Synchrotron Science in the UK: NINA, the SRS and Diamond

S. Samar Hasnain, Molecular Biophysics Group, Institute of Integrative Biology, Faculty of Health and Life Sciences, University of Liverpool, L69 7ZB, UK

C. Richard A. Catlow, Department of Chemistry, University College London, 20 Gordon St. London WC1 HOAJ, UK; School of Chemistry, Cardiff University, Cardiff CF10 3AT, UK

Abstract

The development of synchrotron science over the last 50 years is reviewed from the perspective of the authors own scientific programmes.

Introduction

The application of techniques employing synchrotron radiation now permeates almost all areas of science. Here we give a personal account of how our science in the fields of structural molecular biology, materials and catalytic science developed and evolved using synchrotron techniques. SSH first describes his early work using the NINA Synchrotron Radiation Facility (SRF) at Daresbury and the subsequent development of the Synchrotron Radiation Source (SRS); the growth of the molecular biology programme at the SRS and the increasing involvement of computation and theory are also discussed, as is the expansion of the international usage of the SRS and the transition to the Diamond Light Source. In the later sections, CRAC shows how early work with the SRS contributed to key areas of materials chemistry and describes the development of the SRS diffraction facilities; the major impact of both the SRS and the Diamond facility on catalytic science is also highlighted.

Arriving at the NINA Synchrotron Radiation Facility (SRF)

Having been awarded a J R Ashworth Research Scholarship by the University of Manchester for a project to work in the extended group of Prof Frank Read, FRS (who was a reader at the time), I arrived at Manchester airport on an autumn Sunday evening on 29th September 1974. I was met by Ian Munro and taken to his family home where I lived for a whole week. This moving from home to home enabled me to adjust to the change (that were oceans apart) seamlessly. During the first fortnight, Prof Read asked me to meet various sub-groups of the Atomic and Molecular Physics group covering his own interest *"*electron collisions with atoms and molecules", atomic/molecular physics undertaken at Jodrell Bank and photophysics/photochemistry. Three weeks later, having visited Jodrell Bank observatory and NINA at Daresbury, I was able to tell Prof Read that I was most excited by what I saw at Daresbury and what I had gleaned from Ian Munro's excitement. Frank Read generously agreed. Ian became my official supervisor with Scott Hamilton as my additional supervisor. What a lucky combination – the two pioneers who started it all (the journey of synchrotron radiation science in 1967) at Daresbury were my supervisors. Given the isolated nature of Daresbury and difficulties of travelling from Manchester, I moved to Daresbury and stayed at the lovely Hinstock Mount for the rest of the time for my PhD. I was fortunate at the time that the North Beamline at the NINA Synchrotron Radiation Facility (SRF) had some instruments already installed, commissioned and initial results were coming out.

In addition to Ian and Scott, Manolis Pantos and Malcolm Howells were the PDRAs in the Manchester team with a visiting scientist Professor Itzhak Steinberger from Tel Aviv on his sabbatical leave (see photo 1). Manolis's enthusiasm was infectious and Itzhak was like a 'child in a toy store'. Our instrument intercepted the first portion of the beam on the Northern beamline with the other parts shared by the Reading group and others. Malcolm (who went on to contribute significantly to the Brookhaven light source NSLS and Berkeley's Advanced Light Source, ALS) had wonderfully put together our instrument. We were engaged with trapping organic molecules in rare gas matrices and studying their

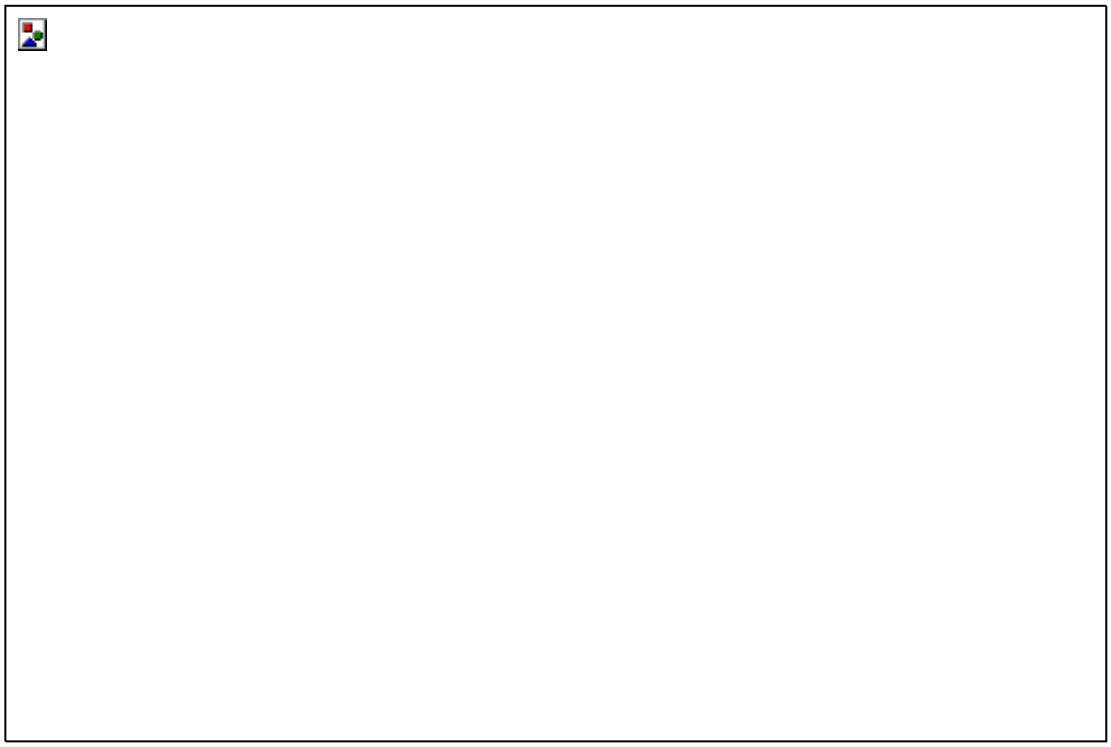


Photo 1. Manchester team in 1976 at the experimental control station. Standing from left to right are Scott Hamilton, Manolis Pantos and Samar Hasnain. Sitting with Ian Munro are Itzhak Steinberger (a visiting scientist from Tel Aviv) and Paul Brint, a PDRA.

photophysical/photochemical properties. Anything we touched provided new results. The pioneering spirit was all around both on the North and South beamlines. This small team of enthusiasts (photo 2) with the community were able to put together a case for what became the first dedicated multi-GeV Synchrotron Radiation Source (SRS). Mike Hart played an important part in incorporating hard X-rays option via a superconducting wavelength shifter. When the NINA SRF closed with the switching off of NINA at midnight of 31st March 1977, a number of us went away to other SR facilities – Ian Munro to SSRL (Stanford), Malcolm Howells and Gwyn Williams to Brookhaven (New York), Joan Bordas to EMBL outstation and I went to DESY at Hamburg leaving my 3 years PDRA fellowship with the Manchester team that had commenced in October 1976.

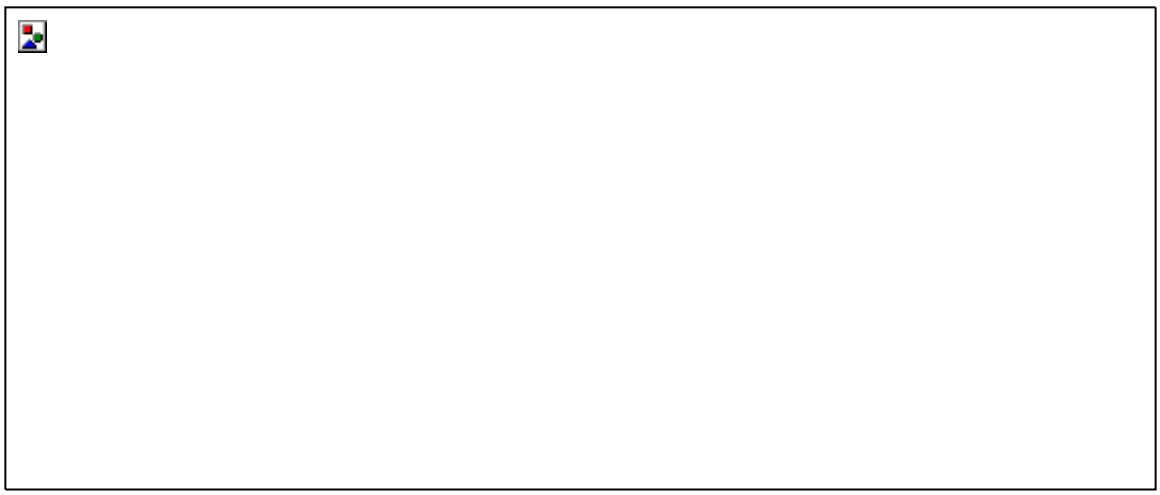


Photo 2. A photograph of the NINA SRF team taken a few hours before the final switch off of NINA on 31st March 1977. At the time, there were 10 user groups coming from the universities of Manchester, Reading, Oxford, Coleraine, Durham, Bristol, Warwick, Leicester, Edinburgh and MRC Cambridge who successfully put the case with the wider potential users community to build the world's first dedicated SR source, the SRS. From left to right: (sitting) John West, Ian Munro, Jeff Worgan and Ken Lea. (standing) Pat Ridley, Iggy McGovern, Bill Smith, Tony Bourdillon, John Beaumont, John Morton, Paul Brint, Samar Hasnain, Robert Pettifer, Joan Bordas, and Tony Cox.

