU cores (specialised AI processors only available on Google's cloud service) to several days on 40 TPU cores. To put that in perspective of cost, that means it would cost up to 16,000 dollars to model just one large target protein. So, completing even just the remaining human protein structure space would require a lot of time and expense (maybe 50 million dollars or so). Cheaper by far than equivalent experimental work, of course, but still surprisingly resource hungry. Until we get more details on exactly what DeepMind are doing, the question as to why AlphaFold is so expensive to run will remain open. For this reason alone, it may be difficult for DeepMind to make AlphaFold available as a free Web server, say. Also, being a commercial organization, one would not unreasonably expect them to want to generate some income from their work, but how much would a biologist be prepared to pay for a single predicted model generated by such an impenetrable "black box", albeit likely a very good one? Even if AlphaFold is finally released as open source software, which we have to hope for, how easy (or expensive in terms of computational costs) will it be for biologists to run the code? Researchers are going to need massive upgrades in their high throughput computing capabilities to keep up. Answers to some of these questions, at least, will hopefully come after the relevant papers are published.

## Implications for Experimental Structural Biologists

So, what are the implications of this breakthrough for labs currently involved in experimental structure determination? Reactions on social media from crystallographers ranged from the almost ridiculously enthusiastic to something close to panic. Some clearly think that no prediction can ever replace an experimental structure. Some simply do not believe the results, or at least don't believe that they are representative of the problems they are currently working on. At the extreme end is the worry that some may be out of a job. We don't feel that any of these positions make sense. Firstly, AlphaFold certainly represents a step change in our ability to predict the structures of proteins from amino acid sequences. Any biologist who currently uses any kind of protein modelling or structure prediction tool today is only likely to benefit from these new technological developments.

The first challenge for crystallographers will be to test the accuracy of these predictions through a wide range of appropriate test cases. We need to quantify better the accuracy of the predictions and the limitations of the method. Secondly, many crystallographers have unresolved datasets in a drawer like the aforementioned target T1100 – which might find a solution with a more accurate model for molecular replacement. Approaching DeepMind for predictions may well help to resolve many of these structures – using a combination of experimental data and predicted models.

The other big challenge is of course studying protein interactions with all sorts of ligands. Without such knowledge, the interpretation of how the structure determines the function becomes very difficult. The hope is that progress towards improving our ability to predict such interactions using machine learning will also be made using similar techniques to AlphaFold. Currently accurate placement of ligands remains challenging, although it is possible in some situations.

At a broader level, in principle we need to work together towards complete structural coverage of the proteome at least for the model organisms and of course those bacteria and parasites that cause diseases. The combination of predicted and experimental data will surely move us more rapidly towards this goal. One approach (mirroring the Structural Genomics Initiatives of the 90s), would be to have available structures for all identified domains, which are common throughout life. Such an encyclopaedia would accelerate our ability to interpret genomes, proteomes and their biological functions, and in the longer term empower cellular tomography to improve our understanding of the proteome content and its distribution throughout all types of cells.

From our perspective, the most exciting thing about this achievement is that it isn't the end of anything, but is really the beginning of many new things. We are convinced that this will enable the field of structural biology to grow and contribute even more to our understanding of life at the molecular level. Now, where's that grant application form…?

**David T Jones** (UCL)
**Janet M Thornton** (EMBL-EBI)

# BCA-BACG 2021 Joint Spring Meeting

## 29th March-1st April 2021 · Online

https://registrations.hg3conferences.co.uk/hg3/165/home.

## YCG-BACG Early Career Satellite Virtual Meeting

## SESSION DETAILS

### Monday 29 March, 2021

**09.30 – 17.40**

Chairs: **Natalie Tatum (Newcastle) and Tom Roseveare (Sheffield)**

The YCG satellite meeting is an opportunity for all early career researchers in the field of crystallography to present their work in a supportive and friendly environment, which will be run by fellow early career scientists. This year's meeting will be the first joint meeting with BACG early career members and will be held virtually. There will be four sessions of talks on Monday chaired by: session 1: Stephen Dodsworth; session 2: Emma Wolpert; session 3 Natalie Tatum, session 4 Natalie Johnson, along with a short presentations session (chaired by Tom Roseveare and Natalie Pridmore) with presenters given 2-3 mins to present their data (similar to flash presentations).

**09.30 – 10.00**

**YCG Plenary talk**

Speaker: **Cheryl Doherty (GSK)**

***Exploring digital design for pharmaceutical solid forms***

**13.20 – 13.50**

**Parkin Lecture**

Speaker: **Elizabeth Driscoll (Birmingham)**

***The Building Blocks of Battery Technology: Inspiring the next generation of battery researchers***

## BCA Spring Meeting 2022

The Spring Meeting in 2022 will be held at The University of Leeds from 11th – 14th April. The Programme Chair will be **Iain Oswald** from The University of Strathclyde. Iain is currently Chair of the Chemical Crystallography Group of the BCA.

## BCA-BACG 2021 Main Meeting Virtual Programme

### Tuesday 30 March, 2021

**09.45 – 10.00**

**Opening remarks and welcome to the conference**

## 10.00 – 11.30 Parallel Sessions

### Parallel Session 1
### CCG: Advances in Software for Crystallography

Chair: **Lucy Saunders (Diamond Light Source)**
Keynote: **Florian Kleemis (Bern, Switzerland)**

***NoSpherA2: Non-spherical atom refinements for general application***

This session aims to reveal the latest and exciting developments happening in crystallographic software. We encourage abstracts from those in the community working on software for chemical crystallography research. We want to know about the latest tools on offer. This could be in the areas of data processing, structure refinement, property calculation or structure investigation to name a few… and we want to hear about them!

### Parallel Session 2
### BSG: Structure-based drug design

Chair: **Jane Endicott (Newcastle)**
Keynote: **Puji Pathuri (Astex)**

***Fragment-based discovery and characterization of ERK1/2 Inhibitors***

Protein structures can assist drug development at all stages of the discovery pipeline, from choosing targets, through identifying hit matter, to supporting iterative medicinal chemistry to enhance potency, pharmacokinetics and pharmacodynamics. Historically, structure-based drug design has addressed well characterised active sites by identifying potential molecular interactions to inform subsequent chemical synthesis. Application of this approach has already contributed to the development of many potent and selective drugs. However, molecular targets with

clear disease linkage can be extremely difficult to find, and for this reason more is being asked of structures in drug discovery campaigns. Examples of these new contributions include characterising and capturing biologically relevant protein conformations to help in the targeting of allosteric sites, and identifying novel classes of target that depend on protein-protein and protein-DNA/RNA/lipid interactions. The keynote lecture will review key advances in the field over the last decade and future possible directions while reflecting on what a drug discovery campaign looks like from the structural biologist's point of view.

### Parallel Session 3
### BACG: *In situ* monitoring of crystallisation

Chair: Tariq Mahmud (Leeds)
Keynote: Zoltan Nagy (Purdue)

This is an area of growing importance and the session has a broad scope. Historically *in situ* monitoring was largely limited to thermal microscopy. However, with advances in analytics, opportunities at light source facilities, and the development of new techniques, probing the detail of crystallisation is possible. This session is a platform to present studies of this type and demonstrate the new insights that can be glimmered. The scope includes contributions outside the area of diffraction or scattering.

### Parallel Session 4
### BACG: Crystal Growth – theory to practice

Chair: Linda Seton (Liverpool)
Keynote: To be confirmed

The session offers a platform to present our current understanding of crystal growth theory, including the contribution of simulation in understanding the mechanism and control of growth processes. The scope embraces the nature of the crystal growth front, evolution and intervention of morphology and analytical techniques to probe processes, leading to our observed experimental outcomes imparted, through the fundamentals of which we aim to understand this important process.

## 13.30 – 14.30 Parallel Plenary Talks

### CCG Plenary

Chair: Hamish Yeung
Speaker: Franziksa Emmerling (BAM, Berlin)

***Shaken not stirred: enhancing the flavour of mechanochemistry***

### IG Plenary

Chair: Helen Blade (AstraZeneca)
Speaker: Marcus Neumann (Avant Garde Materials Simulation)

***Detecting and avoiding disappearing polymorph cases by crystal structure prediction***

### PCG Plenary

Speaker: Vaclav Petricekval

***The role of crystal structure analysis in investigation of crystals with important physical properties***

### BSG Plenary: Rosalind Franklin Centenary Lecture

Chair: Elspeth Garman (Oxford)
Speaker: Gabriel Waksman (UCL/Birkbeck)

***Mechanism of effector targeting by the Legionella type IV secretion system***

## 15.30 – 17.00 Parallel Sessions

### Parallel Session 1
### PCG: Entropy & Structure

Chair: Anthony Phillips (QMUL)
Keynote: Xavier Moya (Cambridge)

***Giant caloric effects near structural phase transitions***

In recent years, entropy has become an explicit target of materials design and synthesis: configurational and magnetic entropy can stabilise materials' structures or form the basis of their functionality. Understanding such disorder requires a variety of experimental and computational techniques drawn both from the conventional crystallographic arsenal and beyond. In this session we welcome talks on all aspects of order and disorder: quantifying, designing, and exploiting entropy for materials ranging from high-entropy alloys to calorics.

### Parallel Session 2
### CCG: Electron Crystallography

Chair: Simon Parsons (Edinburgh)
Keynote: Lukas Palatinus (The Czech Academy of Sciences)

***Structure refinement from 3D electron diffraction: where are the limits?***

Electron diffraction is one of the mostly rapidly developing and exciting areas of crystallography. The publication of a number of recent papers describing its application in chemical crystallography has led to a great deal of comment and anticipation in the chemical community. The technique enables crystal structures to be obtained from samples with dimensions of the order of a few microns, or even hundreds of nanometres The strength of the interaction between electrons and matter that enables such small crystals to be studied carries with it the problem of multiple scattering, meaning that the kinematical model which has been so successful for X-ray and neutron diffraction no longer applies, and dynamical effects need to be taken into account. This session will give an overview of the most recent advances in the field and of progress towards making electron diffraction a more widely used technique in the chemical crystallography community.

### Parallel Session 3
### BSG: Time-resolved crystallography

Chair: Briony Yorke (Bradford)
Keynote: Jasper van Thor (Imperial)

***Optical control of protein structural dynamics by ultrafast X-ray crystallography***

Time-resolved crystallography allows the observation of molecular mechanism in real time, providing unique insight into the dynamics that link structure and function. The use of X-ray free-electron lasers has pushed the boundaries of time-resolved crystallography, allowing structural changes to be determined with femtosecond time-resolution. The development of serial crystallographic techniques has also initiated a resurgence in synchrotron time-resolved experiments. This session will focus

on the exciting developments being made at free-electron laser and synchrotron sources and the science that has been made possible due to these developments. Contributions describing these and other structural time-resolved methods are welcomed.

