LabManager

2019 AUTOMATION RESOURCE GUIDE

Questions to Ask When Buying Laboratory Automation

Laboratory automation and robotics can facilitate repetitive processes and increase laboratory throughput. They can also help prevent variability and errors and increase reproducibility of lab experiments and assays. Applications for automation and robotics in the lab include microplate handling, sample preparation, liquid handling, live cell imaging, and autosampling.

What sample throughput do you need?

The sample throughput of an automation platform will depend on how many samples it can process at once and how fast it can process those samples. When purchasing laboratory automation, think about your present and future sample throughput needs. If you see your sample throughput growing, look for a modular system that can be expanded in the future to accommodate more samples if needed.

How much space do you have available in your lab?

Laboratory automation comes in all shapes and sizes – from compact benchtop instruments to larger floor models. The size will depend on the throughput of the instrument as well as the number and types of functions it can perform. Before deciding on the right automation platform for your lab, make sure you have the space necessary to accommodate it.

How user friendly is the software?

Software is a key component of any automation platform. Look for a user-friendly interface that comes with pre-programmed protocols that can be easily adapted. When purchasing, look for a vendor that will work with you to build any custom protocols, so you aren't left to learn how to code the software yourself.

PURCHASING TIP

Laboratory automation and robotics solutions come in a variety of configurations. When purchasing, look for a company that will work with you to identify the instrument that will work best with your needs. For complex or custom applications, look for manufacturers with modular instruments that can be exactly tailored to your purposes. These instruments are also more likely to be expandable in the future and will therefore meet your needs for years to come.

Automating Your Lab

Automation can improve the efficiency of a lab and more, but figuring out the best "here" or "there" creates the challenge

By Mike May

How to get the greatest benefits of automation and still meet your budget

Getting the most from automation depends largely on the specific application. Nonetheless, some general planning helps in almost any approach to automating a lab process.

First, a scientist must know what goals to pursue. Scientists automate a lab to increase throughput, walk-away time, and data reproducibility. Implementing automation can help remove a bottleneck and increase overall throughput. In reality, the bottleneck is simply moved to another step in the overall workflow. Done properly, though, the new bottleneck is smaller than the one it replaces.

That means that a lab manager should know what bottleneck is being addressed with automation and where it will create a new one. Careful planning and coordination of lab expansion efforts can help increase throughput as efficiently as possible, ensuring that all the different processes grow in sync and funds are spent productively.

Pick the places

A lab manager probably has a few spots in mind for automation. Even if you are running multiple assays, budget restrictions likely mean you can only automate a few.

At the Center for Chemical Genomics at the University of Michigan in Ann Arbor, HTS (high-throughput screening) director Martha Larsen faces these very challenges— the balance between getting the best benefits of automation while meeting a budget. As she says, "We think about the cost and benefit of each item. If we are going to spend x number of dollars, what will be the return to the lab?"

In some cases, doing something faster is a driving force to automate, but that is not always true for Larsen. "Since we are an academic lab," she says, "we don't focus on faster. Instead, the benefit we look at might be that you can save hiring someone."

Sometimes, finding out what automation works, though, is an empirical question. As an example, Larsen describes purchasing an instrument to fit plates on a deck. She says, "By the time a scientist learned how to automate this, they'd spend far more time than they would have if they just kept putting the plates on the deck by hand." Part of the issue with that automated system arose from the frequency of usage. As Larsen says, "If you're only doing something four times a month, it might be quicker to do it manually."

Moreover, that automation failure taught Larsen a crucial lesson. She says, "Now we evaluate an automation decision based on historical usage, then think of the automation investment and how long it will take to get the time back that it takes to install and make the system work."

That kind of analysis led Larsen to not automate her lab's flow cytometer. "Lots of people buy a robotic arm that puts on plates. We found that it only takes 10 minutes to put on the plates, and we only do it two days a month," she says. Plus, she uses a student to do it.

