Institution: University of Leeds

Unit of Assessment: 9 Physics

Title of case study: Development of the world's best-selling Raman Microscopes for Renishaw plc

1. Summary of the impact (indicative maximum 100 words; Leeds researchers in **bold**)

Professor **Batchelder** at Leeds undertook key aspects in the research, design, development and application of Raman microscopes. His partnership with Renishaw plc (Spectroscopy division) led to the development of a new generation of imaging Raman microscope, with performance improved by an order of magnitude. This instrument not only offers dramatically faster performance, meaning spectra could be acquired in seconds rather than tens of minutes, but requires much less laboratory space and maintenance, and offers a wider range of performance compared to other systems on the market. Consequently, the Renishaw system has been the world's best-selling research Raman microscope 2008-13. Wide impact has been generated from the economic benefits of the emergence of the Raman microscope products, from their application within the customer base in terms of improved imaging performance and from the fact that these instruments have since found new applications in a wide range of fields from space research to Forensic Science (see section 4), effectively expanding the customer base.

2. Underpinning research (indicative maximum 500 words; Leeds researchers in **bold**)

The Raman microscope was developed and extended over many years. In **1993 Batchelder** (Leeds), and Renishaw plc, obtained a US patent (5,194,912) for the concept of Raman Analysis Apparatus based on the use of a CCD detector for the detection of Raman scattered light. A key ingredient was the use of an angle-tuned interference filter, which allowed the move away from a conventional monochromator, plus entrance and exit slit based geometries and hence to the formation of a more compact system with higher optical throughput. The step change in Raman analysis performance came about through the application of filters. This initial research has formed the basis of all the microscopes subsequently developed; however, further research and refinements were made including extension into UV and IR excitation regimes, as well as the development of compact systems for drugs and explosives detection and importantly a Raman microscopy capability [1]. The technological importance of **Batchelder**'s initial research work, was recognised with award of the *Annual Achievement Award of the Worshipful Company of Instrument Makers* in ***1994***.

In order to exploit the filtering improvements to Raman technology, in **1997** Leeds (**Batchelder**) and Renishaw obtained a US patent (5,623,342) for the "Raman Microscope" based on tuneable filters. Following this, in **1998** (5,818,047) a US patent was granted between the University of Leeds, Renishaw plc and the Home Office (Prof. Richard Lacey) for a "detector of explosive substances", to implement a simplified instrument in airport ticket handling systems [2,3].

In **2001 Baldwin** and **Batchelder** developed a model that takes into account spherical aberration from refraction through a planar surface when performing Raman spectroscopy. They found that there is an optimum numerical aperture for collected light intensity at a given depth. As Raman microscopy is often carried out on microscopic objects that are designed to operate in air, the air/particle interface will adversely affect the confocal properties of the microscope. When performing Raman confocal microspectroscopy, the interaction of light with a planar surface can cause spherical aberration through refraction, which subsequently causes problems and can substantially degrade the performance of the microscope. The spherical aberration increases the range of focal depths accessible by the rays of the illuminating laser. The scattering volume defined by the confocal aperture thus becomes distorted which leads to a dramatic fall in collected light intensity with increasing depth. The refraction model provides guidance on how to select the dimensions of the aperture to give the least effect of distortion for a given depth. The refraction model has thus provided an important tool for minimising these adverse aberration effects in Raman technology [4].

As Raman microscopes are used to obtain spectroscopic readings from various materials and substances, these devices can be found in many academic research and industrial R&D laboratories worldwide. The work of **Baldwin** and **Batchelder** has therefore made a significant impact in laboratories globally, by optimising numerical apertures for selected focal depths. Furthermore, the model has a wide reach as it can be applied to any situation that requires probing deep through an interface, such as depth profiling of layered materials, identifying inclusions within minerals, and investigating sub-cellular features in biological specimens.

In **2002** Batchelder and co-workers developed a simple chemical method (mirror reaction) to form a silver substrate that can obtain a strong surface enhanced Raman scattering (SERS) signal. This method is particularly suited to the preparation of metalised nanoscale probes for near field imaging applications [5]. Such imaging is essential for some of the Raman applications identified in section 4.

