December 2019 Volume 14 • Number 11

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LAB OF THE FUTURE

STREAMLINING WORKFLOWS WITH SMART TECHNOLOGY

Lab Automation Guide

TRAINING & EDUCATION


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December 2019

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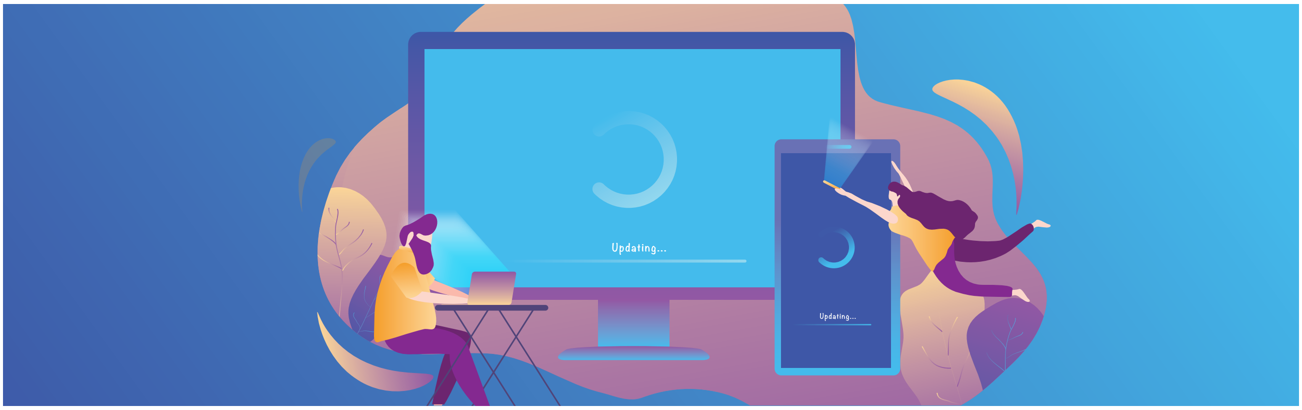

A NEW LOOK ONLINE FOR 2020

As we close out another great year, *Lab Manager* looks ahead to 2020, which holds plenty of new offerings for our readers. One key change you'll see is our website, which is being completely overhauled for the New Year with a cleaner, easier to navigate design. Most of our old categories will remain, but without the clutter of the current site, and we'll be adding some exciting new online offerings going forward. Be sure to explore the revamped site when 2020 arrives and let us know what you think: www.labmanager.com

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DEPARTMENTS

industry insights

ask the expert

special feature

product focus

in every issue

wrapping up 2019

As we prepare to enter a new year (and new decade), it's only fitting to reflect on what this past year has brought to the *Lab Manager* team and our readers. One of the most exciting announcements was the launch of two new live events—the Lab Manager Leadership Summit and Lab Safety Summit—both of which will be returning in 2020, with the addition of the Lab Design Summit and Lab Design Excellence Awards. These events allow us to make more meaningful connections with our readers, while providing you the opportunity to learn from expert speakers and network with fellow lab professionals in a casual, comfortable setting. We thoroughly enjoyed hosting the Leadership and Lab Safety events this year, and hope to see more of you next year.

This time last year, we introduced the first of the mini Product Resource Guides, which quickly grew in popularity throughout the year and covered areas such as sample preparation, lab design, supplies and consumables, and lab automation (featured in this issue).

We revisited important editorial topics from past issues, and analyzed new trends and challenges. To close out this fantastic year, we added laboratory design to our regularly featured article sections in print, developed a lab design E-newsletter, and built a dedicated space online to house more informative content for those involved in the design, build, or renovation of lab facilities.

For the final issue of 2019, the focus is on lab automation, robotics, and smart technologies. Our cover story profiles two companies aiming to revolutionize the way research is conducted and how labs are managed. For example, Magadelna Paluch, co-founder and CEO of LabTwin, interviewed lab managers and their staff from more than 100 labs around the world to better understand their biggest pain-points in the lab. She found that scientists spend up to 70 percent of their time at the bench, but have no easy way to access information during an experiment. Thus, LabTwin, the first voice-powered digital lab assistant, was born. Flip to page 10 to learn more.

Our Asset Management article (page 22) provides great insight on how to give your used equipment and consumables a second life through recycling. As author Michelle Dotzert explains, "Recycling services have the expertise to guide the preparation process and aid in removal and transportation, making the 'greener' choice an easy one." Other highlights of the issue include tips on preventive maintenance for lab equipment (page 18), our Health & Safety feature on ergonomics (page 32), and an Industry Insights article on preventing cell culture contamination.

We have also included a special gift in this issue—10 of them, actually. Turn to page 40 to check out *Lab Manager*'s Holiday Gift Guide, a collection of hand-picked, STEM-themed gifts to give loved ones, or to treat yourself with, this holiday season.

Wishing you a safe and happy holiday season. See you in 2020!

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LAB OF THE FUTURE

STREAMLINING WORKFLOWS WITH SMART TECHNOLOGY by Lauren Everett

The concept of "lab of the future" can mean a variety of things depending on who you ask, but one consistency is clear: new "smart" technologies are at the forefront.

Applications of smart technologies can be found all around us—from vehicles that sense and alert drivers to other vehicles entering their blind spot, to thermostats that automatically adjust your home's temperature throughout the day, to voice-activated devices that can inform you about the weather forecast or set reminders for you. However, innovative technologies like these, that make our daily tasks more convenient and safer, have been slow to enter the lab space. Researchers are expected to think creatively, solve complex problems, and unlock the latest breakthroughs, yet are limited by mostly manual, laborious processes and workflows. How can the innovations we utilize in our everyday life be adapted to simplify work in the lab? A new wave of emerging companies is developing solutions.

At the bench

Magdalena Paluch, co-founder and CEO of LabTwin, and her team visited more than 100 laboratories across the globe, interviewing lab managers and scientists to learn about their biggest pain points and limitations when working in the lab. They found that data entry errors and issues with reproducible research, siloed or fragmented information, and interruptions to experiments were some of the top issues for lab staff.

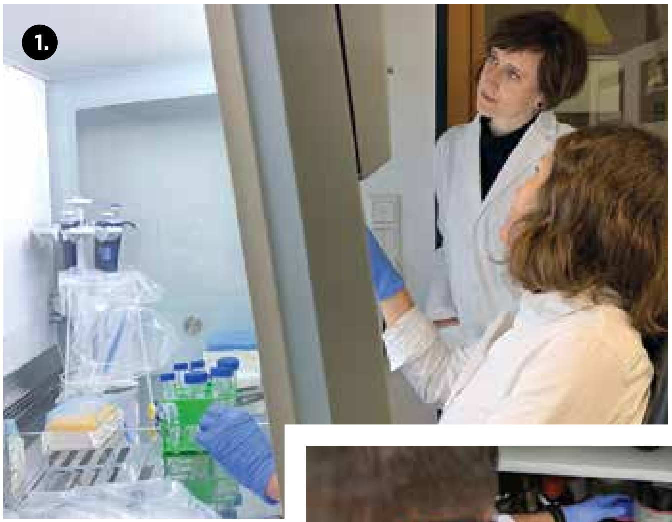
> "When we think about the lab, we should think of how it 'just works' around the scientists."

"We learned that scientists spend the majority of their time [50-70 percent] at the lab bench. At the bench, they have no good way to access information, so that was our initial inspiration for creating LabTwin—to enable real-time information documentation and access at the very point of experimentation," explains Paluch, who has more than 13 years' experience building new technologies.

LabTwin, which is described as the world's first voice-powered digital lab assistant, is transforming the way scientists conduct experiments, input data, and complete reports. The tool is accessible via a mobile app as well as through a web-based platform for desktop computers and tablets. Imagine scientists at the bench with their phone in their pocket, a headset in one of their ears, and an app on their phone that enables verbal communication with the digital assistant. The assistant is triggered to begin real-time documentation and provide access to information through a "wake" word, which can be customized by each scientist to avoid any potential confusion caused by multiple scientists working at the same time with the same generic wake word. "With our open API, we offer integration with an external database and lab informatics software to make work much more insightful and data-driven when at the bench," says Paluch.

In a white paper detailing the benefits of digitization and artificial intelligence in the lab, LabTwin cites that more than $28 billion is lost annually in the US on research that is not reproducible. While electronic lab notebooks (ELNs) are a good start to digitizing data, challenges still remain for workers at the bench. To help prevent human error and combat the reproducibility crisis, LabTwin offers the ability to have interactive protocols. As Paluch explains, scientists often print protocols before entering the lab, and take those printouts with them to the bench. But with LabTwin, that is no longer necessary. The digital assistant will verbally provide each step of the protocol, and the scientist can annotate or change the protocol as they go through it, so the steps or change of value is automatically recorded in real time. This transforms the traditional process of having to fully complete the experiment first, and then manually document what was done throughout the day, which runs the risk of information being lost or inaccurate.

"Scientists can work on four to five experiments in one day, and they have to keep track of all changes they've made, and later document them. We enable scientists to capture it right at the time of change," says Paluch. "We have also witnessed scientists having to leave the bench and the lab, which requires them to take off their gloves, wash their hands, etc., just to check information on a dilution for an experiment they ran a week earlier." By simply asking LabTwin to check that information for them, scientists no longer have to pause from their work. The tool knows scientific terms and acronyms,



1. Magdalena Paluch (back) CEO of LabTwin, is seen with Augusta Modestino (front), a scientist at Leonyte Biosystems. Credit: LabTwin **2.** LabFellows software provides labs unlimited streamlining of electronic ordering and reordering direct with suppliers in one place. Credit: LabFellows **3.** Environmental Health & Safety teams capture safety data sheets and important CAS numbers to create hazardous materials reports for seamless e-filing to local, state, and federal regulatory compliance agencies like the Environmental Protection Agency. Credit: LabFellows

such as ELISA, so scientists truly feel like they have a knowledgeable personal assistant at their disposal. The web application allows for further analysis, reporting, and connection to other systems when the scientist is no longer working at the bench.

To ensure security, the app complies with regulatory guidelines on data privacy and uses data encryption, user access tiering, and private networks to protect lab data. The app allows labs to create a complete audit trail of their work with automatic timestamps, electronic signatures, and (soon-to-be-launched) secure data storage.

When asked about what other needs have yet to be met in the lab, and what emerging trends may be here to stay, Paluch highlighted the continued use of machine learning and automation. "Many trends are driving this space," says Paluch. "Everyone speaks about machine learning, and how we can automate some of the very mundane processes that take place in the lab. That's our vision—to enable and empower scientists. They are at the center of what we do."

Less admin work, more science

To keep research and everyday lab activities on track, time needs to be dedicated to administrative tasks like taking inventory of supplies, submitting purchase orders, and checking equipment maintenance needs.

LabFellows is a newly launched software tool that helps lab managers build operational intelligence. The platform allows the user to set up all the lab's suppliers in one place, and provides solutions for four main areas of concern—procurement, inventory, lab compliance, and integrations. The software enables the user to manage vendors, approvals, and purchases all in one place. You can keep track of the lab's samples, chemicals, and reagents without the use of spreadsheets or notebooks. The software automatically adds purchases to your inventory, so everyone on staff knows what is available and where in the lab it is. It also stores and organizes your safety programs and documents, and connects with your other existing management systems and accounting software.

Like LabTwin, LabFellows aims to save time, and allows researchers to focus on the actual science instead of admin tasks. For example, according to the company, on any given day lab managers can spend up to 90 minutes setting up new vendor and payment terms; 120 minutes taking inventory by spreadsheet on a shared drive; and 30 minutes scheduling instrument maintenance and upkeep.

"When we start to figure out how to do science as a business, we find it really hard to do our work because a lot of the materials [needed] for an experiment are regulated materials," says Julio de Unamuno IV, co-founder and CEO of LabFellows, adding that establishing relationships with new vendors, verifying your lab is compliant, and receiving the materials needed for your lab requires a lot of paperwork and admin work to complete, which takes away from conducting research.

"Our 'secret sauce' is our B2B integrations, which allow you to directly connect with suppliers to do things like execute purchase orders," says de Unamuno. While many other systems create a PDF of your purchase order, which you then have to manually fax or email to your vendor to ensure the order is submitted, with LabFellows, it is automatically sent to the supplier.

"The number one order entry method in our space is the fax machine," says de Unamuno, highlighting the need for better solutions in the lab. "As technologists, we have traditionally failed the lab environment when it comes to these applications. Scientists don't have a problem with new technology, we're just not offering good enough products—that they would rather use a fax machine to place an order."

de Unamuno envisions the "lab of the future" will involve fusion of a variety of different apps and technologies to streamline processes, offer intelligent data, and provide a centralized system. "You're going to see more about how to better manage projects, and tools to get things done without getting your hands dirty. [For example] if your CO_2 cylinder runs low, an alarm will go off to have the supplier automatically come in and replace it. You're going to see an ecosystem of these different apps and tools come together and work together to be more unified. That trend is just starting."

"When we think about the lab, we should think of how it 'just works' around the scientists," says de Unamuno. LabFellows aims to help with this concept of seamless navigation around the lab. The system is able to learn from data the user enters and use that data to automate other lab operation processes. For example, it eliminates the need for double data entry of a lab's inventory, and can automatically populate inventory after the user simply hits one button saying they received the shipment. "Scientists like that all [they] have to do is shop, and then everything else gets automated," says de Unamuno.

What comes next?

As Paluch and de Unamuno both point out, there are still many opportunities to improve the modern lab. Over the years, lab staff have transitioned from recording data with pens and notebooks to utilizing cloud-based technologies and ELNs. But now, another wave of innovations is taking hold.

The ways in which research is conducted, and even the physical lab environment, may look quite different in the coming decade as emerging technologies simplify processes and more features become automated. Armed with a variety of smart technologies, lab managers will be better equipped to make informed decisions and lead their teams.

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Donald Danforth Plant Science Center's Advanced Bioimaging Laboratory

NEW CUTTING-EDGE TECHNOLOGIES WILL ACCELERATE DISCOVERY

by Lauren Everett

A facility within the Donald Danforth Plant Science Center (St. Louis, MO) not only has a new name, but also a wealth of new capabilities to drive research discoveries. The Advanced Bioimaging Laboratory (ABL), previously known as the Integrated Microscopy Facility, is incorporating machine learning and automation, as well as state-of-the-art instruments to accelerate the field of plant science.

