Institution: The University of Manchester		
Unit of Assessment: 8 (Chemistry)		
Title of case study: New paradigms for 3D materials analysis using polyatomic projectiles: changing capacity and industrial practice		
Period when the underpinning research was undertaken: 1 January 2000 onwards		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (*e.g.* job title):**	**Period(s) employed by submitting HEI:**
Nicholas P. Lockyer	Professor (2019 – present) Reader (2014 – 2019) Senior Lecturer (2008 – 2014) Lecturer (2002 – 2008) Special Research Fellow (2000 – 2002)	2000 – present
John C. Vickerman	Professor Emeritus (2012 – present) Professor (1970 – 2012)	1970 – present
Period when the claimed impact occurred: 1 August 2013 - 31 July 2020		
Is this case study continued from a case study submitted in 2014? N		

1. Summary of the impact

Pioneering research at The University of Manchester (UoM) developed polyatomic ion beam systems, resulting in a paradigm shift in materials chemical analysis using secondary ion mass spectrometry (SIMS). The introduction of a C_{60}^+ ion beam allowed for the first time 3D depth profiling of organic materials on the micrometer scale and spawned the development of second-generation polyatomic beams based on massive gas clusters. Together these ion beams have changed both practice and capacity across industrial sectors spanning manufacturing to healthcare *e.g.* organic electronics, battery technologies, pharmaceuticals and cancer research, leading to accelerated product development and improved quality of life. Novel analytical methodology and capabilities have enabled measurements that have never before been possible resulting in new products, economic benefits and business expansion in the coatings/materials industry and new markets for analytical service providers and instrument manufacturers worldwide.

2. Underpinning research

The key UoM researchers were Nicholas Lockyer and John Vickerman, in collaboration with industrial research partner Paul Blenkinsopp (Ionoptika Ltd, Southampton, UK).

Surface chemistry determines how a material interacts with its environment. Analytical techniques that scrutinise the chemical composition and distribution in the surface region of materials (the top few microns) are therefore of critical importance in many areas of technology and in a wide range of industries including healthcare and manufacturing. One such technique for studying surface chemistry is secondary ion mass spectrometry (SIMS), using high energy ion projectiles at low dose to eject or desorb surface molecules for chemical determination and imaging.

In the early 'static' SIMS approach for molecular analysis, high-energy beams of ionised atoms are used to analyse a surface. On impact, these atomic ion beams can cause chemical components of the surface to fragment. This fragmentation limits the technique's ability to interrogate the surface's chemical structure, usually to about 1% of the total surface area. As such, 'dynamic' or 'depth-profiling' SIMS analysis of the chemistry of sub-surface and buried interfaces was limited to elemental species that could survive prolonged bombardment from the ion beam.

In the late 1980s researchers suggested that projectile clusters, comprised of *n* atoms, would shatter on impact with a surface, confining their kinetic energy transfer to the surface region and resulting in high molecular desorption yields. This is the general principle of the polyatomic SIMS technique. Between 2000 and 2003, Vickerman & Lockyer, along with Ionoptika Ltd, developed the world's first polyatomic (n>6) ion beam system for SIMS. This system used Buckminsterfullerene (C_{60}^+) as the polyatomic projectile cluster. It demonstrated a ~1000-fold increase in sensitivity for molecular surface analysis **[1]**, and sub-micron spatial resolution when applied to imaging applications relevant to life sciences and organic materials **[2-4]**. Moreover, using C_{60}^{+} resulted in a substantial reduction in bombardment-induced damage of the sample, allowing up to 100% of the sample volume to be analysed. This improvement in sensitivity enabled unprecedented depth-profiling of successive layers and 3D chemical imaging of organic materials **[2, 4]**, including the first 3D molecular SIMS analysis of a single biological cell **[3]**. Polyatomic SIMS was quickly applied in fields such as biomedical sciences, organic materials, manufacturing and other sectors, where micrometer-scale 3D chemical characterization was beyond the limitations of other analytical techniques. Corning Inc., a major US-based materials company, state, "*Prior to the advent of polyatomic SIMS, we were limited to surface analysis in organic coatings and thin films due to the damaging nature of the mon-atomic primary ion sources. Polyatomic SIMS is the only methodology capable of 10 nm-resolution depth profiling of soft materials and coatings and is the only technique with the required chemical specificity to fully assess chemical changes in these materials*." **[A]**.