From the NINA SRF to the Synchrotron Radiation Source (SRS)

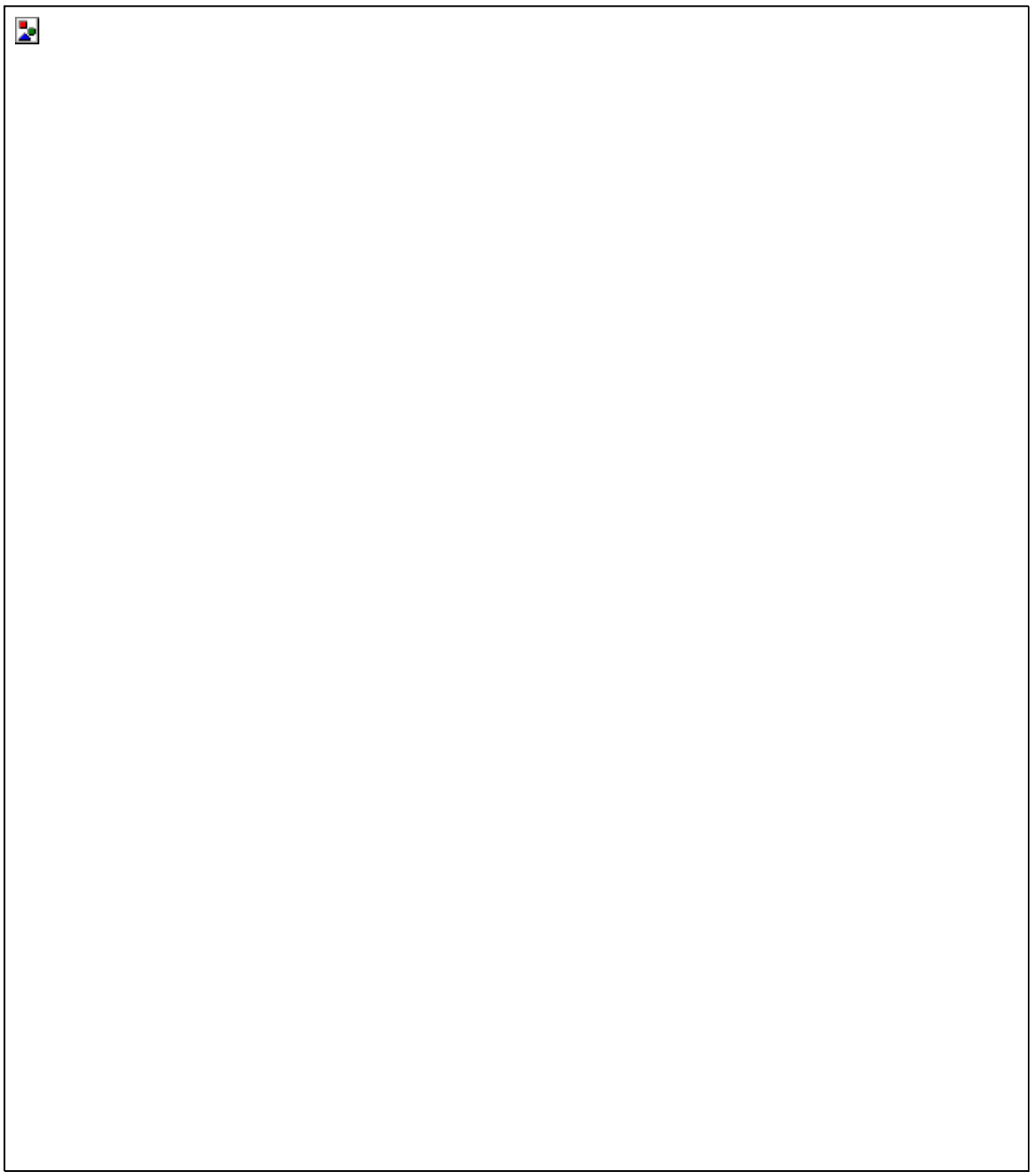
I joined the late Prof Ernst Eckard Koch at DESY in Hamburg as a DESY Fellow where I was able to participate in a variety of experiments ranging from spectroscopy to diffraction of molecular crystals. Koch was again one of the pioneers who together with Ruprecht Haensel and Christoph Kunz had established the synchrotron radiation facility on the DESY synchrotron. During my stay at DESY, the synchrotron radiation team established HASYLAB. On my return to the UK in October 1978, I took a conscious decision to use my physics and synchrotron radiation background at the interface of chemistry and biomedical science, thus joining an interdisciplinary team at Manchester derived from the Chemistry (Dave Garner, FRS) and Medical Biophysics (David Hukins) Departments who had just started the UK's first biological XAFS project working on metalloenzymes and biological calcification. Again, I decided to locate myself at Daresbury where I had the good fortune of being given a temporary office (which became my office for the next 15 years) that was only two doors away from Sir John Pendry, FRS, who had put forward the most comprehensive modern theory of EXAFS (more of this later)[1]. A year later, in 1979, I joined the national effort of establishing the world's first dedicated synchrotron radiation source (SRS) as a full time scientific staff member of the Daresbury Laboratory where I remained until March 2008, having formed a Molecular Biophysics Group in 1989 after returning from a sabbatical in the protein crystallographic laboratories of Charlie Bugg (Birmingham) and Lyle Jensen (Seattle) during the high brightness lattice shutdown of the SRS. I became Max Perutz Professor of Molecular Biophysics at the University of Liverpool in April 2008.

Establishment of XAFS as an important structural biology technique at the SRS.

The two-year period 1978-80 was a steep learning curve getting to grips with X-ray instrumentation (no gratings but radiation-resistant single perfect crystals such as germanium or silicon; mirrors of different size, smoothness and quality and detectors ranging from solid-state devices to ionisation chambers), data analysis and interpretation of extracted EXAFS data. I was fortunate, as mentioned above, to have Sir John Pendry

two doors away, whom I found most welcoming for a science discussion, prepared to translate difficult theoretical concepts into simple language for experimentalists such as me. Even though an approximation known as “the plane wave approximation” of the theory was readily usable requiring little computer time, I immediately grasped the importance of the curvature of the electron wave for accurate structure determination and began to put effort into its full implementation in the form of EXCURVE[2,3] (Norman Binsted, Steve Gurman and Richard Strange played major roles). From John, I also learnt an “open door policy” to encourage younger members of the team to come and talk, that I still maintain at the University. Likewise, I was inducted into the new and emerging field of bioinorganic chemistry by David Garner, FRS, who was one of my supervisors for a year of post-doctoral research (1978-79) and then a great collaborator until the early 90s when my science interest and approach began to change. In these early years many leading biochemists placed their trust in us with their precious protein samples that they obtained with hard labour in a highly purified form in the hope that we would be able to provide some important structural information that would provide support to a particular mechanism. An initial success came from the late Bob Bray of the University of Sussex who had provided more than a gram of purified lyophilised molybdenum containing xanthine oxidase in two forms. We were successful in collecting data and extracting reliable structural information that resulted in the first significant biological XAFS publication from the UK[4].

Towards the end of 1980, Max Perutz approached me to see if I was prepared to help him resolve a serious challenge to his stereochemical mechanism of haem-haem interaction that had come about from some EXAFS work that was conducted in the United States by some leading and highly influential scientists[5]. I accepted the request despite the obvious difficulties (see below).



Max Perutz's view on the James Lauterbrunner (in real life Peter Eisenberger) result was that his theory of a stereochemical mechanism was dead. Typical of him, not knowing the technique, he set about making arrangements for doing the XAFS measurements on a sample prepared by himself. He recruited his friends worldwide to get the measurements done at the Stanford Synchrotron in May 1980 on BL15 and BL23. But Max then faced the problem of data analysis. This brought him luckily to me in late 1980 when I had joined Daresbury as a staff scientist. I was aware of the controversy and had learnt of the difficulties of anyone looking at the data in the USA, for fear of their career. In fact, an Englishman who had done his PhD at Stanford was at the EMBL in Hamburg at the time; he could have analysed the data but decided not to, as he did not wish to rule out the possibility of working in the USA.

Over the next nine months, I rigorously analyzed the data using the most accurate curved wave implementation of EXAFS theory where it took overnight computation on the best IBM computer available at Daresbury (Daresbury was one of the major national computer centres at the time) to complete a single iteration for a fraction of the XAFS data range. In May 1981, I had the result, which confirmed the original EXAFS structural parameters. This compelled me to think where the problem regarding the lack of movement of iron from the porphyrin plane in Eisenberger's study might originate. I set about looking at all of the chemical porphyrin compounds that had been used for comparison and as standards in the original study and our own. The answer was obvious – Eisenberger had used the triangulation method where the assumption was made that the distance of the centre of the porphyrin plane to nitrogens between the compounds and haemoglobin is transferable. Eisenberger had used a value of 2.045Å for centre to nitrogen distance rather than the more commonly used value of 2.02Å. I wrote a detailed letter to Max on 14th May 1981 describing the problem in detail. I received an instant response via a handwritten letter on 18th May expressing his excitement. With some additional data on related compounds collected and analysed, we quickly wrote the paper and submitted it to *Nature* on 22 September 1981. This was just a few months after the SRS had come into operation with its initial energy of 1.8GeV and two bending magnet beamlines, line 7 for for X-rays and line 6 for VUV and soft X-ray primarily for Surface Science experiments. The paper was accepted in December 1981 and published on 11th February 1982[6]. It is remarkable that both of us were so focussed on getting the data analysed and resolving the problem scientifically that we never met prior to the publication. This was remedied by many visits including him staying at our home. On one of my visits to LMB, he mounted a very large MbCO single crystal for the first angle resolved XANES study of a protein crystal using polarised X-rays from the SRS[7]. This early work led to two distinct major contributions: first the realization that multiple scattering events in XAFS needed to be handled accurately and second that the combination of XAFS and crystallography would be very powerful for structure-function studies of metalloproteins, hence giving birth to a combined methods approach that I have continued to develop with new approaches joining the toolbox of structural biology.

Through a BBSRC/MRC grant, we were eventually able to build a dedicated experimental beamline for combined crystallography and single crystal XAFS at the SRS that was opened by Cherie Blair on 28th January 2005[8-10]. The use of this combined approach has led to a global effort to pursue damage-free crystallographic data collection by using spectroscopic methods to validate redox states. Using the most advanced synchrotrons and X-ray lasers, the serial crystallography approach is being developed for obtaining damage-free structures of functional states of redox enzymes[11-14].

