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LETTER FROM THE PRESIDENT

President's Letter – Fall 2024



Group photo from The International School on Fundamental Crystallography, which took place before the LACA VI meeting. Photo given by Massimo Nespolo.

Santiago García-Granda

The summer and early autumn of 2024, like every year between congresses, has been a period of implementation of the changes and transformations resulting from the decisions that were taken at our last General Assembly, a period in which the continuation of the scientific debate is transferred to the Regional Associations.

The IUCr Executive Committee, the Finance Committee and our Commissions and Committees have been working in their respective areas with a specific focus on our next global meeting in Calgary, Canada in 2026.

The administrative heart of our Union, in Chester, is behind all of this activity, keeping the activity of the Union orderly in the service of global structural science. This involves maintaining the momentum of our editorial force, which is so important for the maintenance of scientific programs, support for young researchers and the promotion and dissemination of structural science through our 'Open Labs', and for the establishment of new infrastructure in the most disadvantaged regions. Among these are the initiatives in the LAAAMP environment for building new light sources and the Laboratories for Structural Science in Benin and Jamaica. Vice-President Graciela Diaz is the IUCr representative on the LAAAMP Executive Committee.

Following the implementation of more frequent Executive Committee meetings, taking advantage of the ability to meet online, with bimonthly face-to-face meetings, the Finance Committee has adopted the same model, while incorporating two advisors with profiles that complement those of its statutory members. Ilia Guzei and Ed Mitchell, who were already advising the Finance Committee on its decisions, have now been incorporated as advisors.

The Finance Committee is doing a good job in containing expenses consistent with fulfilling our mission and obtaining the maximum return on our investments.

Given the importance of the various dissemination projects throughout the world and in order to provide a channel for response to requests for support, the Executive Committee has created an Advisory Committee to evaluate, in an agile and fair manner, the various requests for support; this committee is chaired by the Past-President.

I have had the opportunity to attend and participate in various meetings and congresses of the Regional Associations. Last July in Denver, after the meeting of the Executive Committee and the Finance

Committee, where we had the opportunity to discuss the preparations for the 27th General Assembly and Congress in Calgary, we were also able to exchange projects with the Council of the American Crystallographic Association during its 74th meeting.

Later, at the end of August, the meeting of the European Crystallographic Association (ECM34) took place in Padova in combination with the meeting of the European Powder Diffraction Conference (EPDIC18), a very fortunate combination that had not occurred since 2010 at the Darmstadt congress.

At the end of September, I had the opportunity to represent the IUCr at the meeting of the Latin American Crystallographic Association (LACA) in Montevideo.

All of these meetings of our Regional Associations have been extraordinarily satisfactory, not only in the high quality and variety of the research that was presented, but especially in the high proportion of young researchers, the initiatives to increase the influence of women scientists and the growing connection of structural science with society and sustainability.

Unfortunately, this year I shall miss the Asian Crystallographic Association (ASCA) meeting, which takes place at the beginning of December in Kuala Lumpur, Malaysia, but I will be at the African Crystallographic Association meeting in Algeria in April 2025 and will be present at the 2025 ASCA meeting.

As a consequence of the generational changes in our Chester office, Louise Jones has been promoted to the new position of Head of Publishing Operations, and we have recruited a new person to fill the position of Head of Publishing Strategy. Kezia Bowman is now responsible for the publication of this *Newsletter*, in addition to her other duties.

An important step in the incorporation of new blood into the IUCr has been the first meeting of a group of young researchers in structural science, this meeting was attended by young scientists proposed by the five Regional Associations, together with our CEO Alex Stanley, Louise Jones, Manfred Weiss and myself. This inaugural meeting was highly satisfactory and inspiring for the future of the IUCr. A calendar of actions was designed for the full operation of this group and for its gradual incorporation into the various bodies and commissions of the IUCr before its formal approval at the 27th General Assembly. This movement and its success will be fundamental for the future of the International Union of Crystallography and the maintenance of our leadership in structural science.

The International Science Council (ISC) Elections Committee presented a shortlist of candidates for renewal of the ISC Governing Board. The list of candidates promoted by the IUCr, together with the rest of the Unions making up the ISC, had relative success, with some candidates from the Unions' list being included in the final shortlist. Nevertheless, our candidate Hanna Dabkowska was excluded, and the presidency and some other positions were reduced to only a single candidate. This lack of capacity to elect the general assembly results in an obvious democratic deficit and a consequent deterioration in the public image and in the legitimacy of representation, and to a deficit in the confidence of the associates, in particular of the Scientific Unions.

The Nobel Prize in Chemistry 2024 was awarded to the researchers David Baker, for his work on computational protein design, and Demis Hassabis and John M. Jumper, for their work on the *AlphaFold* tools for protein structure prediction using artificial intelligence. This award is also a great encouragement to the many of you who work in this field, and particularly the members of the Biological Macromolecules Commission.

The International Programme Committee (IPC) for the Calgary congress is now being formed, and it is very important that the Commissions are able to nominate the most scientifically appropriate persons, so that the IPC is a true reflection of the diversity that characterizes our International Union, in particular in gender, geography and age.

At the beginning of next year the IUCr award call for nominations (the Ewald, Bragg and Struchkov Prizes) will be announced. The committees are being decided and the rules are being revised, and for the

maximum success of the prizes it is important that the community is prepared to nominate the most outstanding researchers, particularly in areas and sectors that have not been recognized by past awards.

As usual, I end this letter with profound gratitude to all those who form and make our organisation work, the Regional Associates, the IUCr Commissions and Committees, Editors, Co-editors, referees and authors of our journals, our Chester staff and all individual crystallographers, women and men.

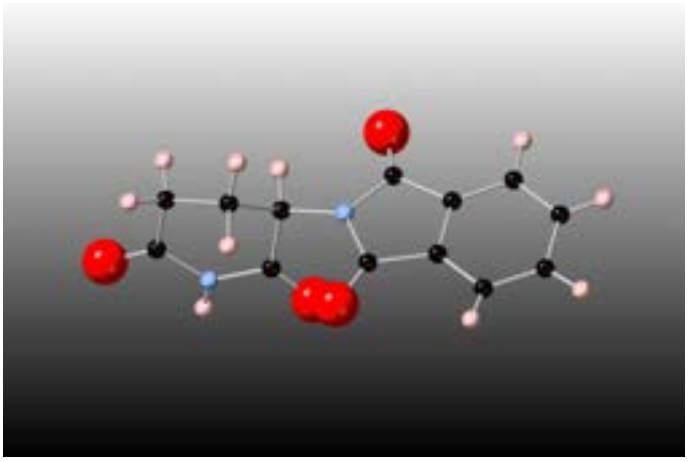
Thanks to *IUCr Newsletter* Editor Mike Glazer and his team, welcome to Kezia, and thanks to all contributors for making possible, as in every quarter, a new quarterly issue that continues to be the reference communication for our community.

Many thanks to all for contributing to maintaining the momentum of the IUCr, wherever they are in the world.

Enjoy practicing structural science!

EDITORIAL

Editorial



The molecular structure of thalidomide.

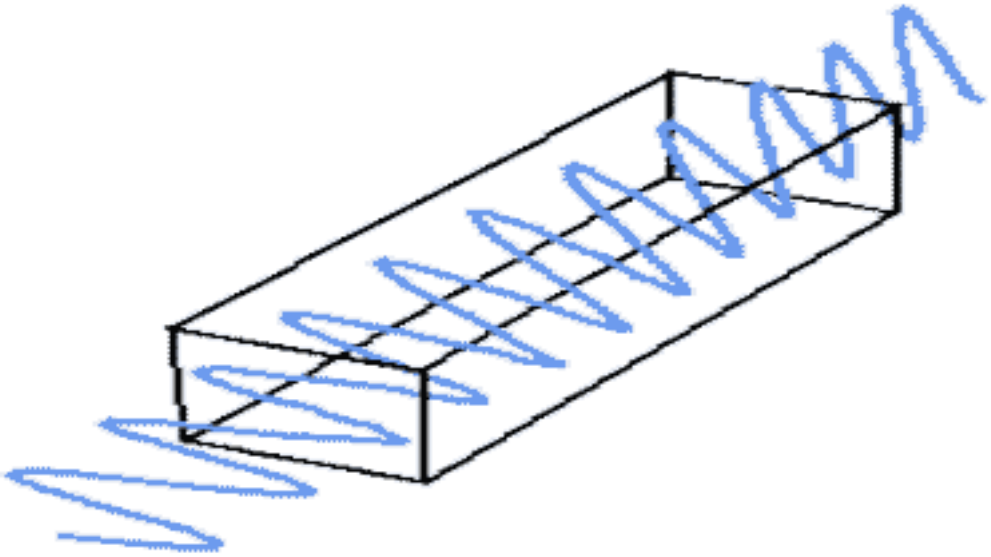
Mike Glazer

This summer, I had the pleasure of attending the European Crystallographic Meeting held in the beautiful city of Padova. As always, an excellent opportunity to meet old friends and to make some new ones. I always enjoy visiting Italy, and we took this opportunity to do some touring after the meeting: Bologna, Verona, and Venice. After all that sunshine and heat (and not to forget the food!), it came as a severe letdown to return to a wet and grey Britain.

The meeting was very well attended, and many interesting talks were given. Here, in this latest issue of the *IUCr Newsletter*, we have a report on the meeting, see https://www.iucr.org/news/newsletter/volume-32/number-3/european-crystallographic-meeting-34. One fun thing was the Science Slam, sponsored by Stoe & Cie, in which a number of contestants presented topics in a novel and entertaining way to a non-expert audience. The audience then judged these in terms of how loud the applause was. The winner was the indomitable Bill Clegg, who chose to sing his contribution to the tune of Mozart's Horn Concerto number 4 (K495), 3rd movement, but in the style of Flanders and Swan (https://en.wikipedia.org/wiki/Flanders_and_Swann). I could not resist asking Bill to let me have a copy for the *IUCr Newsletter*, and so, for your enjoyment, here it is: https://www.iucr.org/news/newsletter/volume-32/number-3/a-crystallographers-concerto. Do have a go at singing along with the script. The music can be found at https://www.youtube.com/watch?v=VHbLV7G4vno. Who says crystallographers are not fun people?

Chirality, sometimes called "handedness," is a special type of symmetry that can be found in many surprising places. Think of the direction in which, say, a screw turns: left or right? It can also be confusing: witness the number of times one sees pictures of the DNA molecule in the media where the sense of hand is incorrect, *i.e.* left-handed helices rather than right-handed. Another interesting fact is that there has historically been much confusion about what is meant by the terms left-handed or right-handed in the science of optical rotation. This is where polarised light has its polarization rotated through an angle when passing through certain media (liquid or solid) (see image below). This phenomenon was first reported by François Arago in 1811 and since then has been studied extensively. Louis Pasteur, in 1848, famously showed that the sense of rotation in certain tartrate crystals was correlated with their external morphology or shape, thus linking optical rotation to the chirality of the molecules within. Since optical rotation was known in fluids of biological origin, it was a small jump to understand that chirality was a major feature of living organisms! However, difficulties arose regarding whether one should consider the sense of rotation for light viewed from the source of the light, as originally used by physicists, or from the point of view of the observer, as used by chemists. The result

was that one could often not be certain when reading scientific manuscripts on optical rotation as to which frame of reference the author was using. Very confusing. This was not resolved until relatively recently when the chemists' convention was universally adopted. You can read much more about this fascinating type of symmetry (including a significant case involving thalidomide, whose model structure is displayed above) in this article by Istvan and Magdolna Hargittai: https://www.iucr.org/news/newsletter/volume-32/number-3/eternal-chirality.



Optical rotation through a medium.

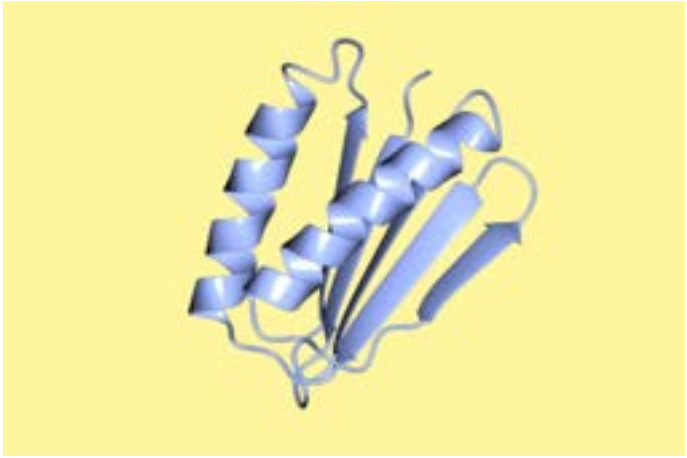
You will undoubtedly have seen that the Nobel Prize in Chemistry this year has been awarded to David Baker, Demis Hassabis and John Jumper for their astonishing work on the use of AI. John Helliwell talks about the importance of their work in determining protein structures here: https://www.iucr.org/news/newsletter/volume-32/number-3/protein-design-and-folding-prediction-endorsed-by-the-nobel-prize-for-chemistry-2024.

The success of this international *Newsletter* is such that the IUCr has decided that it should be published six times from next year instead of four. This will, of course, mean extra work for the staff at Chester, especially for Kezia Bowman, who only recently joined the IUCr.

Finally, it gives me great pleasure to note that, for once, we have no obituaries this time!

FEATURE ARTICLE

Protein design and folding prediction endorsed by the Nobel Prize for Chemistry 2024



John R. Helliwell

I have written before in the *IUCr Newsletter* [1] on the breakthrough made in protein folding prediction by Google DeepMind's *AlphaFold* [2] and on the PDBe (Protein Data Bank Europe) facilitating availability for users of some 200 million *AlphaFold* predicted proteins [3]. Protein folding prediction was one of the decades-old grand challenges of science. Since my student days, I have been fascinated by the physics-based hunt for the Gibbs free energy minimum, which must be the protein 3D structure identified by Anfinsen's protein denaturation and renaturation studies [4]. However, it was not energy minimum methods that solved it; it was a combination of learning from protein sequences and precise protein experimental structures carefully curated in databases [5]. These AI and ML (artificial intelligence and machine learning) methods based on big data are applied to many different prediction challenges in science and, more widely, in society. The continued wish for a physics-based energy minimum approach has led to further debate on whether the protein folding challenge has been solved [6, 7].

On October 9th, 2024, the Nobel Prize for Chemistry was awarded [8]:

"*David Baker has succeeded with the almost impossible feat of building entirely new kinds of proteins. Demis Hassabis and John Jumper have developed an AI model to solve a 50-year-old problem: predicting proteins' complex structures. These discoveries hold enormous potential.*"

Protein design is a reverse procedure to protein fold prediction, which involves designing a protein structure and determining the amino acid sequence that would produce that designed protein. This is a fantastic breakthrough by David Baker and his coworkers at the University of Washington in Seattle. The first of these was published in 2003 [9], see Fig. 1. As remarked by the authors of [9]:

“The ability to design a new protein fold makes possible the exploration of the large regions of the protein universe not yet observed in nature.”

They also recognised the potential for a sweeping change in protein crystallography phase determination:

“Remarkably, a strong molecular replacement (MR) solution to the phase problem was found with the use of the design model. (So) the design model was quite close to the true structure: even the small deviations of NMR solution structures from X-ray crystal structures can make molecular replacement searches fail."

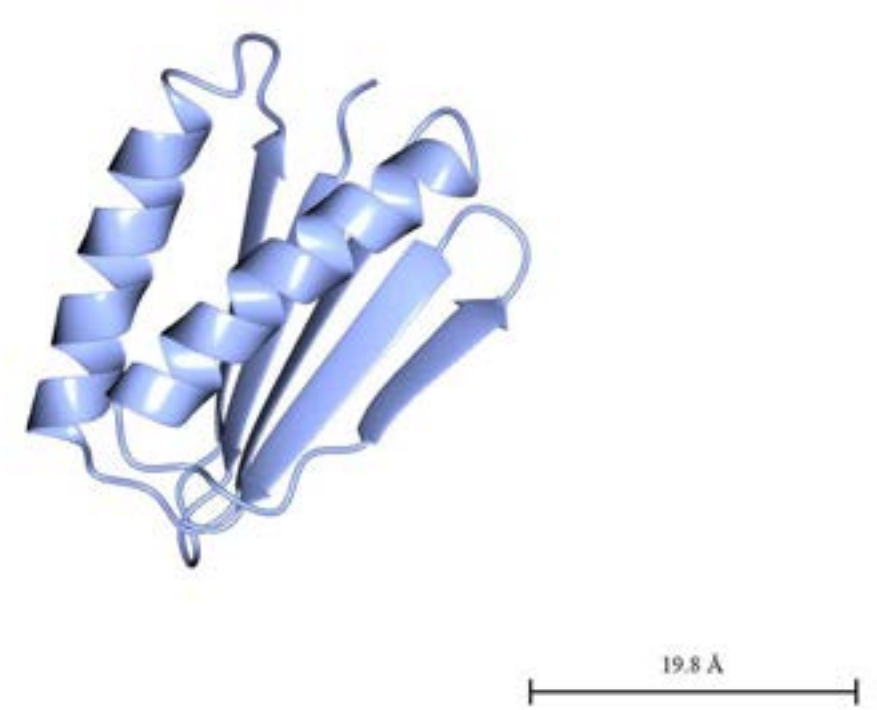


Figure 1. The first designed novel globular protein fold by David Baker and coworkers confirmed with a 2.5 Å X-ray SAD (single wavelength anomalous diffraction) phased crystal structure, PDB code 1qys [9]. Figure prepared by me using *CCP4mg* [15].

Why did I not write about it [9] these past 20 years in the *IUCr Newsletter*? I certainly admired it, but I imagined it as mainly about molecular biophysics, at that time. Meanwhile, protein fold prediction I could always see, if fully solved, would have a massive impact on my efforts in protein crystallography phase determination using tuneable synchrotron radiation. This was a topic that Dorothy Hodgkin drew my attention to in 1975 when she received a pre-print from the SSRL (Stanford Synchrotron Radiation Laboratory) via Sir Ron Mason of the seminal work of Keith Hodgson and colleagues there [10]. Indeed, we are approaching the 50th anniversary of that momentous paper, and a special issue of articles in the Journal of Synchrotron Radiation is underway (https://journals.iucr.org/s/services/specialissues.html), endorsed, of course, by Keith Hodgson himself.

An interesting feature about this year's Nobel Prize in Chemistry was a seeming coordination of topics with the Physics Nobel Prize announced the day before to John J. Hopfield and Geoffrey E. Hinton [11]:

"*...for foundational discoveries and inventions that enable machine learning with artificial neural networks.*"

The Nobel Prize in Physics led to comments on X (formerly known as Twitter) that the Prize had been hijacked by computer scientists. The Nobel Committee explanation, seemingly to anticipate such criticisms, had already emphasised that the Hopfield contribution was statistical physics and that Hinton's contribution involved a so-called Boltzmann machine. Interestingly, the applications of the Hopfield and Hinton methods emphasised in the main press conference were things like interpreting medical imaging data and particle physics data. It seemed to carefully exclude protein folding prediction. However, in a detailed explanation and interview of a Nobel Physics Committee specialist after the main announcement event, he cited application of their methodology in that domain.

So, what next for the two domains of protein prediction and protein design? Google DeepMind, which is based in London, recently launched its *AlphaFold3* software for predicting biomolecular interactions, including proteins, nucleic acids, small molecules, ions and modified residues [12]. For the domain of protein design, the list of impressive applications described by David Baker in his telephone interview at the press conference already includes a designed protein suitable for incorporation in a nasal spray

against the COVID-19 spike protein and a designed protein sensitive to environmental pollutants. As was remarked in the Nobel Chemistry Prize ceremony's subsequent discussions, the limit is not the possibilities but our imagination.

In my own tweet about it on X (formerly known as Twitter) (@helliwelljohn) I wrote:

"*Hearty congratulations to all three Laureates. Both domains, protein design and prediction, are fantastic breakthroughs. Hearty thank yous too to the great care of the sequence data bases and of the PDB experiments' structures database. @rcsbPDB @PDBeurope @PDBj_en"*

Where are we today in my view as a protein crystallographer then? Recently I was asked this by the ESRF communications office, who were writing a piece about the 30 years of user operation at the ESRF since it came online, since I had been involved in the ESRF since the early days. I replied that*: "in the mid 1980s I led the ESRF MX (macromolecular crystallography) Working Group and wrote the MX sections for the ESRF Foundation Phase Report (Red Book)* [13]*. Since then, MX crystals have got ever smaller, tuneable wavelength resonant scattering phasing got supplanted by AlphaFold2 about four years ago, CryoMX (at 100K) is getting more and more supplanted by room temperature MX, structural dynamics (including time resolved MX) keeps growing in importance rather than structure determination per se, neutron MX is growing in importance and X-ray wavelength tuning for site specific metal or ion determination in MX remains very important. For the future, using the new ESRF Extremely Bright Source upgrade of two years ago, it will be dominated by the physiological relevant MX and structural dynamics (time resolved) MX studies. Of course, another major breakthrough is that crystallisation failures of large complexes now have a different way forward with cryoEM."*

Inherent in this personal assessment for the ESRF communications office is that predictions of protein folds have somewhat elaborated into predictions and designs of protein structures including complexes, not 'only' folds. Thereby, the emphasis for the experimental protein crystallographer is apparently shifting to determining structures closer to the conditions of the living cell itself, be it temperature or pH. For example, my colleagues and I recently published a body temperature (37°C) study of a protein with a bound rhenium theranostic compound seeking a truly physiologically relevant structure [14]. I also note that in an unusual move the EuroXFEL have promptly announced the day after the Nobel Prize that David Baker is one of their users, stimulating my thinking that he is moving into the design of protein structure **and** dynamics. Clearly, close fit predictions to the current predominantly 100K database entries of protein structures is one thing, but the need is with us for an expanded number of experimental structures at a wide range of physiologically relevant conditions if there are to be attempts at a close fit of predictions to the living cell situation. Of course, any protein 3D structure prediction or design has to be experimentally validated by crystallography, cryoEM or NMR spectroscopy.

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John R. Helliwell, Department of Chemistry, University of Manchester, Manchester M13 9PL.

