# Introducing Automation to Your Lab

A step-by-step reference guide for the 21st Century biologist

**Written by**

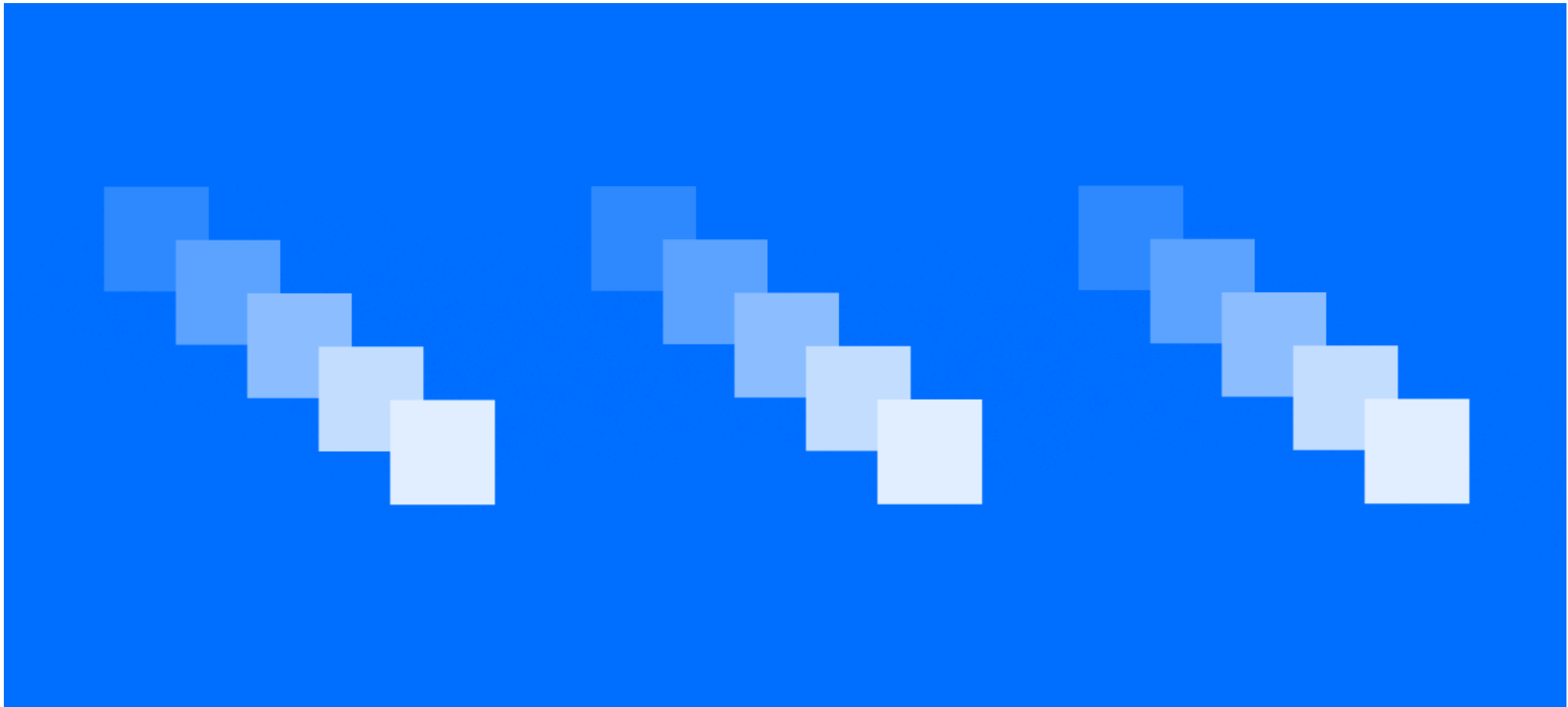Opentrons

INTRODUCTION

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# Dispelling the Myths of Lab Automation

"Repetitio est mater studiorum," says the Latin proverb: "Repetition is the mother of all learning." Scientists live this ancient saying every day, winning hard-earned discoveries by repeating the same process over and over. In some cases, this simply builds a large enough sample size to create statistical significance in the results. In other circumstances, researchers subject different samples to the same procedure or similar samples to different conditions. All of these techniques include a common factor—repetition. To a life scientist holding a pipette and sitting in front of a pile of multiwell plates, the word repetition really hits home. Repetitive processes can be the most painful part of a workflow—but they are also, thankfully, ideal processes to automate.

Many researchers like you have dreamed about automation while pipetting hundreds of samples, but believe it is too complicated, too costly, or too high-throughput to have in their lab.

That simply isn't true.

This e-book debunks these and other myths of lab automation (see "Figure 1: Busting the Top 5 Automation Myths"), and shows that robots can be a great help for the majority of wetlabs.