Conversely, Larsen says that the robotic arm for her high-content microscope really saves time. "It has been worth the investment," she says.

The budgetary side of automation, though, does not end after the sale. As Larsen says, "It's not the initial cost of the automation that matters the most; it's actually the yearly fee we face with it." She adds, "You can buy a car for under $20,000 and get a three-year warranty, but I spend $150,000 on automation and they give me six months or one year of warranty. The manufacturers should be willing to stand behind products longer and build that into systems, especially for academic labs, because I can't afford some of the service contracts." For instance, she says, "One robot costs $40,000 a year for service, and I dropped it." Such costs have made Larsen decide against automation in some cases.

Get the goals in order

To figure out the best way to add automation to a specific lab, the goals must be considered carefully. Consider high-volume DNA extraction from blood or plasma samples. This is a routine assay that doesn't change much and is often labor-intensive, requiring many liquid transfers and lots of mixing. Any user error in labeling tubes or wells could be critical and pipetting errors could lead to concerns about cross-contamination. Consequently, automation can really benefit this assay.

In other cases, the goals might not be as singular. For example, using detection with cell-based assays. This process typically requires moving microplates between a multimodal reader and a fluorescent microscope located down the hall and shared with many others. The overall workflow is inefficient and, what could be done in a couple of minutes, might be stretched over several hours. To consolidate this protocol into a minutes-long process, though, a scientist needs a device that provides a multimodal reader and an inverted fluorescent microscope in one, thereby automating the transition from detection to imaging.

Better biobanking

Some forms of lab work might seem more suited to automation than others. For example, biobanking—collecting and storing samples for research and clinical applications—sounds like a natural fit for automation. In biobanking, sample integrity and quality are paramount. Using automation for biobanking helps center the process around the sample. For example, controlling the temperature improves a sample's quality. Manual biobanking subjects a sample to greater temperature variation, as much as ten degrees, as a freezer gets opened and closed, and even left open longer than necessary. By automating this process, many steps can be completed without opening the freezer, which can produce temperature stability to within single degrees.

Also, automation adds an audit trail to a sample, so researchers can be confident in the quality of the samples they are getting out of the biobank. This can be especially useful in any regulated industry, such as biobanking samples for pharmaceutical research.

Automating a biobank benefits organizations and labs across a wide range of sizes, from large organizations with more than 10 million samples to university labs with just tens of thousands of samples.

When thinking about automating a biobank, though, researchers need to think ahead. The solution should be adaptable and capable of meeting future needs. Sometimes, one simple change helps biobank researchers today and tomorrow. As an example, standardizing tube formats for automating tube storage and retrieval, such as using 2-D bar codes. Using barcodes, automation can act like a vending machine in a freezer and researchers can track and pull samples that have been stored previously.