In **2006** Batchelder and co-workers used the Raman microscope to investigate the effect of changing wavelength on 4 different drug substances. This work was able to demonstrate the dependence of the Raman spectra of certain pharmaceutical substances upon laser excitation [6]. The Raman spectroscopy research carried out in this work has a wide reach as it is easily applicable to any field that needs to identify substances based on their molecular properties. The Raman microscope can obtain spectroscopic data, by using a laser to probe the vibrational energy levels of molecules. The Raman spectrum obtained from this process exhibits a set of characteristic peaks that are indicative of the characteristic vibrational frequencies of the substance or material. In particular the various organic molecules that can be synthesised to make pharmaceuticals have characteristic peaks depending on their carbon, OH and other bonds. As such the Raman microscope has particular significance in identifying illicit drugs and can thus make an important contribution to forensic science. In addition, Raman spectroscopy can also identify inorganic molecules by detecting low frequency shifts that can be associated with the internal dynamics of inorganic molecules. This opens the door to a much wider applicability of the Raman microscope, such as the study and characterisation of gunshot residue (organic and inorganic), paint chips and historical artefacts. An initial example of applied Raman research was demonstrated by **Batchelder**'s role for 18 months as an expert witness for SmithKline Beecham vs Apotex, establishing a dedicated Raman laboratory in Leeds for testing polymorphism in Paxil (a $3.2billion dollar per annum worldwide market).

3. References to the research (indicative maximum of six references; Leeds researchers in **bold**)

[1] Williams KPJ, Pitt GD, **Batchelder DN**, Kip BJ., Confocal Raman Microspectroscopy Using a Stigmatic Spectrograph and CCD Detector, *Applied Spectroscopy* 1994;48(2):232-235; http://dx.doi.org/10.1366/0003702944028407 [cited 103 times].

[2] US Patent 5,818,047; 1998, Detector for Explosive Substances, Chaney, **Batchelder**, Lacey.

[3] Pitt GD, **Batchelder DN**, Bennett R, Bormett RW, Hayward IP, Smith BJE, et al., Engineering aspects and applications of the new Raman instrumentation. *IEE Proceedings-Science Measurement and Technology* 2005;152(6):241-318; http://dx.doi.org/10.1049/ip-smt:20050015 [cited 11 times].

[4] **Baldwin KJ**, **Batchelder DN**, Confocal Raman microspectroscopy through a Planar Interface. *Applied Spectroscopy* 2001;55(5):517-524; http://dx.doi.org/10.1366/0003702011952190 [cited 91 times].

[5] **Saito Y**, **Wang JJ**, **Smith DA**, **Batchelder DN**, A simple chemical method for the preparation of silver surfaces for efficient SERS. *Langmuir* 2002;18(8):2959-2961; http://dx.doi.org/10.1021/la011554y . [cited 89 times]

[6] **Thorley FC**, **Baldwin KJ**, Lee DC, **Batchelder DN**, Dependence of the Raman spectra of drug substances upon laser excitation wavelength, *Journal of Raman Spectroscopy* 2006;37(1-3):335-

341; http://dx.doi.org/10.1002/jrs.1446 [cited 13 times].

4. Details of the impact (indicative maximum 750 words; Leeds researchers in **bold**)

The emergence of commercially viable Raman microscope technology has produced a very broad spectrum of impact, that can be divided into two classes: (i) impact of the technology itself – Raman technology is now used for a very wide range of applications; (ii) economic impact, as demonstrated by the success of Renishaw plc through their sales of the technology.

Pathway to Impact and (i) Wide-Ranging Applications of Raman Technology
The underpinning research at Leeds led directly to a range of commercial Raman technology for Renishaw plc, clearly incorporating the innovations of **Batchelder** *et al.* [A-C]. This technology is now widely used in many applications, some of which also link directly back to the work of **Batchelder** *et al.* on explosives detection [2] and drug identification [6].
Current Raman technology applications include:

- Pharmaceuticals [D]: Raman spectra are used to generate chemical images and thus for applications such as rapid screening and polymorph discrimination.
- Carbon and Diamond [E]: Raman spectroscopy is used for quality control of carbon and diamond coatings.
- Materials Science [F]: Raman analysis is used extensively, for many materials such as composites, polymers and catalyst reagents.
- Geosciences and Gemology [G]: Raman spectroscopy is used widely for analysis of geological materials and also for the classification and valuation of gem stones.
- Forensic Science [H]: Raman techniques are employed widely in evidence analysis, for their ability to identify without contamination very small samples of substances such as drugs, gunshot residue, paint chips, ink, etc.. In particular, the use of Raman spectroscopy for the identification of gunshot residue is on the increase due to the introduction of “non-toxic/lead-free” ammunition increasing the chances of false positives from previously applied methods.
- Nanotechnology [I]: Novel Raman techniques enable analysis below micron scales and thus characterisation of nanomaterials such as carbon nanotubes.
- Art and Heritage [J]: Raman spectra can identify pigments and authenticate works of art. The technology has been used for investigation of the Turin Shroud, the Lindisfarne Gospels and demonstrating the Vinland Map as a fake.
- Semiconductors and Devices [K]: Raman analysis can reveal stress, strain and impurity or dopant levels in semiconductors and devices, providing a tool for R&D and quality control during manufacturing.