Establishment of the SRS as the home for structural biologists

The efforts to make the SRS the home for structural molecular biology dates as far back as the establishment of the NINA SRF. To understand some complexity, it is worth mentioning that the UK's Science Research Council (SRC) established NINA and subsequently the SRS at Daresbury. There were a number of other research councils at the time including the Medical Research Council and the Agricultural and Food Research Council, each jealously guarding their territories and budgets. Simply said, anyone outside the scope and remit of the SRC had to get their funding council to pay their way for the use of the NINA SRF but more so for the SRS owing to what was a significant investment by a single research council.

Insert 1. Some correspondence between MRC and SRC.

29th November 1972 MRC

Dear Mr Thatcher,

May I confirm the gist of the telephone discussion we had on Monday of this week about the proposals for the joint use by Professor Wilkins and Dr Kendrew of the Synchrotron facility at Daresbury ?

When the question was raised in general terms by Mr Jolliffe (his letter of 2nd December 1971 to Dr Lush), we asked all the interested directors of MRC establishments to let us have their views, and the MRC's answer was given in Dr Neale's letter of 22nd June to Mr Jolliffe. The second paragraph of that letter sets out the position at that time in relation to the teams at King's and at the Laboratory of Molecular Biology.

We have now discussed the matter again with Professor Wilkins and with Dr Perutz and they do not feel that the new proposals in any way run contrary to their earlier views. Professor Wilkins regards his contribution to the joint programme as a departmental activity and the MRC will therefore be involved only if he decides to submit grant applications to us for support of this work; I understand that he is, in fact, intending instead to approach the SRC. Dr Perutz is still emphatic that Arndt's use of the facility is in a consultant capacity (in relation to the Daresbury Laboratory) and that no charge should be levied. It may well be that Professor Wilkins may also wish to take up this stance.

NOTE OF A MEETING ABOUT USE OF THE SRF FOR MOLECULAR BIOLOGY

The following were present at a meeting in State House on 22 January 1973:-

Mrs J O Paton
Professor A Ashmore
Dr M F Perutz
Professor D C Phillips
Dr T Vickers
Professor M H F Wilkins
Dr J A Fendley
Mr D Thatcher

Dr Perutz indicated that the equipment presently under construction by Dr Arndt in the MRC Laboratory of Molecular Biology at Cambridge is essentially a copy of what was developed by Professor Holmes (ex-MRC) under EMBO auspices at DESY in Hamburg. When the MRC equipment is working its use will be shared with Professor Wilkins' group at Kings College (the Department of Biophysics and within it the MRC unit) and Professor Phillips' Laboratory of Molecular Biophysics (MRC grant supported) in the Oxford Department of Zoology. The equipment should be completed in late 1973 but would need to be tested in the SRF from Easter 1973 awards.

Insert 2. Max Perutz identifying Hugh Huxley as the key driver from MRC.

Aug 1973 MRC Laboratory of Molecular Biology
University Postgraduate Medical School
Hills Road, Cambridge, CB2 2QH
England
telephone Cambridge (0223) 48011

F/AL/14/C7 3rd August 1973

Mrs J.O. Paton
Science Research Council
State House
High Holborn
London, WC1R 4TA

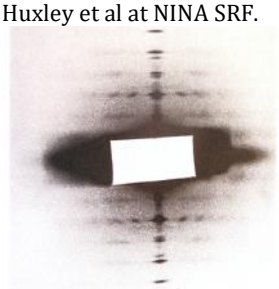
Dear Mrs Paton,

Thank you for your letter of July 16th which I have discussed with Huxley. He is agreeable to your proposal that the MRC should give one year's notice before removing the equipment installed at Daresbury except where removal is necessary for such purpose as overhaul, repair or modification. For this purpose the "MRC equipment" should include the camera and film holder as initially installed, but not any timing or counting equipment which we may take to use with it from time to time. For instance, we may take a multichannel scalar there, use it for a while, and then bring it back here for another experiment.

We also agree to beam time referring to high energy and beam conditions, as you suggest.

Yours sincerely,

Insert 3. Muscle Diffraction obtained by Huxley et al at NINA SRF.



1974 DL Annual Report

Fig.39 X-ray diffraction photograph of a specimen of muscle. The exposure time was approximately one hour for 5 GeV and 14 mA circulating current in NINA.

Max Perutz (MRC Cambridge), David Phillips (Oxford Molecular Biophysics) and Maurice Wilkins (King's College) represented the interests of MRC at meetings on 22nd January and 3rd August 1973 – inserts 1 & 2. Fibre diffraction was identified as the main beneficiary and as such Hugh Huxley was nominated to coordinate the activities at the NINA SRF. Huxley was able to obtain impressive static diffraction pictures from frog muscle (insert 3) in early 1974 and was able to progress towards initial time resolved muscle diffraction using this synchrotron source before the closure of NINA on 31st March 1977. In 1978 when Joan Bordas moved to EMBL Hamburg, where fibre diffraction and XAFS instruments had been located on the storage ring DORIS, Hugh Huxley joined in the effort. He only returned to the SRS in the mid 1980s. Joan returned to Daresbury as the head of

MRC's Structural Biology Laboratory in 1983. At this time MRC also decided to build a dedicated beamline 2.1 for biological solution scattering and fibre diffraction.

John Helliwell, who was a DPhil student at Oxford with Dr Margaret Adams, attended the 10th IUCr Congress in Amsterdam in August 1975 where he heard Keith Hodgson (Stanford) talk about some early crystallographic experiments performed at the 3.7GeV SPEAR storage ring at Stanford[15]. When he asked his supervisory team to go to Stanford to gain experience, he was taken to David Phillips who told him about the existence of the Daresbury Synchrotron Radiation Facility. This turned out to be good fortune for the development of crystallographic activities. It also clearly showed how important the 1973 meeting was where David Phillips was present. John obtained his beamtime on the NINA SRF in December 1976 but the tests were unfortunately inconclusive, primarily due to insufficient intensity and the operating mode of NINA – one would have to wait until the SRS storage ring came on line providing steady intensity. In the meantime, elsewhere in Europe, Roger Fourme had put together a dedicated facility for protein crystallography on the positron storage ring DCI at LURE using an electronic detector[16], which began to attract users, including some from the UK, as the news of possible gains of up to 20 over a 24 kW Elliott GX6 rotating anode spread among the community. It attracted groups from Oxford led by Louise Johnson in which Dave Stuart, FRS and Keith Wilson were also involved[17] and MRC Cambridge led by Max Perutz[18].

With the closure of NINA SRF in spring 1977, the construction of the SRS began. On the X-ray beamline, XAFS (station 7.1: Greaves/Hasnain), fibre diffraction (station 7.2: Watson Fuller), topography (station 7.5/7.6, the longest beamline on a synchrotron for some time: Brian Tanner) and X-ray interferometry (station 7.4: Michael Hart) were planned and built. Neville Greaves led the first publication from the SRS using the XAFS station 7.1 in November 1981[19]. Watson Fuller who was a Professor of Biophysics at Keele University negotiated a lectureship position jointly funded by Daresbury and Keele and advertised the position so that the individual could take the responsibility for station 7.2 as a station scientist. Fortuitously, John Helliwell decided to apply and was appointed to this important job; he was then able to steer the design of this important station to include both fibre diffraction and protein crystallography. The versatility of the instrument provided evidence for many crystallographic groups to join the UK's effort of SR structural biology while providing some exciting science related to fibre diffraction[20].

While line 7 was beginning to produce first results, I started working on a plan to develop beamline 8 where the source properties were much superior to the initial beamlines as the source was at an upstream point of an even-numbered magnet. The beamline was to provide XAFS facilities for dilute systems, particularly biological systems and solution scattering/fibre diffraction. Hugh Huxley, among others, was also involved in detailed specification of the SAXS component of the beamline. The beamline received a real boost with the arrival of the Dutch when NWO signed an agreement in 1982 with SERC to fund this beamline and its two experimental stations. Things began to move rapidly. In 1983 Joan Bordas arrived as part of the MRC signing a cooperation agreement with the SERC for building a biology support laboratory and another dedicated beamline for SAXS/muscle diffraction. SERC funded several experimental stations on the first superconducting wavelength shifter where crystallographic station 9.6 was to be installed; this eventually helped solve the foot and mouth disease virus structure[21] (capturing the national television high spot at 9 pm News in 1989) and F1-ATPase structure[22] that brought the first Nobel prize to the Synchrotron world in 1997 to Sir John Walker from MRC LMB[23]. My own efforts to combine all of the X-ray techniques (XAFS, SAXS and crystallography) came to fruition at the end of the first decade of the SRS[24-26] on iron transport protein, transferrins.

This became the integrated approach of my career since then – fostered by the interdisciplinary environment of the SRS where scientific and technical approaches had no boundaries – the only important aspect of the enterprise was the scientific question.

Collaborative Computational Projects (CCPs) helped to expand the community and science

The SRC's Science Board approved the CCP programme proposed by the Atlas Laboratory (which became a division of Rutherford laboratory in 1975) in October 1973 with the following aims:

- to provide rapid interchange of information in the selected area of study
- to collect, maintain and develop relevant items of software
- to encourage basic research in a given area
- to disseminate information by organising symposia and workshops

A CCP steering panel was established with Prof Phil Burke, FRS and Prof John Murrell, FRS (Sussex) as members. CCP1 (Quantum Chemistry) was initiated in February 1974 with John Murrell as the Chair. Membership included Prof Ian Hillier (Manchester) and Martyn Guest and Vic Saunders from ATLAS. Scientific results from the NINA SRF and the anticipated science from the SRS became a stimulus for a number of new CCP projects. The Science Research Council (SRC) agreed in 1976 that 10 posts supporting science board work should move from Rutherford to Daresbury. Phil Burke played a crucial role in the development of theory and CCPs. He had a joint appointment with Queen's University and the Daresbury Laboratory as Head of the Theory and Computational Science Division from 1977 until 1982 when he returned to Belfast full time. In September 1977, Vic Saunders, Martyn Guest, Mike Elder and Pella Machin moved to Daresbury; all played a major role in the success of CCPs. During the construction phase of the SRS, eight CCP projects were funded and established, four of which were directly linked to the SRS, namely CCP2 (atomic and molecular processes, 1978, Mike Seaton and Phil Burke), CCP3 (Surface Science, 1979, John Pendry, Tom Grimley and Martin Prutton), CCP4 (X-ray Diffraction and Crystallography, 1979, David Phillips, Tom Blundell, Mike Elder and Pella Machin) and CCP9 (electronic structure of solids, 1981, Balaza Gyorffy and Volker Heine). Each of these had and are continuing to have a major impact on science and access to methodology by a much larger community than would otherwise have been possible. In the context of structural molecular biology, the success of CCP4 is only matched by 'user friendly' facilities at SR centres. CCP4 continues to support collaboration between researchers working on methods and software development for protein crystallography in the UK. It has expanded to become a global example of collaboration and has been one of the key contributory factors in the success of biological crystallography (photo 1). The world map showing CCP4 usage and location of training workshops that are held neatly illustrates this.