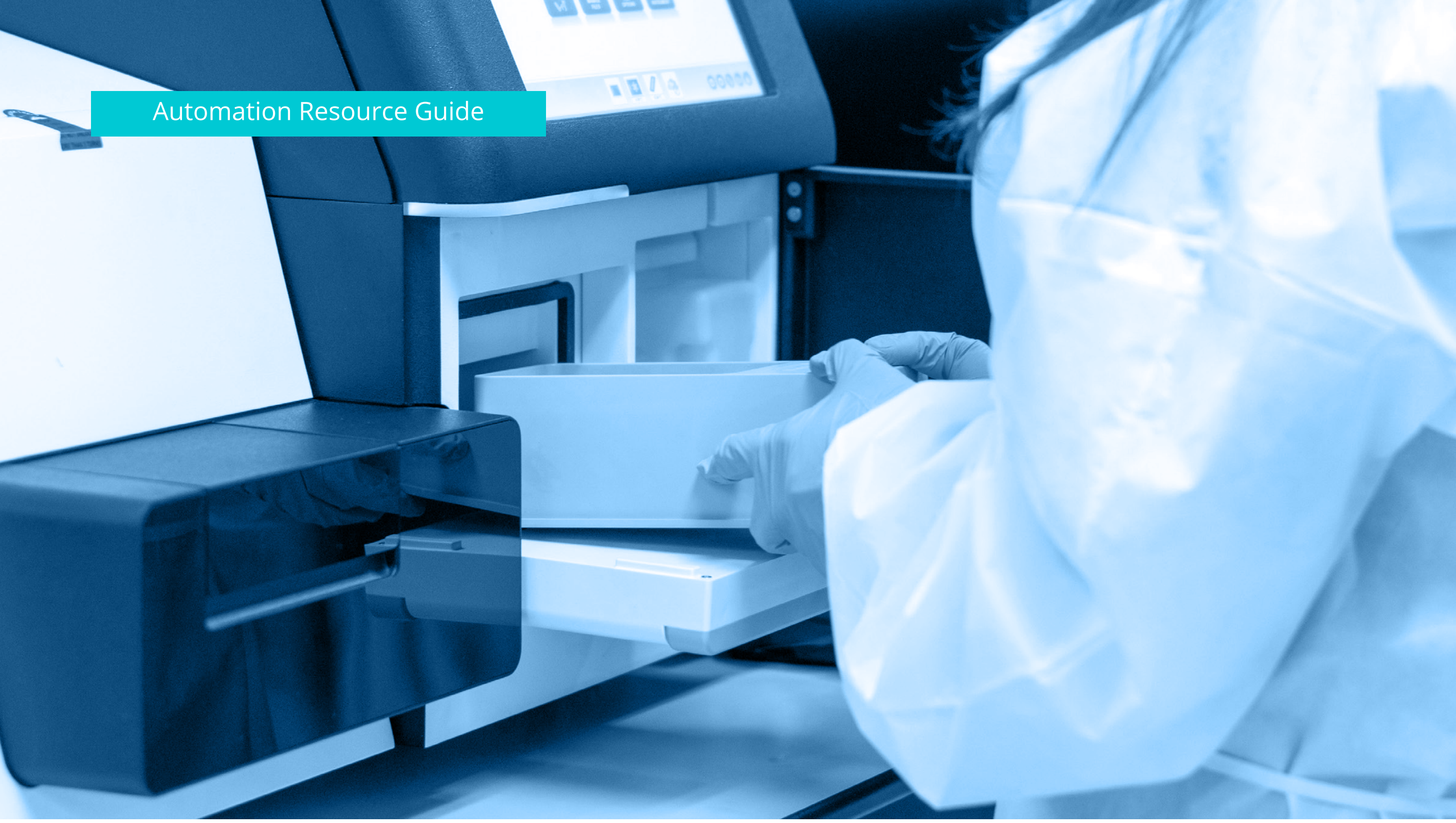
Keep it simple

Not long ago, even the concept of automation sounded complicated. That surely kept many labs from adding automation to anything that could be handled even somewhat efficiently by hand. Today's technology significantly reduces that obstacle.

Part of the simplification in automation comes from an ongoing trend. Lab equipment manufacturers started by building large systems that covered massive workflows in one go. However, they are now focused on providing workstations for small parts of a workflow. Those smaller systems can be integrated in a lab more easily. Also, they allow for future flexibility, so that the same device might reduce one bottleneck today and a different one in the future.

At the same time, vendors keep trying to make automation easier. Users of lab automation are often scientists, not computer programmers. As a result, manufacturers are aiming to have interfaces that work more like smartphones. For example, a simple user interface on a touchscreen that is customizable. In general, a scientist should not need to write code to make an automated system work. The interface should be visual, using drop and drag and copy and paste functions. For scientists with some programming skills, a system built on an open software platform still makes it easier to tailor instructions to individual needs.

