I, scientist

Will robots at the bench leave scientists free to think?

The history of human civilization is a story of increasingly advanced technology. Ever since our ancestors began to sharpen sticks to hunt, we have invented tools and machines to make our lives easier. From the wheel to the steam engine, from aeroplanes to computers and robots, there is no aspect of human life that has not been touched and often improved by technology.

Science is no exception, of course, but the latest piece of sophisticated technology—a robot called ‘Adam’, which stands for ‘A Discovery Machine’—could profoundly change the way a lot of scientific research is conducted (Fig 1). This artificial scientist, which—like its Biblical namesake—is essentially the first of its kind, was designed to analyse data, suggest hypotheses and then carry out experiments to test them. Adam is fully automated and can run for days at a time on its own, requiring only occasional cleaning by a human technician.

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Ross King, head of the Computational Biology Group at the University of Wales’ Department of Computer Science (Aberystwyth, UK) and a member of the Adam team, said that the robot has so far investigated yeast genes of unknown function. “It’s giving us parts of metabolism which are not understood yet. So it’s automatically doing experiments, trying to find some missing enzymes in these metabolic pathways. We know these enzymes must be there, but we don’t know which genes encode them. And we’re trying to discover that,” he said, but cautioned, “We’re doing the data analysis at the moment to convince ourselves that these are correct before we try to publish them.”

Steve Oliver, another member of the team and Professor of Genomics at the

University of Manchester, UK, thinks that such machines—which combine robotics with sophisticated modelling software for data analysis and hypothesis generation—will become more widespread, especially in microbiology and drug screening. “Much more of the drudgery of science will be eliminated. It’s difficult to know whether that’s a good thing or a bad thing. If it’s drudgery that requires a fairly plodding level of thought, but nonetheless thought, then that’s a good thing,” he said. “An example of where robotics has come in to help with bad drudgery is DNA sequencing, which we used to do entirely by hand. It was bad drudgery because you really had to concentrate. You couldn’t think about other things while you were doing the drudgery.”

Adam, in an earlier, unnamed incarnation, first made the headlines in January 2004. British scientists, including King and Oliver, published a letter in *Nature* about a hypothesis-generating programme linked to automated equipment that performed experiments without human intellectual intervention (King *et al*, 2004). King said the idea first emerged in 1999 when his group was working on the quantitative structure–activity relationships of chemicals and he did not have enough chemists to make new compounds. He was already working on software to generate hypotheses, so it was a natural extension to link these programmes to machines in the laboratory and automate the process.

“What was new was to get this computer, this piece of laboratory equipment, to actually do the experiment itself,” King said. Initially, the robot worked with knockouts of known yeast genes. King noted that this first version was not completely automated but depended on humans to move plates from a reader to an incubator.

Despite this, the robot already made hypotheses about what enzyme a gene might encode and then ran tests. The researchers developed a simulator to compare the machine to human scientists doing the same work. “The robot scientist was as good as the best human and better

than the average human,” King said, adding that the machine also proposed the most cost-effective way of running these experiments—its name is also a nod to the economist Adam Smith.

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King stops short of saying that these are the first discoveries made by a robot. “I would not want to make such strong claims until I have a refereed paper to support it, and we are still analysing and checking data,” he said. Certainly, if Adam’s findings were regarded as ‘real’ discoveries, it would contribute to a long-standing philosophical dispute in computer science. According to Lady Ada Lovelace (1815–1852), a colleague of the mathematician Charles Babbage (1791–1871) who invented the analytical engine, computers cannot create anything original because they have to be programmed to do so. However, as King pointed out, “the case against Lady Lovelace is that they can be programmed to be original. But it is controversial.”

No matter the philosophical dispute, robotics and sophisticated modelling software are increasingly taking over some of the heavy routine work in areas such as drug discovery and genomics. But, according to King, machines have a much greater potential to undertake research than is currently realized. “I think if biologists are ever going to get to grips with any system that’s as complicated as even a yeast cell, it’s going to require a fantastic number of experiments,” he said. “The only way I can see this number of experiments being done is through automation. The robot scientist idea is just taking automation one step forward. It’s involving doing simple hypothesis formation, simple testing.”

For James Bischoff, Director of the Experimental Therapeutics Programme at the Centro Nacional de Investigaciones Oncológicas in Madrid, Spain, who runs a cancer drug discovery programme, the use of robotics in screening programmes is already invaluable for speed and accuracy. The robots in his laboratory can process 4,000 compounds in three hours, which would take at least one week to do manually. But he pointed out that it is sometimes easier to conduct experiments by hand rather than to programme a machine. "With robotics, some people who are really into the technology want to use it for everything," he said. "[W]e use it where it really saves us the time. We're not really interested in robotics *per se*; we're just using it as a way to do things accurately and quicker. If we could do it quicker by hand, we'd do it by hand," he said.