### Parallel Session 4
### BACG: Nucleation – theory to practice

Chairs: Bart Vorselaars (Lincoln) and Matteo Salvalaglio (UCL)
Keynote: Klaas Wynne (Glasgow)

Integration of approaches is critical to achieve insight into the influence this step in the crystal growth journey imparts on the crystallisation process. This session will cover all aspects of nucleation, exploring the synergy between theory, simulation and experimental studies, along with novel techniques to probe nucleation.

## Wednesday 31 March, 2021

## 10.00 – 11.30 Parallel Sessions

### Parallel Session 1
### PCG: <3D: Structure and Properties of Low-Dimensional Materials

Chair: Lucy Clark (Liverpool)
Keynote: Maria Grazia Francesconi (Hull)

***One-dimensional oxide and non-oxide materials***

There are many examples of crystalline solids whose structures feature quasi-one-dimensional chains or two-dimensional planes of atoms giving rise to low-dimensional interactions. This results in a diverse array of intriguing physical phenomena, from high-temperature superconductivity in, for example, layered iron arsenides to pronounced magnetocaloric effects in one-dimensional framework solids. Furthermore, since the isolation of graphene, there has been an explosion of activity in the discovery and characterisation of different classes of two-dimensional crystals with remarkable properties that may underpin future advanced technologies. As such, this session is dedicated to showcasing recent developments of crystallography and complementary characterisation methods in the determination of the fascinating structure property relationships in a variety of low-dimensional solids.

### Parallel Session 2
### BSG: Enzymes

Chair: Wyatt Yue (Oxford)
Keynote: Peter Moody (Leicester)

***Using neutron crystallography to watch hydrogens in heme enzymes***

Metabolic enzymes catalyse the biochemical reactions associated with survival and homeostasis in living organisms while the processes governing the behaviour of cells are mediated by tightly regulated cascades and complexes of cell signalling enzymes. Enzymes that perform various types of chemistry are therefore studied intensively in the fields of biochemistry and molecular cell biology. The essentiality of metabolic enzymes is underscored by various genetic and common disorders associated with their deficiency. Enzymes are also central to the field of biotechnology, where they are engineered to manufacture novel products or act upon novel substrates. This session will include examples of work in which structural biology methods are answering important questions relating to the activity and regulation of enzymes, with a view to understanding their functional, biotechnological and therapeutic applications.

### Parallel Session 3
### IG/BACG: Crystal growth/pitfalls and challenges in industrial crystallisation

Chairs: Natalie Johnson (CCDC, Cambridge) and Helen Blade (AstraZeneca)
Keynote: Adam Keates (Syngenta)

***Crystallisation in agrochemicals: The good, the bad and the ugly***

The control and prediction of crystallisation processes is a challenge but vital in many areas of industry. This session will cover practical and computational methods that aim to link understanding with the development of control strategies and predictive approaches. Talks from the perspectives of crystallisation, solid form and characterisation will be welcome.

### Parallel Session 4
### CCG/BACG: Crystal growth of framework materials (incl. MOFs)

Chairs: Nick Blagden (Lincoln) and Michael Zaworotko (Limerick)
Keynote: Michael Zaworotko (Limerick)

Within this session the framework aspects of crystal engineering will be covered. The focus is on MOFs and allied extended networks in clays, zeolites and minerals, along with energy capture and green processing applications.

## 12.00 – 13.00 Exhibition Session and live Q and A chat

### 13.30 – 15.00
### Bragg Lecture

Speaker: Richard Henderson (Cambridge)

## 15.30 – 17.00 Parallel Sessions

### Parallel Session 1
### PCG: >3D: Structure and Properties of Higher-Dimensional Methods

Chair: Phil Lightfoot (St Andrews)
Keynote: Fabio Orlandi (ISIS)

***Superspace formalism and materials properties***

This session targets crystals and materials that go beyond a conventional description using three dimensional axes and indices. This includes aperiodic crystals, quasicrystals and incommensurately modulated crystals, structures, magnetic structures etc. Examples may include compounds exhibiting compositional, structural or spin disorder at the 3D level, but which are amenable to better description and rationalisation using 4D or higher dimensionality. We are interested in examples where the dimensionality may significantly affect materials' properties, as well as in the fundamental description and understanding of the higher-dimensional crystallography.

## Parallel Session 2
## BSG: Computational Biophysics

Chair: Matteo Degiacomi (Durham)
Keynote: Franca Fraternali (King's)

***Protein-protein interactions in health and disease: the importance of 3D structure***

To successfully carry out their task in an organism, biomolecules must interact with their designated substrates in a controlled manner. The function of a biomolecule thus emerges from its specific atomic structure and associated dynamics. Many computational techniques, as diverse as molecular dynamics simulations, homology modelling and protein-protein/ligand docking, can leverage crystallographic data to characterize molecular structure, dynamics and interactions. This session will focus on the application and development of such techniques.

## Parallel Session 3
## IG/CCG: Control & Predictions of Crystals

Chairs: Angeles Pulido (CCDC, Cambridge) and Helen Blade (AstraZeneca)
Keynote: Sten Nilsson-Lill (AstraZeneca)

***A Smörgåsbord of Predictive and Analysis Tools for Crystal Structures. Usage in pharmaceutical industry***

This session aims to cover a wide range of research used to control and predict crystal structures including both experimental and computational tools. Talks will be welcome on the control and prediction of solid forms, particle and mechanical properties, and the session will be open to researchers from a wide range of fields: computational chemistry, informatics, solid state/crystallisation and materials science.

## Parallel Session 4
## BACG: Pharmaceuticals

Chair: Grahame Woollam (Novartis)
Keynote: Susan Reutzel-Edens (Eli Lilly and Company)

All aspects of dosage from selection, pre-formulation considerations and pharmaceutical materials processing are within the remit of this session. The impact of screening, processing and stability on pharmaceutical products, along with system specific examples of hydrates, solvates, salts and polymorphs relevant to dosage forms will be included. Contributions in the area of *in silico* tools for aiding screening and selection are of particular interest.

## 17.30 – 18.30 BCA AGM

# Thursday 1 April, 2021

## 10.00 – 11.30 Parallel Sessions

## Parallel Session 1
## CCG: Chemistry at Extreme Conditions

Chair: Hamish Yeung (Birmingham)
Keynote: Colin Pulham (Edinburgh)

***Putting the Squeeze on Molecular Materials***

Crystallography has traditionally been a major technique with which to understand the structures and reactivity of molecules. This session focusses on how crystallography and other methods can reveal insight into phenomena that occur away from ambient conditions, such as at very high or low temperatures, high pressure or in electric fields. Think bonding, mechanics, distortions, phase transformations, changes in physical properties etc. – *in* and *ex situ* studies allowed!

## Parallel Session 2
## CCG/PCG: Structure Solutions from Powders

PCG Chair: Karen Johnston (Durham); CCG Chair: Jeremy Cockroft (UCL)
Keynote: Kenneth Shankland (Reading)

***Accelerating and enhancing the effectiveness of crystal structure determination from powder diffraction data***

This joint session between the CCG and PCG explores structure solution from powders in a variety of organic, inorganic and mixed organic/inorganic systems. Despite considerable advances in the field, structure solution from powder diffraction is by no means routine and, increasingly, complementary methods are being used to aid structure determination. We are interested in recent examples where structure solution has been aided by complementary methods, including *in situ* and *in operando* techniques as well as total scattering methods. Examples where the combination of experimental and computational methods has resulted in successful structure solution are also of significant interest.

## Parallel Session 3
## BSG: Membrane Proteins

Chair: Bonnie Wallace (Birkbeck)
Keynote: Amandine Marechal (UCL)

***Respiratory supercomplexes: what can we learn from yeast?***

Membrane proteins span a wide range of structural and functional types, ranging from multimeric complexes to monomeric or multimeric channels, receptors, and enzymes They perform very important functions in cells and many are of interest for pharmaceutical development. However, they have proved to be challenging for structural studies due to their amphipathic nature, with both hydrophobic and hydrophilic domains, and the requirement for detergents, amphipols, nanodiscs, and other amphiphiles to solubilise, purify, and stabilise them. This session will include examples of work demonstrating how recent developments in sample preparation and in the complementary techniques of cryoElectron Microscopy and X-ray Crystallography are enabling structural studies of key membrane proteins.

## Parallel Session 4
## BCA/BACG: Crystal Engineering

Chairs: Nick Blagden (Lincoln) and Bucar Kreso (UCL)
Keynote: Bucar Kreso (UCL)

***Respiratory supercomplexes: what can we learn from yeast?***

Within this session the molecular, non-framework aspects of crystal engineering will be explored. The main focus will be the influence the supramolecular process imparts to the crystal science of these materials, and contributions are invited from areas including solid form, particle properties and gel to crystal transformations.

## 12.00 – 13.00 Poster Session and live Q and A

### 12.00 – 13.00
## Lonsdale Lecture
Speaker: Lucy Clark (Liverpool)

### 13.30 – 15.00
## BACG Annual Lecture and Medal Talk
Each year the BACG invites an individual who has made a significant contribution to crystal science to present The BACG Annual Lecture on a topic of interest to the community.

# 13.30 – 15.00 BCA Early Career Prize Lectures

# 15.30 – 17.00 Parallel Sessions

## Parallel Session 1
## PCG: Phase Transitions
Chair: Lewis Owen (Cambridge)
Keynote: Joe Hriljac (Diamond Light Source)

***Phase transitions in zeolites driven by pressure and ion exchange***

Phase transitions are of critical importance to our understanding of a material's structure and its physical and chemical properties. This session will aim to explore a broad range of structural phase transitions; from crystalline solid state transformations to crystalline-amorphous transitions. Particular interest will be placed on novel characterisation including novel experimental set-ups and techniques (e.g. Bragg diffraction, PDF, NMR etc.), data-processing methodologies, and structural parametrisation.

## Parallel Session 2
## BSG: Protein-Protein Interactions
Chair: Richard Bayliss (Leeds)
Keynote: Elton Zeqiraj (Leeds)

***Structure and function of ubiquitin signalling complexes***

Cellular processes depend entirely upon interactions between proteins, either for the transient or regulated recognition of one molecule by another in interaction networks or the stable assembly of individual proteins into higher order complexes. Specific molecular recognition in protein-protein interaction networks is crucial in cell signalling while protein complexes function in cells as molecular scaffolds, hubs for cell signalling or as molecular machines carrying out concerted functions. This session will include examples of work in which structural biology methods have been used to determine the molecular basis of interaction between proteins and their assembly into multiprotein complexes.

## Parallel Session 3
## CCG: Hot Structures
Chair: Charlie McMonagle (ESRF)
Keynote: Sven Lidin (Lund)

***The simple, the challenging and the confusing: Making sense of complexities in reciprocal space***

In this session we look at the latest hot structures coming from the chemical crystallography community. These could be those found at very high temperatures (hot, hot, hot) or that feature an exciting design element or neat properties.