The key to keeping automation as simple as possible starts at the beginning. By identifying the specific spots where automation could do the most good and exploring a variety of solutions, a lab manager increases the odds of a successful implementation. Also, today's scientists should not accept hard-to-use products, because modern automation should be easier than ever to install, customize, and use. Plus, don't forget to get a system that can adapt to tomorrow's needs—giving you a fighting chance of handling unforeseen workflows.



Automating Sample Preparation

Automation seeks to reduce human contact, thereby gaining speed, throughput, and reproducibility

By Angelo DePalma

The operational space of sample preparation is huge, with tens of thousands of possible starting materials and hundreds of relevant methods. The desired readout adds a third dimension to the decision matrix. In all cases, the objective is to "clean up" the sample, so the analyte of interest is preserved to the greatest degree possible, while removing potential interferences. Within that context, automation seeks to reduce human contact at critical points, thereby gaining speed, throughput, and reproducibility while eliminating human error.

Preparing samples for chemical analysis involves routine methods (or a combination thereof), for example extraction, digestion, grinding, preparative chromatography, filtration, dilution, reagent addition, crystallization, distillation, and other processes. Many of these operations are fully manual, while some occur nearly completely within robotic platforms. In either case, sample prep is straightforward and familiar.

Molecular analytic workflows present a different set of challenges. Although many of these methods are already automated, sample collection and preparation are labor- and resource-intensive due to sample complexity.

Sample prep leading to next-generation sequencing, for example, usually involves the collection of human tissues or body fluids. That's all well and good when the objective is quantitation of the obvious, for example plain vanilla genomic DNA.

Sequencing gets interesting when the object is detecting or quantifying circulating tumor cells or tumor DNA from plasma, or fetal DNA in a mother's blood. These applications stand sample prep on its head, as "normal" patient DNA becomes not the target but an unwanted obfuscator to detecting rogue genes from cancer cells.

Moreover, the capture and analysis of such diagnostic DNA is confounded by the presence of circulating nontumor DNA arising from a patient's healthy cells, and the fact that their concentration varies significantly with different cancers and stages of disease.

The standard for pulling such low-abundance analytes from plasma, systems is magnetic beads that attract cell-free DNA. More advanced systems have been developed that, instead of applying a magnet to the outside of the sample vial to collect the beads, insert magnetized rods into the sample, withdraw them, and then re-suspend the beads in a wash flask by demagnetizing and rotating the rods. These more advanced systems claim high yields and purities, which is a requirement for medical diagnostics based on sequencing.

Sample prep for molecular analytical workflows carries the same conundrum as for chemical-analysis workflows, namely whether to purchase a complete analytical system, including sample preparation, from one vendor or to cobble something together with components from several manufacturers.

The choice depends on the end market. For example, basic researchers are better at putting systems together, so they can often purchase components from several vendors that will work well together. In clinical settings, time is money and relying on a single vendor for troubleshooting simplifies the process. Using an entire workflow from a single manufacturer brings comfort as the system has been tested extensively including taking samples, extracting DNA, quantifying it, and delivering it to the sequencer.

What cost barrier?

Small companies and academic labs cite high costs as justification for sticking with manual sample preparation. Manufacturers are trying to overcome this barrier. Basic liquid-handling robots are available at one-tenth to one-hundredth of the cost of premium robots from well-known vendors.

The secret is in the sourcing of technology and components. Manufacturers have tapped into the extensive and growing hardware supply chain in Shenzhen, China, and embrace open-source technology. The global growth of desktop 3-D printers has made things like precise stepper motors and 3-axis controllers more affordable and higher quality than ever before.

Those same components are available to top-tier robotics companies; and given that, why don't those companies use them? It has been suggested that companies with high-margin products cannot afford to cannibalize their own products; this is an idea posited by the highly successful book by Clayton Christensen *The Innovator's Dilemma* (https://goo.gl/s8uANp).

