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The Next Big Developments – The Lab of the Future

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1.1 Introduction

Steve Jobs once said that "the biggest innovations of the 21st century will be at the intersection of biology and technology"; in this (r)evolution, the lab will most definitely play a key role.

When speculating on the future digital transformation of the life sciences R&D, one must consider how the whole lab environment and the science that goes on in that lab will inevitably evolve and change [1, 2]. It is unlikely that an R&D lab in 2030, and certainly in 2040, will look and feel like a comparable lab from 2020. So, what are the likely new big technologies and processes and ways of working that will make that lab of the future (LotF) so different? This section endeavors to introduce some of the new developments in technology and in science that we think will change and influence the life science lab environment over the upcoming decade.

1.2 Discussion

Before going into the new technology and science in detail, it is important to recognize that this lab evolution will be driven not just by new technologies and new science. In our view, there are four additional broader, yet fundamental and complementary attributes that influence how a lab environment changes over time. They are:

1. People and culture considerations
2. Process developments and optimization
3. Data management improvements
4. Lab environment and design

When we add the fifth major driver of change – new technology (including new science) – it becomes clear that digital transformation is a complex, multivariate concept (Figure 1.1).

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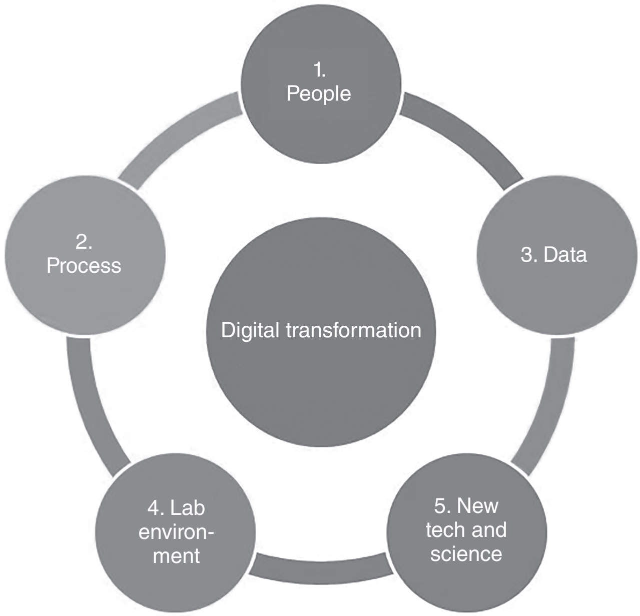

Figure 1.1 Complex, multivariate concept of lab transformation.

In this section, we discuss how each of these high-level attributes will influence the changing lab and the expectations of the users. For all five areas, we include what we think are some of the most important aspects, which we believe will have the most impact on the "LotF."

1.2.1 People/Culture

The LotF and the people who work in it will undoubtedly be operating in an R&D world where there is an even greater emphasis on global working and cross-organization collaboration. Modern science is also becoming more social [3], and the most productive and successful researchers will be familiar with the substance and the methods of each other's work so breaking down even more the barriers to collaboration. These collaborative approaches will foster and encourage individuals' capacity to adopt new research methods as they become available; we saw this with the fast uptake of clustered regularly interspaced short palindromic repeat (CRISPR) technology [4]. "Open science" [5] will grow evermore important to drive scientific discovery. This will be enabled through the increased use of new cryptographic Distributed Ledger Technology (DLT) [6], which will massively reduce the risk of IP being compromised [7]. The LotF will also enable more open, productive, collaborative working through vastly improved communication technology (5G moving to 6G) [8]. The people working in these labs will have a much more open attitude, culture, and mindset, given the influence of technology such as smartphones on their personal lives.

Robotics and automation will be ubiquitous, but with more automated assistance, the density of people in the lab will likely drop, allowing scientists to focus on key aspects and complex parts of the experiments. As a consequence, issues around safety and "lone working" will grow, and a focus on the interaction points which scientists have with automation will develop to ensure they are properly protected. For the few remaining lab technicians, not only will safe working become of increased importance, but the need for organizations to deliver a better "user experience" (UX) in their labs will become key to help them both attract the smaller numbers of more expert technicians and also retain them. The lab technician's UX will be massively boosted by many of the new technologies already starting to appear in the more future-looking labs, e.g. voice recognition, augmented reality (AR), immersive lab experience, a more intelligent lab environment, and others (see later sections).