Photo 1. Location of CCP4 Usage (yellow) and regular workshops/schools (red).

Bringing the international community together

During 1978-80 when I was getting to grips with XAFS instrumentation, theory and analysis, David Garner was asked in the summer of 1980 by the Royal Society of Chemistry to organise a workshop for the chemistry community so that the technique would become more widely accessible to that community. I was acutely aware that EXAFS groups worldwide were working on similar problems (theory, instrumentation and data analysis packages) in this rapidly developing field. It was thus an opportunity to bring together experts from Europe and the United states. Daresbury was good at organising focussed meetings called “study weekends”, which were held over a weekend. After some discussions, Dave agreed to make it an international workshop/conference and that if we were to include ‘inorganic systems’ in the title, the RSC would be happy. This was needed as the request had come from the Inorganic Division of the RSC. We thus called the study weekend “EXAFS for Inorganic Systems”. With a modest contribution from the RSC and strong backing from the Daresbury directorate, we were able to include three speakers from the USA (Peter Eisenberger from Bell Labs, Ed Stern from Seattle and Steve Cramer from Exxon), three from continental Europe (Peter Rabe from DESY/Keele, Antonio Bianconi from Rome and Alain Fontaine from Orsay) and a number of speakers from the UK (John Pendry, the late Robert Pettifer, David Norman and myself). It was sufficiently successful and filling a much-needed gap, so it was spontaneously decided to make this a conference series that is still growing. Daresbury Laboratory published the proceedings of the meeting[27]; and the conference is held every 3 years now. The last conference in this series was held in Krakow, Poland on 22-27 July 2018 with some 500 delegates. In 1990, it returned to the UK when I organized the conference in York.

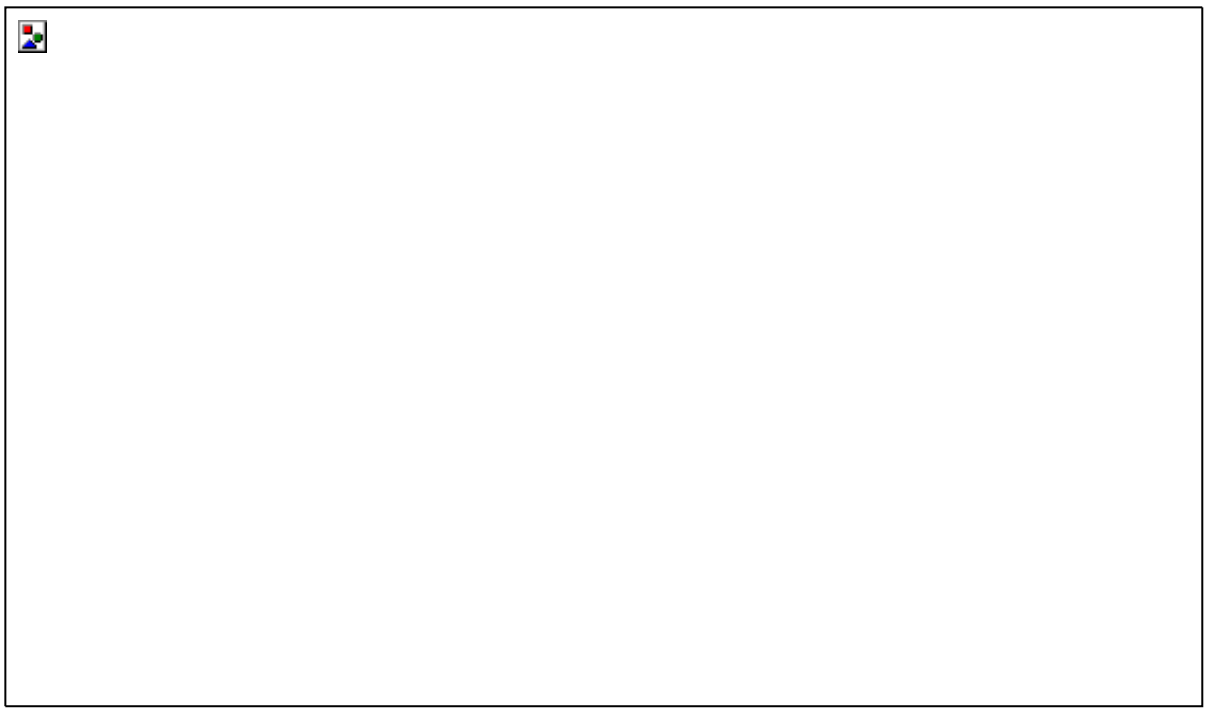


Photo 2: Delegates of the 9th Intenational BSR conference jointly organised by Louise Johnson and Samar Hasnain in Manchester 13-17 August 2007. From left to right SSH is 4th with Tom Blundell. Louise Johnson and Hans Deissenhoffer in the front row.

The availability of synchrotron radiation provided a real boost to biophysical methods in the early 1980's. Following a study weekend organised by Greg Diakun in 1984, the first international conference on 'Biophysics and Synchrotron Radiation (BSR)' took place in Frascati in 1986. In 1988 I, together with Joan Bordas, organised the second conference in the series in the beautiful city of Chester only 15 miles away from Daresbury with generous support from the International Union of Crystallography (IUCr). The conference produced a well referenced book "Synchrotron Radiation and Biophysics" published by Ellis Horwood where many of the synchrotron pioneers (Ian Munro, Roger Fourme, Keith Hodgson, Louise Johnson, Janos Hajdu, Watson Fuller, John Helliwell, David Garner, Wayne Hendrickson, Heinrich Stuhrmann, Yoshiyuki Amemiya, Malcolm Howells, Ed Rubenstein, Ron Burge, etc) contributed authoritative chapters. I was pleased to bring this conference back to the UK in 2007 when I had the pleasure of chairing the 9th conference in the series with one of my mentors, the late Dame Louise Johnson, FRS (photo 2). The conference attracted some 300 delegates with a number of Nobel laureates (Venki Ramakrishnan, Hans Deisenhoffer and Hartmut Michel) as plenary speakers. Other plenary speakers included Tom Blundell, David Stuart, Keith Hodgson, Janos Hajdu, Dmitri Svergun, Malcolm Irving and So Iwata. The 13th conference in the series will be held in Shanghai 21-24 September 2019.

25 years of synchrotron research at the SRS

To mark 25 years of the SRS, a celebratory science event was organised on 12th September 2005, combining it with the annual UK SR users meeting. The purpose of the occasion was not only to highlight the achievements but also to recognise the collaborative spirit which the SRS helped to engender in the scientific community. In addition to many of the UK pioneers, several major SR facilities (ESRF, SPring-8 and SSRL) were represented by their Directors and others. The growth of SR science around the world is a testimony to the collaborative spirit fostered by the SRS community.

I helped to assemble the scientific programme with a small advisory committee (Sir Tom Blundell FRS, Phil Burke FRS, David Garner FRS, Sir John Pendry, FRS, and Michael Woolfson, FRS). The programme was organised under 6 themes namely CCP, Theory-SR science interaction, Materials Science, Advances in SR sources, Instrumentation, Structural Biology and a forward-looking session. The two-days event was held in Manchester with a visit to the laboratory on the evening before. There was a reception for many of the pioneers of synchrotron radiation, who had travelled far and wide at their own expense including the head of the Anglo-Dutch collaboration, Dr Guy Luijkcx and Dr H Weijma. The photograph below (photo 3) shows many of the leading delegates who attended the special reception.