But it is the combination of robotics and sophisticated software that has the potential to efficiently analyse an enormous amount of data and design the right experiments. This is the point where modelling software, such as Potter's Wheel, developed at the University of Freiburg in Germany, steps in. "If you have a certain biological phenomenon and you have two hypotheses in mind that could explain this phenomenon, this software can create an experiment that helps you to best discriminate between the two hypotheses," explained Jens Timmer, a physicist at the Center for Data Analysis and Modelling at Freiburg University. "[I]n this sense, it saves experiments, but it does not replace them. It just helps you design the best one possible. Using all this modelling software is not a competition to biology but just an extension of biology."

In particular, such software is increasingly necessary to understand complex networks. "You can't figure out the dynamics of these networks by using the traditional tools of biology," Timmer said. "[I]n order to really understand, you have to put it together in the form of mathematical models and then analyse these models. Intuition is just not good enough to understand what the systems are doing."

Bischoff, however, whose 50-strong staff includes three experts in modelling and two robotics specialists, is more sceptical. "I believe the model allows you to form a hypothesis that then normally has to be tested by traditional methods," he said. "[T]he ultimate test and demonstration of the model is to show it in the real system.

Fig 1 | Adam: the robotic scientist. Bottom left: Professor Ross King, together with the original robot (Biomek 2000 liquid handler, and Victor plate reader in the background). Bottom right: The original laboratory robot used for the initial rediscovery task and for the subsequent genuine discovery task. From January 2006, the main functions of this robot will be performed by a shiny new automated laboratory (main image). The original robot will then be used in a project investigating how the production of multiple-knockout yeast strains can be automated. Reproduced with permission from Ross King, University of Wales, Aberystwyth. © University of Wales, Aberystwyth, UK (www.aber.ac.uk/compsci/Research/bio/robotsci/).

We used models to generate hypotheses in order to test our systems. We don't just generate models and then validate the models electronically in the computer. We validate them in our experiments."

If software and robotics will take over the 'grunt' work in the laboratory, data analysis, experimental design and hypothesis generation, what room is left for human scientists? Oliver does not think that machines will replace humans at all. "The scientists don't have to worry about that any more than anybody did about disappearing from offices as soon as there were computers," he said. "The pattern of work is going to change. I think it's already changing. People are spending a lot more time analysing their data with the computer than actually generating it. That will become even more true."

...the advent of modelling software and robots in the laboratory could have interesting consequences for human-computer interactions

In fact, Oliver feels that there is a growing need to delegate routine work. "Increasingly, scientists are too busy and not spending enough time thinking," he said. Even so, the advent of modelling software and robots in the laboratory could have interesting consequences for human-computer interactions. "There will be some laboratory members who get instructions to do experiments from a robot rather than a principal investigator. It's going to be something that will be very difficult to deal with psychologically and sociologically," Oliver said. "Equally, the principal investigators will have to get used to the fact that their whole thinking process is going to be an interplay between them and the computer

to design experiments. A lot of psychological and sociological adjustments will have to be made by scientists on all levels."

Eberhard Krauß, head of the High-Throughput Technology Development Studio at the Max Planck Institute of Molecular Cell Biology and Genetics in Dresden, Germany, also thinks that automation and modelling will certainly change the nature of research jobs. "People will need a different profile. The modern biologist not only observes, but he also needs computer skills, programming skills," he said. "I grew up with frogs and toads and running through woods and collecting wild animals and describing them. Now I'm completely in informatics."

"Maybe it's just something that happens from time to time when biology undergoes a major shift and needs to draw upon additional expertise and additional conceptual approaches," Oliver said. "People from mathematics and physics and computer science and the engineering disciplines are being attracted to biology at the moment. On the other hand, you could say that sort of process happened also in the 1950s, when a lot of people came out of the physical sciences into biology and founded molecular biology."

However, even as biology becomes more of a 'dry science', Oliver feels that there will always be a need for students to do the traditional 'wet' legwork. "One of the major constraints now, in my thinking, [of] using yeast as a model is that we know remarkably little about the ecology of these organisms," he explained. "We've come a point where we've pushed laboratory experimentation an awful long way. If we had more insight into the natural history of the organism, we'd be able to design better experiments." Bischoff agreed that the move towards more automation could even boost the demand for human scientists. "I think the more we use robotics and modelling, the more there is a need for

traditional scientists because we generate so much data and so much information that can only be validated by scientists working at the bench," he said.

"The main focus for scientists or biologists is to think and not to perform the experiments"

James Collins, Professor of Biomedical Engineering at Boston University (Boston, MA, USA), also believes that, in the end, you need human ingenuity and creativity. "I've not yet seen that robotics will step in and make a difference in terms of the creative process, where you're going to look at a small number of situations, or try to find the exception or insight into something special," he said. Accordingly, he still sees a crucial role for humans. "Frankly, most of the interesting things that happen come from the unexpected of somebody assessing an apparent mistake or what might be deemed uninteresting or not central and then following up on it. I'm sure you can probably programme machines and use robots to do the same. I haven't seen it yet."

As Krauß pointed out, it is humans who analyse the current knowledge and develop new models, hypotheses and ideas, and plan the next step of the experiment. "There are a number of advantages to using automated aid, but for me the scientist is the brain, not the hands," he said. "The main focus for scientists or biologists is to think and not to perform the experiments."

REFERENCE

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