LCGC INTERNATIONAL

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Improving HPLC Routines

Automating HPLC Operations

Automation and Confidence in HPLC Results

The Strategic Advantage:

Assistance Systems in Liquid Chromatography

The promise of more automation, fewer errors, and increased system uptime in HPLC routine work

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Today's Reality and Tomorrow's Vision:
How the Daily HPLC Routine Could be Improved

Oliver J. Schmitz (University of Duisburg-Essen) and Hui Wu (School of Bioengineering, Dalian University of Technology) share their insights on improving modern high-performance liquid chromatography (HPLC) labs. They highlight automation, AI-driven method development, and enhanced data evaluation as key drivers of efficiency. This Q&A explores how the future of HPLC will be shaped by micro- and nano-scale systems, real-time error detection, and fully autonomous workflows with minimal human intervention.

Q What are the biggest obstacles for more efficiency in your LC lab today?

SCHMITZ: The shortage of skilled workers in the industry is becoming increasingly noticeable in the field of analytics. As a university working group, we naturally have a high turnover of employees, and constantly training new employees takes a lot of time. In my opinion, Agilent has been a great help with the Infinity III LC system. The digital support for the maintenance of the HPLC system along with the purchase of consumables (listing of article numbers) will make the day-to-day work of less experienced users much easier. Better compatibility between HPLC and detectors of different manufacturers and standardized data formats are also urgently needed.

WU: For our biological fermentation laboratory, the biggest obstacle is that the samples are very complex. We often spend a lot of time doing the pretreatment and, after injecting the sample, the LC system would show higher pressure, and the column or injector would show a blockage. That forces us to spend more time on instrument maintenance, affecting the efficiency of the LC system.

Q Which is the biggest driver for more efficiency in your opinion: more automation, fewer errors, or increased system uptime?

SCHMITZ: Even if the latest HPLC systems don't come close to the legendary lifetime of an Agilent 1100 HPLC system due to the increased requirements, I don't see a need to extend the already great operating times of HPLC systems. Rather, it would help to further minimize the connections between the individual components (autosampler, pump, column, detector) and pay less attention to optics or space requirements on the bench–at least from a chromatographic point of view.

In addition, when using a mass spectrometric detector, a column oven directly at the inlet of the ion source would be useful to further increase efficiency without too much effort. With errors related to injection accuracy and abortion of a sequence, the current HPLC systems are so powerful that I do not expect any major increase in performance. The dead volumes and memory effects of most HPLC systems are now also extremely low. Only for sticky molecules, i.e. analytes that exhibit strong adsorption on surfaces, is there still room for improvement.

However, there are already devices such as the Agilent Infinity Bio LC system that show significant improvement for sticky analytes. Further automation, such as the automatic identification of sample vials, is certainly helpful and reduces possible errors. Otherwise, I see the greatest potential in improving data evaluation.

WU: I think the biggest driver is more automation. We're often doing continuous fermentation work. During the process of the fermentation, we hope the LC system can collect, pre-process, and inject the fermentation products automatically. We even hope the LC system can access the industrial software systems and exchange the data and information mutually, which would achieve full automation and improve our team's efficiency.

Q What will your HPLC lab look like in seven years and how will people work in it?

SCHMITZ: I expect that for most applications, due to ecological and economic necessities, the column diameter of HPLC systems will be reduced from the current 3.5 mm and 2.1 mm to 1 mm or less. First, this would significantly reduce the cost of organic solvents during purchase/disposal and, second, improve the

sensitivity of the increasing number of mass spectrometric detections. This means that I expect a shift towards micro- or even nano-HPLC.

Sample preparation and data evaluation will increasingly become fully automated and machine learning will make it possible to develop new methods (gradients) without chromatographic knowledge on the part of the user. This will lead to less specialized personnel, which is why the Infinity III tools are forward-looking. More complex analytical questions still must be answered in the manufacturing industry in rare cases and will therefore be passed on to specialist laboratories.