## Parallel Session 4
## PCG/BACG: Biominerals and Biomaterials / Carbonaceous Materials
Chair: Julia Parker (Diamond)
Keynote: Melinda Duer (Cambridge)

***The Bare Bones of Biomineralization: new insights into bone mineral composition, structure and formation***

From the exquisite morphologies of coccoliths and the incredible hierarchical architecture of bone, to the engineering of implants and joint replacements, the structure of biominerals and biomaterials plays an integral role in determining their properties and function. This session will examine the importance of structure in both natural systems and biomedical devices, explore how their composition and assembly controls physical properties and look at how this can be exploited in the development of novel bio-inspired materials.

# Physics World 2020 Breakthrough of the Year

**THIS annual award has gone to an international team for creating a silicon-based material that emits light at wavelengths used for optical telecommunications[i]. Silicon might be the wonder material of electronics, but its specific structure can be critical. In its normal cubic diamond structure, its indirect band gap means it's a poor light emitter. However, predictions have suggested that in a *hexagonal* structure, a silicon-germanium alloy would have a *direct* bandgap and could be an efficient light emitter. This team have realised this prediction by developing hexagonal Si-Ge nanowires that do indeed emit light at practical wavelengths, and which, in addition to applications in optical computing and telecomms, might also be used to create new chemical sensors.**

Structure-based advances were also central to four of the nine other highly commended breakthroughs: the discovery of a ferroelectric nematic liquid crystal phase[ii]; a thin-film perovskite extremely sensitive X-ray detector[iii]; dispersion- and diffraction-free light propagation in twisted layers of 2D α-$MoO_3$[iv] which has implications for nano-imaging and low energy optical signal processing. And at last: a room temperature superconductor![v]

So 50% of the top ten advances shortlisted by Physics World depended critically on structure.
***Crystallography is alive and kicking!***


References:
i. E.M.T. Fadaly *et al. Nature* **580**, 205 (2020).
ii. X. Chen *et al. Proc. Nat. Acad. Sci.* **117**, 14021 (2020).
iii. H. Tsai *et al. Science Advances* **6**, eaay(0815) (2020).
iv. G. Hu *et al. Nature* **582**, 209 (2020).
v. E. Snider *et al. Nature* **586**, 373 (2020).

# BCA 2020 AGM Minutes

## Draft minutes of the 2020 Annual General Meeting of the British Crystallographic Association

Zoom Webinar 13:00, Thursday 18th June 2020

1. **Approval of Agenda**
   The agenda was approved; proposer: Elspeth Garman, seconder: Charlie McMonagle.

2. **Apologies for absence**
   No apologies received.

3. **Minutes of the previous AGM 2019**
   These were published in the December 2019 issue of Crystallography News and also on the website. No corrections were needed and the minutes were accepted. Proposer: Charlie McMonagle, seconder: Helen Playford.

4. **President's report**
   The President, Simon Phillips, started with the sad report of the loss of a Founder member of the BCA with a few details; Michael Woolfson (1927-2019) Fellow of the Royal Society (1984) and recipient of many prizes and also the loss of BCA Honorary Life member and Editor of Crystallography News (2008-2019) Carl Schwalbe (1942-2019).

   The President welcomed John Finney (UCL) as the new editor of Crystallography News and thanked Simon Coles for his contributions in keeping the newsletter running so efficiently and seamlessly in the interim period.

   Congratulations were given to Elspeth Garman who had been awarded the Eleventh Max Perutz Prize of the ECA in recognition of her invaluable contribution to the field of macromolecular methods and for monitoring and mitigating radiation damage in protein crystals.

   Thanks were given to Tom 'Ed' Edwards, Simon Parsons, Hg3 and teams for dealing with rescheduling the Spring meeting in the midst of the COVID-19 crisis. The 2021 Spring Meeting will be held in Leeds, 29th March – 1st April as a special joint meeting of the BCA and British Association for Crystal Growth (BACG). The 2022 Spring meeting will be held at the University of Sheffield, 11-14th April 2022 with Richard Cooper (University of Oxford) taking on the role of Programme Chair.

   The President thanked the BCA Officers: Simon Parsons, Alex Stanley and Elizabeth Shotton and especially Elizabeth who is retiring from Council this year. The Education and Outreach Coordinator (EOC) Simon Coles who is also retiring this year was thanked, especially for his recent work on Crystallography News. The members of the BCA Council were thanked for their input, enthusiasm and willingness to endure long Council meetings. Thanks were also given to John Finney, the new editor of Crystallography News, Nicola Hardaker and all the team at Hg3 and to all the BCA members for their continued support of the Association.

   The President presented the slides of the EOC, Simon Coles (absent) for an update on education and outreach activities: Points covered included that EOC were looking to migrate learn.crystallography.org.uk/learningresources/ to github, and that no applications for the outreach bursary scheme had been made. For the International Year of Crystallography there was a collaboration between the CCDC and BCA to populate the online periodic table. It was reported that this was nearly complete with worldwide author participation and that there would be a competition for best element. RSC funding to develop educational resources based on this was mentioned, though the report was unclear whether this was being applied for or had been awarded. Finally a Battlecard game was developed and launched as a part of the online Southampton Science and Engineering Festival (SOTSEF); it is available from the CCDC website.

5. **Secretary's report**
   The Secretary, Alex Stanley, reported that the September Council meeting utilised video conferencing facilities in order to reduce travel costs and time. It was successful.

   It was reported that there is a future plan to increase exhibitor attendance (and income) by creating a marketing brochure to promote the benefits of exhibiting at the Spring meeting.

6. **Hg3 Report**
   The Hg3 representative, Nicola Hardaker, reported that the total BCA membership as at 28th May 2020 was 565 and the names of the corporate members were given. Crystallography News has the following current advertisers: Bruker, Oxford Cryosystems and Rigaku Oxford Diffraction (all issues), ICDD (March and September). Thermofisher (June only).

   The cancelled Spring meeting had 147 registrations prior to cancellation with 71 delegate registrations carried over to 2021. Out of 22 originally registered, 15 Plenary/keynote speakers carried over to 2021 as did 10 of the 18 exhibitors. Leeds University has agreed to carry over the deposit to 2021 and did not hold us to any cancellation fees. Georgina Rosair enquired about accommodation to which the reply was that all booked accommodation had been cancelled without charge and would need to be rebooked for the following year. John Helliwell added a note that the IUCr committed to a poster prize for the Spring meeting of which he was in possession. Similarly, the ACA had also committed to sponsor a poster prize for structural dynamics.

7. **Report of the Treasurer including presentation of the Accounts for 2019 and Examining Accountant's Report**
   The Treasurer, Elizabeth Shotton, reported that a copy of the account summary for the period from January 1st to December 31st 2019 had been circulated and a full breakdown of the accounts was included in the BCA annual accounts available by email or online at the Charity

Commission website. Summaries of the income, Spring meeting finances and outgoings (governance and charitable expenditure) were presented.

Looking at last 3 years the Spring meetings made a small surplus in 2017 and 2018 but 2019 made a significant loss. This was reviewed by the Treasurer and Hg3 and it was discovered that the complicated structure for registration rates was the cause of the budgeting issues. As a result, registration rates were simplified for the 2020 Spring Meeting. One of the advantages of Leeds as the venue for the 2020 meeting was that the accommodation would be independent and off-campus, further simplifying the budgeting. Due to the cancellation of the Spring 2020 meeting it is estimated that there is a non-recoverable loss of approx. £14,000. Full details will be available in next year's accounts.

For the governance expenditure, administration fees and expenses were lowered, and the accounting fee was lower due to all groups submitting their accounts in good time. Elizabeth Shotton thanked all the treasurers of the groups for their timely responses.

In response to a question submitted in Q&A by Elspeth Garman, the Treasurer answered that our insurance explicitly stated that we are not covered for losses in the event of a pandemic. Iain Oswald indicated that the fees for printing and stationary were double in 2019. The Treasurer agreed to investigate this and return a response.

In summary, the aim continues to be to try and reduce the governance costs and to maintain a cautious, balanced investment of funds. Although we incurred a surplus over the year, 2020 is likely to have a deficit due to the cancelled meeting. Members were urged to encourage colleagues to join the BCA as membership is our lifeline, and also to encourage their students to apply for bursaries. Thanks were given to Hg3, Council members, BCA group treasurers, Charles Stanley Bank and UHY Hacker Young accountants.

The accounts were accepted; proposer: Iain Oswald, seconder Jeremy Cockcroft.

8. **Appointment of the Examining Accountant for 2019**
The proposal was to appoint the Young Company with an annual fee of £5400. This was approved; proposer Iain Oswald, seconder Jeremy Cockcroft.

9. **Elections to Council**
The President reported that elections had been carried out by electronic ballot. BCA members were notified by email that voting had opened and provided with a personal link to the voting site. The results were as follows:

| | |
|---|---|
| Treasurer | Claire Naylor (2020-2023) |
| BCA Council Ordinary member | Anna Warren (2020-2023) |

It was highlighted that in 2021 there would be elections for President, Education & Outreach Coordinator and an Ordinary Member. Candidates are identified by the Nominating Committee or by BCA members and nominations are made to the Secretary, with a deadline of 30th September 2020. For 2020-2021 the nominating committee is Chris Frampton (Chair), Phil Lightfoot, Elspeth Garman, Lee Brammer and Chick Wilson.

10. **Honorary members**
Honorary members are chosen for their contributions to both crystallography and to the BCA. There are no new Honorary Life Members for 2020. The nomination deadline for 2021 honorary members was given, August 31st 2020. Nominations should be sent to the BCA President with a brief case for support of not more than 400 words. Nominations will be considered at the September Council meeting. New honorary members may not be awarded every year and there is a maximum of two in any calendar year.

11. **Membership, annual subscriptions and subventions**
Membership figures were presented showing a high of over 800 members in 2003, a low of less than 400 in 2012 and a slight decline of recent years to 552 members at 31st December 2019. The President encouraged members to encourage colleagues to join.

12. **Equality, Diversity and Inclusivity (EDI) report**
The BCA EDI policy was adopted in March 2018 and the President restated the policy on a slide and that the intention is to ensure quality and equality. Programme Committee members for 2021 were also encouraged to be mindful of this and invited feedback to the President. Since there was no Spring meeting, figures were reported for the membership from 2019 (estimated) with student members 48% female, Young Crystallographers not including students 47% female and standard members 28% female (128 female, 324 male). Programme Committee members and speakers at the current (and previous) Spring meetings were also given; for 2019 the main meeting figures were as follows (YCG in parentheses), percentages given are female: Programme Committee 53%, plenary speakers 29 (0)%, keynotes 44%, speakers 38 (36)% and chairs 37 (25)%.

13. **Proposals to update the Statutes & By-Laws**
Three proposals were sent to the membership ahead of the AGM, outlining proposed updates to the BCA Statutes and By-Laws. The first was to propose including the option of holding an electronic AGM should the need arise. The second was to define more clearly how the minutes are kept during the AGM and the third related to updating the language in the Statutes and By-Laws to remove any gender-specific references.

