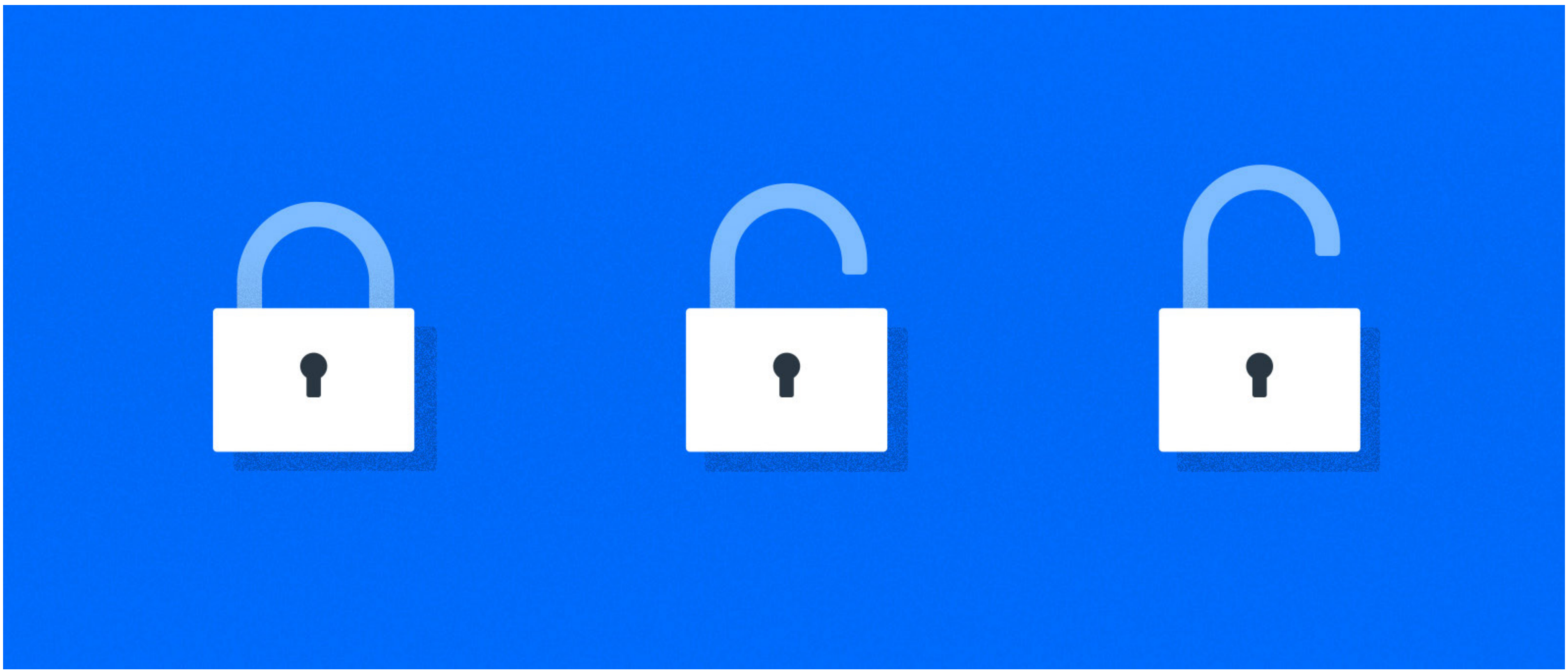
The Life Scientist's Guide To Open-Source

From experts to the uninitiated, free access to information behind software, hardware and science opens more opportunities and accelerates advances in basic research, healthcare and more.

Written by
Opentrons



INTRODUCTION

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CHAPTER 1

The Evolution Of Open-Source

"Open-source" is an idea that appeals to most scientists because of its potential to remove barriers in wet labs and enable an exchange of ideas. But the idea of open-source is a complex one that has evolved over time. We spoke to dozens of life scientists about what open-source means to them and how it can benefit their labs—and science as a whole.

