

<b>Institution: Aberystwyth University</b>
<b>Unit of Assessment: 11</b>
<b>Title of case study: The Robot Scientist</b>
<p><b>1. Summary of the impact</b></p> <p>This impact case concerns the stimulation of public discourse, informing the awareness, attitudes and understanding of the public as to the potential for automating science, and the consequences that then arise regarding ethics, rights and the acquisition of knowledge. It also concerns debate among legal practitioners.</p> <p>The Robot Scientist was the first system to fully automate the process of scientific investigation. This work showed that it was possible. The idea was immediately picked up by the popular press and covered worldwide (the fourth most significant discovery in 2009 according to TIME magazine, reported by TV, radio, national newspapers and magazines, and bloggers). It engaged the public in debate about AI, robotics, lab automation, and science.</p>
<p><b>2. Underpinning research</b></p> <p>This work on the automation of science encompassed the generation of scientific hypotheses, the design of experiments which would discriminate between the hypotheses, the execution of the experiments on laboratory robots, the analysis of the results and the model-update to complete the investigation cycle and feed into the next round of hypothesis generation. The work was carried out at Aberystwyth, the majority from 2004 to 2009, with some work after this date, and prototypes which were investigated before this time (our early work was the winner of the BCS Machine Intelligence Award in 2006). The following are the research areas and technologies which were brought together to make the Robot Scientist:</p> <p><b>Lab automation:</b> Our automation requirements pushed technology to limits that other laboratories still do not yet use, and industry is not yet able to provide [3.1]. We required lights-out reliable automation for on-the-fly-designed yeast growth experiments that took up to 5 days to complete, and ran in overlapping batches. To achieve this we worked with a company (Caliper Life Sciences) to specify, build and test the hardware needed. We then had to further develop software, create monitoring systems, engineer our own equipment modifications (for problems such as temperature, humidity, contamination, dessication, gripper pressure and tolerance), develop biological protocols, create user and machine interfaces, and generally perform robot maintenance.</p> <p><b>Lab information management:</b> This required the formalisation of lab protocols down to the level where they could be automated, and thus led to the creation of one of the first ontologies to express biomedical protocols, and to a discussion of the issues in formalising protocols to such depth [3.2]. The substantial relational database designed to support the automated collection and recording of far more data than human biologists collect was developed and published as AutoLabDB [3.3]. This database schema is re-usable by other automated laboratories.</p> <p><b>Models of Systems Biology:</b> Computational models of yeast metabolism were constructed and released as part of this work [3.4, 3.5]. Aberystwyth became part of an EU consortium ("UniCellSYS") to understand and model the fundamental characteristics of eukaryote unicellular organism biology, concentrating on yeast, and work is ongoing to refine the models of yeast metabolism. One of our contributions to this work was to create new hypotheses about parts of the model, and test out the results on our lab automation, providing real data to support these hypotheses.</p> <p><b>Inductive Logic Programming:</b> We made use of logic based models (using Prolog) and relational learning methods to model metabolism, to interpret the complex data produced by the Robot Scientist, and to provide automated hypothesis generation [3.5, 3.6].</p>

**Hypothesis generation:** Two methods of automatic inference were investigated in order to generate new hypothesis from the model: logical abduction and the replication of human process of reasoning (gene sequence similarity implying gene function similarity) [3.6].

**Yeast deletion strain biology:** A new method of gene deletion was investigated (and proven to work) which is amenable to automation for a Robot Scientist but does not leave genomic scars, and hence can be used to delete multiple genes, and investigate more complex genetic effects.

We brought together these strands of research to create a physical robotic system in the laboratory, which used AI techniques to produce new biological knowledge.

The research was carried out by a team at Aberystwyth, including Ross King (PI) (01/11/1996-31/01/2012), Wayne Aubrey (01/06/2009-28/02/2011), Emma Byrne (13/03/2006- 18/01/2008), Amanda Clare (01/11/2006), Maria Liakata (01/06/2005- 31/12/2012), Chuan Lu (01/02/2005-31/03/2008 (IBERS); 01/04/2008), Jem Rowland (01/06/1980-30/09/2012), Larisa Soldatova (05/04/2004- 04/04/2012), Andrew Sparkes (05/12/2005- 30/04/2011), Ken Whelan (03/12/2001-30/09/2010), Mike Young (01/11/1977- 31/08/2011) and Aberystwyth research technicians.