John Finney identified that the phrasing of the following under item 1. Electronic AGM could be improved.

***Members will be informed at least two weeks prior to the date of a meeting if it is to be held electronically and provided with joining instructions.***

Due to technical issues, this was not addressed in the meeting.

The proposals were approved by anonymous electronic Poll: 34 people took part. 33 approvals and 1 abstention.

14. **AOB**
Lindsey Sawyer asked how many members are present to which the response was 45 (a quorum is 15). Elspeth Garman thanked the panel for making the virtual AGM possible. Iain Oswald asked if there are any guidelines with respect to fees for virtual (winter/autumn) meetings for the groups.The answer was no, not at the moment. Tony Bell asked if the BCA was planning to bid for any future IUCr world congress. The response was no but that Council has been asking people to think about it as the lead time is long. The next bid to be prepared would be for 2028. Elspeth commented that even the ECM has a four year lead time.

The President thanked the panel for helping set up the electronic AGM and everyone for attending.

The meeting closed at 13:45.

# PCG-ISIS / CCG / BSG Group Meetings 2020

## PCG and the ISIS Crystallography Group

**THIS annual meeting, 2-3 November 2020, held jointly between the PCG and the ISIS Crystallography Group and with contributions from the Diamond Crystallography Group, has become a popular fixture in our November calendars.**

In 2020, the coronavirus pandemic meant that it was not possible to hold the meeting in its usual format. Nevertheless, feeling that a day devoted to everyone's favourite topic (structural science!) would be a very welcome distraction from everything else going on in the world, I decided we should go virtual.

I reduced the length of the sessions to mitigate Zoom fatigue (a concept of which most of us, I'm sure, were blissfully unaware this time last year!) and, with some trepidation, sent out an invitation to the community. Would anyone want to come? More importantly, would anyone want to give a talk?

I needn't have worried. I received an amazing response, with over 100 people from all over the world registering for the meeting, and all 16 talk slots filled with a great variety of science.

The first speaker was **Mark Senn** (Warwick), whose talk focused on studying the structure of layered perovskites in order to understand their phase transitions and the physical properties that are closely coupled to subtle structural features. He explored an intriguing case of a second-order phase transition in a hybrid improper ferroelectric, and ultimately concluded that entropic differences between phases, arising from dynamic octahedral tilts and rotations, were the root cause of this observation. The perovskite theme continued with **Wesley Surta** (Liverpool), who began by telling us that there are no lead-free canonical relaxors and ended, after a journey through Rietveld analysis and maximum entropy methods, by revealing that the subject of his talk, KBMN ($(K_{1/2}Bi_{1/2})(Mg_{1/3}Nb_{2/3})O_3$), is in fact an example of a lead-free canonical relaxor!

Next, **Jakob Ahlburg** (Aarhus) treated us to something completely different with a talk about the development of an induction furnace for use on the Polaris neutron diffractometer at ISIS. Sometimes it's necessary to get your sample really hot really fast, and induction is the way to go, although making the technique neutron compatible poses a unique set of challenges.

**Anna Herlihy** (Warwick/ISIS) brought us back to perovskites with an example of a manganite that exhibits an unusual coupling between orbital ordering and ferroelectricity, and whose complex local structure, as revealed by X-ray pair distribution function (PDF) analysis, is apparently at odds with its long-range average structure.

It was during Anna's talk that I recorded the highest number of attendees – 92!

After a tea break (sadly, all attendees had to provide their own refreshments!) we were introduced to the world of lithium-conducting disordered rock-salts by **Maria Diaz Lopez** (Diamond). These materials are particularly interesting for practical applications because lithium ions can move in and out without a phase transition. Sticking with disordered materials, **Adam Sapnik** (Cambridge) was next, with an interesting example of *in silico* polymerisation used to produce an atomistic model of an amorphous metal-organic framework (MOF) and its comparison with PDFs of both the amorphous MOF and its crystalline counterpart. Next, **Gabriel Clarke** (Warwick) presented a fascinating example of an *in situ* diffraction experiment where diffraction patterns were collected under an applied electric field in order to elucidate the mechanism of a hybrid improper ferroelectric. The final speaker of day 1 was **Fi MacIver-Jones** (Edinburgh), whose work on uranium-containing minerals aims to provide better understanding of the stability of these phases that are used to "lock up" soluble uranium species in the solid state and prevent further contamination of the environment.

Day 2 was kicked off by **Ivan da Silva** (ISIS) whose talk explored the strategies he uses to study the structures of porous materials. It was a case of "No single crystal? No problem!" as Ivan talked us through the process of structure solution from powder data. **James Annis** (Warwick) was next, with an example of nanocrystalline cerium germanates that required the combination of both X-ray and neutron diffraction data to properly determine their structures. It was a worthwhile reminder that even an excellent fit to X-ray diffraction data is not always sufficient to call a structure solved!

**Ashok Menon** (Uppsala), joining us all the way from Sweden, revisited rock-salt derived lithium conductors. He discussed the challenges involved in studying layered materials that exhibit both intra- and inter-layer cation disorder and stacking faults, and reminded us of the importance of synthesis route as he found the cation distribution in a sol-gel derived material was far more homogeneous than that in a sample made by solid state reaction. The final speaker before a well-deserved coffee break was **Sam Moody** (Durham), whose knot-in-a-rope analogy for a topologically protected state was probably the clearest I've ever come across. He discussed the observation of strange split magnetic skyrmions in zinc-doped $Cu_2OSeO_3$ and its explanation using a mixed-phase model.

Suitably refreshed, we explored the concept of non-negative matrix factorisation (NMF) with **Harry Geddes** (Oxford). As explained by the analogy of an experienced music producer being able to easily identify the individual parts of a track, NMF is a tool for breaking down complex patterns (e.g. diffraction or total scattering data) into their component parts. Harry discussed possible applications of the method, in particular the example of *in operando* studies of functional materials.

Frustration was the name of the game next, or at least magnetic frustration, with **Alasdair Bradford** (St Andrews) discussing two apparently isostructural oxalate-based magnets, with a strong two-dimensional character arising from a layered structure. Using a combination of elastic and inelastic neutron scattering and muon spectroscopy, surprising differences between the materials were observed, and a more detailed picture of the mechanisms governing these types of systems has been developed. The penultimate talk was given by

**Struan Simpson** (Aberdeen), who continued on the theme of magnetic materials with a barium-containing 6H perovskite. Neutron diffraction data revealed an unexpected phase segregation at low temperature, which was traced back to the magnitude of octahedral tilting. The tilting could in turn be related to the oxygen stoichiometry, suggesting that the material separates into oxygen-rich and oxygen-deficient regions below the transition temperature.

They say you should always end on a high, so it was fitting that the final talk from Hanna Bostrom (Stuttgart) featured the use of high pressure to explore structural distortions in Prussian blue analogues. The "Prussian blue family tree" was a particular highlight for me, and it was interesting to see how small compositional differences can lead to big changes in behaviour under compression.

Overall I thoroughly enjoyed the virtual Winter Meeting, and while I very much hope the 2021 edition can return to an in-person format, I am incredibly grateful that the community was still able to come together to celebrate physical crystallography (and related subjects) in this way.

**Helen Playford**
ISIS Instrument Scientist & PCG Secretary

# Chemical Crystallography Group (CCG)

**THE British Crystallographic Association Chemical Crystallography Group (CCG) hosted their Autumn Meeting on Wednesday 18th November 2020. The event took place in one day, and due to the current limitations on gatherings it was held virtually.**

The first session was chaired by **Lucy Saunders**, deputy chair of the CCG, and began with the plenary speaker **Rachel Crespo-Otero** from Queen Mary University of London, who described her work modelling photochemical processes in organic crystals. In this presentation Rachel used embedded modelling techniques to compare the differences between solution verses solid-state relaxation pathways upon excitation. Rachel used a crystal engineering approach to improve emission properties of the materials investigated. In the first instance she compared three related propeller-shaped molecules and clearly showed that in both concentrated solution and the solid state the emission can be quenched. This is nicely explained by showing that in the solid state, selected torsions are hindered which leads to increasing the energy of excited states and therefore decay via this route is restricted, resulting in brighter emission. In a second study, the radiative pathway was investigated by substituting 2-hydroxchalcone (HC) and 2-hydroxyphenylpropenone (HP) with different functional groups. By changing functional groups, selected radiative pathways were prohibited and therefore an in-depth understanding of the excited state mechanics and quantum yields was achieved.

The second speaker was **Ed Broadhurst** from the University of Edinburgh who presented some impressive and ambitious work in studying polymorph evolution during crystal growth using 3D electron diffraction. Ed and co-workers were able to clearly identify different polymorphs of glycine during crystal growth and follow them as they interconverted within minutes of crystal formation. The advantages of using electrons to study such dynamical chemical processes on crystals grown *in-situ* was clear, including the ability to detect processes on shorter timescales than has previously been possible using solid state NMR. The use of such cryoTEM approaches to chemical crystallography offers substantial promise for a huge range of fundamental and technical advances in the pharmaceutical industry and beyond. Recent developments in the application of dynamical scattering models to the refinement of electron diffraction data were discussed in the follow-up question and answer session.

The final speaker before lunch was **Eleanor Jones** from the University of Strathclyde, who provided a very clear presentation on some of her work involving pressure-induced phase transitions in isonicotinamide polymorphs. The material is used in a wide variety of supramolecular applications, making it a good candidate to probe the effect of pressure on polymorphism. The research involved utilising multiple techniques to study the single-crystal to single-crystal transformation of this system, including microscopy, Raman spectroscopy and single crystal diffraction. One particularly important finding is that the pressure needed to be increased gradually to ensure crystallinity is maintained. The result was a dramatic evolution not only of crystal structure, but also in the macroscopic morphology of the crystal itself.

While the online format has some advantages in opening up participation, sadly for lunch, participants had to rely on their own resources. 'Highlights' included macaroni pie, beetroot on toast and some questionable sushi, but at least there were no queues for the coffee.

After lunch, the session was chaired by **Iain Oswald** and began with the CCDC CCG Younger Scientist Prize being formally awarded to winner **Karen Robertson** from the University of Nottingham. The prize was awarded by **Andrew Maloney** from the CCDC. In her talk, Karen provided a clear and entertaining tour of her career path and research highlights in recent years. Her research focusses on developing a range of crystallisers for specific materials and modes of self-assembly including cooling, pH, reactive and anti-solvent crystallisation. She showed how these crystallisers can be directly used with online analytical techniques such as confocal Raman spectroscopy as well as how the design can be adapted for techniques including online X-ray diffraction. The types of materials she applies these techniques to include pure phase polymorphic small molecule organics, co-crystals, coordination polymers, and metal-organic frameworks. She presented some particularly impressive results showing how single crystals can be probed in this uniquely dynamic environment.

