

CASE STUDY



Collaborative Automation Development Delivers Industry-Wide Modularity and Flexibility



Automation Accelerates Innovation

AstraZeneca is world class when it comes to developing advanced, life-changing pharmaceutical and biopharmaceutical medicines.

One of the crown jewels supporting AstraZeneca's research mission is the Discovery Centre (DISC), located in Cambridge, UK.

This drug discovery and development hub is occupied by over 2300 people who collaborate, interact, and most importantly, identify therapies that can improve patient lives.

A Gem of An Idea



“The automated devices on the old HTS platforms had to be shielded for safety requirements, so basically viewed as impenetrable boxes.”

Helen and Darren Plant work in the High Throughput Screening (HTS) Group at AstraZeneca as Associate Director of the HTS Automation Team and High Throughput Screening Associate Principal Scientist, respectively. The high throughput screening team is responsible for delivering critical compound screening data to both internal AZ projects and also to collaborations with external academic partners. In 2013, when the vision for the DISC was in its infancy, Darren and his colleague, Paul Harper, were tasked with designing new high throughput screening systems.

As they had scope for a complete redesign, they identified several key requirements to enable the AZ HTS group to continue to deliver a wide range of technologies to the business. One of these was flexible & adaptable automation platforms, as the ability to quickly reconfigure systems to screen the next project would be vital to meet portfolio timelines. Another important aspect for

any new automation was to make it as accessible as possible for users to interact with equipment on the platforms, for teaching, error recovery etc. “The automated devices on the old HTS platforms had to be shielded for safety requirements, so basically viewed as impenetrable boxes,” recalls Darren. “Even though the shielding was meant to protect users, it gave many scientists the impression of something scary, imposing, and dangerous.” Scientists weren't keen to use the automation despite the known benefits of automated workflows.

In taking on the new system design project in tandem with the DISC site construction, Paul, Darren, and Helen, decided that half of the new systems would be implemented as soon as possible in AstraZeneca's Alderley Park facility, where other screening equipment had been consolidated. The other half of the new systems would be held and installed in the DISC labs once the facility's labs were constructed.

A Step Forward in Automation Design

The first step in the new high throughput screening system project was to identify goals. First and foremost, the new solutions needed to push beyond the boundaries of existing automation technologies. This meant avoiding off-the-shelf products with narrow capabilities and lifetimes. The ideal automation partner would work with the team to craft something radically novel. Flexibility & modularity were important concepts to be incorporated into any new automation systems.

Second, the system had to be compact. Maximizing value per square meter allowed for future growth and expansion while keeping efficiency top of mind.

Third, the automation software had to be robust and reliable, and also accommodate the very precise timing requirements necessary in high throughput screens. Any delay in the software could impact operations and waste precious time and reagents.

The final goal was more of a push-the-envelope experiment. At the time, the team was very aware that all large-scale lab automation in the UK were shielded, but they wanted to find a way to close the gap, both physically and metaphorically, between the scientists and the automated systems. To do so would encourage use without fear but had to be done without compromising UK safety requirements.

