Bioscience research supports UK equipment manufacturers

Partnerships between UK researchers and equipment manufacturers aid the UK scientific instrumentation manufacturing sector and enable academics in the UK to address cutting-edge research questions. Such interactions helped create the best-selling protein crystallography robot in the world, developed a new sample cell for a technique called linear dichroism, which is now a commercial product, and encouraged manufacturers to make changes to software which have since been incorporated into commercial products, providing on-going feedback on their latest technologies.

"The UK is a great place for the development of pioneering instrumentation in terms of science... it's crucial to maintain it," says Dr Marek Brzozowski from the York Structural Biology Laboratory (YSBL) at the University of York[1].

A 2007 report found that the UK's scientific instrumentation sector was worth around £7.5Bn in 2006/07[2]. The strength of this industry depends in part on collaborations with UK academics and, for the biosciences, particularly those funded by BBSRC.

Modern instrumentation is essential to research activities. "We can't do good research without high quality equipment," says Professor Alison Rodger, Director of the Warwick Centre for Analytical Science at the University of Warwick. As a result, academic researchers often work with industry to ensure their equipment is at the cutting edge, allowing them to address new research questions and collect more, and more detailed, data than ever before.

For industry, such collaborations help them develop new products, test their equipment on the latest research challenges, and get expert feedback which allows them to make modifications and improvements to meet customers' needs. According to Rodger, "Research Councils are facilitating innovations that industry won't do."

In particular, the instruments needed to push the boundaries of scientific research often have to be adapted and improved beyond what is available 'off the shelf', resulting in unique pieces of equipment. This is only possible through strong partnerships between academics and manufacturers. Academic involvement in R&D also demonstrates to industry the continuing need for their equipment, ensuring they retain the people and skills required.

Between 2002 and 2007 BBSRC ran the Research Equipment Initiative (REI), which provided grants for researchers to buy 'mid-range' equipment[3]. Many academics took the opportunity to use REI funding to work with manufacturers to improve their existing equipment or develop entirely new instruments. The scheme required academic applicants to secure a commitment from an external partner such as an equipment manufacturer.

The examples here illustrate how BBSRC funding for research equipment has played an important role in developing products and opportunities not only for the academics who were funded, but also for collaborating companies.

Examples of Impact

UK company TTP Labtech has sold almost 500 Mosquito protein crystallisation robots to researchers in the UK, Europe, the USA, Japan, China, India and elsewhere. The robot was designed with input from BBSRC-funded researchers at the York Structural Biology Laboratory.

A sample cell and instrumentation for linear dichroism spectroscopy, designed by researchers at the University of Warwick with the help of REI funding, was built by Jasco UK Ltd and Crystal Precision Optics in Rugby, UK. The cells have been made available commercially by the researcher's company, Dioptica Scientific Ltd

Instrument manufacturers Molecular Device Ltd have incorporated changes to their commercial software based on the requirements of University of Cardiff researchers supported by BBSRC. The researchers continue to provide input on the latest automated microscopy technology designed by the company, helping them make decisions on product direction.

Further Information
In February 2012 BBSRC published an evaluation of the Research Equipment Initiative, which includes other examples of collaborations between equipment manufacturers and researchers. It can be found at: http://www.bbsrc.ac.uk/organisation/policies/reviews/funded-science/1202-rei-evaluation.aspx

"They were very keen to listen"

In the 1990s, Dr Marek Brzozowski was looking for a protein crystallisation robot to improve the efficiency and reduce the manual labour required to crystallise proteins, a vital step in any structural biology research. "We were trying to find something useful on the robots market, at the very beginning of the use of robots for protein crystallisation, so there was no real user-friendly and affordable robot developed," he says.

The market leader at the time had no interest in collaborating with users to understand what they needed from a protein crystallisation robot, and few other companies were working on this technology. "Then I found a small company [called TTP] in Cambridge who were doing robots for liquid handling, but they were very keen to listen to users and to develop this type of robot which would be best for the market and for protein crystallisation," says Brzozowski.

He added, "Very quickly we improved the software and the hardware with them... and they presented a prototype which we used. This prototype [called Mosquito[4]]... is now the best selling model of crystallisation robot in the world."

Joby Jenkins, from TTP Labtech[5], says, "We've sold near enough 500 units. It's had a huge impact on our business."

"Every laboratory, every person who is dealing with structural biology, has to grow crystals and has to use some equipment to grow crystals," explains Brzozowski. A robot reduces the manual labour involved in the process, freeing researchers' time for other work. It is also more precise and uses a smaller sample of protein, which is particularly important for proteins that are hard to isolate in large quantities, including many human proteins.