*Figure 1: CCDC CCG Younger Scientist Prize-winner **Karen Robertson**, preparing to give her lecture.*

The second speaker in this session was **Rebecca Scatena** from the University of Oxford, who presented her work investigating formate-mediated magnetic superexchange in

the model hybrid perovskite $[(CH_3)_2NH_2]Cu(HCOO)_3$. She used a combination of powder elastic neutron scattering and single crystal magnetometry measurements to determine the ground state magnetic structure to analyse both antiferromagnetic and ferromagnetic interactions, while the charge density distribution and orbital occupancy were determined by high-resolution X-ray diffraction. This analysis of the chemical bonding allowed for detailed correlation between structural, electronic, and magnetic properties in the system. Importantly, she showed that the Goodenough–Kanamori–Anderson rules, which are often employed to predict magnetic exchange in purely inorganic perovskites, can be applicable to these hybrid organic-inorganic materials.

The final speaker before the tea break was **Rosemary Young** from the University of Nottingham, who described her work on investigating reactive metal complexes in metal-organic frameworks (MOFs), including solvent-induced isomerism. In one system Rosie was able to post-synthetically modify a Mn-based MOF with $Mn(CO)_5Br$. Upon irradiation with visible or UV light, the framework released carbon monoxide, which was accompanied with visible colour change from yellow to white. Impressively, during the transformation, the MOF retained crystallinity and the process could be followed using FTIR or *in-situ* X-ray diffraction experiments.

Following the tea break, the last scientific presentation of the day was given by **Nick Funnell** from ISIS, who presented a high-pressure investigation of the well-known polymorphic material 5-methyl-2-[(2-nitrophenyl)amino]-3-thiophenecarbonitrile, often abbreviated to ROY owing to its red, orange and yellow polymorphs. Nick used a combination of high-pressure diffraction and hybrid density functional theory to demonstrate that despite the abundance of polymorphs observed at ambient pressure, no transitions have yet been observed with pressure. This suggests large kinetic barriers to interconversion that may rationalise the high degree of polymorphism observed at ambient conditions. His work shows nicely that the origin of colour in this system may well be more complicated than simple changes in molecular conformation, involving a significant role from intermolecular interactions.

The day concluded with a virtual AGM of the CCG. Despite the change in format of the Autumn meeting to online, more than 70 people registered for the conference, with some even attending from as far afield as Perth in Western Australia. Clearly the online nature of the meeting allowed many people to attend who would not otherwise have been able to travel for an in-person meeting. Though it's clear many of us look forward to meeting in person in future, it was great to see that an online event can be so successful in disseminating such a wide variety of science amongst the community.

*Figure 2: Some of the speakers preparing to give their talks from home. l-r:* ***Eleanor Jones, Rosemary Young*** *and* ***Nick Funnell.***

**Mark Warren** (Diamond Light Source)
**Helena J. Shepherd** (University of Kent)

# Biological Structures Group (BSG)

**"Celebrating Rosalind Franklin's 100-year Birthday: New Structures, New Challenges"**

**THIS year the meeting, held on 18th December 2020, was organised by Kate Brown (Cambridge) and Mark Roe (Sussex), who both did an excellent job of assembling a really fascinating programme of first-class speakers. The meeting was held virtually for the first time and had a historical emphasis on the many pioneering achievements of Rosalind Franklin, as well as the role of today's structural biology in combatting the current coronavirus pandemic.**

Following opening remarks by the chair of the first session, **Kate Brown** (Cambridge), the meeting began with a very interesting historical lecture by **Matthew Cobb** (Manchester) entitled: *The life and times of Rosalind Franklin*. The speaker described how Franklin studied chemistry to Ph.D. level at Cambridge from the late 1930s to mid-40s before moving to Paris for post-doctoral studies on X-ray diffraction of coal with Jacques Méring. The speaker explained how Rosalind's early work had been greatly influenced by Adrienne Weill, a former student of Marie Curie. In 1951 Franklin was awarded a fellowship to return to the UK and work with John Randall at King's. The post was initially described as being on structural studies of proteins, but was later changed to DNA. The speaker explained that, whilst Randall oversaw a truly outstanding research team, communication was somewhat impeded by Franklin's well-known rift with Maurice Wilkins, with whom she was supposed to work initially. This disunity appears to have worked in favour of the Crick and Watson team in Cambridge, who published the first correct model of DNA, based on a sneak-preview of the key fibre diffraction pattern obtained by Franklin's Ph.D. student, Ray Gosling. Nevertheless, these studies by the King's and Cambridge teams led to several very famous papers in Nature with Rosalind as co-author in 1953.

Franklin then moved to Birkbeck where she worked on plant viruses and later polio in the department of J. D. Bernal. Here she obtained a prestigious (multi-million in today's money) NIH grant in 1957 (source: wikipedia), but very sadly passed away from ovarian cancer in the Spring of 1958. Her research was continued by contemporaries, colleagues and students whom she had supervised at Birkbeck in the 1950s, including Aaron Klug, Don Caspar and Ken Holmes, leading to several Nobel prizes.

Next, this year's early-career prize lecture, entitled: *Developing new tools for time-resolved crystallography*, was given by **Briony York** (Bradford) who began by describing the timescales on which various biomolecular processes occur. The speaker then described how pump-probe experiments allow studies to be performed on the nano-second timescale and how the use of multiplexing in data collection and the Hadamard transform give an improved signal-to-noise ratio. Briony then outlined the field of serial crystallography in which hundreds of thousands of micro-crystals are destructively exposed to an intense pulsed beam. As time-resolved studies tend to involve crystals being exposed for longer times, they require a synchronised way of initiating the reaction, such as the use of photolabile groups. The speaker then described studies of the enzyme aspartate decarboxylase and concluded by outlining experiments being undertaken at Diamond Light Source on UV-induced damage in the eye-lens protein γ-crystallin, to gain an improved understanding of

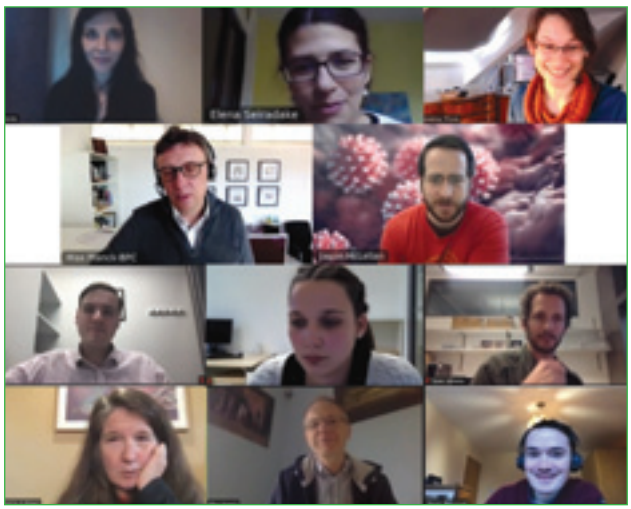

*Figure 1: Speakers from top:* ***Briony Yorke*** *(Bradford),* ***Elena Seiradake*** *(Oxford),* ***Andrea Thorn*** *(Hamburg),* ***Patrick Cramer*** *(Göttingen),* ***Jason McLellan*** *(Austin, Texas),* ***Donald Benton*** *(Crick),* ***Tânia Custódio*** *(Hamburg) and* ***Sjors Scheres*** *(Cambridge) along with session chairs in the bottom row:* ***Kate Brown*** *(Cambridge),* ***Mike Hough*** *(Essex) and* ***Simon Newstead*** *(Oxford).*

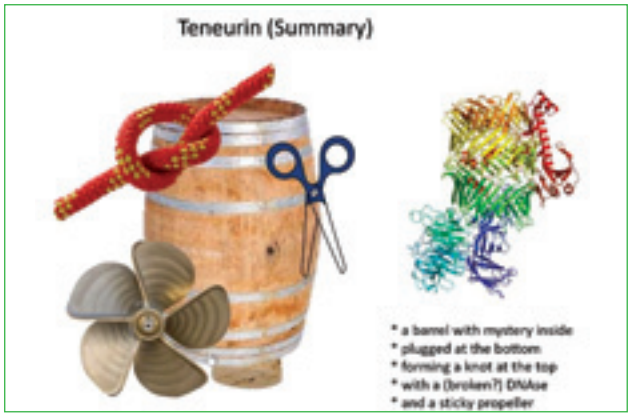


*Figure 2: A slide from the lecture by* ***Elena Seiradake*** *(Oxford)*

cataract formation. Next, **Elena Seiradake** (Oxford) gave a presentation entitled: *Receptor-ligand complexes in the brain: combining structural and biological methods to understand the biology*. She described the techniques involved in immunofluorescent staining of brain slices and gave a review of the different receptor types before outlining her studies of the intriguing protein, teneurin. This 200 kDa synaptic cell-adhesion molecule is found in the hippocampus and appears to have evolved in early eukaryotes by gene fusion with a bacterial toxin. The speaker described structural studies of a complex this protein forms with latrophilin 2 and outlined a model for the roles of teneurin, latrophilin and the protein FLRT in guiding cortical migration, the movement of neurons to their final locations in the brain.

After lunch, Session 2, which was chaired by **Mike Hough** (Essex), began with a presentation by **Andrea Thorn** (Hamburg) entitled: *The coronavirus structural taskforce: a 2020 effort*. The speaker outlined the setting up of the Coronavirus Structural Taskforce in the spring of 2020 in response to the SARS outbreak and to utilise the many experimentalists rendered home-bound by the pandemic. The aim of the taskforce is to validate deposited coronavirus structures determined by X-ray crystallography, NMR and EM, and, if necessary, reprocess, remodel and re-refine them, making the new structural data available for improved structure-based drug and vaccine development. The team also conducts simulation studies and has a very

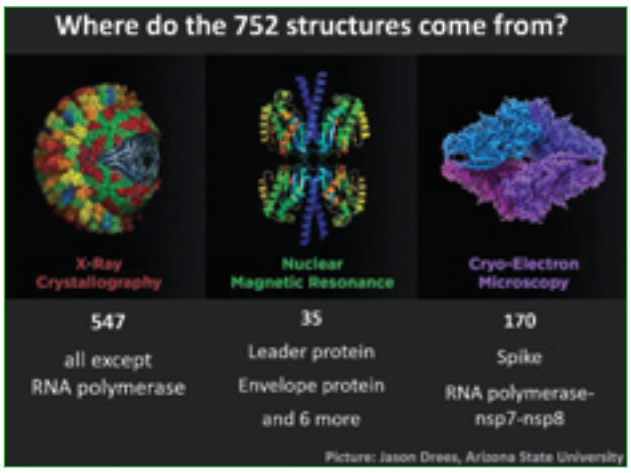


*Figure 3: The work of the Coronavirus Structural Taskforce was presented by its leader* ***Andrea Thorn*** *(Hamburg).*