**FIGURE 1**

## Busting the top 5 automation myths

| MYTH | REALITY |
|---|---|
| ✗ Liquid-handling automation costs $100,000! | ✓ Scientists can get started with as little as $5,000. |
| ✗ You need a robotics and/or coding expert on staff. | ✓ Any biologist can run some systems. |
| ✗ A room must be dedicated to the equipment. | ✓ Some automated liquid-handling systems sit on a bench—with a footprint of about one-third square meter (less than 2 sq ft.) |
| ✗ The learning curve for personnel is daunting! | ✓ Running some systems is similar to using a smartphone app. |
| ✗ Only biotechnology and big pharmaceutical companies can benefit from automating liquid handling. | ✓ Almost any lab requiring repetitive liquid handling can save time and reduce errors with automation. |

If you want to explore the idea of automating some repetitive processes in your lab, this e-book will help guide you toward figuring out if automation is right for you.

If you're curious about automating liquid handling, use this ebook as a resource to help you walk through every step and learn more about this technology. You can start by learning about the sorts of workflows that really benefit from automated liquid handling (and those that don't), and then explore a wide range of capabilities that should be considered when choosing the right robot for your lab.

A liquid-handling robot's range of technical capabilities must meet the variety of ways that scientists use them. In *Lab Manager*'s "**2017 Automated Liquid Handling Survey Results,**" the top uses included serial dilution, plate replication and PCR setup, as well as plate reformatting, high-throughput screening and whole-genome amplification. Nearly 30% of respondents purchasing an automated system are first-time buyers, but that number is on the low side: at Opentrons, for example, nearly 70% of our customers are new to automation. Automation is more accessible than ever and many labs are adding robotics for the first time -- and you can too! All you need to do is learn some basics and you're off to the races.