The origins of open-source begin in academia. In the 1950s and 60s, the majority of computer software was created by universities and widely shared by academic scientists to collaborate on research.[1] This is the origin of open-source software, the most widely known application of the open-source idea—and the most familiar use case to scientists. Open-source software is when someone writes a piece of code and shares it with others who use or modify it for their own purposes, for free and with no restrictions on how the software is changed.

In the early 2000s, advancements in manufacturing and technology enabled open-source's expansion into the hardware realm. Open-source hardware is when someone designs equipment or technology and shares those specifications with others to use and modify, also for free and with no restrictions. This type of hardware enables researchers to build or customize equipment that they otherwise would not be able to access in their labs due to cost, access, and the rapid pace of technological advancement. It was also enormously disruptive to the lab automation industry because it enabled labs besides the largest, most well-funded ones to have access to the latest technology to fuel their discoveries, which in turn enabled widespread adoption of some of the best technologies on the market.

Between 2002 to 2016, about 225 3D printing patents expired and that technology became public domain.[2] This enabled bench scientists to create and share components that could be printed in any lab with high-resolution 3D printers.

In short, a barrage of innovation sparked the marriage of open-source software with open-source hardware, and greatly amplified the potential of open-source in the life science industry. Newly available open-source hardware could be controlled and tweaked by open-source software, and open-source hardware could be built and connected to other open-source hardware. All of this development led to an open-source revolution that's just beginning to take hold. Plus, the multiplying effect of critical mass adoption accelerates the trend, ensuring more innovation to come.

FIGURE 1

Open-Source Evolution Timeline

1950s – 1960s
Open-source computer software created and shared by academic researchers

2000s
Open-source hardware first created by lab researchers

2012 – 2016
3D printing patents expire, making technology public domain

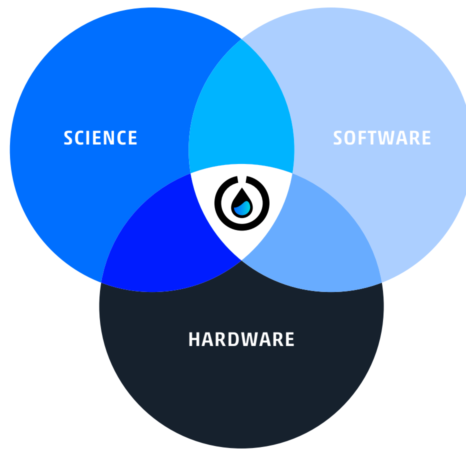
CHAPTER 2

The Many Benefits Of Open-Source: Creation, Customization, Accessibility, And Transparency

As a life science company born from and founded upon this revolution, **Opentrons** is proof of the potential unlocked in the lab by open-source products. "So much of life science is closed off, proprietary, centralized, and opaque," said an Opentrons co-founder when asked to describe the company's mission. "We provide an opportunity to change the way life-science is done, and to give more people access to the tools and knowledge that could accelerate their research."

> **"We're adapting protocols based on what we're doing," one scientist noted. "It's hardly ever the case where you're following a standard protocol across all labs...[protocols are] suited to their individual needs, and so the hardware and software need [the ability to] incorporate those ideas."**

As the maker of a fully open lab automation system, Opentrons lives at the intersection of open-source in science, hardware and software—which is a crucial driver of innovation. "We're adapting protocols based on what we're doing," one scientist noted. "It's hardly ever the case where you're following a standard protocol across all labs...[protocols are] suited to their individual needs, and so the hardware and software need [the ability to] incorporate those ideas."



Thanks to its versatility and variety of applications, life scientists have a range of benefits to reap from open-source. As an example, open-source enables wet lab devices' features to be fine tuned for particular assays, or even modified wholesale enough to create entirely new ones such as turning a liquid handler into a colony picker. Imaging expert Eric Greenwald of the University of California, San Diego did exactly that: he created an opening in his OT-One, added legs, and mounted it to an inverted microscope. Greenwald uses this combined liquid handling–imaging system with fluorescent sensors to study how drugs impact biochemical signaling in living cells.

