By John R Helliwell

(Recent news! - John has just been awarded the 8th Max Perutz Prize of the European Crystallographic Association for his dedication to developing all aspects of the use of synchrotron radiation for crystallography)

In 1976 I proposed synchrotron radiation protein crystallography experiments at the UK's Synchrotron Radiation Facility (SRF). I have been told that these were the first in the UK. The research is described in an Appendix to my Oxford University DPhil thesis which I reproduce below as an Appendix to this narrative. The full text of my thesis can be consulted at the STFC Daresbury Laboratory Library which holds a copy as I personally lodged it there.

My thinking was that, as a young experimental physicist, the state of the art of experiments and of apparatus in this one of the leading Laboratories in the World was rather primitive. I did not directly see how matters might be improved until I was presented by my DPhil supervisor Dr Margaret Adams to Prof Dorothy Hodgkin OM FRS Nobel Laureate; Dorothy Hodgkin occupied an office next to mine and which I shared with Ms Joyce Dargay, Dorothy Hodgkin's last DPhil student. Dorothy Hodgkin said that the thing about protein structure is that there are three probes of the structure of matter: X-rays, electrons and neutrons. This is very true. Indeed my York University final year undergraduate physics project was on *The use of the electron microscope to determine the Burgers vectors of dislocations in thin metal films* . More importantly she mentioned the research going on at the Laboratory of Molecular Biology in Cambridge on low dose electron microscopy of bacteriorhodopsin. She then went on to say that she had received a letter from Sir Ron Mason describing his research visit to the Stanford Synchrotron Radiation Laboratory (SSRL), where he had sight of the preliminary experiments on protein crystallography, and included in his communication to her a preprint of Phillips et al 1976 (see below in the references list). The first sentence of this paper refers to this topic being controversial. Ron Mason criticised other UK senior protein crystallographers' negative view of synchrotron radiation, including the Head of the Laboratory of Molecular Biophysics, Prof David Phillips (later Sir David Phillips and then Lord Phillips) himself. Dorothy Hodgkin asked my opinion. I went away and studied the preprint. The first reference was to a paper by Rosenbaum, Holmes and Witz (1971) in Nature; Synchrotron radiation as a source for diffraction, focussing on muscle fibre diffraction. Importantly it also mentioned a protein crystal as a possible sample. These efforts to me looked like the obvious answer to how to better

address the phase problem in protein crystallography and to better utilise our small crystals (since our X-ray exposure times to record a full diffraction data set were long and my samples prone to radiation damage effects).

I reported back to Margaret and Dorothy that I would like to go to Stanford to learn more. I was ushered in to see David Phillips. He listened intently; he had a rather stern demeanour - see the caricature in the New Scientist interview of him here - but I held to the core facts of my thinking. He said "you don't need to go to Stanford, there is a Synchrotron Radiation Facility (SRF) near Warrington, which runs off the high energy physics synchrotron NINA. But it is just 'toys for the boys'which I took to mean a derogatory reference to high energy physics. I replied that "Warrington would be fine, and they also have a good rugby league team." He laughed. In spite of my innate criticisms of his Lab the meeting ended amicably and he was very helpful, as was Dr Guy Dodson, Dorothy's right hand man, and Margaret. I got the Daresbury SRF beam time application form and filled it out. My proposal was accepted and scheduled. With another student of Margaret's, Ian Archibald, I co-owned an 'old banger' car, a dark blue Morris Oxford. We kept about a gallon of petrol in it at any one time. For this trip I filled it with a full tank. I got permission from David Phillips to take a precession camera, photographic film and developing/fixing chemicals in the boot of the car to Daresbury. I took my thesis project samples (the enzyme 6 phosphogluconate dehydrogenase (6PGDH) crystals) as well as despentapeptide insulin crystals (a gift from Guy Dodson), too small for X-ray crystal structure analysis in the home Lab.

At Daresbury in the SRF all the instruments were in one large experimental area. In my 24 hour NINA beamtime period I made myself an absolute pain to all the other experimenters, as alignment of my camera was not via a motorised stage and we had to keep going in and out, which meant turning off the beam to all the instruments to gain access. Dr Joan Bordas and Dr Ken Lea who assisted me were very patient and explained a great number of new things to me about the NINA machine as an X-ray source and about beam line X-ray optics. NINA of course was devoted primarily to high energy physics. Dr Ian Munro was the SRF Director. I found this all very forward looking in its vision for SR as a source for spectroscopy, photophysics and diffraction (topography and energy dispersive but also powder diffraction). There was a Cambridge Medical Research Council Laboratory of Molecular Biology (MRC LMB) muscle diffraction camera, but 'was not used much' I was told.

