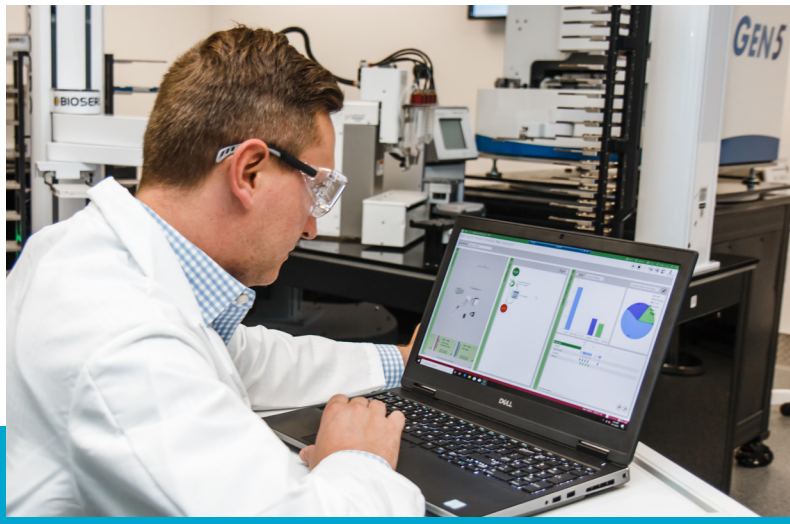


Pharmaceutical Manufacturers Accelerate Drug Discovery with Automated LC/MS Workflows

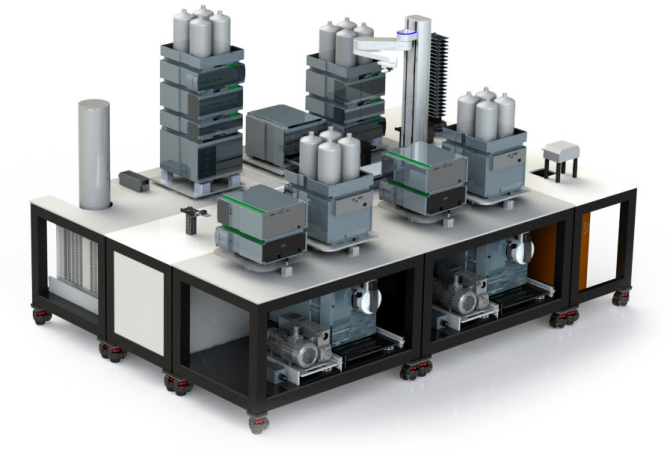
By David Dambman, Director of Engineering, Biosero

One in three adults worldwide has multiple chronic conditions. The Center for Disease Control predicts cancer cases will increase by 24% between 2010 and 2020. Patient lives depend on new drug discoveries and continuous improvement of existing treatment options.

Pharmaceutical manufacturers play a vital role in the health and well-being of people worldwide. The pressure is always on manufacturers to expedite innovation in the drug discovery process and discover a cure or develop drugs that address specific disease states. The faster companies introduce new drugs to the market, the greater the benefits for patients and drug development companies alike. How can manufacturers accelerate tedious and lengthy drug discovery processes while controlling the cost of drug development?

Automation creates efficient, cohesive lab ecosystems

Despite many technological advances, laboratory research equipment is still fragmented and pharmaceutical manufacturers remain dependent on manual labor. Equipment and instruments are often from multiple original equipment manufacturers (OEMs) and lab operators spend most of their time shuttling samples from station to station, troubleshooting errors and collecting data from multiple instruments and workcells. Because a scientist's time



Seamless integration and full automation of a liquid chromatography and mass spectrometry (LC/MS) workcell can be tricky. A dozen or more individual pieces of equipment can make up one workcell. Automation scheduling software automates LC/MS workflows to shorten cycle times, handle error recovery situations and provide more rapid result analysis to help pharmaceutical manufacturers iterate faster and accelerate the drug discovery process.

is consumed with following protocols and managing each step of a process, it's challenging for them to capture and audit each workflow thoroughly. The lack of data and information about a protocol contributes to the lack of reproducibility in experiments.