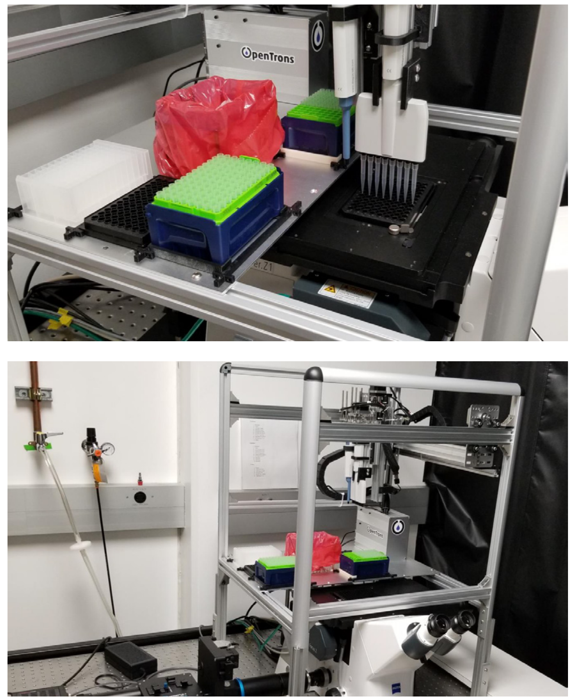
Another example is customizing the operation of a device. With just a few pieces of high-precision 3D-printed parts, a gear system and some screws, most any scientist can make a gripping device. Greenwald did exactly this, building a **gripping device to move petri dishes** on the deck of his OT-One. This open-source hardware enhances the capabilities of the Opentrons robot in a way that's custom tailored to his lab's workflow.

But there are many more applications of open-source hardware.

Scientists at another lab utilized Greenwald's idea, extending it to run an array of molecular cloning protocols on an Opentrons OT-2. Simply by downloading a collection of software **modules**, anyone can turn their OT-2 into an *E. coli*-transforming, colony-picking, plasmid-prepping machine, and more. As the site for these tools points out: "All code for this project is freely distributed for academic and commercial uses under the MIT license."

Another benefit open-source offers life scientists is that even lab members who aren't interested in tweaking a device's hardware or software themselves are able to use the tools created by, and made available to, the community. Some of those tools include 3D printing files for **customized labware**, custom lab devices like Greenwald's petri dish grabber, and even entire workflow setups like **an assembly system for genomics**.

All of this openness is uncommon but refreshing to life scientists. Many lab devices come in cookie-cutter packaging, revealing little about what's inside or how the device works. They also run on proprietary hardware and software whose inner workings are opaque and unchangeable. This lack of transparency can be unhelpful in a lab, as one scientist told us. "I have always liked being able to get into the workings of the device, whether that's software or a microscope. I'd like to be able to see what's happening inside." Some of that thinking comes from a scientist's natural curiosity and some, as this scientist noted, comes from the fact that "you can often get strung along quite a bit if you have to have the latest software and you have to have a license." That stringing along doesn't happen with open-source technology.



Photos of Greenwald's custom OT-One setup.
CREDIT: Greenwald

These examples show some of the potential of open-source, and why it's gaining traction across hardware, software, and even science in general. This traction emerges from the desire to make scientific devices that provide a custom fit to an application, as well as giving scientists who want a better understanding of how an instrument works and better access to tweaking its inner workings.

But as encouraging as these benefits are, implementing open-source in the lab comes with a slew of challenges.

CHAPTER 3

Challenges Of Implementing Open-Source

One major challenge facing the widespread adoption of open-source in the life science community is that a critical mass of members must not only be invited to the community, but active within it. This means that everyone participating in both making and using the open-source tools is not only contributing to the outcomes provided by them, but also benefiting from them. Given the complexity of both hardware and science, and the relatively sluggish speed at which new scientific technology is adopted, gaining critical mass is no simple undertaking.