Kirk J. Czymmek, PhD, who joined ABL as the director in May 2019, has been leading the charge and setting the vision for the facility's upgrade. Czymmek came to the lab with more than 30 years of advanced microscopy experience. He is an expert in light and electron microscopy, atomic force microscopy, single molecule imaging, super-resolution microscopy, cryo-techniques, and correlative microscopy. As he points out, plant research has been about a decade behind animal research in terms of using the latest technologies available to make new discoveries that can benefit humankind.

"Keep in mind fungi, bacteria, and viruses are all microscopic, so to understand the basic mechanisms of how these work, you need a microscope. You can see the effects of disease eventually, but if you want to stop it or understand the underlying causes, you will need to magnify it and use special probes and technologies to interrogate," Czymmek says. That is why he wants to apply new approaches and technologies to plant research at the Danforth Center, but believes the results will improve plant research across the globe. "I've heard the expression that St. Louis is the 'Silicon Valley of plant research' and it feels true to me. I feel a lot of energy here," says Czymmek.

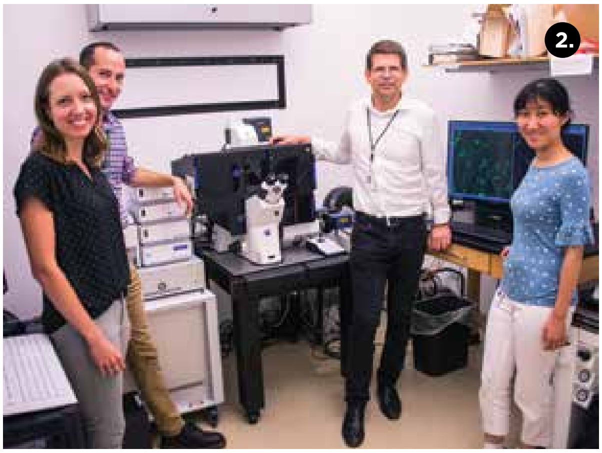
▲Super-resolution using single-molecule localization microscopy shows cell wall components (white/light-blue foci) in grass plant structures. *Credit: Dr. Yunqing Yu and Dr. Elizabeth Kellogg Lab, Donald Danforth Plant Science Center*

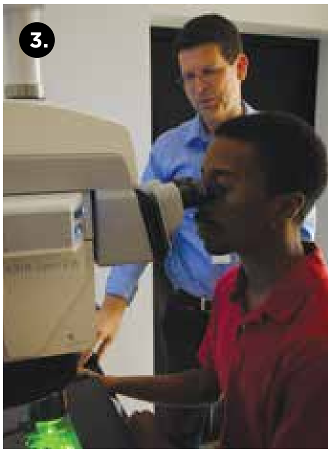
The ABL team uses contemporary molecular cytology, preparation, and imaging technologies to better understand the aspects of plant-microbe interactions and fungal cell biology. "Ultimately, our goal is to combine advanced imaging methodologies along with the latest molecular and genomics tool[s] to provide new insights into microbe interactions with plants and their environment to understand the disease-state and promote plant health," explains Czymmek on the lab's website.

Catching up

When trying to study plants, unique challenges arise that researchers don't encounter when working with animal cells. One of the biggest challenges with plants is that they have cell walls that act as rigid barriers, and are often impermeable. Plant cell walls are also made up of different chemicals and carbohydrates, which makes them difficult to analyze, unlike animal cells that have a simple membrane as a barrier. Despite these hurdles, plants have great potential to help improve our environment and educate us on how to maintain a healthy world.

"When it comes to plant disease, we can't fall asleep at the wheel and sometimes breeding and genetics isn't fast enough to stay ahead. We have to find other strategies to prevent disease when it arises, and to understand the fundamentals of how it is caused, which is a lot of what I focus on," says Czymmek.





Elevating research

ABL is the Danforth Center's hub for state-of-the-art cellular imaging instrumentation and services. Czymmek utilizes his expertise to help users design and implement their specific imaging experiments. "The number one thing I do when talking to a collaborator is ask 'what are the scientific questions you are trying to answer?'" says Czymmek. "And then I consider what microscopy tool(s) are most appropriate to help open a door that they weren't thinking about before." Just a few months after becoming director of ABL, Czymmek unveiled a suite of new instruments that will further assist researchers in accelerating their projects. One such instrument is the ZEISS AxioZoom microscope, which enables advanced automation to create large area maps and sophisticated multi-location and analysis routines. When asked how ABL has incorporated automation and machine learning into its workflows, Czymmek says, "What I need[ed] is a system that has versatility where it's not just about taking one picture and walking away from it, it's about probing the same organism or sample multiple times over a period of time to look at the changes that might be happening to it."

In the fall of 2019, Czymmek also demonstrated the potential of additional technologies the lab intends to implement. One highlight of the demonstration involved the ZEISS Elyra 7, a high-speed 3D and 4D super-resolution microscope that allows researchers to break the diffraction limit using structured illumination microscopy and single molecule localization microscopy techniques using antibodies or fluorescent proteins. This approach creates a two-fold resolution increase compared to traditional fluorescence microscopy, and makes it possible to see the faintest signals and tiniest structures in living and fixed samples.

Another important upcoming addition to ABL will be the Leica EM ICE High-Pressure Freezer—an innovative cryo-preparation approach for light and electron microscopy. As mentioned above, the cell walls of plants create a barrier that makes it difficult to analyze or get probes inside. Traditionally, to resolve this challenge and prepare samples in a lifelike state, samples are immersed in conventional chemical solutions. But during this preparation process, the plant slowly dies, and many changes can take place. "Depending on the biological question you're going after, using a cryogenic approach where you rapidly freeze the sample and preserve it in a more lifelike state can be highly beneficial," says Czymmek. This method also allows researchers to handle larger samples. "Previously, we had to cut a sample down to a three-millimeter dimeter size (A = 28.27 mm) and a fair bit of damage can happen to large plant specimens under this constraint. Now we can freeze plant structures that are six millimeters in diameter (A=113.1) with the new design and it is so much easier to use."

1. An exterior view of the Donald Danforth Plant Science Center, located in St. Louis, MO. **2.** A team of imaging experts and scientists evaluate the application of single-molecule super-resolution imaging to plant cell wall components with the ZEISS ELYRA 7 microscope. From left to right, Renee Dalrymple (ZEISS super-resolution specialist), Matthew Curtis (ZEISS 3D imaging specialist), Kirk Czymmek (director, Danforth ABL), and Yunqing Yu (postdoctoral associate, Elizabeth Kellogg Lab). **3.** Kevin Cox, a Howard Hughes Medical Institute postdoctoral fellow, examines a fluorescent plant specimen using the ZEISS Axio Zoom microscope with Czymmek. *Credit for all photos: Danforth Plant Science Center*

Although this initial expansion of instrumentation and techniques is significant, the ABL team is not stopping there. Czymmek intends to bring even more technologies to the facility, and to update other existing ones.

"Every five years, a major change in optical light microscopy occurs that will change the landscape of how we actually explore plant and animal cells and tissues at a microscopic level. That is why I am pushing for single molecule approaches, super resolution techniques, and techniques where we break the diffraction limit," says Czymmek.

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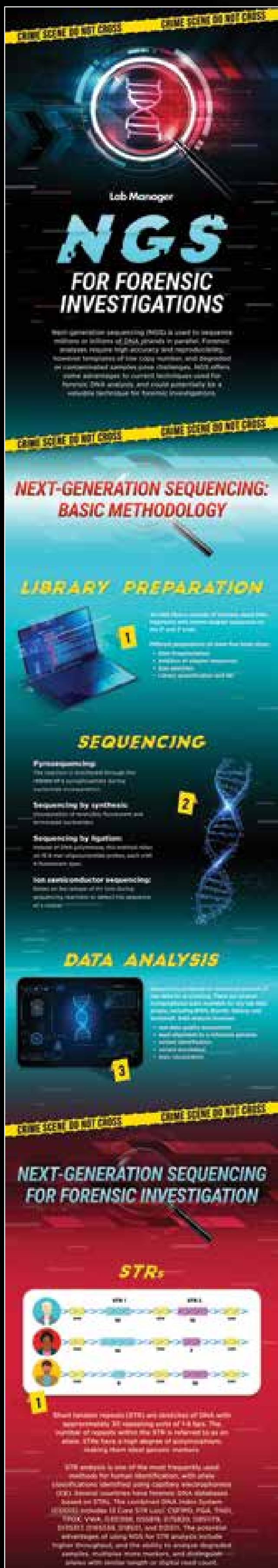

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Lab Equipment Maintenance

BE PREPARED FOR THE UNKNOWN WITH PREVENTIVE CARE

by Donna Kridelbaugh

Prasanna Tamarapu Parthasarathy, a research lab manager at Memorial Sloan Kettering Cancer Center, likens lab equipment to the "backbones" of any successful project. Without the properly functioning tools in place, you are unable to move forward with your work. She explains, "There's certain equipment that we use everyday. If any one of these is broken, an entire experiment will be postponed. It will have a domino effect."

Thus, it is critical for lab managers to keep equipment maintained in top condition to avoid any downtime and also costly repairs. While lab managers are ultimately responsible for operational efficacy, Parthasarathy empathizes that equipment maintenance is a team effort. This means having "people involved at the right place and at the right time."

Within the laboratory, Paris Grey, a research lab manager at the University of Florida and co-founder of the website Undergrad in the Lab, advises that an effective equipment maintenance program should start with the proper training and onboarding of lab members. She says, "This should include learning what sounds and equipment behavior is normal and what to do if something doesn't seem right."

Lezlee Dice, a laboratory manager at the University of Tennessee-Knoxville, also says overseeing equipment maintenance is a daily task. She explains that a lab manager needs to stay active in the lab and establish open lines of communication with team members to remind them of their responsibilities and to detect any issues that may arise. She cautions, "Prevent the creation of an environment where workers are afraid of getting in trouble if they report problems with equipment." While Lucy J. Towler, laboratory supervisor at American Acryl, has worked in different labs of varying sizes and functions, she underscores that the same best lab management practices apply for equipment maintenance, no matter where you work. Her overarching principle is to "keep a lab neat and organized." This goes a long way to prevent contamination or spills that can damage equipment. Towler also involves the entire lab team by requiring a weekly lab inspection checklist to be filled out by technicians on a rotational basis who then report any issues to her. This checklist includes components related to equipment operations, waste management, and safety items. She comments, "Prior to weekly assignments, one tech was doing them all and the other ones got complacent."

> "Lab managers also can get assistance with equipment maintenance from outside the organization through equipment manufacturers and third-party service providers."

It's also best practice to put systems in place to schedule time for performing preventive maintenance. These can include chore calendars for routine tasks and calendar reminders about regular preventive maintenance items. For example, when Grey's -80C lab freezer almost had

a meltdown more than a decade ago, she set up a monthly calendar reminder to do the required maintenance (e.g., vacuum the filter, check seal) to avoid near-catastrophic events in the future. She has stuck to the schedule ever since.

Dice further suggests using equipment sign-in sheets, especially for instruments located in shared facilities, for accountability purposes. This paperwork also documents usage to demonstrate the need for funding repairs or replacement in the future and who should be charged for consumables or other related expenses.

Responsibilities for equipment maintenance extend beyond the lab to other departments, depending on the internal organizational structure and overlapping functions or oversight duties. It is imperative for lab managers to maintain regular communications with these departments and ask for assistance when needed. In Parthasarathy's organization, the facilities management department runs regular operational checks on instruments and reports back to her on the status. After she has reviewed the reports, they work together, as required, to schedule maintenance events. In turn, she makes sure that lab members openly communicate with other departments (e.g., facilities management, EHS) as soon as equipment issues occur (e.g., equipment malfunction, biohazardous material spill).

For Towler, who oversees a quality lab in the chemical industry, she has other instrument control requirements to meet. For example, her lab runs weekly QA/QC checks on instruments and control charts the results. Additionally, she maintains a predetermined calibration schedule and documents these results. Other efforts include physically tagging equipment that is in or out of service and making sure to have backup equipment in case something goes down.

Towler points out that most of these efforts stem from their recent ISO 9001 certification achievement. However, she says, "Honestly, ISO is no different than other quality programs that are in place. Most are just good quality practices that should be set up in any quality lab." Therefore, lab managers can learn a lot by looking at such guidelines and reaching out to their own quality management professionals in-house to set up sound instrument control processes.

Lab managers also can get assistance with equipment maintenance from outside the organization through equipment manufacturers and third-party service providers. A range of services may be offered, from site visits to online trainings for lab managers. For some equipment, especially high-dollar items, purchasing a service contract with features that include routine maintenance and repairs by a qualified technician may be a good option to invest in.

Don Newton, a clinical laboratory consultant, explains it may make business sense to devote resources to service and maintain an instrument, instead of replacing in a few years. He says, "Keep in mind that, while lab technology changes rapidly, sometimes, based on what that [equipment] does, it doesn't change much at all. So, assess the condition and function of the [equipment], and what, if anything, has changed for that area of the lab. If your changes are small and it's still like new, then a longer service contract might be a good fit."

Newton also says that service contracts can be used as a bargaining chip in the purchasing process, and further cost savings can be achieved by partnering with another lab facility. Although, he warns, "While price is a driving factor, it's not the only factor. In the case of service contracts, you get what you pay for. So, sometimes it's better to pay a bit more now for stronger services later."

Another option may be an extended warranty. Parthasarathy says they buy a warranty for most of the equipment in their lab to have safeguards in case of a malfunction and to minimize the number of emergency maintenance site visits. Overall, lab managers need to do their homework to know what's covered by any service contracts or warranties and what can void any contracts in place (e.g., using nonapproved parts or reagents).

Field technicians are another valuable resource for lab managers. Dice advises to take advantage of their technical know-how during a site visit and have them train a responsible user on the proper way to maintain that equipment. Additionally, Newton says, when deciding on a service provider, it's important to evaluate the service reps for their areas of expertise, that they are certified on the specified equipment, and what their response time may look like based on multiple factors (e.g., workload, commute).

Lab managers also can strive to take a data-driven approach to identifying equipment maintenance needs and detecting potential malfunctions early on. This is now further enabled by the use of remote monitoring and smart technologies that provide real-time data collection and insights that can be accessed from anywhere. For example, Elemental Machines is a company that leverages the power of artificial intelligence and data science to streamline lab workflows and improve processes. Clients use the company's Internet of Things devices to remotely monitor equipment conditions and look for data anomalies that may indicate problems. The use of these devices provides a more complete dataset (e.g., temperature readings every 15 seconds) from which lab managers can base decisions.