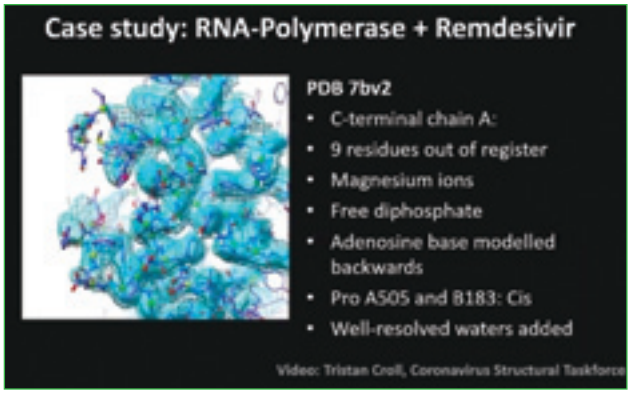


*Figure 4: A re-determination of one of the SARS CoV-2 targets by the Coronavirus Structural Taskforce.*

interesting educational website (**https://insidecorona.net**). The talk concluded with an account of the group's work on improving a published drug-bound structure of the SARS-CoV-2 RNA-dependent RNA polymerase, which was originally studied by EM. The next lecture was given by **Patrick Cramer** (Göttingen) and was entitled: *Coronavirus RNA polymerase: structure and inhibition by remdesivir*. He explained how coronavirus has the largest genome of all RNA viruses and is unusual in that its RNA polymerase has proofreading activity, which stops many antiviral agents from being effective. The speaker described progress on structure analysis by cryo-EM of the enzyme bound to a trojan-horse inhibitor, remdesivir.

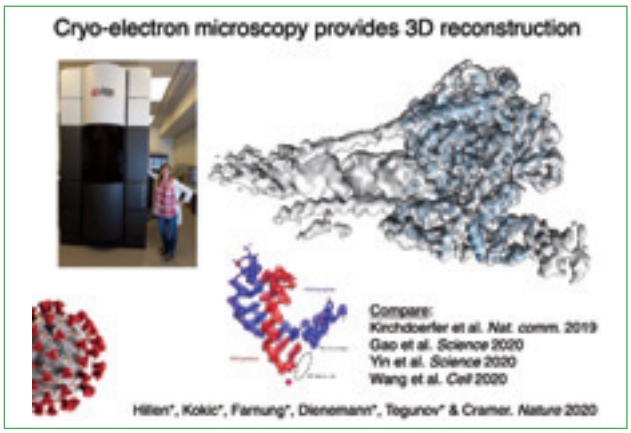


*Figure 5: Patrick Cramer (Göttingen) spoke on the structure and inhibition of the coronavirus RNA polymerase analysed by cryo-electron microscopy.*

This compound is administered as a prodrug and becomes triphosphorylated within cells where it acts by stalling the viral RNA polymerase due to steric hindrance. The speaker emphasised that this compound is not a chain termination inhibitor and its effects can be overcome by increasing the substrate concentration.

The final lecture in this session was given by **Jason McLellan** (Austin, Texas) and was entitled: *Development of antibodies and vaccine antigens for SARS-CoV-2*. The speaker gave an interesting account of the origin of the term 'coronavirus' which stems from a very brief 1968 letter to Nature suggesting that the 200 Å petal-shaped projections from the viral surface, which are visible by EM, are redolent of solar corona. These projections are, of course, made of the spike proteins which are the targets of the newly developed vaccines. Jason explained how the S2 spike protein undergoes a large conformational change from a compact pre-fusion state to a very elongated fusion state which is the infectious form. The aim of the project was to generate mutants of the spike protein which stabilised its compact pre-fusion state as a basis for therapeutic antibody- and vaccine-development. Initially, they worked on MERS, but switched to SARS-CoV-2, as soon as its genome was released. Proline scanning mutagenesis of the spike protein yielded a two-proline mutant with high levels of expression and immunogenicity. Interestingly, this form of the protein has been used in most of the ongoing vaccine development work. These studies also resulted in a 4 Å resolution EM structure of the S2 spike protein being determined and shed much light on the dynamics of its structural transitions. The mutant protein has also been used to generate camelid single-domain therapeutic antibodies (see below) and further work has yielded an improved EM structure for a hexa-pro mutant which has even greater immunogenicity.

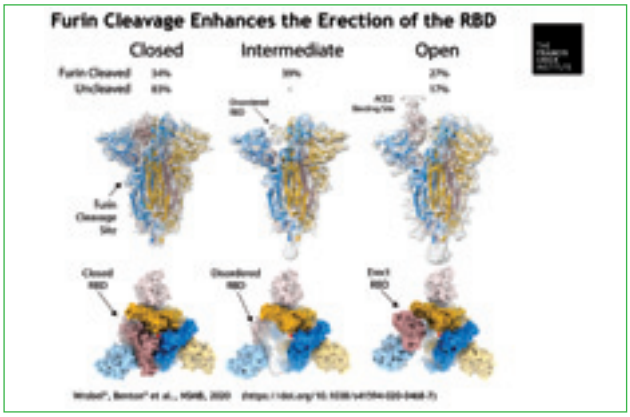


*Figure 6: **Donald Benton** (Crick) emphasised the role of the subtilisin-like protease furin in activation of the SARS-CoV-2 spike protein.*

After a much-needed coffee break, Session 3, which was chaired by **Simon Newstead** (Oxford), began with a lecture by **Donald Benton** (Crick) entitled: *Structural basis of SARS-CoV-2 receptor binding*. The speaker described further EM structural studies of the covid S1/S2 spike protein assembly and the complex that S1 forms at the cell surface with angiotensin-converting enzyme-2, otherwise known as the ACE2 receptor. Donald showed a movie of how the receptor binding domains (RBD) of the spike protein project towards the three ACE2 molecules which are bound to it. This causes a conformational change that exposes the membrane fusigenic region of the spike protein. These studies were undertaken with the now very abundant G614 covid variant of the spike protein which also possessed the same two stabilising proline mutations described by the previous speaker. The next lecture was given by **Tânia Custódio** (DESY/EMBL, Hamburg) who spoke on: *Selection and structural analysis of synthetic nanobodies neutralizing SARS-CoV-2*. The speaker described the use of antibodies derived from *Camelidae* such as camels, llamas and alpacas which consist of single antigen-binding domains. These nanobodies have great therapeutic potential as pathogen-neutralising agents, not least in the current pandemic, and have been used as tools for crystallisation of membrane proteins. Tânia described SAXS and cryo-EM studies of a complex between the covid prefusion spike protein and the synthetic nanobody, or sybody, Sb23 which has nanomolar affinity for the RBD domain. The speaker mentioned that fusion of sybodies improves their affinity further.

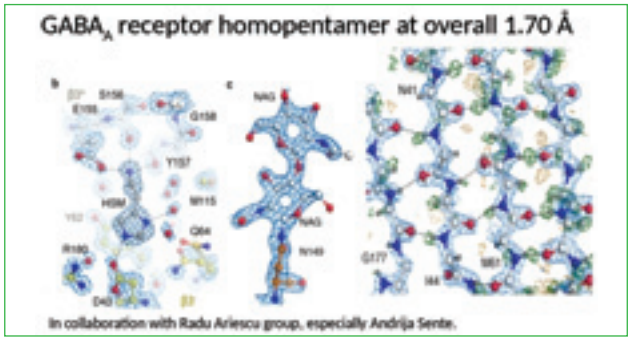


*Figure 7: Density for individual hydrogen atoms in the EM structure of the GABA$_A$ receptor presented by **Sjors Scheres** (Cambridge).*

The closing lecture of the meeting was given by **Sjors Scheres** (Cambridge) and was entitled: *Cryo-EM single-particle analysis to atomic resolution*. The speaker summarised recent developments in the high resolution cryo-EM field including advances in direct detectors and image processing. Further progress includes the study of beam-induced motions and Bayesian polishing, as well as corrections for optical aberration and curvature of the Ewald sphere, the latter being very significant for larger particles. Sjors explained how the resolution in EM is limited by radiation damage, sample heterogeneity and misalignment as well as the envelope function in the contrast transfer function. Sources of noise include the detector itself, ice, charging, shot-noise and inelastic scattering. The speaker described the very new instrumentation that was used in this particular study, namely a Falcon 4 detector, a Selectris energy filter and a cold field emission gun. This microscope was able to achieve a resolution of 1.22 Å with mouse apoferritin, easily revealing the positive electrostatic potential of individual hydrogen atoms in difference maps. A similar study of the GABA$_A$ receptor yielded a structure for this membrane protein at 1.7 Å resolution, again with convincing difference map features for hydrogen atoms. This, of course, raises very exciting prospects for structure-based drug design for membrane receptors using the cryo-EM technique.

This concluded an exceptionally interesting meeting for which the speakers must be sincerely thanked for their excellent presentations. The organisers **Mark Roe** (Sussex) and **Kate Brown** (Cambridge) must also be congratulated for their hard work and organisational skills. In addition, the BSG is very grateful to **SWISSCI** for their generous sponsorship of the meeting, which was attended by around 40 members. Attendees had the opportunity to meet with each other in smaller groups during three excellent online networking sessions, which were held between and after the scientific sessions.

**Jon Cooper** (UCL) & **Shabir Najmudin** (King's)

# Down Memory Lane – A Y290 on the western edge of Europe[i]

**IN August 1981 a small ad in Chemistry in Britain placed by Professor George Ferguson advertised a Hilger and Watts Y290 for £5,000. I contacted George in Guelph about buying it and he stressed that a Weissenberg camera was needed to get data collection started on the Y290. I knew of a long forgotten Weissenberg camera that was lying in a cupboard in another University in Dublin. I got permission to use the Weissenberg and I was sure that it could be added to one of the spare X-ray windows on our JEOL PXRD. I went to Professor Frank Coll, the head of the Chemistry Department in Galway, and said to him that we had recently spent more than £5,000 each on IR spectrometers and that I thought I could set up single crystal diffraction in Galway for £5,000. He told me that the University accountant would give me a cheque for £5,000 and he wished me good luck.**

With my long-time friend and colleague **Des Cunningham** I went to Guelph and we stayed for a week with George Ferguson learning how to operate the Y290. We gave George the cheque and he told us that John Ralph had serviced the Y290 in Guelph and that we should get him to come to Galway when we had the machine setup.

We had absolutely no funds and setting up the Y290 in Galway could not have been done without the help of many people, especially Professor Philip Walton from the physics department[ii] who had experience with X-ray generators, Kevin Carey of Digital Equipment in Galway and John Ralph. The existing X-ray setup in Galway had one generator connected to JEOL PXRD and XRF machines. Philip said he knew where there was a high voltage switch and 20 meters of HV cable which was out of use in one of the hospitals. To illustrate the type of practical help provided I have indicated in figure 1 the setup we had and the HV switch labelled S.