For Opentrons, creating critical mass for open-source technology meant building lab automation platforms and putting them into the hands of researchers using shared or overlapping techniques. This allowed them to assess and innovate the platforms, and ensure they would be as useful as possible... and why we will continue to make lab automation platforms affordable, easy-to-use, and flexible enough to be adopted as quickly as possible by as many labs as possible.

Another major challenge in implementing open-source into life science labwork is the balance between standardization and flexibility. Depending on a lab's methods and research areas, they will likely need a highly specific, customized setup—even if they're using the same protocol as another lab. And even if they're using a community-created assay, researchers often have to tweak and re-optimize the entire thing to achieve their intended results. Understanding which parts of an open-source protocol can be usefully shared—and which work best when controlled by the robot's operator—is the heart of this challenge. This principle applies to any aspect of an open-source platform: the benefits of what can be shared must outweigh the work required to customize and re-optimize.

> **"... the benefits of what can be shared must outweigh the work required to customize and re-optimize."**

In a similar vein, another big challenge scientists face in utilizing open-source tools is adapting them to meet precision and accuracy standards. Since many open-source tools need to be customized to work in each lab, there's an additional element of tweaking required to ensure that they perform up to standard to provide verifiable results. Many traditionally trained bench scientists do not necessarily have the technical expertise to do that, so there's an additional learning curve required to successfully utilize open-source tools in lab work.

FIGURE 2

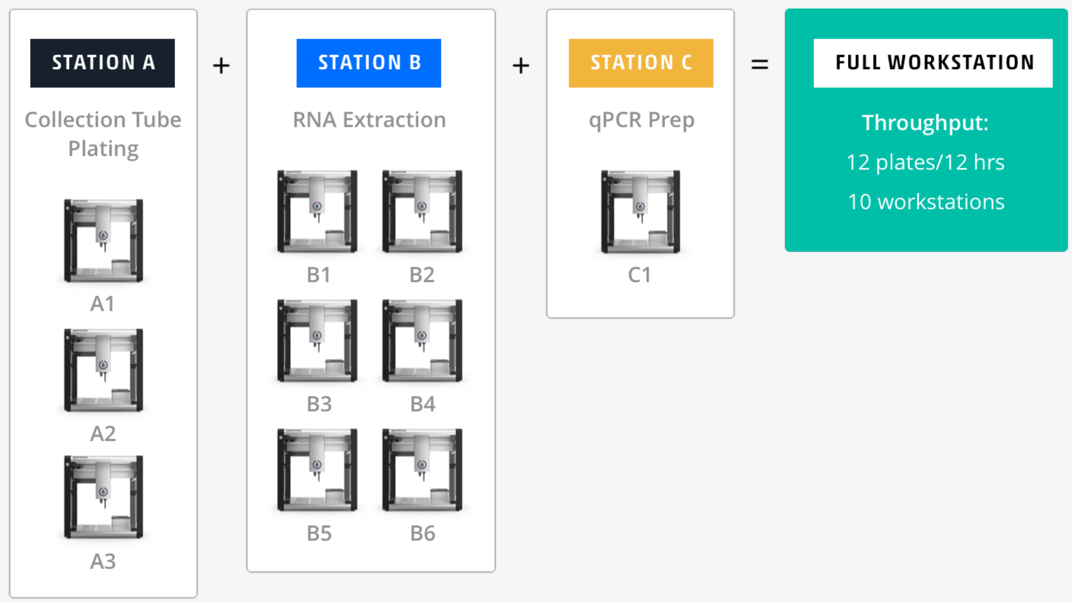
Challenges of implementing Open-Source

- How do we help foster and develop an active community?
- How do we find a balance between standardization & flexibility?
- How do we adapt our tools to meet precision accuracy standards?
- How do we shift the perspective around open-source?