### 3. References to the research

#### References:

- [3.1] Sparkes, A., King, R. D., Aubrey, W., Benway, M., Byrne, E., Clare, A., Liakata, M., Markham, M., Whelan, K. E., Young, M., Rowland, J. (2010) An Integrated Laboratory Robotic System for Autonomous Discovery of Gene Function JALA 15 (1), 33-40. doi:10.1016/j.jala.2009.10.001.
- [3.2] Soldatova, L., Aubrey, W., King, R. D. and Clare, A. (2008) The EXACT description of biomedical protocols. *Bioinformatics* 24: i295-i303. Special issue for ISMB 2008. doi:10.1093/bioinformatics/btn156. REF2 submitted.
- [3.3] Sparkes, A. and Clare, A. (2012) AutoLabDB: a substantial open source database schema to support a high-throughput automated laboratory, *Bioinformatics*, 28(10) 1390-1397. doi:10.1093/bioinformatics/bts140. REF2 submitted.
- [3.4] PD. Dobson, K. Smallbone, D. Jameson, E. Simeonidis, K. Lanthaler, P. Pir, C. Lu, N. Swainston, WB. Dunn, P. Fisher, D. Hull, M. Brown, O. Oshota, NJ. Stanford, DB. Kell, R. King, SG. Oliver, RD. Stevens and P. Mendes, Further developments towards a genome-scale metabolic model of yeast. *BMC Systems Biology*, 2010; 4:145. doi:10.1186/1752-0509-4-145. REF2 submitted.
- [3.5] Whelan, K. E. and King, R. D. (2008) Using a logical model to predict the growth of yeast. *BMC Bioinformatics* 2008, 9:97 doi:10.1186/1471-2105-9-97.
- [3.6] King, R. D., Rowland, J., Oliver, S. G., Young, M., Aubrey, W., Byrne, E., Liakata, M., Markham, M., Pir, P., Soldatova, L. N., Sparkes, A., Whelan, K. E., Clare, A. (2009) The Automation of Science. *Science* 324(5923):85-89, 3rd April 2009. doi:10.1126/science.1165620. REF2 submitted.

#### Grants:

- [3.7] BBSRC BB/D00425X/1 (Robot Adam, £587289, A robot scientist for yeast systems biology)
- [3.8] BBSRC BB/F008228/1 (Robot Eve, £1029580, A robot scientist for drug design and chemical genetics),
- [3.9] SRIF2 and SRIF3 funding for the robot hardware (approx £450K and £540K for the two robots).
- [3.10] RAEng/EPSRC Research Fellowship (Amanda Clare, approx £500K, Engineering the Intelligent Scientific Laboratory),
- [3.11] BBSRC BB/G000662/1 (£100K, The Modelling Apprentice: A tool to aid the formation of cell signalling models).
- [3.12] EU FP7 UNICELLSYS (£298424, Eukaryotic unicellular organism biology – systems biology of the control of cell growth and proliferation)

#### 4. Details of the impact

The Robot Scientist was chosen as the fourth most significant discovery in 2009 according to TIME magazine. TIME stated that "In April, 'Adam,' a machine designed at Aberystwyth University in Wales, became the first robotic system to make a novel scientific discovery with virtually no human intellectual input". They went on to say that this was a "major breakthrough" and "the first to complete the cycle from hypothesis to experiment to reformulated hypothesis without human intervention" [5.1].

Our research had led to a paper in Science in April 2009. This paper described the project as a whole, the automation setup, the philosophical implications, and the new biological knowledge that had been discovered. The high profile of the journal helped to bring the paper to the attention of the media. The research group and the University also helped to encourage interest in the work by providing video, images, a detailed set of web pages, and a preprint of the paper online.

The Robot Scientist has now appeared in national newspapers around the world, including the US, Australia and Singapore (newspapers included the Times, Financial Times, Guardian, Sydney Morning Herald, Straits Times, New York Times and others [5.7]). The work has also been discussed on radio, TV, and magazines, online news sites and in technology magazines. These included the BBC, Wired, NewScientist, Scientific American, CNET, Reuters and others [5.4,5.5,5.6,5.8,5.9]. It also now has its own Wikipedia page [5.12].

To give some examples of the impression made on the public we can look at the comments they left next to online articles. The NewScientist article received 62 comments from the public, including "I've been looking forward to living through leaps in human history like this" and "This is going to speed scientific progress exponentially. Hurts my mind just thinking about the possibilities...". Comments left after the article in Wired include the concerned "Why are we compelled to build machines that do our thinking for us?... I for one am not looking to replace myself with a machine" and the philosophical "No matter how many 'scientific discoveries' these robots make, does it count until a conscious entity (for now that means us) says that it is a scientific discovery?"