John Morgan, director of marketing at Elemental Machines, says clients most often monitor cold storage equipment, incubators, and animal facilities where a controlled environment is required. In these cases, he notes an equipment malfunction could result in a catastrophic loss of valuable specimens and reagents. Morgan relays they have had multiple clients who noticed unusual temperature patterns emerging from their cold storage equipment data.[1,2] In both cases, these labs were able to show data collected with Elemental Machines devices to the manufacturer and obtain hardware or software fixes.

Additionally, a lab manager can be alerted if a temperature exceeds a specific threshold. Morgan says, "For instance, we recently had a power outage here in Cambridge on the weekend. One of our clients is right around the corner. He got a text alert at 6:30 a.m. on a Saturday and was able to go into the lab and load up his freezers with dry ice to save his samples."

Finally, Morgan explains the need to use data to optimize laboratory operations and improve the overall reproducibility of science. "You can't control what you don't understand," he says. "Our CEO, Sridhar Iyengar, often talks about the 'unknown unknowns.' What might be going on in your lab environment that could be affecting your processes? Sometimes you don't even know what it might be. Why not measure everything?" Therefore, lab managers should try to measure as much as possible to pinpoint issues and ensure laboratory conditions are reproducible. Case in point, Morgan mentions a client who observed irregular readings from their HPLC instrument, resulting from room temperature fluctuations due to the HVAC system.[3] Once the issue was identified, the lab was able to take steps to correct it.

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Breathing New Life into Old Equipment

NEARLY EVERY PIECE OF EQUIPMENT HAS THE POTENTIAL TO BE RECYCLED, WITH SOME HELP FROM THE EXPERTS **by Michelle Dotzert, PhD**

Recycling is an environmentally friendly way to dispose of lab equipment no longer in use. Depending on the condition of the instrument, maintenance and repair may return an item to manufacturer specifications for resale, or if it is no longer functional, working parts may be salvaged and sold, and the remaining scrap materials recycled.

That being said, there are some limits to consider, and determining which items may and may not be recycled is largely based on safety. Whether preparing a small benchtop centrifuge, or an MR system that requires a dedicated room, decontamination and removal of any hazardous substances is the top priority. "Most instruments can be recycled, but those presenting a radiation risk or extreme biological hazards should not be," explains Dante Boyer, president of The Lab World Group (Woburn, MA). "Certain molds that may have developed can present health problems as well as decontamination problems and may be better off being permanently disposed of." In addition to biological contaminants, cryogens and radiation must be considered for X-ray, CT, and MR imaging equipment. "Items we receive from medical facilities and labs must go through a certification process with the state to ensure harmful substances like cryogens have been removed before we pick it up," says Lou Ramondetta, president of Surplus Service (Fremont, CA). "If a piece of equipment meets the decontamination criteria to be recycled, then the call is really based on the useful life," explains Boyer.

> "If a piece of equipment meets the decontamination criteria to be recycled, then the call is really based on the useful life."

Once the equipment is deemed safe for recycling, there's the matter of transporting it. Depending on the size of the instrument, it may involve scheduling a simple pick up, or a complete deinstallation for larger, more complex systems. Companies have the expertise required to remove and transport all types of equipment. "We act as a turn-key, one-stop solution for our customers," says Boyer, "Once contacted by customers, we do an initial assessment of the assets along with the logistics of the overall project," he explains. For larger imaging systems, "We can deinstall CT and MR systems, and carry out all types of transport depending on the customer's needs, ranging from local pickup in the Bay Area, to white glove service. Depending on the price range and value of the device, we are able to offer different options to get the item to our facility," says Ramondetta.

Wondering what happens to that equipment when you've managed to get it out of the lab? "About 85 percent of what comes into our facility gets repaired, refurbished, and reused," says Ramondetta. "We have a team that goes through the equipment to evaluate it, and if it's a piece that goes directly to recycling, we have partners we work with that will recycle metal, plastic, or electronics." Sometimes when an instrument can't be repaired, its working parts may hold value. "This usually pertains to higher-end items like mass spectrometers or gas chromatographs. In addition, lasers, mirrors, and filters can be valuable," explains Boyer. To determine if an instrument is suitable for refurbishment, The Lab World Group uses "traceable NIST tools, ranging from data-loggers, thermometers, tachometers, CO_2 analyzers, etc. to see if items are working to manufacturers' specifications," he says.

> "Sometimes when an instrument can't be repaired, its working parts may hold value."

In light of growing concern over the accumulation of single-use and disposable products, new recycling solutions have emerged. MilliporeSigma's Biopharma Recycling Program uses a process from waste management company Triumvirate Environmental to recycle "bioreactor, buffer and sampling bags (multi-layered films), and assemblies and filters," says Jacqueline Ignacio, global manager, customer sustainability solutions at MilliporeSigma. "We also often recycle disposable protective gear, such as nitrile gloves, shoe and hair covers, and other items used in the manufacturing suite that are made from plastic materials," she explains. The program is available to MilliporeSigma's customers on the east coast of the US and begins with an on-site meeting during which Triumvirate performs a waste assessment. "This assessment helps identify all the products that can be included while outlining the most efficient logistics, containers to be used, and pick-up schedule," says Ignacio. "Each site has different needs, so many different collection schemes can be developed," she adds.

Recycling laboratory instruments and single-use products is an excellent way to keep them out of the landfill, and in some cases, repair and refurbishment adds years of functionality for subsequent owners. Recycling services have the expertise to guide the preparation process and aid in removal and transportation, making the "greener" choice an easy one.

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Continuing Education in the Laboratory

THE MOST SUCCESSFUL TEAMS NEVER STOP LEARNING **by Sara Goudarzi**

When James A. Kaufman caused an accident in the lab within two weeks of his start date of working for a biochemical company at age 30, he realized that school hadn't fully prepared him for the laboratory environment. That incident was the tipping point for Kaufman. Ever since, he's spent more than four decades trying to figure out how to share with others some of what he has learned about safety through the Laboratory Safety Institute (LSi), which he founded.

"Since then, we've educated over 100,000 people in 30 countries, in 130 different kinds of laboratories," says Kaufman, LSi's founder and president emeritus. "We [also] publish a small document called the Laboratory Safety Guidelines, of which six million copies have been given away in 21 languages." The institute provides courses, lectures, seminars, and workshops to labs. They also inspect laboratories, where representatives from LSi go in and compare what is, with what should be. Kaufman and his organization approach training through an important lens—safety—and he believes that in addition to initial training, continuing education is important in the success of a laboratory. "We all get careless," he says. "We all need reminders from time to time. Everybody needs regular refresher training, whether it's every year, every day, [or] every week."

"In addition to helping labs thrive and produce reliable results, training can allow individuals to further their personal goals."

During trainings, people come up to Kaufman and tell him that they've been at the job for decades and never had a problem, and ask in earnest why they should make a big deal about safety now. To that, he replies: "Congratulations, I'm glad you haven't had a problem, but that's not the question, the question is what would be the acceptable number of times to have x, y, or z happen? And I usually ask, how many times in a 40-year career do you want to have a piece of glass in your eyeball and generally the answer is zero."

Training for Success

Safety is just one facet of continuing education. At Nelson Laboratories LLC, a full-service contract microbiology and chemistry lab serving the healthcare industry, with headquarters in Salt Lake City and several large labs in various states and smaller labs around the globe, frequent and wide-ranging training is an important aspect of ensuring operations run smoothly. "We have a variety of methods to determine training needs at Nelson Labs, including monitoring quality trends, doing annual talent reviews, and annual employee training documentation reviews," says Jennifer L. Wilson, professional development manager, Nelson Laboratories LLC.

Training, Wilson explains, is not just key to a successful lab but the health of those depending on lab results:

"In our industry, every test matters because the products that we test will be used on patients. Obtaining accurate results can literally be a matter of life and death. Getting and keeping our employees trained enables us to perform tests without deviating from the procedure and ensuring our customers get exact results."

In addition to helping labs thrive and produce reliable results, training can allow individuals to further their personal goals. Such is the case for many scientists who might require additional skills to do so. The Association of Public Health Laboratories (APHL) is an organization that serves public health by representing US laboratories that monitor and respond to potential threats, such as a rabies or anthrax outbreak. Part of APHL's work is training staff and scientists from the public health laboratory network throughout the country and in Puerto Rico. There are several modalities APHL utilizes, one of which is a year-long emerging leadership program.

> "An important part of our culture is also to listen to employees for feedback on what works and continually improve our processes."

"All of these people who are laboratory scientists at public health labs really know their science—they have got that down, no problem," says Eva J Perlman, senior director, Training and Workforce Development at APHL. But as those people progress through their careers and become promoted to being supervisors or other management positions, they come to realize they might be missing certain leadership skills, effective communication tactics, ideas on how to motivate their team, good laboratory practices, ethics, safety issues, and how to tell a really good story, which involves translating analytics for people not in the sciences, in an effort to show impact. APHL's program can help such folks make the career transition or take on additional roles and responsibilities. They also develop programs by utilizing a variety of modalities based on training assessments, new regulations that might come up, and new methodology or protocols by the Centers for Disease Control and Prevention (CDC). "We will do webinars, seminars, [and] workshops that are experiential," Perlman says. Workshops "have a component that requires the students actually sit at the bench, look through the microscope, prepare media, whatever it is. Those particular activities in most cases, especially those hands-on experiential workshops, are around topics that are very unique to a state or local public health laboratories."

Such programs are important because the science continues to become more and more complex and people need to stay updated. "When you overlay or underpin the advances in technology, it becomes sort of that hamster wheel or almost trying to keep up with all of those advancements in evolution of the science and the technology," Perlman explains.

Training approaches

Every lab is unique and when it comes to continuing education, the leaders of each one must decide what works best for their team and goals. For some, intermittent formal training has a positive effect on keeping staff abreast of techniques and safety, while a less formal approach might be useful for others. At times, both are needed to meet the lab's objectives. And even within a lab, the learning styles of staff members are not homogenous. It's up to management to understand and decide on how best to train their personnel.

"Each person learns differently," says Zachary S. Anderson, director, Laboratory Operations, Nelson Laboratories LLC. "Our Professional Development Department has done an excellent job of creating content and criteria for developing training materials and trainer approaches. The breakdown of tasks, qualification steps, and employee assessments also helps us to ensure that employees are prepared to succeed. An important part of our culture is also to listen to employees for feedback on what works and continually improve our processes."

Further, everyone's goals vary. Some employees want to broaden their knowledge. Others like to focus on one specific topic and become experts in that particular area. "For those employees, we have roles where they can focus on one test, one industry, or one sterilization method, and learn all they can about it," Wilson says. "We send them to external industry training and to standards committee meetings through organizations such as AAMI, ISO, PDA, or ASTM."

Another consideration is budget. Labs have a finite amount of resources to dedicate to training, which can be expensive and take the scientists or technicians away from their everyday work. When Perlman of APHL's team performed a training assessment in 2018 and asked what the participants' preferred learning method was, the top two responses were classroom and workshops, both of which can be costly.

"In order for you to go someplace and attend a workshop it means you're away from the bench so the work that you would typically be doing has to get rerouted to somebody else, if there is somebody else," she says. "And when it comes to things like an online course, for example, then most often it's very difficult for a laboratory scientist within the public health lab to be able to access the computer to be able to participate in that online course during business hours."

But training doesn't always have to be formal. Managers could instill a culture of learning as part of the lab's routine activities, whether it's by giving a short presentation at the beginning of weekly meetings or putting up a bulletin board, as a passive learning center with relevant information on techniques, procedures, or chemical safety sheets.

Whatever combinations of methods each manager chooses, it's ultimately a means to allow the staff and the laboratory to grow in order to produce reliable results for their clients.

"The most important aspect of the work we do is that at the end of every study and product life cycle is a person in need of care," says Anderson. "When we hire great people, keep them motivated and engaged through challenging and important work, we positively affect global health. Supporting training and education is critical to our values."

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Automation and Robotics in Laboratory Design

HOW TECHNOLOGY AFFECTS THE FUTURE OF DATA ANALYSIS **by Mark Paskanik**

Viewing window for inspections and safety.
Credit: Triggs Photography

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

1. Lab equipment without automation. 2. Lab equipment with automation line and robot. *Credit: Triggs Photography*

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."[1] The robot in the laboratory will never have these problems and will also allow people to have more time for collaboration and innovation.

> "Really, the question is: why are you *not* using automation and robotics in your laboratory?"

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 (as seen in Image 1). If you trace the footsteps, you will see a very irregular pattern of flow that is inefficient. By installing the new automation line (seen in Image 2), 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.

"Tracking, data collection, and accountability can be enhanced or improved with automation and robotics."

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 of 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. A Tecan type liquid handler, for example, may only cost a few thousand dollars. 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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Ergonomics in the Lab

WHAT YOU NEED TO KNOW ABOUT REPETITIVE MOTION **by Vince McLeod**

Carpal tunnel is a term that strikes fear into everyone that uses a computer, and we all know how much computers are used in laboratories and research in general. Everything from data entry to notation and protocol documentation to grant, article, and proposal writing is digital today. But repetitive motion and associated musculoskeltal disorders (MSD) are not limited to computer users.[1] In this article, we will discuss the technical aspects of repetition/duration and force as it applies to ergonomic risk in lab and office settings. And we will offer solutions to get you through the days and weeks pain-free.

Breaks and rest combat repetitive motion

The definition of repetition is doing things over and over again. In repetitive work, the same motions are performed using the same parts of the body in the same way, time and time again. In activities such as typing, mousing, or entering data by referencing paper source documents, the affected muscles, tendons, and joints can be used thousands of times a day, week after week, year after year. The risk of injury is even greater when repetitious jobs involve awkward posture (e.g. bent or flexed wrists) or forceful exertions such as repetitive overreaching for the mouse (which can lead to shoulder and neck pain).

Our goal from an ergonomic standpoint is to, first and foremost, strive for neutral and balanced actions. Additionally, reducing the number of repetitions experienced by each set of muscles, tendons, and joints throughout the workday and allowing time for recovery is paramount. The body has great capacity to repair itself. Problems arise, however, when the amount of damage or stress accumulated over the course of time overtakes the body's ability to repair. This is when we experience pain. If the cumulative damage continues without allowing time to recover and heal, there is the potential for serious injury.

In order to introduce healing time, short breaks in repetitive tasks bring significant benefit. Break up data entry with variations in activity such as filing, reading, using the copier, or any other task that uses different muscles and motions than computer use. It is also good to include micro-breaks of just a minute or two every half hour or so during long data entry periods. Research has shown it is often better to take many small breaks than one long work break during the day. Try using software that tracks keystrokes and mouse movement and alerts you when breaks are appropriate.