I explained to the SRF scientists my ideas about SR in protein crystallography, which I believed were exciting and not to be regarded at all as controversial. Subsequently I listened to talks by Dr Keith Hodgson in Amsterdam in 1975 at the International Union of Crystallography (IUCr) World Congress of Crystallography and Prof Ken Holmes at the 4th European Crystallography Meeting (ECM4) held in 1978 in Oxford. After these two lectures I heard at first hand, from other people leaving the two lectures, that actually no one believed that SR could ever become

relevant to protein crystallography. I had the opposite view; it was extremely exciting.

Fortunately a post was advertised from Keele University Physics Department jointly with Daresbury Laboratory for a person with expertise in Biophysics and who would take a role at the new SRS, the first dedicated SR source for X-rays in the World. I applied and was offered the job. So, I left my Oxford University Post Doc job with Margaret Adams as well as my Linacre College Junior Research Fellowship and started my new job in February 1979. I laid out my plans for SRS Protein Crystallography (PX) in the Daresbury Laboratory Study Weekend that January organised by Ian Munro and Bob Cundall (Helliwell 1979; see weblink).

In my first weeks at Daresbury, and I was there 50% of the time, I made it known that I would build a protein crystallography beamline on the first X-ray bending magnet beamline of the SRS, beamline 7. Dr David Norman, in a meeting, stated that I could not do that because I had no community support from the UK's protein crystallographers. So, I called a meeting of the UK's protein crystallography Laboratory Heads, which was during a Biochemical Society conference in Oxford. I had a good attendance, maybe 15 or so people, and obtained their support. I still heard regular mutterings eg from students and staff that SR would not be relevant to them. When I showed David Phillips SRS PX 7.2 he was clearly thrilled; it was a very proud moment for me. What was it that convinced the UK's PX Lab Heads to support me? The answer is maybe as trite as " my determination to do it impressed them". A key step obviously was 'passing' my interview with David Phillips that I described in detail above.

For SRS PX 7.2 and SRS PX 9.6 I led the design, the build, the commissioning and various categories of pioneering demonstration experiments as well as the user support. I obtained the funding for SRS PX 9.5 (from the Swedish Research Council), led the design and then assisted in detail with its build and development and use; the instrument scientist in charge was Andrew Thompson.

Throughout this early period it was clearly essential to move forward from photographic X-ray film as our detector. We took part in pioneering efforts with various technologies namely TV, MWPC, image plate and CCD detectors. There were many incremental, hard won, steps in a process that has finally culminated in revolutionary capabilities at the current SR facility MX beamlines.

The early days of CCP4 (Collaborative Computational Project for Protein Crystallography) at Daresbury are described in two abstracts - *Acta Cryst* **A37** C8 (1981) and C311-C312

(1981) , presented at the IUCr World Congress in Ottawa in 1981. I led the first of these, showing explicitly the importance of the link in protein crystallography between state of the art beamline development of the time and software. Further details can be found in an informal blog by T N Bhat.

By then I had become increasingly preoccupied with leading the European Synchrotron Radiation Facility Macromolecular Crystallography (MX) instruments suite Working Group; see :-

J.R. Helliwell and R. Fourme 'The ESRF as a facility for protein crystallography: A report and design study'. ESRP Report IRI-4/83(1983), pp. 1-36.

My formal links with Daresbury SRS were stopped in 1993, stated to be because of my preoccupation with the ESRF as well as my increasing academic projects at Manchester University, where I took up the Chair of Structural Chemistry in January 1989. Gladly I was able to rejoin the Laboratory in 2000. I finally became Director of SR Science for the Central Council for the Laboratory of the Research Councils (CCLRC) and Director of the SRS in 2002. This brought various responsibilities assisting with the development of the Diamond Light Source, a marvellous initiative for the UK.

Detailed scientific and instrument development descriptions of the above and their wider impacts, which have been considerable, including re-energising neutron macromolecular crystallography, are in the references below.