Perhaps the biggest challenge is adoption of the open-source concept. Scientists need to think a bit differently to gain the full benefits of going more open-source, and changing that kind of culture and perspective is extremely difficult. Due to the publication-focused model of academic research, there is little monetary incentive for scientists to share proprietary ideas. But, sharing ideas and information could solve problems that closed-source science cannot. With lives at stake, especially given the global coronavirus pandemic, science cannot afford to withhold knowledge.

FIGURE 3

Opentrons COVID-19 Testing System



CHAPTER 4

Creating New Knowledge

Although many scientists appreciate the value of sharing knowledge, the processes for doing science aren't open. For example, a scientist working on a key set of experiments might keep it secret for fear of having someone else replicate them and publish before them. Even once results get published, they often can't be read because peer-reviewed journals cost a lot in print or live behind paywalls online.

Thankfully, there are open-source solutions for these issues, too.

Another open-source enthusiast pointed out the value of open-source approaches in bioengineering, noting that while working with non-government organizations, "open-source is the difference between a remote lab having access to knowledge as opposed to keeping something secret and behind a paywall."

She added that open-source methods speed up sharing knowledge across groups, helping to create solutions more quickly than traditional methods of collaboration—which is perhaps the single biggest benefit open-source offers life scientists: maximizing the impact of their time.

OPEN ACCESS JOURNALS

Open-access publishers like **PLOS** make all scientific articles available for free. There's even a **Directory of Open Access Journals** (DOAJ), which describes itself as a "community-curated online directory that indexes and provides access to high quality, open access, peer-reviewed journals." At the time of writing this e-book, DOAJ included 14,350 journals with more than 4.7 million articles.

OPEN PROJECTS

Matt Todd, professor of drug discovery at University College London School of Pharmacy started **opensourcemalaria.org**. At this site, anyone can get involved with the search for a cure to malaria, which kills more than 400,000 people a year.

OPEN METHODS & DATA

To bring even more of the open-source ethos to science, some research groups focus entirely on sharing methods and data. Synthetic biologists working with plants can find free tools at **Open Plant**. Other life scientists can share experimental methods at **protocols.io**, which reduces the need to reinvent the wheel over and over—and helps lead to better experimental processes. As one scientist told Opentrons: "I just like the idea of being able to run someone else's experiments in my own laboratory."

CHAPTER 5

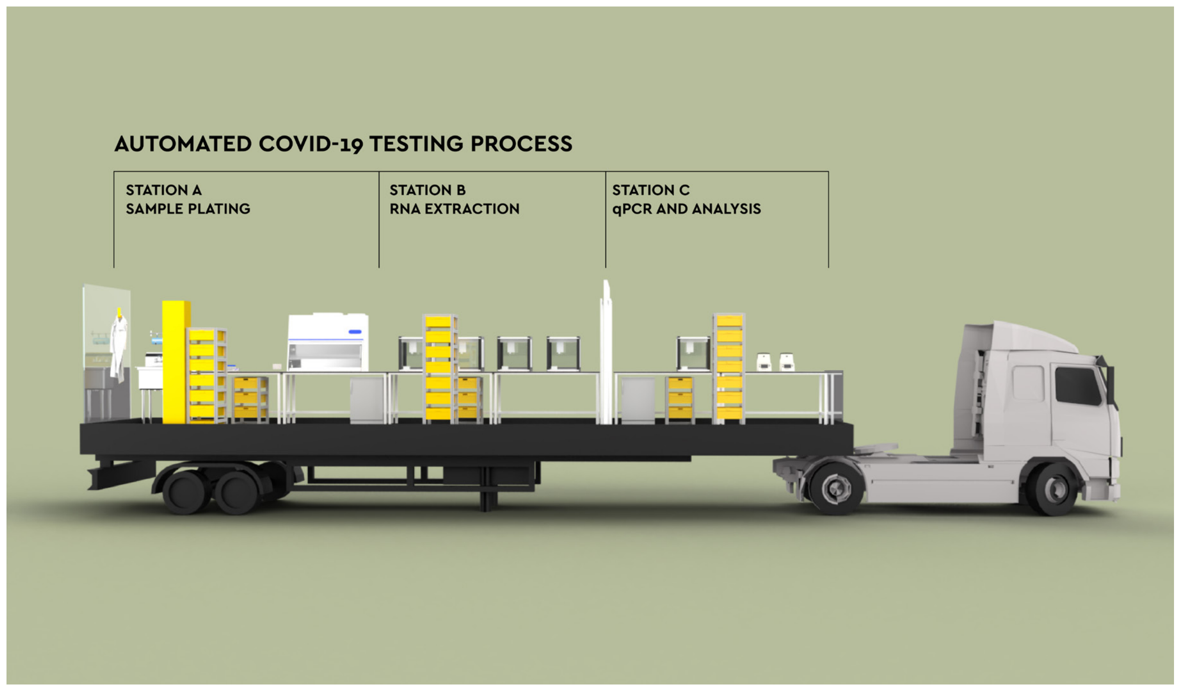
Maximizing Time, Skill Sets, And Collaboration

