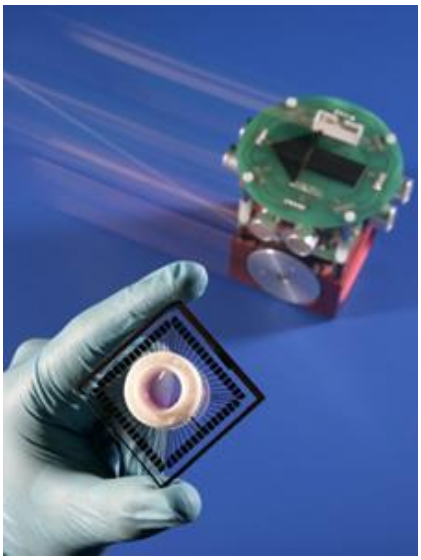
Institution: University of Reading

Unit of Assessment: 3 Pharmacy

Title of case study: Public and Commercial Engagement with brain-computer interfaces

1. Summary of the impact

Brain diseases cost European healthcare agencies approximately €800 billion each year, but are very poorly understood. Neuroscientists and cyberneticists at the University of Reading study how individual brain cells subserve higher cognitive functions, using brain-computer interfaces to understand how individual cells form neuronal networks. This work has engaged the public imagination through mainstream media, attracted investment from pharmaceutical companies whose drug development programmes demand an understanding of how cellular networks function in the brain and enhanced the use of stem cell derived human neural tissue, thereby enabling a reduction in the use of animals in such research.



'Gordon', the mobile robot that wirelessly embodied a brain cell culture grown on a multi-electrode array (in close-up).

2. Underpinning research

One of the largest challenges facing neuroscience is how we can reconcile our understanding of cellular and molecular neuroscience with the emerging recognition of the network that underlies higher cognitive functions, such as memory and attention. A collaboration between Dr Ben Whalley (School of Pharmacy) and Professors Kevin Warwick and Slawomir Nasuto (School of Systems Engineering) at the University of Reading has developed and exploited new technologies that enable the monitoring of networks of live brain cells grown from rodent tissue in the laboratory and connected to computer systems[a,b]. Our research shows that viable, functional cultured neuronal networks can be embodied within a computer system for 3-4 months and such embodiment can influence the responses of the neuronal networks themselves. Crucially, we have demonstrated that these neuronal networks share the specific bioelectrical[a,b,d-h] and neurochemical[c] features shown by higher organisms to control cognitive function, thereby paving the way for behavioural investigations using embodied neuronal networks.

We have extended this research by demonstrating that embodied neuronal networks can also be created with human embryonic stem cells—a world first [i] - by applying advanced cell culture techniques, stem cell technologies, biocompatible 3D scaffolds, multielectrode array electrophysiological methods and conventional pharmacology / immunohistochemistry to confirm the presence of spontaneously active, stem-cell derived neuronal networks [d]. The research required close working with major multinational sponsors in the pharmaceutical industry to realise the real-world impacts of the research in drug development [j]. As a consequence of our collaboration, a multi disciplinary laboratory, the Brain Embodiment Laboratory (BEL), has been established at Reading to study how neuronal information flows between the brain and body to better understand mechanisms underlying healthy function and specifically identify targets for the treatment of neurodegenerative and neuromuscular diseases. Dr Ben Whalley joined the University of Reading in 2005 as a Lecturer in Pharmacy Practice and is now a Senior Lecturer in Pharmacology. Professor Kevin Warwick joined the University as Professor of Cybernetics in 1988. Professor Nasuto joined the University in 2000 as a Reader in Cybernetics, becoming Professor in 2012.

