Institution: Durham

Unit of Assessment: 8

Title of case study: Structural science – equipment and software for industry

1. Summary of the impact

Durham Chemistry has a long history of research in cutting edge crystallographic methods and innovative instrument design which has led to the commercialisation of scientific apparatus and software with significant sales value. Durham-developed apparatus and crystallographic software are used globally by both industry and academia. Autochem2, for example, is sold exclusively to Agilent via the spin-out company OlexSys, and hundreds of researchers rely on Durham's contributions to the Topas software pacakge. Crystallographic research for pharmaceutical and other companies, research-based consultancy, commercial analytical services and provision of international PhD+ level training schools have led to further significant impact.

2. Underpinning research

Research in the development of crystallographic methods at Durham has been carried out by the groups of Professor Judith A K Howard (JAKH, 1991–), Dr. Andres Goeta (AEG, 1998–2011dc), Professor John S.O. Evans (JSOE, 1998–) and Dr Ivana Evans (IRE, 1999–). Their work forms part of our Research Grouping in Materials Synthesis and Structure (MSS), and is supported and exploited by others working in structural science and, in particular, solid state NMR.

Durham Chemistry has a strong focus on the synthesis and understanding of functional materials. Examples include superconductors, molecular magnets, materials with electronic and magnetic phase transitions, gas storage materials, structural materials and molecular switches. In order to understand, develop and exploit structure-property relationships in these materials, high resolution X-ray-derived structural information is required across a wide temperature range. Low temperatures also provide higher quality structural information than ambient studies and allow study of otherwise unstable systems. JAKH therefore designed, constructed and developed the unique Fddd diffractometer [1] integrating closed cycle cryo-refrigeration and a high intensity X-ray beam to enable crystallographic studies of very small crystals down to 9 K. Single crystal X-ray diffraction studies in the UK had been restricted previously to temperatures above 100K using liquid nitrogen temperatures as coolant. The unique facilities developed in Durham enabled low temperature studies on a number of important systems with exploitable macroscopic properties, but, using a point detector, experiments were slow and only a limited number of temperatures could be studied.

The advent of CCD detectors for laboratory diffractometers provided a solution to the speed problem, but the data quality obtainable at sub 100 K temperatures was severely limited by the complex cryostat environment, with heat shields and windows severely attenuating the beam and giving rise to their own strong X-ray scatter. JAKH therefore initiated research into the development of an open-flow cooling device, similar to the now ubiquitous liquid nitrogen devices, but capable of reaching much lower temperatures [F1]. The cryostat developed, the HeliX, allowed the first rapid full structural investigations of novel systems maintained at sub 100 K temperatures in an open environment, allowing rapid data acquisition. The design also enabled laser excitation of samples allowing full structural investigations of thermally trapped, optically induced, excited spin state complexes [2,3].

Many of the new materials prepared and studied in Durham are in polycrystalline (powdered) form, but there is still a need to study their low temperature structural properties. Examples of materials include those showing negative thermal expansion behaviour [F2], electronic phase transitions or light-induced changes. The need to study these materials [3,4] led to [F3] research by JSOE/AEG to develop and exploit the pHeniX cryostat for powder diffraction. The design incorporated novel features to allow operation on a range of lab-based instruments with a variety of different sample types.

The experimental structural and materials science undertaken at Durham has required parallel development of computational methods and software tools. In the area of single crystal diffraction the JAKH group has an extensive research programme in the development of computational tools for data analysis. With EPSRC funding they designed and delivered an innovative, future-proof, toolbox based software suite (Olex2) based on Python-integration of a series of small modules [F4]

using fit-for-purpose programming codes, informed by X-ray crystallography expertise. This approach allows the efficient use of established routines and the parallel development of new algorithms [5]. In the area of powder diffraction, JSOE has been involved in the development of the Topas suite of software and its application for novel data analysis since the late 1990s. He has developed data analysis methods for parametric fitting of huge bodies of diffraction data, for analysing neutron and energy dispersive diffraction data, and distortion-mode modelling of functional materials; these are used by industry and academics [6,7].

3. References to the research

[1] R.C.B.Copley, A.E. Goeta, C.W. Lehmann, J.C. Cole, D.S. Yufit, J.A.K. Howard and J.M. Archer, "The Fddd four-circle diffractometer for single-crystal X-ray studies at temperatures down to 9K", *J. Appl. Cryst.*, 1997, **30**, 413–417. **DOI**: 10.1107/S0021889897002525. **[8 citations]**

[2] A.E. Goeta, L.K. Thompson, C.L. Sheppard, S.T. Tandon, C.W. Lehmann, J. Cosier, C. Webster and J.A.K. Howard, "[Cu_2{1,4-bis[(3-methyl-2-pyridyl)amino]-phthalazine-H}$(N_3)_3$] at 40K", *Acta Cryst.*, 1999, **C55**, 1243-1246. **DOI**: 10.1107/S0108270199005648. **[19]**

