Institution: Imperial College London



Unit of Assessment: 9 Physics

Title of case study: P10 - Optical sectioning microscopy - Aurox Ltd

**1. Summary of the impact** (indicative maximum 100 words)

Aurox Ltd is an Oxfordshire spin-out company formed in 2004 by Prof Mark Neil (at Imperial since August 2002) with former colleagues from Oxford University. Its main product line consists of wide field optical sectioning fluorescence microscopes based on the principle of structured illumination and detection using patterned disks. The microscopes use conventional (lower cost) light sources and do not require a scanning system which sets them apart from competitors. Research at Imperial has impacted on the design of disk patterns for optimising performance and has played a critical role in bringing these microscopes to market. Aurox's systems are supplied to and marketed by Carl Zeiss (as VivaTome<sup>™</sup>) and Andor Technology (as Revolution DSD<sup>™</sup>) for application in the biomedical sciences, generating successful sales over the period 2008-2012 and enabling Aurox to embark on a second-generation development programme. Since 2008 Aurox have sold more than 150 units with market value in excess of £3M. The majority of this £3M in sales have been since 2010 when an optimisation step which was developed and devised at Imperial College was incorporated into the Aurox products.

## 2. Underpinning research (indicative maximum 500 words)

Stemming from original research (*Nature*, 383, 804-806) conducted by Prof Mark Neil (MN) and his colleagues at Oxford University in the late 1990s, MN has continued to work on wide field optical sectioning microscopy at Imperial. The results of his research have had significant impact on product developments and improvements in, spin-out company, Aurox's own programmes via his role as "Principle Scientist" with the company.

Research undertaken at Imperial College between 2004 and 2008 under a Basic Technology Research Award [G1] focussed on the application of micro-led arrays [1] to optical sectioning microscopy [2]. This large multi-partner project was led by Strathclyde university whose own role was the fabrication of micro-LED arrays, but with Imperial's role looking in particular at applications in microscopy and imaging. A particular emphasis of the work lead by Imperial within this project was using customised micro-LED arrays as programmable structured illumination light sources in fluorescence microscopy as a means to achieving optically sectioned imaging. This is a feature, commonly associated with more complex laser scanning confocal microscopes, where an image is obtained of just the in-focus parts of the specimen, while signal from the out-of-focus parts is rejected.

Significant outputs of the work at Imperial included the development of theoretical analyses of optical sectioning performance [3] of such structured illumination microscopy systems that have helped in the understanding and thus further refinement of Aurox's own microscopy units. This has enabled Aurox to produce disk designs that optimise the balance between optical sectioning strength - how thick is the optical section - and signal level - how bright is the optical section. The significant steps in the research were undertaken wholly at Imperial by Prof Mark Neil and his research team.

Key personnel:



- Mark Neil, Professor of Photonics (2009-present), previously lecturer and reader (since 2002), Physics Department, Imperial College London
- Paul French, Professor of Photonics, Head of Photonics Group, Physics Department, at Imperial 01/10/89-present.

3. References to the research (\* References that best indicate quality of underpinning research)

- \*Zhang, H. X., Gu, E., Jeon, C. W., Gong, Z., Dawson, M. D., <u>Neil, M. A. A.</u> and <u>French, P. M.</u>
  W., '*Microstripe-array InGaN light-emitting diodes with individually addressable elements*', IEEE
  Photonics Technology Letters, 18, 1681-1683 (2006). <u>DOI</u>, **14 citations (as at 25/7/13)**
- [2] <u>\*Poher, V., Zhang, H.X., Kennedy, G.T., Griffin, C., Oddos, S., Gu, E., Elson, D. S.</u>, Girkin, J.M., <u>French, P.M.W.</u>, Dawson, M.D. and <u>Neil, M.A.A.</u>, 'Optical sectioning microscopes with no moving parts using a micro-stripe array light emitting diode', Optics Express, 15, 11196-11206 (2007). <u>DOI</u>, **19 citations (as at 25/7/13)**
- [3] <u>\*Poher, V., Kennedy, G. T., Manning, H. B., Owen, D. M.</u>, Zhang, H. X. X., Gu, E., Dawson, M. D., French, P. M. W. and Neil, M. A. A., 'Improved sectioning in a slit scanning confocal microscope', Optics Letters, **33**, 1813-1815 (2008). DOI, **4 citations (as at 25/7/13)**

## Grants:

[G1] EPSRC, <u>GR/S85764/01</u>, 'A Thousand Micro-emitters Per Square Millimetre: New Light On Organic Materials & Structures', RCUK Basic Technology Programme, PI Martin Dawson (Strathclyde) with Co-Is from Strathclyde, Imperial, Sheffield and Heriot-Watt, 01/07/04-31/10/08. £2.7M total funding, £430K to Imperial Photonics.

## 4. Details of the impact (indicative maximum 750 words)

Aurox Ltd [A] was formed in 2004, is based in Oxfordshire, and now employs 5 full time staff in both development and manufacturing. The company's goal is "to make 3-D microscopy accessible and affordable to the masses – to individual researchers, not just imaging facilities in large institutions" [B]. Aurox products use lower cost light sources than competitors and do not require a scanning system which sets them apart from other microscopes. The company testifies that Imperial research carried out by Prof Mark Neil's group has "directly influenced developments and improvements to Aurox products" and, in particular, the research in paper [3] has led to "a better understanding of optical sectioning in the Aurox SD62 series of microscopes". This has enabled the company to optimise the microscopes performance "to better accommodate end user requirements" [B].