Scientists must repeat research experiments hundreds of times to identify the compounds that will serve as the foundations for drug development. This requires highly repetitive laboratory tasks and the analyzing of substantial amounts of data. If done manually, it can take weeks or even months to determine which compounds to abandon or develop further. With every experiment, the goal is to obtain reliable results consistently. The longer a cycle takes, the more data it generates and the more difficult results are to replicate. Innovative automation can eliminate the variability introduced by humans and improve the drug discovery process.

These days progressive pharmaceutical scientists who are on a mission to discover new drugs for diseases and treatments look to leverage breakthroughs in automation, artificial intelligence (AI), machine learning (ML), Internet of Things (IoT), big data and robotics to expedite the drug discovery process.

Expediting the path to high-quality drug candidates

Pharmaceutical researchers seek the quickest route to finding high-quality drug candidates, the compounds that will have the right effect for a patient with specific disease states. The quicker researchers can cycle through the compounds — the faster they will discover new drugs that save lives. The shorter the cycle times, the more quickly pharmaceutical researchers can iterate and find the right compounds for new drugs.

Liquid chromatography and mass spectrometry (LC/MS) have become an essential method to support preparative and analytical research applications. The LC/MS method is useful because it can analyze large volumes of material with specificity and sensitivity. Preparing samples for these technologies requires hundreds of steps, leveraging several pieces of sophisticated instrumentation and multiple sample transfers. LC and MS devices are inherently incompatible and thus highly manual and dependent on large teams of lab technicians to execute the workflows when used in tandem.

To accelerate drug discovery, lab automation is critical. New hardware and software are now available to integrate steps of the LC/MS process

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autonomously. An effective and well-implemented laboratory automation design will:

- Achieve around the clock, 24/7 operation to expedite discovery
- Minimize software hang-ups and hardware malfunctions to maximize uptime
- Increase lab technician walk-away time so they can manage more platforms at once and make better decisions by analyzing the increased data output

Seamless integration and full automation of an LC/MS workcell can be tricky. A dozen or more individual pieces of equipment can make up one workcell. Individual workcells may be required for each step of the evaluation process. Each device in a workcell might be made by a different manufacturer and come with its own operational software, as well as with its own promise of integration. Once these workcells are built up in the laboratory, many automation engineers find that the equipment simply won't work together.

Biosero, a company with a long history in the life science industry, has developed a software solution to address this quandary. Green Button Go Automation Scheduling Software is a device-agnostic software suite that integrates any manufacturers' equipment, automating workcells to complete application processes unattended.

The software supports a vast library of device drivers, as demonstrated in **Figure 1**, each designed to connect a specific piece of lab equipment, such as a: robotic arm, scanner, liquid handler, washer, centrifuge, incubator or reader.

Software hang-ups and hardware malfunctions stymie complex workflows

Although an LC/MS workcell can generate high-value chemistry analysis, running the process is not without headaches. When running a complex workcell with the amount of equipment an LC/MS method requires, the software can get hung up. When that happens, a technician needs to slow or halt the process to troubleshoot the problem, or worse, manually restart the whole process. Not only does this stall the progress of discovery, but it also increases the risk of sample processing errors.

Due to high sample volumes that circulate through a preparative system, the purification columns can frequently clog, impeding the workflow and requiring intervention by researcher or scientists to manually unclog columns.

No matter how cutting edge the equipment, an LC/MS workcell with no automation platform still requires human intervention to shuttle plates from station to station and troubleshoot errors. This limitation restricts the platform to operate during the eight-hour workday, only when lab technicians can be present. Unautomated systems also supply fragmented data, requiring a lot of manual curation and analysis.

Automation software creates a fluid ecosystem for LC/MS methods

The cure for the prevailing operational hang-ups of LC/MS systems is automation. Green Button Go software automates LC/MS workflows to shorten cycle times, handle error recovery situations and provide more rapid result analysis to help pharmaceutical manufacturers iterate faster and accelerate the drug discovery process.

With Green Button Go automation scheduling software, pharmaceutical manufacturers can integrate and accomplish full-length LC/MS processes. Multiple LC/MS units, in single or multi-unit workcells, can be employed to perform various sample processing tasks at the same time.