Various of the details above I have not described before, which I offer here as my contribution to the SRS History website. This project, instigated by Dr Ian Munro as an important addition to the History of British Science, is a tribute to the innovative nature of the SRS.

Appendix 1

Extract from John R Helliwell DPhil Thesis University of Oxford 1978

“X-RAY STUDIES CONCERNING THE STRUCTURE OF 6-PHOSPHOGLUCONATE DEHYDROGENASE”

JRH Supervisor Dr Margaret J Adams, Laboratory of Molecular Biophysics and Somerville College, Oxford University.

JRH Local Contact at the Daresbury Laboratory SRF was Dr Joan Bordas.

APPLICATION OF SYNCHROTRON RADIATION TO PROTEIN CRYSTALLOGRAPHY: PRELIMINARY EXPERIMENTS ON 6PGDH CRYSTALS USING THE NINA SYNCHROTRON, DARESBURY, U.K.

Earlier in my thesis the important application of synchrotron radiation to protein crystallography in optimising the anomalous scattering of heavy atoms was discussed. The work of Phillips et al. (1976) involved crystals, of various sizes, of rubredoxin, azurin, nerve growth factor and L-glutaminase asparaginase to test the beam from the storage ring SPEAR (Stanford, U.S.A.) as a possible X-ray source in crystal structure analysis. The data obtained at several different wavelengths above and below the Fe K edge (1.74 Å) from the iron containing protein, rubredoxin (M.W. = 6000) were analysed in detail (Phillips et al. (1977)).

The work described here involved similar experiments directed at optimising the anomalous scattering of the heavy atoms in the $KAu(CN)_2$ and $K_2Pt(CN)_4$ derivatives of 6 phosphogluconate dehydrogenase (6PGDH), respectively. The values of f ' and f " at the wavelengths of the Ag, Mo, Cu, Fe and Cr Kα lines are shown in Table AI.1. In Table AI.2, the values of the wavelengths for the L and K absorption edges for Au and Pt are given. The aim of this work was to test the usefulness of the synchrotron as an X-ray source in the structural analysis of a large protein molecule (6PGDH has a molecular weight of 100,000 Daltons).

One 24 hour shift was available (December 1976) in one of the NINA machine cycles; the closure of the source in March 1977 prevented continuation of the experiments. The experiments proposed were the recording of precession photographs on a Stoe precession camera of:-

(i) the h 0 1 centric zone of the Au and Pt derivatives of 6PGDH, respectively on the long wavelength side of the appropriate absorption edge;

(ii) the h h 1 acentric zone of both derivatives above and below the edge. Photographs of type (i) were aimed at observing the variation of f ' with λ and of type (ii) maximizing f ".

Table AI.1 Variation of f' and f" of Au and Pt at 5 different wavelengths. (From International Tables for X-ray Crystallography.)

	CrKα		FeKα		CuKα		MoKα		AgKα	
Element	f'	f"	f'	f"	f'	f"	f'	f"	f'	f"
Pt	-4.6	12.8	-4.5	9.9	-5.2	6.9	-2.4	8.4	-1.3	5.7
Au	-4.7	13.5	-4.5	10.4	-5.1	7.3	-2.7	8.8	-1.4	6.0

The wavelengths of the $K\alpha_1$ emission lines for Cr, Fe, Cu, Mo, Ag, are respectively: 2.29, 1.94, 1.54, 0.71, 0.56 Å.

Table AI.2 Wavelengths of the K and L absorption edges of Au and Pt in Å. (From International Tables for X-ray Crystallography.)

Element	K	L
Pt	0.15816	1.07259
Au	0.15344	1.03994

The apparatus was located 47 m from the electron orbit and the machine parameters at the time of the experiment were 4 GeV, 18 mA (average), 25 mA (peak). The beam was monochromated

using a Si [1 1 1] channel cut computer controlled monochromator with a band pass delta $\lambda/\lambda = 10^{-4}$ and which then entered a pin hole collimator on the Stoe camera. The camera had been previously roughly aligned with a laser beam reflected onto beam axis by a plane mirror. Final adjustment was achieved by observing the spot shape of the main beam on Polaroid film. The main advantage of the Stoe camera was the optical system for centering the crystal specimen involving a telescope, whose axis was perpendicular to the collimator axis.