In 2008, Vickerman and Lockyer introduced a new-generation of time-of-flight SIMS instrument (*J105 3D Chemical Imager*), designed with Ionoptika Ltd **[4]**. The significance of this work is highlighted by the UK's National Physical Laboratory (NPL), who stated: "*The ground-breaking J105 pioneered the concept of using a mass spectrometer designed to work with a continuous flow of secondary ions, optimally designed for use with a focussed polyatomic ion beam"* **[B]**. This represented a further paradigm-shift in analytical protocol, improving analysis speed 1000-fold and improving the measurement precision (mass resolution).

The introduction of the C_{60}^{+} beam revolutionized the capabilities of SIMS. The NPL state, "*The C_{60}^{+} ion beams developed at Manchester gave impetus to the field and were the forerunner of the modern Gas Cluster Ion Beam"* **[B]**. These massive Gas Cluster Ion Beams (GCIBs, *n*>1000), had been used in the semiconductor industry for surface cleaning, but never-before in materials analysis. Research by Vickerman and Lockyer (with Ionoptika Ltd) and independently by Matsuo (University of Kyoto, Japan) developed the first high energy, focused, mass-selected GCIB sources for SIMS applications **[5]**. Collaboration between Vickerman and Ionoptika Ltd led to the first commercial GCIB for SIMS in 2011 and in 2013 demonstrated that the chemistry of the GCIB projectile can be exploited to further enhance analytical sensitivity ~100-fold **[6]**.

Corning Inc. stated that, "*The University of Manchester group has been pivotal in the development of technologies and methodologies for the practical implementation of polyatomic SIMS*" **[A]**.

The US National Institute of Standards and Technology (NIST) stated that, *"We view the work done by* [The University of Manchester] *as revolutionizing the analytical capabilities and availability of this approach to the scientific community and industry."* **[D]**.

3. References to the research

As a result of research described in this case study, Vickerman received the following international awards: 2004 Rivière Prize of the UK Surface Analysis Forum for advances including 'the recent developments of the *polyatomic ion sources* that will be of major importance for the growing work in the advanced technologies surrounding nano-biotechnology'; 2009 RSC Theophilus Redwood Award 'Awarded for his outstanding contribution to the development and application of secondary ion mass spectrometry techniques for surface analysis and *3D chemical imaging of organic and biological systems*'; 2012 the Médaille Chevenard of the Société Française de Métallurgie et de Matériaux for 'outstanding contribution in *scientific instrumentation* and methods of characterizing materials'. Since 2000, Lockyer has delivered 26 invited and plenary talks on polyatomic SIMS at international meetings. Vickerman has delivered a similar number. The research has been published in high-quality, peer-reviewed journals, including *Analytical Chemistry*, a top-tier analytical chemistry journal from the American Chemical Society. Citation data are from Scopus, and accurate as of 5 March 2021.

[1] D. Weibel, S. Wong, **N. Lockyer**, P. Blenkinsopp, R. Hill, **J.C. Vickerman**, A C_{60} primary ion beam system for time of flight secondary ion mass spectrometry: Its development and secondary ion yield characteristics, *Analytical Chemistry* 75 (**2003**) 1754-1764. [456 citations] DOI: 10.1021/ac026338o.

[2] E.A. Jones, **N.P. Lockyer, J.C. Vickerman**, Depth profiling brain tissue sections with a 40 keV C-60(+) primary ion beam, *Analytical Chemistry* 80 (**2008**) 2125-2132. [77 citations] DOI: 10.1021/ac702127q.

[3] J.S. Fletcher, **N.P. Lockyer**, S. Vaidyanathan, **J.C. Vickerman**, TOF-SIMS 3D biomolecular imaging of Xenopus laevis oocytes using buckminsterfullerene (C-60) primary ions, *Analytical Chemistry* 79 (**2007**) 2199-2206. [254 citations] DOI: 10.1021/ac061370u.

[4] J.S. Fletcher, S. Rabbani, A. Henderson, P. Blenkinsopp, S.P. Thompson, **N.P. Lockyer, J.C. Vickerman**, A New Dynamic in Mass Spectral Imaging of Single Biological Cells, *Analytical Chemistry* 80 (**2008**) 9058-9064. [204 citations] DOI: 10.1021/ac8015278.

