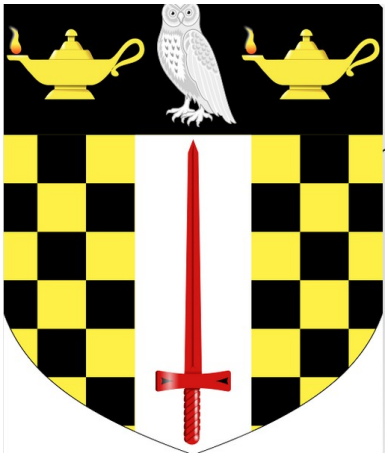
Crystallography at Birkbeck



Birkbeck, University of London celebrates its 200th Anniversary in 2023. As it was where much crystallographic development took place – and was the location of the first Department of Crystallography – it seemed appropriate to mark the occasion. So we are publishing here a personal account by Rex Palmer – apart from Alan Mackay, the longest surviving member there from earlier days – his personal account of some of people and some of the crystallographic work done in the College over the past eight or so decades since Bernal took over the Chair in Physics there from Patrick Blackett.

This is an extended version of a shorter article by Rex that was published in the March 2023 *Crystallography News*. You might also like to refer to the articles in the Bernal special issue of *Crystallography News* (September 2021), where Christine Slingsby, Paul Barnes and John Finney respectively discuss more of the biological, materials and liquids work that came out of the Department in the Bernal era.

John Finney
UCL

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CRYSTALLOGRAPHY AT BIRKBECK COLLEGE

Some of the people and some of their science

Before getting to Birkbeck, it's perhaps useful to introduce the polymath crystallographer who brought crystallography to the College.

After his graduation in Cambridge, **John Desmond Bernal** began research under William Henry Bragg in the Davy Faraday Laboratory at the Royal Institution in London. In 1924 he determined the structure of graphite (the Bernal stacking describes the registry of two graphite planes) and also did work on the crystal structure of bronze. His strength was in analysis as much as experimental method, and his mathematical and practical treatment of determining crystal structure is widely recognised. He also developed an X-ray spectro-goniometer using odd bits and pieces he found lying around such as an old alarm clock (see figure 1), and developed the **Bernal** Chart for interpreting X-ray photographs taken with this oscillation camera, the commercial version of which (Unicam) was used extensively in crystallographic laboratories for many years.

Figure 1:

Bernal's prototype rotation camera.

In 1927, Bernal was appointed as the first lecturer in Structural Crystallography at Cambridge, becoming the Assistant Director of the Cavendish Laboratory in 1934. There, he started applying his crystallographic techniques to organic molecules, starting with oestrin and sterol compounds including cholesterol in 1929, forcing a radical change of thinking among sterol chemists including corrections to the immensely incorrect structure of cholesterol which two scientists had received the Nobel Prize in Chemistry for (see Appendix)! While at Cambridge, he analysed vitamin B_1 (1933), pepsin (1934), vitamin D_2 (1935), the sterols (1936) and the tobacco mosaic virus (1937).

He also worked on the structure of liquid water, publishing a landmark paper in the first volume of *Journal of Chemical Physics*[i] showing the boomerang shape of its

molecule (1933) and foreseeing the kind of charge distribution often used today in computer simulations of water and aqueous systems. It was in Bernal's research group that after a year working with Tiny Powell at Oxford, Dorothy Hodgkin continued her early research career. Together, in 1934, they took the first X-ray photographs of hydrated protein crystals using the trick of bathing the crystals in their mother liquor, giving one of the first glimpses of the world of molecular structure that underlies living things. Max Perutz arrived as a student from Vienna in 1936 and started the work on haemoglobin that would occupy him most of his career.

The move to Birkbeck

Crystallography came to Birkbeck when Bernal took over the chair in physics from Patrick Blackett in 1938. He had been refused fellowships at Emmanuel and Christ's Colleges, and also refused tenure by Ernest Rutherford, who disliked him. With his appointment he brought with him a wealth of knowledge and experience of crystallographic studies of a huge in-depth range of materials from water, metals, proteins and viruses.

Figure 2:

The Birkbeck lab. from 1948 to 1966.

After World War II (again see September 2021 *Crystallography News*), he established Birkbeck's Biomolecular Research Laboratory in two war-damaged Georgian houses in Torrington Square (figure 2). This would be a multidisciplinary department that would seek to investigate the structure and function of proteins using all the available physical techniques, including not only X-ray crystallography (where he envisaged making developments in X-ray tubes and instrumentation suitable for both large unit cell systems such as viruses and also liquids), but also the newly invented electron microscope. His plans also included inorganic work relevant to the building industry, with special emphasis on understanding the shrinkage of cements. So his initial team was made up of **Harry Carlisle** from Oxford[ii] to head the section on proteins and viruses, **Helen Megaw** to lead the cement work, **Werner Ehrenberg** to develop new apparatus (especially fine focus, high intensity X-ray tubes), and **Donald Booth** to develop the application of computing to crystallography. When **Helen Megaw** left in 1946 for Girton, she was succeeded by **Jim Jeffery**, who acquired **Alan Mackay** as a part-time Ph.D. student to work on the structure of calcium phosphate.