In *The Cathedral & the Bazaar*, Eric Raymond wrote:

Perhaps in the end open-source culture will triumph not because cooperation is morally right or software "hoarding" is morally wrong ... but simply because the closed-source world cannot win an evolutionary arms race with open-source communities that can put orders of magnitude more skilled time into a problem.

What Raymond means is that the very nature of open-source creates a wide net of interdisciplinary cross-team collaboration that often yields results much more quickly than traditional, proprietary structures can. Open-source teams are often composed of people with specialized skill sets that can be combined to more efficiently and effectively create the "orders of magnitude more skilled time" that Raymond noted by pulling in creators from disciplines that aren't traditionally involved in resource development. Better still, those teams can create those innovations and time savings without needing to work in the same place—or even know each other.

Perhaps the biggest and best proof of this idea is the way the scientific community has rallied to combat the global coronavirus pandemic. Researchers all over the world pivoted their research and switched workflows to find ways to create diagnostics, therapeutics, and antibodies to fight SARS-CoV-2. The amount of information, resources, and sharing to create scalable diagnostic testing solutions using open-source is unprecedented. Experts from various disciplines—clinical care, drug discovery and development, epidemiology, molecular biology, public health, virology and more—must combine datasets and analyze them together whenever possible. To create and compare results, open-source methods enhance the opportunities from making research more affordable to increasing the ability to understand the methods used to generate data. One group, led by researchers at the Hospital Clinic de Barcelona in Spain, detailed their open-



OpenCell's Mobile COVID-19 Testing Station. CREDIT: OpenCell source diagnostic testing solution in a bioRxiv paper: "**ROBOCOV: An affordable open-source robotic platform for SARS-CoV-2 testing by RT-qPCR**"[3]

The OT-2 stations are a promising solution to increase the SARS-CoV-2 testing capability since it is an affordable open-source platform for liquid handling. Open-source platforms have advantages compared with other platforms such as cost-effectiveness, flexibility and fast adaptation to laboratory needs. Open-source platforms are as strong as their community. Working with them can be challenging at first but every actor should greatly benefit as the community of users and developers grow, testing and improving existing code and developing new functions and capabilities for the platform.

The global scientific response to COVID-19 would simply not be possible without the collaboration and diverse skill sets enabled by open-source.