1.2.2 Process

The lab processes, or "how" science gets done in the LotF, will be dominated by robotics and automation. But there will be another strong driver which will force lab processes and mindsets to be different in 5–10 years time: sustainability. Experiments will have to be designed to minimize the excessive use of "noxious" materials (e.g. chemical and biological) throughout the process and in the cleanup once the experiment is complete. Similarly, the use of "bad-for-the-planet" plastics (e.g. 96/384/1536-well plates) will diminish. New processes and techniques will have to be conceived to circumvent what are standard ways of working in the lab of 2020. In support of the sustainability driver, miniaturization of lab processes will grow hugely in importance, especially in research, diagnostic, and testing labs. The current so-called lab on a chip movement has many examples of process miniaturization [9]. Laboratories and plants that are focused on manufacturing will continue to work at scale, but the ongoing search for more environmentally conscious methods will continue, including climate-friendly solvents, reagents, and the use of catalysts will grow evermore important [10]. There will also be a greater focus on better plant design. For example, 3D printing [11] could allow for localization of manufacturing processes near to the point of usage.

In the previous paragraph, we refer to "research, diagnostic, and testing labs" and to manufacturing "plant." We believe there is a fundamental difference between what we are calling hypothesis- and protocol-driven labs, and this is an important consideration when thinking about the LotF. The former are seen in pure research/discovery and academia. The experiments being undertaken in these labs may be the first of their kind and will evolve as the hypothesis evolves. Such labs will embrace high throughput and miniaturization. Protocol-driven labs, where pure research is not the main focus, include facilities such as manufacturing, diagnostic, analytical, or gene-testing labs. These tend to have a lower throughput, though their levels of productivity are growing as automation and higher quality processes enable ever higher throughput. In these labs, reproducibility combined with robust reliability is key. Examples in this latter area include the genomic screening and testing labs [12, 13], which have been growing massively in the

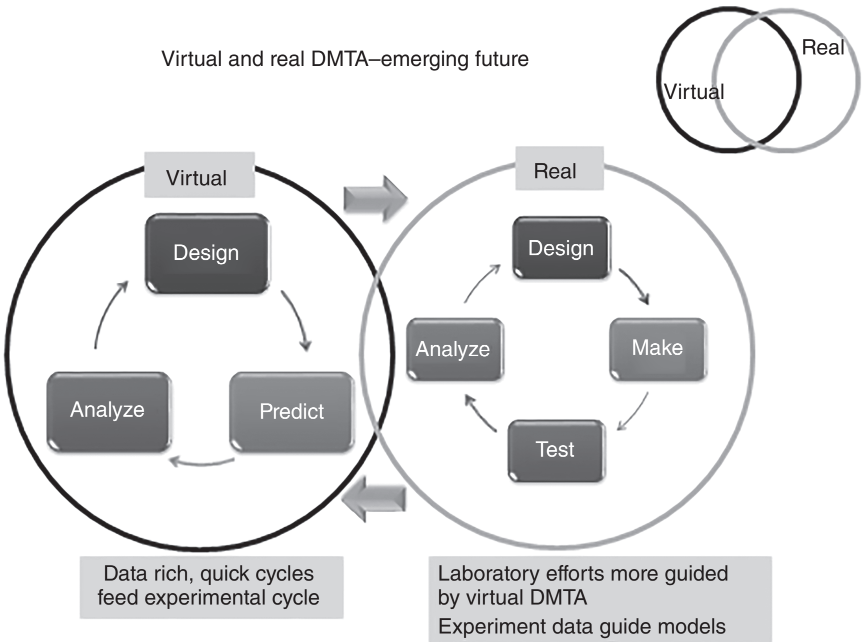

Figure 1.2 Virtual and real design-make-test-analyze (DMTA) concept.

past few years. For these labs the already high levels of automation will continue to grow.

In the hypothesis-driven lab [14] with the strong driver of sustainability combined with the growth of ever higher quality artificial intelligence (AI) and informatics algorithms, there will be more in silico, virtual "design-make-test-analyze" (vDMTA) and less, tangible Make and Test (see Figure 1.2). Fewer "real" materials will actually be made and tested, and those that are will be produced on a much smaller scale.

Finally, as labs get more sophisticated – with their high levels of automation, robotics, miniaturization, and data production (but with fewer staff) – combined with the need for those facilities to be both safe and sustainable, the concept of "laboratory as a service" (LaaS) will grow [15]. The LotF will not be a static, self-contained, and single scientific area facility. It will be a blank canvas, as it were, in a large warehouse-like facility or cargo container [16] which can be loaded up on demand with the necessary equipment, automation, and robotics to do a contracted piece of lab work. That piece of work might be a chemical synthesis or a cell-based pharmacological assay one day, and an ex vivo safety screen in the same area the next day. The key will be use of a modular design supported by fully connected devices.