(ii) Economic Impact during the REF period
Major economic impact has arisen from the creation of new Raman microscope technology that is commercially viable, based on the underpinning R&D work by **Batchelder** *et al*.. This technology generated expansion of the Renishaw product range to include Raman microscopes, with all the accompanying jobs and economic benefits. The Raman Spectroscopy Division now represents a multi-million pound pa revenue stream within Renishaw plc.
The major economic impact of Raman lies predominantly within the Healthcare section of the Renishaw group. Renishaw Healthcare contributed £21.7 million to the revenue of Renishaw in 2011, amounting to 8% of the group’s total income, with the predominant income source being the spectroscopic instrument range based on the patents and technology developed by **Batchelder** [L]. The first half of 2012 saw a streamlining of Renishaw Healthcare but nevertheless still with growth in the Raman spectroscopy range (Raman AFM package introduced) leading to a 27% increase in revenue compared with the same period of 2011 [M]. Furthermore, from [P]: *The Healthcare section of the group contributed £29 million to the revenue of Renishaw in 2013, some 9% of Renishaw total turnover. The Chairman’s statement on Healthcare for the 2013 annual report stated “Spectroscopy sales continued to be the main driver in this business segment and were at a record level.”*
Renishaw offer a product line including a very large number of flexible configurations of a

fundamental Raman microscope device, within which the innovations of **Batchelder** *et al.* are highly visible in the optical setup of all the available Raman configurations [C-E]. From 2008-13, Renishaw have produced the world's best selling research Raman microscope, the inVia [N]. As evidenced from [P]: *The innovations of **Batchelder** et al. have been incorporated in the inVia microsope product which has been the world's best-selling research Raman system 2008-13.*

New Directions and Applications

Raman analysis continues to have growing impact as a research tool. For example, Renishaw Raman microscopes based on the work of **Batchelder** *et al*. have been used by Oxford, Cambridge and other leading universities to research the role of defects in graphene [O], paving the way towards industrial manufacture and application of graphene in the future.

5. Sources to corroborate the impact (indicative maximum of 10 references; Leeds staff in **bold**)

All the web pages used as corroboration of this impact are on record at Leeds, along with all relevant documents as pdfs. All web pages and links last accessed 25/09/2013. A letter from Renishaw, corroborating all the aspects of the impact, is also on record at Leeds [P].

[A] Detailed Renishaw product note: http://goo.gl/G6Uw2v
[B] **Baldwin KJ**, **Batchelder DN**, Confocal Raman microspectroscopy through a Planar Interface. *Applied Spectroscopy* 2001;55(5):517-524; http://dx.doi.org/10.1366/0003702011952190 [cited 91 times].
[C] Renishaw website, Raman spectroscopy section: http://www.renishaw.com/en/raman-spectroscopy--6150
[D] Pharmaceutical applications: http://www.renishaw.com/en/pharmaceutical--7977
[E] Carbon and Diamond applications: http://www.renishaw.com/en/carbon-and-diamond--8269
[F] Materials Science applications: http://www.renishaw.com/en/materials-science--7978
[G] Geosciences and Gemology: http://www.renishaw.com/en/geosciences-and-gemology--7979
[H] Forensic Science: http://www.renishaw.com/en/forensic-science--7980 The website features a document on drug detection which includes work by **Batchelder**. Paint chip analysis features at http://goo.gl/XnFmhI
[I] Nanotechnology applications: http://www.renishaw.com/en/nanotechnology--7981
[J] Art and Heritage applications: http://www.renishaw.com/en/art-and-heritage--7982
[K] Semiconductors and Devices: http://www.renishaw.com/en/semiconductors--7983
[L] Renishaw annual report for 2011: http://goo.gl/XSUYP3
[M] Renishaw interim report for 2012: http://goo.gl/IR9mLg
[N] The Renishaw inVia system: http://www.renishaw.com/en/invia-raman-microscope--6260
[O] Renishaw Raman microscope investigating graphene: http://goo.gl/DYREHo .
[P] Letter from the Director and General Manager, Spectroscopy Products Division, Renishaw plc.