This founding team (figure 3) grew over the years to be a major influence in the development of crystallography, and led to the establishment (after many bureaucratic battles) of a full Department of Crystallography in 1964. Among those joining the team were **Aaron Klug,** who worked shortly on Ribonuclease before turning to viruses, in which pioneering work he was joined by **Rosalind Franklin.** Klug took the virus work to Cambridge before publishing any of the results in the name of Birkbeck College. Other names that played major roles in the early decades include **Don Caspar**, **Isidor Fankuchen**, **John Finch** and **Ken Holmes**. Again, see the September 2021 *Crystallography News* for a fuller account of this and other biology-related work.

Figure 3:

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

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

The M.Sc. in Crystallography

In the early years the only taught course was the M.Sc. in Crystallography. This was a highly intensive course for both part-time and full-time students. It gave a thorough and comprehensive grounding to prospective researchers in the field of X-ray crystallography. Part-timers attended lectures from 6 to 9 p.m. five days a week for two years and had practicals on Saturdays (!). Full time students were usually supported by grant-giving bodies and covered the lecture courses and practicals by

attending special sessions put on for them by members of staff during the day. This was for many years an outstanding course and was held in esteem by many science departments world-wide – many researchers from the UK and abroad have claimed that this was the start of their scientific careers. About 10 to 15 students per year graduated and many continued studying in the Department for part-time or full-time Ph.D. degrees. One of its external examiners was Kathleen Lonsdale of nearby UCL (who also taught on the course). Another was Arnold Beevers, famous for his part in inventing the computational aid Beevers-Lipson Strips. I remember one day in 1964 meeting someone by chance at the Pasadena Institute of Technology in California who asked me where I was from. I told him I was from Birkbeck College to which to my amazement and joy he immediately responded: “I know…the M.Sc. in Crystallography”.

A new building!

In 1952 a new Birkbeck College building was opened in Malet Street. However, the Crystallography Research Laboratories remained in the two Georgian houses in the adjacent Torrington Square. The Computer Section was also in one of these houses (actually in a static water tank about 60 feet long that had been used in the war for fire fighting!). The M.Sc. lectures and practicals were held in another house at 32 Torrington Square (see figure 4).. Eventually, in the later 1960s, new lecture theatres and laboratories for both student courses and research were opened in the new building, with Bernal now Head of an independent Department of Crystallography.

Figure 4:

A student on the steps of 32 Torrington Square in Summer 1961. This building housed the M.Sc. Crystallography lecture rooms and practical laboratories which moved to the main Birkbeck College building on its completion in the mid 1960s. Credit: Rex Palmer.

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

Some of the people and their work

Harry Carlisle (see figure 5) succeeded Bernal as Head of Department in the early 1970s, having interests in the X-ray analysis of both small organic molecules and the much larger molecular weight proteins, concentrating the latter on the medium sized protein Bovine Pancreatic Ribonuclease A. This was extracted, from pancreases purchased from a local slaughter house, by Ph.D. student **Michael Rosemeyer** who also grew the crystals and prepared heavy atom derivatives. Michael later became Professor of Biochemistry at UCL. As mentioned earlier, Harry Carlisle's small molecule analysis experience had started when he worked with Dorothy Crowfoot (later Hodgkin) on the structure of cholesteryl iodide[iv]. Some 50 or so years later the original crystals were found in a phial in the Department in unblemished state and were subjected to a modern high resolution analysis[v].

Figure 5:

Harry Carlisle (standing) in the Crystallography Library (aka tea room – for idea generation, only second to the bar) in the new building around 1972, possibly the occasion of Harry Carlisle's birthday. L-R: Alan Mackay, Nick Moore, Andy Morphew, Harry, John Finney. Credit: Rex Palmer.

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

By the mid 1960s more sophisticated methods were being developed for measuring X-ray intensity data from both large and small molecule crystals. The early linear diffractometer of Hilger and Watts (Y190/A328) designed by Arndt and Phillips was manually operated. The later 4-circle instrument (Y290) was controlled by a PDP-8 minicomputer. The Enraf-Nonius CAD4 diffractometer is characterised by a kappa goniometer. It had therefore become much faster to measure the data, and with greater accuracy, to solve crystal structures. The breakthrough with respect to Ribonuclease came in 1967 with the publication of a low resolution structure[vi], and Harry's group worked on ribonuclease until his retirement. Ribonuclease work continued after Harry's retirement resulting in several publications (for example see figure 6).[vii] [viii].