FEATURE ARTICLE

A crystallographer’s concerto



Words by Bill Clegg (in the style of Michael Flanders and Donald Swann’s *Ill Wind*).

Music by Wolfgang Amadeus Mozart: Horn Concerto number 4 (K495), 3rd movement: https://www.youtube.com/watch?v=VHbLV7G4vno.

Written for the ‘Science Slam’ entertainment session at ECM34, Padova, 2024:

I made a new compound and needed its structure
But spectroscopy doesn’t tell me enough.
Now X-ray diffraction will give me a picture
So I can be sure that I made the right stuff.
Tutti

For crystal growth, I had to dissolve it and let it cool.
Upon my oath! It’s incredibly boring to see.
But to my surprise, and in front of my eyes,
A crystal did grow to useful size.
Oh, what a pain of learning to cope
With peering for hours down a microscope!

But that was yesterday, and now today
I looked for diffraction effects.
There were the spots, but they didn’t fit a lattice.
What on earth does it mean?
Single crystals give patterns without a flaw.
Oh, could it be a twin?
Yes indeed! Now I need
Clever software to find me a twin law.

Next integrate
And corrections apply to sigma and I.
Then I can use direct methods in structure solution.
If that doesn’t work, I’ll try flipping the charge
To look for electrons and their distribution –
Molecular fragments that I can enlarge.
Tutti

What a joy! Finding atoms in a Fourier,
Hydrogens showing up in a difference map.
This is easy, I learnt how to do it at Erice
With SHELX, or OLEX, or some other app.
Now everything's found, the structure is sound.
It's time to start the tricky part –
The first refinement round.
Now, I urge: please converge!

Away now we go with our least-squares refinement,
Constraining, restraining, and weighting it all.
The model gives data approaching alignment
With measured diffraction; the R factor's small!
Tutti

It's looking fine; the goodness of fit is precisely 1 –
A pleasing sign! Shout out loud: I'm on cloud nine!
Now on the screen the structure is seen,
No more density showing between.

A lovely molecule – it's really cool!
I'll show it at ECM.
I'll devise a surprise
And I'll snaffle the main poster prize!
I just need a nice diagram
Showing the molecules in the cell
And ellipsoids to prove I am
Not just a fraud.
Cadenza

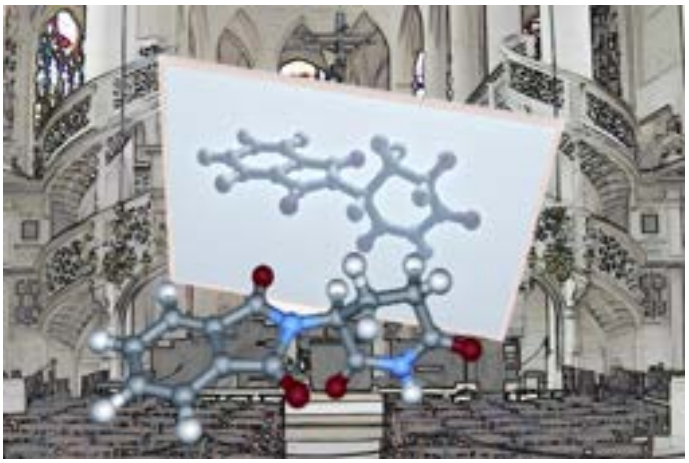
And then publication – the very best journal,
Attracting citations all over the place.
My new reputation will blossom eternal,
I'll enter the database!
Tutti

I'm getting excited! I should wait till later,
My fingers are flying around.
I've just hit DELETE and I've lost all my data
And made an unprintable sound! ***#***!***
And now comes the moment I dread,
Those crystals are looking quite dead.
I'll have to use powder instead!!!
EPDIC!!*

**European Powder Diffraction Conference*

HISTORY OF CRYSTALLOGRAPHY

Eternal chirality



Istvan Hargittai, Magdolna Hargittai

Chirality as a phenomenon in nature has always been present. As a concept in science, it has been around for some time. It began as a curiosity, then became a fundamental component in scientific research, and today, it is a crucial consideration in medicine. It is important in crystallography, though not always recognized explicitly; for example, it does not appear in the Subject Index of the excellent *Historical Atlas of Crystallography* [1].
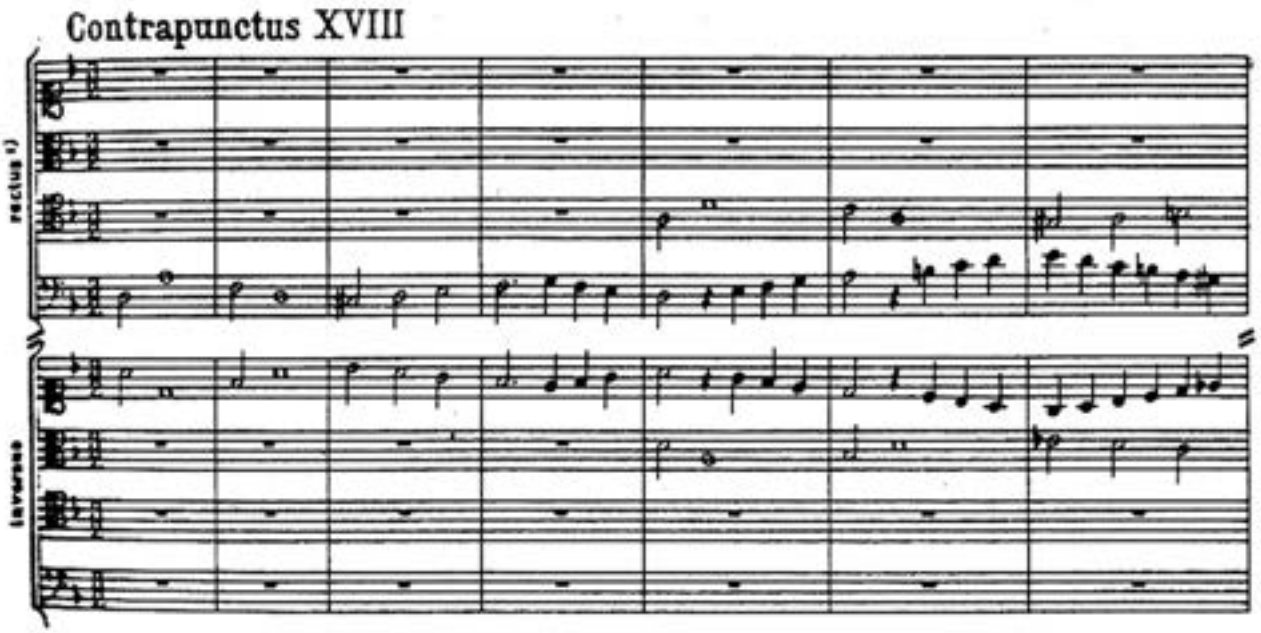
The main thrust of our research careers has been determining and modeling molecular structures. We were not concerned with chirality when using gaseous electron diffraction to determine internuclear distances because the same set of internuclear distances characterizes both chiral versions. However, chirality has fascinated us due to our broader interest in symmetry [2−4]. This essay surveys a set of selected examples of chirality.

Many objects, both animate and inanimate, have no symmetry plane but occur in pairs that are related by a symmetry plane. They are each other's mirror images but cannot be superimposed. This is called chirality or handedness from the Greek word for hand, *cheir* (χέρι). Below, we present examples of a homochiral pair, a heterochiral pair of hands and a heterochiral pair of feet — the concept could just as well be called 'podality' (from *pódi* — πόδι). The phenomenon belongs to the more general concept of dissymmetry, which signifies the absence of certain symmetry; in the case of chirality, it is the absence of a symmetry plane.



From left to right: homochiral pair of hands: Auguste Rodin, *The Cathedral*, Rodin Museum, Paris; heterochiral pair of hands: tombstone in the Jewish cemetery, Prague; legs: detail of the sculpture *Wave*, by Kay Worden, Newport, Rhode Island. Photographs by the Hargittais.

Not only material objects can have handedness: there is a beautiful example in Johann Sebastian Bach's (1685−1750) *The Art of the Fugue*.



Chiral pair: J. S. Bach, *Die Kunst der Fuge*, detail.

The German philosopher Immanuel Kant (1724−1804) wrote about the puzzle of the isometric left and right hands that cannot be made to coincide in space. He called the non-superposable mirror images "incongruente Gegenstücke" (incongruent counterparts) [5].



Immanuel Kant: stipple engraving by J. Chapman, 1812 (Wellcome Collection).

In 1811, D. François J. Arago (1786−1853) described the optical activity of quartz crystals. Some rotated the plane of polarized light in one direction, while other quartz crystals rotated it to the same extent but in the opposite direction. [6]. This discovery was one of Arago's many discoveries in several areas of science. For one of them, on the magnetic properties of substances not containing iron, he received the most prestigious Copley Medal of the Royal Society (London) in 1825.

In 1812, Jean Baptiste Biot (1774−1862) discovered the optical activity of quartz crystals [7] and observed that some solids, even when dissolved in water, showed the same effect. Biot's genius manifested in his conclusion that the effect is a molecular property. It was then left to Louis Pasteur (1822−1895), decades later, to understand the correlation of dissymmetric crystals and the optical activity in solution. Chirality and optical activity have been intimately related, and laevo-active (L) and dextro-active (D) chiral substances have been distinguished. Optical activity does appear among the entries in the Subject Index of the *Historical Atlas of Crystallography* [1]. Indeed, it is a more general concept than chirality. If a molecule or a crystal is chiral, it is necessarily optically active, whereas the converse is not true. There are symmetry classes of crystals that are non-enantiomorphous yet may exhibit optical activity.



D. François J. Arago and Jean Baptiste Biot: lithographs (Wellcome Collection).

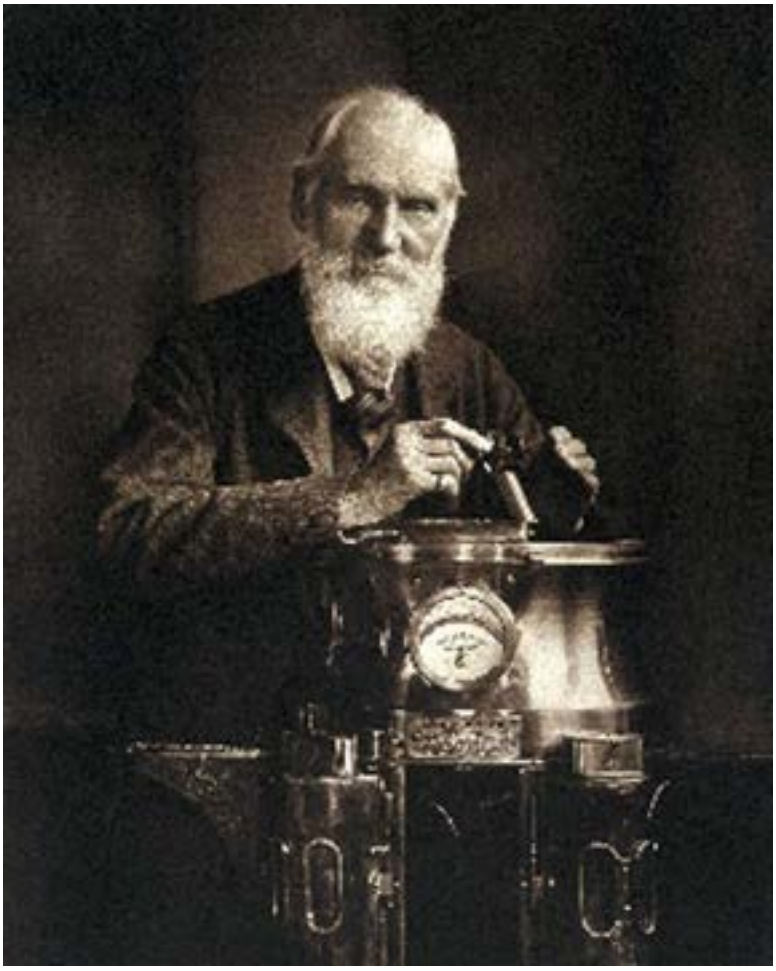
What Pasteur did in this connection in 1848 may be called the reverse experiment. He crystallized sodium ammonium tartrate from a solution he prepared from the optically inactive salt. He obtained crystals of two kinds, which were each other's mirror images. One of the two was identical with the crystals of the naturally occurring optically active tartrate — a product of the fermentation of wine. But the other, its mirror image, had never been seen before. Pasteur separated the two forms by hand. Tartrate was a lucky choice because manual separation is rarely possible. In his next experiment, Pasteur dissolved the two kinds of crystals separately in water, and the two solutions showed optical activity of the same magnitude but opposite in direction. The old Biot presented Pasteur's findings of crystal and molecular dissymmetry (today, we prefer the term chirality) to the French Academy of Sciences. Biot realized the magnitude of Pasteur's discovery, so he had Pasteur first demonstrate it to him in the laboratory before reporting about it to the Academy. When Biot could see the experiment with his own eyes, in Pasteur's words [8] he became: "...very visibly affected, the illustrious old man took me by the arm and said, 'My dear child, I have loved science so much throughout my life that this makes my heart throb.'"



Louis Pasteur's bust in front of the central building of the Institut Pasteur, Paris, and his models as exhibited there. Photographs by the Hargittais.

Pasteur's discovery had broad implications. J. Desmond Bernal (1901−1971) pointed out that it arose at a meeting place of three great distinct disciplines: crystallography, physics, and chemistry. In his treatise *Molecular Asymmetry* [9], Bernal charted the developments that could be related to Pasteur's discovery. Here and already once above, the term 'molecular asymmetry' figures, whereas the term 'molecular dissymmetry' often occurs in describing chirality. It is a little confusing, so we better define them: asymmetry means the complete absence of symmetry and dissymmetry means the absence of certain symmetry. Accordingly, in this case, indeed, dissymmetry and asymmetry could be used interchangeably. When Bernal discusses the significance of Pasteur's discovery, he reaches back to other classics of science, to R. J. Haüy, J. F. W. Herschel, J. J. Berzelius, and Auguste Bravais. He shows how they contributed to the development of the concept and to the development of X-ray crystallography in the early 1910s.

Lord Kelvin (1824−1907) wrote [10]: "I call any geometrical figure, or group of points, chiral, and say that it has chirality if its image in a plane mirror, ideally realized, cannot be brought to coincidence with itself."



William Thomson, Lord Kelvin: photograph by Harry Herman Solomon (Wellcome Collection).

Pierre Curie (1859−1906) formulated the most general and fundamental concept related to symmetry that involves dissymmetry, including chirality: "c'est la dissymétrie qui crée le phénomène" (dissymmetry creates the phenomenon) [11]. A phenomenon is expected to exist and can be observed only if certain elements of symmetry are absent from the system. A forerunner of this concept was put forward in 1833 by Franz E. Neumann (1798−1859) in his studies of the physical properties of crystals: "The physical properties of crystals always conform to the symmetry of the crystal" [12].



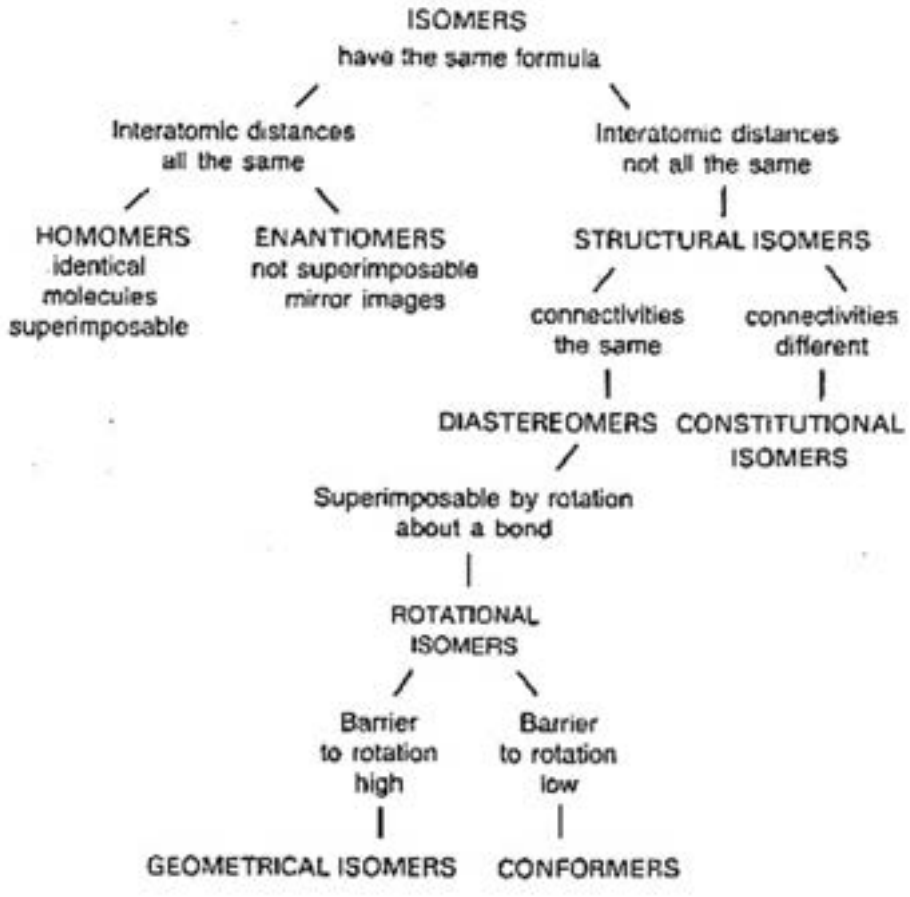
Statue of Marie and Pierre Curie in the Marie Curie Garden, Paris 5 — Latin Quarter, photograph by the Hargittais; and *Chiral Pierre Curie* by and courtesy of the graphic artist Istvan Orosz [3].

The emergence of stereochemistry could be a direct consequence of Pasteur's discovery. Its birth was in 1874, which is 150 years ago [14, 15]. The basic concepts were proposed by J. H. van 't Hoff (1852−1911) and J. A. Le Bel (1847−1930). Van 't Hoff published a booklet, *La Chimie dans l'Espace* (*Chemistry in Space*). Viktor Meyer (1848−1897) first used the term stereochemistry in 1890. The idea of extending the description of materials structures into the third dimension reaches back at least to Johannes Kepler in the early 18th century [16] and John Dalton in the early 19th century [17] in their discussions of the stacking of the building elements in water and ice. Still, even as late as 1956, the distinguished crystallographer Albert F. Wells (1912−1994) felt the need to stress that the description of "...the three-dimensional arrangements of atoms in crystals was an integral part of structural chemistry" [18].

The possibility that chirality leads to two different versions of the molecules of the same substance causes a well-defined isomerism in molecular structures. This is shown in the scheme below summarizing molecular isomerism. According to Vladimir Prelog (1906−1998), Hans Erni's *ex libris*, shown below, contains all three basic paraphernalia necessary for dealing with chirality. They are human intelligence, a pair of left and right hands, and two enantiomorphous tetrahedra [19]. Prelog was a co-recipient (with John W. Cornforth) of the 1975 Chemistry Nobel Prize "...for his research into the stereochemistry of organic molecules and reactions."



Hans Erni's *ex libris* bookplate for Vladimir (Vlado) Prelog with a dedication to one of the present authors (courtesy of the late Vladimir Prelog). A peculiar feature of this drawing is that the two hands appear inverted due to the two arms being crossed [13]. Erni made other versions of this drawing in which the two hands appear non-inverted.



Hierarchy of molecular isomerism ([2], p. 100).

Returning to the multitudes of consequences of Pasteur's discovery, it brought about the realization that biologically important substances occur in one of the two possible versions in living organisms. The Nobel laureate biologist George Wald (1906−1997) noted: "No other chemical characteristic is as distinct of living organisms as is optical activity" [20]. The great question is: how did it start, and how was one version of the two possibilities chosen? Already, Pasteur contemplated this, and Vladimir Prelog called this a question of molecular theology in his Nobel lecture titled *Chirality in Chemistry* [21]. Prelog gave his own definition to chirality: "An object is chiral if it cannot be brought into congruence with its mirror image by translation and rotation. Such objects are devoid of symmetry elements which include reflection: mirror planes, inversion centers or improper rotational axes."

The philosopher and theoretical physicist Lancelot L. Whyte (1896−1972) extended the definition of chirality: "Three-dimensional forms (point arrangements, structures, displacements, and other processes) which possess non-superposable mirror images are called 'chiral'" [22]. This extension made it convenient to describe chiral point groups, such as chiral molecules, and space groups, such as left-handed and right-handed helices. One of us (IH) discussed the possible origin of handedness in biological macromolecules in 1998 with Nobel laureate Ilya Prigogine (1917−2003), who said [23]: "Some people had proposed that the preference of left-handed amino acids may be related to electroweak interactions which stabilize very slightly the left-handed amino acids. Indeed, bifurcations are very sensitive to very small differences of energy. If the transition goes very slowly over years, then even such small differences in energy will introduce a slight effect in favor of one of the two amino acids." The polymath science historian Stephen F. Mason (1923−2007) did a great deal of pioneering studies on biomolecular homochirality and on the recognition of the electroweak origin of biomolecular handedness (see *e.g.* in [24]). The handedness of the biologically important helices has a vast literature.



Left-handed and right-handed helices at the Monastery in Zagorsk (left), and in a church in Paris (right). Photographs by the Hargittais.

At the birth of stereochemistry, it was impossible to tell when there was a molecule that could exist in two mirror image forms which isomer was which, and there was no way to establish the absolute configuration. The organic chemist Emil Fischer (1852−1919) took the bold step in 1894 of arbitrarily assigning an absolute configuration to sugars [25]. There was a 50% probability that he might be right. Luckily, he was, which could be established only in the early 1950s when the crystallographer Johannes M. Bijvoet (1892−1980) and his team determined experimentally the sense of molecules [26]. Their technique was revolutionary but tedious, because for each new molecule the chemical relationship with the initial one had to be established for which they had determined the absolute configuration. Prelog succeeded in simplifying the procedure a great deal.

In conclusion, we mention two remarkable stories in connection with molecular handedness.