For instance, robot arms can move along a track and provide tubes or plates to units simultaneously for sample preparation and analysis. The software can also monitor and adjust sample storage temperatures to ensure sample integrity. Maintaining the appropriate temperatures ensures high-quality and reproducible results and saves costly hours recreating compounds that would otherwise be lost.

Once processes are complete, lab techs can review data logs stored in the Green Button Go dashboard to see if any errors occurred and how those errors were mitigated to complete the run. They can also monitor the data in real-time as samples are processed, demonstrated in **Figure 2**.

The software allows multiple copies of instruments in a workcell to operate in a pooled configuration. This parallel processing of samples increases system throughput dramatically and minimizes downtime. In this scenario, Green Button Go can identify software or hardware issues and automatically address them by using only the functional components in the workcell to keep the laboratory processes moving.

If the software identifies an error on one LC/MS platform that is not correctable in real-time, the software triggers the system to unload all of the affected samples and re-queue them for processing on another LC/MS workcell. The robotic arm removes all affected samples from the disabled instrument, puts them into storage, and reschedules them to run on the other LC/MS automatically — all without human intervention.

The last barrier to full LC/MS automation was achieving a seemingly simple task humans do every day at home or work — opening and closing a drawer. Up until now, humans have been essential to opening the drawers of most LC/MS autosamplers — the last barrier to full LC/MS automation. Controlling a robotic arm to transfer plates from a feeder to a reader is easy. However, commanding the same robot arm

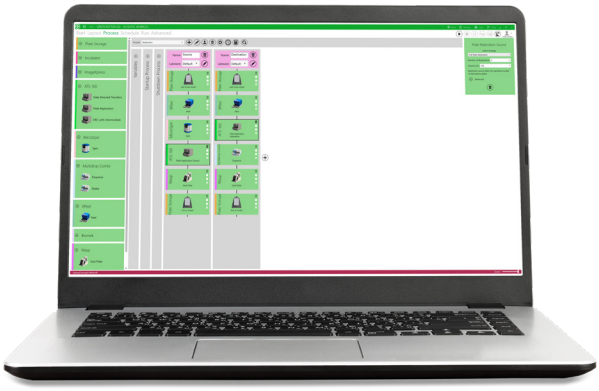

Figure 1
Layout – Easily arrange instruments in the layout to configure your workcell.

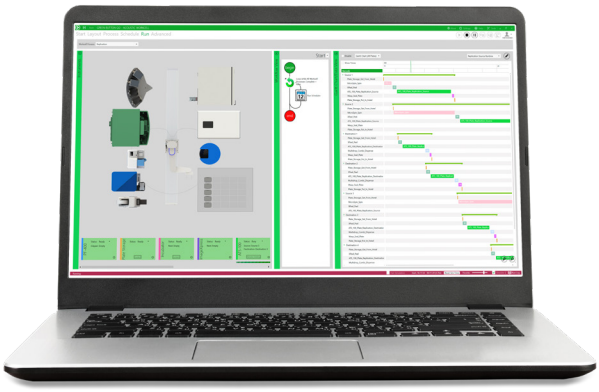

Figure 2
Process – Drag and drop instrument steps into the workflow to define your process.

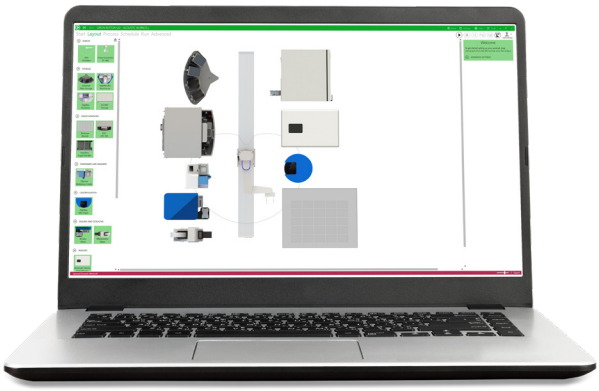

Figure 3
Run – Monitor the execution of the workcell at runtime.

conduct the refined movements of opening and closing the door — that takes innovation. Using a unique gripper and a device driver developed by Biosero, a robotic arm can now open an autosampler door, place plates inside, and close the door, achieving full LC/MS workflow automation, as shows in **Figure 3**.