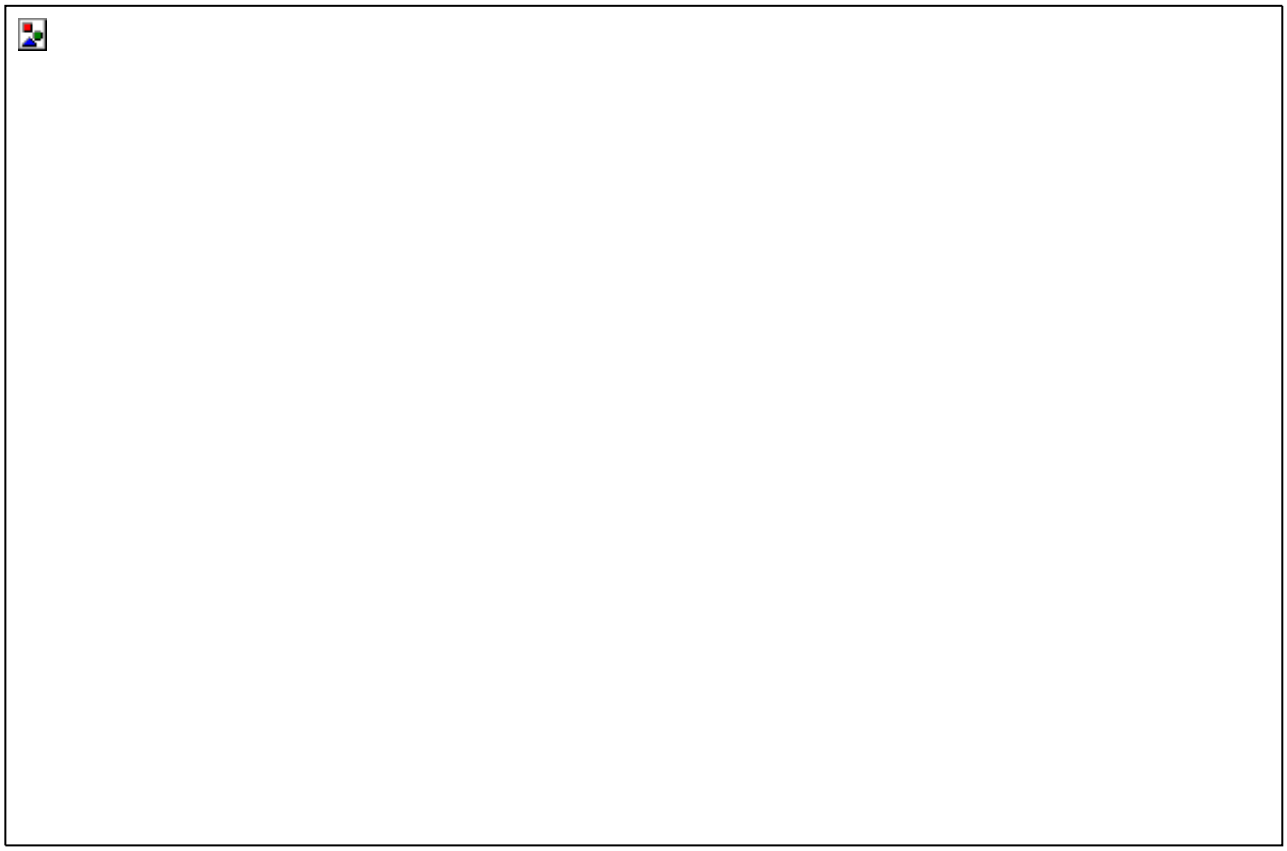


Photo 3: A group photo of many of the eminent scientists associated with the SRS and the SR world. In the front row Samar Hasnain, Herman Winick, Louise Johnson, John Pendry, Ian Munro, Mike Chesters (Director at the time), Hugh Huxley, Akira Kira, Michael Woolfson, Gerd Materlik, Alan Leadbetter are clearly visible. Pat Ridley, John West, Phil Burke, John Inglesfield, John Evans. Keith Hodgson, Richard Catlow and Bill Stirling are visible in the third and 4th rows.

From the SRS to Diamond

The SRS closed in 2008, having pioneered many of the techniques and research areas in the X-ray region. These are continuing to thrive at the Diamond Light Source (photo 4), and pioneering new frontiers. My inauguration as the first holder of the Max Perutz chair of Biophysics at Liverpool University took place in September 2008 (photo 5) with opening of the Barkla X-ray Laboratory of Biophysics in July 2011.

DIAMOND has broken new grounds in rapid data collection, on-the-fly data processing and remote access. It has been the first synchrotron centre to extend the structural biology capabilities to include a national cryo-EM facility under the same roof utilising the same.

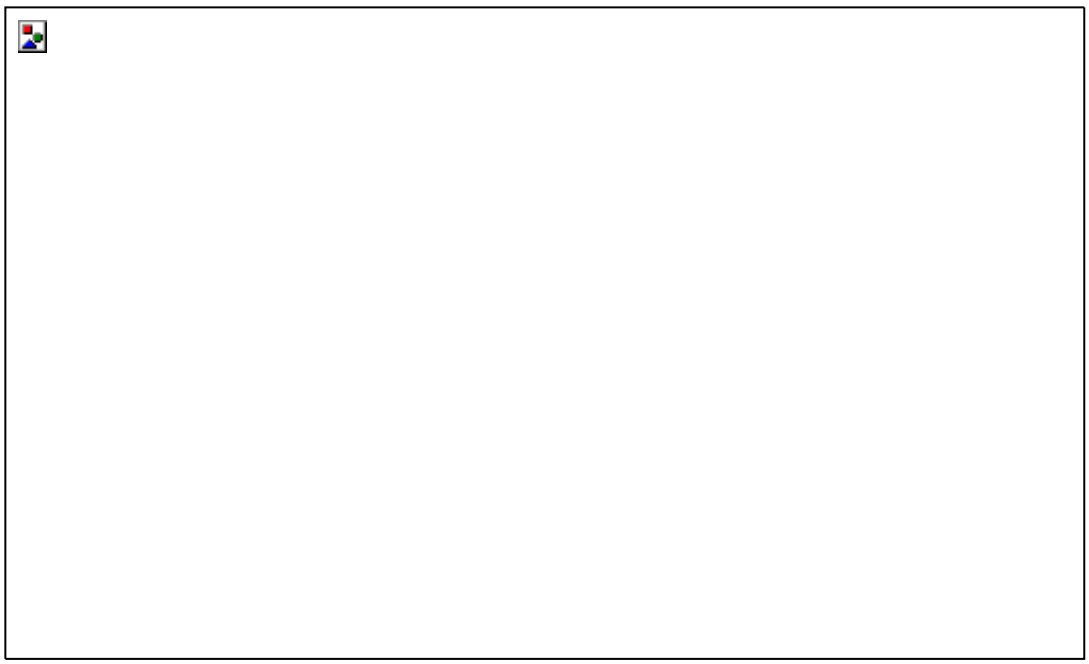


Photo 4. SRS gives birth to Diamond which has become an exemplar facility for Structural Biology.

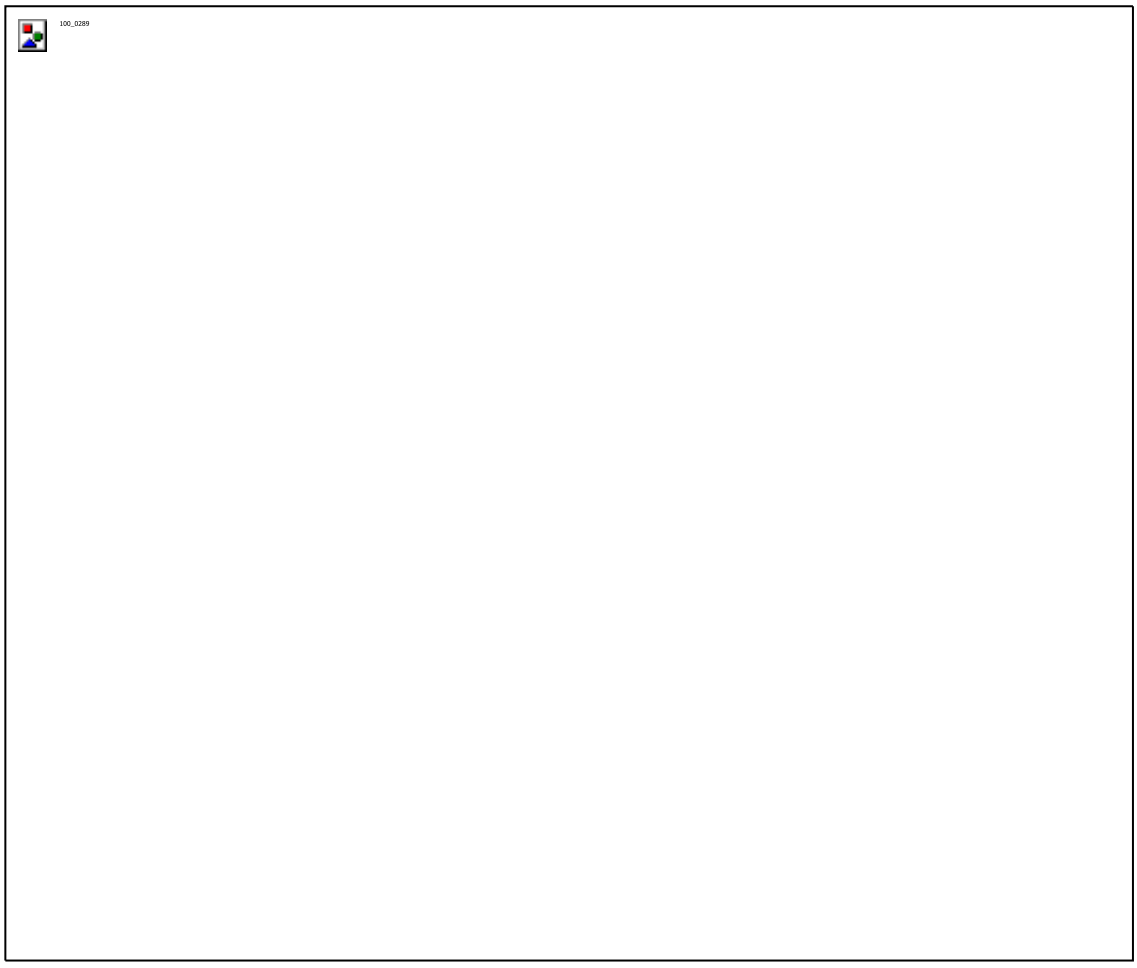


Photo 5. Installation as the Max Perutz Chair of Molecular Biophysics at the Liverpool University. Front row from left to right are Kyosho Nagai, Tom Blundell, Robin Perutz, SSH, Yasmeen Hasnain, Giorgina Ferry, Richard Henderson and Louise Johnson. In the 2nd row Roger Fourme, John Collinge, Colin Nave, Slaman Hasnain, Keith Hodgson, Simon Phillips and Michel van der Rest among others are present. In the final row first from right is Michael Woolfson.

infra-structure for access, user support and scheduling. It clearly has become an exemplar structural biology centre encouraging several other leading synchrotron centres to include cryo-EM in their structural biology toolkit[28,29]. We will also see below, how it has made major contributions to the development of materials and catalytic science.

Synchrotron Radiation, Materials Chemistry and Catalytic Science

Techniques based on synchrotron radiation have had a major impact on the fields of materials chemistry and catalytic science. In the sections which follow, a personal account is presented of CRAC's involvement in these fields, together with a discussion of the likely future developments. I will discuss first my early work with the SRS, which focussed on the application of EXAFS to defective ionic materials; next the development at the SRS of the diffraction facilities. From the 1990s onwards I became increasingly involved with the harnessing of Synchrotron techniques in catalytic science initially with colleagues in the Royal Institution, but more recently with the team in the UK Catalysis Hub. I hope that this account illustrates how synchrotron based techniques have grown over the decades from specialised niche applications into core and crucial experimental methods in mainstream areas within chemistry and materials science.