Since 2008 Aurox has sold more than 150 units with market value in excess of £3M [B]. The "majority of these sales have been since 2010 when the optimisation step described in paper [3] was incorporated into [their] products" [B]. The sales have been made through distributers Carl Zeiss MicroImaging GmbH, who market the products as Vivatome<sup>TM</sup> [C, D], and Andor Technology PLC, who market it as Revolution DSD<sup>TM</sup> [E]. In the case of both customers it was initial feedback from beta-site testing with end users that pointed to the need for a fuller understanding of the impact of disk pattern design on the competing requirements of optical section strength and signal level. That understanding was provided by the research undertaken at Imperial described above and which informed the design of new disk patterns that was a crucial step in the development of the eventual systems that went to market [B].

As distributers both Carl Zeiss and Andor (headquartered in Germany and Northern Ireland respectively) have in turn benefitted from the addition of Aurox units to their fluorescence



microscopy product lines, providing a low cost optical sectioning microscopy solution that is capable of operation at relatively high speed. In Carl Zeiss this has filled a niche at the low cost end of their already extensive product line, effectively phasing out their previous ApoTome<sup>™</sup> product. Within Andor this has formed part of a concerted effort to expand from a small, but successful, scientific camera manufacturer to a worldwide supplier of complete optical microscopy systems. In marketing the Revolution DSD<sup>™</sup> Andor Technology PLC has "made significant use of the research in paper [3] to help explain the operation of the Revolution DSD through both webinars and other promotional material" [B]. As end users, biomedical scientists find that with a low cost and relatively compact device such as this they are no longer held up in their work by waiting for access to centralised facilities where more expensive and bulky laser scanning microscope systems are often sited, and that they can now access some of the same functionality as provided by such traditional microscope systems in their own laboratories.

Through the development of first-generation systems with Carl Zeiss, Aurox was awarded R&D 100 award in 2010 [F]. Most recently, in May 2012, Aurox received a Queen's award for innovation [G] and an Institute of Physics Innovation Prize [H] in October 2012. All of these awards were based on the success of the first-generation systems that benefited from the Imperial research highlighted here [B].

As a result of the success of the first generation systems produced by Aurox, it is currently actively involved in the development of a second generation of systems that will both improve on overall performance for existing customers Carl Zeiss and Andor, and expand their respective customer bases in new directions. The design of the second generation of microscopes produced by Aurox continues to be, in part, underpinned by the analysis developed in paper [3] [B].

Aurox continues to work with Prof Neil's research group at Imperial to develop the next generation of microscopes. An example of the continued collaboration is Aurox's role as the industrial/commercial sponsor an EPSRC DTA/CASE award which has been held at Imperial since October 2010 [B, I]. The student Lionel Fafchamps is working under the supervision of Prof Mark Neil at Imperial and industrial supervisor Dr Rimas Juskaitis at Aurox on further developments to spinning disk pattern design to include more complex patterns that can mitigate some of the residual artefacts of simple line patterns, and the behaviour of systems using such masks in bright field microscopy such as are used in material inspection applications. A particularly interesting recent development under this program has been in mask designs that give significant improvements in resolution for fluorescence systems. It is expected that these developments will feed into the second and future generation systems under development at Aurox.

## 5. Sources to corroborate the impact (indicative maximum of 10 references)

- [A] Aurox Ltd. web pages, <u>http://www.aurox.co.uk</u> (archived at <u>https://www.imperial.ac.uk/ref/webarchive/7qf</u> on 03/09/13)
- [B] Letter from Managing Director of Aurox Ltd, indicating the significance of the research to their product development and subsequent sales performance (available from Imperial on request).
- [C] Carl Zeiss VivaTome page, <u>http://microscopy.zeiss.com/microscopy/en\_de/products/imaging-systems/vivatome.html#Introduction</u> (archived at <u>https://www.imperial.ac.uk/ref/webarchive/3qf</u> on 3/9/13)
- [D] Carl Zeiss VivaTome brochure, <u>http://applications.zeiss.com/C125792900358A3F/0/398009EAE6C4F189C125790600482250/</u> <u>\$FILE/60-2-0038\_e\_VivaTome.pdf</u> (archived <u>here</u>)
- [E] Andor Revolution DSD page, <u>http://www.andor.com/microscopy-systems/revolution-dsd</u>



(archived at https://www.imperial.ac.uk/ref/webarchive/4qf on 3/9/13)

- [F] R&D100 award announcement: <u>http://www.rdmag.com/Awards/RD-100-</u> <u>Awards/2010/08/Putting-fluorescence-into-focus/</u> (archived <u>here</u>)
- [G] Queen's award announcement <u>http://www.businesslink.gov.uk/Horizontal\_Services\_files/2012\_QA\_Winners.pdf</u> (archived <u>here</u>)
- [H] Institute of Physics Innovation Awards 2012 announcement. <u>http://www.iop.org/news/12/sep/page\_56982.html (archived at https://www.imperial.ac.uk/ref/webarchive/6qf</u> on 3/9/13)
- [I] Lionel Fafchamps EPSRC DTA/CASE award 10/10 3/14.