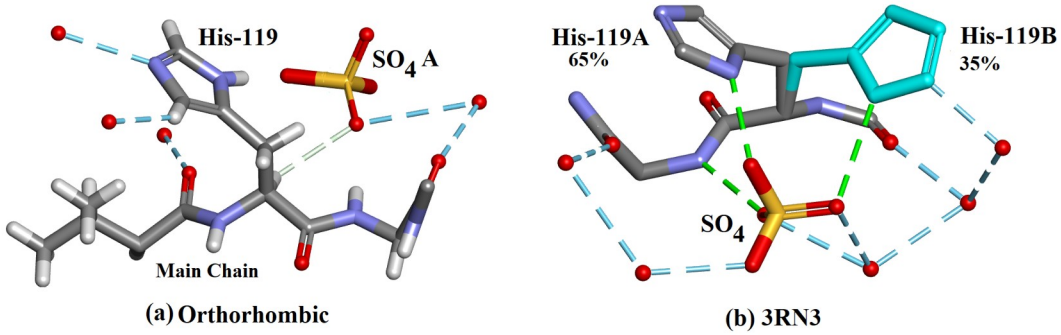

Figure 6:

(a). Orthorhombic RNase A. His-119 occupies a single site. The SO_4^{2-} is disordered in this structure. Only the major SO_4^{2-} A site is shown. (b) Monoclinic RNase: 3RN3[1] His-119: major site A (65%) and minor site B (35%). The SO_4^{2-} is ordered. From reference vii.

Jim Jeffery was Head of the Materials Research team until his retirement. He originally studied at Cambridge University where the first course project was to construct a working X-ray tube and use it to collect X-ray photographs from crystals. His work in the Department initially focussed on cement-related systems: why cement sets was a pressing industrial problem after World War II, a time when there was a lot of reconstruction work taking place. Bernal thought that "the properties of hydrated cements are closely related to those of many biological gels and are strongly influenced by the same long range forces". Jim's work expanded to a wider

range of inorganic materials such as corrosion products in power station boilers[ix] and phase separation in, and the crystallisation of, glasses[x] – of contemporary importance in the manufacture of glass ceramics. He was also enthusiastically concerned with instrument development (the Department for many years made its own arcs in its workshop) and experimental methodology, on which he published a book, *Methods in X-ray Crystallography*, in 1971. He was awarded a personal chair in recognition of his many achievements.

Though **Alan Mackay** began his time at Birkbeck in the late 1940s as part of Jim Jeffery's cement-centred group, his interests soon broadened, publishing more broadly than might be expected of a 'normal' crystallographer. It was not only Istvan Hargittai who considered him "one of the rare generalists of our time"[xi]. He contributed to the development of the science of structures generally, and was a major driver in developing Bernal's concept of 'Generalised Crystallography'[xii]. Like Bernal who thought that local five-fold symmetry might be relevant to the structure of liquids, much of Alan's focus has been on systems that so-called 'classical crystallography' rejected – for example an icosahedral packing of equal spheres that became known as the Mackay icosahedron, which according to one Chinese researcher "made tremendous impact on particle, cluster, inter-metallics, and quasicrystal researchers"[xiii]. And it's perhaps in relation to quasicrystals that Alan might be mainly remembered for. Having designed a regular non-periodic two-dimensional structure from regular *pentagons* that was different from the Penrose tiling – and simulated its diffraction pattern (see figure 7) – he predicted[xiv] the possibility of what were to be called 'quasicrystals' three years before their experimental discovery by Dan Schechtman. Though missing out on the Nobel Prize given for quasicrystals, Alan was belatedly elected a Fellow of the Royal Society in 1988.

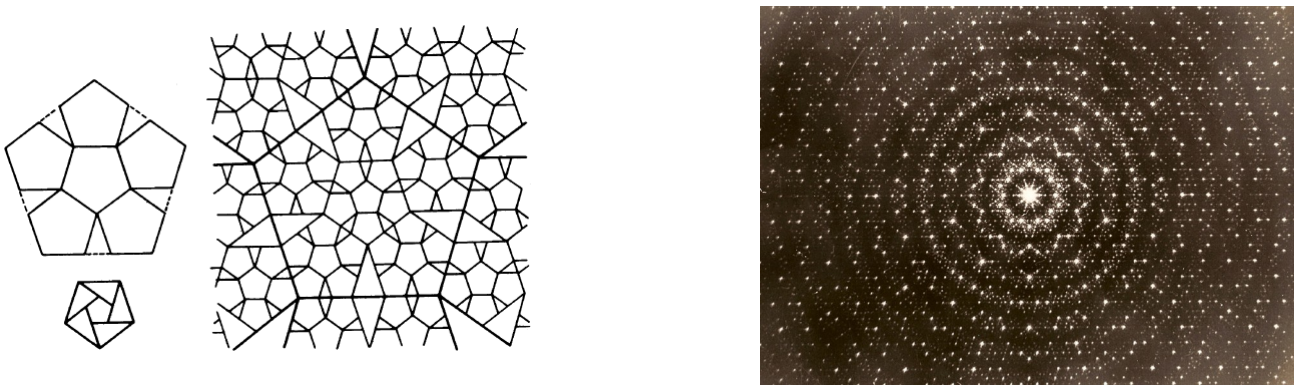

Figure 7:

Alan Mackay's five-fold space-filling tiling (L) and its optical diffraction pattern (R)

Expansion

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

Rex Palmer joined the Department as a Lecturer in 1964, following his Ph.D. on Ribonuclease under Harry Carlisle in 1962, and a year each as a Research Fellow at

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

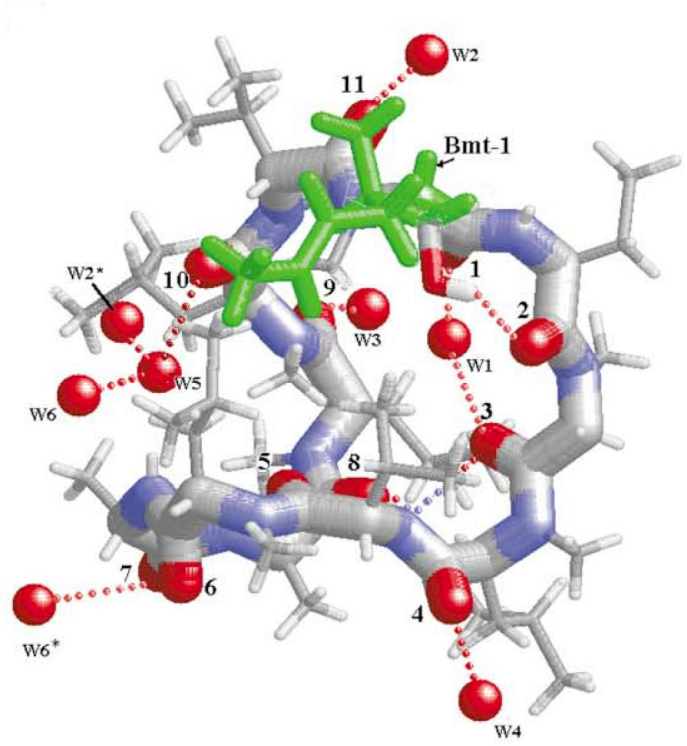

Figure 8:

Secondary structure of Cyclosporin H[xvi] illustrating the convoluted figure-of-eight folding and water structure. Water 2 is related by symmetry to water 2 and forms a cluster with waters 5 and 6 in CsH form-II. Water 6 occurs only in form-I and links two symmetry-related CsH molecules; waters 1–5 are common to both forms. The hydroxyl of residue MeBmt-1 forms an intramolecular H-bond with* Ñ*-Abu-2 CO, i.e. O2. Work from Brian Potter's Ph.D. Thesis.*

Beatrice Gorinsky (née Woolhouse) came to Birkbeck in the early 1960s to study for the M.Sc. Crystallography degree. Subsequently she registered with Harry

Carlisle as a Ph.D. student working on the Ribonuclease project, after which she was awarded a Lectureship in the Department. She continued to be a key worker on the Ribonuclease project and also worked in the team with Peter Lindley (see below) on the structure of Serum Transferrin. Both of these projects were highly successful, the work on Transferrin being a highly innovative project on a biologically very important protein.

David Moss joined the Department in the late 1960s as a Lecturer in electron microscopy. His research interests ranged from molecular biology and protein crystallography to bioinformatics, with special reference to symmetry and statistics. He led Birkbeck's efforts in the ImmunoGrid collaborative project to build and deploy a virtual human immune system using computer simulation. The system aims to mimic immune responses to help design treatments for cancer and chronic infections, which it is hoped will assist in understanding autoimmune diseases such as rheumatoid arthritis, celiac disease, allergies and leukemia relapse. In the latter case, he worked to develop immunotherapies where donor T cells can be used to kill residual leukemia cells.

David was perhaps ahead of his time in introducing internet-based education in 1995, working part-time to run these courses, (even if it meant giving tutorials in the middle of the night to catch students on both sides of the Pacific Rim – Birkbeck being one of the first universities to use the internet for teaching). He was Head of what became the School of Crystallography from 1987 to 1996, and again from 2001 to 2006 – many colleagues are grateful for his sacrificing time that could be spent of academic work for effective management. One of his achievements in his 'retirement job' as a part-time Senior Research Fellow has been (with **Ajit Basak)** to provide the first detailed description of the alpha toxin in certain bacteria and explain how it disrupts the signalling function of cells. The alarming prospect of the use of such toxins in bioterrorism gives this work a strong contemporary importance. His computing expertise has been crucial in research developments in the area of bioinformatics, and the use of computer databases and algorithms to enhance biological research, especially in the area of genetics.