All the crystal specimens were mounted in glass capillaries in Oxford and the diffraction tested on a GX 6 rotating anode run at 40 kV, 40 mA. The specimens were then transported by car to Daresbury. No facilities existed at NINA for mounting crystal specimens.

The positions of the L absorption edges of the Pt and Au atoms were located in the azimuthal coordinate space of the monochromator stepping motor by monitoring the transmitted intensity of the beam through the appropriate foil with an Argon ionisation chamber.

No useable precession photographs of the crystals were obtained on this run. In the absence of focussing of the beam in the horizontal and vertical planes the crystal intercepts only a small solid angle of the available beam intensity. Since the divergence of the beam in the vertical plane is 0.1 mrad the vertical dimension of the beam 47 m from the source is 4.7mm . A crystal that presents a face of size 0.2 x 0.2 mm to the beam intercepts only a small fraction of the available intensity. A mirror/ monochromator system in a working protein crystal diffraction experiment has been described subsequently by Webb
et
al (1977).

The X-ray diffraction of the crystals was re-tested on return to Oxford and found to be weak, though present. Transport of the samples in this manner was not ideal.

Appendix 1 references-

Phillips J.C., Wlodawer A., Yevitz, M, Hodgson K.O. Applications of Synchrotron

Radiation to Protein Crystallography: Preliminary Results. (1976) PNAS USA 73, 128-132.

Rosenbaum, G.; Holmes, K.C.; Witz, J. Synchrotron radiation as a source for X-ray diffraction Nature (London), 1971, 230, 434, (

Webb N.G, Samson S., Stroud R.M., Gamble R.C. and Baldeschwieler J.D. **A focusing monochromator for small-angle diffraction studies with synchrotron radiation** (1977) J.Appl.Cryst. 10, 104-110.

Appendix 2 The Plan for PX development at the UK's SRS

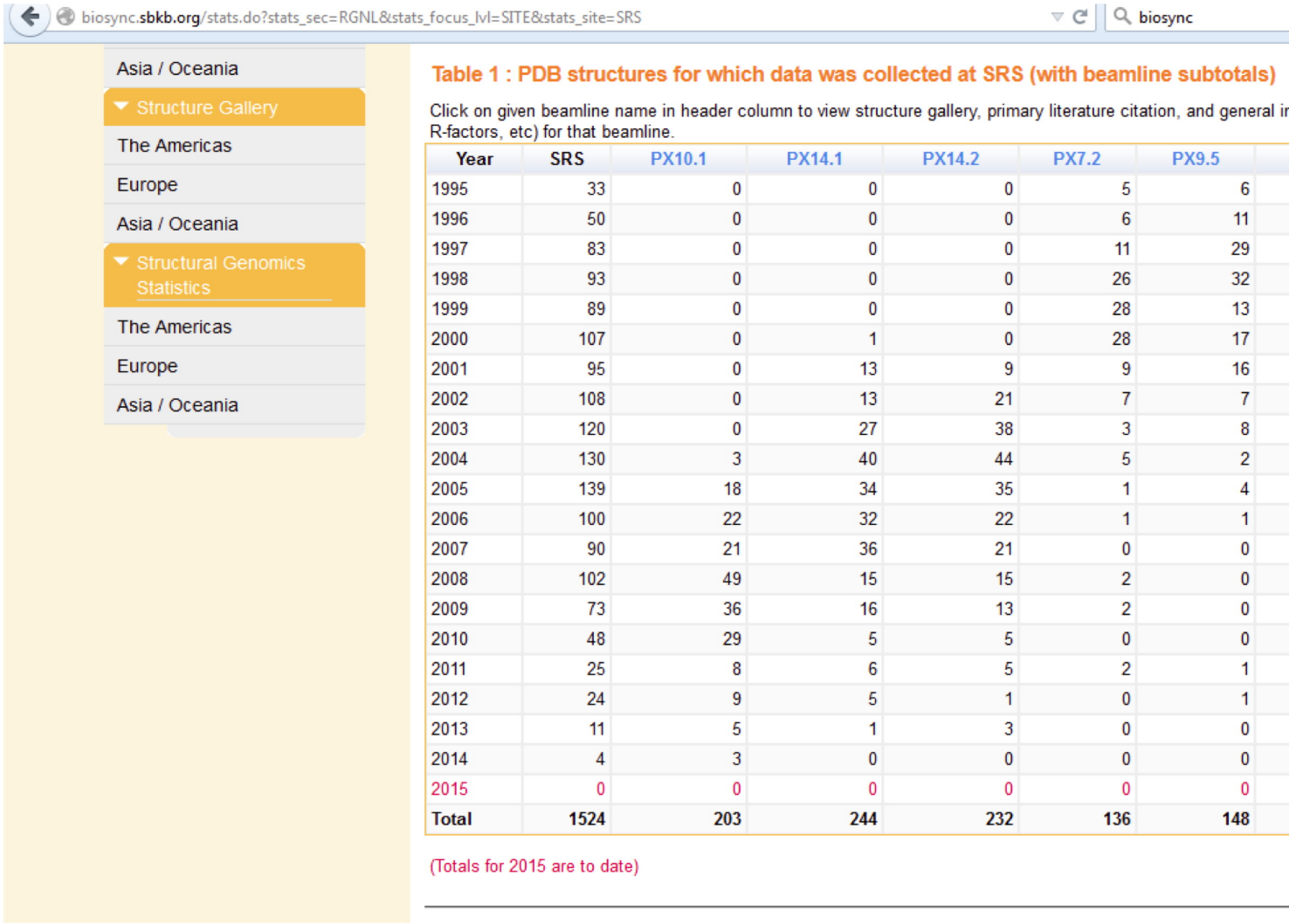
J.R. Helliwell 'Optimisation of anomalous scattering and structural studies of proteins using synchrotron radiation', Proc. of Daresbury Study Weekend, 26-28 January 1979 DL/SCI/R13. (1979) pages 1–6.