Yet before Marek contacted TTP, the company hadn't thought about developing a protein crystallisation robot. "We were in the process of developing a nanolitre pipetting instrument," explains Jenkins. "We hadn't given protein crystallisation a second thought. That's when Marek and the YSBL got involved."

Image caption here

"Fortunately the technology we had developed was extremely well suited to the application... we did tailor the user interface aspect of the software and hardware and developed a few peripheral items to tailor it to that application, based on advice from Marek and YSBL users. Then we had a beta unit which we sold to them at a low price to road test it. That was fed back to us and we made a series of design improvements and changes."

Jenkins adds that one of the reasons it's been so successful is that it is so intuitive and easy to use. "A lot of that credit goes to [Marek and colleagues] explaining to us how to design it in that way."

Brzozowski puts this success down to the willingness of the company to work with academic users. "I think this is because we came up with a very practical approach; they were working very closely with us, and they were listening to us and implementing everything."

Jenkins agrees that they definitely helped. "They came along at the right time and guided us. It was pretty important."

When Brzozowski bought a new, more advanced Mosquito model from TTP using funding from the REI, he received a significant discount in recognition of the help he had given to develop the equipment.

Since then, Brzozowski has continued working informally with TTP Labtech, which is leading to new ideas and advances in equipment technology. "This type of personal contact, and maintaining people and interest to do things is crucial, because now if I have an idea in this direction I know where to go."

Other researchers who received REI funding have also established strong partnerships with equipment manufacturers, providing constant feedback on their

equipment and help them design new products. "Every time the engineer comes we take some step forward in instrumentation and instrumentation design," says Professor Alison Rodger.

"It's a constant dialogue between us that works really well, because of the complementary nature of their instrumentation expertise and our knowledge and skills." she adds.

Such relationships also have clear benefits for the researchers, allowing them to access the engineering expertise of manufacturers. According to Dr Rachel Errington, Reader in Biomolecular Imaging and Systems Cytometry at Cardiff University, "If you have a good relationship with a manufacturer you get the best of both worlds – the nimbleness and flexibility to make changes [to the equipment], but also the robustness you need."

"A great sounding board for new ideas"

Feedback and collaboration with academics also provides equipment manufacturers with the information they need to improve existing products to meet the needs of their customers. For instance, working with Dr Rachel Errington at Cardiff University, equipment manufacturer Molecular Devices (UK) Ltd developed new software to allow Errington to incorporate a spectral imaging camera with their microscope configuration. It also enabled Errington to link the camera to acquisition software from a different manufacturer to process the data.

The new capability has since been incorporated into different products sold by the company. "This link between our software, Metamorph, and the third party software was a new thing for us which, without Rachel, we wouldn't have developed," says Dr Emma Robertson, Imaging Account Manager at Molecular Devices (UK) Ltd.

"We'd been discussing our aspirations and functionality for the instruments, which were, and still are, quite unique," says Errington. She used an REI grant to update and expand their imaging and microscopy equipment so they could carry out dynamic high-throughput cell assays. Importantly, they needed to embed their spectral imaging camera with the new microscopes.

As Errington needed more than just off-the-shelf functionality, they asked the research and development team at Molecular Devices to write new software, including a driver for the camera and a dynamic data exchange application. This would allow the Molecular Devices microscopes to share data from the spectrum imaging camera with processing software from a different manufacturer.

"It was a two-part development," explains Robertson. "It was the specific camera driver for the specific camera Rachel wanted, but it was also the more general second application that helped Rachel do what she needed to do. Off the back of that, it's also now a function other customers find useful."

"That's obviously of great benefit to other customers as well... it's not just specific to that camera, but can be opened up to other third party software," Robertson adds.
The collaboration between Errington and Molecular Devices has since extended beyond the REI funding. Errington regularly travels to Molecular Devices to use their high-content imaging equipment, and to look at how high content cell-based assay capability and novel image analysis can be advanced. This provides valuable feedback which Molecular Devices can incorporate into future equipment.

"What we're looking to have is a good solid product that does what the researchers need it to do," says Robertson. "Rachel has always been a great sounding board for new ideas, and she's always been eager to provide feedback to us. That's a real advantage when trying to make decisions on product direction," she adds.

What was the Research Equipment Initiative?

The Research Equipment Initiative (REI) provided funding for researchers at UK Higher Education Institutions and Independent Research Organisations to purchase and install mid-range (£50K to £500K), multi-user, multi-project equipment.

It aimed to enable high-quality research and to promote sharing of equipment and partnership between departments, institutions and external sponsors of research

Applications also needed to include funding for the equipment from external partners.