Peter Lindley joined the department in 1967. He started work at Birkbeck in the cement area and small molecule crystallography. He established a small molecule service for chemists and biologists which was used by many chemists in the UK and Europe. He played a major role in the Department's fight back against an attempt to close it in the early 1970s, and as part of the internal reorganisation agreed by the staff that followed, he changed tack from small to large biological molecules, working on structures of proteins such as Serum Transferrin, Human Serum Ceruloplasmin, Cupredoxin, Lactoferrin and (with Christine Slingsby – see below) γ-Crystallin II. His persistence against great odds in sorting out problems with the water supply system in the basement was instrumental in keeping the lab. operational! In the 1990s, he moved to senior science management positions at large scale facilities, first at the Daresbury synchrotron and then at the ESRF in Grenoble.

John Finney arriving in the Department in 1965 as Bernal's Research Assistant to work on his structural model of liquids with a most imaginative Experimental Officer **Ian Cherry**. Following his (part-time) Ph.D. in 1968 he joined the staff as a Lecturer. With the departure of **Shirley King** from Bernal's Liquid Group (Shirley had worked

on adapting Bernal's model of simple liquids to the structure of water), he expanded his interests to water in all its forms, especially its role in biological processes[xvii]. Here, he teamed up with the protein crystallographic expertise in the Department to examine the detailed structure of disordered water in proteins and other biomolecules – both by X-ray and neutron structure determination and, with Julia Goodfellow (see below) the early application of computer simulation to these complex systems. With great support from Dorothy Hodgkin, he and Ph.D. students **Hugh Savage** and **John Bouquiere**, in collaboration with Peter Lindley (see above), produced a very high resolution neutron structure of the disordered water in Vitamin B_{12} coenzyme (see figure 9) [xviii] that led to Hugh, on a late night train back home to Littlehampton, determining a set of repulsive regularities that appeared to control not only the observed solvent structure, but also the organisation of water in hydrates and ices[xix].

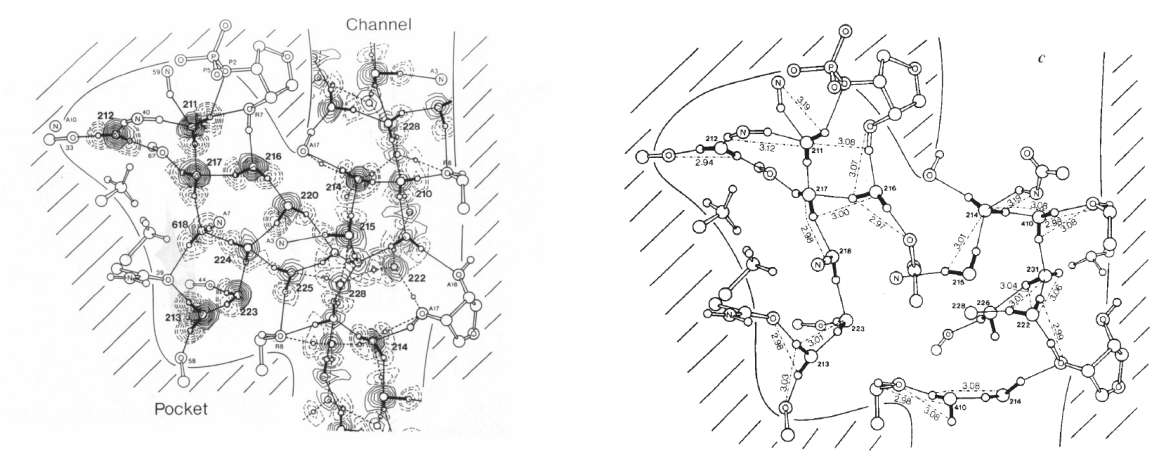

Figure 9:

Left: Water networks in the 15K crystal of vitamin B_{12} coenzyme. Dotted lines between atoms indicate alternative networks. Right: Rationalisation of the water orientations on the basis of minimum oxygen to remote-hydrogen contacts of ~3.0Å.