Automation scheduling software can also resolve clogged columns, typically an operation-ending problem for chromatographers. If the software detects increased pressure in a column, it will automatically trigger the system to back-flush the column and recalibrate it using specified protocol(s). If a system detects that connectors are leaking, the software will shut off the system and automatically notify a lab operator about the issue via text message email, tweet or any multimedia notification the user desires.

Automation increases walk-away time for laboratory technicians and scientists

Naturally, people are incredibly agile and can move items very quickly, but only in one location and with two hands. Repetitive and mundane work is prone to error when done by humans.

Without automation, lab technicians must oversee workflows minute by minute to make sure their assays are running smoothly. Automation software frees up technician time, the time they can spend on more valuable analytical work.

Because the software controls and monitors the progress and outcome of the workflows, it frees technicians and scientists from highly-repetitive tasks and empowers them with more freedom. Simply put, it allows pharmaceutical companies to utilize their skilled workforce in more meaningful ways. Instead of standing at a computer screen, clicking something 20 times to keep processing samples or manually troubleshooting issues, researchers can walk away and focus on the imperative work of analysis.

User-defined workflows and advanced driver development future-proof the lab

Another significant advantage of scheduling software is that technicians can easily modify laboratory protocols using a drag-and-drop interface to add or delete instruments and device control commands. The technician can use the software to schedule different methods to run simultaneously or at scheduled times, allowing labs to run tests 24/7/365.

> Moreover, the Green Button Go software suite provides a future-proof network because users can easily access drivers (also known as instrument plug-in modules) rapidly develop them as labs adapt and expand their workflows over time.

Biosero's dedicated team of developers is continuously creating new drivers. Already more than 300 common device drivers are available. To develop a new device driver, as well as application program interfaces (APIs), the team starts by acquiring the instrumentation or the API for another software stack Green Button Go needs to automate or integrate. Dedicated software engineers focus solely on developing the driver for API, no matter who manufactured it. Thus, the software can automate with equipment from any manufacturer. It also integrates with other essential lab systems such as Lab Information Management Systems (LIMS) or analytical systems. Biosero updates drivers regularly and adds new drivers to their library frequently. Green Button Go is configurable so that only specific employees can be given administrator privileges to access new drivers.

Compliance, security and support essential to reliable lab automation software

Green Button Go Automation Scheduling Software is available in a version that is certified compliant with Food and Drug Administration (FDA) 21 CFR Part 11. The verification was carried out by an independent third party to ensuring the software incorporates audit trails, electronic signatures and other encrypted documentation required for electronic records.

The software is compatible with Microsoft Windows operation system. Because the software is deployed locally on lab PCs, it can operate safely behind the organization's firewalls and security systems as well.

Biosero offers extended service and warranty agreements that include all major and minor software upgrades, as well as hot fixes, for Green Button Go software. Customers can also enlist the help of Biosero service engineers, stationed throughout North America and Europe, to install software upgrades. Labs can choose to procure drivers and upgrades for the software and install them locally and if they purchase a Biosero service agreement then can download drivers via the cloud.

Training is available for users who want to learn how to install and set up the software, execute layouts changes, learn basic scripting, add new instruments and create methods and advanced usage scenarios.

Developer training is also available for people who already have programming experience. In this training, developers learn how to customize Green Button Go Automation Scheduling software to their organization's needs using C#, JavaScript, Visual Basic, or Python.

Automation software: a flexible platform accelerating drug discovery methods

Pharmaceutical companies can accelerate drug assessment and discovery with automation, which ultimately benefits patients with better treatment products. In a rapidly evolving environment, automation is essential for shorter cycle times, reaction monitoring, error handling, quality control and bringing new drugs to market more quickly.

Software that is flexible enough to grow as demands increase and is agnostic to the hardware components is vital in every drug discovery lab. Discovery requires implementing entirely novel processes and being nimble. With the help of innovative automation, pharmaceutical manufacturers can now have dynamic software that enables them to make complex decisions in less time, while upholding the utmost quality assurance and data tracking methods.

For more information about laboratory automation visit www.biosero.com.

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