In Dorothy L. Sayers' (1893–1957) detective story, *The Documents in the Case*, an expert identifier of wild mushrooms dies of poisoning. The question arose: was this death a consequence of accidental poisoning or even suicide, or was it foul play, *i.e.* intentional poisoning and murder? The analysis of the toxin in the victim's body showed the presence of only one of the two possible versions of the poisonous molecule, pointing to a man-made product, hence, murder. Sayers had a co-author for this book, Robert Eustace (pen name of Eustace Robert Barton, 1869–1943). He was a physician and himself a prolific author whose plots often included references to scientific innovation. He probably provided the scientific basis for Sayers' detective story; everything presented in the story was correct, even from today's perspective. Sayers' book has been kept in print ever since it appeared in 1930. The date of the original publication is significant as it was anticipated for decades by the current legislation that rigorously prescribes chiral purity for pharmaceutical products. Pharmacology necessitated this legislation because the physiological impact of left-handed and right-handed versions of the same molecule may vastly differ. This is not what Sayers' story exposed. It exposed some physiological relevance of chirality, which was sufficiently pioneering to deserve our appreciation [27].



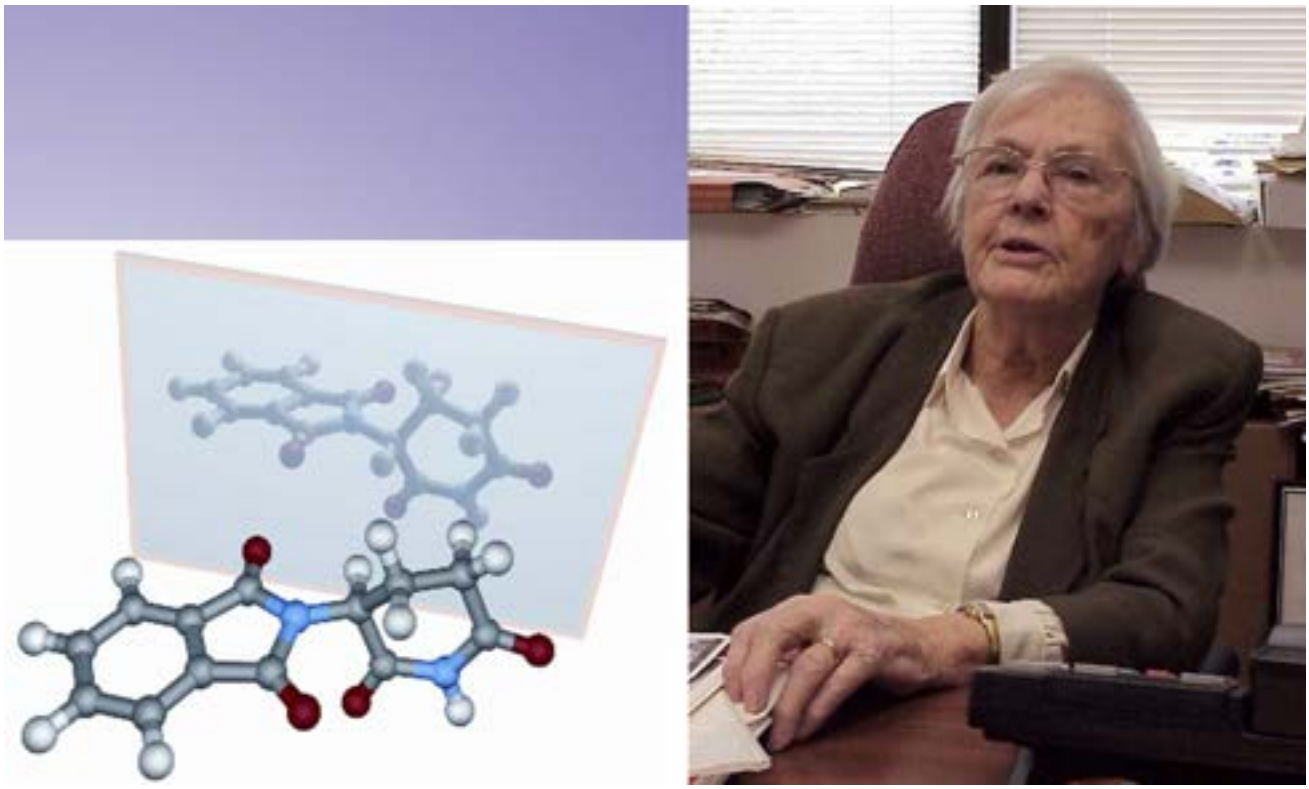
Dorothy L. Sayers, 1925, publicity photo from her American publisher, in the public domain (Sayers-whose-body-image.png - Wikimedia Commons).

Here, we present a few examples of differences in the properties of chiral versions of the same substance. We list the names of the substances with selected properties of the right-hand/left-hand versions in that order:

(1) Ethambutol — treats tuberculosis/causes blindness.
(2) Penicillamine — treats joints/is toxic.
(3) Naproxen — reduces inflammation but risks heart disease/is toxic for the liver.
(4) Propoxyphene — pain reliever (Darvon)/cough medicine (Novrad). Note that the names of these two medications are each other's mirror images.
(5) Asparagine — bitter/sweet.
(6) Carvon — caraway smell/spearmint smell.
(7) Limonene — lemon smell/orange smell.

A tragic example was the thalidomide case — *N*-phthaloyl-α-aminoglutarimide (its model is shown below and here). It was known as Contergan in Europe. Originally, it was marketed as a sedative in the late 1950s. It was given to pregnant women suffering from morning sickness. The drug was marketed as a racemate (*i.e.* consisting of both chiral molecules), and by the early 1960s, many birth defects in Western Europe were associated with Contergan. Slowly, the correlation between its consumption and the occurrence of birth defects was recognized, and it was finally withdrawn from the market. Eventually, it was understood that one of the two chiral versions of thalidomide was teratogenic; the other was harmless. The tragedies occurred worldwide except in the Soviet bloc, where it was not available, and the United States, where the Food and Drug Administration (FDA) had never approved it. A young and conscientious official of the FDA, Frances O. Kelsey (1914−2015) [28], resisted approval and demanded more and more tests and thorough investigations. Her work contributed to establishing a regulatory regime — the Kefauver-Harris Amendments of 1962 and the Investigational New Drug Regulations of

1963. Today, and for some time, it has been the case, in the European Union and elsewhere, that molecules that may have two enantiomeric versions may be marketed for medicine only in the version that has the desired effect. This has resulted in a huge industry of chiral separation.



Computer drawing of thalidomide molecular structure (courtesy of Ilya Yanov) and Frances O. Kelsey, 2000, in her office at the US Food and Drug Administration. Photograph by the Hargittais.

On the one hand, this has added to the costs of medicine, while, on the other hand, it has saved enormous amounts of substances that are not consumed and wasted. For fairness, we add that chiral separation would not solve the problem of thalidomide causing birth defects because the harmless version rapidly converts into the other version in the organism. Note also that thalidomide has other beneficial uses in medicine, but it should never be administered to expectant mothers.

Here, we make a big jump to allude to the enormous significance of chirality — or, more generally, dissymmetry — on a universal scale. In 1960, there was less than a half-page note in *Nature* [29] in which the physiologist John B. S. Haldane (1892−1964) returned to Pasteur in the wake of the recent discovery of parity violation. Haldane's starting point was T. D. Lee and C. N. Yang's discovery [30], which led to the acceptance of the notion of the asymmetrical universe. Pasteur first enunciated this [31], and Haldane quotes him in the French original.

Here, we provide the quote in English translation (courtesy of Alan L. Mackay): "It is inescapable that dissymmetric forces must be operative during the synthesis of the first dissymmetric natural products. What might these forces be? I, for my part, think that they are cosmological. The universe is dissymmetric, and I am persuaded that life, as it is known to us, is a direct result of the dissymmetry of the universe or of its indirect consequences. *The universe is dissymmetric*." (emphasis in the original).

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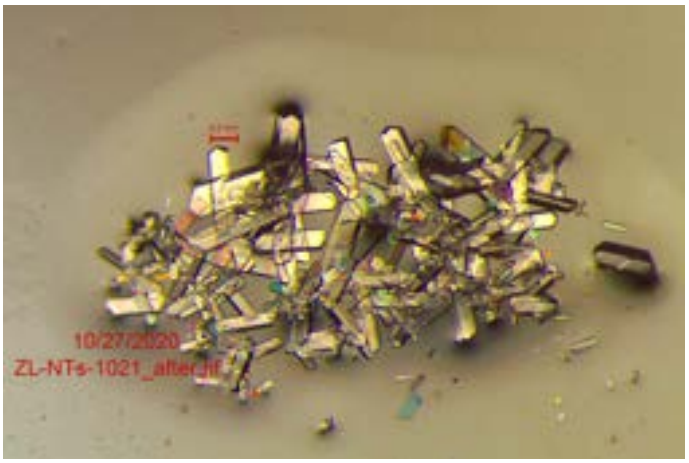
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FEATURE ARTICLE

How to grow crystals for X-ray crystallography



Roger D. Sommer

Part of the Best practice series.

Growing high-quality crystals remains a necessary part of crystallography and many other techniques. This article tabulates and describes several techniques and variations that will help individuals grow high-quality crystals in preparation for crystallographic techniques and other endeavors, such as form screening. The discussion is organized to focus on low-tech approaches available in any laboratory.

1. Introduction

Sample preparation is a key aspect of any analytical technique. In X-ray crystallography, this means growing crystals of sufficient size and quality to fit the instrument and the technique. A modern instrument can harvest diffraction data from needles as thin as 20 microns. Instruments of an earlier vintage may need crystals with dimensions closer to ten times that. Neutron diffraction experiments require crystals still larger. In all cases, the quality of the crystals grown is a deciding factor for success. This article presents techniques for growing high-quality crystals for single-crystal X-ray diffraction (SCXRD). The focus is on techniques available in nearly any chemistry laboratory doing organic/organometallic chemistry. Many of these will be well-known conventional approaches. There is also a mention of more systematic approaches that offer high-throughput screening for industrial applications. Comments about refinement to these techniques are born of experience chasing crystals of uncooperative samples that only eventually yield diffraction-quality crystals. There are myriad variations on the themes below. Consider this an outline, with tips and tricks and resources that might further your efforts in pursuing great crystals. Also available are numerous books (Holden & Morrison, 1982), papers (Müller, 2009; Etter *et al.*, 1986), and websites with contributions from respected crystallographers that offer advice for crystal growth (Boyle, 2023; Blake, 2024; Mueller, 2024; Dinger & Klosin, 2015).

The time, effort, material, and resources needed to grow crystals ranges widely depending on the compound, from `minimal' to `impractically high' on all four fronts. So why do this? Why advocate for growing crystals on fast-moving projects where material is precious and resources may be limited? The answer is the same as always: unambiguous structural characterization moves projects along, keeps them on track (or gets them back on one), and provides insight to the chemical process. X-ray analysis of diffraction-quality crystals can unlock a project's potential from almost any point in its cycle: from early confirmation of regiochemistry or stereochemistry in starting materials, to the `cherry-on-top' structure at the end of a multi-step synthesis. In the middle, crystal structures of isolated intermediates support and direct synthetic routes and mechanistic studies, while also giving process-relevant details for later

scale-up. Crystallization is still favored today by industry as a purification technique because it is scalable. It also offers myriad choices for selecting the form that is isolated – a key factor in the pharmaceutical field. Either from a user or facility manager point of view, getting the best data possible is most important. Users depend on the facility to advance their projects, careers, hopes, and dreams. The crystallographer needs to minimize the required instrument time and refinement effort to make the structure publishable. This frees up resources for more samples and experiments, and deepens the relationship between the users and the facility. The crystal-growing effort is also an opportunity to collaborate openly on the project. The most value from the crystal-growing effort may be seen when the chemical drawing of the proposed structure *might not be* the structure of the actual material. And all parties must keep an open mind about what is actually in that vial. This fosters a culture that benefits everyone involved. The resources needed to start growing crystals are as little as a few milligrams of material and a weekend of quiet evaporation. So why not do this?

2. Options to consider

2.1. Chemical assessment

A crystallization begins with an assessment of the compound's solubility and chemical stability. Is the material air/water sensitive? Is it thermally stable? Does the reactivity of the compound preclude the use of certain solvents? Many of these answers are usually known by the time a crystallization is undertaken. If not, they are readily addressed with a few qualitative tests.

2.2. Solubility profile

The most common medium for growing crystals is liquid solution. It is also the most convenient approach, requiring the least equipment and infrastructure. A first step here is to collect information about the solubility of the material in question. It is also critical at this point to have a chemical context for the compound of interest. Look at the reaction steps leading up to it, and keep in mind that impurities such as solvents or by-products from previous chemical steps can be carried through the process despite careful work and good separation technology. A simple chemical drawing can be highly useful in making solvent choices. Based on the functional groups present, some chemical reasoning can be used to make rational choices about where to start. A `like dissolves like' approach is reasonable. Nonpolar compounds, or those with significant nonpolar regions, may be highly soluble in ethers or aromatic solvents. Polar protic compounds will likely need polar protic solvents to get them into solution. Other factors to be considered are molecular shape and the presence of hydrogen bonding. Large flat molecules, and systems with extensive intermolecular hydrogen bonding, often have lower solubility in common solvents. Fig. 1 shows a typical solubility profile at the bench. *N*-(*o*-Tolyl)acetamide demonstrates a range of solubilities as the polarity/polarizability of the solvent increases.



Figure 1. The `line-of-vials' approach to solubility testing for 20 mg samples of analyte in 0.5 ml of solvent. From left to right: heptane, diethyl ether (Et_2O), toluene, ethyl acetate (EtOAc), dichloromethane (DCM), and acetonitrile (ACN).

At the bench, a good tactic is to assemble a line or grid of vials containing a small amount of material. This is as simple as scooping some material into a vial, adding a few drops of solvent, swirling the vial, and observing. Starting with solvents that evaporate quickly allows easy recovery for further tests before progressing to polar solvents until significant solubility is observed. The range of solvents used in this process will inform decisions about crystallization protocols. The choice for this range will vary by analyte. Solvents like dimethylformamide (DMF), dimethyl sulfoxide (DMSO), and water may be reserved for cases when nothing else works because they are difficult to remove.

3. Techniques

This section organizes crystallization techniques with an eye toward the economical use and re-use of material. Observations from the solubility tests can guide decisions about what solvents and techniques to try. Comments for each technique include a description of the procedure, discussion of limitations/risks, and how to avoid common mistakes.

3.1. Slow evaporation

Sometimes, making a solution and leaving the cap off produces a viable batch of crystals that diffract sufficiently for SCXRD. This technique can directly follow the solubility screening by simply walking away. The real advantage here is that slow evaporation requires minimal effort. Other examples of this technique include:

– NMR tubes left in the back of the hood over a holiday.

– A vial with a loose cap placed on a quiet shelf. Or a sealed septum vial with a needle inserted.

– Schlenk line apparatus with a slow purge of inert gas.

– High-throughput nanodrop evaporation under oil (Tyler *et al.*, 2020).

There are some drawbacks to the slow evaporation approach. If experiments go to dryness before the crystals are discovered, harvesting the crystals by scraping the vial may degrade or destroy them. Solvated crystals may lose their interstitial solvent, resulting in poor diffraction. The compound of interest may decompose over time due to oxygen or water vapor in the laboratory, or other chemical pathways. In addition, loose solvent vapor from slow evaporation is unwelcome in the environment. Good technique, knowledge of reactivity, and monitoring the progress can decrease the risks associated with slow evaporation. Evaporation experiments can also be set up in sealed chambers by using the

vapor-diffusion concepts discussed later.

3.2. Slow cooling

Slow cooling exploits the change in solubility as a function of temperature. In the case of the example compound in Fig. 1, toluene would be a good choice. A large ΔT between ambient and boiling temperature typically translates into a greater recovery of solid when the mixture returns to room temperature. Heat a slurry until a clear solution is obtained. It is useful to have a reserve of heated solvent available to add if needed. Don't skimp on the size of the vessel, as it may take more solvent than anticipated. Remove the heat source and allow the solution to cool slowly in an insulated container. If low-boiling solvents are used, cool a saturated solution in the freezer. Some examples of this technique:

– Beaker of solution on a hotplate. Turn off the hotplate and let stand to cool.

– Place a vial of hot solution inside a vacuum jacketed container. Pack with glass wool. Refrigerate.

– Run a Soxhlet extractor to make a concentrated solution. Remove the solvent vessel, seal it, and place it in a vacuum flask, cover with glass wool and allow to cool.

– A thermostat-controlled oven with software to design temperature ramping and cycling strategies.

Some drawbacks to the slow-cooling technique are obvious. Heating flammable solvents is inherently dangerous and should be done with proper safety measures in place. Cooling flammable solvents requires a refrigeration unit that is suitably safe for that purpose (*i.e.* `explosion proof') and vials should be well sealed. Thermally-sensitive compounds may have a limited temperature range available. It sometimes requires very slow cooling to produce X-ray-quality crystals of sufficient size. Dissolution of some materials might be slow, and an impatient person can end up with too much solvent. In this case, the experiment becomes slow evaporation. Or the sample is returned to the rotovap for reduction and restart.

Slow cooling is a simple, accessible, and effective way to grow X-ray-quality crystals for many compounds. There are easy ways to use basic equipment to make effective setups. There are also advanced systems (Technobis, 2023) to control temperature and other conditions so that complex crystallization protocols can be developed. A variation of slow cooling that deserves mention is thermal cycling. This moves the system back and forth across the boundary of supersaturation. As a result, crystals are ripened to larger size and sometimes better quality (Mullin, 2001).

3.3. Layering

Solvent layering relies on the solubility difference of the analyte in two solvents. A typical setup starts with a solution of the material in a polar solvent. A (usually less polar) counter-solvent is gently layered on top of the solution. The vessel is capped, and diffusion slowly moves one layer into another. This lowers the polarity of the system to the point that precipitation begins, hopefully producing crystals. This is best done in a narrow vessel like an NMR tube or capillary. The choice of solvent/counter-solvent pairing is critical. Planning is needed to ensure the denser liquid is the bottom layer. The typical arrangement is solution on the bottom and counter-solvent on top. Miscible liquids from opposite ends of the `line-of-vials' are good choices for this technique. This method is gentle, relatively quick (1–5 days), simple, and inexpensive. Example setups are shown in Fig. 2.

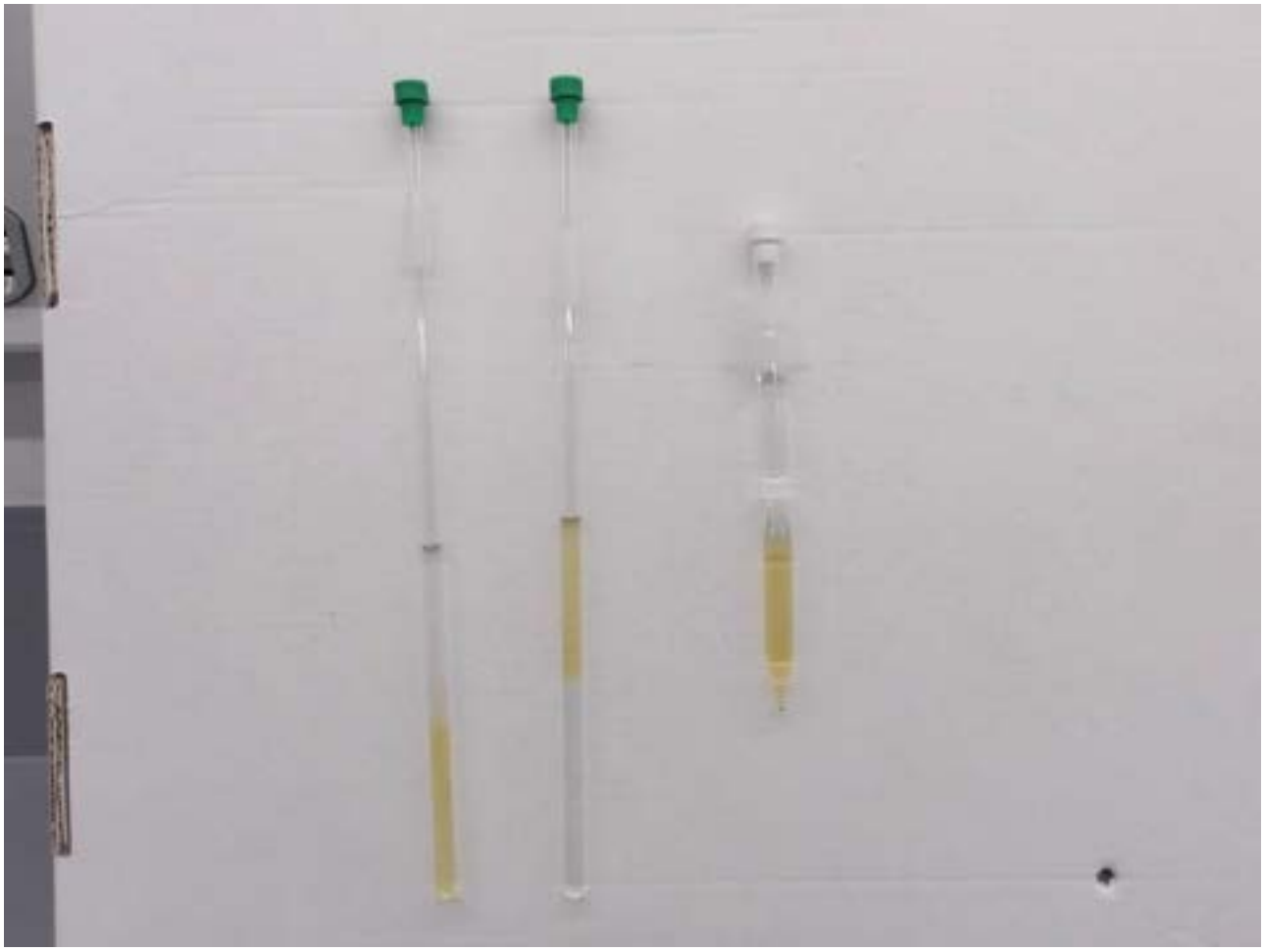


Figure 2. NMR tube prepared for crystallization by (left) layering heptane onto a yellow THF solution, (middle) layering a yellow THF solution onto dichloromethane counter-solvent and (right) layering solution/counter-solvent in a lab-built constriction tube made from a Pasteur pipet.