**That's why we created this guide.**
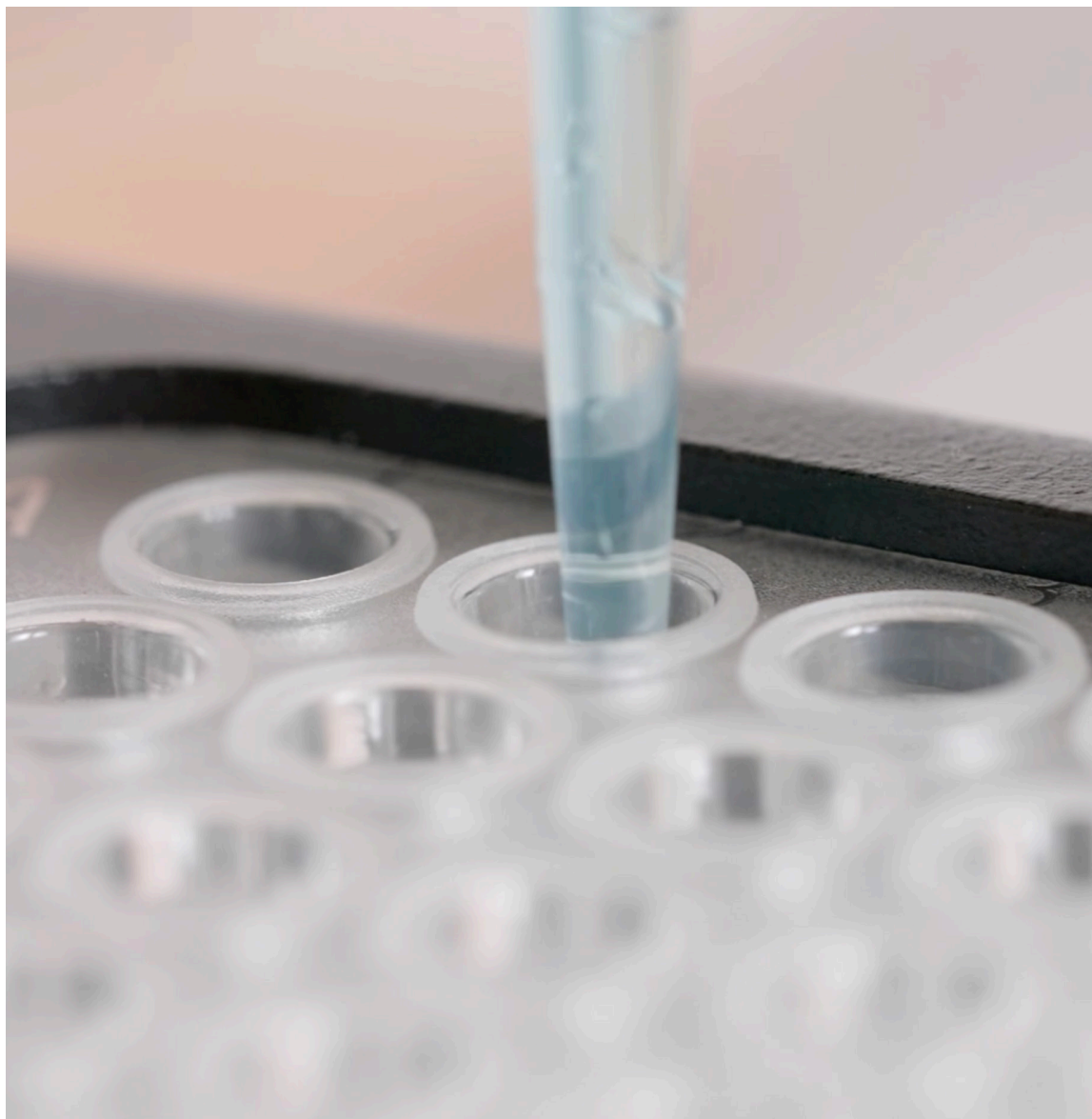
# Overall Benefits of Lab Automation

When put together in an efficient and effective way, automation improves liquid handling in many respects. First, scientists will save time when they don't need to do pipetting on top of all their other lab work. Second, automation increases throughput and enables efficient workflow scale up. Third, automation allows for greater accuracy from each liquid-handling step to the next because it minimizes human errors that would normally be introduced in the workflow. Fourth, you get a receipt at the end of an automation run—meaning, you can keep very close tabs on exactly what has happened to your samples, and producing data in this way enables more sophisticated analysis. Fifth, humans don't do well with repetitive motions; our joints get injured when doing the same action over and over. Automation frees researchers of repetitive stress injuries often associated with pipetting.

> **"When put together in an efficient and effective way, automation improves liquid handling..."**

## Top 5 benefits of lab automation

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**01**  Saving time

**02**  Increasing throughput by doing each liquid-handling operation faster – or by doing more than one at a time

**03**  Greater accuracy from one liquid-handling step to the next compared to pipetting by hand

**04**  Enhances reporting of what was done and when

**05**  Lab personnel avoid some of the movements that trigger repetitive strain injuries to their hands, wrists, necks or backs

As a lab accrues all of these improvements from automation, lab personnel are free to do other, more meaningful activities in the lab—like data analysis, experiment design, and writing up results for publication.

> **"Liquid-handling automation is complicated, but using it doesn't have to be."**

Getting all of those benefits, though, emerges from some pretty complex technology and processes. Liquid-handling automation is complicated, but using it doesn't have to be. Even more, making the decision to move from manual pipetting to automated liquid handling can be simplified. Scientists must consider many things—in their own labs and in the automation market—but this e-book makes it easy to get started. When automation makes the right fit with a research group's liquid-handling needs, life in that lab changes for the better—results become more accurate and repeatable, running experiments gets easier, and productivity increases dramatically.

# Choosing the Best Workflow to Automate

To really dig in, let's consider what makes a good workflow for automation—and what doesn't. The key general concepts can be applied to almost any protocol. To get started, review "Figure 3: Your Workflow is a Good Candidate for Automation if…" table below and compare that to the workflow you're considering for liquid-handling automation.

If all five features in the table are true for a common workflow in your lab, you should automate it! If some of them are not true for the workflow you are considering, it is probably most practical to stick to manual pipetting.

Let's think about these features in a bit more detail. First, you should aim for an automation solution that will easily accommodate the liquid volumes you use most often in your workflows—if this is between 1μl and 1000μl, you'll find a lot of automation options available for you. With smaller or larger volumes, there are robots that will work, but they are usually more expensive or may only work with more restricted use cases.

Second, you should apply automated liquid handling to processes that are troublesome, time-consuming, error-prone, and monotonous.

Third, the automated workflow should be one that a lab runs often enough—at least once a week—to really justify the transition to automation. Less than this and your return on investment in both dollars and time will take awhile to become net positive. If you do it once a week, automating a workflow can pay back the initial investment in both time and money in 8 - 12 months. If you automate a workflow daily, some lab robots pay for themselves in a matter of weeks.

Fourth, you need to consider how much of a given workflow can be automated within your budget—how long you can "walk away" from the labwork. You can buy robots with automated incubators and centrifuges, for example, but these are too expensive for most labs. However, it is important to keep in mind that just because you use a centrifuge 5x in a manual protocol to spin things down doesn't necessarily mean you need to run it the exact same way on a robot; there are many good work-arounds that can make tricky manual steps automation friendly (See "Figure 4: Translating Manual Processes to Automation").

> **"there are many good work-arounds that can make tricky manual steps automation friendly…"**

**FIGURE 3**

## Your workflow is a good candidate for automation if…

——

**01**  The liquid transfers are between 1-1000 μL

**02**  One or more steps include time-consuming and/or tedious liquid handling

**03**  Your lab runs the workflow at least once a week

**04**  You can afford a walk-away automation solution

**05**  5% precision is enough

Lastly, 5% precision with respect to pipetting volume needs to be enough for the workflow in mind. 5% precision works best for low volumes, but we've expanded on that in the "Precision and Lab Automation" chapter.