Break down and analyze tasks

It is critical to examine and analyze the work being performed. Examine the job on a task-by-task basis. In many cases we have seen unnecessary repetitive work performed due to poor process design or evolution over time. When evaluating, ask yourself "can parts of this process be automated? Can equipment be linked directly for data collection? Can steps be eliminated or modified to improve flow or actions?" Investigate use of barcodes and readers to reduce data entry or entry readable/scanable forms or other types of information collection. It is always worth investing time to engineer a solution that will save significant time and effort in the long run.

An example: mouse use

Pain is often reported from mousing and usually attributed to over-use, and is often combined with poor mouse location. The conventional mouse requires a great amount of work to be directed through one arm, shoulder, and hand. It is a good idea to try to distribute this work and share it between both sides. One approach is the use of keyboard commands. Most operating systems contain keyboard commands or shortcuts for common tasks. Taking the time to explore and use these can greatly reduce mouse use, and once you get familiar with them will actually speed up your work.

Another remedy is to try one of the many "alternative" or "ergonomic" mice now offered. Some allow one to use both hands for mousing, sharing work between hands. Software programs allow you to automate common tasks (e.g. autofill) and develop scripts called macros to perform, reduce, or eliminate many actions. Their use can significantly decrease the amount of typing you need to do.

Exertion force

Force is the amount of muscular effort needed to perform work. Fatigue and injury track with the amount of force exerted. The more force required, the higher the risk of both.

Exertion force depends on many factors, including:

- The effort used to strike an object (e.g. key depression when typing)
- The shape and dimensions of an object you are working with
- How you grip an object or tool
- The precision of motion required to perform the task
- Duration of force applied by the muscles (e.g., the amount of time spent without a muscle-relaxation break)
- Awkward postures (bending, twisting, over-reaching)

Goal number one is to always have a neutral and balanced posture. Goal two is to reduce the number of repetitions or duration of exertion experienced by each set of muscles, tendons, and joints throughout the workday.

Number three is to reduce the force applied to perform the task. OSHA provides excellent help through their eTool on ergonomics.[2] Strive to recognize and reduce all the risk factors both on and off the job to effectively reduce the potential for repetitive motion pain and injury.

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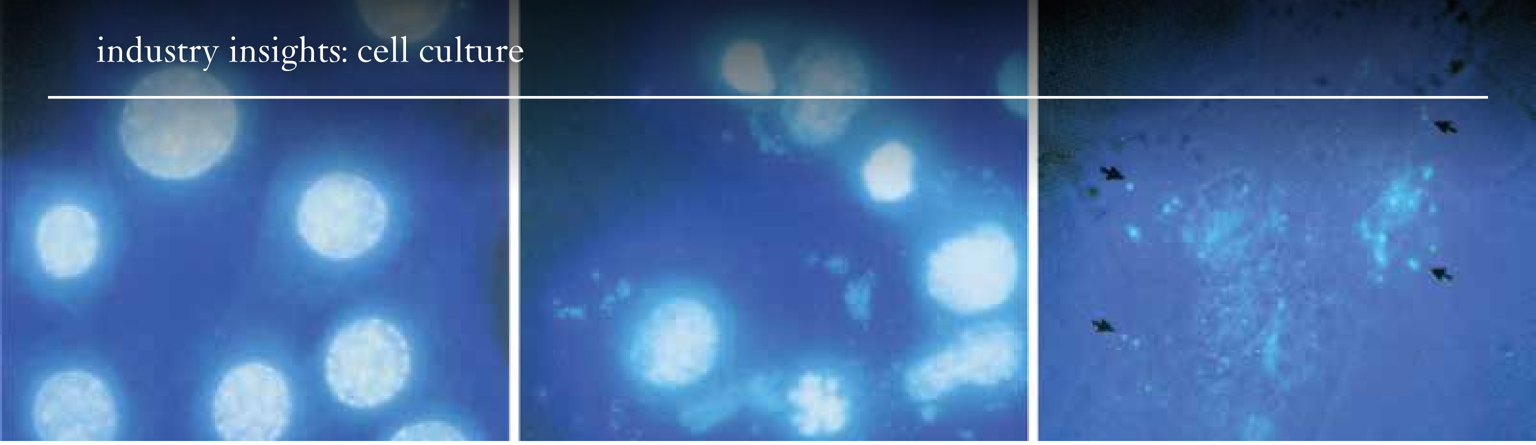

▲Photomicrographs of mycoplasma-free cultured cells (left panel) and cells infected with mycoplasma (center and right panel). *Credit: Thermo Fisher Scientific*

Cell Culture Contamination: An Ounce of Prevention is Worth a Pound of Cure

CONTAMINATION HAS SERIOUS CONSEQUENCES, AND PREVENTION IS ESSENTIAL FOR SUCCESSFUL OUTCOMES **by Michelle Dotzert, PhD**

The concept of cell culture was first explored more than a century ago, beginning with Wilhelm Roux's experiments culturing chick embryos in saline solution, and Ross Harrison's attempts to grow nerve fibers *in vitro*. Since then, cell culture has become a fundamental technique to examine cell growth, differentiation, and response to stimuli ranging from new drugs to toxins, with applications in vaccine research, protein therapeutics, and cancer research, among countless others. The basis of the technique is to grow and maintain cells *in vitro*, under controlled conditions, using either primary (finite) cells, prepared directly from tissues, or immortalized cells that may be cultured indefinitely. Common to all cell culture experiments is the threat of biological and chemical contamination, as well as cell-line cross-contamination, each having potentially disastrous effects. Adhering to best practices and working with specialized instruments designed to prevent contamination are critical for successful cell culture experiments.

> "Adhering to best practices and working with specialized instruments designed to prevent contamination are critical for successful cell culture experiments."

A MYRIAD OF POTENTIAL CONTAMINANTS

"There are two significant sources of cell culture contamination," says Mary Kay Bates, senior global cell culture scientist, laboratory equipment, Thermo Fisher Scientific. "The most common source of contamination is the flora present on laboratory workers, which can come from hair, breath, or skin. The second significant source is the laboratory environment itself; the incidence of contamination increases when a laboratory is not cleaned regularly." According to Jaleel Shujath, vice president of marketing at Absorption Systems, "biological contamination is most often caused by people not wearing the appropriate protective equipment (e.g., gloves, lab coats, goggles) or using improper techniques (e.g., not wiping down the cell culture hood, blocking laminar flow, and using the same pipettes between plates of different cell types)."

Biological contaminants include bacteria, fungi, viruses, mycoplasma, and even other mammalian cells. Contamination with bacteria, fungi, and yeast is generally easy to detect, either through increased turbidity of the medium, or microscopic visualization. Mycoplasma however, pose a serious threat to cell cultures and have unique features that make them difficult to detect. They eppendorf

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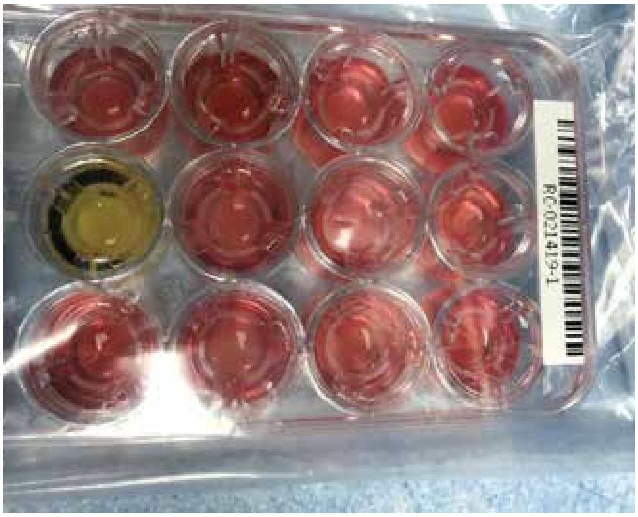

An example of cell culture contamination *Credit: Jaleel Shujath, Absorption Systems*

are smaller than bacteria, and lack a cell wall, meaning antibiotic treatment is futile. "Unfortunately, routine use of antibiotics can enable contamination by mycoplasma," says Bates. "Not only do antibiotics not work against mycoplasma, but they kill off other organisms such as *Staphylococcus aureus*, which might otherwise indicate a broad contamination early, allowing contaminated cultures to be discarded. As a result, undetected mycoplasma can thrive," she explains.

Cell culture is also susceptible to chemical contamination, occurring "when fumes from chemicals used circulate in the air and dissolve into the culture media," says Bates. Cleaning disinfectants and other volatile organic compounds including phenol-chloroform, β-mercaptoethanol, and isoamyl alcohol are all potential sources of contamination. Generally, poor technique also contributes to chemical contamination, says Shujath. Dimethyl sulfoxide (DMSO) is a cryoprotectant that is toxic to cells, and exposure at room temperature should be limited to no longer than absolutely necessary. "When cells are removed from liquid nitrogen to be plated, they must be quickly thawed in a warm water bath and the DMSO quickly removed," he explains.

The consequences of contamination may be severe. "Unexpected experimental results and premature cell death are the primary consequences of contamination," says Shujath. "For example, if running a standard cell-based assay, and contamination by other cells occurs, the assay results may drift over time. While this may also be due to high cell passage number, one cannot discount cell contamination," he says. Bacteria and fungi exert these detrimental effects by altering the pH of the culture medium. "Bacteria and fungi often produce lactic acid as a byproduct of metabolism, which makes the culture medium more acidic, leading to toxicity and cell death," explains Bates. Mycoplasma contamination does not have lethal effects, but "has been shown to cause chromosomal aberrations and morphological changes as well as reduce transfection efficiency," she says. Once detected, the process of rectifying cell culture contamination is time-consuming and costly. Shujath recalls a case of mycoplasma contamination: "acquiring and growing up new cells and redoing all the experiments set the research program back months, costing hundreds of thousands of dollars in material and labor costs."

ARE THOSE BREAST CANCER CELLS ACTUALLY BLADDER CELLS?

Working with multiple cell types is commonplace, but foregoing precautions can lead to cell line cross-contamination. "While tempting to save time by working with multiple different cell lines at the same time in the biological safety cabinet (BSC), this can result in the transfer of cells, for example, from a breast cancer cell culture to an ovarian cancer cell culture," says Bates. "If incoming cells grow faster, there may soon be none of the original cell culture remaining."

Alarmingly, there is evidence to suggest that up to one-third of tumor cell lines being used in scientific research are affected by inter-or intraspecies cross-contamination. "This is a big issue because experiments are no longer reproducible nor in most cases even valid," explains Shujath. "Retracted or withdrawn publications, harm to scientists' reputation[s], and wasted time and resources" may result, says Bates. Fortunately, there are ways to reduce the risk of potential cross-contamination. "The easiest precaution one can take, besides proper technique, is to get the cells from a reliable source (ie. biorepositories), expand and freeze down appropriately, and frequently thaw a fresh vial bi-weekly or monthly to use in experiments. In other words, don't keep using the same batch for months on end," says Shujath. Many journals are also implementing measures to ensure validity, and "most reputable journals now require cell line authentication before manuscripts can be published," says Bates. "Cell lines sourced from cell banks, such as the ATCC and the European Cell Bank will have been authenticated. For other cell lines, DNA analysis is available to secure authentication."

AN OUNCE OF PREVENTION

Between the numerous types of contaminants and sources of contamination, it would seem that cell culture contamination is inevitable. Fortunately, a combination of good technique and the right equipment can prevent most contamination.

Using proper aseptic technique is a simple way to reduce the risk of contamination. "Wear proper PPE and clean gloves with ethanol before entering the BSC," says Shujath, and "make sure that the laminar flow of the hood remains intact by placing only the needed supplies in the hood, and use slow and deliberate movements to allow the laminar flow to adjust. Do not use the same pipette between different cell types to prevent cell line cross-contamination and even within the same cell lines, pipettes should be changed often to prevent other biological contamination," he adds. Other considerations include "working with one cell type at a time, cleaning the laboratory, or resisting answering cellphone calls and texts while working with cells," says Bates.

Working with specialized equipment will also help to prevent contamination. "Instruments and equipment that have been specifically designed to prevent contamination are essential, such as using a biocontainment lid in a centrifuge, working in a properly designed and certified BSC, or using a CO_2 incubator with 100 percent solid copper interior and in-chamber HEPA filtration providing ISO Class 5 cleanroom conditions," explains Bates.

IMPLICATIONS FOR INDUSTRY

Contamination is a serious concern for the biopharmaceutical industry. Mycoplasma are especially concerning, as they may contribute to human disease. Since mycoplasma infection can't be detected with microscopic methods, specialized techniques are required. The US Code of Federal Regulations, FDA's Points to Consider, the International Conference on Harmonization, and US Pharmacopeia provide technical documentation for the detection of mycoplasma. Unfortunately, the established culture method requires a long incubation period and several sub-cultures, taking up to 28 days to complete, and is therefore not conducive to rapid screening required for products with short half-lives. This also delays the initiation of corrective measures, potentially resulting in the loss of downstream product. As a result, much more rapid microbiological methods have been developed and validated, and several companies offer rapid biopharmaceutical product testing. Given the detrimental effects of biological or chemical contamination, and even with more rapid testing methods, the best approach is to implement preventive measures including using good aseptic technique and equipment designed to minimize contamination.

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Richie Kohman, PhD

ASK THE EXPERT

INNOVATIONS IN NEXT-GEN SEQUENCING: FOCUS ON *IN SITU* RNA SEQUENCING

by Tanuja Koppal, PhD

Richie Kohman, PhD, senior research scientist and lead, Synthetic Biology, Wyss Institute for Biologically Inspired Engineering, Harvard Medical School, talks to contributing editor Tanuja Koppal, PhD, about the recent advances in *in situ* RNA sequencing (RNA-seq) and its emerging applications.

Q: What can you tell us about *in situ* RNA-seq and how it can be applied?

A: *In situ* sequencing allows RNA-seq to be performed directly on biological samples and therefore retains the spatial context of the transcripts. It follows a similar conceptual workflow as conventional RNA-seq, where RNA gets converted to DNA amplicons. Sequencing then occurs on custom microscopy equipment with integrated fluidics. This process essentially converts the biological sample into a next-generation sequencing flow cell. *In situ* sequencing provides a spatial context that is lost by other methods. As cells exist in a dynamic and complex microenvironment, preservation of their spatial relationship can be crucial for understanding their fundamental biology or being able to effectively study and diagnose diseases. *In situ* sequencing can be applied to many different sample types ranging from whole zebrafish to mouse brain sections to human induced pluripotent stem cells. The technique is agnostic to sample type and hence, the applications can be very diverse. The hope is that once commercialized, the technology can be made available to more laboratories.