There are several pitfalls related to the layering approach. Mixing outside of diffusion is the enemy. Even holding the tube in hand cause enough temperature fluctuation to produce unwanted stirring. Sometimes mixing goes too quickly and only tiny crystals or amorphous precipitate are recovered. Layering on a counter-solvent requires some skill. These challenges can be addressed with some simple strategies: a layer of `blank' solvent can be added to the tube before the counter-solvent is layered. This helps prevent disturbing the layer of solution in the bottom. Another approach is to flash freeze the lower solution in liquid nitrogen, then add the counter-solvent layer on top of the solid. It is also possible to make tubes with a tapered middle, which slows mixing and prevents disturbing the lower layer during setup.

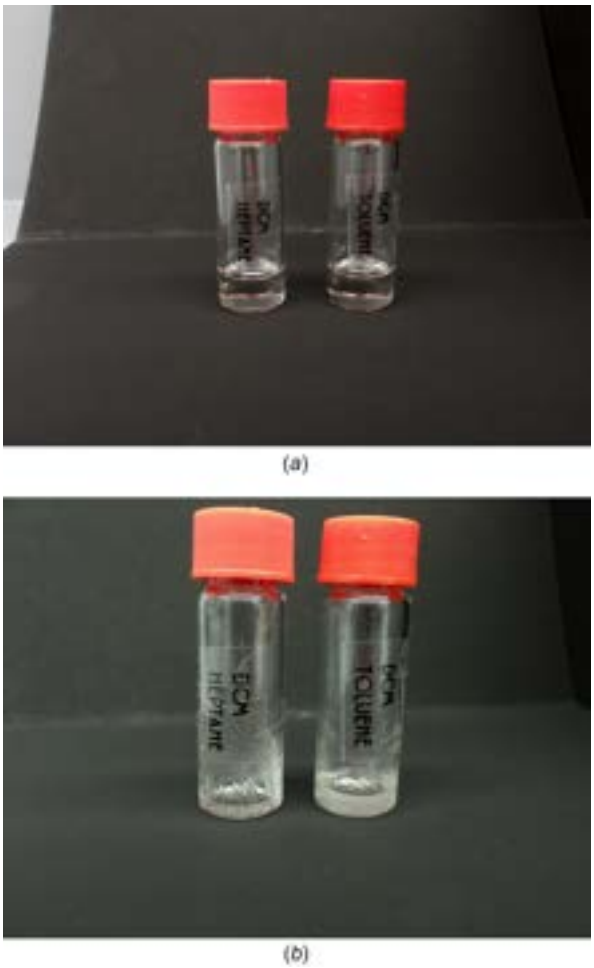
3.4. Mixed evaporation

Evaporation of a mixed-solvent solution offers the simplicity of slow evaporation with some insurance against the sample drying out. A low-boiling solvent is paired with a higher-boiling counter-solvent, and slow evaporation is allowed to progress. As the volume of solvent decreases, the solubility of the analyte in the vial drops. The high-boiling counter-solvent ensures that the mixture does not go to dryness. Mixed evaporation does not require the dexterity needed for layering. A good starting ratio is 2:1 solvent–counter-solvent. If needed, more solvent can be added, knowing that it will evaporate later. Table 1 lists a few handy solvent pairs for mixed evaporation with boiling points in °C.

Table 1
Examples of solvent pairs useful for mixed evaporation crystallizations

Solvent (b.p. in °C)	Counter-solvent choices (b.p. in °C)
Dichloromethane (35)	Heptane (98), toluene(110), *n*-butyl acetate (126)
Tetrahydrofuran (66)	Water (100), toluene (110)
Acetone (56)	Water (100), toluene (110)

This approach is well suited for an intentional `first try'. The DCM/heptane and DCM/toluene pairings, shown in Fig. 3, typically finish in 24 to 48 h. As little as 10 mg can permit three or four tests in the first set of vials. An additional advantage is that the material and vials themselves are generally easy to reuse for a next set of solvents.



(*a*)

(*b*)

Figure 3. (*a*) Mixed evaporation crystallizations using 20 mg of *N*-(*o*-tolyl)acetamide in 0.5 ml DCM, with 0.2 ml of counter-solvent added. The caps are loosened 1/4 turn. (*b*) t = 24 h.

Mixed evaporation works best with a large difference in boiling point between solvent and counter-solvent. This approach limits the choice of high-boiling liquids to those that are also poor solvents for the material. Materials that require polar high-boiling solvents like DMF or DMSO are less well suited to this approach. Whenever other crystallization attempts are combined in a larger vial to recover material, a mixed evaporation experiment is inadvertanlty started. Documentation and reproducibility become difficult when this mixture turns out to be where the crystals grow.

3.5. Vapor diffusion

Vapor diffusion is perhaps the gentlest and most versatile approach to crystal growth that is readily available in a standard chemistry laboratory. The analyte is dissolved in the less-volatile solvent and paired with a volatile counter-solvent. The pair should be miscible, with the analyte having a much lower solubility in the counter-solvent (from opposite ends of the line-of-vials in Fig. 1). The experiment is arranged as nested vials. The inner vial contains the analyte solution and the outer holds a reservoir (the `pool') of the counter-solvent. There should be headspace available for vapor exchange to happen. As the counter-solvent vapor dissolves into the solution, the solubility of the analyte decreases. This continues until the solvent is saturated with counter-solvent, or the pool is completely transferred to the inner vial. The timeframe depends widely on solvent choice and conditions. Diethyl ether and pentane will transfer overnight, while higher-boiling counter-solvents take more time. Fig. 4 shows microscope images of before and after, as well as the setup at various stages of vapor transfer.

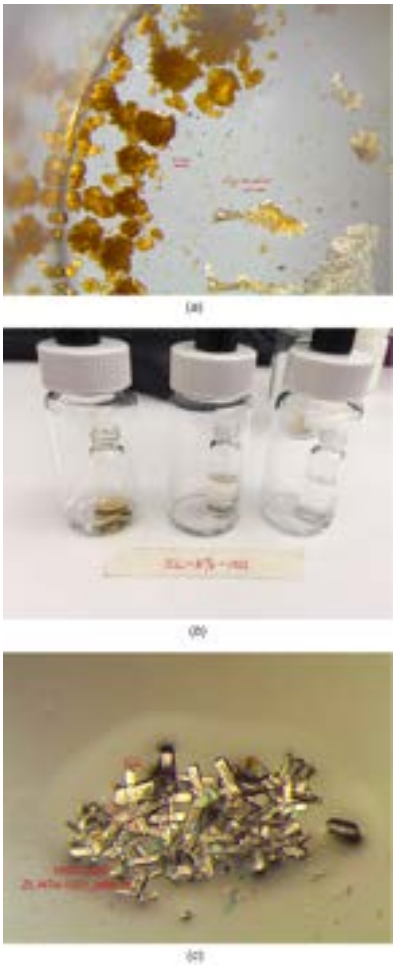


Figure 4. (*a*) Before, (*b*) during, and (*c*) after pictures of successful vapor-diffusion crystal growth. The solvent/antisolvent pair was ethyl acetate/pentane.

Vapor diffusion tends to work best starting with a saturated solution of material. A dilute starting solution may mean that nothing precipitates. It is also important not to overfill the inner vial. Otherwise, it may overflow when counter-solvent transfers in. Reproducibility can be a challenge without careful portioning of the material and solvents. Some recommendations are listed in Table 2.

Table 2
Some common solvent/counter-solvent pairs useful for vapor-diffusion crystallizations

Solvent (b.p. in °C)	Counter-solvent choices (b.p. in °C)
Ethyl acetate (77)	Pentane (36)
Acetonitrile (82)	Diethyl ether (35), pentane (36)
Methanol (65)	Dichloromethane (35)
Water (100)	Ethanol (78)
DMF (153)	Diethyl ether (35)
DMSO (189)	Water (100)

There are many more options for vapor-diffusion conditions (Spingler *et al.*, 2012). For example: (i) if a crystallization using MeOH/DCM crashes out, giving microcrystals, then charge the pool with 1:1 MeOH–DCM instead of neat DCM. This will decrease the driving force for transfer and provide a gentler approach to a supersturation in the inner vial. (ii) If slow evaporation of DCM leaves only desolvated crystals trapped in a crust, slow evaporation can be equilibrated before dryness by setting the DCM solution in a vapor chamber with *just the right amount* of methanol (or a DCM/MeOH mix as above) in the `pool'. (iii) If crystallization of a particular form requires just the right relative humidity, the vapor chamber can be charged with salt solutions to regulate that variable. Biochemists have numerous techniques to explore a vast landscape of conditions for vapor-diffusion crystallizations (McPherson & Gavira, 2014). There are also many commercial products to control vapor-diffusion conditions.

3.6. Sublimation

Sublimation can be a good option for some compounds as a purification and crystal-growth method. It also offers a good way to grow crystals that are unlikely to be solvated forms. The variable of solvent choice is replaced by the combination of pressure and temperature. Thermal stability of the analyte is an important consideration. Some materials like iodine, phenol, and ferrocene can grow dramatically large and beautiful crystals. Many other materials grow preferentially into very thin needles and plates. The setup can be as simple as a flask or test tube on a hot plate or as elaborate as a specialty apparatus built for vacuum sublimation. Fig. 5 shows a simple arrangement used to crystallize adamantane by sublimation.



Figure 5. Crystallization of adamantane by sublimation in a septum-top vial. The temperature was maintained at 65°C using a hotplate and the vacuum held at ~200 mbar (1 bar = 10^5 Pa) using house vacuum and a syringe needle pushed through the septum. Sublimed crystals are seen on the vial walls.

3.7. Dealing with oils

It is common in organic chemistry that new molecules are first isolated as oils even after careful purification. Residual solvent, stopcock grease, or other contaminants may be the issue. If drying under vacuum doesn't help, stirring the oil with a small amount of hexanes or ether may extract these adulterants, and yield something that can be recrystallized. This doesn't always work. But it is worth trying something like this to see if the material can be isolated as a solid.

3.8. Salts and cocrystals

When sufficiently good specimens are not available from the above techniques, a salt or cocrystal of the desired material may afford better crystals. This topic is larger than the scope of this article (Quere & Wouters, 2011; Wouters & Quere, 2011). Suffice it to say that these represent their own chemical endeavor that deploys an understanding of molecular structure and intermolecular interactions that may result in achieving large high-quality crystals suitable for SCXRD. There are also techniques deploying chaperone molecules (Virovets *et al.*, 2021), complexing agents (Etter & Baures, 1988), and molecular networks (Fujita, 2021; Carroll & Coles, 2023) that may also yield SCXRD-quality crystals containing stubborn molecules.

4. Conclusion

Beyond the structural insights gained from crystallography, other benefits come from the work put into crystallization. Notably, documenting the chemical behavior in multiple systems (solubility, stability, *etc*.) is of use for advancing the project or program. For uncooperative samples that `never' crystallize, the question is `When do I give up and move on?'. There is always another thing to try, right? This can only be answered by, and with support from, the team. Regardless of the outcome of crystallization attempts, the discussion, collaboration, and hands-on experience built around the effort unlocks another benefit – comaradery with others in the field which gives strategies, options, and encouragement for making a regular repeating habit of growing great crystals. Good hunting.

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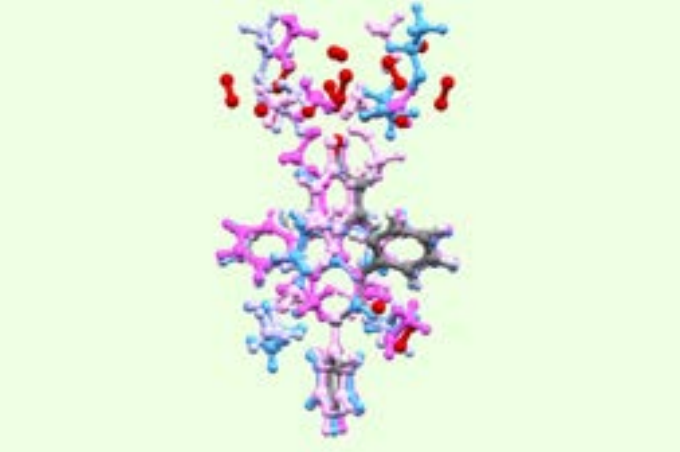
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COMMENTARY

Relating solvatochromism and solvatomorphism in organic dyes using high pressure



Elena Boldyreva

I remember my early childhood experience with `secret ink' that only became visible when a sheet of paper was sprayed with ethanol. This was a manifestation of *solvatochromism*, color change in different solvents (Marini *et al.*, 2010). Cobalt chloride hexahydrate is pale pink and any text made using its aqueous solution is hardly visible on a white or pinkish background. However, once cobalt chloride is dissolved in ethanol or dried, the resulting dehydrated form is blue, so that the text becomes clearly visible. Later I learnt that the color difference is related to the coordination of cobalt (octahedral in the hydrate and tetrahedral in the anhydrous form that is formed on contact with ethanol) and to the ligand field splitting of the orbitals (Griffith & Orgel, 1957).

Fascinating color change of solutions of transition metal salts in different solvents is one of the main attractions to the world of chemistry for many children. Organic compounds are also known to form solutions of different colors when dissolved in different solvents. This is due to different supramolecular associates formed by a dissolved molecule (solute) and the solvent molecules. Solvatochromism is commonly used in many areas of chemical and biological research to study bulk and local polarity in macrosystems (membranes *etc.*), or even the conformation and binding of proteins.

Despite its wide use, solvatochromism remains a largely unexplored phenomenon due to the extremely complex coupling of the many different interactions and dynamic processes that characterize it.

It is difficult to get direct information on the environment of a chromophore in solution. This challenge is exacerbated by the dynamics of the environment itself, which is labile and versatile in solution, in contrast to the solid state. Crystal structures of crystal solvates shed some light on the relation between the immediate environment of a chromophore in the condensed state and the optical spectrum that defines the observed color. Therefore, crystallization from different solvents can be used to model the solvation process, at least to some extent.

Pressure can fine tune the interatomic distances with or without changing the general symmetry and geometry of coordination; in this way optical properties can also be fine-tuned. The phenomenon is known as *piezochromism* (Reichardt, 1992). The mechanisms of piezochromism may be related to molecular rearrangement, conformational changes, breaking chemical bonds, or multiple cooperative phenomena (Li *et al.*, 2021). In crystals, structural changes can be followed directly by diffraction techniques and then related to changes in optical properties measured spectroscopically. It is more difficult to get such information for a molecular environment in solution.

In an article in this issue of **IUCrJ** (Sobczak & Katrusiak, 2024), the techniques of high-pressure crystallization, *in situ* X-ray diffraction and UV–vis spectroscopy were combined to understand structural aspects of solvatochromism. The authors focused their attention on a representative of a large class of the *N*-betaine dyes, Reichardt's dyes, namely 4-(2,4,6-triphenyl-1-pyridinio)phenolate [ET(1)]. These dyes are particularly sensitive to changes in the solvent environment and are thus used as probes for studying solvent–solute interactions (Reichardt, 1994). Their molecules comprise an extended conjugated and polarizable system, with a large permanent dipole moment. Additionally, the oxygen atom on the phenolate moiety is highly basic and prone to form hydrogen bonds with solvent molecules. The solvatochromic effect in this group of compounds was postulated to originate from differences between solvation spheres formed around the dye's highly dipolar electronic ground state and its less dipolar excited state (Reichardt, 1994).

The ET(1) crystals were put into a diamond anvil cell (DAC) immersed in a solution of ET(1) in a selected solvent (acetone, methanol or ethanol) and then compressed. Optical spectra of the solutions were measured as a function of pressure. At certain pressures, the original ET(1) crystals were found to recrystallize into solvates, and could be prepared *in situ* as single crystals at high pressure, facilitating their structure determination by single-crystal X-ray diffraction (Fig. 1).



Figure 1. Schematic overview of experimental procedures from Sobczak & Katrusiak (2024).

A detailed analysis of the chromophore environment in the solid state helped shed light on the relation between molecular structure, solute–solvent interactions and optical properties. By comparing the optical spectra in the solid state and in solution, the authors used this information to indirectly probe solution structure. Interestingly, on approaching crystallization, there were anomalous changes in the pressure dependence of the absorbance spectra, indicating clearly that while the zwitterionic form of the ET(1) was stabilized in the solvation sphere, the interactions formed with the solvent molecules were significantly altered above the hydrostatic limit of the solvent.

Relations between *solvatochromism* and *piezochromism* have attracted significant attention for a long time. Research has usually dealt with the effects of pressure on solutions of piezochromic compounds in different solvents (Burgess *et al.*, 1998). However, solvents may also have a pronounced effect on the piezochromism of solids. To achieve hydrostatic compression, solids are not studied at high pressure in isolation, but are immersed in a pressure-transmitting fluid. This fluid can interact with the solid and result in high-pressure solvate formation, solvent-assisted polymorphic transitions, or recrystallization (Zakharov & Boldyreva, 2019). One could expect that a pressure-transmitting fluid may also affect the piezochromism of crystals under hydrostatic compression. This phenomenon has not been studied yet though one can consider the recent contribution by Sobczak & Katrusiak (2024) as the first step in this direction. The pressure-transmitting medium in their work affected solid-state piezochromism *via* the formation of different solvates. One can also expect that other mechanisms are possible for other compounds, perhaps related to surface solid–liquid interactions or liquid-assisted recrystallization into other polymorphs (not a solvate). Studies of solvatochromic shifts under varying pressure conditions are challenging, but, as the recent work by Sobczak & Katrusiak illustrates so clearly, they open new avenues for understanding solvent-mediated effects in molecular systems. They also pave the way for exploring potential applications in pressure-sensitive molecular sensors and materials science, particularly in the development of advanced photonic materials.

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COMMENTARY

The challenges of growing great crystals – or at least good enough ones!

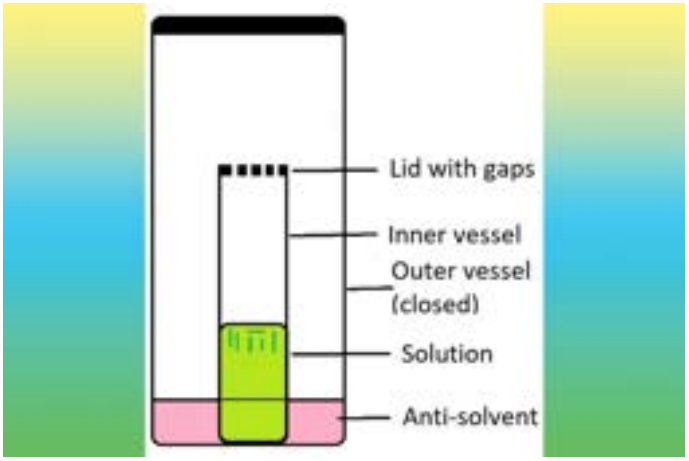


Figure 1. A possible setup for vapour diffusion. Note that the outer vessel is sealed. The more volatile anti-solvent passes through the gaps in the lid of the inner vessel and dissolves in the green solution. This transfer slowly reduces the solubility of the solute and results in the controlled growth of the green crystals.

Alexander J. Blake

The first challenge when composing a guide to growing crystals for crystallographic studies is deciding which techniques to include and, by implication, which to exclude. This question arises because across chemistry and materials science a wide range of techniques are used. Some are highly specialized but are vital to particular fields of study, one example being solvothermal methods for the synthesis of zeolites and metal–organic frameworks.

In this first contribution to the *Best practice* series in *Acta Crystallographica Section C: Structural Chemistry*, Roger Sommer (2024) sensibly concentrates on the solution methods which are the most relevant to the majority of chemists. After a detailed consideration of the advantages of crystallization and of structure determination, the methods outlined are organized so that the simplest, most accessible and most economical techniques are described first. Thus, there are explorations of the potential of slow evaporation, slow cooling and layering; these are followed by descriptions of somewhat more advanced techniques, such as mixed evaporation and vapour diffusion. This last technique (Fig. 1) is flexible, controllable and widely applicable: it does not demand any specialized equipment and so can easily be carried out in a typical chemistry laboratory. It is not uncommon that once the vapour diffusion technique is introduced to a research group, its obvious advantages mean that it rapidly becomes their method of choice.

A short section on sublimation, a technique which offers the possibility of solvent-free crystals, complements the description of the various solution methods. The first two entries in the list of references (Boyle, 2024; Blake, 2024) in the article have more details about sublimation techniques. In fact, the list of references itself comprises a valuable resource: it consists of both refereed publications and online resources, with the latter providing not only more detailed descriptions of some techniques but also links to even more resources.

Overall, the review article provides a concise and effective introduction to the subject of growing crystals suitable for structure determination. For many readers the techniques as outlined will suffice, but for others the article will serve as a springboard to finding the method that works best for their materials.

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COMMENTARY

Exploring crystal structure–physical property relationships with pressure



David R. Allan

In this issue of **IUCrJ**, Zwolenik *et al.* (2024) present a study of the evolution of the crystal structure and spectroscopic properties of a previously unobserved polymorph of 1,3-diacetylpyrene under both variable temperature and pressure. This material is an example of a molecular conjugated system; these systems are of significant interest for their structure–property relationships. The new β-form polymorph is structurally distinct from the α-form [also reported by the authors (Tchoń & Makal, 2021)], as the molecules are arranged in π-stacked layers, which leads to pronounced photoluminescence. The authors studied the systems piezochromism and piezofluorochromism and their relationship with the variation in interplanar π-stacking distances using single-crystal X-ray diffraction, UV–Vis fluorescence spectroscopy and DFT calculations. Their results show that the optical properties relate directly to the variation of the interplanar distances within the π-stacking.