EXAFS and the SRS

I first became aware of the potential of synchrotron radiation for my science in the late 1970s when my research programme had a strong focus on disordered ionic materials – both halides and oxides – for applications in solid state electrochemistry. Much of my work was in computer modelling which was then emerging as a powerful technique in materials chemistry for developing models of structural and dynamical properties of materials and in particular of defect and dopant structures and energies. However, I had a strong interaction with experiment – particularly the group of Alan Chadwick at Kent which was at the forefront of experimental studies of ionic mobility in solids. At Alan's instigation, we attended a "Study Weekend" at Daresbury where we learned of the EXAFS technique and it was clear that EXAFS had huge potential in our field, by providing unique information on local structural properties in disordered solids. We began a very fruitful interaction with Neville Greaves at Daresbury and shortly after the SRS was opened, we succeeded in winning a grant from the SRC, "Synchrotron Radiation Facilities Committee" for EXAFS studies of ionically conducting solids. We recruited a talented post doc, Lee Moroney, and together with her and Neville, we faced the challenges of collecting and analysing data from the EXAFS beam line (station 7.1).

Despite the difficulties, it was immensely exciting working on this pioneering facility and our science made rapid progress. Developments in data analysis software were crucial and our success owed much to our interactions with Norman Binsted who was developing effective EXAFS data reduction procedures. I will pick out just two highlights of this highly productive period. The first concerned rare earth doped fluorite (CaF_2) – a widely studied system in the 70s and 80s owing to its ionic conducting properties and to applications in laser technology. There had been a long standing debate about the local structure around the dopant ions and EXAFS data when combined with computational modelling demonstrated that the dominant structure was a beautiful octahedral dopant cluster surrounded by a cloud of fluoride ion interstitials. This work, published in Nature[(30)] and highlighted on the front cover of the journal (reproduced in Fig, 1) clearly demonstrated the power of the technique, especially when combined with computational modelling. The second was a study of yttrium stabilised zirconia[(31)] – amongst the most intensively studied ceramic materials, owing to its applications as a structural ceramic and as an oxygen ion conducting solid. Yttrium ions replace those of zirconium and are

compensated by oxygen vacancies; and the location of the latter with respect to the dopant had been a matter of controversy. A careful and detailed analysis of the Yttrium and zirconium EXAFS data showed conclusively that the vacancies occupied not the nearest, but the next nearest oxygen site with respect to the dopant. The conclusions of the EXAFS analysis were again supported by computer modelling.

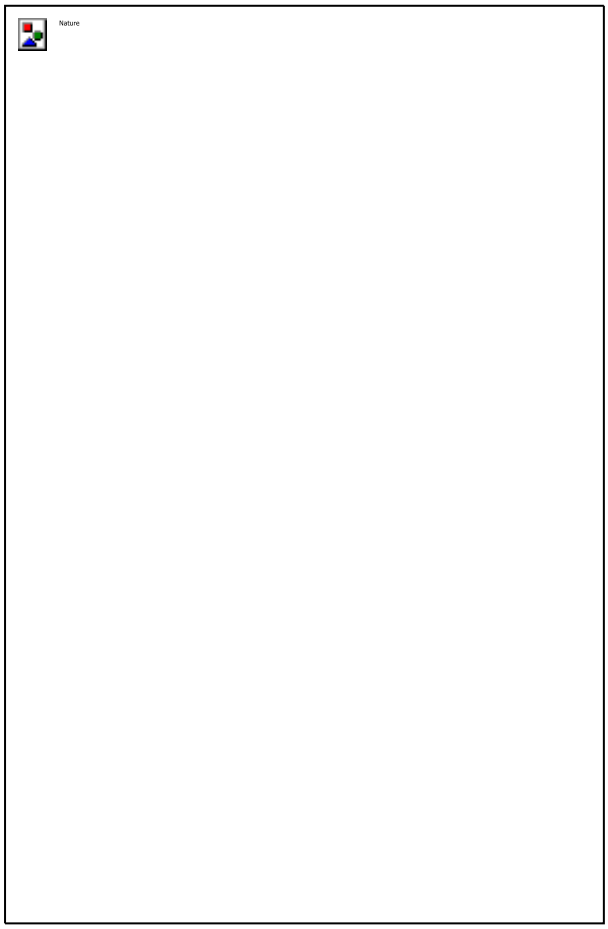


Fig (1): *Front Cover of Nature illustrating dopant interstitial cluster in rare-earth doped calcium Fluoride*

Many others contributed to the developing field of X-Ray spectroscopic studies of complex and disordered materials and the technique is of course now standard in materials chemistry. The early work on the Daresbury station 7.1 played a very important role in this development.

The Development of Diffraction Facilities

Although the first successful application of SR techniques in materials chemistry were in the exploitation of X-Ray spectroscopy, it was clear that powder diffraction had a great potential for the field. In the 1970's, high resolution powder diffraction (HRPD) using neutron sources had had a major impact, owing to the possibility of using Rietveld techniques enabled by the Gaussian line shapes of neutron PD reflections; structures as complex as those of zeolites had been solved. Synchrotron based techniques presented exciting opportunities as the peak shapes, although more complex than those of neutron data, can nevertheless still be parameterised; and they

have the additional advantage of being narrow, due to the high collimation of the synchrotron beam, thereby minimisation peak overlap – the intrinsic difficulty with powder data.

The potential of SR based PD had been recognised early in the development of the instrumental programme on the SRS, with the construction of a high resolution instrument (station 9.1 on the wiggler beam line). In 1985, I moved to a joint professorial appointment between Keele University and The Daresbury Laboratory, where my role was to assist in the development of the PD instrumentation and community. I was given great support and encouragement from the then Vice-Chancellor of Keele, Brian Fender, and we were fortunate enough to recruit Andy Fitch (now leading the powder diffraction programme at ESRF) as a lecturer who brought valuable and extensive experience of neutron based PD. The team at Daresbury included Peter Hatton and Graham Bushnell-Wye, and was soon augmented by Bob Cernik, Phil Pattison and Simon Clark. We were also helped by the expertise and vision of Michael Hart who was then playing a crucial role in developing the instrumental and scientific programme of the SRS

It soon became clear that the instrument on beam line 9.1 was being required to function in too many modes, including operating both as an angular and energy dispersive (ED) diffractometer. The team therefore developed and implemented a plan for a suite of three instruments: station 9.1 was optimised for high resolution angle dispersive studies; a second station (9,4 – again on the wiggler beam line) was constructed for energy dispersive work; and a third (station 8.3), for intermediate resolution angular dispersive XRPD. The latter had an intriguing design, proposed by Michael Hart with a set of long collimators between the sample and the detector, (often referred to as the Hart-Parrish design), which improved line shape and resolution.

The plan proved to be a great success. Andy Fitch's expertise in structure solution using Rietveld techniques helped to develop station 8.3 into a workhorse diffractometer which solved a large number of crystal structures; there were also crucial contributions from Bob Cernik and an early success was the solution by Cernik et al.[32] of the structure of cimetidine ($C_{10}H_{16}N_6S$) – a powerful histamine antagonist – which clearly showed the ability of synchrotron based powder techniques to solve complex structures. (9.1) operated successfully as a high resolution instrument and was reserved for more specialist applications including anomalous dispersion experiments; while 9.4, proved highly successful as an ED diffractometer and made a key contribution to the emerging field of kinetic crystallography owing to the ability to collect data very quickly in the ED mode.

The three stations continued to operate throughout the lifetime of the SRS. They were followed in the 1990s by a microcrystalline single crystal diffractometer in a project led by Bill Clegg, of which I was co-Investigator and which is discussed in detail in Clegg's article in this issue. With these instruments, synchrotron based diffraction at the SRS made a marked and important contribution to structural materials science.

Catalysis and the Royal Institution

In 1989, I moved to a professorial position at the Royal Institution where, together with the then Director, Sir John Meurig Thomas – one of the leading figures worldwide in catalytic science - we began to explore the potential of SR techniques in studying catalytic materials. EXAFS had been used to considerable effect by John Evans and others in homogeneous catalysts, but application to heterogeneous catalysis was less common. Our work centred around microporous catalysts, both zeolites and alumino-phosphates and was greatly assisted by Gopinathan Sankar, who had recently joined the team from CNR Rao's group in Bangalore. An early success was our study of nickel zeolite Y[33] – a widely studied catalytic material – where by combining results from separate XRD and EXAFS

experiments we are able to characterise in detail the local environment of the nickel, located within a the cages of the microporous crystal structure of the zeolite. The next step was to combine XRD and EXAFS in one experiment. The Daresbury team led Greaves, Dent and Derbyshire successfully developed techniques in which diffraction and spectroscopy data could be measured simultaneously. Progress in detector design and technology reduced the data collection time and it now became possible to monitor the evolution of both local and long-range structures during a solid-state reaction. The RI/Daresbury team was at the forefront of exploiting these developments, with a pioneering study of the conversion of the mineral aurichalcite to a copper catalyst, which was able to follow the decomposition of the mineral and the growth of the metal particles during the reaction[34].

Other highlights from this very productive period relate first to the location of organic templates within microporous solids. Templates are used in the synthesis of these materials as they can direct the structures towards specific architectures. In the 1990s, Dewi Lewis and Dave Willock developed "*de-novo*" design methods for the prediction of templates for specific architectures and successfully predicted a template for the synthesis of a microporous alumino-phosphate – DAF-5 – shown in fig (2). Following the synthesis of the solid, the structure was determined using the recently developed microcrystalline diffractometer on station 9.8, referred to earlier and the location was revealed as shown in the figure. It was exactly as predicted by the computational modelling[35].