Q: How did you get interested in this technology?

A: My introduction to the field came through the *in situ* work I was doing with a team of researchers in Dr. George Church's lab at the Wyss Institute. They were developing a foundational technology in the field and some members of the group founded the company ReadCoor Inc. to commercialize the technology. Since the spinout, I have been running a team at Wyss to create new variations of the technology, as well as find ways to apply it in new directions. For instance, I was recently co-PI with Dr. Church on the Machine Intelligence from Cortical Networks (MICrONS) project funded by Intelligence Advanced Research Projects Activity, which aims to use *in situ* sequencing to map the neural connectivity within the mouse visual cortex. I became interested in the technology because of the multidisciplinary challenges it posed, as well as the number of applications it can be used for. In particular, I was drawn to its use in studying the brain, as there are still many fundamental questions that remain unanswered in neuroscience.

> "I became interested in the technology because of the multidisciplinary challenges it posed, as well as the number of applications it can be used for."

Q: What are some of the current technical challenges when doing *in situ* RNA-Seq?

A: With regular RNA-seq, there is not much information obtained on spatial resolution at the sub-cellular level. However, doing *in situ* RNA-seq by coupling microscopy with sequencing is a formidable engineering challenge and is probably not something that can be set up in a lab for a single experiment or project. There are issues associated with sample handling, sample movement, heat transfer, fluidics, and more that need to be addressed before the imaging and sequencing come into play. There is also the challenge surrounding data acquisition and analysis that needs to be tackled after iterations of sequencing data are generated. The company ReadCoor Inc. that is commercializing this technology is currently developing instruments and reagents so that laboratories can perform *in situ* sequencing themselves.

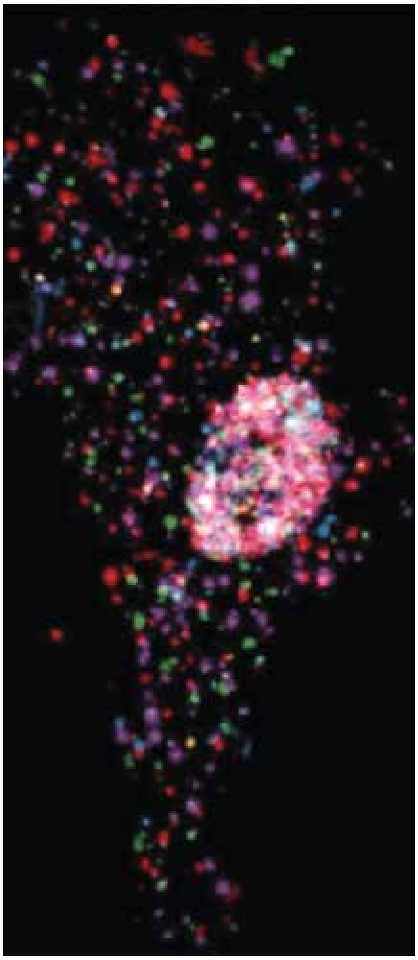
Q: What are some of the upcoming trends and technologies in sequencing that we should be aware of?

A: The inclusion of the 3D context for gene expression introduces many additional, multi-disciplinary challenges relating to instrument engineering, microscopy, and data analysis. Fortunately, the field has solved many of these problems and industrial *in situ* sequencing is emerging. Soon, it will be increasingly common to analyze the identity of endogenous transcripts within their spatial, biological context.

Two additional trends in the field can be seen emerging. One is that *in situ* sequencing will be coupled with synthetic biology approaches for writing molecular signatures into biological samples. In this case, the targets of interest will not be natural molecules but rather engineered ones. For instance, in the Synthetic Biology Platform at the Wyss Institute, we engineered a mouse that records its development through evolving CRISPR guide RNAs. By performing *in situ* sequencing of this RNA, one can obtain 3D lineage maps that are very difficult to obtain from other methods.

Another trend will be the coupling of *in situ* RNA detection with the simultaneous analysis of other molecular modalities such as proteins and genomic DNA. Because of the scalability of sequencing chemistry, it will be possible to analyze large numbers of different molecular types provided they can be made compatible with the current sequencing pipelines. By analyzing additional target types, a more complete molecular profile of cells and tissues can be obtained.

> "There are issues associated with sample handling, sample movement, heat transfer, fluidics, and more that need to be addressed before the imaging and sequencing come into play."



▲Image 1: A representative image of a sequencing round performed on a primary fibroblast. Credit: "Highly Multiplexed Subcellular RNA Sequencing *in Situ*" - Je Hyuk Lee et al. *Science* 343, 1360 (2014); DOI: 10.1126/science.1250212

Richie Kohman, PhD, is a senior research scientist and the lead of the Synthetic Biology Platform at the Wyss Institute for Biologically Inspired Engineering at Harvard University. He received his BS from Santa Clara University and PhD from the University of Illinois Urbana-Champaign, both in chemistry. Subsequently, he was postdoctoral fellow in the Department of Biomedical Engineering at Boston University, an affiliate of the MIT Media Lab, and group leader at Expansion Technologies, Inc. Currently, he oversees all research conducted by the Synthetic Biology Platform including advances in nucleic acid synthesis, *in situ* sequencing, gene editing, genome recoding, neurotechnology, gene therapy, stem cell therapy, anti-aging, and all aspects relating to the intersection of synthetic biology and synthetic chemistry.

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Holiday Gift Guide

BY *LAB MANAGER*

Our editorial team has hand-picked 10 STEM-themed gifts to give your loved ones this holiday season. Share your passion of science and technology with friends, colleagues, and family, or treat yourself to one of these fun products. With a range of price points and options for every age group, you can put a smile on everyone's face on your gift-gifting list this year.

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1 **littleBits Star Wars Droid Inventor Kit.** *Chosen by Laura Quevedo, eMarketing coordinator.* Winner of 50+ toy awards, this customizable droid product is great for the ultimate *Star Wars* fan. Kids eight years and older can create their own droid and bring it to life using littleBits electronic blocks. The app includes 22 coding missions for users to level up their computer science skills. Available at amazon.com. Price: $64.99

2 **National Geographic Scientist Barbie Collection.** *Chosen by Catherine Crawford-Brown, digital media coordinator.* Barbie is an adventurous spirit, always enthusiastic about exploring the world. Now, Barbie has partnered with National Geographic to encourage imagination, expression, and discovery through play. Choose from a marine biologist, astrophysicist, entomologist, or other science professions to kickstart your child's interest in a STEM career. Available at shop.nationalgeographic.com. Price: $45.95

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3 **'Forget Lab Safety' T-Shirt.** *Chosen by MaryBeth DiDonna, lab design editor.* We all know lab safety is a top priority, but a little humor never hurt anyone! Embrace your inner superhero with your new go-to casual shirt. Sizes range from juniors to adults, and can also be purchased as a tank top. Available at snorgtees.com. Price: $20

4 **Apollo 11 50th Anniversary Framed Print.** *Chosen by Lauren Everett, managing editor.* Want to own a piece of the actual Apollo 11 Command Module? This commemorative print of the Apollo 11 Moon landing also includes a space-flown fragment of the Kapton thermal insulation. Available at scientificsonline.com Price: $179.95

5 **Its Atomic – Periodic Table Game.** *Chosen by Rachel Muenz, associate editor.* Perfect for family game nights or for classroom use, everyone can enjoy this scientific twist on the classic brick tower game. Each brick is printed with an element name and atomic number, and the game features three rule variations: traditional, atomic, and for advanced geeks only. Available at scientificsonline.com. Price: $32.95

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6 Giant Microbes Vaccine Pack. *Chosen by Michelle Dotzert, scientific technical editor.* These plush toy friends may look cute, but don't let them fool you. The four-pack includes minis of Hepatitis, Polio, Tetanus, and Rotavirus and can serve as a reminder to get vaccinated. Browse the site for other plush vaccine collections. Available at giantmicrobes.com. Price: $16.95

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7 Beaker Terrarium Kit. *Chosen by Trevor Henderson, editorial director.* Do you know a DIY enthusiast? This terrarium kit comes with everything you need to test out your green thumb, including a beaker, accent stones, moss, and an air plant. A great addition to liven up an office or home. Available at etsy.com. Price: $27

8 KiwiCo Crates. *Chosen by Danielle Gibbons, art director.* Fun and educational science projects delivered right to your door. This monthly subscription allows you to choose from a variety of plans based on age (from infant to 16-years-old) and topic of interest. The kits inspire children to think creatively and become problem solvers—young scientists in the making! Available at kiwico.com. Price: starting at $16.95/month

9 Botanical Friends Bud and Mary Jane. *Chosen by Andrea Cole, business coordinator.* This botanical plush toy pair is the ideal gift for horticulturists, hydroponics lab workers, or chemistry and cannabis enthusiasts. Make Bud and Mary Jane the new mascots of your cannabis research lab, or use them to help teach others about cannabis science and cultivation. Available at labratgifts.com. Price: $19.98

10 *Lab Manager* Live Events. The *Lab Manager* team will be hosting three unique events in 2020—the Lab Manager Design Summit, Leadership Summit, and Lab Safety Summit. Come meet us or send employees to one (or more) of these educational events, geared specifically toward lab managers and others in leadership positions. Learn more at: summit.labmanager.com/design; summit.labmanager.com/leadership; and summit.labmanager.com/safety. Registration pricing varies.

Disclaimer: The products in this gift guide were chosen at the discretion of the Lab Manager *team, and no additional compensation was received. Any product claim, statistic, quote, or other representation about a product or service should be verified with the manufacturer, provider, or party in question.*

AUTOMATED LIQUID HANDLERS

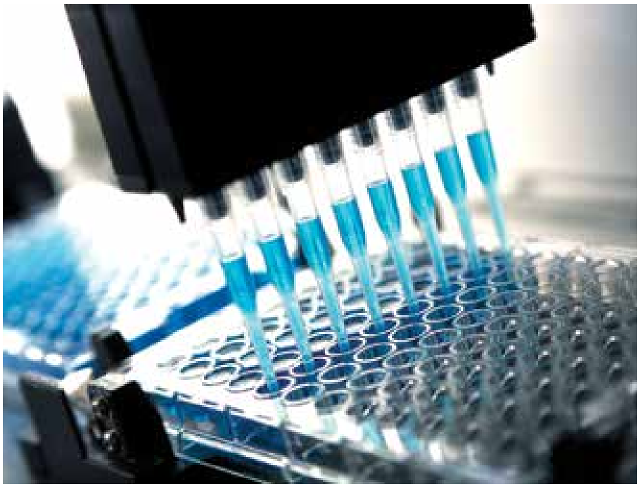
AUTOMATION IN CHEMICAL SCREENING AND BEYOND

by Brandoch Cook, PhD

The identification of new drugs from among an infinite combination of atoms and linkages has, for most of its history, been restricted by the slow crawl of low throughput intrinsic to the technology available. A classic example of drug discovery that has evolved along with gains in throughput is the identification of microtubule targeting agents (MTAs). For several hundred years, botanicals derived from the autumn crocus have been used to relieve gout and other inflammatory immune disorders. The active ingredient, colchicine, was identified and characterized in the 1940s, but its actual activity was not defined until the 1960s. Because colchicine treatment accentuates mitotic figures in cell preparations, allowing easy visualization, its use in research led to definitive proof that human cells have 46, not 48, chromosomes. Forward chemical genetic investigations later linked a cellular function, mitosis, to discovery of a protein, tubulin, via binding of colchicine. Another MTA, Taxol, was identified shortly thereafter, and surprisingly displayed an opposing function to colchicine, promoting rather than inhibiting microtubule polymerization. Like colchicine, Taxol is botanical in origin, from the bark of the Pacific yew. Because of the strength of its microtubule binding activity, Taxol was used to biochemically pull down, purify, and characterize components of protein complexes that reside there along with tubulin. Throughout the next two decades, the anti-tumor activities of Taxol were investigated and defined, and since its initial FDA approval in 1992, it has been used widely in chemotherapeutic regimens, particularly for breast and ovarian cancers.

The existence of two perfectly opposing MTAs in the limitless chemical wilderness prompts the tantalizing idea that there are many more out there, and that perhaps problems like chemotherapeutic drug resistance can be overcome by using them in series or parallel, analogously to classes of antibiotics. Or that activities and specificities can be optimized, and toxicities minimized. The great contemporary leap in capability for chemical screening using extensive natural product and synthetic libraries unlocks the possibility that investigators may actually find them. Hence, modern MTA drug discovery has evolved to incorporate assays with ever-greater sensitivity and throughput. Initial improvements relied on detection of changes in refracted light sent through purified microtubule samples stained with nucleic acid-binding dyes. Recent improvements have increased sensitivity many-fold by using enzymatically applied fluorophore tags, and automating microscopic assays to detect slight changes in fluorescent emissions. As a result, there are many new candidate MTAs somewhere along the pipeline from the wilderness to the door step.

These developments have only been possible with the reduction of human error. To a certain extent, the more human hands manipulate things in the realm of the very small, the more they skew the results in ways that are, by contrast, very large. In chemical screening and many other high-throughput protocols, automated liquid handlers have stepped in where human hands would otherwise fail. Liquid handlers apply robotics and software to program and manipulate liquid distribution tasks into adaptable outputs. This can take a form procedurally indistinguishable from pipetting small volumes into microwell plates, but using movable arms and interchangeable stages by calibrating compressed air through plastic tips. It may also be something as divergent as automating the flow of bacterial colony picking, culturing, and genetic analysis, guiding robotics with sound waves. Consequently, outputs for liquid handlers cover a broad range of categories, including chemical library deposition, stepwise qPCR setup, and biochemical or cellular biology-based screening using techniques such as ELISA or flow cytometry. Because of the diversity of outputs, liquid handlers come in multipurpose formats



that can be customized to different assays, or specialized formats adapted to specific repetitive tasks that can automate immunohistochemical staining, antibody purification, and more.

Hamilton Robotics offers the multipurpose Microlab series of liquid handlers. The Microlab Vantage model coordinates pipets and tips with compressed O-ring expansion (CORE), and comes in an array of modular, stacking cabinets that includes: 1) a pipettor with customizable arms, channels, and transport; 2) a logistics cabinet with storage, waste, device integration, and transport ports; 3) a track gripper with transportation between pipettor and logistics cabinets or third-party output instruments; and 4) a rear integration cabinet with storage and device integration space. The PerkinElmer JANUS and Beckman Coulter Biomek series offer analogous setups, although each differs in its ability to combine with other models, its available number of decks for microplates (and therefore its optimal throughput), and range of pipetting volume. For instance, the Janus MDT nanohead extension enables pipetting down to 50 nanoliters, making it competitive with specialized drug discovery-oriented liquid handlers such as Labcyte Echo.