The properties of a material are intrinsically linked to its structure at an atomic level, and it was with the development of X-ray crystallography that these fundamental relationships could begin to be unpicked with unprecedented detail. The foundational X-ray diffraction studies were performed by William Lawrence Bragg and William Henry Bragg who, in one of their seminal papers of 1913, determined the structures of zincblende along with the simple alkali halides, sodium chloride and potassium chloride (Bragg, 1913). For what would now be considered extremely well-known and comparatively simple structures, their discovery proved revolutionary and controversial, with contemporary chemists not readily accepting them. In sodium chloride, for example, no individual molecules were observed, and this profoundly contradicted what was expected from molecular theory at the time, where the precise integer stoichiometries were considered to be a consequence of the valency of atoms in molecules (Authier, 2013). Even after fourteen years, with the X-ray diffraction technique becoming more established, the leading chemist, H.E. Armstrong, still found Bragg's structure for sodium chloride `more than repugnant to the common sense, not chemical cricket' and `chemistry is neither chess nor geometry, whatever X-ray physics may be' (Armstrong, 1927). However, the profoundly definitive nature of X-ray crystallography was demonstrated unequivocally in 1929 with the determination of the molecular structure of benzene by Kathleen Lonsdale (Lonsdale, 1929). The shape of the molecule had been the subject of significant conjecture since its discovery by Michael Faraday in 1825 (Julian, 1981) with August Kekulé, who established the theory of chemical structure through valence (Kekulé, 1857), providing a preliminary model of the benzene structure in 1865 (Kekulé, 1865). The structure was the subject of speculation over the next few decades with the X-ray crystallography studies of Lonsdale, finally, providing a definitive resolution to the conjecture – offering new insights into the nature of the bonding within the benzene molecule and the electron-sharing nature of this archetypal conjugated system.

From its inception, therefore, X-ray crystallography studies not only provided a means of observing atomic positions within crystalline solids, but they also gave a unique insight into the nature of bonds, providing an unparalleled means of examining the properties and potential function of materials. The study of the correlation between the properties of crystalline materials and their structure has undergone considerable growth during the intervening period and encompasses a variety of physical effects, such as electrical conductivity, magnetism, catalysis and optical properties (Konar & Vittal, 2019). The use of the thermodynamic variables of temperature and pressure can strongly influence these physical properties, which can, in turn, be mapped to the accompanying variation of the structure. As the variable of pressure provides the most direct means of altering the chemical bonding and structure of a material, and it can be varied in the laboratory by several orders of magnitude (in comparison to temperature) from ambient to megabars, its application can, consequently, have a profound effect on the properties of a system (Tse, 2020). A prominent example is the observation of superconductivity in dense metallic hydrides, with very high critical temperatures (T_c) reported in compressed hydrogen sulfide [200 K, Drozdov *et al.* (2015)] and lanthanum hydride [260 K, Somayazulu *et al.* (2019)].

The extreme pressures required are often generated through the use of diamond-anvil cells that allow the sample to be probed with X-rays, for crystallographic studies and, as diamond is also sufficiently transparent to electromagnetic radiation across a wide energy range, the cells can also be used for both IR and UV–Vis spectroscopy. The diamond-anvil cell does impose restrictions on the level of data that can be collected, however, and for IR spectroscopy type-II diamonds (which are essentially free of nitrogen impurities) are required as they have low luminescence and are transparent to IR radiation (Mao, 2007). For single-crystal X-ray diffraction, the volume of accessible reciprocal space is restricted by the opening angle of the X-ray apertures and limits the completeness of a data set – particularly for low-symmetry systems. To improve completeness, two or more crystals can be loaded with sufficiently random relative orientations so that the portion of reciprocal space from each sample can be summed into a more complete set of data or, the sample can be mounted in the cell with an orientation that maximizes the potential data completeness for the crystal symmetry (Tchoń & Makal, 2021). The latter approach was adopted by Zwolenik, Tchoń and Makal who further improved both the completeness and resolution using synchrotron radiation, which can access X-ray wavelengths shorter than can be achieved on a lab source (Zwolenik *et al.*, 2024). They also adopted Hirshfeld Atom Refinement (HAR), which moves away from the more generally adopted spherical atom approximation and uses repeated *ab initio* molecular density calculations to successively determine the aspherical atomic scattering factors between cycles of least-squares structural refinement, with the calculated densities and refinements iteratively reaching convergence (Capelli *et al.*, 2014). This quantum crystallography approach (Grabowsky *et al.*, 2017) can provide dramatically improved refinement of atomic positions and ADPs for light atoms, particularly hydrogen atoms, and, in the current work, gave demonstrably improved structural models for the 1,3-di-acetylpyrene molecules.

To provide a deeper insight into the observed structural changes and the variation in the optical properties, Zwolenik, Tchoń and Makal utilized DFT calculations (Becke, 2014) to determine how the compression of the π-stacks affected the energy gap. They found that the accompanying DFT simulations accurately calculated the piezochromism associated with the π-stacking, which gave a 50 nm red-shift of the emission maximum in the high-pressure luminescence spectra from ambient pressure to 4 GPa. The work, therefore, provides a complete overview of the structure–optical property changes of the β-form of 1,3-diacetylpyrene with methodologies that are, encouragingly, becoming increasingly accessible to non-specialist laboratories.

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COMMENTARY

Chromic and dynamic: soft crystals of platinum(II) complexes pave the way for multi-responsive materials

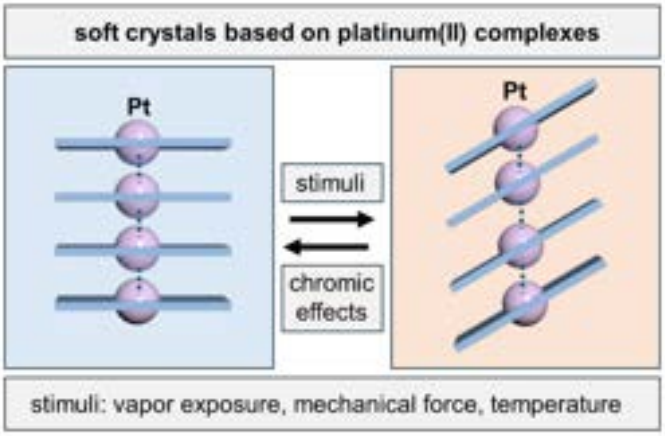


Figure 1. Reversible changes in color and luminescence in soft crystals of Pt(II) complexes triggered by gentle stimuli. Alterations in supramolecular architecture and interactions (π···π stacking and Pt···Pt contacts) generate changes in emission and optical phenomena.

Gonzalo Campillo-Alvarado

Smart materials and modern sensing technologies demand molecular systems capable of responding to external stimuli without damaging the structural integrity. Ideally, materials should be robust yet flexible to accommodate molecular changes that result from external stimuli. In the current issue of **IUCrJ**, a topical review by Kato (Kato, 2024) discusses a remarkable class of luminescent platinum(II) complexes that assemble into soft crystals. Soft crystals (*i.e.* crystalline materials easily deformed near room temperature) respond to external stimuli such as light, heat, moisture, or chemical vapors with structural transformations and phase transitions. Combined with the luminescent properties of platinum(II) complexes and metallophilic interactions (*i.e.* Pt···Pt contacts), the soft crystals display intriguing chromic behavior in response to stimuli. These materials hold exciting promise as design elements for sensors and probes.

Recent discoveries in soft and dynamic crystals have challenged the enduring perception that crystals are predominantly static and used solely to determine molecular structures via X-ray diffraction (Naumov *et al.*, 2020; Kato & Ishii, 2023). Indeed, a plethora of recent reports of single-crystal-to-single-crystal (SCSC) transformations and other mechanical effects have demonstrated that single crystals and solids can be far from static. Mechanical effects have been broadly categorized into disintegrative and restorative (Awad *et al.*, 2023). Disintegrative effects cause crystals to break down after external stimuli in a one-time event, often leading to separation accompanied by a leaping or `salient' effect. Conversely, cooperative and concerted molecular motions result in restorative effects, which enable crystals, including soft crystals, to retain macroscopic integrity, gain reversibility, and establish structure–property relationships by X-ray techniques (Posner *et al.*, 2015). Despite significant progress in the study of soft and dynamic crystals, establishing clear design elements and routes has long remained a major challenge in the field of crystal engineering, often relying on serendipity. The pertinent topical review by Kato (Kato, 2024) summarizes collective and systematic efforts on the development of Pt(II) complexes to generate resilient, adaptive and luminescent chromic crystals. These crystals respond to alterations in the molecular assembly with corresponding changes in color and luminescence, *i.e.* chromism (see Fig. 1). The review highlights chromism arising from alterations in the geometries of π···π stacking and Pt···Pt

contacts caused by vapor exposure, mechanical stimuli, heating and counterion engineering.

A key element in the review by Kato (Kato, 2024) relies on discussing changes to the molecular structures in crystals arising from external stimuli by single-crystal X-ray diffraction (SCXRD). SCSC transformations and phase changes provide unique insights into chemical transformations in solids and help correlate with chromic luminescent effects (Posner *et al.*, 2015; Atwood *et al.*, 2002; Chaudhary *et al.*, 2017; Naumov & Bharadwaj, 2015). For instance, SCSC transformations have been used to understand molecular underpinnings of photochemical reactions and polymorphic transformations in pharmaceutics and organic semiconductors (Pettersen *et al.*, 2020; Chung & Diao, 2016; Sherman *et al.*, 2020). In the review, Kato discusses the relationships between Pt···Pt distances and emission color changes using variable-temperature SCXRD and emission spectra (Saito *et al.*, 2020). The results showed a high dependency of color on stacking patterns and Pt···Pt distances, which are further affected by the temperature changes and substituents in a series of Pt(II) complexes. The work is reminiscent of mechanical effects in crystals involving metallophilic interactions with gold (*i.e.* Au···Au contacts), which exhibit similar electronic and luminescent phenomena (Seki *et al.*, 2015).

The second part of Kato's review discusses vapochromic transformations and triboluminescence in soft crystals of Pt(II) complexes, which are induced by vapor exposure and mechanical stimulus, respectively. Notably, single crystals exhibit numerous multi-stimuli transformations, allowing for cycling through vapor exposure, heating and grinding (Shigeta *et al.*, 2016) in a rare complex shape-memory behavior. Overall, Kato and collaborators have shown that SCSC transformations are an unparalleled analytic tool for understanding structure–property relationships of soft and dynamic crystals, as well as for developing advanced and reversible multi-functional materials.

Developing soft, dynamic crystals using Pt(II) complexes as building blocks, as discussed in the review by Kato (2024), represents a significant step forward for the rational and systematic design of stimuli-responsive chromic materials. Given the prominence of Pt(II) complexes in medicinal chemistry and catalysis, novel systems are expected to continue demonstrating unusual and attractive optical properties for materials design. Future development may include soft crystals using more than one metalophillic contact (*e.g.* Pt···Pt, Au···Au) or incorporating cooperative supramolecular interactions (*e.g.* chalcogen bonds, boron coordination). Advances could result in multi-responsive crystals capable of mechanical deformation and exhibiting reversible chromic phenomena in response to stimuli, potentially resulting in molecular-based sensors and devices that adjust to the curvature of surfaces such as human skin or plant leaves (Wang *et al.*, 2017; Wang *et al.*, 2024). The topical review by Kato (2024) is a clear and concise reference for crystal engineers and material scientists interested in developing a rational and systematic approach to designing multi-stimuli responsive soft crystals.

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MEETING REPORT (IUCR SUPPORTED)

Practical courses on advanced methods in macromolecular crystallization: 20 years of history and future perspectives



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The first Federation of European Biochemical Societies Advanced Course on macromolecular crystallization was launched in the Czech Republic in October 2004. Over the past two decades, the course has developed into a distinguished event, attracting students, early career postdoctoral researchers and lecturers. The course topics include protein purification, characterization and crystallization, covering the latest advances in the field of structural biology. The many hands-on practical exercises enable a close interaction between students and teachers and offer the opportunity for students to crystallize their own proteins. The course has a broad and lasting impact on the scientific community as participants return to their home laboratories and act as nuclei by communicating and implementing their newly acquired knowledge and skills.

1. Introduction

Macromolecular crystallography is one of the most powerful structural biology techniques. Many fundamental fields of science benefit from this technique, such as chemistry, biology, physics and environmental science. The experimental procedure requires the growth of well diffracting crystals. Knowledge on how to nucleate, grow, analyse, handle and improve crystals is therefore an essential requirement to obtain the necessary X-ray diffraction data that will enable the scientist to determine a three-dimensional arrangement of atoms. Even though basic crystallography principles are theoretically taught at universities, practical training on how to obtain the required crystals is typically missing.

This lack of formal education has already been identified in our community, and the International Union of Crystallography (IUCr) has a permanent Commission on Crystallographic Teaching with its own microsymposia accompanying the regular congress. Still, most of the effort of our community has been focused on the potential of web technologies to better reach students (Kantardjieff, 2010; Kantardjieff *et al.*, 2010). Recently, Gražulis *et al.* (2015) and Dawe *et al.* (2022) highlighted the role of crystallography as an educational tool taught at different levels. From this series of articles, the need for specialized hands-on workshops or schools to teach crystallization, not only the fundamentals but also the methods and procedures, has been recognized. Under this premise, the Federation of European Biochemical Societies (FEBS) Advanced Crystallization Course was born two decades ago to fill the gap between basic theoretical knowledge and concrete hands-on skills. The FEBS organization provides detailed guidelines for advanced course programmes for course organizers

(https://www.febs.org/events/advanced-courses/for-advanced-courses-organizers) with which the course layout must comply. This year, the tenth edition of the FEBS crystallization course took place from the 9th to the 15th of June at the Faculty of Science, University of South Bohemia in Ceske Budejovice, Czech Republic, and included contemporary topics like fragment screening, *in cellulo* protein crystallization and basic cryo-electron microscopy (cryo-EM) principles.

2. Historical context

Crystallography is one of the scientific disciplines whose importance has been decisive for the development of chemistry during the last third of the 20th century, due to its contribution to the knowledge of the state of aggregation of matter, in which the components (atoms, ions, molecules) are arranged in an orderly and repetitive manner to form the crystalline state. Over the course of history, many Nobel Prizes (NPs) have been awarded for scientific achievements directly related to, or involving the use of, crystallographic methods and techniques. Starting in 1901 with the NP in Physics awarded to W. C. Röntgen for the discovery of X-rays, to the most recent NP in Physiology or Medicine, 2021, to D. Julius and A. Patapoutian for their discovery of receptors to sense temperature and touch, a total of 33 prizes have been given to crystallography-related investigations and discoveries. Crystallography, when applied to macromolecules, has profoundly influenced biology, biochemistry, physiology and medicine. It is the basis of structural biology and structural genomics, helping us study proteins, nucleic acids, and their complexes such as ribosomes and viruses. Detailed knowledge of the structure of biological macromolecules allows us not only to understand the relationship between structure and function but also to make rational proposals for functional improvement of medication, which is a top priority in today's biomedicine.

Unfortunately, there is no widely accessible formal education in this field at either the undergraduate or graduate level. Therefore, the aim of the FEBS Advanced Course on macromolecular crystallization was, from the very beginning, to close this gap of knowledge while exposing the student to focused hands-on practice.

The first concept of this kind of practical crystallization course emerged in the form of the crystallization course (CC) that took place in 2001 and was repeated in 2003 and 2005 in Nové Hrady (Czech Republic) as a locally organized and supported event. In 2004, the course was supported by FEBS and opened to a much broader international community of students and early career researchers. Renamed to `Advanced methods in macromolecular crystallization', it was from thereon organized biennially. Ongoing support from FEBS, along with a strong commitment of the local organizing team and participating international lecturers and tutors, enabled the firm establishment and continuance of the now 20-year-old tradition (Fig. 1). Despite the difficulties encountered during the COVID pandemic, the FEBS Advanced Crystallization Course took place as one of the rare in-person events in August 2021 (ninth edition), attended by a consistent number of participants. However, the COVID pandemic left its mark and prompted us to postpone the tenth edition by one year.



Figure 1. Timeline and snapshots of the FEBS Advanced Course on macromolecular crystallization.

From 2004 to 2018, the courses were held in the castle of Nové Hrady, located in the south of the Czech Republic (South Bohemian region). This distant and rather remote place allowed all participants to be offered accommodation either on-site or in the vicinity of the castle and thus spend the whole course and free time either informally interacting with each other or working on their scientific project, discussing problems in the laboratory with peers and tutors. Since 2021, the event has been organized at the Faculty of Science of the University of South Bohemia in Ceske Budejovice (Budweis), in the lecture halls and the laboratories of the Structural Chemistry department. The participants are accommodated on the university campus in the student dormitories, close to the venue at the Faculty of Science.

Compared with the very first CC event, the number of applicants almost doubled and increased every year in comparison with the number of available places (Fig. 2). According to the guidelines for practical FEBS Advanced Courses, the ratio between the number of teachers and students should be close to one or higher, which requires careful selection of the students based on their curriculum vitae, motivation letters and recommendation letters from their supervisors.

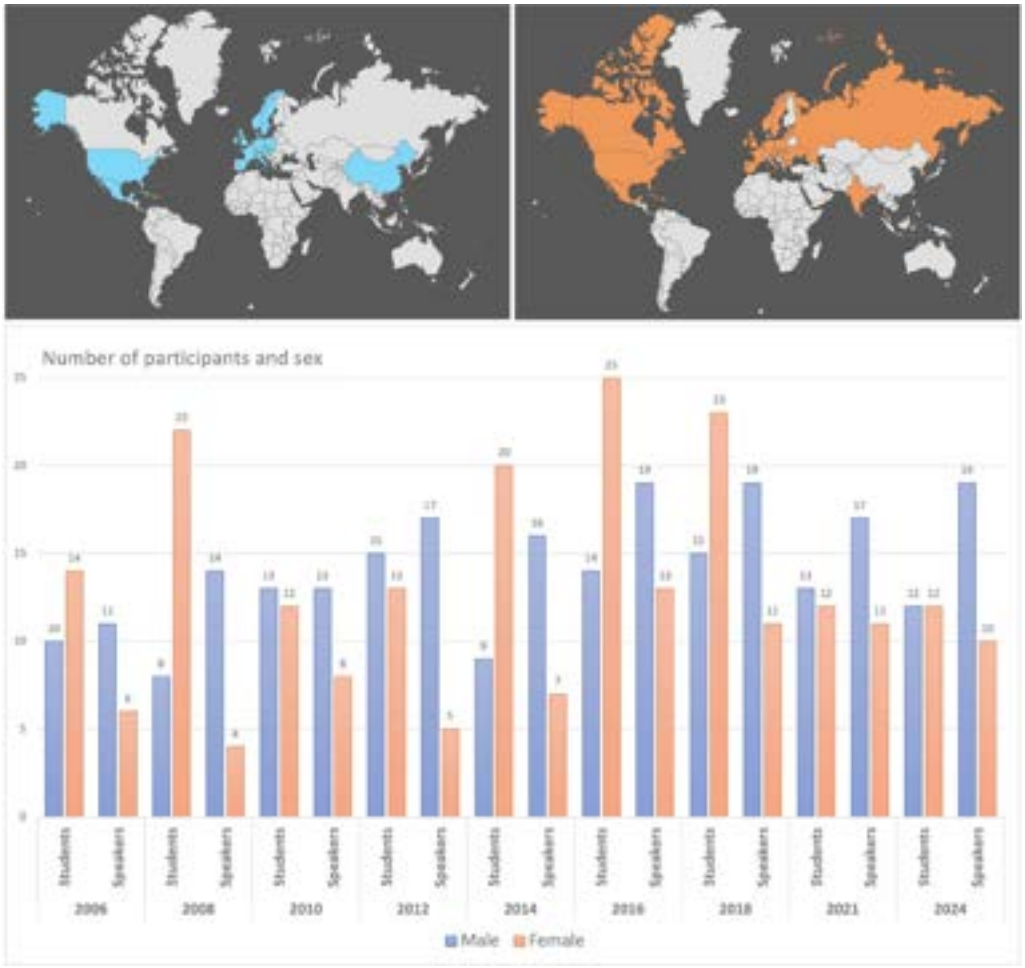


Figure 2. Graphs representing the origin and total number of students and speakers over the past nine editions (2006–2024) of the course. The upper maps show the country of origin of speakers (blue) and students (orange) and the lower graph the total number and sex of students and speakers.

3. Description of the course

The course not only offers theoretical lectures, covering the fundamental principles of crystallography, sample preparation for crystallization experiments, nucleation and crystal growth, the principles of various crystallization techniques, and experimental strategies for screening and optimizing crystallization conditions, but also incorporates current advancements in structural biology methods, including *in cellulo* crystallization and cryo-EM basics.

The FEBS Advanced Crystallization Course is organized as an event lasting six days, starting on Sunday afternoon with some introductory lectures and finishing on Saturday morning, with practical exercises on crystal flash-cooling and data collection. A typical day of the course starts with morning lectures on different crystallization topics given by expert speakers and followed by discussions (Fig. 3). During the breaks between the lectures or practical exercises, participants can also interact directly with the speakers and discuss their ideas and scientific problems. After lunch, the practical sessions start in the laboratories; the topics usually relate to the morning lectures. Some of the hands-on training sessions are compulsory, some of them are optional, and students can decide according to their preferences and needs. After dinner, the teaching continues with non-compulsory lectures on the theoretical background of crystal structure determination; these optional lectures are not a part of the regular programme of the crystallization course (Fig. 3).



Figure 3. Lectures and practical sessions. From top left to bottom right: participants sitting in the theatre hall during lectures; lunch in the Mirror Hall of the castle; laboratory practical exercise with Martin Caffrey demonstrating the lipid cubic phase; optional evening lecture with Jeroen Mesters explaining Bragg's law and Ewald's sphere of reflection.

Two evening sessions are also devoted to the students' own posters, where students not only present their data but also discuss their difficulties and problems with their peers and the specialists. A scientific committee comprising various specialists also assesses the posters using a standardized scoring sheet, and outstanding ones are awarded poster prizes.

Besides the get-together evening sessions, various social events, such as an excursion, historical dancing, concerts or gala dinners, were organized during the courses to let the participants interact in a more informal atmosphere (Fig. 4).



Figure 4. Social activities, poster sessions and poster prizes. From top left to bottom right: visiting the Budweiser Budvar: Czech National Brewery; dancing lesson in the castle; poster session; best poster prizes (awarded in 2021 and 2024 by the IUCr).

3.1. Topics – theoretical lectures

The FEBS Advanced Crystallization Course was designed to teach the participants a wide range of crystallization and structural biology techniques; the lectures and hands-on practical exercises are given and supervised by experts from all over the world (see Tables S1 and S2 in the supporting information).