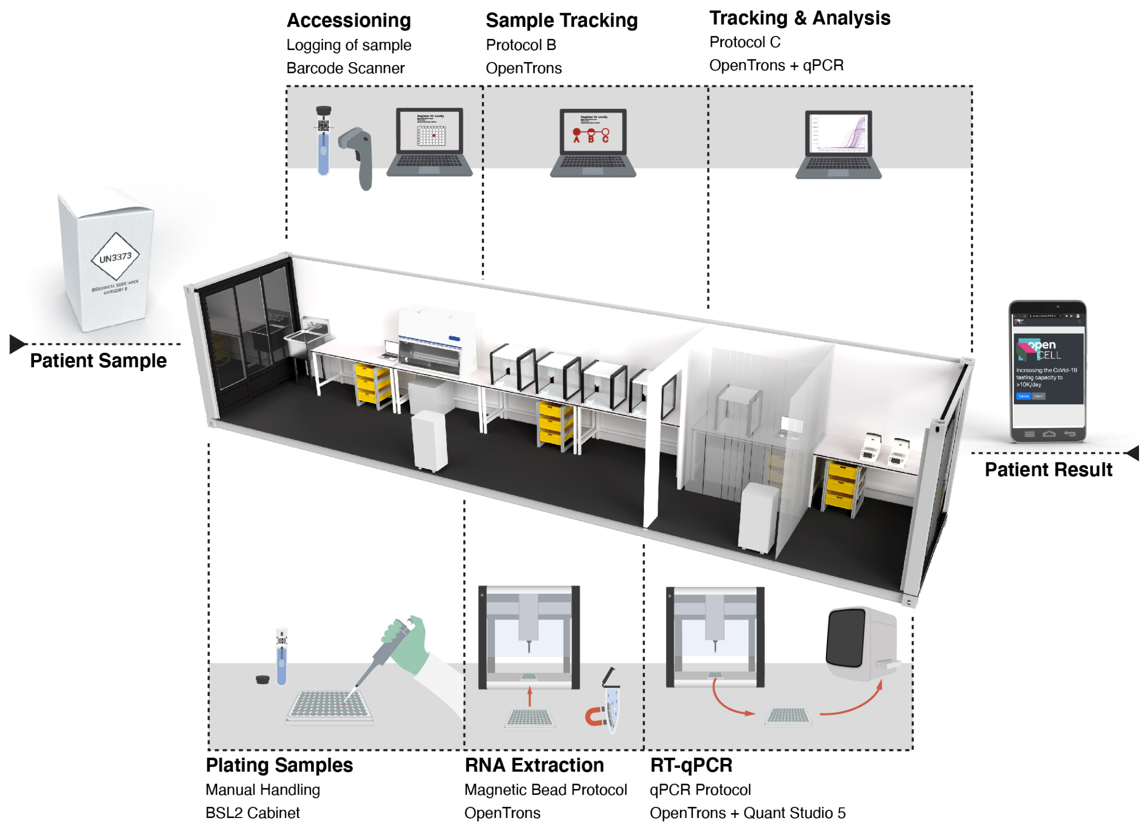


Illustration Of OpenCell's 3-part qPCR COVID-19 Testing Station. CREDIT: OpenCell