WU: My hope is that there will no longer be people in the HPLC lab, and that most of the LC preparation and analysis work will be automatically completed by the LC instruments, including mobile phase preparation and sample preparation. The LC system could judge and solve problems like AI does. Hopefully, people won't spend time on the LC system; rather, they could tell it what to do and the system would complete the entire process as mentioned above. The people will have more time to focus on their professional field.

Q From your point of view, can you define the most important steps to a fully autonomous LC system?

SCHMITZ: The most important steps would be coupling sample preparation. This also includes more complex sample preparation with HPLC, automated sample detection, excellent automated error detection with simultaneous system response, and improved data evaluation with standardized data formats.

WU: I think the performance of the LC system should be very good, including UHPLC, powerful valve technology, highly sensitive detectors, and so on. Currently, the most important step to a fully autonomous LC system is the automated pre-processing technology for complex online samples. The technology is very important because the sample, which would be injected into the LC system, must be clean with no particles or gas. The solution should be compatible with the starting mobile phase; as such, automation online pretreatment technology is key.

How to Achieve More Automation, Fewer Errors, and Increased System Uptime in Today's HPLC Operation

Automation enhances productivity, minimizes errors, and boosts system uptime for today's HPLC laboratories.

High-performance liquid chromatography (HPLC) is a fundamental analytical technique used to separate, identify, and quantify compounds dissolved in a solution. Widely employed in laboratories across pharmaceutical drug development, quality control, quality assurance, food safety, and environmental testing, HPLC plays a critical role in ensuring accurate and reliable results.

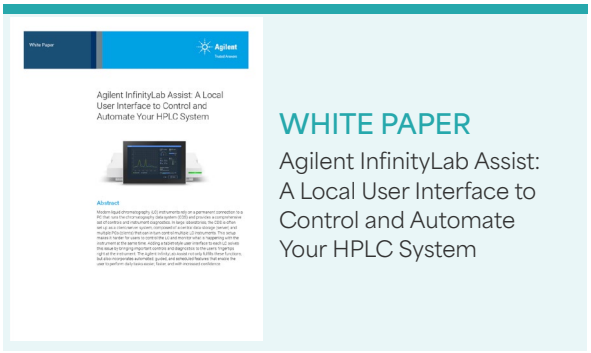
However, as the demand for greater productivity, fewer operational errors, and improved system uptime grows, HPLC laboratories are increasingly turning to automation. Although many labs start by automating individual steps, the leading

industry vendors now provide comprehensive solutions that integrate automation across entire workflows. This approach offers a more seamless, efficient, and accurate way to manage HPLC operations.

Current Challenges and Automated Solutions

Despite ongoing advancements made in technology and workflows, today's HPLC laboratories continue to encounter several bottlenecks. Manual operations and maintenance consume a substantial portion of the analyst's time, reducing efficiency overall. In addition, complex sample management and inconsistent methods not only strain productivity but also increase the likelihood of manual errors, often resulting in time-consuming test reruns. Additionally, preventable system issues, reagent shortages, and troubleshooting delays contribute to unnecessary downtime, further impacting lab performance.

In an effort to address these challenges, a variety of automated solutions have been introduced into the HPLC landscape. For example, automated start-up and shutdown routines simplify system preparation and closure, reducing the need for manual intervention and saving valuable time. Similarly, automated system purging and solvent blending technologies streamline solvent preparation and management, minimizing human error and ensuring consistency across workflows. Additionally, features like automated method transfer, which encompass the entire workflow including sample preparation, analysis, and data processing, along with sequence creation templates, can enhance cross-system compatibility and optimize sample sequencing. These comprehensive advancements significantly improve overall workflow efficiency, enabling laboratories to overcome common bottlenecks, improve reliability, and enhance operational productivity.