Mainly in order to follow the same experimental path required to produce structural information, the first topic is protein purification, including purification of protein complexes and adaptation of the protein sequence, for example, increasing its solubility (Table 1). How to characterize a protein solution in terms of purity, state of aggregation *etc*. is stressed as a fundamental part of the process prior to crystallization. Before starting with more commonly used crystallization techniques, the concepts of the protein phase diagram, supersaturation, and the thermodynamic principles of crystal nucleation and growth are introduced. The many routes to find initial crystallization conditions are shown and discussed prior to being implemented by the students during the hands-on sessions. From the beginning for each edition, the programme is pre-evaluated and, where needed, adapted following suggestions by tutors and former participants. For example, in the latest edition (2024) we have included a talk on fragment screening. The full list of past and present topics covered during the theoretical lectures is provided in Table 1 and detailed further in Table S1.

Table 1
Topics offered at the FEBS practical crystallization courses

Fundamentals	Nucleation; crystal growth mechanism; phase diagrams
Sample preparation	Construct design; sequence adaptation; entropy reduction; expression; purification
Sample characterization	Dynamic light scattering/static light scattering/differential scanning fluorimetry; microscale thermophoresis; UVEX crystal imaging systems; ultracentrifugation
Crystallization methods	Vapour diffusion, hanging and sitting drop; crystallization under oil; high-throughput methods; lipidic cubic phase and micelles; dialysis and temperature control methods; complexes, protein–protein/protein–nucleic acid
Advanced methods	Liquid diffusion methods: capillaries/microfluidics; fluorescent trace labelling; seeding/microseed matrix screening; ionic liquids, nano/microcrystals for X-ray free-electron lasers; *in cellulo* crystallization; fragment screening
Complementary methods	Small-angle X-ray scattering/small-angle neutron scattering; NMR; cryo-EM
Other methods	Crystal handling; diffraction measurement; publication of scientific results

3.2. Topics – hands-on practical exercises

The freshly acquired knowledge from the morning lectures is implemented and applied during the four-hour afternoon practical exercises. On average, there were approximately 28 students, who were typically divided into six groups. During the online registration process, students were solicited to bring their own proteins. Students who would like to test their own samples were evenly spread between the different groups to increase their chances to discuss their own problems with the specialist. A T-shirt colour-code was introduced to identify each group composed of approximately four to six students (Fig. 5). All groups completed all practical exercises according to a prearranged time schedule. In addition, free time slots were available to deepen a particular hands-on skill or to further crystallize students' own samples as required, choosing one of the techniques offered in the course. A detailed list of past and present topics covered during practical exercises is given in Table S2.



Figure 5. Hands-on training. From top left to bottom right: crystallization in capillaries (Jose A. Gavira); the secret life of crystallization drops (Bernhard Rupp); observation of crystal growth and seeding (Terese Bergfors); crystallizing own proteins (Jeroen R. Mesters); crystallization under oil (Lata Govada); intracellular protein crystallization (Lars Redecke).

Students bringing their own protein(s) were also required to provide a minimum amount of information such as the final purification column elution profile, Coomassie stained SDS–PAGE gel of the protein and its final concentration, together with a full description of the composition of the solute and storage condition. In addition, model proteins such as lysozyme, thaumatin or xylanase are used to carry out hands-on crystallization experiments.

The students' proteins were firstly characterized in solution by biophysical methods (*e.g.* dynamic light scattering). The tutors individually discussed the students' samples and proposed an optimal experimental strategy to obtain crystals. The crystallization trials were observed under a microscope and promising conditions were subsequently optimized using standard and advanced crystallization methods (Fig. 5). If the desired crystal was obtained, the crystal could be fished and cryocooled in liquid nitrogen with cryoprotection agents and measured later at the home-source diffractometer or sent to a synchrotron. The direct interaction with the experts, allowing more personalized discussions on specific scientific issues, has resulted in various collaborations and publications: see for example de Wijn *et al.* (2018, 2019) and Benedek *et al.* (2019).

3.3. Course organization

Each edition of the course is carefully organized at least one year in advance. The main organizer of the course prepares a proposal for FEBS for the advanced practical course according to the instructions available at https://www.febs.org/events/advanced-courses/for-advanced-courses-organizers. After the selection process, the course organizers may be asked to clarify several points concerning the evaluation of the proposal and filed appendices. Meanwhile, the organizers (Fig. 6) structure the web pages and course administration, arrange for the communication with all participants, handle the students' applications and admissions, propose Youth Travel Fund (YTF) grant awardees (see the FEBS web page for further information; https://www.febs.org/events/advanced-courses/for-advanced-courses-organizers), and finalize the programme schedules for lectures and laboratory exercises.



Figure 6. Organizers of the FEBS practical crystallization courses. From left to bottom right: FEBS2004–FEBS2012 (Pavlina Rezacova, Rolf Hilgenfeld and Ivana Kuta Smatanova); FEBS2014–FEBS2018 (Ivana Kuta Smatanova, Juan Manuel Garcia-Ruiz and Pavlina Rezacova); FEBS2021 (Jose A. Gavira, Ivana Kuta Smatanova, Pavlina Rezacova and Jeroen R. Mesters).

At the earliest opportunity, potential sponsors are contacted to seek their support for the course. Sponsors have the option to select the way in which they would like to contribute. Typically, companies provide consumables for hands-on practical exercises, support coffee breaks or evening activities (refreshments during evening lectures), or cover registration fees for individual students. All forms of sponsorship are highly appreciated. The sponsor's logos and advertisements are prominently displayed

on all course materials, on the web page, and in the lecture hall and poster display area.

With the support of FEBS and the University of South Bohemia, along with the strong commitment of the local organizing team and the participating international lecturers and tutors, we have been able to keep the registration fee low for an extended period, especially in comparison with other similar courses worldwide.

The collected abstracts of all lectures, laboratory exercises and poster presentations are published in a special issue of the Bulletin of Czech and Slovak Crystallographic Association, *Materials Structure in Chemistry, Biology, Physics and Technology* [ISSN 1211–5894 (print), ISSN 1805–4382 (online)].

3.4. Participants

The number of students participating in FEBS Advanced Courses is generally limited to 24, with a ratio of tutors/teachers to students of 1:2, in agreement with the FEBS criteria. The maximum capacity of the Laboratory of Structural Chemistry is 30 students, and with prior consent of the FEBS Advanced Courses (AC) committee the number of students admitted to the CCs was frequently increased to on average 28 students (Fig. 7). The steady interest of students for this course over the past 20 years has stimulated and convinced us as organizers, tutors and lecturers to continue to offer this course.

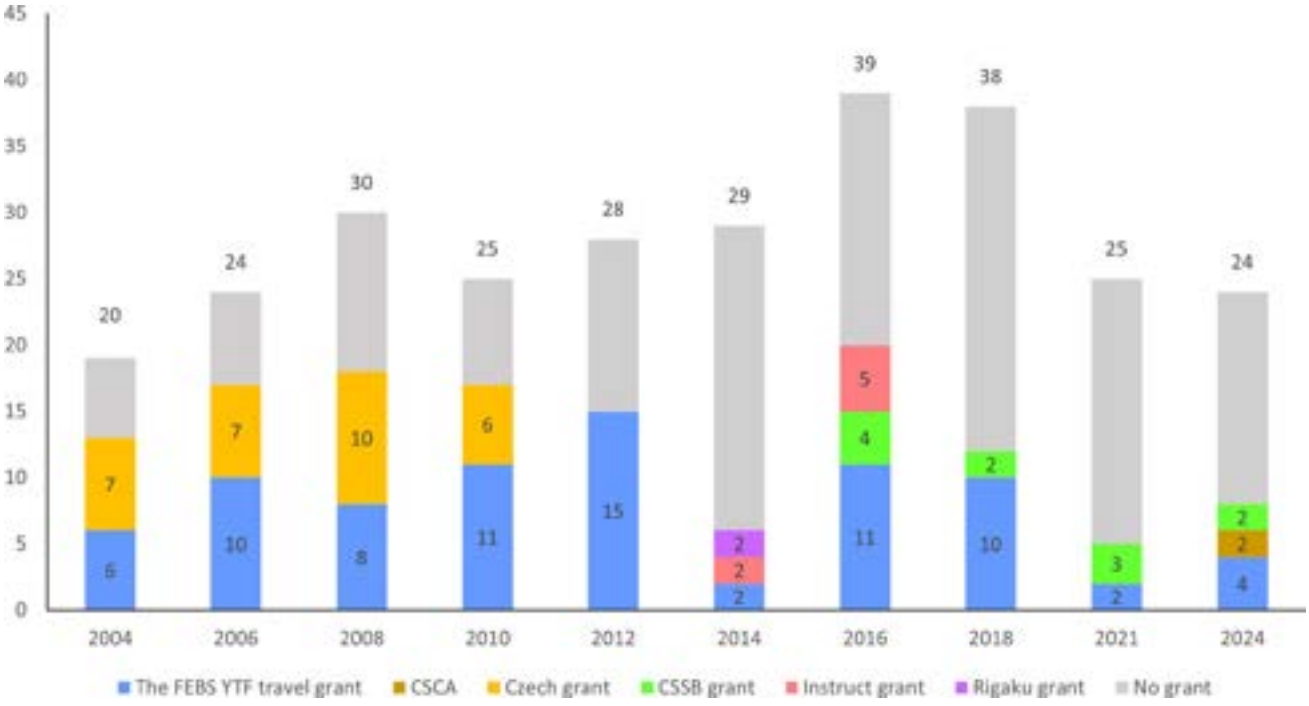


Figure 7. Number of grants provided to students by institutions, associations and companies.

Applicants such as PhD students and junior postdoctoral scientists fulfilling the required criteria have the possibility to apply for a FEBS YTF grant supporting their participation at the FEBS course. In addition, a transcontinental YTF award can be offered for the participation of young scientists from outside the FEBS area. Several societies and associations have also supported students at the courses, such as the Czech and Slovak Crystallographic Association (https://xray.cz) and the Czech Society for Structural Biology (https://cssb.structbio.org/) (Fig. 7).

3.5. Course evaluation

During the closing ceremony, participants receive their certificate of participation in exchange for the filled FEBS evaluation questionnaire. In this questionnaire, participants rate (either excellent, good, adequate, poor or inadequate) the programme organization, programme quality, scientific training by the speakers and tutors, subject state of the art, time for discussions, balance between hands-on training and lectures, duration of the course, location and accommodation, and quality of facilities (lecture hall and laboratories) including technical equipment. In addition, space is provided for suggestions for improvements of future courses and for additional comments.

Overall, the participants rated most issues surveyed as excellent or good, with only some solitary/personal adequate to inadequate ratings on one or another single item. The overall averaged rating over all participants is shown in Fig. 8.

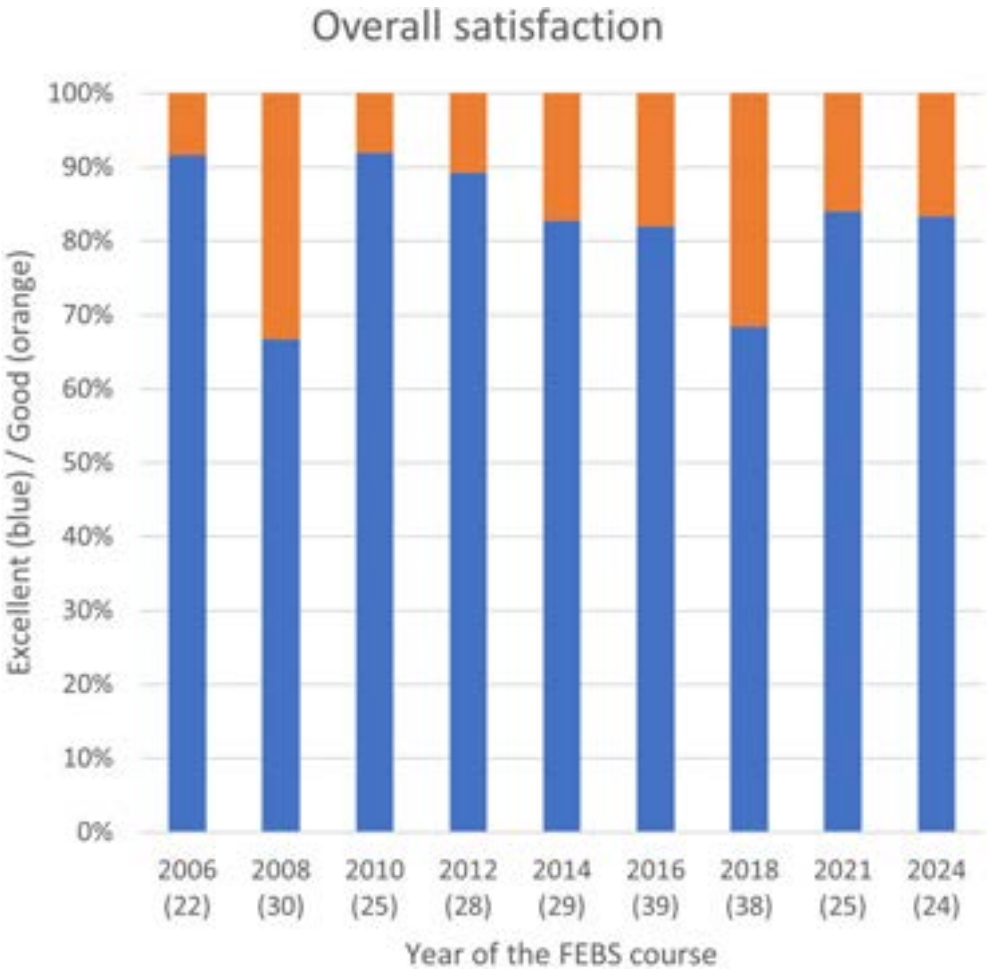


Figure 8. Summary of the averaged scores by year of the FEBS evaluation questionnaire. The number of students that evaluated the courses is given in brackets.

4. Future perspectives

Conventional X-ray diffraction techniques, along with new technologies in X-ray free-electron lasers, neutron diffraction, serial crystallography *etc*., have diversified the number of strategies for determining atomic models of macromolecules and macromolecular assemblies while expanding the requirements for crystalline samples. Nowadays, samples are required to be either a single crystal or a slurry of thousands of nanocrystals of homogeneous size, in the size range of nanometres to millimetres. Samples are characterized either at room temperature or under cryogenic conditions. In any case, the need for a crystal sample still requires the right crystallization conditions, which even today are mainly found by a trial-and-error approach. Although artificial intelligence (AI) may soon contribute to this process, we still require more fundamental knowledge on the mechanisms involved in protein crystal growth, as today's overall knowledge is still insufficient to predict the behaviour of a particular protein in solution. Therefore, spreading basic knowledge on protein crystallization at dedicated practical courses for young scientists and showing how both traditional and advanced methods can be used to screen the phase diagram have not lost their importance, and will remain an important task in the near future.

Due to the course's ongoing popularity and financial support from the FEBS AC committee, this year the tenth-anniversary edition has been held. This CC is unique in the field of macromolecular crystallization thanks to its practical focus and substantial discussions on developments and methodologies, its coverage of a wide range of structural methods, and, most importantly, its continuing acceptance by the students. Building on this success, we plan to continue to offer the course, maintaining the established organizational structure while incorporating relevant topics beyond the recently assimilated *in cellulo* crystallization, fragment screening, cryo-EM basics, or the role of *AlphaFold* and AI in future development. The aim of the course has always been to educate and motivate young scientists to undertake approaches that are more rational to the crystallization of macromolecules and to combine numerous techniques to tackle their structural problems.

5. Conclusions

The legacy of these CCs, which we call advanced because they included unusual techniques and methods, lies not only in their temporal persistence but also in the lasting impact they have had in shaping the research trajectories of a large group of students, industrial applications and academic activities in the wide-ranging field of crystallization. The continuation of these courses serves as a beacon, guiding and inspiring the next generation of scientists and engineers towards new frontiers of discovery and innovation.

Despite the divergent levels of impact on the students' academic development, student participation in these events has formed a cohesive community that transcends individual courses and extends its influence on other educational programmes, including the International School of Biological Crystallization (Granada) and the FEBS practical and lecture course named `Biomolecules in action' (Budweis and Hamburg). Additionally, the community involves its teachers and tutors in global conferences such as the International Conference on the Crystallization of Biological Macromolecules and collaborates with entities such as the IOBCr (International Organization for Biological Crystallization) (https://en.wikipedia.org/wiki/International_Organization_for_Biological_Crystallization). This strengthens networking and knowledge and experience transfer within a wider scientific community.

Supporting information

Supporting information. DOI: https://doi.org/10.1107/S1600576724007106/dv5018sup1.pdf

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Conflict of interest

The authors declare no competing interests.

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INTERVIEW

Women in Crystallography - Dr Julia Contreras-García interview



Women in Crystallography T-shirts at ECM34.

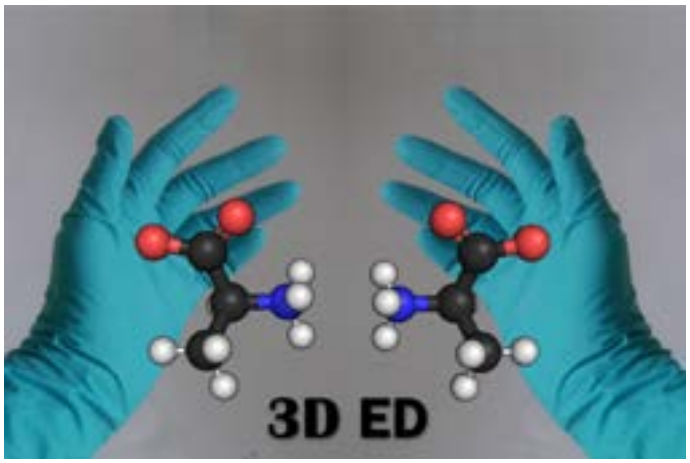
This interview with Dr Julia Contreras-García, President of the "Women in High Pressure" organisation, is part of the "Women in Crystallography - A Video Series", a project of the GIG03 (General Interest Group on Education in Crystallography of the ECA) and funded by the Royal Society of Chemistry within the framework of the "Inclusion and Diversity Fund". Dr Contreras-García discusses her research on electron density and its applications in understanding chemical bonds and predicting properties like superconductivity.

She shares the origins of the "Women in High Pressure" group, which was founded in response to the lack of female representation in the European High-Pressure Committee. The group began by creating an online database to ensure visibility for women in the field. Over time, the initiative grew through events at conferences and the creation of "Women in Crystallography" t-shirts that you can see at conferences today. This initiative has already started funding its first recipients.

Dr Contreras-García encourages students and postdocs to sign up for the "Women in High Pressure" database, emphasising the importance of building awareness of gender biases and becoming part of a supportive community for women in science.

ASSOCIATES NEWS

SIG4 (ECA) Distinguished Publication Award 2024



Stéphanie Kodjikian, Tatiana Gorelik

The “Distinguished Publication Award 2024”, presented by the Special Interest Group on Electron Crystallography of the European Crystallographic Association (ECA SIG4), recognizes the most outstanding paper published in 2023. This award celebrates significant advancements and applications in the field of electron crystallography. Candidate publications were evaluated based on several criteria, including innovation, complexity, high-quality research with a focus on electron crystallography, broad scope, and impact on the community. The jury was made up of internationally renowned experts in electron crystallography. SIG4 extends its thanks to them for their engagement and professionalism.

This year’s winner is the paper titled “Accurate structural models and absolute configuration determination using dynamical effects in continuous-rotation 3D electron diffraction data” by Paul B. Klar, Yaşar Krysiak, Hongyi Xu, Gwladys Steciuk, Jung Cho, Xiaodong Zou, and Lukas Palatinus, published on April 20, 2023, in *Nature Chemistry,* **15**, 848−855 (https://doi.org/10.1038/s41557-023-01186-1).

Klar *et al.* describe a method for analysing continuous-rotation 3D electron diffraction (3D ED) data for routine structure analysis across a broad range of materials, including minerals, framework structures, and organic compounds. The paper introduces the concept of 'virtual frames' to calculate integrated intensities using the dynamical theory of diffraction. This approach is then applied to the dynamical refinement of crystal structure models using 3D ED data from 19 different compounds. The authors demonstrate that this refinement approach, which accounts for the multiple scattering of electrons, is clearly superior to the commonly used kinematical refinement, which neglects multiple scattering. Along with reducing noise in Fourier maps and improving overall agreement between measured and calculated intensities, dynamical refinement reveals structural details more clearly, such as hydrogen sites and guest molecules. A key focus of the paper is the determination of the absolute structure of chiral compounds, demonstrated by successfully assigning the correct handedness based on 3D ED data from 58 chiral molecular crystals.

The jury was particularly impressed by the wide-reaching impact of the work, as the results were based on data from 10 different transmission electron microscopes across various laboratories. This impact is further underscored by the paper’s nearly 50 citations as of September 2024.

We congratulate the winners and look forward to future developments in the field of electron crystallography.



Gwladys Steciuk (left) and Paul Klar (right) at ECM34, Padua, Italy, August 2024.

MEETING REPORT (IUCR SUPPORTED)

European Crystallographic Meeting 34



Some past and new members of the Executive Committee of ECA. From left to right: Marijana Đaković, Delia Haynes, Andrew Maloney, Arie van der Lee, Andrea Ienco, Consiglia Tedesco, Klaudia Hradil, Chiara Massera, Jan Dohnálek, on screen: Antonia Neels, Maria José Sanchez Barrena.

Jan Dohnalek, ECA

During the last week of August (26-30th August 2024) the crystallographic community met in the medieval city of Padova, Italy, to discuss the latest developments and results in the field of crystallography (https://www.ecm34.org/). The Congress welcomed more than 800 participants who contributed in 43 microsymposia spanning from quantum crystallography over applications in material and biological sciences to teaching and crystallography in art, accompanied by about 700 posters. The plenary lectures were given by Kristina Djinovic on the molecular architecture of muscles and by Jonathan Wright providing insights into imaging single crystals in powder samples. The most significant developments in the key directions of instrumentation, computational tools and application of crystallographic approaches in various branches of research were presented in 16 keynote lectures. The social program offered amongst others the Science Slam, a great concert of classical music in Palazzo Liviano, a public lecture *Einstein and Me* by Gabriella Greison, a students' mixer, and an unusual experience in the form of a conference dinner in one of the historical city squares. This Congress was complemented by seven satellite events, including the European Young Crystallographers Satellite Meeting or the special event Crystallography in School promoting teaching of crystallography with school science teachers. The organizing committee chaired by Gilberto Artioli and Giuseppe Zanotti with the help from the chairs and co-chairs of the individual microsymposia managed to prepare a great event with exciting topics, excellent speakers, and plenty of space for social and scientific interactions. The crystallographic song *A musical account of a rather unfortunate trainee crystallographer* by Bill Clegg was performed with the music of Wolfgang Amadeus Mozart in the Science Slam and also during the closing ceremony to great success. It was a treat to all the crystallographers - allowing them to enjoy not just science but also good music and fun.