3. References to the research

Journal articles have been published in peer-reviewed journals. They have also been internally assessed as of at least 2* quality.

a. Spencer, M. *et al.* Spatio-temporal dependencies in functional connectivity in rodent cortical cultures *J. Behav. Robotics* **2**,156-163 (2012) : DOI: 10.2478/s13230-012-0002-7
b. Spencer, M. C. *et al*. Multi-scale evolving complex network model of functional connectivity in neuronal cultures. *IEEE Trans. Biomed. Eng.* **59**, 30-34 (2012). DOI: 10.1109/TBME.2011.2171340 (IF=2.348)
c. Hammond, M. W. *et al.* Endogenous cholinergic tone modulates spontaneous network level neuronal activity in primary cortical cultures grown on multi-electrode arrays. *BMC Neuroscience* **14**, 38 (2013). DOI: 10.1186/1471-2202-14-38 (IF=3)
d. Downes, J. H. *et al.* Emergence of a Small-World Functional Network in Cultured Neurons. *PLoS Comput. Biol*. **8**, e1002522 (2012). DOI: 10.1371/journal.pcbi.1002522 (IF=4.867)
e. Xydas, D. *et al.* Revealing ensemble state transition patterns in multi-electrode neuronal recordings using hidden Markov models *IEEE Transactions on Neural Systems and Rehabilitation Engineering* **19**, 345-355 (2011). DOI: 10.1109/TNSRE.2011.2157360 (IF=3.255)
f. Spencer, M. *et al.* Investigation of Spatio-Temporal Dependencies in Neuronal Functional Connectivity. In proceedings of the 9th IEEE International Conference on Cybernetic Intelligent Systems 57–62 (2010)
g. Hammond MW, *et al.* Controlling a mobile robot with a biological brain *Defence Science Journal* **60**, 5–14 (2010) http://publications.drdo.gov.in/ojs/index.php/dsj/article/view/11
h. Warwick, K. *et al.* Autonomous Mobile Robot with a Biological Brain in *Mobile Intelligent Autonomous Systems*, J. R. Raol and A. K. Gopal (eds), CRC Press, Taylor and Francis, pp.281–294 (2013)
i. Smith, I. *et al.* Functional and spontaneously active networks of human stem cell-derived neurons, cultured on a bio-compatible 3D scaffolds; a multi-electrode array (MEA) study. Poster 415.26/D16, Neuroscience 2013, Nov 9th-13th San Diego, USA
j. GSK Nutrition (H5141600) 2011-2013 PI B. Whalley £235,000 Title: Ginsenoside effects upon spontaneous neuronal activity; EPSRC EP/D080134/1 2006-2010 PI: K. Warwick Co-I: B. Whalley £419,000 Title: *Investigating the computational capacity of cultured neuronal networks using machine learning.*

4. Details of the impact

The substantial non-academic impact of this work lies in three key areas: i) extensive and persistent public engagement with scientific research, ii) reduction of animal use in commercial research and iii) commercial exploitation of our technologies.

Public engagement with scientific research

In 2008, Paul Marks, a journalist with New Scientist, heard about our work during a talk given by Professor Warwick. He then contacted the team to arrange an interview. A feature article, "*Rat-brained robots take their first step*", appeared in New Scientist in August 2008, specifically highlighting the brain-computer interface work being conducted at University of Reading. The magazine's online article, *"Rise of the rat-brained robots"* was published on 13 August 2008. This article linked to a YouTube video of the robot functioning, and the two versions of the video have now received in excess of 2.5 million unique views (see, for example, one version at http://www.youtube.com/watch?v=1-0eZytv6Qk). In 2008, and following the increased public profile of our work, the Science Museum in London enlisted us to produce a special display devoted to our research in this area, with our working 'robot' as the highlight. The display opened on 16 October 2008. Originally planned as a 3 month display, it remained for in place 18 months due to high public demand. The Science Museum receives more than 2.5 million visitors every year, with one third of these visitors coming from overseas. As of 2013, the Science Museum maintains a series of web pages specifically dedicated to our brain-computer research[1]; a resource used by over 250 secondary schools and colleges as an integral part of their course structure.

Our work also led to a cross-disciplinary collaboration with Bill Gaver, Professor of Design at Goldsmiths, University of London, who was funded by EPSRC (EP/E035051/1) to "build new bridges between academic specialism and public engagement by pushing emotive and accessible formats". Specifically, the collaboration examined the impact of our brain-computer research on

public perceptions and engagement with science and society. This work led us to design the '*Neuroscope*', a device installed at the Science Museum's Dana Centre in London and at the LABoral Centro de Arte y Creacion Industrial (Gijon, Spain) in 2008, which enabled public visualisation of, and interaction with, the complex neuronal activity exhibited by networks of brain cells. The results of the collaboration were also published in the book, Material Beliefs (ISBN 978-1-904158-95-0; 2009)[2].