A weblink to this article is provided but I quote from my conclusion which to my mind readily sets the tone:-

"Synchrotron radiation can be of considerable use to protein crystallography and the advantages to the user of a dedicated source like the SRS cannot be over emphasised"

Clearly this was a bold assertion on my part ie given the context of the controversy issues that I have described above. Early feedback that I was correct came from the strength of international interest. USA scientists arrived very promptly (Michael Rossmann himself from Purdue University; Steve Ealick, Howard Einspahr and Bud Suddath from Alabama), we were cited in Scientific American. The Swedish protein crystallographers arrived very promptly including with funds from their Research Council to support our work and allow them formal access. They also paid 50% of the construction of SRS PX 9.5 and provided a staff member (Dr Ron Brammer) to work on the design. Also I was engaged to lead the discussions on protein crystallography uses of the ESRF. Other objective measures were less clear eg my abstract on SRS 7.2 in Ottawa in 1981 at the IUCr Congress was allowed a poster but not a talk whereas at the British Crystallographic Association (founded in 1982) I vividly recall presenting the design of and first, exciting, results from SRS PX 9.6 in about 1984 or so..

Has this all stood the test of time? The BioSync website keeps a record of all the World's beamlines Protein Data Bank (PDB) Depositions and the SRS fares very well. See Table below (March 24th 2015):-



biosync.sbkb.org/stats.do?stats_sec=RGNL&stats_focus_lvl=SITE&stats_site=SRS

biosync

Asia / Oceania

Structure Gallery

The Americas

Europe

Asia / Oceania

Structural Genomics Statistics

The Americas

Europe

Asia / Oceania

Table 1 : PDB structures for which data was collected at SRS (with beamline subtotals)

Click on given beamline name in header column to view structure gallery, primary literature citation, and general ir
R-factors, etc) for that beamline.

Year	SRS	PX10.1	PX14.1	PX14.2	PX7.2	PX9.5
1995	33	0	0	0	5	6
1996	50	0	0	0	6	11
1997	83	0	0	0	11	29
1998	93	0	0	0	26	32
1999	89	0	0	0	28	13
2000	107	0	1	0	28	17
2001	95	0	13	9	9	16
2002	108	0	13	21	7	7
2003	120	0	27	38	3	8
2004	130	3	40	44	5	2
2005	139	18	34	35	1	4
2006	100	22	32	22	1	1
2007	90	21	36	21	0	0
2008	102	49	15	15	2	0
2009	73	36	16	13	2	0
2010	48	29	5	5	0	0
2011	25	8	6	5	2	1
2012	24	9	5	1	0	1
2013	11	5	1	3	0	0
2014	4	3	0	0	0	0
2015	0	0	0	0	0	0
Total	1524	203	244	232	136	148