A final point about workflows: sometimes what you're trying to do is actually totally unique to your lab. Maybe you want to integrate a custom piece of data analysis software that can generate new automated runs based on data coming from your robot. Perhaps you are developing a new hardware module that you need to work on the deck of a robot. Or, you just want to be able to use the core mechanisms of a robot in a way they weren't exactly designed to do. In all these cases, you need a custom automation solution—and there are two ways to make one: pay someone lots of money to do it, or do it yourself (DIY). DIY lab automation is on the rise, according to this **2019 *Nature* article**, and open-source platforms like Opentrons make completing a useful custom automation solution yourself orders of magnitude easier than it was before. You can get a totally custom automation station, but it will take more resources to get running than an off-the-shelf solution for common wet lab protocols.

## Translating Manual Processes to Automation

| PROCESS | MANUAL | AUTOMATION |
|---|---|---|
| Nucleic acid purification | Spin columns | Magnetic beads |
| Mixing | Vortex | Extensive pipette mix |
| Heating | Heat bath | Temperature module |
| Cooling | Ice bucket | Temperature module |
| Repeat dispense | Repeater pipette | Multi-dispense function |

# Precision and Lab Automation

To explore the 5% precision constraint a little deeper, let's look at a specific pipetting volume and platform. Assuming an accurate pipetting volume of 1 microliter (µl), for example, the Opentrons OT-2 pipetting robot has a 5% coefficient of variation. That means that for a programmed volume of 1 µl, the actual pipetted volume of each transfer will be between 0.95–1.05 µl—somewhere within 5% of 1µl. On most robots, the coefficient of variation improves for larger volumes.

This is, again, a place where you can pay for performance. In general, automation solutions that can do better than 5% precision at low volumes are well out of most labs' budget, with capacitive sensing robots like the **Tecan Freedom EVO** and **Hamilton Microlab STAR** series starting around $75k-$100k, and acoustic dispensing robots starting near a quarter million dollars. Less expensive air-displacement pipetting mechanisms generally stick to this 5% precision point—including manual pipettes.

It's worth noting that many air-displacement manual pipettes quote a better CV at 1µl, with some claiming values as low as 2.5%; however, these results are a best-case scenario and can be difficult to achieve depending on the personnel and techniques used. Additionally, a full set of top-of-the-line manual pipettes can be as expensive as some robots. When you factor in human error and inconsistent pipetting technique across lab members, an air-displacement pipetting robot will still prove to be the most precise pipetting solution available for most jobs.

Much of the information about precision presented in this guide is focused on volumes of 1µl because this is the lowest transfer volume needed in many molecular biology workflows. While you can easily automate transfers at volumes above 1µl, it starts getting complicated—and expensive—at lower volumes. Surface tension and capillary action make liquids behave differently at these volumes, and they require special handling by different hardware.

For example, microfluidic devices are super efficient for specific workflows where you can use a bespoke fluidic chip. While more flexible digital microfluidics technologies are just starting to become available to scientists due to companies like **Volta Labs**, microfluidics is still a rigid and inflexible solution for most applications. More specialized and expensive robots can move sub-microliter volumes using acoustic dispensing, like the **Labcyte Echo**, or by using positive displacement, like the **TTP Labtech Mosquito**—but these solutions are typically only workable for labs with a lot of resources and/or very niche workflows.

# How much liquid to move?

To make lab life easier by automating liquid handling, a scientist needs to know how much liquid will be moved and how fast. That all depends on what workflows a lab runs and how quickly steps must be completed. One of the first features that scientists ask about a robot is: How much liquid can it move?

## VOLUME RANGES

As mentioned previously, the liquid-handling sweet spot for most labs is 1–1,000 μl, which can accommodate a wide range of common life science workflows including sample preparation for polymerase chain reaction (PCR), library preparation for next-generation sequencing (NGS), nucleic acid purification, running ELISAs and more. Consequently, most life science lab managers will look for automated liquid handlers that excel in this range. As discussed in the previous chapter, pipetting sub-microliter volumes pushes up the price on a robot enormously. On the other end, pipetting higher volumes usually only happens outside of most research biology workflows and may not be a consideration for most labs.

## LOW, MEDIUM, OR HIGH THROUGHPUT?

In addition to the volume range that a robot can pipette, throughput—meaning, the number of samples you can process at once—is another crucial factor to consider. In many situations, the desire to increase throughput draws life scientists to automated liquid handling in the first place. When deciding which robot to use, you'll want to consider whether you need low, medium, or high throughput.

For a lab that wants to move away from manual pipetting, but doesn't run hundreds of samples a day, only low-level throughput—by the standards of automated liquid handling—is required. To get this amount of pipetting going faster, it just takes a robot that runs a single-channel pipette, or has limited multi-channel capability. Such a system can process a small number of samples, such as tens or hundreds a week, and can carry out most simple liquid-handling steps.