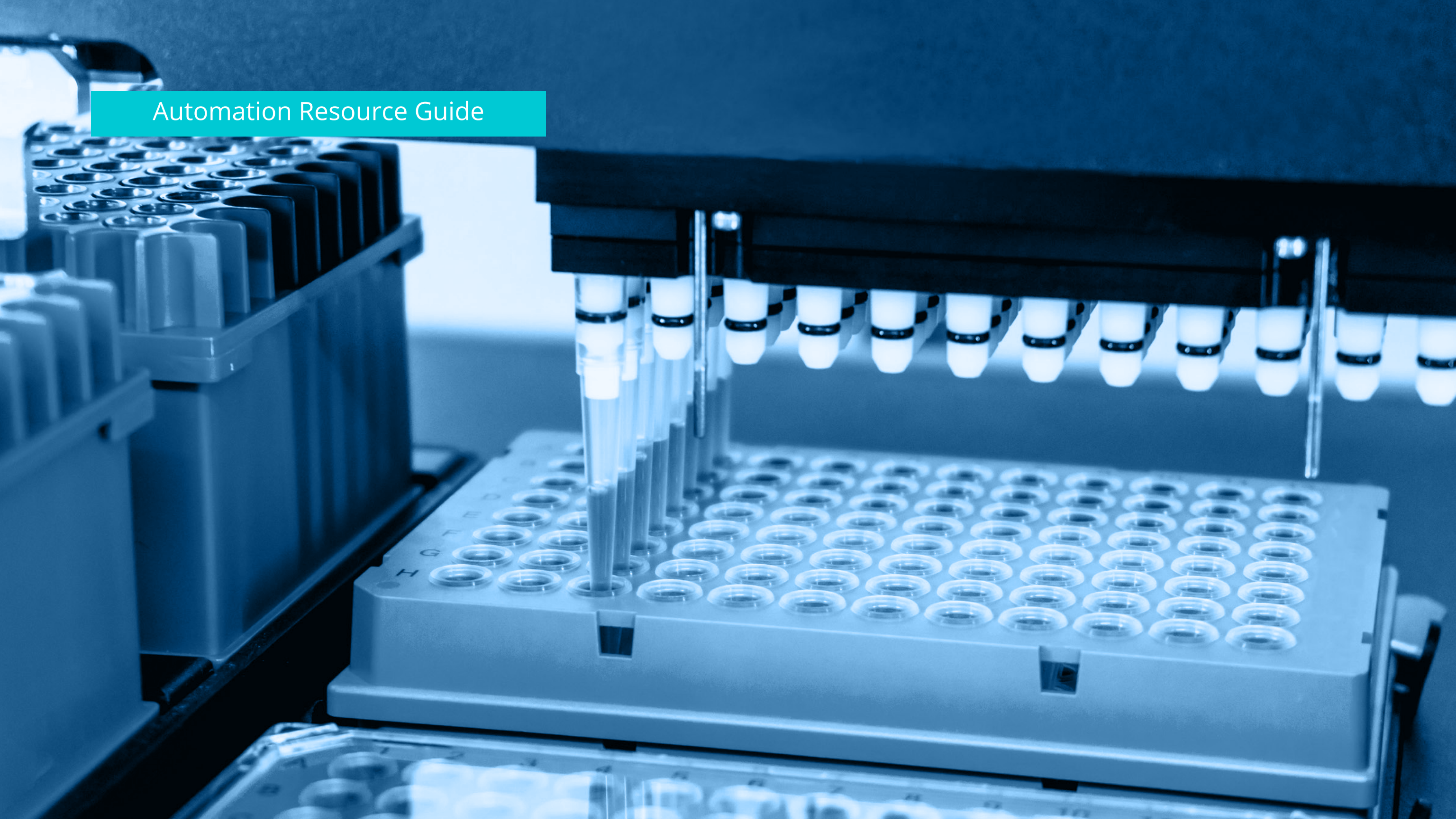
However, even this argument is like comparing apples and oranges. The big automation manufacturers serve laboratories who are conducting highly complex assays in high throughput. Smaller companies are selling to the 90 percent of labs that are currently doing everything by hand.

