by Colin Nave

By 1987, the protein crystallography facilities on stations 9.6 and 7.2 were well established with a high scientific output and station 9.5 was being developed, initially for Laue diffraction, under a collaboration with the Swedish Research Council. With a horizontally and vertically focusing mirror, station 9.5 gave a higher intensity than stations 9.6 and 9.7 which were also used for this technique. The early Laue experiments (by John Helliwell and his collaborators) clarified the capabilities of the technique and acted as a test bed for Laue software developments. The resultant software is still being used for both x-ray and neutron Laue crystallography. After these developments the emphasis for x-ray Laue diffraction moved to the higher intensity facilities on ID9 at the ESRF where time resolved capabilities were developed. For monochromatic data collection, the SRS was an early adopter of data collection at cryogenic temperatures, a technique which, allowed the study of weakly diffracting crystals before radiation damage occurred.

Initial Multi-wavelength Anomalous Dispersion (MAD) experiments had already been carried out (again by John Helliwell and his collaborators) on station 9.6 which allowed wavelength changes, albeit with some difficulty. After this, station 9.5 was equipped with a fast scanning monochromator and this facility contributed to the development of the technique and also produced useful structural results. However station 9.6 had more intensity than the other protein crystallography facilities on the SRS and was used for some very high profile scientific results such as the structures from Oxford of Foot and Mouth Disease Virus, and time resolved studies on Glycogen Phosphorylase. Another highlight is the structure determination of Light Harvesting Protein in which the long standing 9.6 station scientist Miroslav Papiz was closely involved with collaborators from Glasgow. In 1994 the structure of F1-ATPase was published by a team from the MRC at Cambridge with station 9.6 providing again the crucial data. This work resulted in a Nobel Prize for Chemistry, awarded to John Walker in 1997. There was also increasing interest in the use of the SRS by the pharmaceutical industry and agreements were set up with a variety of companies to provide both beamtime and data collection services with Pierre Rizkallah appointed to assist with this work.

The research councils (and later the Welcome Trust), involved in biological and medical sciences were very keen to see that the biology stations on the SRS were maintained at a high level and invested additional funds, coordinated by a Biology Program Joint Steering Committee. This resulted in the stations being equipped with the most up to date detectors and computing equipment, together with upgrades of the optics when necessary. The BPJSC asked for the laboratory to consider an additional facility with similar capabilities to the high intensity station 9.6. Peter Lindley, then Director for Life Sciences at the SRS agreed to look into this and the laboratory responded by proposing the first multipole wiggler facility on the SRS, used to equip two stations, 14.1 and 14.2. These came into operation in early 2000 and late 1999 respectively. Station 14.2 incorporated MAD capability (wavelength change around 1 min) and (according to BioSync) has produced considerably more MAD structures (16) than any other facility on the SRS. Station 14.2 also acted as a focus for automation and incorporated a robotic sample changer which was made available for users in 2003. Further investment from the BBSRC resulted in continued support for the first PX station 7.2, during a period when overall funding for the SRS decreased as a result of the introduction of the “ticket” system by the EPSRC. The grant for this work was awarded to Trevor Greenhough who was involved in the SRS from an early stage via his positions at Keele University.

By this time, the protein crystallography facilities at the ESRF were increasingly being used for the most demanding projects. However, even for these, the SRS was being used for initial investigations including screening crystals to identify the best crystallisation conditions. One notable example of this is the work on 30S ribosome which led to the Nobel prize for Chemistry (Venki Ramakrishnan 2009). The crystals for much of this work were screened on station 14.1.

After the announcement that the new synchrotron was to be built on the RAL site, investment in the SRS nevertheless continued, in order to sustain a key driver for the new facility. A good example was the successful proposal for another protein crystallography facility at the SRS, led by Samar Hasnain, The new facility was again based on a multipole wiggler and had MAD

capability together with a facility for on line spectroscopy. Associated with this new beamline was a structural genomics component where good links were forged with the RIKEN activities in Japan. This resulted in several publications involving RIKEN and Daresbury staff.

The Collaborative Computational Project for Protein Crystallography (CCP4) was based at Daresbury during the lifetime of the SRS and good links were developed between these two activities. An informal collaboration (known for reasons lost in the mists of time as the DNA project) was set up with other European synchrotrons and the MRC Laboratory of Molecular Biology with the aim of automating data collection for protein crystallography. Several successful joint grant applications extended this further including e-HTPX (funded by the BBSRCs e-science initiative) and the BioXHIT contract (co-ordinated from EMBL Hamburg and funded by the EC). See an informal blog by T N Bhat for a detailed account of the early development of CCP4.

Daresbury staff (Colin Nave and collaborators) had investigated radiation damage in protein crystals at cryogenic temperatures in the early 1990s using stations 9.7 and 9.5 in Laue mode. Other investigations included studies of imperfections in protein crystals at cryogenic temperature and the effects of data collection at different x-ray wavelengths on the spot to background ratio in diffraction patterns from protein crystals. The radiation damage studies in particular were extended via the European collaborations. The subject of radiation damage in protein crystallography resulted in a regular series of international workshops which are still ongoing.

The protein crystallography facilities were in regular use by visitors from abroad. As high quality facilities became available in the USA, the visitors from this country decreased. However, regular visits took place from elsewhere with a significant number of European visitors funded by various EC contracts.

The planned transfer of activities from the SRS to Diamond went well for protein crystallography. The developments in automation and data handling which took place on the SRS formed a good basis for further developments at Diamond. SRS staff were involved in the specification and design of the initial facilities at Diamond with some staff (Liz Duke, Katherine McAuley, Alun Ashton, Graeme Winter, Colin Nave) taking up positions at the new facility. The strength of the UK academic user program on the SRS, together with the industrial and European program meant that a high demand existed for the protein crystallography facilities on Diamond when the SRS closed.

Examples of both academic and industrial uses of the protein crystallography facilities on the SRS can be found in the document The Social and Economic Impact of the Daresbury Synchrotron Radiation Source (1981- 2008) , which can be downloaded.

The pace of developments in protein crystallography on synchrotrons shows no signs of abating. These include new and upgraded sources with higher brightness (multi-bend achromats and free electron lasers) together with beamline optics, detectors and data handling. All of this will result in more challenging structural biology projects becoming feasible. Things have come a long way since John Helliwell's proposal to use synchrotron radiation for protein crystallography at Daresbury, nearly 40 years ago. This contribution initiated a strong synchrotron radiation program for protein crystallography in the UK, based on the facilities at the SRS.

Personal note

I joined Daresbury Laboratory in 1982 and worked closely with John Helliwell in developing the initial facilties for small angle x-ray scattering on the SRS before becoming Facility Group Leader for Protein Crystallography in 1987. I continued in this position until 2003 after which I took up an Individual Merit position, concentrating on developments for protein crystallography on synchrotrons. In 2007 I retired from Daresbury Laboratory and took up a part time position at the Diamond Light Source. I am extremely grateful for the opportunity that the SRS has given me for pursuing an interesting career in an exciting area of science together with the productive and enjoyable interactions with the many colleagues at Daresbury and the users of the SRS.