AstraZeneca HTS Automation Goals

1

Push beyond the boundaries of existing automation technologies

2

Reduce hardware footprint

3

Robust and reliable software

4

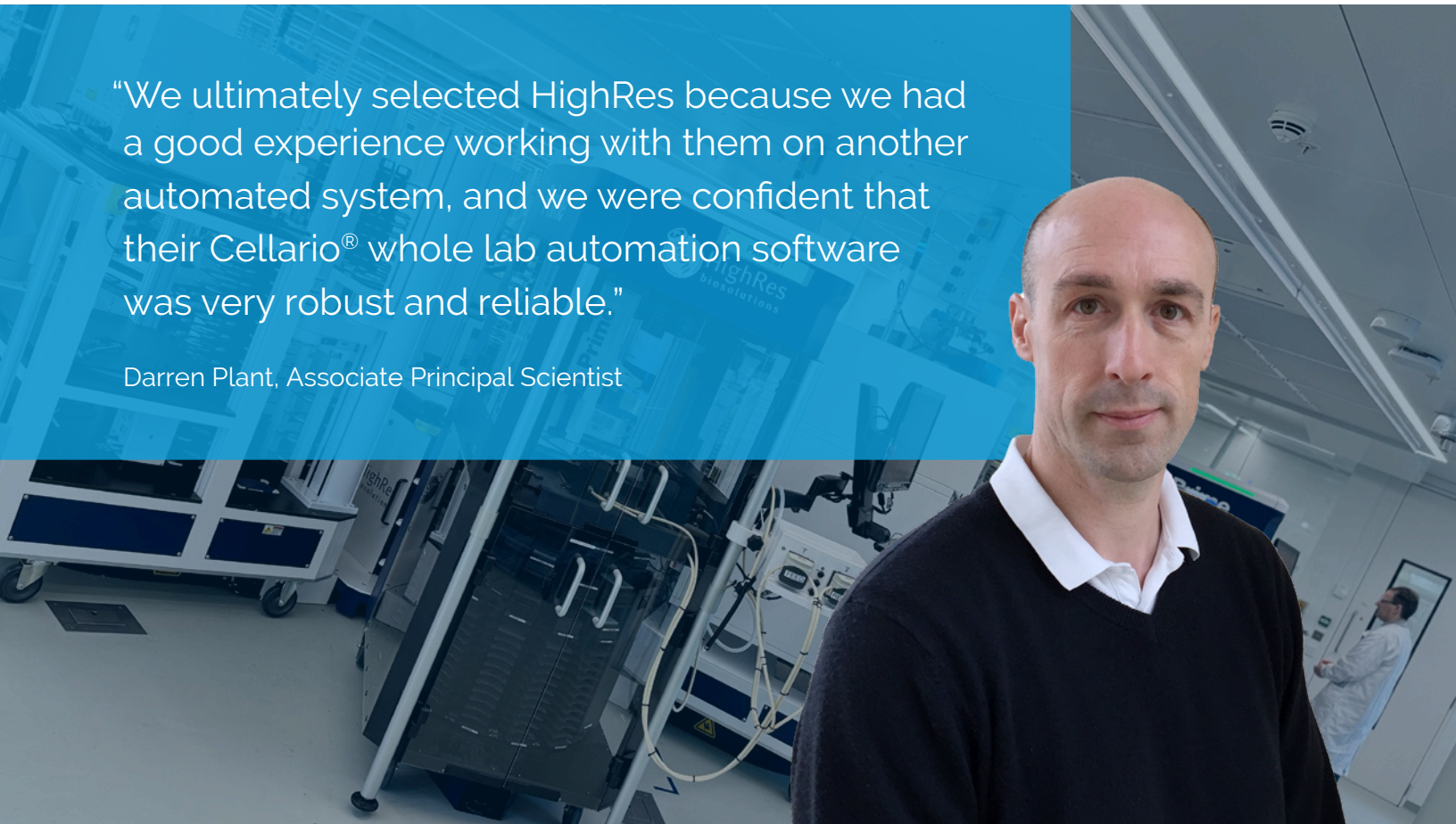
Remove shielding

They were also mindful that AstraZeneca's compound management team was rebuilding their automation system at the same time. Although this was part of the overall DISC project and the two groups shared a joint budget, the decisions were made in parallel to build a joined up, end to end capability.

Connecting with HighRes

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Darren Plant, Associate Principal Scientist



When it came to finding the right automation provider, the decision was relatively easy. “We ultimately selected HighRes because we had a good experience working with them on another automated system, and we were confident that their Cellario® whole lab automation software was very robust and reliable,” Darren says.

The HighRes team eagerly dug into the project. Cellario software evolved to incorporate a list of desired features from the AstraZeneca team. Hardware was adapted, too. Five large robotic work cells were fabricated; each with a central