(Totals for 2015 are to date)

First presentation of SRS PX 7.2 at the IUCr World Congress Ottawa, Canada:-

J. R. Helliwell , T. J. Greenhough , P. Carr , P. R. Moore , A. J. Thompson , G. Hughes , M. M. Przybylski , P. A. Ridley , J. E. Bateman , J. F. Connolly and R. Stephenson

Central data collection facility for protein crystallography, small-angle

diffraction and scattering at the Daresbury Laboratory Synchrotron Radiation Source (SRS)
Acta Cryst.
(1981). A37, C316

J.R. Helliwell, T.J. Greenhough, P. Carr, S.A. Rule, P.R. Moore, A.W. Thompson and J.S. Worgan 'Central data collection facility for protein crystallography, small angle diffraction and scattering at the Daresbury SRS' (1982) J. Phys.E. 15, 1363-1372.

T.J. Greenhough and J.R. Helliwell 'Oscillation camera data processing: reflecting range and prediction of partiality. II Synchrotron sources' (1982) J. Appl. Cryst. 15, 493-508.

U.W. Arndt, T.J. Greenhough, J.R. Helliwell, J.A.K. Howard, S.A. Rule and A.W. Thompson 'Optimised anomalous dispersion crystallography: a synchrotron X-ray polychromatic simultaneous profile method'. Nature (1982) 298 835-838.

Rossmann, M.G.; Erickson, J.W. Oscillation Photography of Radiation-sensitive Crystals using a Synchrotron Source. J. Appl. Cryst. 1983, 16, 629–636.

H. Einspahr, K. Suguna, F.L. Suddath, G.Ellis, J.R. Helliwell and M.Z. Papiz 'The location of the Mn:Ca ion cofactors in pea lectin crystals by use of anomalous dispersion and tunable synchrotron X-radiation'. Acta. Cryst. (1985) B41, pp. 336-341.

Ealick, S.E.; Rule, S.A.; Carter, D.C.; Greenhough, T.J.; Babu, Y.S.; Cook, W.J.; Habash, J.;

Helliwell, J.R.; Stoeckler, J.D.; Parks, R.E. Jr; Chen, S.; Bugg, C.E. Three-dimensional

Structure of Human Erythrocytic Purine Nucleoside Phosphorylase at 3.2A˚ Resolution.

J. Biol. Chem. 1990, 265, 1812–1820.

Bugg, Charles E.; Carson, William M.; John, A. Montgomery Drugs by Design: Structurebased Design, An Innovative Approach to Developing Drugs has Recently Spawned Many Promising Therapeutic Agents, Including Several now in Human Trials for Treating AIDS, Cancer and other Diseases. Sci. Am. 1993, December, 92–98.

M. Cianci, P.J. Rizkallah, A. Olczak, J. Raftery, N.E. Chayen, P.F. Zagalsky and J.R. Helliwell "Structure of apocrustacyanin A1 using softer X-rays" (2001) Acta Crystallographica Section D-Biological Crystallography D57, 1219-1229.

SRS initiatives with electronic area detectors

J.R. Helliwell 'The use of electronic area detectors for synchrotron X-radiation protein crystallography with particular reference to the Daresbury SRS' (1982) Nuclear Instruments and Methods, 201, 153-174.

J.R. Helliwell, G. Hughes, M.M. Przybylski, P.A. Ridley, I. Sumner, J.E. Bateman, J.R. Connolly and R. Stephenson 'A 2-D MWPC area detector for use with synchrotron X-radiation at the Daresbury Laboratory for small angle diffraction and scattering' (1982) Nuclear Instruments and Methods, 201, 175-180.

RAXIS IIc Rigaku Corporation; dual image plate automatic reader. (1985 to 1989)

M. Pokric, N.M. Allinson, A.R. Jorden, M.P. Cox, A. Marshall, P.G. Long, K. Moon, P. Jerram, P. Pool, C. Nave, G.E. Derbyshire and J.R. Helliwell (2002) “Large area high-resolution CCD-based X-ray detector for macromolecular crystallography” Nucl. Instrum. Methods Phys. Res. Sect. A-Accel. Spectrom. Dect. Assoc. Equip. A477, 166-171.