In any high-throughput process, error and contamination can come from a wide variety of human sources: mis-pipetting into adjacent microwells; miscalculation of reagents in master mixes; or contaminants on gloves, tubes, or equipment that transfers into microwells. These errors can magnify discrepancies in final results; this is especially true with contaminating DNAs that can be mis-amplified in qPCR reactions. In a series of tests executed by the Eppendorf Corporation, manual reactions in three separate iterations using the same set of reagents obtained copy numbers diverging by two orders of magnitude. In equivalent automated setups using their EpMotion liquid handler, variability decreased to 1.5 percent, with single copy detection sensitivity.

“In chemical screening and many other high-throughput protocols, automated liquid handlers have stepped in where human hands would otherwise fail.”

Discrepancies in consistency between manual and automated protocols is not only a boon to research science and reproducibility—these differences can have real, life-or-death implications. Accurate and rapid identification of pathogens or emerging disease vectors have the potential to mitigate food-borne illness or tropical disease outbreaks. Projects to streamline DNA profiling workflows, for example with PerkinElmer working to apply their technology to discrete liquid handling steps from pre-processing, to DNA extraction, qPCR setup, DNA normalization, short tandem repeat reactions, and final reaction clean-up can minimize error in the identification of criminal suspects. Automated processing of DNA samples on FTA cards for upload to the FBI’s CODIS database can streamline and standardize national links between criminal acts and DNA profiles, with greater speed and accuracy. With the application of robotics to steps where it is becoming increasingly necessary to do so, researchers can devote themselves more fully to the tasks of data collection and analysis, where robots are not quite ready to tread.

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FOR ADDITIONAL RESOURCES ON AUTOMATED LIQUID HANDLERS, INCLUDING USEFUL ARTICLES AND A LIST OF MANUFACTURERS, VISIT WWW.LABMANAGER.COM/AUTO-LIQUID-HANDLERS

GAS CHROMATOGRAPHY

AUTOMATION FOR GC SAMPLE PREPARATION

by Mike May, PhD

To separate the components in a sample with gas chromatography (GC), proper sample preparation is important. The sample may be cleaned up in various ways to improve the selectivity of the separation, and it must be volatilized prior to injection into a GC platform. The preparation can be manual or automated, depending on the application, as well as the required throughput.

> "For labs that run more GC and at higher throughputs, taking the time to automate sample preparation can be crucial."

In some cases, automating the preparation of GC samples just doesn't make sense in time or financial cost. "We do not have our GC preps automated," says Rachel Behrens, lab manager at the polymer characterization facilities at the University of California, Santa Barbara. As she notes, GC is not used that often in her lab. "My researchers only prepare a few samples at a time, and it is often to help identify analytes that they might not be able to address via other means, such as nuclear magnetic resonance and other techniques."

For labs that run more GC and at higher throughputs, taking the time to automate sample preparation can be crucial, and may be achieved with various methods.

Commercial options

The market offers several options for automating GC sample preparation. In many cases, a scientist can simply buy a device that does the sample prep. As an example, Germany-based GERSTEL offers its MultiPurpose Sampler MPS. This robot can automatically prepare samples for GC and GC-MS (gas chromatography-mass spectrometry). That's just one of many manufactured platforms to consider. California-based Agilent offers a collection of options, including several GC autosamplers that can run dilutions, derivatizations, and more.

Refined research methods

Some scientists started automating sample preparation for GC decades ago. In 1994, scientists working on MIT's NASA-sponsored Advanced Global Atmospheric Gases Experiment (AGAGE) installed an automated GC-MS system in Ireland, as part of AGAGE's mission to study changes in chemicals and climate around the world. This platform could capture a two-liter sample of air, concentrate desired samples with an adsorbent-filled trap kept at about -55°C, and analyze the chemical components, down to concentrations of 0.2 parts per trillion.

That system triggered even more advanced technology. For instance, at the University of California, San Diego/ Scripps Institution of Oceanography, Jens Mühle notes that AGAGE uses "our most advanced GC-MS systems—the 'Medusa' automated gas chromatographic systems with mass spectrometric detection—for ultra-low-level, high-precision, long-term reproducible measurements of ozone depleting substances and synthetic greenhouse gases." This system uses two traps, which are filled with polymer absorbents to automatically concentrate specific analytes. These traps are kept at a colder temperature, about -165°C, to allow the capture of a wider range of chemicals, especially more volatile ones. With dual traps, it uses fractional distillation to purify analytes of interfering compounds, refocusing from a large trap to a smaller one. Consequently, this automatic sample preparation produces reproducible injections for GC-MS.

From the comfort of a lab to some distant testing site, automating parts of GC sample preparation can come in handy in some cases and be indispensable in others. It all depends on the lab and the application.

Mike May is a freelance writer and editor living in Texas. You can reach him at mike@techtyper.com.

FOR ADDITIONAL RESOURCES ON GAS CHROMATOGRAPHY, INCLUDING USEFUL ARTICLES AND A LIST OF MANUFACTURERS, VISIT WWW.LABMANAGER.COM/GC

Protect Fragile 3D Spheroids and Non-/Loosely-Adherent Cells During Automated Media Exchange

CELL-FRIENDLY FEATURES FACILITATE CELL BIOLOGY WORKFLOWS

Q

How to increase media exchange efficiency without harming or losing cells?

Media exchanges, where spent media is removed and replaced with fresh media, may seem routine yet they are critical to cell culture viability and proliferation. Even with deep focus and a steady hand, cell damage and accidental evacuation are often unavoidable when performing media exchanges in 3D and non-/loosely-adherent 2D cell cultures with a handheld pipette. On top of that, this manual method is laborious and variable, which can skew results and slow the overall pace of research activities. Automated liquid handlers increase efficiency, but also risk damage and loss as they lack capabilities specific to cell culture workflows.

A

An automated liquid handler with a specialized media exchange module provides gentle, consistent, and effective aspirating and dispensing.

MultiFlo™ FX, with its Automated Media Exchange (AMX™) module is optimized with cell-friendly features for consistent results that are unmatched by other liquid handlers or manual methods. The modular MultiFlo FX can incorporate up to four dispensers and a washer; the AMX module consists of specialized, autoclavable cassettes with separate aspirate and dispense heads, plus two software controlled peristaltic pumps that remove spent media and deliver fresh media without disturbing sensitive spheroids and cells in 96- and 384-well format. This system is well-suited for integration with BioTek's automated incubator, imagers, or multi-mode readers for further enhanced efficiency.

MULTIFLO FX MULTI-MODE DISPENSER with AMX Automated Media Exchange module increases workflow consistency and walkaway efficiency while protecting 3D spheroids and non-/loosely-adherent cells during critical media exchange steps.

ION CHROMATOGRAPHY

PREPARATIVE CHROMATOGRAPHY: WHEN MOST OTHER METHODS FAIL

by Angelo DePalma, PhD

Preparative chromatography—the non-analytical chromatographic purification of milligrams to kilograms of product—has found applications in many industries and for a diverse set of molecules. Preparative-grade resins and pre-packed columns are now available for most separation modes, including normal phase (e.g. flash chromatography), reverse phase, affinity, size exclusion, HILIC (hydrophilic interaction chromatography), IMAC (immobilized metal affinity chromatography), and both cation and anion exchange.

Over the last 30 years, the purification of therapeutic molecules, especially proteins at manufacturing scale, has driven many of the advances in preparative chromatography. This has given rise to resins and columns applicable to process development and, via scale-down and high throughput experiments, process optimization and troubleshooting. These products in turn have facilitated drug discovery and academic research that relied on purifying proteins and peptides from their often-complex matrices.

Whether these applications employ one of the separation modes mentioned above, or specifically ion exchange, depends on the molecule and circumstances. "Ion exchange lends itself well to purification of many classes of therapeutic proteins. It resolves both process-related impurities such as host cell proteins, and product-related impurities such as charge variants, with scalability and under mild conditions," says Dr. Peter Hagwall, who manages process development and characterization products for GE Healthcare (Uppsala, Sweden). "The emergence of novel antibodies and therapeutic proteins, for example bispecific or trispecific antibodies and antibody fragments, makes ion exchange—including mixed-mode resins—even more attractive."

Preparative ion exchange also works well for viral vectors, which are essential components for both cell and gene therapies. Here, it resolves capsids that are empty versus those containing the therapeutic gene. Even in instances where the standard HPLC analytical method uses reverse phase separation, ion exchange may be preferable at preparative or even manufacturing scale.

Under pressure

The physical conditions that chromatography resins experience during purification is a key factor in resin selection. Among these, pressure is arguably the most significant. Many purification resins, including ion exchangers, are based on agarose beads. GE has historically relied on agarose as a base resin material, and has further refined this material for the high flows and relatively low pressures required at prep scales. GE's high-flow agarose products are all named by some variant on the trade name "Capto™," for example Capto SP/Q ImpRes or Capto S/Q HiRes ion exchange resins. Most of these materials are available both in pre-packed columns and, in some cases, as loose resins.

Higher-flow operation is critical at preparative scales because the shorter the processing time, the less stress the target molecules experience and the more their structural stability is preserved. GE has demonstrated a time saving of approximately half in the elution step for large-scale purification on Capto ImpRes high-flow resin columns, compared with Q Sepharose High Performance resin, a conventional-flow anion exchanger.

According to Hagwall, many researchers still use previous generations of resins, while process developers have mostly adopted high-flow resins. "The productivity improvements of higher flow seem less beneficial in the laboratory than in a production environment," he says. Yet Hagwall notes "frustration" on the part of process developers who must redesign purification trains when incorporating high-flow resins at large scale.

At laboratory scale, pre-packed columns are often viewed as an extravagance, as nearly every manufacturer who offers such columns also offers loose resins at lower cost per resin volume. "However, more and more scientists, even academics, are taking advantage of the consistency and robustness afforded by prepacked columns," Hagwall adds. Vendors typically offer a variety of prepacked options, from off-the-shelf prepacked columns without packing qualification data to custom-packed columns including certificates of analysis for the most important resin and column characteristics. "These columns come with full documentation, which is essential for GMP or GLP work."

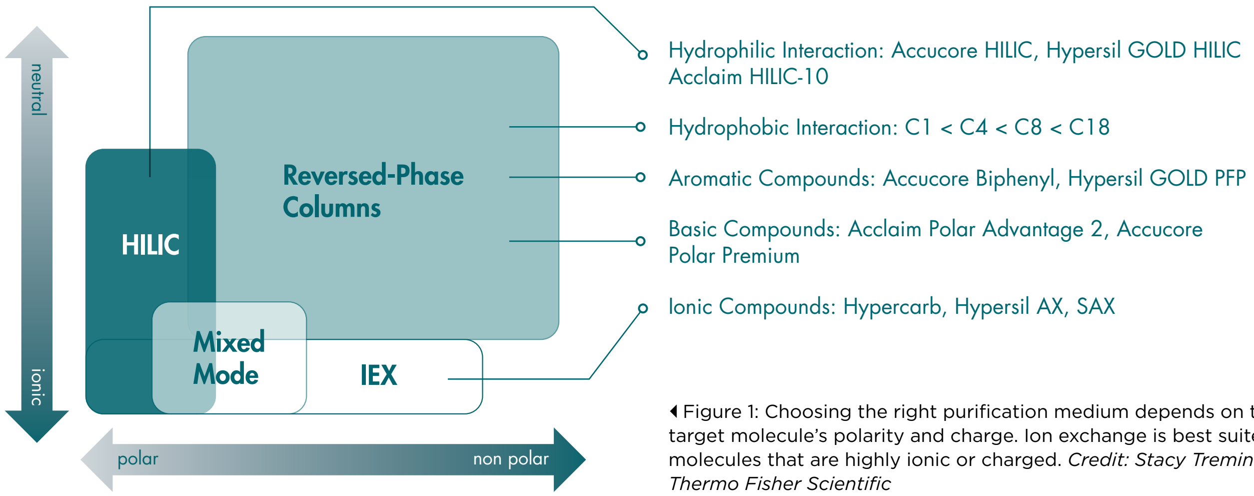

Figure 1: Choosing the right purification medium depends on the target molecule's polarity and charge. Ion exchange is best suited to molecules that are highly ionic or charged. *Credit: Stacy Tremintin, Thermo Fisher Scientific*

As shown in Figure 1, the choice of chromatographic purification mode depends on the target molecule's polarity and charge. Ion exchange works best for charged or highly ionic compounds, including proteins, peptides, and oligonucleotides. That assumes all other factors are equal, which they frequently are not. Immunoglobulin G-based monoclonal antibodies, for example, may be purified by cation exchange. However, these molecules have very high affinity for protein A, which is almost always used to capture antibodies at scales ranging from milligrams to multiple kilograms. Similarly, IMAC is often the method of choice for preparing "research" quantities of proteins that carry or have been labeled with polyhistidine residues.

Mixed-mode opportunities

"There may also be other charged species in the mix, for example proteins, that we would not want to trap," says Stacy Tremintin, product manager for chromatography columns and consumables at Thermo Fisher Scientific (Sunnyvale, CA). "So we exploit the affinity to protein A or IMAC. Affinity provides a cleaner fraction because of the specificity of the ligand-protein interaction."

One preparative ion exchange option available to newer, diverse classes of therapeutic protein is mixed-mode ion exchange. Mixed-mode resins employ ion exchange with an orthogonal separation mode, for example a hydrophobic interaction, on a single resin bead. Mixed-mode resins work especially well for ionic proteins that are either not sufficiently retained or resolved by reverse phase resins. "Mixed-mode resins are uncommon in academic labs and drug discovery but the closer you get to process scale, the more you see them," Hagwall says. "But that is beginning to change. Mixed-mode resins are more expensive than conventional ion exchangers and more difficult to work with. They require substantially more development work than a company or lab that has used conventional resins may be used to. But for the large and growing base of investigators involved with non-traditional proteins, they offer an interesting option."

Mixed-mode preparative chromatography was all the rage about 15 years ago, but has now settled into niche applications, usually ones that require some finesse.

"Mixed-mode chromatography allows better control over resolution, and provides more parameters and options for optimizing resolution," says Tremintin. "For example, mixed-mode media combining ion exchange and reversed phase chemistries allows full resolution of complex samples, which normally contain mixtures of hydrophobic and polar analytes. Reversed phase alone does not retain very polar analytes, while ion exchange would not provide resolution or quantitation of hydrophobic, non-polar species."