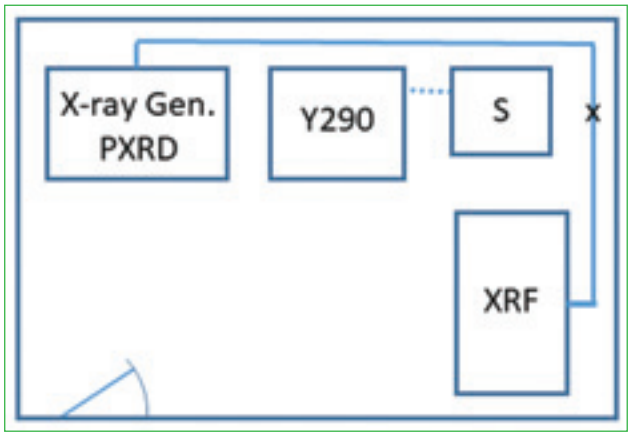


*Figure 1: The set up we had. The HV switch is labelled S.*

I said to Philip: "we don't have any connectors for the ends of the HV cable at the X-ray tube or the switch". He said: "I will get one for the tube made up in the workshop" and then he picked up the cable at the point marked x, cut it with his penknife, stripped the cut ends, pushed the wires into the HV sockets on the switch and filled the sockets with oil.

The other great asset we had in Galway was the only Digital Equipment factory outside the U.S. I realized that we had a serious problem with the teletype in that it would not work with 50 Hz ac. I contacted Kevin Carey and asked him if he knew anyone who had a teletype and he told me that the Colaiste Iognaid secondary school in Galway[iii], known locally as the "Jes", had been given a PDP11 and a room full of VT52 terminals by Digital and that they had teletypes for an older system which was now redundant. There can't have been many schools that had that level of computer facilities in the early 1980s. A few years later Digital gave all Galway second level schools login facilities to a large computer in Galway. When we got the Y290 working, any faults the PDP8 developed were repaired by Kevin Carey who would come during lunch hour and quickly find the flip chip where the fault was. John Ralph had told us that we were lucky not to have a straight 8 which had discrete transistors rather than the 7400 series logic DILs which we had.

I believe that Hilger & Watts built 25 Y290s and then ceased production. John Ralph bought the rights and built 2 further machines, one of which he sold to Max Perutz at MRC Cambridge and the other to the Pasteur Institute in Paris.

The Y290 was operated using a teletype which was used to read in the programs from paper tape and punch the output onto paper tape. A full data set required a tea chest full of paper tape. We soaked the paper tape roll before use with Mazola cooking oil to lubricate the punch. We could not afford X-ray diffraction film for the Weissenberg so we used out of date hospital X-ray film. The paper tape was a lot of trouble and it was just possible to read the tapes into the University DEC20 computer. We collected data on about 50 crystals this way but to speed things up we needed to automate the Y290 operations and stop using Weissenberg unit cell data. I learned some machine code programming using an Acorn Atom microcomputer and a PDP12 manual. I asked the University accounts department for a loan of £400 to buy a BBC micro and then set about upgrading the Y290.

## Automating the Y290

I wrote what I now know to be a disassembler program for the PDP8 on the Acorn Atom and analysed the PDP8 programs.

The plan devised depended on making a tiny alteration to the BIN LOADER program.

The PDP8 RIM loader program was loaded with the data switches and RIM loader was used to load BIN LOADER. BIN LOADER could then read in the programs needed to operate the Y290 from paper tape. BIN LOADER had a go address of 7777. All of the Y290 programs had a go address of 0200.

The last instruction in BIN LOADER was HALT. By great good fortune there was a location on the same page as the HALT instruction which had 0200 in it. I changed HALT to JUMP INDIRECT/ the location containing 0200.

We left the data switches at 7777 and three reed switches were attached to the STOP, LOAD ADDRESS and START

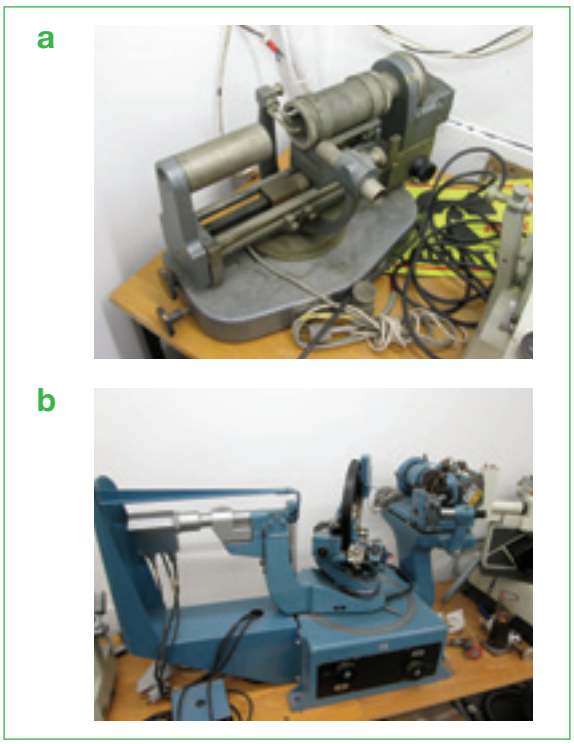


*Figure 2: The retired Weissenberg (a) and Y290 (b) in 2020.*

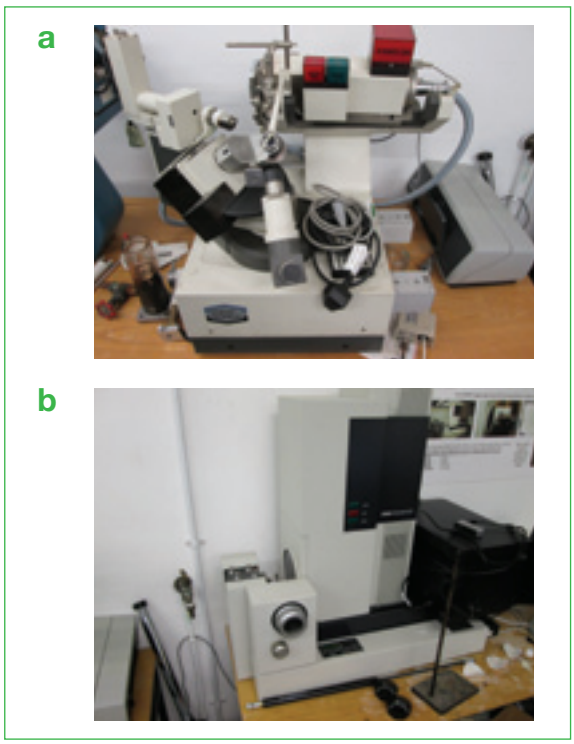


*Figure 3: The CAD4 (a) and MAR image plate (b) in 2020.*

switches. The three reed switches were connected to three of the PIA pins on the BBC micro. Thus the BBC micro could by operating STOP LOAD ADDRESS and START run the BIN LOADER to get the PDP8 to read a program the BBC micro sent to it. The program would then auto start when it reached the JUMP INDIRECT (0200). Complete automation!!! and it worked. Seamus Kellehan, a member of the chemistry department technical staff, built several of these "interfaces" and we sold enough of them at a modest price to repay the University accounts department.

## Getting rid of the need for unit cell and reflection data from the Weissenberg

The plan here was to use the Weissenberg to obtain a random orientation rotation photograph. This would be a curved version of the way other diffractometers used a flat Polaroid Camera to take random orientation photographs. In such a photograph each reflection can appear four times and the x and y values of these spots can be used to calculate Theta and Chi for each reflection. Setting these values on the Y290 allowed Phi to be obtained by spinning the Phi axis until the reflection is found. The second thing that was required was to incorporate the Busing and Levy 4-circle geometry calculations[iv], least squares on the cell dimensions and unit cell transformations into a FORTRAN program. Rex Dark of the mathematics department in Galway had a look at the Busing and Levy paper and said it should be OK. A few days later Rex returned with 7 pages of neat fountain pen equations and matrix transformations and asked if he could have a set of 12 reflections to try it out. I gave him a reflection set and started to write the FORTRAN version of Rex's equations. I had not got very far with the programming when a few days later Rex returned to say that it worked and he handed me many pages of tiny writing. I asked him how he did it, did he use a calculator? "No" he said "I used 7 figure log tables". This was an astonishing feat. The final version of this program was called BRVCEL[v], and I know that BRVCEL was in use in the Royal Military College in Shrivenham during the worst of the troubles in Northern Ireland.

The BBC micro-driven Y290 increased the number of structures to about 200. It was the first 4-circle diffractometer in Ireland north or south and was eventually replaced by a CAD4 which was the second 4-circle diffractometer in Ireland. The CAD4 was replaced by a MAR image plate, the first area detector system in Ireland, which had the Y290 tube shield and monochromator as its X-ray source. The Y290 and the CAD4 were used together for a while and we found that the ESDs on the cell dimensions were better on the Y290. This was a testament to the angle setting accuracy of the Y290 Moiré fringe method which was not affected by gear train wear or slack. The least squares part of BRVCEL was written by Tim Higgins and it showed up some errors in the first version of the unit cell least squares program that came with the CAD4. BRVCEL lives on in the Oscail software package which uses some of its subroutines to check and transform unit cells[vi].

**Patrick McArdle**
National University of Ireland Galway

### References:

i. http://www.nuigalway.ie/crystallography/
ii https://www.google.com/search?source=univ&tbm=isch&q=professor+philip+walton&sa=X&ved=2ahUKEwiClZ_6n7HrAhXTTBUIHUrnDvsQ7Al6BAgJEBk&biw=1920&bih=888#imgrc=hduz-axdil4RIM
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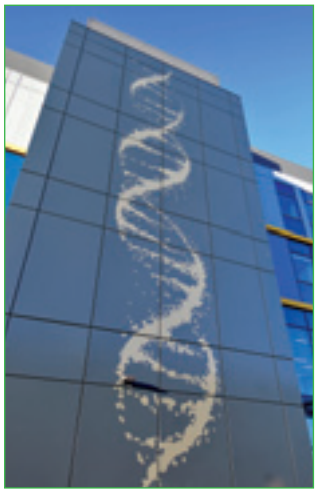
iv. Busing, W.R. and Levy, H.A. 'Angle calculations for 3- and 4-circle X-ray and neutron diffractometers'. *Acta Crystallographica* **1967**, 22, (4), 457-464.
v. Higgins, T., Dark, R., McArdle, P. and Slmmie, J. 'BRVCEL—A computer program for cell reduction and Bravais lattice determination'. *Comput. Chem.* **1990**, 14, (1), 33-36.
vi. McArdle, P. 'Oscail, a program package for small-molecule single-crystal crystallography with crystal morphology prediction and molecular modelling'. *J. Appl. Crystallogr.* **2017**, 50, (1), 320 – 326.