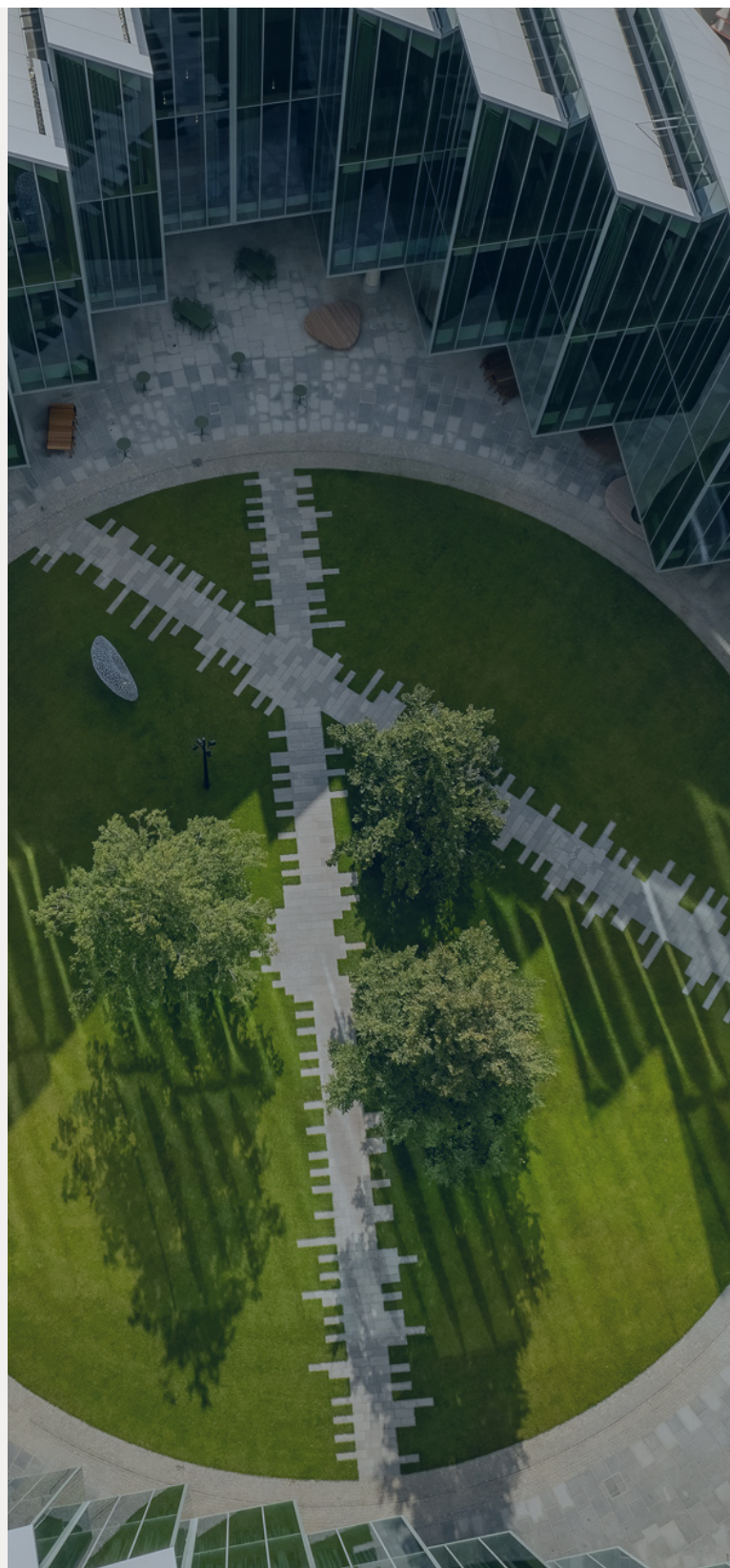
Kuka robot mounted on a six-sided CoLAB base. The robotic arms were equipped with safe operation software to protect users from harm while bypassing the need for bulky shielding. Each CoLAB base included five Nucleus® MicroDock™ docking stations to integrate enabled cart-based or standalone devices easily and quickly without having to reattach positions or reconfigure power, data, and utility connections.

The most novel development in this project opened an unprecedented frontier in life science robotics.

Reaching New Heights in Automation Innovation

The joint team envisioned automation platforms where devices could be introduced to and removed from a workflow as needed. This HighRes innovation is now known as the Nucleus FlexCart™ and is available to any life science lab. Here, mobile carts are each equipped with docking technology and a Precise ACell robot. Shelves in the FlexCart vertically house equipment to minimize lab space, and the robotic arm moves around radially and vertically to reach any device on the cart or in proximity. FlexCarts were also equipped with safe operation software to meet UK safety requirements without incorporating physical shields.