Next-gen proteins

Emerging protein therapeutics present the usual challenges of sequencing and higher-order structures, but often incorporate non-generic chemical modifications. Manufacturers are designing new systems in anticipation of the growing interest in next-generation protein drugs, whose sequencing and mapping is required for full characterization.

These systems provide automated protein affinity purification, protein digestion, peptide cleanup through micro reverse-phase chromatography, and fractionation in preparation for mass-spectrometric (MS) analysis. They can also prepare samples for discovery and analysis of protein and peptide biomarkers.

Automated systems for the analysis of protein sequencing achieve the principal goals of sample prep: eliminating workflow bottlenecks, creating walkaway time, and providing reproducibility. The relevance in today's proteomics environment is that sample preparation has become a rate-limiting step.



Automated Liquid Handlers

Users decide between dedicated and multipurpose systems

By Angelo DePalma, PhD

Demand for automated liquid-handling systems parallels the larger automation marketplace. Generally, the need for automation is based on speed or throughput, consistency of results, and the value of a lab worker's time. Within this multidimensional demand space, requirements range from simple automated pipetting through midrange systems to multiuse, general-purpose automation systems costing hundreds of thousands of dollars, and liquid handling is just one component in demand. Users continue to specify high-end liquid-handling systems that serve "workflow automation" needs rather than single-liquid dispensing operations.

Purpose-built systems

Lab managers must ultimately decide if their liquid-handling needs are based on one or two processes or if they prefer flexibility—and with it greater complexity and higher costs. In the past, organizations have used in-house automation teams to handle the complexities of automated liquid-handling systems. Now, the majority of organizations are looking for a turnkey system that does what it's supposed to. They know they will still need some in-house support, but they would rather have experts configure the system for their specific workflows.

While purpose-built automation is catching on in select markets, flexible workstations are still in high demand. Academic research labs usually have more than one project going, and within each project there are several workflows that could benefit from automation. Research labs often change their priorities and projects. With these ever-changing needs, dedicated workstations are not a viable option unless they come at a very low price where labs can purchase multiple systems. Flexible automation platforms, in contrast, can evolve with workflows, ensuring that the instrumentation will not become obsolete.

This raises the question of who will carry out programming and repurposing of liquid-handling systems – as you build in more flexibility, the platform becomes more complicated.

Graphical user interfaces (GUI) can help reduce the flexibility-complexity conundrum by providing an easy way for users to program their systems. For routine applications, individuals do not need to learn software to create applications. They can open an old method and tailor parameters like sample number, dispensing volume, and washes by answering a series of questions. The GUI asks more questions for complex workflows than simpler ones.

Markets where purpose-built automation makes the most sense are clinical testing and pharmaceuticals. The former usually rely on very large, expensive platforms that perform the same tests over and over. The latter can justify the expense of an application-specific platform for new or ongoing projects based on consistency of results and reduced human resource utilization.

Dedicated but flexible

Some manufacturers believe that purpose-built or application-specific workstations are the wave of the future. For example, in the past individuals performing ELISA assays would purchase a robot with ELISA capabilities. Today, they're probably looking to purchase an automated ELISA workstation instead of an all-purpose instrument.

The impetus for specialization amounts to the division of labor between scientists who do science and the vendor's engineers who specialize in automation. Users don't want to dedicate a lot of time to learning the intricacies of laboratory automation. Application-specific workstations save them from that learning curve. Users want vendors to figure out the set-up, optimization, and tweaking of the system for them.

This raises issues of personalized versus core facility utilization and of instrument proliferation. Top-of-the-line automated liquid handlers, as part of larger, sophisticated automation systems, remain expensive and may still be more appropriately utilized within core facilities. But as prices for automation have fallen across the board, many more labs can now justify the expense of application-specific liquid handlers that sit on individual desktops. If configured with the user and application in mind, routine operations may be conducted without expert input.