# Rosalind Franklin Institute reaches key construction milestone

**THE £40m Hub building which will house The Rosalind Franklin Institute on the Harwell Campus has reached practical completion. The Institute will now commence specialist scientific fit out to create a lab environment which is capable of supporting some of the world's most sensitive research equipment.**

The Rosalind Franklin Institute (www.rfi.ac.uk) aims to transform life science through interdisciplinary research and technology development. It will bring together researchers in life, physical science, and engineering, to develop disruptive new technologies designed to tackle major challenges in health and life sciences. These technologies will be housed in the Hub at Harwell alongside 200 researchers, including collaborators from academia and industry. Researchers will occupy the Hub as soon as the laboratory fit out and installation of research equipment is completed.



Specialist labs for imaging, mass spectrometry, structural biology and chemistry have been designed to promote collaboration. Research already underway at The Franklin on the Harwell Campus and in spokes around the UK has led to the development of nanobodies against SARS-CoV-2, breakthroughs in imaging biological samples using electrons, and the development of chemistry techniques which can enable proteins to be modified within cells.

Professor James Naismith, Director of The Franklin, has commented that "Our scientists coming together in the building for the first time will deliver scientific firsts impacting across the UK nations. By doing so we will honour the legacy of our namesake Rosalind Franklin and try to be worthy of bearing her name."

# *CrystEngComm* celebrates the Cambridge Structural Database in a special issue

**THE journal *CrystEngComm* has published a special issue[i] to mark the Cambridge Structural Database (CSD) reaching 1 million structures, with 33 papers that highlight the breadth of applications made possible with these data.**

This themed issue of *CrystEngComm* comprises articles which highlight some of the many applications of the CSD in celebration of the one millionth crystal structure, a significant community achievement in 2019. The research carried out by the authors demonstrates the breadth of information and the variety of applications arising from the data in the CSD. It also illustrates how, over the last half a century, the complexity and size of structures have expanded, and the techniques and instrumentation used to determine new structures have evolved considerably. The published articles show how far the field has evolved.

To date, the CSD is comprised of 43% organic structures, including drugs, agrochemicals, pigments, explosives and protein ligands, and 57% metal organic structures, including MOFs, catalysts and porous frameworks for gas storage. It is used by pharma companies, start-ups and academic institutions, and retains links to other key datasets including the Protein Data Bank, Drugbank, PubChem and more. The CCDC are investing heavily in a database evolution project to ensure the CSD is flexible and extensible to deal with the growing volume, types and uses of structural chemistry data.

The CCDC celebrated the special issue with a short series of webinars last January, jointly organised with *CrystEngComm*. This "Behind the paper" series invited authors to share the story of how their work started, and where it will go next.

The editorial for this special issue can be found at https://pubs.rsc.org/en/content/articlelanding/2020/CE/D0CE90154G#!divAbstract .

**Reference:**

i. *CrystEngComm* **43**, 7143 (2020)

# Meetings of interest

**IN** the continuing pandemic situation, many meetings are being cancelled or postponed. At the time of writing, all the meetings listed here were scheduled to go ahead either in-person or online, but there are likely to have been further changes since going to press. Further information may be obtained from the websites given. Assistance from the IUCr website is gratefully acknowledged.

Note that many online meetings charge little or no registration, so if there's a topic that's of particular interest you might check it out. Also, some meetings listed with a location may be running a mixed in-person/online format.

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

**29th Mar 2021 – 1st Apr 2021**
British Crystallographic Association Spring Meeting
Online conference.
**https://registrations.hg3conferences.co.uk/hg3/165/home.**

**12th Apr 2021 – 14th Apr 2021**
Directing Biosynthesis VI
Edinburgh, UK.
**https://www.rsc.org/events/detail/39023/directing-biosynthesis-vi**

**18th Apr 2021 – 23rd Apr 2021**
Imaging Materials with X-Rays – Recent Advances with Synchrotron and Laboratory Sources
Seattle, WA, United States.
**https://www.mrs.org/meetings-events/spring-meetings-exhibits/2021-mrs-spring-meeting/call-for-papers/detail/s21/ct03/Symposium_CT03**

**23rd Apr 2021 – 27th Apr 2021**
Crete 2021 – 1st International Cryo-EM Symposium/Workshop
Heraklion, Crete, Greece.
**https://cryoemcrete.com/**

**4th May 2021 – 5th May 2021**
PDB50: Celebrating the 50th Anniversary of the Protein Data Bank
Online.
**https://www.asbmb.org/meetings-events/pdb50**

**14th May 2021 – 16th May 2021**
10th International Conference of the Hellenic Crystallographic Association
Athens, Greece.
**https://sites.google.com/view/hecra2020/home**

**6th Jun 2021 – 17th Jun 2021**
Zurich School of Crystallography 2021: Bring Your Own Crystals
Zurich, Switzerland.
**https://www.chem.uzh.ch/linden/zsc/index.html**

**14th Jun 2021 – 18th Jun 2021**
16th International Conference on Surface X-ray and Neutron Scattering (SXNS16)
Lund, Sweden.
**https://www.sxns16.org**

**15th Jun 2021 – 18th Jun 2021**
17th European Powder Diffraction Conference – EPDIC17
Šibenik, Croatia.
**https://www.epdic17.org/**

**23rd Jun 2021 – 25th Jun 2021**
MOFs for Energy and the Environment: Faraday Discussion
Manchester, UK.
**https://www.rsc.org/events/detail/40612/mofs-for-energy-and-the-environment-faraday-discussion**

**29th Jun 2021 – 2nd Jul 2021**
AFC 2020: Congress of the French Association of Crystallography
Grenoble, France.
**https://afc2020.afc.asso.fr**

**4th Jul 2021 – 10th Jul 2021**
6th European Crystallographic School (ECS6)
Online.
**https://www.ecs6.chemcryst.hu/**

**7th Jul 2021 – 9th Jul 2021**
Challenges in Biological Cryo-electron Microscopy: Faraday Discussion
Sheffield, UK.
**https://www.rsc.org/events/detail/40005/challenges-in-biological-cryo-electron-microscopy-faraday-discussion**

**12th Jul 2021 – 15th Jul 2021**
15th International conference on materials chemistry (MC15)
Dublin, Ireland.
**https://www.rsc.org/events/detail/43710/**

**12th Jul 2021 – 30th Jul 2021**
23rd National School on Neutron and X-Ray Scattering
Online.
**https://neutrons.ornl.gov/nxs**

**18th Jul 2021 – 23rd Jul 2021**
11th Liquid Matter Conference
Prague, Czech Republic.
**http://www.lmc2020.cz/**

**30th Jul 2021 – 4th Aug 2021**
71st ACA Annual Meeting
Online conference.
**https://www.amercrystalassn.org/future-meetings**

**7th Aug 2021 – 9th Aug 2021**
Applications of Synthetic Crystals in Medicine (SCM2021)
Changsha, China.
**http://www.hiesrs.com/page15.html**

**9th Aug 2021 – 14th Aug 2021**
IUCr2020 Computing School
Nove Hrady, Czech Republic.
**https://www.xray.cz/iucr/workshops/nh/default.htm**

**11th Aug 2021 – 13th Aug 2021**
School on SAXS/SANS and BioSAXS/BioSANS Data Analysis
Kutná Hora, Czech Republic.
**https://www.xray.cz/iucr/workshops/kh/default.htm**

**11th Aug 2021 – 14th Aug 2021**
Electron Crystallography School
Tabor, Czech Republic.
**https://www.xray.cz/iucr/workshops/tabor/default.htm**

**12th Aug 2021 – 14th Aug 2021**
TOPAS Intensive Course
Prague, Czech Republic.
**https://www.xray.cz/iucr/workshops/topas/**

**14th Aug 2021 – 22nd Aug 2021**
Twenty-Fifth Congress and General Assembly of the International Union of Crystallography
Prague, Czech Republic.
**http://www.iucr2020.org/**

**6th Sep 2021 – 8th Sep 2021**
Understanding Crystallisation: Faraday Discussion
Leeds, UK.
**https://www.rsc.org/events/detail/41849/understanding-crystallisation-faraday-discussion**

**8th Sep 2021 – 10th Sep 2021**
Peptide-Membrane Interactions: Faraday Discussion
London, UK.
**https://www.rsc.org/events/detail/37143/peptide-membrane-interactions-faraday-discussion**

**12th Sep 2021 – 17th Sep 2021**
15th Biennial Conference on High Resolution X-Ray Diffraction and Imaging (XTOP 2020)
Minsk, Belarus.
**https://www.xtop2020.atomicus.by/**

**16th Sep 2021 – 18th Sep 2021**
23rd Heart of Europe Bio-Crystallography Meeting (HEC23)
Vierzehnheiligen, Franconia, Germany.
**https://www.hec23.uni-bayreuth.de/en/index.html**

**19th Sep 2021 – 23rd Sep 2021**
23rd European Symposium on Quantitative Structure-Activity Relationship
Barcelona, Spain.
**https://www.euroqsar2020.org/**

**11th Oct 2021 – 14th Oct 2021**
International Conference on Materials Science and Engineering 2021
Brisbane, Australia.
**https://www.materialsconferenceaustralia.com/**

**16th Dec 2021 – 17th Dec 2021**
Italian Crystal Growth 2021 - Crystal Growth: from Theory to Application
Torino, Italy.
**https://www.icg2020.net/**

**17th Jan 2022 – 22nd Jan 2022**
Third Pan African Conference on Crystallography
Nairobi, Kenya.
**https://pccr3africa.org/**

**29th Jul 2022 – 3rd Aug 2022**
72nd ACA Annual Meeting
Portland, OR, United States.
**https://www.amercrystalassn.org/future-meetings**

**21st Aug 2022 – 26th Aug 2021**
CMD29 (Condensed Matter Division of the European Physical Society)
Manchester, UK
**http://cmd29.iopconfs.org/Home**

**23rd Aug 2022 – 27th Aug 2022**
Thirty Third European Crystallographic Meeting (ECM33)
Versailles, France.
**https://www.ecm33.fr/**

# The Cambridge Crystallographic Data Centre 2021 User Group Meetings

**THIS year the CCDC will be hosting User Group Meetings virtually. We have followed the feedback received from the 2020 Global UGM and chosen to break up the day, so we could focus on one topic per meeting. We are happy to announce the dates of the events below.**

- **Educators: 16 and 17 March**
- **Science Day: 26 May - hear from the CCDC Ph.D. Students**
- **Discovery Science: 9 and 10 June**
- **Material Science: 7 and 8 September**

All User Group Meetings are open to everyone that wishes to join. You can find more details about each meeting and register to attend by visiting the CCDC events webpage: **https://www.ccdc.cam.ac.uk/News/Events/**

If you would be interested in presenting your work which uses the CSD or CCDC tools in any of the above areas, please send a brief 150-word abstract to **hello@ccdc.cam.ac.uk**.

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