SRS 9.6

First presentation of SRS PX 9.6 at the IUCr World Congress Hamburg, Germany:-□□□□□□□□□□ □ J. R. Helliwell , M. Papiz , P. R. Moore and A. W. Thompson

A new instrument for protein crystallography on the wiggler beam line at the SRS providing a focussed, tunable beam at short X-ray wavelengths
Acta Cryst.
(1984). A40, C394.

J.R. Helliwell, M.Z. Papiz, I.D. Glover, J. Habash, A.W. Thompson, P.R. Moore, N. Harris, D. Croft and E. Pantos 'The Wiggler Protein Crystallography Work-station at the Daresbury SRS; Progress and Results'. Nuclear Instrum. and Methods. (1986) A246, 617-623.

B. Hedman, K.O. Hodgson, J.R. Helliwell, R. Liddington and M.Z. Papiz 'Protein micro-crystal diffraction and the effects of radiation damage with ultra high flux synchrotron radiation'. PNAS.USA (1985) 82, 7604-7607.

S.J. Andrews, M.Z. Papiz, R. McMeeking, A.J. Blake, B.M. Lowe, K.R. Franklin, J.R. Helliwell and M.M. Harding 'Piperazine Silicate (EU-19) - The structure of a very small crystal determined with synchrotron radiation'. Acta. Cryst. B44, 73-77 (1988).

P.J. Baker, G.W. Farrants, T.J. Stillman, K.L. Britton, J.R. Helliwell and D.W. Rice 'Isomorphous replacement with optimised anomalous scattering applied to protein crystallography'. (1990) Acta Cryst. A46, 721-725.

SRS 9.5

R.C. Brammer, J.R. Helliwell, W. Lamb, A. Liljas, P.R. Moore, A.W. Thompson and K. Rathbone 'A new protein crystallography station on the SRS Wiggler beamline for very rapid Laue and rapidly tunable monochromatic experiments: I. Design Principles, Ray Tracing and Heat calculations'. Nucl. Instrum. and Methods, (1988) A271, 678-687.

M.R. Peterson, S.J. Harrop, S.M. McSweeney, G.A. Leonard, A.W. Thompson, W.N. Hunter and J.R. Helliwell "MAD phasing strategies explored with a brominated oligonucleotide crystal at 1.65Å resolution" (1996) J. Synchrotron Rad. 3, 24–34.

SRS PX goes international:-

J.R. Helliwell and R. Fourme 'The ESRF as a facility for protein crystallography: A report and design study'. ESRP Report IRI-4/83(1983), pp. 1-36.

A. Cassetta, A.M. Deacon, S.E. Ealick, J.R. Helliwell and A.W. Thompson "Development of instrumentation and methods for MAD and structural genomics at the SRS, ESRF, CHESS and Elettra facilities" J. Synchrotron Rad. (1999), 6, 822–833.

Whilst the above references are explicitly linked to the SRS I led a project to try and make our **P X diffraction data processing software**
as good as possible, ie akin to the efforts I was making with the instrumentation and experimental methods. Ie:-

J. R. Helliwell , A. Achari , A. C. Bloomer , P. E. Bourne , P. Carr , G. A. Clegg , R. Cooper , M. Elder
,

T. J. Greenhough
,
B. Shaanan
,
J. M. A. Smith
,
D. I. Stuart
,
E. A. Stura
,
R. Todd
,
K. S. Wilson
,
A. J. Wonacott
and
P. A. Machin
Protein crystal oscillation film data processing: a comparative study
Acta Cryst.
(1981). A37, C311-C312.

A major new application was **synchrotron Laue crystallography** for time-resolved protein sturtcural studies and applications to microcrystals as well as spin off into neutron Laue crystallography with what became known as the ‘Daresbury Laue software’:-

J.R. Helliwell, J. Habash, D.W.J. Cruickshank, M.M. Harding, T.J. Greenhough, J.W. Campbell, I.J. Clifton, M. Elder, P.A. Machin, M.Z. Papiz, and S. Zurek 'The recording and analysis of Laue diffraction photographs' (1989) J. Appl. Cryst. 22, 483-497.

Y.P. Nieh, J. Raftery, S. Weisgerber, J. Habash, F. Schotte, T. Ursby, M. Wulff, A. Haedener, J.W. Campbell, Q. Hao and J.R. Helliwell "Accurate and highly complete synchrotron protein crystal Laue diffraction data using the ESRF CCD and the Daresbury Laue software" (1999) J. Synchrotron Rad. 6, 995–1006.