Personalization and task-specificity are ideal for lab groups with minimal liquid-handling needs, for example polymerase chain reaction or simple extraction. For those, systems capable of little more than automated pipetting may be the answer. Even for higher-end lab work, full-blown, application-specific systems satisfy a growing desire on the part of operators to run their own experiments on their own time and terms.

Application specificity is not the dead end its name suggests. True, such systems come ready to use out of the box, but many with built-in mechanical flexibility can provide access to new workflows through programming. Software and method writing are two areas where vendors can provide substantial value, even for systems originally designed for a single major application.

You buy the instrument for the initial workflow – any additional workflows added later on are bonus. And if your needs change again in the future, you can just call the vendor.

Automation and Robotics in Laboratory Design

How technology affects the future of data analysis

By Mark Paskanik

Automation and robotics have both played a role in laboratory design for many years. However, in recent years we have started seeing a larger increase in this type of design with greater success. Where are we headed next, and how can we plan to take advantage of this successful type of design in the laboratory?

The basics

Thomas Edison is well known for his many inventions and an amazing 1,093 patents. Most of his inventions were based on an early model of automation of specific tasks. These days, laboratory equipment is being designed to increase productivity and reduce the number of repetitive tasks that people need to do. These tasks can be very labor intensive and ergonomically difficult to perform. Many products on the market today help to reduce this repetition. An example would be utilizing a robot in liquid handling. Traditionally, a person would sit at a bench with a pipette tool and repeatedly transfer liquid media in small amounts. Now, robotic arms are used to complete this task with artificial intelligence (AI). These robots can adapt to different sizes and techniques and thus, improve efficiency. A large floor mounted robotic instrument can run 24/7, which greatly increases production.

Education

We are now starting to see programs that focus on educating students in the world of automation and robotics in a multi-disciplinary approach. The Stuart Weitzman School of Design at the University of Pennsylvania offers a Master of Science in Design: Robotics and Autonomous Systems. This program explores the means for orchestrating design agency within material and robotic systems for the fabrication or live-adaptation of experimental architectural prototypes.

In the field of life sciences, the Indiana University School of Informatics and Computing offers a course in data acquisition and lab automation. The course covers the entire process by which signals from laboratory instruments are turned into useful data: fundamentals of signal conditioning and sampling; interfacing, communications, and data transfer; markup languages and capability systems datasets; general lab automation; and robotics. A significant portion of this course is devoted to practical learning using LabVIEW.

With these programs becoming more readily available, the workforce of the future will be better prepared to help implement and innovate these new technologies.

When should you automate or use robots?

Really, the question is: why are you not using automation and robotics in your laboratory? Top reasons for doing so include a triple bottom line, ergonomics, data integrity and traceability, process uniformity, and throughput.

The triple bottom line is defined as a framework to evaluate performance in a broader perspective and is based on the social, environmental, and financial framework. Social impact is improved in a variety of ways with automation and robotics. Giving time back to the laboratory staff is a benefit that will greatly improve their productivity. Likewise, the potential to operate a more sustainable laboratory that can run utilizing less energy can have a positive impact on our environment.

Ergonomics is a very important aspect of all laboratories. Tasks such as sitting at a hood or microscope for extended periods of time can lead to musculoskeletal disorders (MSDs). MSDs affect the muscles, nerves, blood vessels, ligaments, and tendons. According to the Bureau of Labor Statistics in 2013, MSD cases accounted for 33 percent of all work-related injury and illness cases. OSHA has published a guidance on "Laboratory Safety Ergonomics for the Prevention of Musculoskeletal Disorders." The robot in the laboratory will never have these problems and will also allow people to have more time for collaboration and innovation.

Data integrity and traceability can be invaluable when it comes to research and collecting data in the laboratory. You may have heard a news story or seen an article based on research that was affected by poor data. Some of this has been the result of human error. Tracking, data collection, and accountability can be enhanced or improved with automation and robotics.