1.2.3 Lab Environment and Design

The lab environment, its design, usability, and sustainability are mentioned previously in this section and elsewhere in the book, but it is fair to say that all labs will face the pressure [17, 18] to design sustainable spaces [19] that can keep up with all the emerging technical trends as well as the usability and design features needed to support a new generation of scientists. These drivers will combine to influence how the LotF evolves and experiments are performed. Research institutions are already creating more "open" labs areas to support interdisciplinary teamwork, collaborative working, and joint problem solving, rather than the previous "siloed" departmental culture. This will continue in the LotF. The growth of innovation clusters [20] and lab coworking spaces will require more consideration as to how shared automation and lab equipment can be effectively and securely used by groups, who may be working for different organizations and who will want to ensure their data and methods are stored and protected in the correct locations. Effective scheduling will be critical in the LotF to enable high productivity and to ensure that the high value of the automation assets is realized.

1.2.4 Data Management and the "Real Asset"

It is true of 2020, just as it was 50 years ago and will be in 50 years time, that the primary output of R&D, in whatever industry, is data. The only physical items of any value are perhaps some small amounts of a few samples (and sometimes not even that) plus, historically, a lot of paper! It is therefore not surprising that the meme "data is the new oil" [21] has come to such prominence in recent times. While it may be viewed by many as hackneyed, and by many more as fundamentally flawed [22], the idea carries a lot of credence as we move toward a more data-driven global economy. One of the main flaws arising from the oil analogy is the lack of organizations being able to suitably refine data into the appropriate next piece of the value chain, compared to oil, which has a very clear refining process and value chain. Furthermore, the "Keep it in the Ground" [23, 24] sustainability momentum makes the data-oil analogy perhaps even less useful. However, within the LotF, and in a more open, collaborative global R&D world, experimental data, both raw and refined, will grow in criticality. Without doubt, data will remain a primary asset arising from the LotF.

At this point then it is worth considering how data and data management fit into the processes that drive the two fundamental lab types, which we have referred to earlier, namely (i) the hypothesis-driven, more research/discovery-driven lab and (ii) the protocol-driven, more "manufacturing"-like lab.

1.2.4.1 Data in the Hypothesis-driven, Research Lab

In a pure research, hypothesis-driven lab, whether it is in life science, chemical science, or physical science, there is a fundamental, cyclical process operating. This process underpins all of scientific discovery; we refer to it as the "hypothesis-experiment-analyze-share" ("HEAS") cycle (see Figure 1.3) or, alternatively, if one is in a discovery chemistry lab, for example a medicinal chemistry lab in biopharma, DMTA (see Figure 1.2).

The research scientists generate their idea/hypothesis and design an experiment to test it. They gather the materials they need to run that experiment, which they then

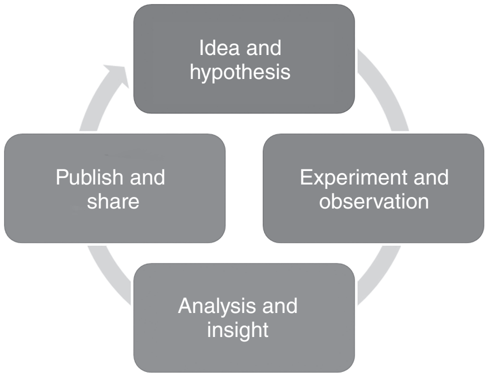

Figure 1.3 Hypothesis-experiment-analyze-share (HEAS) cycle.

perform in the lab. All the time they capture observations on what is happening. At the end they "workup" their experiment – continuing to capture observations and raw data. They analyze their "raw" data and generate results ("refined" data); these determine whether the experiment has supported their hypothesis or not. They then communicate those results, observations, and insights more widely. Ultimately, they move on to the next, follow-on hypothesis; then, it is off round the cycle they go again until they reach some sort of end point or final conclusion. All the while they are generating data: raw data off instruments and captured visual observations and refined data, which are more readily interpretable and can more easily lead to insights and conclusions.

1.2.4.2 Data in the Protocol-driven Lab

In the protocol-driven lab, whether it is in a manufacturing or sample testing domain, there is again a fundamental process which operates to drive the value chain. Unlike the "HEAS" cycle this is more of a linear process. It starts with a request and ends in a communicable result or a shippable product. This process, which we refer to as the "request-experiment-analyze-feedback" (REAF) process, is outlined in Figure 1.4.