Scientists working with multiwell plates from 96 to 384 wells can find manual pipetting tedious at best and error-prone at worst. Here, a medium-throughput robot that works with an 8-channel pipetting head can serve the purpose. While there are robots that use 96- or 384-channel pipettes

## FIGURE 5

### Levels of Throughput

| Low throughput | <1,000 samples / week |
|---|---|
| Medium throughput | <10,000 samples / week |
| High throughput | 10,000+ samples / week |

to do whole plates all at once, they are expensive. Increasing the number of channels obviously increases throughput, and can easily allow for the processing of hundreds or even thousands of samples per week.

For the highest throughput—such as that needed at a large pharmaceutical company screening tens of thousands of compounds or more—robotic liquid handlers can start to take up entire rooms of space, and consume a start-up's entire bank account. But 90% of labs won't need this capacity, so this concern is often moot.

# Space Considerations

One aspect that is sometimes left out of the lab automation purchase process is the type of space you need for your new robot. Automation platforms can have major requirements in terms of lab real estate, and giving up extra bench space can sometimes be the largest cost for bringing in a robot. You need to think about where the robot will fit, and what types of environment the robot itself creates.

### STERILITY

In *Lab Manager's* "**2017 Automated Liquid Handling Survey Results**," scientists selected "Safe sample handling - No cross-contamination" as the top feature on their shopping list, so a robot must not cross-contaminate samples. If it does, no amount of speed or convenience offsets that drawback. The good news is that this is a major consideration for anyone designing wet lab automation, and the robots on the market are much less likely to contaminate samples than a human operator.  But exactly how sterile a robot keeps the samples on its deck is determined by the hardware included with that robot.

Some automated liquid handlers offer no protection between a sample and the wider surrounding environment, which can be fine for some situations. Other robots have simple glass or plastic barriers

to prevent excess airflow across samples during a run, which is enough for many molecular biology workflows.

For those workflows requiring a greater degree of sterility, such as many tissue culture assays, fully enclosed systems with positive pressure and filtering can also be purchased. These platforms keep samples in what amounts to a tissue culture hood, including laminar flow, HEPA filtration, positive air pressure, and often ultraviolet lamps that keep contaminants out and/or destroy unwanted biology that get inside.

For labs handling dangerous reagents, keeping the liquid handler in a biosafety cabinet is the only viable way to keep both scientists and samples safe from contamination. That leads to another feature to consider—size. If a lab plans to keep samples contaminant-free by running a workflow inside a hood, then everything must fit inside that hood. So, in such cases, a robotic liquid handler and any associated equipment must fit inside the lab's hood, and still leave enough room for access as needed. How small the robot has to be really depends on the size of a lab's hood. In general, though, low- and medium-throughput systems are most likely to meet this constraint.

### SIZE

The footprint of the robot is a key consideration in other aspects as well. For example, if a researcher wants to be able to easily move the robot, it needs to be small enough to enable that. Even some medium-throughput systems are small enough and light enough for a two-person lift. Then, a platform of that size and weight can be moved to different spots, between labs, or even in and out of a hood if needed. That kind of robot is not only movable, but also more manageable in terms of bench space. Without taking up so much room, it's easier to put a smaller robot where it's needed, close to associated equipment for a specific workflow.

As a liquid handler gets bigger and more complicated, possibly including multiple arms and various accessories, it takes up more space—too much to sit on a bench. Sometimes, robots just need to be big and take up lots of floor space, but these systems are far from mobile. While they are the right tool for some big jobs, they are also far more than most labs would ever need.

# Cash considerations

Some financial aspects have already been mentioned, and the $100,000-or-more myth could be the biggest stumbling block to automation in some life science labs. As shown, though, it doesn't take $100,000 or even $10,000 to automate a wet lab. $4,000 can be enough for a pipetting robot, depending on the lab's needs. See "Figure 6: Robot Pricing Table" for an overview of what different solutions cost.