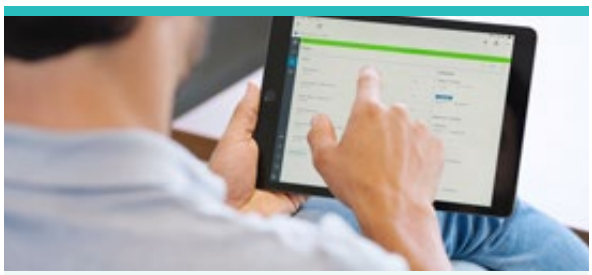
WHITE PAPER

Agilent InfinityLab Assist: A Local User Interface to Control and Automate Your HPLC System

While these solutions address specific challenges, modern techniques can integrate automation across every step of a laboratory's workflow. From automated barcode reading to sample identification and real-time monitoring, these innovations enhance traceability, reduce manual intervention, and minimize the risk of errors. By leveraging comprehensive automation, laboratories can achieve greater accuracy, efficiency, and reliability throughout their operations.

For instance, laboratories can maximize uptime by implementing automated solvent monitoring tools. These systems provide alerts when solvent levels are low, which prevents bottles from running dry, avoids costly re-analyses, and reduces strain on the system. Agilent's InfinityLab HPLC systems, for instance, feature built-in level sensing technology that automatically measures solvent levels and predicts whether sufficient solvent is available to complete a run before initiating a sequence.

To further enhance operational efficiency, laboratories can implement automated diagnostic tools, trend reporting, preventive maintenance protocols, and rapid troubleshooting capabilities within the HPLC workflow, as offered by Agilent's InfinityLab Assist Technology either directly in front of the LC system via the connected tablet/display or remotely in a browser on a PC or mobile device.



VIDEO
Assisting with Your Daily HPLC Routines

Additionally, software solutions like Agilent's CrossLab Instrument Maintenance and Diagnostics Software provide email-based alerts, notifying users when it is time to replace key consumables, perform preventive maintenance, or address instrument issues, thereby proactively maintaining instrument health and ensuring continuous operation.

Finally, in today's landscape, remote work isn't an exception or a luxury—it's a necessity. Remote system management and control tools provide operators with the flexibility to monitor and control systems from off-site locations, which both minimizes disruptions and ensures continuous oversight. Agilent's OpenLab Software is a cloud-based solution that centralizes data storage, enabling laboratory personnel to operate any instrument in any lab, process data from any instrument, and review or approve results securely from any location and device within the network.

Choosing the Right Automation Technology

When selecting automation technologies for the laboratory, it's crucial to consider factors such as budget, compatibility, and scalability.

For instance, laboratories aiming to minimize errors during sample verification can enhance their Agilent 1290 Infinity III Multisampler with an internal barcode reader, the Agilent InfinityLab Sample ID Reader. This low-cost product confirms sample

identity and ensures correct positioning, bridging the gap between barcode registration for analytical workflow tasks embedding acquisition software and keeps this association through data analysis and reporting processes.

Laboratories with higher throughput seeking to minimize manual intervention throughout their workflows may want to consider investing in integrated automated workflow solutions. These comprehensive systems streamline processes by reducing errors, saving time, and enhancing usability from the initial receipt of samples to the generation of final reports. Labs seeking an automated workflow solution can complement their existing Sample ID Reader with a software solution like Agilent Advanced Sample Linking and Agilent Sample Scheduler for OpenLab. These technologies work together to associate each sample container with a unique pre-barcoded vial, creating a closed-loop system that eliminates errors, saves time, and streamlines sample handling from initial registration, optionally in a LIMS, to final reporting. By automating critical steps, this integrated solution strengthens data integrity and significantly improves overall laboratory productivity.

VIDEO
Prevent HPLC Solvent Bottles Running Dry

In addition to considering costs and compatibility, laboratories must prioritize proper training and skills development for their personnel. This includes providing training on new automated systems as well as access to resources such as maintenance guides and troubleshooting tools. Reputable vendors, such as Agilent, support labs by supplying comprehensive materials and training to ensure the seamless integration of their technologies into laboratory workflows.