Five crystallographic prizes were awarded during the Meeting. Firstly, the Max Perutz Prize to Professor Mariusz Jaskólski, Adam Mickiewicz University in Poznań, accompanied with his lecture *A path paved with crystals*; the Erwin Felix Lewy Bertaut Prize to Daniel Mazzone, Paul Scherrer Institute, Villigen; and the Alajos Kálmán Prize to Piero Macchi, Politecnico di Milano. Then, two newly established prizes were awarded for the first time: the Lodovico Riva di Sanseverino Prize in recognition of notable contributions to the dissemination of crystallography in the field of education at all levels to Claire Murray, a Freelance Scientific Researcher in Germany, and the George M. Sheldrick Prize to a non-tenured researcher for outstanding scientific contributions in the field of structural sciences to Marta Morana, University of

Florence. Find more information about the European Crystallographic Association (ECA) prizes here: https://ecanews.org/prizes/.



The Max Perutz Prize awardee Professor Mariusz Jaskólski during his lecture: *A path paved with crystals.*

Eleven poster prizes, supported by companies, IUCr Journals, the CCDC and others, appreciated the best poster presenters, in specific fields of research, instrumentation development or at the start of their career.

The previous Executive Committee of the ECA finished its term and a new Committee was elected by the ECA Council. Achievements of the outgoing Executive Committee were appreciated by the Council and some Committee members have been re-elected into their new roles. Dr Arie van der Lee (Université de Montpellier) has become the new President of the ECA. The ECA Council has approved the organization of the European Crystallographic School 11 in Stockholm, 21st-27th June 2026, and of ECM37 in Athens, August 2028.

MEETING REPORT (IUCR SUPPORTED)

2nd High-Pressure Single-Crystal X-Ray Diffraction Summer School



Group picture taken during the School, with participants and lecturers present. The picture was taken in front of the Centre for Science at Extreme Conditions (CSEC) of the University of Edinburgh.

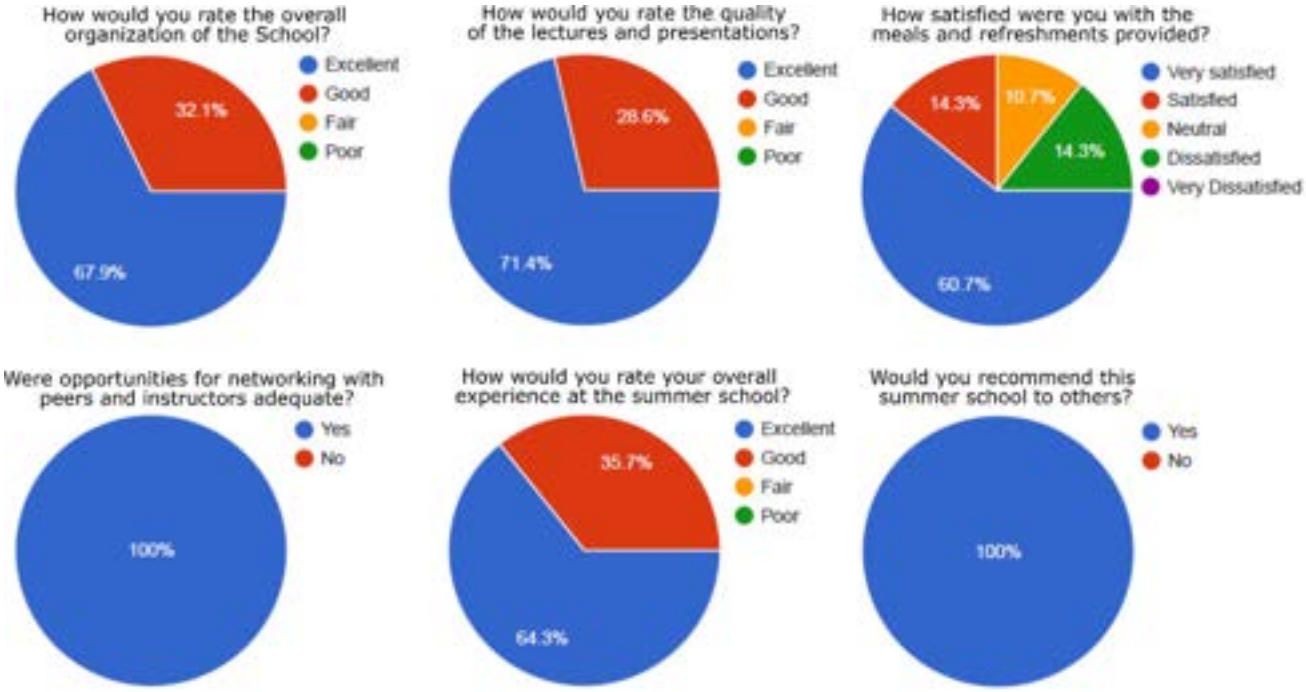
Dominique Laniel, Elena Bykova, Maxim Bykov, Leonid Dubrovinsky, Natalia Dubrovinskaia

The 2nd High-Pressure Single-Crystal X-Ray Diffraction Summer School was held at the James Clerk Maxwell Building of the University of Edinburgh (Edinburgh, Scotland), from July 22nd to July 26th 2024 (https://indico.ph.ed.ac.uk/event/282/overview). The School was supported and approved by the IUCr, through the IUCr Commission on High Pressure. A total of 30 participants from 15 countries and 4 continents attended the full week. These participants were provided an accommodation at the University's Pollock Halls. The School was such a vibrant success that we will hold another one next summer, but this time in Frankfurt (Germany) — and certainly in upcoming years as well, making it an annual event.

The intent of the School was to train young and established scientists in the recent methodological advancements in high-pressure single-crystal X-ray diffraction. These new developments enable solving and refining crystal structures from tiny micrometre- to submicrometre-sized crystallites confined in diamond anvil cells up to pressures of multiple hundreds of gigapascals (GPa). An overview of the necessary fundamental theoretical and methodological principals, including diamond anvil cell preparation, strategy of experiments, laser-heating, introduction to software and single-crystal X-ray diffraction (SCXRD), was covered through lectures. These were accompanied by 13 hours of hands-on sessions, where participants were divided into five small groups of six individuals, each with its own instructor, and guided through step-by-step tutorials and examples. At the end of the School, participants were able to perform basic high pressure SCXRD experiments, as well as data processing and interpretation. The lectures and hands-on tutorials were given by a total of nine experts, including three from the United Kingdom, five from Germany and one from the United States, with a woman-to-man ratio of 4:5.

To maximize discussions between participants as well as between participants and lecturers, snacks, lunches and dinners were provided on-site for the complete duration of the School. All participants were requested to bring a poster presenting their research, which were shown and displayed during two poster sessions. Moreover, extracurricular activities took place during three evenings, namely a whisky tasting, a walking tour of Edinburgh and a ceilidh — a traditional Scottish group dance.

During the last day of the School, the IUCr awardees were given their certificates. The participants were also requested to fill out an online survey to gauge their satisfaction and identify aspects to improve for next editions of the School. Overall, their response was overwhelming positive. Indeed, all 28 participants that took part in the survey said they would recommend the School to others, while 64.3% and 35.7% rated their overall impression of the School as “Excellent” or “Good”, respectively. Among all surveyed aspects, the one with the least positive feedback was meals and refreshments, for which 75% of the participants were either “Very satisfied” or “Satisfied”, but 25% were “Neutral” or “Dissatisfied”. In the future, a different catering company will be used.



Questions and pie chart representations of the answers obtained from the survey filled out by 28 participants at the end of the School.



IUCr Young Scientist Awardees (left to right): Benedito Donizeti Botan Neto (Universitat de València, Spain), Xuejing He (University of Tokyo, Japan), Almudena Inchausti Vallés (Complutense University of Madrid, Spain) and Natalia Sacharczuk (Adam Mickiewicz University, Poznań, Poland).

Given the increasing importance of the diamond anvil cell single-crystal X-ray diffraction of polycrystalline samples methodology, as well as the very positive feedback received from participants at the School, we are confident that new participants will attend the next edition in Frankfurt (Germany), which will undoubtedly be just as successful. Looking forward to summer 2025…!

MEETING REPORT (IUCR SUPPORTED)

26th Heart of Europe Bio-Crystallography Meeting



Markus C. Wahl

The 26th Heart of Europe Bio-Crystallography Meeting (HEC26) took place from 26th to 28th September 2024, in the historic city of Kraków, Poland. Hosted by the group of Sebastian Glatt and Przemysław Grudnik from the Małopolska Centre of Biotechnology, Jagiellonian University Kraków, the event gathered a vibrant community of structural biologists from across Central Europe. The meeting was attended by structural biology experts from numerous research groups, and the participation of scientists from Austria, the Czech Republic, Germany, and Poland contributed to the lively exchange of ideas.

A total of 121 participants registered for this year's meeting at a spectacular venue, the monumental Forest Hotel on the hill of Przegorzały. The program included 50 talks: the *HEC Lecture* by Arwen Pearson (University of Hamburg, Germany), introductory lectures by three new HEC groups, 17 scientific talks, and 25 flash talks by PhD and Masters' students, as well as four sponsor talks. The opening session featured presentations from the three new HEC groups headed by Krzysztof Brzeziński and Miłosz Ruszkowski from the Institute of Bioorganic Chemistry, Polish Academy of Science, and by Michał Szymański from the University of Gdansk, Poland.

Over the course of the three-day program, fascinating research into the molecular mechanisms of biomolecules and their complexes as well as updates on state-of-the-art structural biology methods were presented. A highlight of the event was the *HEC Lecture*, delivered by Arwen Pearson, who captivated the audience with an overview on recent advancements in time-resolved macromolecular serial crystallography.



Participants at the 26th Heart of Europe Bio-Crystallography meeting in Krakow, Poland.

Several companies (Arinax, CGF Biotec, Cytiva, Dectris, Dunn, Formulatrix, Jena Bioscience, NanoTemper, PHCbi, Proteros, Rigaku, Sarstedt, Selvita) participated in the event, generously supporting the meeting through presentations and sponsorships. Their involvement introduced the latest technological advancements to the structural biology community.

The meeting awarded prizes for outstanding presentations. Jana Skerlová from the group of Pavlína Maloy Řezáčová, Institute of Organic Chemistry and Biochemistry of the Czech Academy of Sciences, won the 'HEC Prize' for the best full talk, with Evangelia Nathanail (group of Oliver Daumke, Max Delbrück Center for Molecular Medicine) and Mathias Schenk (group of Miriam Linnert, Fraunhofer Institute for Cell Therapy and Immunology) also being recognized for their excellent contributions. David Speck from the group of Patrick Scheerer, Charité - Universitätsmedizin Berlin, received a special distinction. The prize for the best flash talk was awarded to Duc-Anh Nguyen from the group of Milton Stubbs, Martin-Luther-Universität Halle-Wittenberg.



HEC26 Prize winners: Duc-Anh Nguyen (second from left), Mathias Schenk (third from left), Evangelia Nathanail (third from right) and David Speck (second from right), with organizers Przemysław Grudnik (left) and Sebastian Glatt (right). Jana Skerlová, who was awarded the prestigious 'HEC Prize' for her outstanding presentation, was unable to participate in the group photo.

A social afternoon offered opportunities for relaxed discussions amidst nature, on a guided hike to Piłsudski Mound, and science, on a tour of the SOLARIS Synchrotron. The lively HEC Party at the Forest Hotel on Friday night created a warm and festive atmosphere, encouraging both formal and informal exchanges well into the evening.



Recreational hike to the top of Piłsudski Mound (left) and a visit to the SOLARIS National Synchrotron Radiation Centre (right).

The success of HEC26 sets the stage for the 27th Heart of Europe Bio-Crystallography meeting, which will take place in Halberstadt, Germany, from 25th to 27th September 2025, and will be organized by the

group of Markus Wahl, Freie Universität Berlin. We look forward to another inspiring gathering next year.

MEETING REPORT (IUCR SUPPORTED)

9th European Crystallography School (ECS9)



The ECS9 was held in Nancy (France), 24th–30th June 2024, at the site of the *Faculté des Sciences et Technologies of Université de Lorraine*, as an in-presence event. In this edition, the school targeted the improvement of crystallographic skills for young scientists (PhDs, postdocs, Masters students) working in different fields (chemistry, physics, material science). The lectures and practical sessions covered all aspects from basic structure analysis to understanding of chemical bonds, bonding interactions and structure-properties relationships in materials, with a focus on single crystal X-ray diffraction and structure analysis. Consequently, the program was organized in the following 5 main scientific sections, with lectures on the fundamentals in the morning and practical sessions with applications and tutorials in the afternoon:

(i) An introduction to X-ray diffraction (XRD) theory.
(ii) Structure determination and analysis.
(iii) Packing and interaction analyses.
(iv) Using aspherical models of the electron density distribution.
(v) Crystallography under constraints.

The 18 speakers (9 international, 9 local) plus 3 sponsors (industrials) gave 8 fundamental lectures and 7 practical sessions during which at least 2 tutors were present for guiding and helping the participants. In order to guarantee a reasonable tutor-to-participant ratio, especially for the practical sessions, our laboratory of crystallography (CRM2) was heavily involved with 9 speakers/tutors. Most of the lecturers were present and available for the participants during the whole week, enabling further specific discussions and informal exchanges between lecturers and attendees, during and after presentations. Additionally, coffee breaks and 2 poster sessions helped significantly to develop discussions.

This school brought together a total of 62 (30 F, 32 M) participants of 25 different nationalities, coming from laboratories of 22 countries.



Lecture (top) and practical sessions with hands-on structure solution and refinement (bottom).

Thanks to industrial (STOE, Rigaku, Bruker, Dectris, Cristal Laser) and public sponsors (Region Grand Est, Metropole of Nancy, City of Villers-les-Nancy) as well as local support of the *Université de Lorraine,* registration fees could be proposed at very low rates (350 € for PhDs and postdocs, and 450 € for other people). Registration fees covered participation in courses and materials used, overnight stays, lunches and coffee breaks during the school, as well as the gala dinner and excursion. As a consequence, the school attracted a lot of interest and the 50 available places (constrained by the capacity of the computer room for the practical sessions) were sold out one month before the inscription deadline. In order to enable a maximum of interested young scientists to participate, we accepted a total of 62 inscriptions (out of a total of 78 pre-registrations recorded at the closing date of inscriptions).

Thanks to the support of IUCr, ECA and the French Crystallographic Association (AFC), we could offer 17 bursaries/travel grants for a total of 8784 €. The 17 laureates of the bursary came from 14 countries from Europe, Central Asia, South Africa, North Africa and South America. Additionally, we waived the fee for 2 students, and 2 Italian students were directly supported by the Italian Crystallographic Association (AIC). Finally, 2 poster prizes of 100 £ and 100 € were awarded during the school, sponsored by the CCDC and CRM2, respectively.



Group photo before the school dinner at the Château Mme de Graffigny.

MEETING REPORT (IUCR SUPPORTED)

International School on Fundamental Crystallography: Seventh MaThCryst School in Latin America



Justiniano Quispe

The seventh edition of the School of Mathematical Crystallography in Latin America was recently held from 12th to 16th August 2024, at the Facultad de Ciencias Físicas, Universidad Nacional Mayor de San Marcos, in Lima, Peru (https://www.even3.com.pe/e/ISFC2024-7MathCrystS). This school is part of a series of fundamental crystallography schools that began 17 years ago at the University of Havana, Cuba, and have since been held biennially in various countries across South America, Central America, and the Caribbean. The first school took place in 2007 in Havana, followed by Montevideo, Uruguay in 2010; Uberlândia, Brazil in 2012; La Plata, Argentina in 2014; Havana, Cuba again in 2016; and Bogotá, Colombia in 2018. Unfortunately, the global impact of the SARS-CoV-2 pandemic led to the delay of subsequent schools. The successful realization of the seventh MaThCryst School in Latin America marks a significant milestone, signalling the reactivation of this series after more than five years of inactivity.



Inauguration of the seventh MaThCryst School in Latin America. From left to right: Dr Arbelio Pentón, Dr Leopoldo Suescun, Dr Massimo Nespolo, Dr Justiniano Quispe, Dra Marisel Espinoza, Dr José Niño, Dr Ángel Bustamante, Mg María Luisa Cerón, Dr Mois Arroyo, Dra María Cristina Nonato and Dr Carlos Landauro.

The primary objective of this school was to provide training and education to Latin American students and young researchers on the fundamentals of crystallographic symmetry, with a focus on the application of mathematical and computational tools in various fields. Additionally, the school aimed to encourage collaborative work through interaction and the exchange of ideas between course participants and renowned researchers.



Dr Massimo Nespolo uses a ball to keep the attention of all students.

This year's school attracted 82 participants, including 64 students with a notable representation from Peruvian institutions. The participants came from countries such as Peru, Ecuador, Colombia, Philippines, Cuba, Brazil, Germany, Spain and France. Efforts were also made to promote gender diversity, achieving a 33% participation rate for women. It is noteworthy that this is the second time the school has been organized by a participant from one of the previous editions.

The inauguration on the first day was led by university authorities from the oldest university in the Americas, founded in 1551. Present were Dr José Niño Montero, Vice-Rector of Research and Graduate Studies; Dr Ángel Bustamante Domínguez, Dean of the Faculty of Physical Sciences; Dr Justiniano Quispe Marcatoma, President of the Organizing Committee; Dr Marisel Espinoza Suárez, representing the local organizing committee; and Mg María Luisa Cerón Loayza, who served as the coordinator for gender equality and diversity. The opening lecture, titled *X-ray Crystallography: From Material Science to Drug Discovery*, was delivered by Dr Maria Cristina Nonato. Subsequently, the lecturers Dr Massimo Nespolo and Dr Mois Aroyo presented on various topics including symmetries in crystal families, lattice systems, and crystal systems. On the second and third days, they continued to explore the properties of space groups and their descriptions in the *International Tables for Crystallography*, incorporating exercises and in-class interactions. They also demonstrated the use of mathematical and computational tools to access crystallographic symmetry information from the *International Tables for Crystallography* databases.



Dr Mois Aroyo teaching space groups and their description in *International Tables for Crystallography*.

On the fourth day, professors Dr Arbelio Penton, Dr Maria Cristina Nonato, and Dr Leopoldo Suescun covered topics such as *Crystallographic Calculations in Reciprocal Space*, *Introduction to X-ray Diffraction*, and *Diffraction Symmetry: Space group determination*. A poster session was held on the same day, featuring 15 works selected by evaluators from the local committee. Awards were given to the two best posters, which were evaluated by a jury of the school's professors based on their academic relevance.

On the final day, Dr Gemma de la Flor joined online from Germany for a dynamic session in which students explored various applications of the International Tables online server and the Bilbao Crystallographic Server. The closing lecture, delivered by Dr Maria Cristina Nonato, was titled *Fragment Screening by X-ray Crystallography: An Important Tool to Develop New Therapies Against Infectious Diseases*. The week concluded with a presentation of the *School Proceedings* by Dr Justiniano Quispe, summarizing the events of the week, followed by a musical performance featuring piano and violin by musician Rafael Huaroto Santillán.



Authors and co-authors in the poster session happy to show their work to the attendees.



Dr Allan O. Junio from the Philippines secured first place in the poster session, while Dr Yonathan Parra from Ecuador earned second place.

The success of this school was largely due to the collaborative efforts of the IUCr Commission on Mathematical and Theoretical Crystallography, in coordination with local Peruvian researchers, and the

support of institutions such as the IUCr; the National Council of Science, Technology and Technological Innovation (Concytec); the National Program for Scientific Research and Advanced Studies (Prociencia); the Center for Technological, Biomedical, and Environmental Research (CITBM); the Latin American Council of Physics (CLAF); Thermo Fisher Scientific; and the Peruvian Society of Physics (Soperfi).

MEETING REPORT

International XRD excites: Non-Ambient XRD and Beyond Symposium



Heiner Santner

In July 2024, Anton Paar and the Institute of Inorganic Chemistry at Graz University of Technology successfully hosted the first international edition of the **XRD excites: Non-Ambient XRD and Beyond Symposium**. More than 90 participants from over 20 countries gathered in the Austrian city of Graz for the meeting.

The event brought together an array of users from the field of X-ray diffraction (XRD) and non-ambient XRD, with the aim of encouraging multidisciplinary cooperation and an open exchange of experience between renowned scientists, young scientists and industry professionals. In this unique setting, researchers with different scientific backgrounds – ranging from materials science, crystallography, geology and mineralogy to energy storage and conversion – got together, learned about their individual progress and challenges in the application of non-ambient XRD and other areas, and sparked new ideas for their own research.

The symposium featured 23 high-level presentations from keynote speakers such as Claudia Weidenthaler from the Max-Planck-Institut für Kohlenforschung on *in situ* studies of energy materials, Monica Dapiaggi from the University of Milan on coupling laboratory and synchrotron NA-XRD data, Scott Misture from Alfred University on *in situ* powder XRD and high-resolution XRD studies of oxides, David Walker from the University of Warwick on non-ambient XRD analysis in the laboratory, Rémy Guillet Nicolas from CNRS LCS – ENSICAEN on small-pore zeolites, Volker Kahlenberg on non-ambient powder XRD studies in mineralogy and geology, Vishnu Shanker from NIT Warangal on graphite-based carbon nitrides, and Stefan Weber from Abbvie Germany on the use of non-ambient XRD for biological drug development.

A poster session offered an opportunity to discuss the latest scientific findings in more detail and initiate possible future collaboration projects between the participants. Last but not least, participants were given a deeper insight into non-ambient XRD in a special workshop that also included hands-on sessions with different types of non-ambient XRD attachments.

It wasn’t all work though!