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

In the late 1960s, there was a major scientific controversy when a well-respected Soviet scientist, Boris Derjaguin, reckoned he had discovered a new and denser form of water which many thought might be a polymer of water – hence the name 'polywater'. Having heard a lecture by Derjaguin while a postdoc. in Cambridge, **Paul Barnes** wrote to Bernal asking if he could join the group to work on this. He duly did so – see his article in the September 2021 *Crystallography News* for how this work proceeded. Being taken on to the academic staff, he in due course inherited Jim Jeffery's materials-focussed group. Exploiting X-ray and neutron diffraction and

electron microscopy, he and his group did extensive structural work on materials such as zeolites, ceramics, cements[xx], hydrates (particularly those with an industrial application), bulk rock analysis, drug polymorphism, rubber- based materials and micro-mechanical structures. With respect to his recognition in cement studies, he drew together a multinational team of authors in a book *Structure and Performance of Cements* that highlights the latest global advances in the field of cement technology. The Materials Group was strengthened by the arrival in 1994 of **Jeremy Cockcroft** from the ILL. In addition to his research, Jeremy, assisted by **Huub Dreissen,** was a central force in establishing courses in long-distance learning in the Department.

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

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

The Blundell era and beyond

The arrival of **Tom Blundell** in 1976, becoming Head of Department in 1978, signalled major developments in the structural biology research in the Department. With research interests in elucidating the architecture and function of macromolecules and their multi-component assemblies using methods from biochemistry, protein crystallography, and bioinformatics, he and his team have made major contributions in understanding biological function in many areas (see report in the March 2023 *Crystallography News* on the seminar held in his honour in December 2022). These include the structural biology of polypeptide hormones[xxii], growth factors, receptor activation, signal transduction, and DNA double-strand break repair – subjects important in cancer, tuberculosis, and familial diseases. He has also developed software for protein modelling and understanding the effects of mutations on protein function, leading to new approaches to structure-guided and fragment-based lead discovery. Many of the students and post-docs that worked with him at Birkbeck have gone on to be major players in their own right – examples including **Tim Hubbard** at King's College London, and **Lawrence Pearl**, who in 2008 followed Tom's footsteps in being elected FRS. Early on in his time at Birkbeck, Tom published with Louise Johnson a book on *Protein Crystallography*.

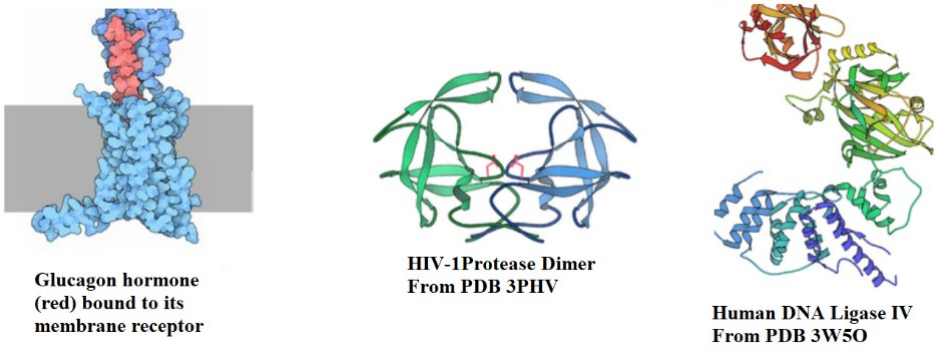

Figure 10:

Three of the very many protein structures worked on by Tom Blundell and his team.

Janet Thornton, now Director Emeritus at the European Bioinformatics Institute, joined Birkbeck in 1980. "I was part-time initially: a wonderful opportunity to spend time with my two children while continuing with my research. Later I understood how lucky I had been and appreciated how much support I'd received at Birkbeck." Her research focussed on bioinformatics, exploiting computers to study protein sequences and structures; she was one of the first to classify these structures and describe them in terms of their component parts. On being made a Fellow of The Royal Society (one more Birkbeck alumnus to be so recognised), Janet said: "I admire Birkbeck immensely, both for its work in giving people the opportunity to study, but also for its world-class research; the words Birkbeck and crystallography are synonymous". An example of one of Janet's projects – that also illustrates the internal collaboration across groups within the Department – was the development of the program PROCHECK[xxiii].

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

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

proteins resulted in being awarded the 2009 Interdisciplinary Prize from the Royal Society of Chemistry and the 2010 AstraZeneca Award from the Biochemical Society. From 1999 to 2006, Bonnie was Director of the Centre for Protein and Membrane Structure and Dynamics at the Daresbury Laboratory, and since 1999 has been Co-Director of the Protein Circular Dichroism Data Bank.

Helen Saibil came to Birkbeck in 1989 as the Bernal Professor of Structural Biology – noting her speciality of electron microscopy and Bernal's early recognition when setting up the Biomolecular Research Laboratory of the potential of 'the newly invented electron microscope' (see Bernal's comment in the last paragraph of page 3 above), occupying the Bernal Chair would seem highly appropriate. She developed the Cryo-EM operation in the Department, with much – though not by any means all[xxvii] – of her research on molecular chaperones and protein misfolding[xxviii]. Helen was also a key figure in the establishment of a cryo-imaging facility at the Diamond Light Source. In 2006 she became yet another Birkbeckian to be elected as a Fellow of The Royal Society.