Since 2008, our work has been featured in over 100 different news articles, including (approximate 2008 circulation figures in brackets): *The Lancet* (29,000), *The Daily Telegraph* (800,000), *Daily Mail* (2,300,000), *Forbes* (900,000) and *The Independent* (250,000). In May 2013, the work was featured as the Medical Research Council's Brain Picture of the Day [3] and been featured on BBC News, ITV News, Fox News, CBS (USA), Discovery Channel, National Geographic Channel, Swiss TV Channel 1, Danish TV Channel 1, and Swedish TV Channel 1. Our work on human brain cells at BEL was featured in the first episode of BBC Radio 4's Frontiers series [4] and reported on the BBC website [5] and ITN news [6].

Change in business practice - reduction in animal research

Public support for the use of animals in research is declining (down to 66%, from 75% in 2010; http://tinyurl.com/kny3fph) but their use in research is actually increasing (http://tinyurl.com/pjka9qb and http://bit.ly/1489LAq). Our approach, using functional human brain cells integrated into robotic systems, has been adopted by GlaxoSmithKline [7] via purchase of an evaluation licence to use our technology. This licence permits this major commercial organisation to assess and adopt the technology in order examine its application in toxicological testing and the development of drugs, with the specific long-term aim of reducing the number of animals used in such studies. Moreover, the technology is sought after to produce results that are more directly relevant to the development of products designed to treat *human* disorders or modify *human* performance. Taken together, these new directions represent a change in business practice that has arisen as a direct result of the development of BCI systems at Reading.

Commercial exploitation of University of Reading intellectual property

Reading researchers have collaborated with GlaxoSmithKline, GW Pharmaceuticals and UCB Pharmaceuticals to further their Research and Development programs by using our BCI systems in areas such as: a) the development of new treatments for drug-resistant epilepsy to the point of clinical use[7], b) identifying mechanisms by which anti-epileptic drugs act to permit development of next generation anti-epileptic treatments[7] and c) identifying mental performance enhancing components of natural products[7].

We have secured funding of approximately £1.8M [7] from GSK, GW and UCB to aid drug development research for both anti-epileptic drugs and cognitive enhancers. Crucially, the intellectual property associated with the embodied human brain cell platform belongs to University of Reading and can be licensed. The purchase of an evaluation license for this technology by GSK Pharmaceuticals and GSK Nutrition, in order to determine the active components ('nutraceuticals') of complex natural product mixtures, reflects a significant change in business practice by a multinational organisation[7].

5. Sources to corroborate the impact

1. http://www.sciencemuseum.org.uk/antenna/ratbrains
2. http://materialbeliefs.com/pdfs/materialbeliefs-book.pdf
3. http://www.bpod.mrc.ac.uk/archive/2013/5/29
4. http://www.bbc.co.uk/programmes/b02qm2sb
5. http://www.bbc.co.uk/news/science-environment-22867070
6. http://www.youtube.com/watch?v=5PWXkcm9hso
7. 11/2011-11/2013 GSK Nutrition (£235,000) *Ginsenoside effects upon spontaneous neuronal activity* PI: B. Whalley; 04/2012-04/2015 UCB Pharmaceuticals (£73,254) *The role of SV2A proteins and ligands in neuronal network activity* PI: B. Whalley ; 01/2012-01/2013 GW Pharmaceuticals (£100,000) Anticonvulsant potential of phytocannabinoids (project expansion)

PI: B. Whalley ; 08/2010-07/2013 GW Pharmaceuticals (~£976,722) Anticonvulsant potential of phytocannabinoids (programme extension) PI: B. Whalley ; 08/2009-08/2010 GW Pharmaceuticals (£140,000) Anticonvulsant potential of phytocannabinoids (project expansion) PI: B. Whalley ; 09/2007-2010 GW Pharmaceuticals (£353,000) Anticonvulsant potential of phytocannabinoids.