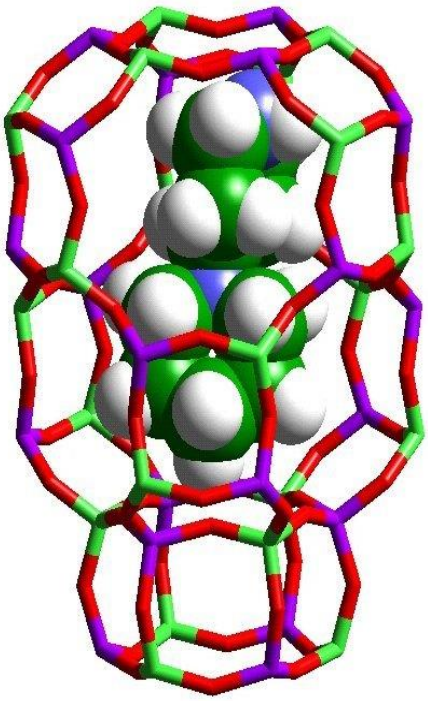


Fig (2) *Predicted and experimentally determined structure of 4 piperidinopiperidine inside the pores of DAF-5.*

Another intensively studied system, was the zeolite "TS1" based on an all silica zeolite – silicalite – in which ~1% of the Si is replaced by Ti and which is an extensively used industrial oxidation catalysts. It also proved possible to develop catalysts with similar functionality by taking "mesoporous" silicas – materials with pore dimensions in the 30 – 50 A range (as opposed to micoporous materials which are typically in the 4 – 12 A range) and grafting tetrahedral Ti species on their internal pores. In a series of studies, EXAFS

was able to confirm in detail the structure of the active site. Computer modelling also probed both the structure and mechanisms involved in using these catalysts in epoxidation reactions using H_2O_2 as oxidant. The predicted structures shown in Fig (3) agree accurately with the results of the *in situ* EXAFS data analysis. The computer modelling was also able to elucidate the reaction mechanism, so that by this combination of modelling and EXAFS, the full catalytic cycle was understood at the molecular level[36], as illustrated in Fig (4).

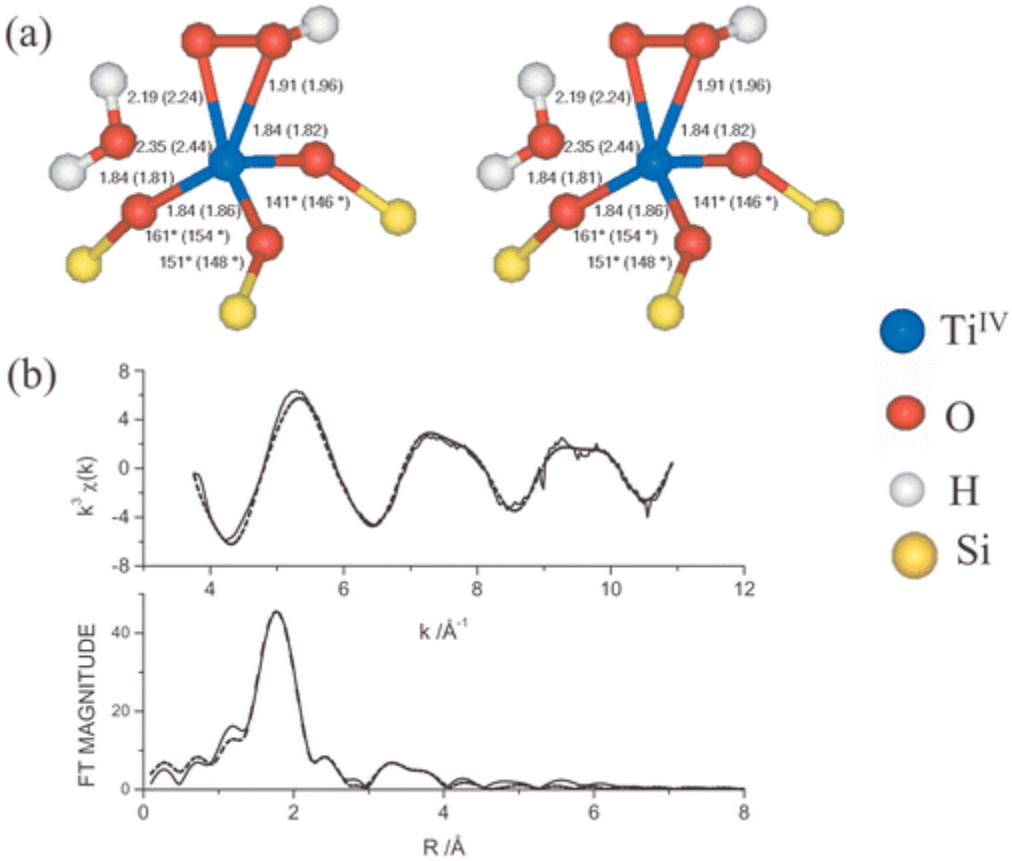


Fig (3) *Intermediate in the TS1 oxidation catalyst created by reaction of the titanium centre with hydrogen peroxide.*

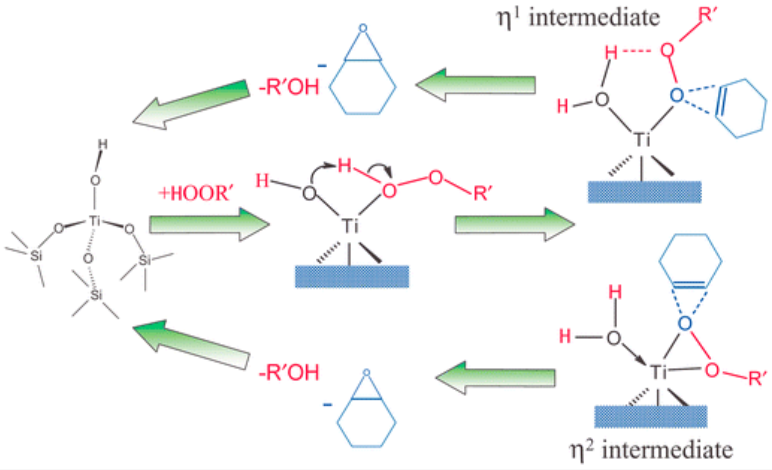


Fig (4) *Proposed epoxidation mechanism for Ti micro/meso-porous catalysts for alkene epoxidation.*

Synchrotron Radiation and the UK Catalysis Hub.

In 2013, Graham Hutchings, Matt Davidson, Chris Hardacre and I, after extensive discussions with EPSRC, successfully bid for funds to establish the *UK Catalysis Hub* involving a coordinated and comprehensive programme of catalytic science in the UK. Importantly, this national network comprising more than 40 university teams, has a physical base and hub in the Research Complex at Harwell (RCaH) on the UK Harwell Science and Innovation campus, which hosts the major facilities including the Diamond Light Source, the ISIS Neutron Source and the Central Laser Facility. The Hub has made and continues to make effective use of all these facilities. The use of X-Ray spectroscopy on the Diamond beamlines, led by Emma Gibson and Peter Wells in collaboration with scientists from Diamond has been one of the major features as illustrated by two recent examples.

The first relates to supported nano-metallic catalysts which are extensively used in heterogeneous catalysts. Bimetallic Au/Pd nanoparticulate systems have diverse catalytic functionality and have been particularly widely studied. In a series of experiments Gibson et al.[37] investigated how the structures of such nano-particles evolve during CO oxidation catalysis. The work built on the development of combined *in-situ* EXAFS with DRIFTS on Diamond Beam Line 18 and by piecing together the evidence from the two techniques, it was clear that the nano-particle undergoes extensive restructuring during the catalytic cycle as illustrated in Fig (5). Interestingly, during the cycle, the gold buries into the interior of the particle giving a gold-core, palladium-shell structure.

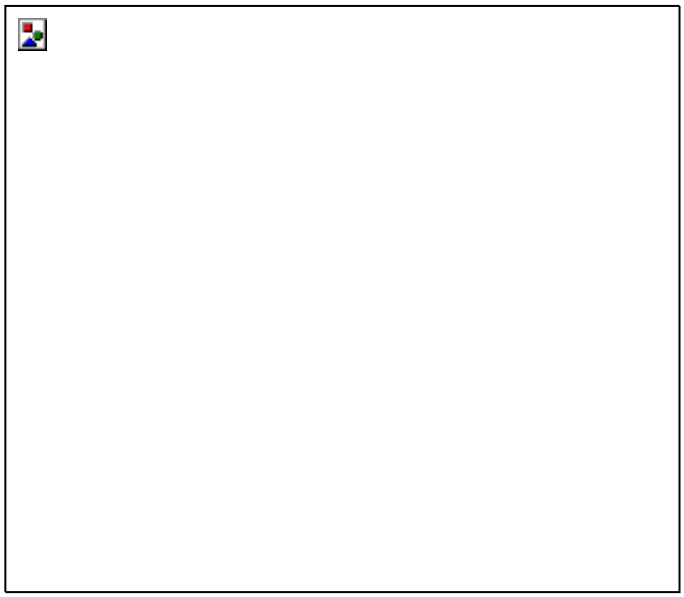


Fig (5); *Schematic of restructuring of Au/Pd nano-particles during CO oxidation as revealed by combined EXAFS/DRIFTS. Initial state of catalyst (A, showing external and B, giving cross-section) has PdO on the surface, of NPs with an Au rich core and an AuPd alloy exterior. The final state (C and D) has a gold core, followed by an Au/Pd alloy and a top layer of Pd.*

The second example relates again to nano-structured catalysts: in this case, gold on a carbon support, which pioneering work of Hutchings had shown to be effective for the catalytic conversion of acetylene to vinyl chloride – a key step in the production of PVC. The catalyst has now been commercialised by Johnson Matthey and is replacing mercury based catalysts, which have been widely used in China and which have substantial associated environmental problems. It had been generally assumed that the active

catalyst comprised Au nano-particles. However, *in-situ* EXAFS clearly showed during the catalytic operation, the gold is predominantly present as single gold cations. Computer modelling work then demonstrated a plausible mechanism for the catalytic cycle based on gold cations as the active site.[38]
Many other examples could be given of the crucial role of *in situ* X-Ray spectroscopy in the wide ranging science of the Catalysis Hub. Another very notable development has been the use of tomographic imaging of real industrial catalysts led by Beale using both facilities at Diamond and ESRF.[39] The role of these techniques in catalytic science has been amply demonstrated in extensive work of Weckhuysen and colleagues[40]

The Future

Synchrotron based techniques are now integral components of biomolecular, materials and catalytic science. Future developments in sources will offer exciting new opportunities in time resolved structural science and in micro-focus experimentation. The power of *in-situ* studies will continue to grow as well as the continuing spectacular developments in imaging of real systems complex materials and catalysts. There will also be continued rapid growth in the combination of synchrotron measurements with other spectroscopies and techniques. For structural biology, synchrotron X-ray crystallography will continue to remain single most important tool for proteins and multiple-protein complexes with molecular weight <200kD. Nearly 90% of the structures in the protein data bank are for macromolecules <200kD[29]. cryoEM is likely to become the most dominant structural biology approach for systems >200kD and for difficult-to-crystallize membrane proteins. For the latter, XFEL crystallography would also play a significant role with a pole position for providing damage-free and time-resolved structures as exemplified by recent examples of photosystem II[14] and retinol isomerisation[41,42]. Synchrotron-based crystallography would remain unique at providing structures at a resolution that provides details at chemical level necessary to define the mechanism of an enzyme or processes such as electron transfer, bond formation and breakage. Synchrotron-based serial crystallography is beginning to emerge and is likely to play important role in kinetic crystallography at sub-seconds to milli-seconds time scale. Light sources will continue to illuminate the science of biomolecules, complex materials and catalysts for coming decades.