[5] S Rabbani, AM Barber, JS Fletcher, **NP Lockyer, JC Vickerman**, TOF-SIMS with Argon Gas Cluster Ion Beams: A Comparison with C_{60}^+, *Analytical Chemistry* 83 (**2011**), 3793-3800. [150 citations] DOI: 10.1021/ac200288v

[6] S. Sheraz, I. Berrueta Razo, T. P. Kohn, **N. P. Lockyer**, and **J. C. Vickerman**, Enhancing Ion Yields in Time-of-Flight-Secondary Ion Mass Spectrometry: A Comparative Study of Argon and Water Cluster Primary Beams, *Analytical Chemistry* 87 (**2015**) 2367–2374. [46 citations] DOI: 10.1021/ac504191m

This research was funded by a series of EPSRC/BBSRC grants exceeding GBP6,000,000 to Vickerman & Lockyer to develop the technology, perform fundamental studies and develop novel analytical applications.

4. Details of the impact

Context

SIMS techniques have been applied to numerous industrial applications, including in the pharmaceutical and life science industries as a tissue and cell imaging technique, and particularly in the microelectronics industry for studying the structure of semiconductor devices. SIMS was previously limited in its utility, primarily to the analysis of inorganic materials. The aggressive nature of the atomic primary ion beam caused significant damage to the underlying surface of the material, restricting the amount of meaningful information that could be obtained to <1% of the sample surface, severely limiting the sensitivity of the measurement. In addition, the low yield of diagnostic secondary ions limited the spatial resolution available in SIMS imaging of molecular materials. Set against this background, UoM's research and collaborations have aimed to overcome these limitations by using new, more gentle polyatomic ion beams, as described above.

Pathway to impact

The research underpinning this case study has been performed to a great extent in collaboration with UK SME Ionoptika Ltd, who provided in-kind support, engineering expertise and routes to commercialisation. This collaboration has been ongoing since 2000, when UoM researchers worked with Ionoptika to develop the first C_{60}^+ primary ion beam source **[B, C]**.

Reach and significance of impact

Changing practice in the scientific community and industry

Virtually all of the ~100 Time-of-Flight-SIMS spectrometers sold since 2013 include a polyatomic ion source, using either C_{60}, GCIBs, or both **[B]**. NPL characterise the importance of polyatomic ion sources in SIMS applications, saying "*These projectiles are **critical in the application of SIMS across industrial sectors** spanning manufacturing to healthcare and have been **universally adopted** by the worldwide SIMS community."* **[B]**. The Manchester group has been pivotal to the implementation and commercialisation of polyatomic SIMS allowing widespread access to these new measurement tools, which have changed analytical practice and capacity **[A, D, E]**.

Industrial sectors including electronics (*[text removed for publication]*), chemical (Dow Chemical, BASF), manufacturing (Dow Corning [a joint venture between Dow Chemical Company and Corning Inc.], Mitsubishi, Fujifilm) and pharmaceuticals (AstraZeneca, GlaxoSmithKline, Novartis) and governmental research labs (UK-NPL, USA-NIST, Korea-KRISS) rely on the enhanced sensitivity and 3D molecular imaging capabilities unique to these ion beams. The NPL stated, "*polyatomic cluster impacts together with novel analytical methodologies enable increased sensitivity of a 1000-fold for thick samples."* **[B]**. The NIST stated, *"Work done by the group at Manchester has revolutionized the analytical capabilities and availability of this approach to the scientific community and industry. We have seen integrated signals improve by factors of 10^5 for certain organic compounds when compared to atomic primary ion beams"* **[D]**.

At Dow Chemical Company, polyatomic SIMS provide unique depth-profiling capabilities to study chemical degradation and segregation on multilayer polymer-based materials *'enabled experiments that have never before been possible'* **[E]**.

Corning Inc. stated, "[Polyatomic SIMS] *has changed the analytical practice and capacity within Corning Inc., enabling us to derive new levels of understanding regarding our products and their performance."* **[A]**.

Leading analytical services company Tascon GmbH, serving customers in the automotive, chemicals, electronics, glass, life sciences, and pharmaceuticals markets stated, "*(GCIB) has opened complete new applicational options. Not only depth profiling has become feasible, but also the reconstruction of the 3-dimensional composition (both elemental and molecular) has entered our daily analytical portfolio.*" **[F]**.

The NIST stated, "*C_{60} and GCIB ion sources are able to derive new chemical information on 3D micro-distributions within a wider range of materials (polymers, biological materials, drugs and semiconductors) than was previously possible with conventional SIMS using monoatomic ion beams"* **[D]**.