Process uniformity is enhanced by improved visual inspection. Humans can have difficulty with visual inspections that determine color, shape, and size. This, of course, can be affected by fatigue and other factors which require hand/eye coordination. Advances in computer imaging technology can evaluate the inspection almost instantly and in a repeatable fashion.

Throughput is an obvious advantage. Many tasks that may have taken a person all day to complete can now be done in a much shorter amount of time. Robots with intelligent vision can perform tasks without breaks and with more reliability in the data.

Case studies

Many laboratory owners are looking at automation and robotics at the equipment level. Other laboratory owners are considering this for their entire laboratory space. Although the laboratories will be occupied by people, you can envision these labs running on their own, independent from human interaction. Of course, this is the extreme case for automation and robotics, but it does lead to an interesting thought on operating laboratories more sustainably and efficiently.

With full implementation of automation and robotics, a laboratory can operate within a closed process environment and one that does not require human thermal comfort. This could greatly impact overall energy consumption and create a new model for laboratory sustainability.

QualTex Laboratories is the largest, independent non-profit testing laboratory in the US for blood and plasma products. The laboratory is FDA and ISO registered, CLIA certified, and an approved and/or accredited testing facility by multiple companies and health ministries worldwide. An automation line was installed to increase production by approximately 10 times. Before the installation, samples were required to be processed with many separate pieces of equipment. This, in turn, required employees to transfer materials by cart or by hand within the facility. If you trace the footsteps, you will see a very irregular pattern of flow that is inefficient. By installing the new automation line, production throughput was drastically increased. The track line receives the samples and sends them to each piece of equipment based on a bar code system. In addition to this line, a robot is used for delivery and receipt of samples at the end of the line and for storage/retainage as required. In effect, this space does not require human interaction except for routine maintenance and inspections.

Medicago is a pioneer of plant-based transient expression and manufacturing and has always sought more effective ways to improve human health. This company utilizes the leaves of tobacco plants to produce the influenza vaccine. Plants are highly efficient at producing proteins of varying complexity, serving as bioreactors—or mini factories—for vaccines and protein-based therapeutics.

Medicago's plant-based production platform demonstrates agility, accuracy, and speed by eliminating the risk of mutation and contamination during production. It also significantly shortens production timelines. A major robotic factor in this technology is based in its fully automated greenhouse. The leaves from 90,000 tobacco plants are used each year in the production of the influenza vaccine. Large scale robotics lift the potted tobacco plants from the automation line, then move them to the infiltration robots. Plants are then incubated for 10 days before being harvested for virus-like particles utilized in the production of the influenza vaccine.

Without this automation line and robotic features, Medicago would likely not have the means to produce and market the same number of vaccines within a four-week time span. They would probably need a much larger space and more employees to meet the same production goals.

Impacts

Generally speaking, costs to implement these strategies can vary greatly. Custom high-end automation equipment can cost $1 million or more, but individually mass-produced equipment made at a significantly lower cost is becoming more of the norm for laboratory equipment. The ability to adapt equipment to existing building conditions is improving as well. Floor flatness and vibration control may have been difficult to obtain with sensitive automation lines, but much of this new equipment can be installed without any special change to the infrastructure of the building.

One would think that with the inclusion of automation and robotics, our labs would require fewer people. However, what we are actually finding is that more people are required for data analysis due to the significant increase in production. Until AI becomes more common, we will also see an increase in office space required for our labs.

The design and planning of your laboratory will be impacted by automation and robotics now and in the future. According to Market Intelligence, the Global Lab Automation Market was valued at $3.14 billion in 2017 and is projected to reach $4.64 billion by 2025, growing at a compound annual growth rate of five percent from 2018 to 2025. We can expect the pace of automation and robotics in the laboratory to incrementally increase over time. Will your lab be ready?

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