This software was adopted by the neutron facilities in the 1990s for neutron macromolecular and neutron chemical crystallography firstly at the Institut Laue Langevin Grenoble (LADI and VIVALDI), then the Los Alamos LANSCE Protein Crystallography Station and then Oak Ridge USA. It has also assisted in the technical simulations at the European Spallation Source in the 'nMX' instrument project (see http://europeanspallationsource.se/sites/default/files/macromolecular_stap_review.pdf).

Overall SR and macromolecular crystallography overviews:-T.J. Greenhough and J.R. Helliwell 'Uses of synchrotron X-radiation in the crystallography of molecular biology'. Invited review for Progress in Biophysics and Molecular Biology (1983)
41
, 67-123.

J.R. Helliwell 'Synchrotron X-radiation protein crystallography: instrumentation, methods and applications'. Invited review for Reports on Progress in Physics. (1984) 47, 1403-1497.

J.R. Helliwell "Macromolecular Crystallography with Synchrotron Radiation" Cambridge University Press (1992). Published in paperback 2005.

J.R. Helliwell "Synchrotron Radiation and Crystallography: The First Fifty Years" (1998) Invited Article for the Acta Crystallographica 50th Anniversary Special Issue, Acta Cryst. A A54, 738–749.

M.P. Blakeley, M. Cianci, J.R. Helliwell and P.J. Rizkallah "Synchrotron and neutron techniques in biological crystallography" Chem Soc Reviews (2004) 548-557.

J R Helliwell (2012) "The evolution of synchrotron radiation and the growth of its importance in crystallography" Crystallography Reviews 18, 2012, 33-93. This article reproduces the letter from Sir Ron Mason to Sir Sam Edwards (then Head of the UK's Science Research Council) that I mentioned above in my narrative. I contacted Sir Ron Mason during the preparation of this

article via Linked In and obtained his permission to do so.

SR PX Science and Spin offs into industry

J.R. Helliwell 'Protein crystallographic drug design using synchrotron X-radiation' Acta Radiologica (1983) Suppl. 365, 35-37.

E.J. Maclean, P.J. Rizkallah and J.R. Helliwell (2006). “Protein Crystallography and Synchrotron radiation; current status and future landscape” European Pharmaceutical Review Issue 2, p71-76.

John R. Helliwell and Edward P. Mitchell Synchrotron radiation macromolecular crystallography: science and spin-offs IUCrJ (2015). 2, 283–291.

Acknowledgements

I am extremely grateful to everyone for their help and / or opposition to these ideas and both of which produced a clarity in my mind as to the way forward. Secondly I was joined by people with diverse skills; together we achieved a ‘can do’ approach. I thank them all. They are coauthors in the references below or acknowledged for their contributions in the publications’ acknowledgements.

The Rutherford Appleton Laboratory is heartily thanked for the SRS wiggler beamline 9 superconducting 5T wiggler with which major new initiatives became possible for us.

The Rutherford Appleton Laboratory is thanked for their development of the Multi Wire Proportional Chamber electronic area detector development; a truly pioneering device.

The Enraf Nonius TV electronic area detector was another truly pioneering device which in turn built upon the initiatives and achievements of Dr Uli Arndt at the MRC LMB Cambridge. I had the pleasure and enjoyed the challenge to work with this and help shape a new future in protein and chemical crystallography. This work was led by my Daresbury colleague Dr Miroslav Papiz.

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On SRS PX 7.2 the establishment of small angle scattering and high angle fibre diffraction was also made. This was in close collaboration with Dr Colin Nave, and who had the necessary specialist expertise in these areas that I did not have, and with whom it became a pleasure to work with Colin for many years. This included the following publication relevant to these Early

Years descriptions:-

C. Nave, J.R. Helliwell, P.R. Moore, A.W. Thompson, J.S. Worgan, R.J. Greenall, A. Miller, S.K. Burley, J. Bradshaw, W.J. Pigram, W. Fuller, D.P. Siddons, M. Deutsch and R.T. Tregear 'Facilities for solution scattering and fibre diffraction at the Daresbury SRS'. DL/SCI/P457E. March 1985. J. Appl. Cryst. (1985) 18, 396-403.