Integrating new automation into a lab also necessitates careful consideration of ongoing maintenance and support. Reliable vendors can assist labs by establishing maintenance schedules, providing timely access to technical support, and ensuring the availability of software updates when needed. This level of support helps laboratories maintain optimal performance and maximize the value of their automation investments.

Laboratories adopting new technology should also prioritize collecting key performance metrics to evaluate impacts on efficiency, accuracy, and system uptime. These insights can identify areas for improvement, guide further system

optimizations, and reveal opportunities where additional automation can enhance the lab's workflow and overall productivity.

Automation for a Better Lab

Automation delivers significant benefits, such as error reduction, enhanced system uptime, and increased productivity. Looking ahead, automation is positioned to play an ever-expanding role in HPLC laboratories, and it is expected that next-generation solutions will marry advanced technologies to create truly synergistic workflows. To remain competitive, laboratories must assess their current HPLC operations and adopt strategic measures toward embracing automation and efficiency—or risk falling behind in an increasingly automated landscape.

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Leveraging Automation for Increased Data Confidence

By minimizing human error by standardizing processes and supporting workflows, automation can improve trust in—and reproducibility of—HPLC results.

Like any powerful and widely used analytical technique, high-performance liquid chromatography (HPLC) still comes with challenges that can ultimately affect the accuracy and reliability of results. Common issues include manual sample handling and preparation, entry errors, and procedural inconsistencies, all of which can increase the risk of human error and lead to inaccurate or non-reproducible results.

Automation offers an effective solution to address these challenges by virtually eliminating the potential for human error. It enhances performance, correctness, and consistency, while streamlining data tracking and improving the overall user experience in HPLC laboratories. With workflow automation, analysts can have greater confidence in both the analytical process and the reliability of their results.

Enhanced Sample Identification and Tracking with Barcode Technology

Many laboratories already use barcode readers to streamline the introduction of sample information into the analytical software to improve their workflow process. However, integrating additional automated barcode scanning technology elevates these benefits further by preventing incorrect sample placement and misidentification. This advanced integration ensures greater accuracy and efficiency in sample management and increased reliability in subsequent analysis and results.

A built-in sample identification reader, such as the Agilent InfinityLab Sample ID Reader, streamlines operations by recognizing sample positions and identifiers without requiring the manual input of vial-in-tray locations. This reader is installed in the vial drawer area of Agilent's Infinity II or III Multisamplers, replacing the bottom drawer, while the upper three drawers (six trays) remain available for vial samples.

Previously, users had to manually input or transcribe vial locations, or ensure that each vial was placed in its designated position. With this advanced technology, neither of these steps are required.

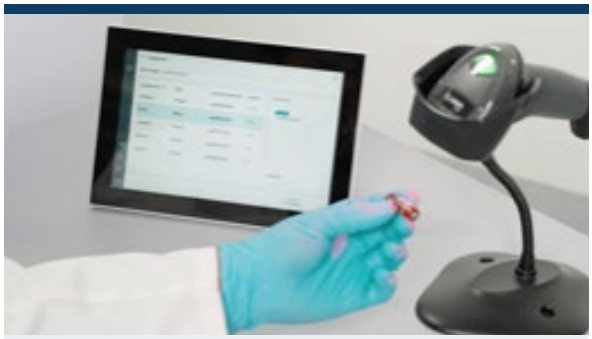
Instead, samples with barcodes on the vials' bottom can be placed in the drawer in any order and position, simplifying the set-up process and saving time. The built-in reader automatically scans for sample identification, position, and analysis information, ensuring efficient, accurate (correct), and traceable sample data acquisition. After data analysis, the barcode confirmation and identified position are recorded in the results table, providing final confirmation of sample measurements. This streamlined approach saves time, enhances ease of use, and significantly reduces errors, ensuring a more reliable and efficient sample analysis workflow.