**FIGURE 6**

## Robot Pricing Table

**Opentrons OT-2**
Starting at $5,500

**Festo
Tekmatic**

| LESS THAN $10K | $10k - 40K | $40k - 80K | $80K - $120 | OVER $120K | OVER $500K |
|---|---|---|---|---|---|

**Gilson PIPETMAX**       **Forumlatrix Mantis**

**Andrew Alliance Andrew+**       **Hudson Robotics SOLO**

**Flow Robotics Flowbot ONE**       **Integra ASSIST PLUS**

**Neotec EZ Mate**

**Hamilton Microlab STAR**       **Beckman BioMek**

**Analytic Jena CyBio FeliX**       **Perkin Elmer JANUS**

**Agilent Bravo**       **Seyonic SeyMotion**

**Tecan Freedom Evo**       **Apricot Designs**

**Eppendorf EPMotion**       **TTP Labtech Mosquito**

**Hamilton Microlab NIMBUS**       **BrandTech LHS Flow**

**Dynamic Devices Lynx**

**Labcyte Echo**

**Hi-Res Bio Systems**

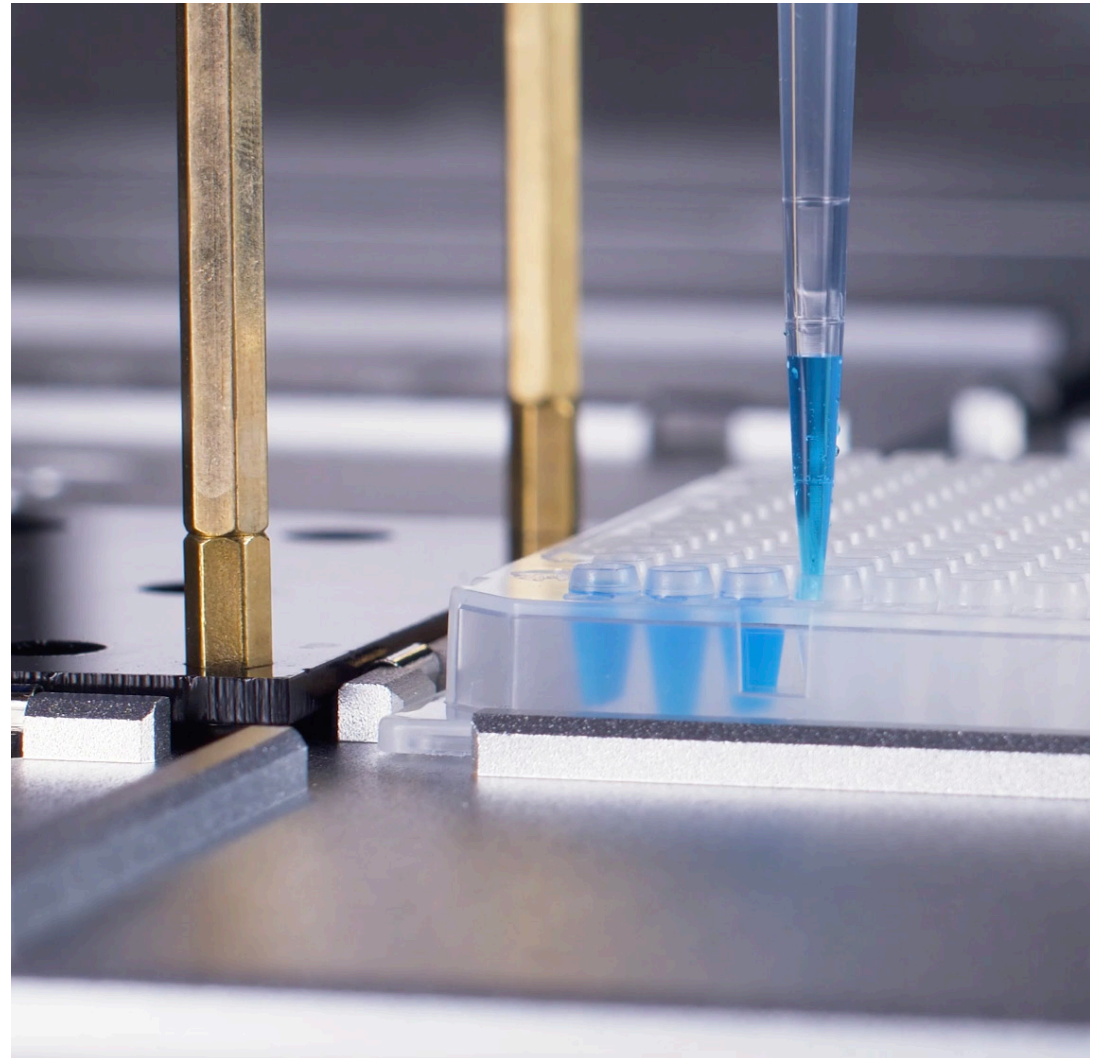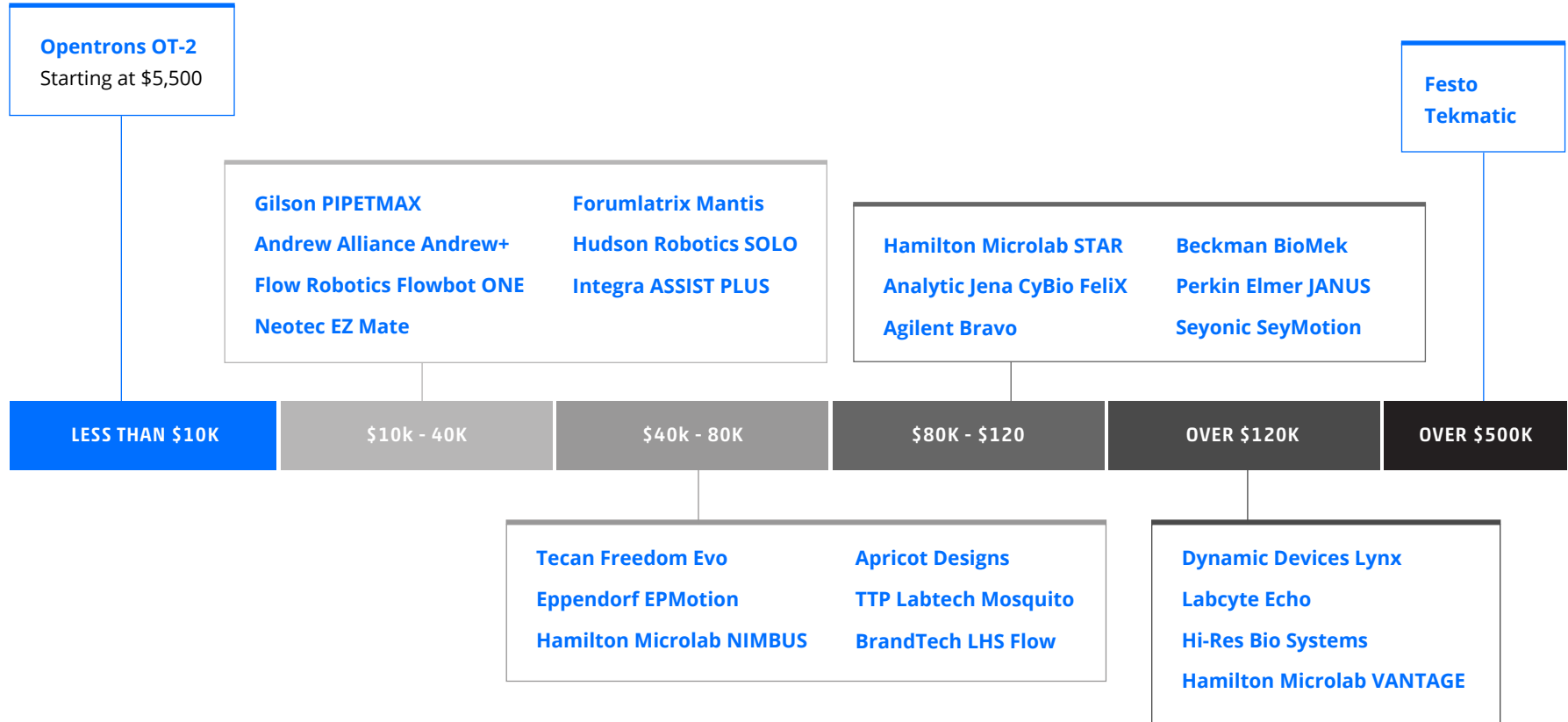**Hamilton Microlab VANTAGE**