Angelo DePalma *is a freelance writer living in Newton, New Jersey. You can reach him at angelodp@gmail.com.*

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MICROPLATE TECHNOLOGY

MICROPLATE OPTIONS FOR ORGANOIDS

by Mike May, PhD

When culturing cells, scientists often pursue one primary goal: create more natural conditions for growth and maintenance. One of the most successful outcomes arises from organoids, which are three-dimensional (3D) collections of cells that replicate some of the structural and functional aspects of a particular organ, such as the intestinal organoids described in 2009 by Hans Clever's group at the Hubrecht Institute in the Netherlands. In fact, scientists often call organoids mini-organs. These cultures can be developed in various ways—often depending on the kind of organoid being made—but some sort of labware is always needed, usually a microplate of some kind. Picking the best microplate for growing organoids often includes some personal preference.

Ups and downs

Despite the sophisticated science that lies behind organoids, an equally fancy microplate is not required. At the University of California San Diego, Alysson Muotri, director of the stem cell program in the Institute for Genomic Medicine, uses regular six-well plates to grow brain-based organoids. "The main reason is for better nutrient distribution under agitation, scalability, and low price," he explains.

In some cases, scientists seek microplates with unique features for working with organoids. Keep in mind that this work can involve several stages. First, the microplate must provide conditions that encourage cells to build 3D structures, which requires a different environment compared to simply culturing cells on a flat slide. Next, scientists typically grow organoids in a matrix, and in some cases, scientists like to observe and monitor the process. Lastly, organoids may be isolated or removed for further analysis.

To meet all of those requirements, scientists could select from a variety of options. One is Corning's clear, round-bottom microplates that are ultra-low attachment. With a plate that cells don't tend to grow on—which is the reason for using ones that are ultra-low attachment—organoids are more likely to grow in the matrix and less likely to stick to the surface of the plate. As an example, Corning's Elplasia round-bottom plates come in six-, 24- and 96-well formats. Plus, the company notes that spheroids (3D cultures of cells without some of the organ-like features of organoids) "may be formed and cultured for 21 or more days."

Nevertheless, what works in one lab or for culturing one type of organoid might not be the best choice for another. In one study, a team of scientists developing human-prostate organoids observed that ultra-low-attachment microplates were not the best option, as cells formed spherical aggregates rather than organoids.

Seeking specializations

As more scientists turn from traditional 2D methods of culturing, vendors will create an increasing collection of specialized labware, which will include microplates recommended specifically for culturing organoids.

Some examples already exist, including UK-based AMSBIO's Lipidure-COAT plates. The company endorses these plates for culturing spheroids, embryoid bodies, and organoids.

At UK-based Newcastle University, professor of stem cell science Majlinda Lako and her colleagues used the Lipidure-COAT plates to grow retinal organoids. Amazingly, these human-induced pluripotent stem cell-derived retinal organoids were able to generate light responses.

Growing a clump of cells that respond to light—immaturely, yes, but responding at all—reveals just some of the potential of organoids. As a neurobiologist and tinkerer in cell culture from decades ago, building any sort of retina in a dish astonishes me. I never expected to see that, and now I wonder what else I will see. With the right methods and microplates that fit the need, I'm sure that I'll be amazed again, and probably soon.

***Mike May** is a freelance writer and editor living in Texas. You can reach him at mike@techtyper.com.*

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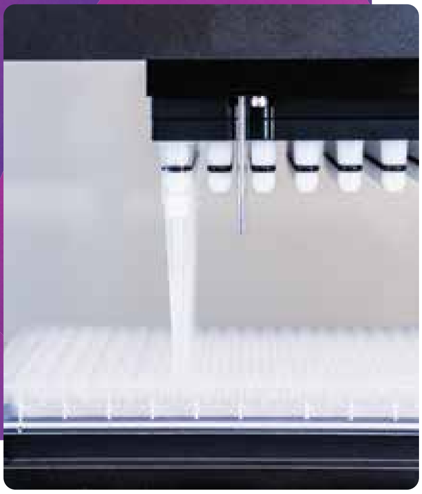
LAB AUTOMATION



AUTOMATED LIQUID HANDLING

Automated liquid handlers employ motorized pipettes or syringes to accurately distribute liquids into sample vessels. Using these instruments can increase the reproducibility and throughput of your experiments while freeing up your lab workers to perform other laboratory tasks.

Purchasing Tip

If you are using your automated liquid handler to pipette extremely small volumes in the nanoliter range, consider purchasing an instrument that uses acoustic liquid dispensing. This method of liquid handling employs pulses of ultrasound to eject droplets of liquid and is more accurate than air displacement at small volumes.

6 Questions to Ask When Buying an Automated Liquid Handler

What sample volumes is the instrument capable of pipetting and how many channels can be pipetted at once?

Do you need to purchase specific pipette tips from the manufacturer or is the instrument compatible with generic pipette tips?

What safety features are available to protect your workers? (e.g. shields, automatic stopping)

What downstream analyses will you be performing? Will the instrument be able to prepare your samples for these analyses?

Will you be using the automated liquid handler for more than one application? Do you require an independent handler, or can it be integrated into a workstation?

What software is available with the instrument and how configurable are the protocols?

List of Manufacturers

Agilent	www.agilent.com
Analytik Jena	www.analytik-jena.com
Andrew Alliance	www.andrewalliance.com
Apricot Designs	www.apricotdesigns.com
Art Robbins Instruments	www.artrobbins.com
Aurora Biomed	www.aurorabiomed.com
Beckman Coulter	www.beckmancoulter.com
BioNex Solutions	www.bionexsolutions.com
BioTek Instruments	www.biotek.com
BrandTech Scientific	www.brandtech.com
Dynamic Devices	www.dynamicdevices.com
Eppendorf	www.eppendorf.com
Formulatrix	formulatrix.com
Gardner Denver	www.gardnerdenver.com
Gilson	www.gilson.com
Hamilton Robotics	www.hamiltoncompany.com
HighRes Biosolutions	www.highresbio.com
Hudson Robotics	www.hudsonrobotics.com
INTEGRA Biosciences	www.integra-biosciences.com
Labcyte	www.labcyte.com
MDZ Automation	www.mdzautomation.com
METTLER TOLEDO	www.mt.com
Opentrons	www.opentrons.com
PerkinElmer	www.perkinelmer.com
ProGroup Instrument	www.serialdilution.com
Promega	www.promega.com
Questron Technologies	www.qtechcorp.com
Sartorius	www.sartorius.com
SCP Science	www.scpscience.com
TECAN	www.tecan.com
Thermo Fisher Scientific	www.thermofisher.com
TTP LabTech	www.ttplabtech.com

AUTOSAMPLERS

Autosamplers automatically draw from a predetermined set of samples and inject these samples into analytical instruments. The reproducibility and accuracy of these instruments, especially at low volumes, have eliminated persistent sources of error when performing analytical assays.

Purchasing Tip

Carryover results when sample left over from the previous injection is injected with the sample and can result in ghost peaks when performing chromatography. Insufficient rinsing of needles when using an autosampler can result in carryover. One way to minimize this issue is to purchase an autosampler that allows for multiple rinse solutions, both internally and externally, so that even samples with different physical or chemical properties are properly removed before the next injection cycle.

5 Questions to Ask When Buying an Autosampler

What type of autosampler do you need? (e.g. liquid, headspace, SPME)

Which application will you be using the autosampler for? Will the instrument be compatible with your analytical instruments?

How many samples can the instrument accommodate? What types of sample vessels are compatible with the instrument?

What range of sample volumes can be injected using the instrument?

How long is the instrument's cycle time? (e.g. how long it takes to perform a single injection)

List of Manufacturers

Agilent	www.agilent.com
Analytik Jena	www.analytik-jena.com
Anton-Paar	www.anton-paar.com
Aurora Biomed	www.aurorabiomed.com
Costech	www.costechanalytical.com
Distek	www.distekinc.com
Elemental Scientific	www.icpms.com
Ellutia	www.ellutia.com
EST Analytical	www.estanalytical.com
Fritsch International	www.fritsch-international.com
GBC Scientific Equipment	www.gbcsci.com
GE Healthcare Life Sciences	www.gelifesciences.com
Gerstel	www.gerstel.com
Gilson	www.gilson.com
Hitachi	www.hitachi.us
iChrom	www.ichrom.com
Hanna Instruments	www.hannainst.com
Jasco	www.jascoinc.com
KNAUER	www.knauer.net
Lumacyte	www.lumacyte.com
METTLER TOLEDO	www.mt.com
OI Analytical	www.oico.com
PerkinElmer	www.perkinelmer.com
Pike Technologies	www.piketech.com
PS Analytical	www.psanalytical.com
Reichert Technologies Life Sciences	www.reichertspr.com
Seal Analytical	www.seal-analytical.com
Shimadzu Scientific	www.ssi.shimadzu.com
Spark Holland	www.sparkholland.com
Teledyne Cetac	www.teledynecetac.com
Thermo Fisher Scientific	www.thermofisher.com
Waters	www.waters.com

BENCHTOP AUTOMATION

Benchtop automation can include a variety of instruments used for applications such as sample preparation, cell-based assays, ELISA, liquid handling, and next-generation sequencing. These instruments have a small footprint, making them practical for most labs, and are more accurate and consistent than lab workers.

Purchasing Tip

When selecting benchtop automation, the best instrument will be one that replaces a task performed frequently in your lab. Evaluate the protocols completed by your lab workers on a daily basis and identify which ones take the longest. Automating these time-consuming tasks will increase your throughput and your lab workers' productivity.

5 Questions to Ask When Buying Benchtop Automation Instruments

How much space is available on your lab bench for benchtop automation?

Can the instrument be integrated with current automation or workflows used within your lab?

Is the instrument modular or is it a complete workstation? If it's modular, how many instruments will you need to purchase to accomplish your task?

Can the instrument be expanded as your sample throughput needs increase?

What software is available with the instrument? How user-friendly is the instrument and how easy are the protocols to configure?

List of Manufacturers

AB Controls	www.abcontrols.com
Agilent	www.agilent.com
Anton Paar	www.anton-paar.com
BioMicroLab	www.biomicrolab.com
Biotage	www.biotage.com
BioTek Instruments	www.biotek.com
BrandTech Scientific	www.brandtech.com
Fluidigm	www.fluidigm.com
Gilson	www.gilson.com
Hach Company	www.hach.com
Hanna Instruments	www.hannainst.com
LICONIC	www.liconic.com
Metrohm USA	www.metrohmusa.com
METTLER TOLEDO	www.mt.com
Molecular Devices	www.moleculardevices.com
Qiagen	www.qiagen.com
Rudolph Research Analytical	www.rudolphresearch.com
Sartorius	www.sartorius.com
SI Analytics USA	www.si-analytics.com
SOTAX	www.sotax.com
Teledyne Cetac	www.teledynecetac.com
Thermo Fisher Scientific	www.thermofisher.com
Unchained Labs	www.unchainedlabs.com

INSTRUMENT/ LABORATORY MONITORING

Instrument and laboratory monitoring tools allow for the detection of equipment failures as well as changes to the laboratory environment and can notify users when these incidents occur. They can be used to monitor equipment including fridges and freezers, incubators, and ovens, as well as laboratory environmental conditions such as temperature, energy use, and humidity. Using instrument and laboratory monitoring tools help keep your samples and experiments secure while providing you with peace of mind.

List of Manufacturers

BioRAFT	www.bioraft.com
CAS	www.dataloggerinc.com
Elemental Machines	www.elementalmachines.io
ELPRO	www.elpro.com
Eppendorf	www.eppendorf.com
Esco	www.escoglobal.com
Grant Instruments	www.grantinstruments.com
MilliporeSigma	www.emdmillipore.com
Monnit	www.monnit.com
Online LIMS	www.onlims.com
PHC Corporation of North America	www.phchd.com/us/biomedical
PerkinElmer	www.perkinelmer.com
Rees Scientific	www.reesscientific.com
Sensoscientific	www.sensoscientific.com
Smart Sense	www.smartsense.co
Tetrascience	www.tetrascience.com
Thermo Fisher Scientific	www.thermofisher.com
Vertére	www.vertere.com

5 Questions to Ask When Buying Monitoring Equipment

What instrument manufacturers is the monitoring system compatible with? Will it work with the instruments in your lab?

Can the system monitor more than one instrument at a time?

What action is taken when an issue is detected? How will you be notified? What is the maximum number of individuals who can receive notifications?

Can the monitoring system be integrated with your laboratory information management system (LIMS)?

What support is offered by the monitoring system service provider? Are they familiar with your instruments and can they help set up the system?

Purchasing Tip

Some instruments come with integrated instrument monitoring. Before purchasing such instruments, decide whether you want a single monitoring system from a third-party manufacturer for all your lab instruments or if you would like to rely on independent monitoring systems included with specific equipment. If you plan on using integrated instrument monitoring, speak to the manufacturer about whether this monitoring can be added to your LIMS so the status of all your instruments is located in one place.

MICROPLATE AUTOMATION

Microplate automation includes instruments such as handlers, stackers, washers, live-imagers, and dispensers. Using microplate automation in the lab, especially for liquid handling, can help overcome the human error often experienced when microplates are handled by lab workers while increasing your sample throughput.

List of Manufacturers

Agilent	www.agilent.com
Analytik Jena	www.analytik-jena.com
BioNex Solutions	www.bionexsolutions.com
Bio-Rad Laboratories	www.bio-rad.com
Biosearch Technologies	www.douglasscientific.com
BioTek Instruments	www.biotek.com
BMG LabTech	www.bmglabtech.com
BrandTech Scientific	www.brandtech.com
Hamilton	www.hamiltoncompany.com
Hudson Robotics	www.hudsonrobotics.com
Labcyte	www.labcyte.com
Molecular Devices	www.moleculardevices.com
Peak Analysis & Automation (PAA)	www.paa-automation.com
PerkinElmer	www.perkinelmer.com
Thermo Fisher Scientific	www.thermofisher.com
Tomtec	www.tomtec.com

5 Questions to Ask When Buying Microplate Automation

Can the instrument be integrated with other equipment or workflows already in place in your lab?

Is the instrument expandable? Can you add on to the instrument as your required sample throughput increases?

What sample volumes and number of wells will the system accommodate? How easy is it to switch between microplate types?

How easy is the instrument to calibrate? Is calibration by your service provider included with your purchase?