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

Some concluding remarks

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

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

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i J.D. Bernal and R.H. Fowler. *J. Chem. Phys.* **1**, 515 (1933).

ii Harry had worked with Dorothy Crowfoot/Hodgkin at Oxford to solve the structure of cholesteryl iodide. That was the first time a complex, asymmetrical biological molecule was visualised directly by X-ray analysis and it opened a new way to determining unknown chemical structures.

iii J.D. Bernal. *Proc.Roy.Soc. A* **280**, 299 (1964).

iv C.H. Carlisle and D. Crowfoot. *Proc. Roy. Soc. A* **184**, 64 (1945).

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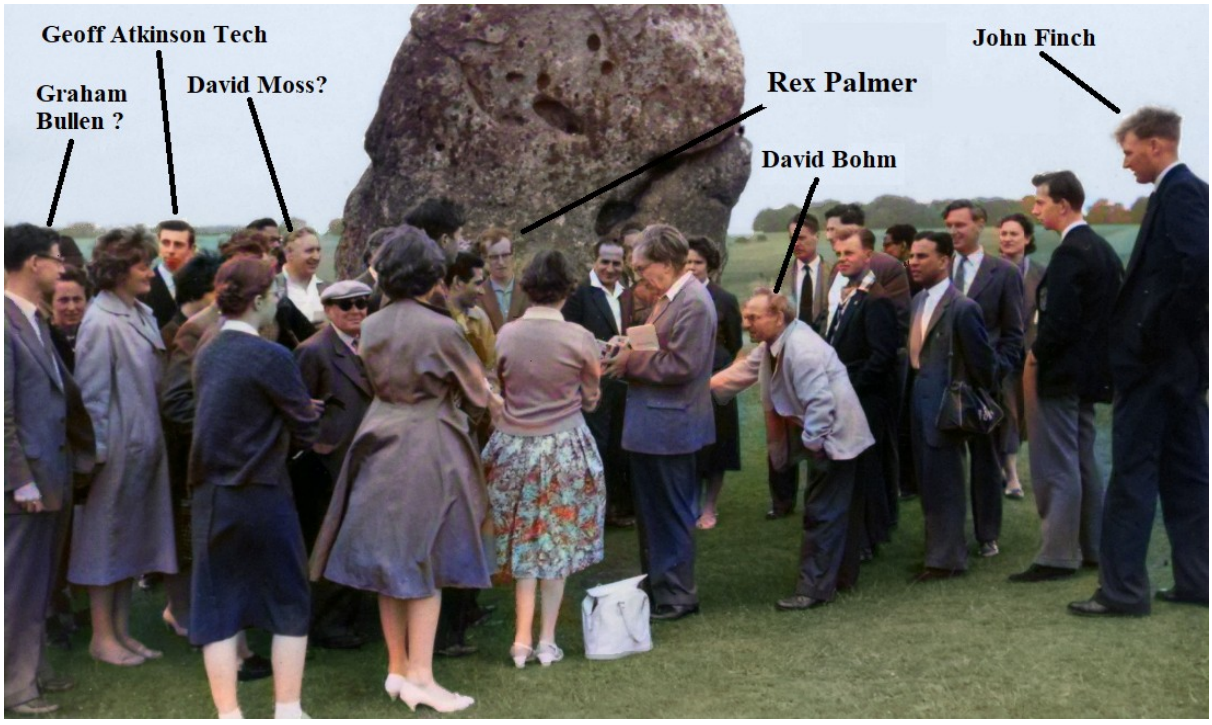
Appendix

Department outings

During the Bernal era, the Department got together in a Department outing. With Bernal's encyclopedic knowledge of everywhere he too k us, we always learned interesting things – not necessarily crystallographic.



The Crystallography Department annual summer outing in 1958. That year we went by coach to Stonehenge where Bernal gave a well-informed guided tour of the monument stones. We checked with David Moss and he was quite sure that the person indicated was not him – it might be Nick Moore. Also, the person labelled as David Bohm is actually Werner Ehrenberg. On leaving Stonehenge we were taken to nearby Salisbury Cathedral where Bernal again demonstrated his in-depth knowledge by making the group gather round the clock which was situated at the back of the cathedral on a table. He told us that it was a very early version of a spring-driven clock and showed us how it worked. The coach then took us to Egham, passing Royal Holloway College, and stopping at a roadside café for a welcome meal before returning to Birkbeck College.

Other outings included trips to Uppark (a 17th century National Trust property), a boat trip to Hampton Court (where David Moss failed to find the way to get *into* the maze, let alone the way out), and to the Eldridge Pope brewery in Dorchester (RIP) where Barry Gellatly stocked up on a cask of Hardy's ale to open on his son's 21st birthday. John Finney has helped a dozen or so bottles survive their 'do not open before' date of 1989.