CHAPTER 6

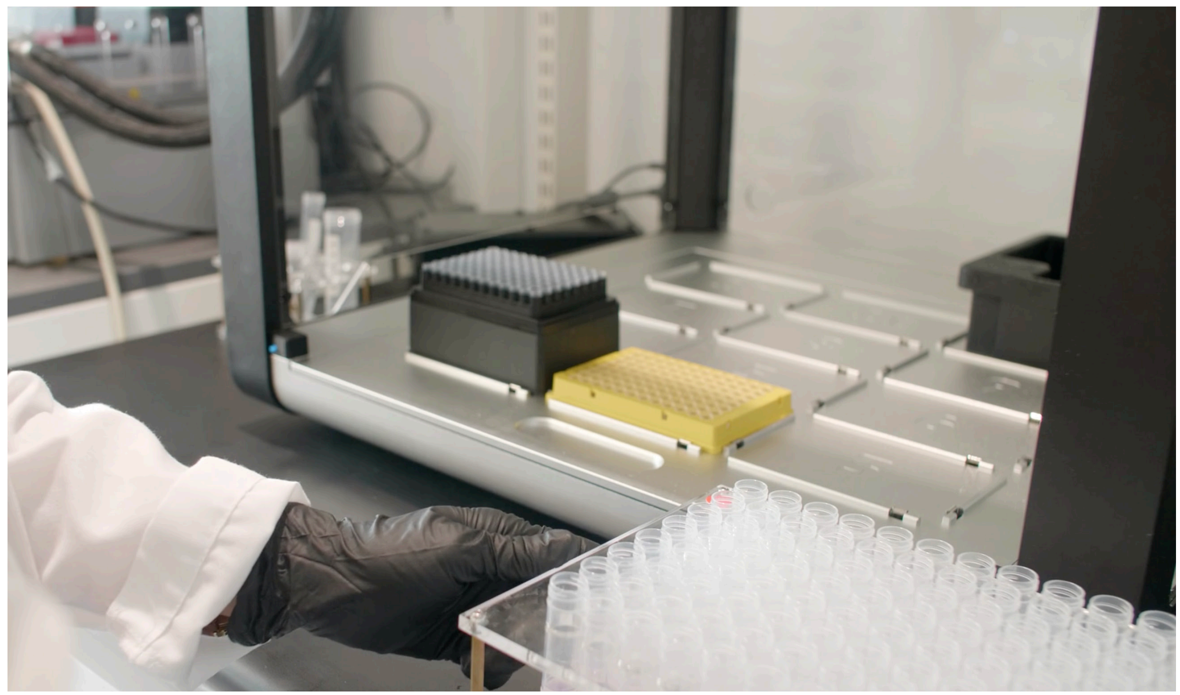
Improving Science And Aiding Society

The research cited in this e-book on sequencing and infectious disease reveals some of the ways that open-source tactics enhance science and benefit society. But there are larger, more long-term benefits to adopting open-source solutions in life science, too.

Perhaps the biggest: utilizing an open-source philosophy toward scientific discovery would improve accuracy and reproducibility for all of science. Transparency in methods and access to controlling software makes it easier for researchers to understand experiments, as well as find and correct errors. With reproducibility being a key goal of science, especially given the complexity of modern experiments, the transparency and teamwork inherent in open-source approaches support that objective. As one scientist said: "We definitely have a push towards reproducibility and robustness in science. And you can imagine, as part of getting a paper published, you also have to release that code for your robots and then any robot in the country can do that same experiment. That would be really cool." It would also make science more productive and the outcomes more useful.

To really make scientific tools useful to society, the tools and what they can do must be affordable. For example, Gencove uses an Opentrons robot as part of an economical DNA-sequencing method. A customer can get ancestral and health-related data for just $60.

As mentioned early, open-source methods encourage teamwork, and people around the world can work together—creating a whole unit that gets more work done than could the parts alone. That's some of the thinking behind India-based **Open Source Drug Discovery**, which works with partners around the world to find treatments for a range of tropical diseases, including leishmaniasis, malaria and tuberculosis.



Part of Gencove's OT-One Setup. CREDIT: Opentrons

CHAPTER 7

Embracing The Unexpected

In thinking about the expansive value that an open-source philosophy can drive, remember these words from Raymond: “Any tool should be useful in the expected way, but a truly great tool lends itself to uses you never expected.”

As Greenwald built an imaging system with an Opentrons robot, other scientists are finding ways to use open-source technology to solve manifold problems in their labs. In many cases, this technology provides just what a lab needs, largely ready to go from the start. Like Greenwald’s imaging system and the colony picker, some scientists will modify the robot to expand its capabilities. With open-source technology, a scientist’s imagination can take the technology to completely new uses, where researchers can collect exciting datasets and answer crucial questions.

With today’s technology, many applications of an open-source instrument don’t require a hacker’s tweaking or an engineer’s modifications. In short, most anyone can use it. And that’s what allows it to be so instrumental in creating scientific technologies of the future.

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How could open-source technology extend the reach in your lab? Everyone at Opentrons is excited to help you answer that question.

APPENDIX

Resources

REFERENCES

1. Open Source Software and the "Private-Collective" Innovation Model: Issues for Organization Science
2. 3D Printing Patents Are Expiring: What Does It Mean?
3. ROBOCOV: An Affordable Open-Source Robotic Platform For SARS-CoV-2 Testing By RT-qPCR

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RESOURCES

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