**NOTE:** These prices are estimated because most manufacturers do not publish their pricing openly—except for Opentrons.

Still, buying a liquid handling robot isn't the end of a lab's automation spending. If a robot doesn't come with software to run it—and it should—then the lab needs to buy it. That could also mean working with software that's not designed for a specific robot, which can make programming more complex— maybe complex enough to require an expert. But that shouldn't happen! Expect a liquid-handling robot to come with software made for that platform and designed to make your life easier, not more complicated.

Some systems require in-person installation from the manufacturer, which can get complicated and costly —but it doesn't have to be. Scientists can select a platform that is nearly plug-and-play— almost as simple as unpackaging it, plugging it in, adding reagents, and hitting 'run' to execute a protocol.

Reagents can also be costly, but they are already factored into a lab's costs. An automated system can use reagents more efficiently by reducing error and pipetting consistently every run, which leads to cost savings over time. That same efficiency can also save on the amount of sample required. In situations where sample is scarce—say, a sample from an endangered species—using a smaller volume of it can lead to extracting more priceless information from it.

Automated liquid handling has additional cost-saving benefits, too. By saving scientists' time in the lab, they can do more—from high-priority tasks like grant and article writing to designing new experiments, and even creative daydreaming. Providing scientists with more time to think about and do science is a key goal of all labs.

> **"Expect a liquid-handling robot to come with software made for that platform and designed to make your life easier, not more complicated."**

That creative thinking will, hopefully, spawn new ideas that require new experiments. Some of those will require new workflows. In those situations, a robot with workflow flexibility will come in handy, so that it can be adapted to new uses. In some labs, multiple uses will be intended all along, and in those cases a versatile robot is valuable from the start.

# Developing Your Protocol

To do a lab any good at all, a liquid-handling robot must run protocols that fit a lab's workflow. Nearly every scientist needs to tweak any protocol to fit their needs, especially as a lab's needs evolve.

The first question is: Does a robot allow a scientist to develop and tweak custom protocols themselves? Some don't. In those cases, scientists must ask the vendor to make any changes they need in the system—or worse, the system is locked down and no changes are possible. With other vendors, a scientist must pay for an engineer from their company to make a custom protocol. Often that can cost $5,000 or more, even for small adjustments. In some cases, the vendor will teach a lab member to create custom protocols, but that training can cost thousands of dollars too.