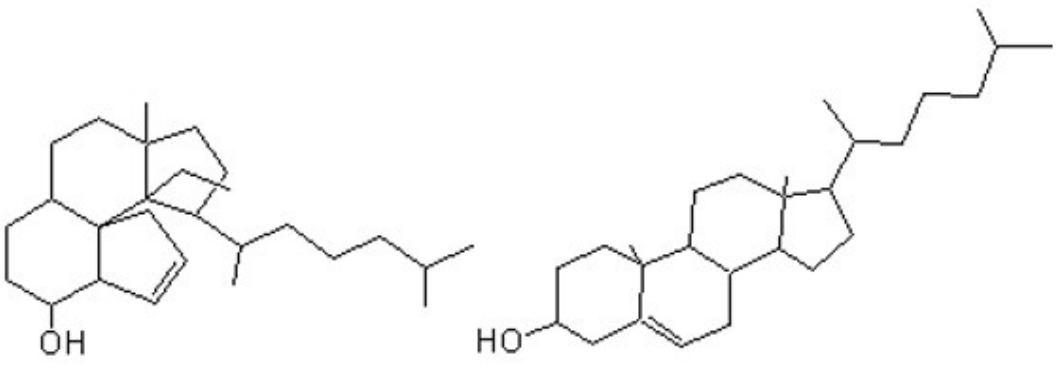
Who discovered cholesterol?

The Daily Mail Reader's Questions featured in December 2005 the QUESTION: Who discovered cholesterol? The following is my reply in January 2006 to one of the answers received.

Further to the previous answer (Daily Mail 14th December 2005), some corrections are required. It is true that Windaus and Wieland were awarded the Nobel Prize in Chemistry but this was in 1928 not 1934, and included studies on vitamins as well as cholic acid and cholesterol. However, this award was probably the biggest gaff ever made by the Nobel Prize Committee.

In 1934 Dorothy Crowfoot (who later became Dame Dorothy Hodgkin FRS and herself was awarded the Nobel Prize for her work on important biological structures including penicillin and insulin) wrote "It is perhaps a warning to us that the brilliant and intricate researches of Windaus and Wieland should have led to a formula so incorrect as that put forward for cholesterol in 1928." Just how incorrect the formula for cholesterol was can be spotted even by the untrained eye. Formula (1) below is the incorrect version while (2) is the correct one. The corrections were in fact made by John Desmond Bernal FRS (later Professor of Physics at Birkbeck College, London) on the basis of detailed but simple crystallographic measurements using X-rays and published in 1932. With Dorothy Hodgkin in Oxford, Harry Carlisle (who later became Professor of Crystallography at Birkbeck) painstakingly carried out the very first 3-d X-ray analysis by Fourier synthesis on crystals of cholesterol iodide (1942) without the use of a computer. This work completely confirmed Bernal's results.

It is of interest to note that the sterol framework of cholesterol is also the structural basis for the hormonal steroids such as progesterone, testosterone and oestrogen, as well as synthetic drugs such as the anabolic steroid stanazolol which has been in the news recently. Rectification of the wildly incorrect formula for cholesterol is a tribute to the depth of insight and tenacity of British scientists. A modern, highly accurate structure for cholesterol iodide is soon to be published in the Journal of Chemical Crystallography. Interestingly this work was carried out by teams from Birkbeck College and the University of Southampton using samples of Carlisle's crystals that had survived in a bottle for over 50 years.



(1) (2)

The Professor's Picasso

To Readers' Letters: Daily Mail 25/5/2010 from Hilda Palmer M.Sc., Birkbeck Alumnus.

Picasso may have been the most evil man Paul Johnson ever met (Daily Mail 24th May 2010) but he was without doubt a hugely talented artist who knew how to portray the Devil, as witnessed by this drawing which he produced in a matter of seconds on the bare wall of the flat in 21-22 Torrington Square, Bloomsbury in 1950. The flat was used by Professor of Physics J D Bernal FRS in an annex of Birkbeck College, which housed the Crystallographic Laboratories and Workshop. Bernal was a leading pioneer in the field of X-ray Crystallography. About the wall sketch, Picasso is supposed to have said to Bernal (known as Sage) after drawing the Angel and the Devil, "That's you on the right!"

Bernal had many other celebrity acquaintances including the singer Paul Robeson and the actor Miles Malleson with whom he had common political leanings. The story goes that Malleson turned up at the flat late one cold very foggy night in November 1959 with a young lady in tow, Bernal being away at the time. He told one of the students that Bernal had given him permission to use the flat and somewhat filled with trepidation the student let him in having recognised who he was. I personally was fortunate to see the Picasso *in situ* in the late 1950s before the wall was removed, finally coming to rest at the Wellcome Building in Euston Road and being resited in the Wellcome Gallery where it can still be seen.

Hilda Palmer **The Professor's Picasso**