Economic benefits and capacity building for instrument manufacturers and industrial users

The co-development, with UoM, of polyatomic ion sources for SIMS, firstly C_{60} and more recently GCIBs, are at the centre of Ionoptika's business model and emergence into an international leader in SIMS technology **[C]**. Ionoptika stated, "*commercialisation of the J105 has led to Ionoptika moving to a larger manufacturing facility in 2014 and has resulted in the creation of 23 specialist manufacturing jobs since 1 August 2013, tripling our workforce*." **[C]**. The C_{60} source is protected by three patents and the SIMS instrument developed to maximise polyatomic projectiles the subject of two more (2014).

Industrial users worldwide apply polyatomic SIMS measurements to derive new levels of understanding on products and their performance, leading to economic impact.

For example, at Dow this technology is used to develop new multilayer coatings and [text removed for publication] **[E]**. Corning Inc. state: "*I cannot say enough about the impact polyatomic ion sources have on industrial product development….Since the introduction of the polyatomic ion beam source to Corning, there has been at least a 300% increase in sample volume."* **[A]**.

Influenced new instrumentation products

As a result of UoM's underpinning research since 2000, all three major manufacturers of time-of-flight SIMS, Ionoptika Ltd (UK), IonToF GmbH (Germany) and Phi Inc. (USA) supply C_{60} and/or GCIB sources with their instruments with each ion source valued at GBP100,000–400,000. The *J105* instrument design results directly from our pioneering work with C_{60} [B] which demonstrated for the first time a projectile beam combining high brightness, high molecular sensitivity and the capability to operate in a dynamic mode for full 3D-analysis **[1]**. These instruments (~GBP1,500,000 each) have sold across three continents, to industrial and academic labs **[C]**. The same principle of continuous bombardment has led to another instrument platform from Thermo/IonToF GmbH – the 3D orbiSIMS, launched in 2017 and selling 8 units worldwide *[text removed for publication]* **[B]**.

Beyond SIMS, the rather gentle molecular erosion under polyatomic bombardment allows other 'surface analysis' methods including X-ray Photoelectron spectroscopy (XPS) to probe sub-surface chemistry. GCIB sputter-etch sources allow this highly-quantitative technique to measure buried molecular layers and clean-up contaminate surfaces. At Dow, product development was impaired by "*a gap of chemical analysis over the information depth of about 10 nm (usually thought of as the maximum depth for XPS) and a couple* [of] *microns (about the information depth of IR)…cluster beam etching coupled with SIMS and/or XPS analysis has eliminated this information gap… meaning the impossible is now possible*" **[E]**. XPS market-leader Kratos Analytical stated, "*Depth profiling with retention of chemistry was not possible before the development of GCIB technology. [text removed for publication]*". [text removed for publication] **[G]**.

Enhancing quality of life through new measurement capability

Polyatomic beams provide novel capabilities for chemical imaging in biomedical and consumer product fields. Examples include studies of drug distribution in single biological cells and drug release studies in biomedical implants **[B]**. A collaborative study between Novartis and Penn State University used a J105 instrument and micro-focused GCIB to image antimicrobials in single bacteria, shedding new light on the biological mode of action. Such studies demonstrate the downstream impact in personalised medicine and future healthcare. In a wide range of industrial applications, polyatomic beams provide answers to critical questions regarding product performance and failure which were simply not available previously **[F]**.

At NIST polyatomic SIMS has opened several new application areas in healthcare and bioanalysis including (i) development of next generation drug delivery films, (ii) assessing potential health hazards associated with Homeland Security Application and (iii) public health and safety issues related to drug contamination and adulteration **[D]**.

Corning Inc. stated, "*Polyatomic SIMS was used to understand the chemistries and failure mechanisms in our pharmaceutical vial coatings which are currently being employed for use in COVID vaccines* [and] … *has accelerated product development significantly and has led to improved quality of life for our global customers*." **[A]**.

5. Sources to corroborate the impact

[A] Letter from Principal Scientist, Corning Inc, USA, 8 September 2020
[B] Letter from the Director of the National Centre of Excellence in Mass Spectrometry Imaging, National Physical Laboratory, UK, 7 September 2020
[C] Letter from the Director, Ionoptika Ltd, UK, 2 July 2020
[D] Letter from Supervisory Research Chemist, National Institute of Standards & Technology, USA, 11 June 2020
[E] Letter from Research Scientist, Dow Chemical Company, USA, 15 June 2020
[F] Letter from the Managing Director, Tascon GmbH, Deutschland, 9 July 2020
[G] Letter from Marketing Manager – Surface Analytics, Kratos Analytical Ltd, UK, 23 June 2020