Ultimately, the automation of critical steps like sample injection and tracking

ensures correct and efficient sample processing by virtually eliminating identification errors. Users can avoid accidental sample mix-ups, as each sample is automatically recognized throughout the analysis process. Real-time verification ensures optimal traceability, while Agilent's InfinityLab Sample ID Reader adds an extra layer of reliability by providing immediate error alerts.

Improved Data Integrity

By automating steps that were previously manual, barcode scanning and other automated technology enhances the performance throughout the workflow, from sample preparation and injection through analysis and results. The result is improved data accuracy and integrity.



VIDEO
Ensure Safe Sample Journeys

First, consistency in routine operations (such as sample loading) enforces standardized protocols, ensures that every sample is processed uniformly, and minimizes variables for optimal reproducibility. Next, automated data logging eliminates the need for manual entry, significantly reducing the risk of human error and minimizing data inaccuracies. It also safeguards against unauthorized data manipulation, ensuring secure, reliable, and high-quality record-keeping for enhanced data integrity.

Data automation provides secure, auditable trails from sample processing to final reporting. These robust data storage and transfer protocols not only enhance traceability but also support compliance with regulatory requirements, ensuring peace of mind during audits and inspections.

User-Friendly Workflows

Automation not only delivers better and more reproducible data, but also introduces intuitive interfaces and streamlined workflows into the lab. By design, automation simplifies processes, eliminates manual tasks, and saves time, which leads to a more efficient and productive laboratory environment overall. Additionally, automation reduces training requirements and minimizes user errors, further enhancing operational efficiency.

While full automation refers to the total replacement of human intervention

with robotic or cobot systems, workflow automation focuses on optimizing specific processes within the laboratory to reduce human-related errors and improve performance. As such, workflow automation allows laboratories to maintain human oversight while automating repetitive tasks, ensuring a balance between efficiency gains and the flexibility of manual control.

With user-friendly systems, analysts can prioritize data quality over manual procedures. These simplified and reliable operations inspire confidence in system outputs, ensuring consistent protocols while virtually eliminating the risk of human error.

Implementing Automation for Data Confidence

Agilent offers a comprehensive range of automation technologies designed to enhance laboratory efficiency and data integrity. When selecting solutions, laboratories should align their choices with specific objectives, considering factors such as sample throughput, regulatory compliance, and existing infrastructure (Agilent automation can be seamlessly integrated with existing systems, including the 1260 and 1290 Infinity III Multisamplers).

For instance, the Agilent InfinityLab Sample ID Reader facilitates accurate sample identification and tracking, while the Agilent Sample Scheduler for OpenLab optimizes workflow management. These plug-and-play automated solutions are compatible with current laboratory equipment, enabling straightforward implementation and immediate benefits in operational efficiency and data reliability.

Selecting a reputable vendor is also crucial when implementing automated systems. Responsible vendors, such as Agilent, not only deliver high-quality technology but also provide comprehensive training to ensure lab personnel are confident and proficient in using the new systems.

Additionally, regular updates and consistent maintenance are essential to keeping automated systems reliable and ensuring they maintain optimal data accuracy and traceability. Partnering with a vendor that offers strong support services will maximize the value of automation in the laboratory and sustain long-term efficiency.

Modern, Automated Labs are Possible

The integration of automation into HPLC workflows represents a transformative step toward improving laboratory efficiency, accuracy, and data integrity. By

eliminating manual processes, workflow automation can reduce the risk of human error, ensure consistent sample handling, and enhance traceability through advanced tools such as barcode scanning and sample identification readers. Laboratories can then achieve greater confidence in their analytical results while simplifying workflows and minimizing training requirements.

Moreover, automation supports compliance with regulatory standards by providing secure, auditable data trails. Choosing the right vendor, like Agilent, ensures access to not only cutting-edge technology but also the training, updates, and support needed to maintain reliable and effective systems. As automation continues to evolve, laboratories will be freed up to focus on delivering high-quality data and driving innovation in their analytical processes, rather than wasting resources on manually inputting data, performing maintenance, and conducting other time-consuming tasks.

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