A guided city tour in Graz – a UNESCO World Heritage Site – and company tour at Anton Paar ended with a visit of the Anton Paar Sudhaus brewery, where head brewmaster Gebhard Sauseng explained the details of the brewing process. Of course, no brewhouse tour would be complete without the option to also sample the beers fresh from the tap. From there, it was only a few steps to the conference dinner.



With this first **XRD excites: Non-Ambient XRD and Beyond Symposium**, Graz University of Technology and Anton Paar – together with all the participants – placed impressive emphasis on non-ambient XRD in a city that has a long history and deep connection to the field.

For more information please click here:

https://www.anton-paar.com/corp-en/xrd-excites/?utm_source=IUCr_Newsletter_pr&utm_medium=media&utm_campaign=hq_education-research&utm_content=C-00066872.

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MEETING REPORT

Inaugural MSI Crystallography Workshop at Howard University with the University of the District of Columbia and NSF's ChemMatCARS



Participants at the first MSI Crystallography Workshop in Howard University, Washington, District of Columbia, USA.

Timothy R. Ramadhar, Yu-Sheng Chen, Raymond J. Butcher, Steven P. Cummings, Xueqing Song, Matthew V. Tirrell, Richard B. Fenner

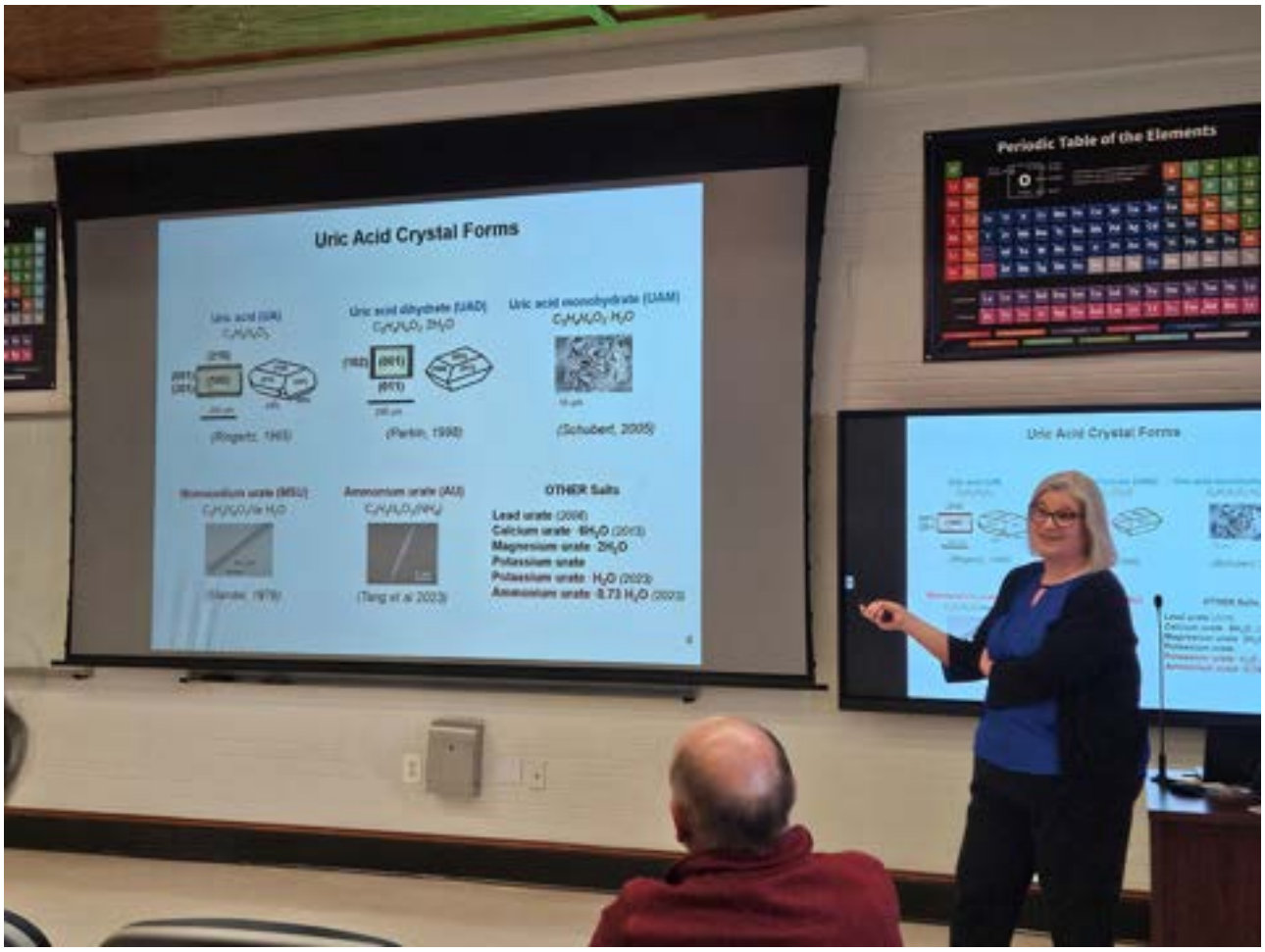
Engaging the next generation of synchrotron X-ray crystallography researchers is of the upmost importance to sustain and build the future of this critical field. The universities that train experimentalists and the national facilities that harbor the infrastructure for cutting-edge research recognize their roles and responsibilities to grow the crystallographic discipline. Exploring partnerships between minority-serving institutions (MSIs) and national facilities can establish pathways to support this effort. These partnerships also promote further diversification in science, technology, engineering and mathematics (STEM), leading to a stronger national workforce.

On April 6–7, 2024, the first crystallography workshop between Howard University (HU), the University of the District of Columbia (UDC), and NSF's ChemMatCARS was held in the HU Department of Chemistry. A total of 36 attendees, mostly undergraduate and graduate students along with faculty and presenters, attended this inaugural workshop. HU and UDC are Historically Black Universities (HBCU) located in the heart of the nation's capital: Washington, DC, nestled amongst nearby landmarks such as the Washington Monument, the Lincoln Memorial, the United States Capitol, and the White House. HU is a private doctoral research university founded in 1867, and UDC is a public land-grant Master's institution established in 1851. NSF's ChemMatCARS is a synchrotron beamline facility (Sector 15) in the Advanced Photon Source at Argonne National Laboratory near Chicago, Illinois that uses high-brilliance and high-energy X-rays to study matter at the atomic and molecular levels. This beamline, which uses an undulator insertion device, specializes in advanced small-molecule crystallography, liquid surface and interface X-ray scattering, and anomalous small and wide-angle X-ray scattering (ASWAXS) to shed light on structural problems in chemical and materials science. Advanced crystallographic studies that have been performed at NSF's ChemMatCARS include resonance diffraction/diffraction anomalous fine structure (DAFS), photocrystallography, *in situ* structural dynamics, high-resolution charge density studies, high-pressure studies, and microcrystallography.

This first-of-its-kind workshop was co-organized by HU, UDC, and NSF's ChemMatCARS and was funded by a National Science Foundation Partnerships for Research and Education in Chemistry (NSF PREC) Planning Grant. Timothy Ramadhar [HU and NSF PREC Planning Grant Principal Investigator (PI)] and Yu-Sheng Chen (University of Chicago and leader of the NSF's ChemMatCARS Advanced Crystallography Program) collaborated in organizing this workshop. While planning an agenda that would engage attendees, Ramadhar and Steven Cummings (HU and NSF PREC Planning Grant Co-PI) also ensured that attendees would be well nourished with catered meals throughout the entire workshop.

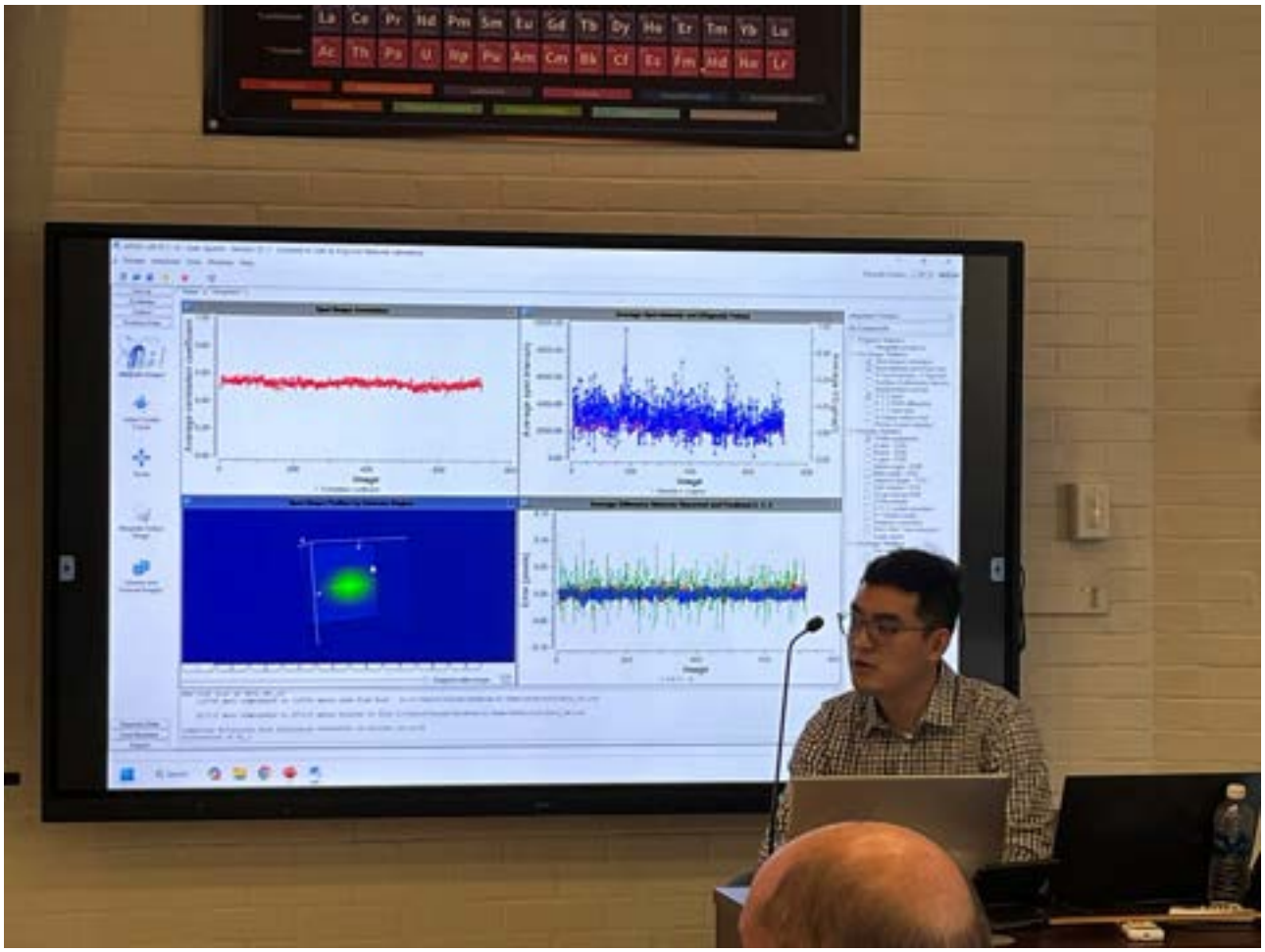
Welcoming remarks were delivered by Ramadhar, Xueqing Song (UDC) and Raymond Butcher (HU and NSF PREC Planning Grant Co-PI). Both Song and Butcher provided background and current information on the UDC Division of Science and Mathematics and the HU Department of Chemistry, respectively. Matthew Tirrell (University of Chicago and NSF's ChemMatCARS PI) presented a history and overview of the NSF's ChemMatCARS facility along with the beam time application process. Butcher subsequently introduced single-crystal X-ray diffraction and discussed his collaborative research on spin crossover complexes with Greg Brewer (Catholic University of America). Chen concluded the morning session by presenting details of NSF's ChemMatCARS Advanced Crystallography Program and its technical capabilities.

Scientific talks highlighting crystallographic research using in-house diffraction instruments and synchrotron light sources were also featured. Jennifer Swift (Georgetown University) and Samuel Dunning (Carnegie Institute of Science) gave presentations on the research that demonstrated how X-ray diffraction can be used to solve important scientific problems through structural studies. Swift delivered a talk on the first morning about biogenic uric acid. Dunning presented his research the next morning on carbon nanothread formation.



Jennifer Swift (Georgetown University) presenting a scientific lecture on biogenic uric acids.

Practical sessions on analyzing data from single-crystal X-ray diffraction experiments were held after lunch on the first workshop day. Pierre LeMagueres (Rigaku Americas Corporation) gave a virtual presentation introducing attendees to crystallographic data processing using *CrysAlis*^{Pro}. This software is used for the in-house Rigaku Synergy single-crystal X-ray diffractometers at HU and UDC that were funded by the National Science Foundation Major Research Instrumentation grants program [HU: DMR-2117502 (PI Ramadhar), UDC: CHE-2117621 (PI Song)]. Next, Tieyan Chang (NSF's ChemMatCARS) gave a walkthrough on processing crystallographic data using the Bruker *APEX* software, which is used extensively at the beamline. In the sessions for *CrysAlis*^{Pro} and *APEX*, attendees learned how to perform reflection indexing, reciprocal lattice examination, integration, absorption correction, and space group determination. Jinxing Jiang (NSF's ChemMatCARS) discussed *SHELX* and *Olex2* software programs, which can be used together for structure solution, refinement, finalization, and visualization. Before dinner, the practical sessions concluded with a hands-on tutorial where smaller group attendees had the opportunity to solve and refine sets of X-ray diffraction data collected at the NSF's ChemMatCARS beamline.



Tieyan Chang (NSF's ChemMatCARS) showing attendees how to integrate reflection data in Bruker *APEX*.

After the first day, all attendees were strongly encouraged to put what they had learned into practice and apply for beam time at NSF's ChemMatCARS.

The second day featured an extensive listening session with undergraduate and graduate students at HU and UDC followed by a farewell lunch. Students had the opportunity to share their journey in STEM, noted why they chose to attend HBCUs, and presented ideas about how to increase student recruitment and retention in science. The workshop organizers left this session with valuable insights on ways to develop an impactful partnership between HU, UDC, and NSF's ChemMatCARS for a future submission to the NSF PREC grant program.

The organizers are in the planning stages of hosting another crystallography workshop this year at NSF's ChemMatCARS, which is being equipped with new capabilities along with a second beamline via a canted

undulator to utilize a brighter X-ray beam (approximately 1000-fold at most energies) afforded through the recent Advanced Photon Source upgrade. Improvements to the Advanced Crystallography Program as a result of the upgrade include the ability to perform small-molecule serial diffraction, resonant diffraction applicable to all transition elements for element-specific location and redox states, and high-throughput processing of microcrystalline samples through automation involving the use of a data collection robot that can be accessed via a mail-in service.

This workshop was financially supported solely by the National Science Foundation through a PREC Planning Grant (CHE-2334957). The NSF's Chemistry Division (CHE) PREC program is dedicated to fostering, establishing, and enhancing collaborations between MSIs and CHE-supported facilities, centers, and institutes. Its main goal is to increase recruitment, retention, and degree attainment among underrepresented groups in chemistry. The program concurrently aims to boost outstanding research and educational initiatives that reinforce these partnerships. Underrepresented minorities supported through this program include Blacks or African Americans, Hispanics or Latinos, American Indians, Alaska Natives, Native Hawaiians, Other Pacific Islanders, and persons with disabilities. The PREC Planning Grant program that has funded this workshop aims to catalyze collaborative partnerships with CHE-supported facilities, institutes, and centers to facilitate the creation of competitive proposals for the PREC program in future solicitations. NSF's ChemMatCARS, a CHE-supported center, has established scientific partnerships with several MSIs. NSF's ChemMatCARS is supported by the Divisions of Chemistry and Materials Research of the National Science Foundation under grant number CHE-1834750.

MEETING REPORT

12th Training Course on Symmetry and Group Theory (a student's perspective)



Group photo of the 2024 English basic course.

James Steele

I first heard about this course from a colleague, an experienced experimentalist in diffraction-based characterisation, at the end of a long day of working together on a structural refinement that was proving troublesome. Like many PhD students in solid-state chemistry, or condensed matter physics (the same thing in my opinion), I had studied X-ray diffraction, and a small amount of group theory through the lens of molecular symmetry, during my undergraduate degree. "*Excellent!*" I thought, "*I am fully prepared to tackle complex structural characterisation of novel materials and their phase transitions, based on symmetry relations, group theory, and space groups...*" Of course not.

When I started my PhD, I had a limited grasp of what a space group even was. Rietveld refinements were a wonderous black box that you fed data, then marvelled at the structure that popped out (which was, more often than not, an unphysical mess). Programs such as *TOPAS*, *GSAS*, and *FullProf* are incredibly powerful and valuable tools to the experimental structural scientist. However, they are infamously poor at dealing with symmetry, particularly in the hands of a student with limited understanding of the underlying concepts.

"*Garbage in, garbage out.*"

This is, of course, not for lack of trying. There are numerous resources (both online and in print) for the learning of crystallography. However, these can often seem impenetrable, riddled with confusing conventions, field specific jargon, and mathematics one may not have encountered in many years (if at all). Further, experimentally focused research groups don't necessarily have theoreticians on hand, or experimentalists with the specific expertise (or free time) required to build up the knowledge and confidence of new students. This often adds up to make crystallography seem insurmountable to the budding crystallographer, and is one of the main reasons I was so excited when I heard about this course. The training course on symmetry and group theory has run for many years now, primarily in Japanese, but additionally in English since 2019, in response to the demand shown by students who are not native Japanese speakers. Primarily, the course was motivated by the many obstacles commonly faced by early career researchers, owed to the somewhat limited crystallographic training provided by (already busy) undergraduate curricula. The course is hosted at the High Energy Accelerator Organisation site in Tsukuba (KEK), and is provided free of charge.[1] It is sponsored by the Crystallographic Society of Japan, the Institute of Materials Structure Science, and supported by many other Japanese scientific societies

and associations. From 2019, it has been certificated as a common lecture by SOKENDAI (The Graduate University for Advanced Studies). All lectures and exercises are delivered by Professor Massimo Nespolo (Université de Lorraine, France).

Unlike any other course I have previously studied, which required students to make unsatisfying concessions, accept axioms without explaining how they arise, and learn relations by rote, Professor Nespolo starts truly from first principles, with basic algebra. This lays necessary foundations, which are built up procedurally and developed throughout the course into a rich understanding, with many satisfying relations that become apparent as more advanced concepts are introduced. Further, the opportunity to participate in frequent guided exercises, where the taught concepts are explored in greater detail, allows participants to really absorb the content of the course and solidify their understanding. The condensed nature of the course facilitates a breadth of topics to be taught, starting from the required fundamental algebra, building to point/space groups and their constituent properties from a geometric/graphical perspective. This then facilitates understanding of the physical meanings of the following crystallographic calculations via matrices, and how all of this adds up to macroscopic properties and phase transitions in the materials, which is the subject of our research.

I study battery cathode (positive electrode) materials. As alkali ions are removed from between transition metal oxide layers, this class of materials undergo a range of complex phase transitions, including layer glides, vacancy orderings, and static/dynamic distortions (such as the well-known Jahn-Teller effect). Each of these factors has the potential to result in symmetry lowering effects, from the original high-symmetry parent cell. As an example from my own work, combined refinement of structural models against X-ray and neutron diffraction data has allowed us to find that removing 1/3 of the sodium ions from sodium nickel oxide ($NaNiO_2$ -> $Na_{2/3}NiO_2$) results in symmetry lowering from $C2/m$ to $P2_1/c$. Electrochemically desodiating the material in this way results in multiple extra symmetrically distinct crystallographic sites (where only single Na, Ni, and O sites existed in the parent), and is associated with sodium/vacancy ordering and transition metal orbital ordering, both of which combine to affect the resultant structure of the new cell.



Participants receive certificates for completing the course.

I look forward to applying what I have learned regarding fundamental crystallographic symmetry, and group-subgroup relations, to solving the remaining novel structures throughout the $Na_{1-x}NiO_2$ phase-space, and would gladly participate in the advanced course (provided my Japanese improves over the next few years!). I strongly recommend this course to any other students who have struggled to understand the underlying crystallographic concepts that inform the necessary decisions required to devise physically meaningful (and symmetrically sensible) Rietveld refinements for novel structural elucidation.

1 It is unfortunately not currently possible to provide financial support for travel, which is probably the main factor limiting participation by students outside of Japan. I was fortunate to receive a professional development grant from my funder (EPSRC NanoDTC), without which I could not have taken part in the course.

James Steele is a PhD student co-supervised by Professor Siân Dutton and Professor Dame Clare Grey at the Cavendish Laboratory and Yusuf Hamied Department of Chemistry (University of Cambridge, UK).

IUCR SUPPORTED EVENTS

IUCr supported meetings

These forthcoming meetings are supported by grants from the IUCr Calendar Committee.



11th Oct 2026 - 16th Oct 2026

Indaba10

Skukuza, Kruger National Park, South Africa



5th Dec 2026 - 10th Dec 2026

African Materials Research Society (AMRS 2026)

Nairobi, Kenya

MEETINGS CALENDAR

Meetings calendar

This is a list of meetings of interest to crystallographers occurring within the next twelve months, as recorded in the IUCr Calendar of Events. Please let us know of any that are missing by completing this form or sending an email to forthcoming.meetings@iucr.org.



Indaba10 South Africa 11th Oct 2026 - 16th Oct 2026



Synchrotron Radiation: Science, Knowledge, Innovations, Future (SKIF-2026) Russian Federation 18th Oct 2026 - 23rd Oct 2026



CCP-EM/Diamond Icknield Workshop United Kingdom 9th Nov 2026 - 13th Nov 2026



Instruct-ERIC hands-on workshop on Advanced cryo-FIB-SEM methods Germany 9th Nov 2026 - 13th Nov 2026



Crystal36-AXAA 2026 Meeting Australia 26th Nov 2026 - 2nd Dec 2026

African Materials Research Society (AMRS 2026) Kenya 5th Dec 2026 - 10th Dec 2026

Joint Polish-German Crystallographic Meeting 2027 Germany 15th Feb 2027 - 18th Feb 2027