At AstraZeneca, FlexCarts are also configured together on smaller semi-automated bays to support simpler HTS assays. Two FlexCarts can be connected via two MicroDocks, with one ACell robot handing plates over to the other FlexCart. For example, one Dispenser FlexCart with liquid handling equipment for reagent additions, is combined with a Reader FlexCart that houses microplate readers to read the assay plates at the end of the protocol. These semi-automated bays can be reconfigured very easily by simply undocking & redocking different FlexCarts. This flexibility allows varied FlexCart combinations to be paired depending on the screening technology and desired sample throughput.



The Impact of HighRes Automation Today

With half of the new HighRes automated systems temporarily installed at AstraZeneca's Alderley Park facility, the HTS group and scientists were able to familiarize themselves and debug the systems before they were permanently installed, along with the rest of the HighRes automated systems at the DISC facility.

"I'm really proud to have seen this project evolve from concept to an actual platform that has delivered millions of screening wells in the lifetime that we've had it so far," comments Helen. "And to know that our automated systems will help us to identify chemical equity that will improve patient lives is very humbling."

Anyone involved with AstraZeneca's high throughput screening can be confident that every compound, in every well and every plate, is treated identically so that results can be compared. As the bridge between engineering and science, Helen's team is empowered to write custom Cellario scripts for enhanced agility and reliability in the screening process and to train scientists on basic script creation. Gantt charts and flow gates help to visualize the movement and timing of a run before precious reagents and samples are used and can even be reconfigured in the middle of a run.

Helen is also delighted with the mindset change from the perspective of scientist interactions, noting, "Scientists now often ask, 'Can I automate


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this assay?' whereas previously they might have asked, 'Do I have to automate this assay?' when our older automated systems were in place."

Even error recovery is well managed in Cellario software. Scientists are trained to handle simple error recovery themselves, and Helen's team is brought in to resolve more complex situations. The experiment to remove physical shielding around the systems proved successful. Gone is the fear of breaking equipment or potential harm. Fear and apprehension are replaced with confidence and an eagerness to unleash the imagination on what's now possible using the HighRes automated systems and FlexCarts. Fully automated high-throughput screens of up to 1.8 million compounds now routinely take place in 1536-well format microplates, and some screening times have been significantly reduced.

Embedded Expert Support Further Enhances the Experience

In addition to the HighRes hardware and software, the AstraZeneca HTS group took advantage of second-to-none HighRes expertise. In the DISC HTS lab a dedicated HighRes support engineer is embedded full time, working with the AstraZeneca automation specialists on Cellario and the automated work cells. This expert assists with everything from quick fixes to complex coding and everything in between. Helen and Darren agree that this extra measure has been a huge help and success.



"From a sustainable point of view, I appreciate that we are reusing something rather than throwing it away and starting again."

Helen Plant, Automation Team Associate Director

Next Steps in the Automation Journey

As the quest to discover new medicines will never stop, neither shall the HTS group's automation evolution.

Helen says, "Now that we've got our automation platforms together, we can reach out to groups outside HTS to maximize the value of our automation and use the real estate even more effectively." The automated HighRes systems are easily reconfigured with devices to suit any

assay and programmed to run unattended or overnight in response to an increase in demand. She adds, "From a sustainable point of view, I appreciate that we are reusing something rather than throwing it away and starting again." Darren is aiming towards more speed to process more plates and compounds and facilitate specialized complex biology.

Conclusion

HighRes Biosolutions automated systems, including the ground-breaking FlexCarts, are now an integral part of high throughput screening operations at AstraZeneca. Screening data on two recent automated projects has demonstrated high repeatability that would likely not have happened in a manual format, increasing the possibility of finding a drug.

As visitors visit our lab, they are impressed when they watch any of the automated HighRes systems in action. The visual appeal of the automated systems, with plates and arms moving here and there in the workflow, is a delight. But more importantly, as Helen notes, "It also ties people more closely to the idea that we're doing something really big, not just in the lab, but as a company."



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