Acknowledgements

We are grateful to all the colleagues mentioned in this article for their long-standing collaboration. We would also like to thank SRC, SERC, CCLRC, STFC, BBSRC, EPSRC and MRC for funding and support over the years. CRAC would like to thank John Matthey for funding and collaboration. SSH would like to thank Prof Robin Perutz and Vivien Perutz for supporting naming of my chair after Max Perutz. We are grateful to members of our groups over the years for their contribution, enthusiasm and passion for scientific research. We thank Tom Blundell, Alan Chadwick, Bob Cernik and Tom Blundell for reading the manuscript and their encouragement.

References

1. P. A. Lee & J. Pendry, *Phys Rev* **B11**, 2795-2811, 56-63 (1975).
2. N. Binsted, R. W. Strange and S.S.Hasnain, *Biochemistry*, **31**, 12117-12125 (1992)
3. N. Binsted and S.S. Hasnain, *J. Synchr. Rad.* **3**, 185-196 (1996)).
4. J.Bordas, R.C.Bray, C.D.Garner, S.Gutteridge and S.S.Hasnain, *Biochemical J.* **191**, 499 (1980)).

5. P. Eisenberger, R. G. Shulman, B. M. Kincaid, G. S. Brown & S. Ogawa. *Nature* **274**, 30-34 (1978)).
6. M.F.Perutz, S.S.Hasnain , P.J.Duke, J.L.Sessler and J.E.Hahn, *Nature* **295**, 535 – 538 (1982)
7. A. Bianconi, A.Congiu-Castellano, P.J.Durham, S.S.Hasnain and S. Phillips, *Nature*, **318**,685-687 (1985)
8. M. Cianci, S. V. Antonyuk, N. Bliss, M. W. Bailey, S. Buffey, K. C. Cheung, J. Clarke, G. E. Derbyshire, M. J. Ellis, M.J. Enderby, A.F. Grant, M.P. Holbourn, D. Laundy, C. Nave, R. Ryder, P. Stephenson, J.R. Helliwell and Hasnain, S.S., *Journal of Synchrotron Radiation* **12**, 455-466 (2005),
9. A. Arcovito, M. Benfatto, M. Cianci, S.S. Hasnain, K. Nienhaus, G.U. Nienhaus, C. Savino, R. W. Strange, B. Vallone, and S. Della Longa, *Proceedings of National Academy of Sciences***, 104**, 6211-6216 (2007)
10. M. A. Hough, S. V. Antonyuk, R. W. Strange, R. R. Eady and S.S. Hasnain, *Journal of Molecular Biology***, 378,** 353-361 (2008)
11. S. Horrell, S. V. Antonyuk, R. R. Eady, S. S. Hasnain, M. A. Hough and R. W. Strange. *IUCrJ **3***, 271-281 (2016),
12. T. P. Halsted, K. Yamashita, K. Hirata, H. Ago, G. Ueno, T. Tosha, R. R. Eady, S. V. Antonyuk, M. Yamamoto and S. S. Hasnain, *IUCrJ **5***, 22-31 (2018)
13. Suga, M.; Akita, F.; Hirata, K.; Ueno, G.; Murakami, H.; Nakajima, Y.; Shimizu, T.; Yamashita, K.; Yamamoto, M.; Ago, H.; et al. *Nature* **517,** 99–103 (2015).
14. Suga, M., Akita, F., Sugahara, M., Kubo, M., Nakajima, Y., Nakane, T., Yamashita, K., Umena, Y., Nakabayashi, M., Yamane, T., Nakano, T., Suzuki, M., Masuda, T., Inoue, S., Kimura, T., Nomura, T., Yonekura, S., Yu, L.-J., Sakamoto, T., Motomura, T., Chen, J.-H., Kato, Y., Noguchi, T., Tono, K., Joti, Y., Kameshima, T., Hatsui, T., Nango, E., Tanaka, R., Naitow, H., Matsuura, Y., Yamashita, A., Yamamoto, M., Nureki, O., Yabashi, M., Ishikawa, T., Iwata, S. & Shen, J.-R. (2017). *Nature*. **543**, 131–135.
15. J C Phillips, A Wlodawer, M M Yevitz, and K O Hodgson, PNAS, **73**, 128-132, (1976)
16. M. Lemonnier, R. Fourme and F. Rousseaux and R. Kahn, *Nuclear Instruments & Methods*, **152**, 173-177 (1978)
17. K. S. Wilson, E. A. Stura, D. L. Wild, R. J. Todd, D. I. Stuart, Y. S. Babu, J. A. Jenkins, T. S. Standing, L. N. Johnson, R. Fourme, R. Kahn, A. Gadet, K. S. Bartels and H. D. Bartunik, *J. Appl. Cryst.* **16**, 28 (1983)
18. G. Fermi, M. F. Perutz, B. Shaanan, R. Fourme, *J. Mol. Biol.* **175**, 159 (1984)
19. Greaves, G. N.; Durham, P. J.; Diakun, G.; Quinn, P. Nature 294, 139-142 (1981)
20. A Mahendrasingam, VT Forsyth, R Hussain, RJ Greenall, WJ Pigram, W Fuller, *Science* **233**, 195-197 (1986)
21. R. Acharya, E. Fry, D. Stuart, G. Fox, D. Rowlands & F. Brown, *Nature,* **337**, 709-716 (1989)
22. J. P. Abrahams, A. G. W. Leslie, R. Lutter & J. E. Walker, Nature 370,621-628 (1994)
23. S. S. Hasnain, J. R. Helliwell & H. Kamitsubo, *J. Synchrotron Rad.* **6**, 809-811 (1999)
24. R.C.Garratt, R.W.Evans, S.S.Hasnain and P.F.Lindley. *Biochem Journal*, **233**, 479 (1986),
25. S. Bailey, R. W.Evans, R.C. Garratt, B. Gorinsky, S.S.Hasnain, C.Horsburgh, H. Jhoti, P.F. Lindley, A. Mydin, R.Sarra, and J.L.Watson, *Biochemistry*, 27, 5804 - 5812 (1988)
26. G. J. Grossmann, M. Neu, F. J. Schwab, R. W. Evans, E. Townes- Andrews, P. F. Lindley, H. Appel, W.G. Thies and S.S.Hasnain. *J Molecular Biol,* **225**, 811 - 819 (1992)
27. C. D. Garner and S. S. Hasnain, DL/SCI/R17 (1981)
28. Saibil, Grunewald and Stuart, ACTA CRYST D71, 127-131 (2015)
29. Muench, Antonyuk & Hasnain, IUCrJ, 6, 167-177 (2019)).
30. Catlow CRA, Chadwick AV. Greaves GN and Moroney LM, *Nature*, **312**, 601-604 (1984)

31. Catlow CRA, Chadwick AV, Greaves GN and Moroney, LM, *J.Am.Ceram.Soc.,* **69**, 272-277 (1986)
32. RJ Cernik, AK Cheetham, CK Prout, DJ Watkin, AP Wilkinson and BTM Willis, *J.Appl.Crys,* **24,** 222-226, (1991)
33.Dooryhee E., Catlow CRA, Couves JW, Maddox PJ, Thomas JM, Greaves GN, Steel AT and Townsend RP, *J.Phys Chem,***95,** 2514-2521, (1991)
34. Couves JW, Thoma JM, Waller D, Jones RH, Dent AJ, Derbyshire GE and Greaves GN, *Nature,* **354,** 465-468, (1991)
35. Lewis DW, Sankar G, Wyles JK, Thomas JM, Catlow CRA and Willock DJ*, Angewandte, Chemie, Int Ed*; **36,** 2675- 2677 (1997)
36. Thomas JM, Catlow CRA, Sankar G., *Chem Comm*, 2921-2925 (2002)
37. Gibson EK, Beale AM, Catlow CRA, Chutia A., Gianolio D, Gould A., Kroner A., Mohammed KMH, Perdjon M, Rogers SM and Well PP, *Chem Mater,* **27,** 3714 – 3720, (2015)
38. Malta G, Kondrat SA, Freakley SJ, Davies CJ, Lu L, Dawson S, Thetford A., Gibson EK, Morgan DJ., Jones W, Wells PP, Johnston P.,Catlow CRA, Kiely CJ. and Hutchings GJ, *Science,* **355,** 1399 1402, (2017)
39. Senecal P, Jacques SDM, Di MM, Kimber SJ, Vamvakeros A., Odarchenko Y, Lezcano-Gonzalez I., Paterson J, Ferguson E. and Beale AM. *ACS Catalysis,* **7,** 2284 – 2293, (2017)
40. Meirer F and Weckhuysen B., *Nature Reviews Materials, **3,*** 324-340, (2018)
41. Nango, E., Royant, E., Kubo, M., Nakane, T., Wikstand, C. *et al*. *Science* **354**, 1552–1557 (2016).
42. Nogly, P., Weinert, T., James. D., Carbajo, S., Ozerov, D., Furrer, A., Gashi,D., Borin,V., Skopintsev, P., Jaeger, K., Nass, K., Båth, P., Bosman, R., Koglin, J., Seaberg, M., Lane, T., Kekilli, D., et. al. *Science* **361**, 145 (2018).