[3] V.A. Money, I.R. Evans, M.A. Halcrow, A.E. Goeta and J.A.K. Howard, "Light induced excited high spin-state trapping in [FeL_2]$(BF_4)_2$ (L = 2,6-di(pyrazol-1-yl)pyridine)", *Chem. Commun.*, 2003, 158–9. **DOI**: 10.1039/B210146G. **[53]**

[4] S. Allen and J.S.O. Evans, "The kinetics of oxygen migration in $ZrWMoO_8$", *J. Mater. Chem.*, 2004, **14**,151–156, RSC Hot Article. **DOI**: 10.1039/B310137A. **[18]**

[5] O.V. Dolomanov, L.J. Bourhis, R.J. Gildea, J.A.K. Howard, H. Puschmann, "OLEX2: A complete structure solution, refinement and analysis program", *J. App. Cryst.*, 2009, **42**, 339–341. **DOI**:10.1107/S0021889808042726. **[650]**

[6] A.A. Coelho, J.S.O. Evans, I.R. Evans, A. Kern, and S. Parsons, "The TOPAS symbolic computation system", *Powder Diffraction*, 2011, 26, S22–S25. **DOI**: 10.1154/1.3661087. **[8]**

[7] G.W. Stinton, J.S.O. Evans, "Parametric Rietveld refinement", *J. Appl. Cryst.*, 2007, **40**, 87–95. **DOI**:10.1107/S0021889806043275. **[40]**

Selected research funding:

[F1] EPSRC Grant GR/L16903/01 (1996-1999), £180K, JAKH. "Open Heart Crystallography at (virtually) Helium Temperatures".

[F2] EPSRC Grant GR/N00524 (2000-2003), £270K, JSOE. "Negative Thermal Expansion and Oxygen Mobility in Framework Materials".

[F3] EPSRC GR/M35222 (1999-2002), £121K. JSOE, JAKH, & AEG. Joint Research Equipment Initiative grant leading to development of the pHeniX cryostat.

[F4] EPSRC EP/C536274/1 (2005–2011), £1.2M (£943K Durham). "Age Concern; Crystallographic Software for the Future" led to Olex2, spin-out OlexSys and other outputs.

The quality of the research described in section 1 is evidenced in several ways. Much of it was enabled by peer-reviewed EPSRC grants (listed F1-F4) above. When required, final reviewed reports on these received outstanding/internationally-leading grades. Several of the papers cited above were returned in previous RAE exercises and, we infer, were graded > 2*. Several of the references listed have also been highly cited. Reference [5] has been cited over 850 times and reference [7] over 40 times and we have received numerous invitations to present research at international meetings. Our software user base (>5000 for single crystal, >650 for jEdit/Topas Academic) attests to the quality of these research-derived packages.

4. Details of the impact

Research at Durham aimed at developing an open-flow cryostat capable of cooling below liquid nitrogen temperatures [1] was performed as part of an EPSRC-funded project in collaboration with Oxford Cryosystems (OC). OC is an Oxfordshire based company which employs 20 staff and has an annual turnover of £3–£3.5M. The prototype was completed in 1998 and the commercial version was launched by OC as the HeliX at the IUCr Congress in Glasgow, 1999. IP for the Helix is owned by OC who have sold around 20 units in the 2008-2013 period to academic institutions and central facilities globally [Im1].

Figure: N-HeliX (far left) and pHeniX (middle) cryostats commercialised by Oxford Cryosystems [2,3]; Olex2 and Topas Academic crystallography software (right).

The successful development of the HeliX suggested similar technology could provide a 12–310 K cryostat for powder diffraction experiments, filling a market gap for apparatus that was (a) easy to use and low maintenance, (b) compatible with a range of diffractometer configurations and (c) usable by those without cryogen expertise and did not require expensive liquid He. A prototype pHeniX powder cryostat [4] was co-developed with OC, installed in Durham in 2002, and the commercial version launched later that year. pHeniX units have been sold to industry in South Korea, China, United States, mainland Europe and the UK as well as to national facilities and academic institutions directly by OC and through the X-ray manufacturers PANalytical and Bruker AXS. Approximately eight units are sold annually. The Director of Sales and Marketing at Oxford Cryosystems, said: “it is fair to say that without the research excellence of Durham University, we would not be manufacturing and selling these cooling devices as we are today. OC’s product range has expanded greatly over the past ten years and being able to offer these products is very important in allowing us to move into new applications.” [Im1]

EPSRC “Age Concern” funding to JAKH enabled development of Olex2 software [5, Im2], a modern, powerful and easy to use package for the solution, analysis and refinement of single crystal X-ray data. The open source version is available free of charge from the internet and has been downloaded extensively, providing an estimation that there are over 5000 users worldwide. The original paper has been cited > 650 times, demonstrating impact on the global academic community and in training students, future academics and industrial scientists. Future development of Olex2 has been secured through the Durham spinout company OlexSys [Im2]. OlexSys was established in December 2010 (Company No 07465154) with the legal assistance of Durham University Business and Innovation Services. It has been trading since June 2011 has a growing turnover, employs full and part time staff and is chaired by JAKH. OlexSys has two complementary and parallel work strands. To keep Olex2 at the scientific cutting-edge they maintain and develop the open source version for and on behalf of the global academic community. They also provide bespoke software solutions for industry and have commercial contracts with instrument manufacturers Agilent, Rigaku and the Cambridge Crystallographic Data Centre.