Over the course of the initiative, BBSRC's REI funded 221 grants with a total value of £29.6M.

"Something that didn't exist before"

Working at the cutting edge of research, scientists often have unique requirements for instrumentation. However, most do not have the technical engineering expertise required to turn their ideas into dependable instruments. Professor Alison Rodger[6] used an REI grant[7] to support her work with equipment manufacturers Jasco UK[8] and a small engineering company Crystal Precision Optics[9] to create a new sample cell and to adapt Jasco's spectrometer to accommodate it. The sample cell allows Rodger to use much smaller samples for a technique called linear dichroism, which can determine the structure of certain molecules and membrane systems.

"We pulled lots of ideas together to create a new instrument that does something that didn't exist before," says Rodger. She has since set up her own company, Dioptica Scientific Ltd, to make their unique cells available to others interested in using similar methods. "The cells we've made are not available anywhere else," says Rodger.

Linear dichroism uses polarised light to study the structure of protein fibres, DNA and membrane systems that can be aligned in a flow. "It's particularly good for the molecular assemblies that are not amenable for NMR or X-ray crystallography -- which are the techniques you'd choose because they give atomic-level resolution. Linear dichroism doesn't give such good resolution, but it gives us the data more quickly and easily, and it works on systems on which [NMR and X-ray crystallography] don't work," explains Rodger.

To build and use the cell, Rodger first had to work with Jasco UK, who supplied the spectrometer, to adapt the software it used: although the equipment had the potential to measure what Rodger wanted, the software had to be recoded to allow it to detect it. "They reconfigured the instrument for us in ways that weren't quite normal," says Rodger. "The actual spectrometer, as it is configured, is still probably unique in the world."

The Jasco engineers then worked with another company, Crystal Precision Optics in Rugby, to design the sample cell and a mounting to go on the instrument.

The new cell allows Rodger to use much smaller samples for analysis, making it easier to study biological systems where it can be difficult to isolate large quantities of the molecule or system being investigated. "We have developed quite a number of new flow methods," explained Rodger. "What they let us do is reduce the sample volume significantly."

"We've taken the sample volume down by three orders of magnitude, which doesn't sound stunning but it's opened up possibilities," she adds. "The other development we've made with that instrument is cutting the timescale down," Reducing the amount of time it takes to place the sample into the spectrometer and start data collection allows Rodger and colleagues to study, as they occur, reactions that take place very quickly.

Rodger has since continued to work with Jasco UK. "We have been named 'The Jasco Centre of Excellence in Polarized Light Spectroscopy' and host visitors to our equipment for Jasco UK Ltd," Rodger adds.

Other benefits of industry-academic collaborations

Collaborations like this help sustain and nurture the UK's strong and innovative scientific instrumentation sector, ensuring academics and manufacturers remain at the forefront of scientific discovery, technical innovation and commercial opportunities.

Demonstration sites

Brzozowski's laboratory was a demonstration site for TTP Labtech's Mosquito robot. By volunteering their laboratories as demonstration sites for specific pieces of equipment bought through the REI, academics secured discounts and regular equipment servicing from manufacturers. In return, manufacturers could use the equipment in the demonstration site to show new customers how the equipment was being used in a real-world setting.

Training

Manufacturers often contributed to training courses run by their academic partners. "Every year a couple of the Jasco people come to the circular dichroism and linear dichroism workshop I run at Warwick, with colleagues from around the UK, and they contribute to the training," says Rodger. Rodger also visits Jasco UK to provide training for new customers and engineers. In return, she receives a discount on instrument servicing.

Similarly, Robertson and colleagues from Molecular Devices run a session on a training course run by Errington; "Rachel's involved in running an imaging course, so we're going to be running one of the sessions there, talking about high-content imaging, teaching, doing hands-on workshops and lectures," Robertson says. "It's spreading the word about the technology to educate the up-and-coming [researchers]," she adds.

References

1. See: http://www.york.ac.uk/chemistry/research/ysbl/

2. UK scientific instrumentation sector: https://connect.innovateuk.org/c/document_library/get_file?uuid=59ffbe03-8e62-467b-819b-7660297e888c&groupId=230986

3. i.e. equipment in the £50K to £500K price range.

4. See: http://www.ttplabtech.com/products/mosquito/

5. See: http://www.ttplabtech.com/

6. See: http://www2.warwick.ac.uk/fac/sci/chemistry/research/arodger

7. See: http://www.bbsrc.ac.uk/pa/grants/AwardDetails.aspx?FundingReference=REI20503

8. See: http://www.jasco.co.uk/

9. See: http://www.crystal-optics.u-net.com/home.htm