The internet also produced many widely read blog posts debating the issues that are raised by the prospect of an automated scientist. The public engaged with the idea and left many comments on these blogs. While some fearful reactions were raised by the public, there was also a hugely positive response, and it would seem that the public can understand the potential for greater knowledge that can come from the automation, and that this is inspiring. An example of a comment posted following a blog post written by Ed Yong is "I love computers and robots! I really want to make these kinds of things when I graduate." [5.10]. On a forum belonging to xkcd, people wrote "This is quite awesome though" and "We need to get thousands of these to work. Bring on the singularity!" [5.11].

The work has also raised discussion amongst legal practitioners about patents. This is demonstrated by a letter to Science in 2009 by two patent attorneys and a technical advisor, which they state was directly inspired by the Robot Scientist work [5.2]. They said "As two patent attorneys and a technical adviser at a long-established Philadelphia intellectual property law firm, we read R. D. King et al.'s Report about robotic inventors ("The automation of science," 3 April, p. 85) with interest. We wonder whether the products invented by robots will ultimately become free to the public without the possibility for patent protection." The legal issue raised by the Robot Scientist regards whether discoveries made by robot can be patented and if so, by whom, or would it be necessarily patent-free and available to the public. This is an issue that could potentially be worth billions and must now be resolved. Their letter discusses current law in the US and Europe and the existing protection that it might provide. Bloggers also picked up this point [5.3].

The research has also had impact in the lab automation industry. Caliper Life Sciences, an international lab automation company with a UK office, who won the tender to produce the robot hardware, have used the Robot Scientist as a leading example of what can be done with

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automation [5.13]. The senior applications specialist for Caliper Life Sciences told us that the company could not have imagined a better marketing campaign for the future of lab automation, and as a result, sold us the equipment at a heavy discount, undercutting the opposition tenders to the point of making a loss. The Sparkes et al (2010) paper in the Journal of the Association of Laboratory Automation, which described the automation and included a member of Caliper Life Sciences as a co-author, appeared in the January issue of this journal, which was given out to more than 4000 delegates of the LabAutomation conference at Palm Springs, California. This conference is predominantly the leading trade fair, with industry-related technical talks in parallel. Again, Caliper Life Sciences were extremely pleased at this impact.

**5. Sources to corroborate the impact**

- [5.1] TIME magazine's 4th most significant discovery of 2009: [http://www.time.com/time/specials/packages/article/0,28804,1945379\\_1944416\\_1944423,00.html](http://www.time.com/time/specials/packages/article/0,28804,1945379_1944416_1944423,00.html)
- [5.2] The issues of patents is discussed in: Robot Inventors: Patently Impossible? Stevenson, et al. Science 22 May 2009: 1014
- [5.3] The issue of patents is also discussed in blog articles such as <http://www.reportergene.com/2009/05/freedom-of-robots.html>
- [5.4] BBC article: <http://news.bbc.co.uk/1/hi/sci/tech/7979113.stm>
- [5.5] NewScientist article: <http://www.newscientist.com/article/dn16890-robot-scientist-makes-discoveries-without-human-help.html>
- [5.6] Reuters: <http://uk.reuters.com/article/2009/04/02/us-science-robots-idUKTRE53167K20090402>
- [5.7] NYTimes: <https://www.nytimes.com/2009/04/07/science/07robot.html>
- [5.8] CNET: <http://news.cnet.com/robo-scientist-makes-gene-discovery-on-its-own/>
- [5.9] Wired <http://www.wired.com/wiredscience/2009/04/robotscientist/>
- [5.10] Ed Yong blog <http://blogs.discovermagazine.com/notrocketscience/2009/04/02/enter-adam-the-robot-scientist>
- [5.11] XKCD <http://forums.xkcd.com/viewtopic.php?f=9&t=37381>
- [5.12] The Robot Scientist has its own Wikipedia page [http://en.wikipedia.org/wiki/Robot\\_Scientist](http://en.wikipedia.org/wiki/Robot_Scientist).
- [5.13] Press release from Caliper Life Sciences (please contact Mike Benway of Caliper Life Sciences for Caliper's opinion) <http://www.caliperls.com/about/news-media-center/press-releases/press-release-20100121.htm>