One commercial contract is with Agilent [Im3], who install Olex2 with all of their X-ray systems (each typically costing > ~£300K). Agilent commissioned OlexSys to create the exclusive bespoke commercial product AutoChem. Autochem provides automated, intelligent, real-time structure solution and refinement during data collection. Although Agilent company policy states that specific sales figures can’t be released, the University believes a significant number of licences have been sold to date. A major update, Autochem2.0 was commissioned in 2011. It is derived from Durham research and OlexSys developments, and described on the Agilent website as: “The ultimate productivity tool for chemical crystallography, AutoChem - now as AutoChem2.0 - provides fast, fully automated structure solution and refinement during data collection. Developed exclusively for Agilent by the authors of Olex2, AutoChem2.0 is a seamlessly integrated, optional plug-in for CrysAlisPro, offering an advanced approach for automatic structure determination, and now with an even higher rate of success.”

JSOE has been heavily involved in the development of Topas – the leading software for analysis of powder diffraction data and Rietveld refinement (e.g. [6]). He has worked closely with Alan Coelho

and Bruker in implementing new ideas and methodologies in this software [Im4,5]. In particular his methods for analysing variable temperature/time/chemical environment data are used worldwide and the time-of-flight neutron and distortion mode/magnetism methods he introduced underpin numerous experiments at UK central facilities (e.g. [7]). The jEdit interface he developed and distributes for "power-use" of the software is used by many academic and industrial groups, and Durham has trained in excess of 500 people in its use at predominantly industrial workshops worldwide (USA, Germany, Italy, UK, Australia). Many of these innovations are now incorporated in the commercial version of Topas [Im4], which has a list price around £10K. Sales figures for Topas are commercially sensitive information that Bruker cannot release. Many licenses have been sold and that their distribution would be approximately 50:50 between industry and academia. Many copies of the academic version have been sold to groups worldwide (80% in REF period) [Im5]. The Topas community wiki site and discussion forum is run through Durham (topas.dur.ac.uk/dokuwiki.php) and has a vibrant and expanding community with about 300 members. This includes industrial members from industries in the chemicals (e.g. Johson Mathey, BASF), cement, pharmaceutical and mining sectors.

Our structural expertise also has significant and direct impact on industry via the service/consultancy work we perform under the auspices of the departmental services. Within the REF period the Department has performed many single crystal, powder diffraction and related analyses. We have also supported industrial users with structure-related problems via Durham's industry-funded solid state NMR service, helping 49 companies with work between January 2008 and July 2013.

The impact of all our crystallographic research is enhanced by regular international training schools run in Durham [Im6], e.g. the Powder Diffraction and Rietveld refinement School (biennial since 2004) and BCA X-Ray Single Crystal Structure Analysis Intensive Training School (biennial in Durham since 1995), targeting both academics and industry on an international scale. Since 2008 the X-ray Single crystal school has trained over 250 participants over 3 schools held biennially and the powder school has trained >200 delegates from around the world. An overseas PhD student at the 2008 powder school stated "I think it was one of the best teaching courses I have ever attended" and a UK academic "I would have no hesitation in recommending it to any academics or students….there is a huge need for this in the UK"; the International Union of Crystallography powder commission described it as a "school others should aspire to". The problem-based learning example set for the powder school features many examples derived from Durham research (http://www.dur.ac.uk/john.evans/topas_workshop/pcg_workshop_menu.htm) to help train others in our methods.

5. Sources to corroborate the impact

[Im1] Helix and pHenix: Director of Marketing & Sales, Oxford Cryosystems (http://www.oxcryo.com; http://www.oxcryo.com/coolers-for-diffraction/n-helix/; http://www.oxcryo.com/coolers-for-diffraction/phenix/)
[Im2] Olex2: Olex2 CEO – OlexSys (http://www.olexsys.org); UK registered company 07465154.
[Im3] Olex2 and Autochem2.0: Oliver Presley, Program Marketing Manager (XRD), Agilent (www.agilent.com). (http://www.chem.agilent.com/en-US/products-services/software-informatics/autochem/Pages/default.aspx).
[Im4] Topas: Head of Global Product Management XRD, Bruker AXS has provided information confirming JSOE's contribution to Topas. See also: http://www.bruker.com/products/x-ray-diffraction-and-elemental-analysis/x-ray-diffraction/xrd-software/applications/xrd-software-applications/topas.html.
[Im5] Topas Academic: Alan Coelho has provided information confirming TOPAS sales and impact. http://www.topas-academic.net ; http://www.dur.ac.uk/john.evans/topas_academic/topas_main.htm topas.dur.ac.uk/dokuwiki.php
[Im6] Powder diffraction and Rietveld refinement school: EPSRC proposals, testaments of previous delegates and comments of referees in school funding applications.