Many robotics companies have graphical interfaces for you to develop your own protocol in a point-and-click manner, as well as programming languages that allow you to write your protocol in code. Check to see what options are included with the price of

**FIGURE 7**

## The Opentrons Approach:

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Opentrons offers four FREE options for protocol development. You can:

- **choose a free protocol from the open-source Protocol Library**

- **use the free point-and-click Protocol Designer**

- **use Opentrons's free Python API (application programming interface) to write protocols in Python yourself**

- **work with a dedicated Opentrons Applications Engineer to get custom protocol developed for you (the first one is free!)**

the robot, and what software you have to pay extra for. You should also consider your learning curve for any tool. If you do not write code, sometimes a graphical user interface (GUI) is the only option—but not all GUIs are simple, and some can have learning curves as difficult as learning to code. The same goes with coding interfaces: these can be extremely complicated, or very simple—make sure you know what you're getting into!

Many automation companies will also have relationships with reagent makers where they have verified certain kits and protocols that work well on their robotics. Sometimes, this 'verification' is effectively just saying: "we got this to work, maybe you can too." Sometimes, the reagent company will send a field application scientist out to load the correct protocol onto your robot to run the desired kit. And sometimes, companies provide verified protocols for commonly used reagent kits for free to download from their website—which is what Opentrons does.

# Choosing The Right Vendor

The robot vendor can either smooth your transition to automated liquid handling from manual pipetting, or make it a mess. A few good rules of thumb go a long way toward picking the best robot from a reliable vendor. These are all things that should be expected and provided during the decision-making process.

One crucial area involves the performance data of the robot. Anyone can publish data—but it needs to be reliable. In order to help you determine the reliability of a robot's data, a vendor should readily provide:

- **pipetting volume ranges and accuracy**

- **pipetting precision (meaning coefficient of variation, or CV)**

- **how both were measured**

Scientists also need to consider a robot's performance over time. To do that, a vendor should provide guidelines for maintaining quality assurance over the life of the platform.

Ideally, a liquid handling robot should be easy to use—meaning, it should be relatively straightforward for you to setup and execute protocols on. It should be beginner friendly.  If an automated liquid handler is truly easy to use, the vendor should be prepared to validate that. This could be done through tutorials, customer testimonials, demonstrations of applications loaded with a system, and so on.

That said, a liquid-handling robot platform also needs to work long and hard while staying within spec for pipetting precision and movement for as long as possible. For that, scientists need a warranty, and it's reasonable to expect a one-year warranty on repair or replacement. On expensive robots—say, $50,000 or more—look for at least a two-year warranty. Also, keep in mind that some vendors charge for a warranty, but some include one as part of the purchase.

To handle performance problems, some companies require a support contract as part of a robot purchase, and the support contract alone can cost thousands of dollars a year. Conversely, Opentrons provides free online support as needed.

> **"Look for a vendor who does what it takes to keep a lab running with minimal downtime."**

In some bad-luck situations, no amount of support is enough to get a broken robot back online. For some vendors, the solution is a repair visit scheduled weeks away. Opentrons, on the other hand, express delivers the customer a new robot. Look for a vendor who does what it takes to keep a lab running with minimal downtime.

# Next Steps on the Path to Automation

Now you know that robots can be a key factor in doing the day-in day-out repetitive lab work that is the foundation of advancing scientific understanding. You have identified ideal workflows to automate, determined the type of robot you need, and understood what you can expect from different types of lab automation vendors. You should feel empowered to take your next step in purchasing an automated liquid handling robot.

As you explore automation in your lab, use this e-book and add a little of your own repetition—read this again or skim the key spots for reminders. There's no need to memorize the details. Just come back to this ebook as needed to refresh your memory. If any of the old thinking creeps in and you start wondering if you could ever use a lab robot, take another look at "Figure 1: Busting the Top-5 Automation Myths."

**Just remember: lab automation is within your reach, and it will supercharge your lab's productivity. All you need to do is apply the steps in this guide and get started. Greater efficiency, productivity, and accuracy awaits. What are you waiting for?**

**FIGURE 8**

## Next Steps When Purchasing An Automated Lab Robot

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Now, with this information in hand, take the next steps:

- [ ] reach out to a few vendors

- [ ] discuss possibilities for your workflow

- [ ] find out how easy or difficult it would be to automate

- [ ] set up an online or in-lab demonstration and see for yourself

# Resources

**RESOURCES**

**2017 Automated Liquid Handling Survey Results**

**Tecan Freedom EVO** Liquid Handling Robot Information

**Hamilton Microlab STAR** Liquid Handling Robot Information

**Volta Labs** Information

**Labcyte Echo** Liquid Handling Robot Information

**TTP Labtech Mosquito** Liquid Handling Robot Information

**Nature Paper on DIY Lab Automation**

**Why Lab Robots Are the Personal Computer of the Automation Revolution**

**Manual Pipetting is a Pain (Literally): Here Are 10 Ways to Make It Better**

**3 Ways Automation Produces Better Biology Lab Results**

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