Does the instrument come with pre-programmed protocols? How easy is it to create new protocols using the available software?

Purchasing Tip

Microplate automation is available as integrated workstations or as modular components that can be used to build a system. Workstations are typically designed to complete a specific task such as nucleic acid or protein extraction/purification or cell-based assays. Before purchasing, consider what you will be using your microplate automation for and whether this application will change in the future. If you anticipate that future needs will change, a modular system might be a better fit.

ROBOTIC WORKSTATIONS

Robotic workstations automate multi-step procedures and can complete entire protocols without human intervention. These workstations are designed for specific applications such as ELISA, hematology, protein and DNA extraction or purification, next-generation sequencing library preparation, and PCR. The walk-away processing performed by these instruments increases lab throughput and worker productivity.

Purchasing Tip

Robotic workstations have many moving parts that could break. When purchasing a robotic workstation, make sure to include a service contract. This will save you money in the long run when it comes to instrument repairs, and a regular service schedule will help keep your instrument calibrated and accurate.

5 Questions to Ask When Buying Robotic Workstations

Can the workstation be used for more than one application?

What safety features are available to protect your workers? (e.g. shields, automatic stopping)

Does the instrument require specific tips, sample vessels, or consumables? How will this affect your purchasing?

What protocols come pre-built into the instrument's software and how easy is it to modify these protocols?

Can you work with the manufacturer to build a workstation that exactly fits your experimental needs?

List of Manufacturers

Agilent	www.agilent.com
Analytik Jena	www.analytik-jena.com
Beckman Coulter	www.beckmancoulter.com
Biosearch Technologies	www.douglasscientific.com
BioTek Instruments	www.biotek.com
BrandTech Scientific	www.brandtech.com
Eppendorf	www.eppendorf.com
Hamilton	www.hamiltoncompany.com
HighRes Biosolutions	www.highresbio.com
Hudson Robotics	www.hudsonrobotics.com
Labcyte	www.labcyte.com
Labman Automation	www.labmanautomation.com
Molecular Devices	www.moleculardevices.com
Peak Analysis & Automation (PAA)	www.paa-automation.com
PerkinElmer	www.perkinelmer.com
ProGroup Instrument	www.serialdilution.com
SEAL Analytical	www.seal-analytical.com
Sirius Automation	www.siriusautomation.com
Tecan	www.tecan.com
Thermo Fisher Scientific	www.thermofisher.com
Tomtec	www.tomtec.com

SAMPLE MANAGEMENT

Your laboratory samples are invaluable. Automated sample management systems use barcoding to track your samples and robotics efficiently store your samples. Software makes it easy to access any sample at any time. These instruments can increase your lab's throughput by decreasing the time it takes for your lab workers to store and retrieve samples.

List of Manufacturers

BioMicroLab	www.biomicrolab.com
BioNex Solutions	www.bionexsolutions.com
Brooks Life Sciences	www.brookslifesciences.com
Hamilton	www.hamiltoncompany.com
HighRes Biosolutions	www.highresbio.com
LICONIC	www.liconic.com
NBS Scientific	www.nbsscientific.com
Scinomix	www.scinomix.com
Sirius Automation	www.siriusautomation.com
TTP Labtech	www.ttplabtech.com
Vertére	www.vertere.com

6 Questions to Ask When Buying a Sample Management System

What temperature do you need to store your samples at? (e.g. ambient temperature, 4°C, -20°C, -80°C)

How many samples can the system accommodate? Can it be expanded if you need to store more samples?

What types of sample vessels are compatible with the system?

Can the sample management system be integrated with other automated workflows? (e.g. decapping, automated liquid handling)

What software is available with the system? How easy is it to find samples using the software?

Does the system have integrated instrument monitoring? Are there alarms or alerts to inform you of system failures?

Purchasing Tip

Are you working with sensitive samples? When purchasing, look for automated sample management systems that have been designed to keep samples at consistent temperatures, even during sample processing. Temperature fluctuations can put your samples at risk by increasing the potential for sample degradation.

technology NEWS

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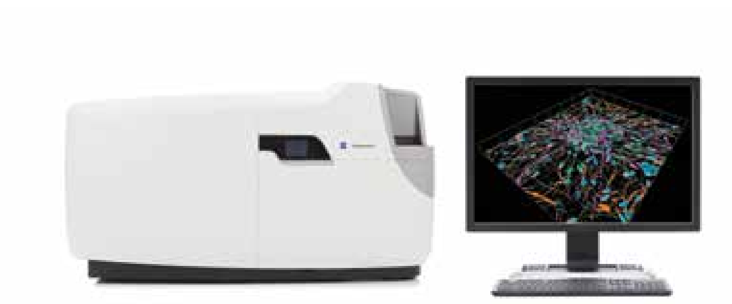
Thermo Fisher Scientific
www.thermofisher.com



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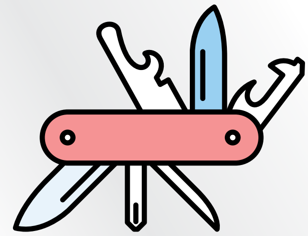
Olympus
www.olympus-lifescience.com

QUICK TIPS FROM LINDA

PREPARING FOR THE WORST



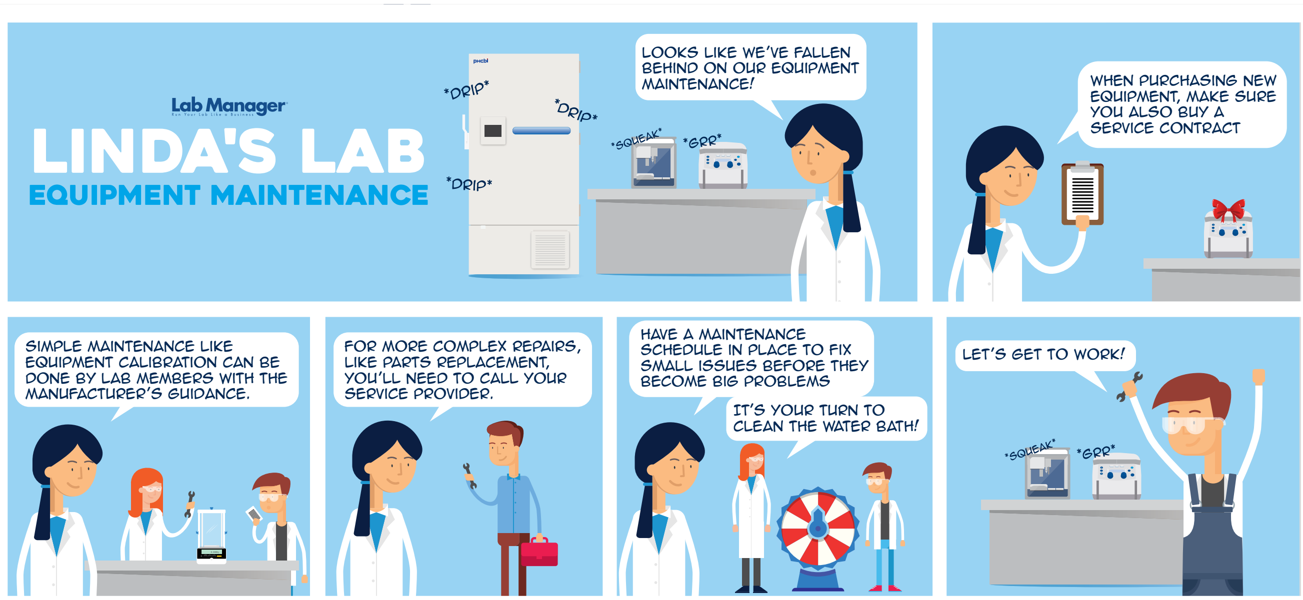
DID YOU KNOW:

Fires and floods are the most common and widespread types of natural disasters. Flooding can occur in all 50 states, and 90 percent of all presidentially-declared US natural disasters involve flooding. Do you have a plan in place to protect your precious equipment, samples, and other lab assets if a flood or other natural disaster hits your facility?

It is important to have both a disaster response plan, as well as a recovery plan, since recovery efforts can range from days to weeks or months. As the leader of your lab, you should develop plans that are specific to your facility, and go beyond the general plan for your overall institution. Outline roles and responsibilities for your team before, during, and after the disaster, including those considered essential personnel and decision-makers. Review and update these roles as needed (at least annually).

It is also a good idea to invite local fire departments and first responders to your facility to become familiar with the layout of your lab, and any potential hazards they should be aware of prior to answering an emergency call.

FOR MORE INFORMATION, VISIT:
LABMANAGER.COM/DISASTER-PLAN



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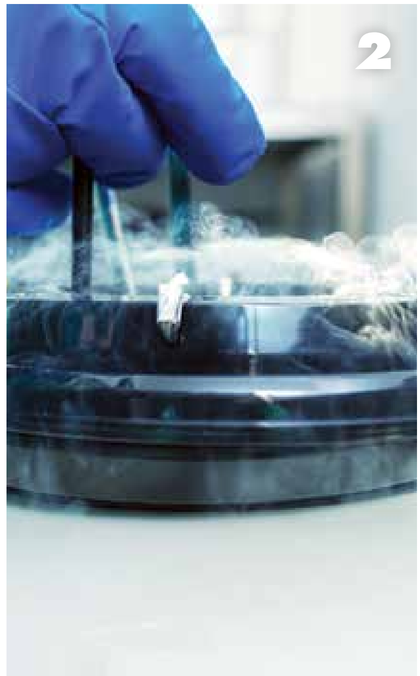


LM ONLINE

We look back at our web content since the November issue and look forward to what's in store for the first issue of 2020.

1 Turning Common Lab Design Challenges into Benefits

Researchers need labs purposefully designed to enable their science. Successful labs are created when all stakeholders and the design team have an aligned vision. Every detail must be exhausted during planning to ensure labs are functional, efficient, and safe. While lab projects are expensive and complex, there are steps designers can take to mitigate challenges.

Read more at **LabManager.com/lab-design-challenges**

2 Trending on Social Media

As of November 13, *Lab Manager*'s top November issue article posted to social media was our Health & Safety feature, "Working with Liquid Nitrogen." Use of liquid nitrogen has grown rapidly the last several years, due in part to the growth in stem cell research and other medical uses. Unfortunately, so have the number of serious accidents and injuries. This article discusses the physical and physiological hazards of liquid nitrogen, and how to prevent accidents.

Read more at **LabManager.com/liquid-nitrogen**

3 Most Popular Webinar

Our most recent top webinar on LabManager.com with 498 registrants was "Impact of Human Error in Titration." This Product Spotlight webinar helped attendees learn how to improve weighing, assess the risk of using manual burets, and integrate sample preparation to help control the impact of human error and increase the accuracy of results. Though it ran on November 12, you can still register to watch on-demand.

Read more at **LabManager.com/titration-webinar**

LabManager.com

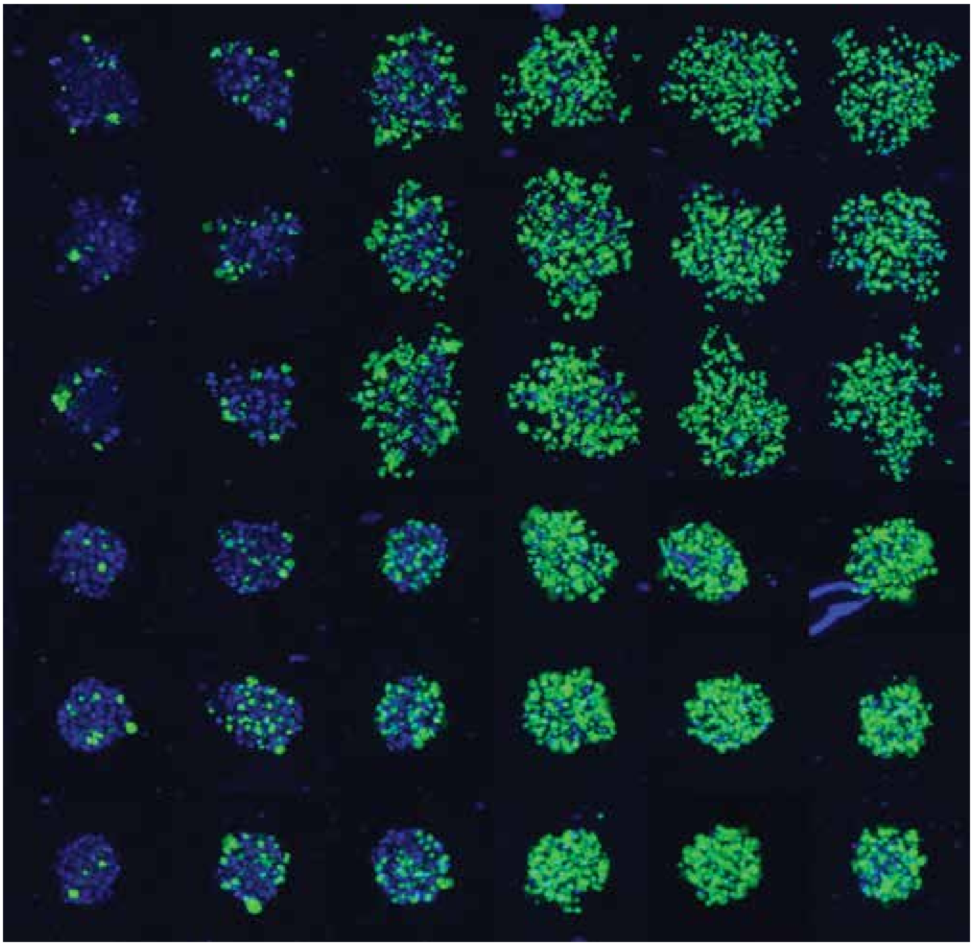
NEXT ISSUE

Run Your Lab Like a Business

While every laboratory is unique, there are some common traits of successful lab leaders. The January/February 2020 cover article will offer guidance on managing the business side of lab operations, and discuss topics such as employee engagement and productivity, strategies to ensure you are meeting annual goals, and getting staff on board with the facility's overall mission.

Olympus NoviSight™ 3D Cell Analysis Software

Olympus NoviSight™ 3D cell analysis software provides fast, accurate statistical data on spheroids and other 3D models to reduce the time and cost of drug discovery research.



OUR SOFTWARE'S TRUE 3D TECHNOLOGY delivers spatial and morphological data to an intuitive, interactive user interface. Data is always connected to images for easy validation and interpretation on one screen. The software works with all Olympus confocal systems and comes with ready-to-use 3D cell-based assays for efficient observations.

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