There are many similarities, often close, between the linear REAF process and the HEAS cycle especially in the Experiment/Observe and Analyze/Report steps, but the REAF process does not start with an idea or hypothesis. REAF represents a service, which starts with a formal request, for example to run a protocol to manufacture a good or to test a sample, and ends with a product or a set of results, which can be fed back to the original customer or requester. As we noted in Section 1.2.4.1 above, it is increasingly likely that the LotF will be set up with a Laboratory as a Service (LaaS) mentality; REAF may therefore be much more broadly representative of how labs of the future might operate.

Figure 1.4 Request-experiment-analyze-feedback (REAF) process.

It is important to acknowledge that the data and information, which drive Request and Feedback, are quite different in REAF than in the corresponding sections in HEAS. With the focus of this book being on Experiment/Observe, and to a degree Analyze, we will not say anything more about Request and Feedback (from REAF) and Hypothesis and Share (from HEAS). Instead, the remainder of this section focuses on what the Experiment and Analyze data management aspects of the LotF will look like, whether that LotF is a hypothesis- or a protocol-driven lab. This is made simpler by the fact that in the Experiment/Observe and Analyze/Report steps, the data challenges in the two different lab types are, to all intents and purposes, the same. In the remainder of this section we treat them as such.

1.2.4.3 New Data Management Developments

So what new developments in data management will be prevalent in both the hypothesis- and the protocol-driven labs of 2030? In the previous two sections we asserted that these labs will be populated by fewer people; there will be more robotics and automation, and the experiment throughput will be much higher, often on more miniaturized equipment. Building on these assertions then, perhaps the most impactful developments in the data space will be:

a) The all pervasiveness of internet of things (IoT) [25, 26]. This will lead, in the LotF, to the growth of the internet of laboratory things (IoLT) environments; this will also be driven by ubiquitous 5G communications capability.
b) The widespread adoption of the findable, accessible, interoperable, and reusable (FAIR) data principles. These state that all data should be FAIR [27].
c) The growing use of improved experimental data and automation representation standards, e.g. SiLA [28] and Allotrope [29].
d) Data security and data privacy. These two areas will continue to be critical considerations for the LotF.
e) The ubiquity of "Cloud." The LotF will not be able to operate effectively without access to cloud computing.
f) Digital twin approaches. These will complement both the drive toward labs operating more as a service and the demand for remote service customers wanting to see into, and to directly control from afar what is happening in the lab. Technologies such as augmented reality (AR) will also help to enable this (see Sections 1.2.5 and 1.2.6).
g) Quantum computing [30–33]. This moves from research to production and so impacts just about everything we do in life, not just in the LotF. Arguably, quantum computing might have a bigger impact in the more computationally intensive parts of the hypothesis- and protocol-driven LotF, e.g. Idea/Hypothesis design and Analyze/Insight, but it will still disrupt the LotF massively. We say more on this in Sections 1.2.5 and 1.2.6.

The first three of these developments are all related to the drive to improve the speed and quality of the data/digital life cycle and the overall data supply chain. That digital life cycle aligns closely to the HEAS and REAF processes outlined in Figures 1.3 and 1.4 and can be summarized as follows (see Figure 1.5):

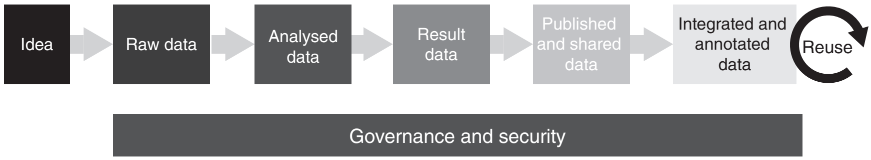

Figure 1.5 Digital data life cycle.

IoT technology [34] will allow much better connectivity between the equipment in the LotF. This will enable better, quicker, and more precise control of the lab kit, as well as more effective capturing of the raw data off the equipment. This in turn will allow the next stage in the life cycle – "Analyze Data" – to happen sooner and with more, better quality data. This improved interconnectedness in the lab will be made possible by the same 5G communication technology which will be making the devices and products in the home of 2025 more networked and more remotely controllable.

As improved instrument interconnectedness and IoLT enable more data to be captured by more instruments more effectively, the issue of how you manage the inevitable data flood to make the deluge useful comes to the fore. The biggest initiative in 2020 to maximize the benefits of the so-called big data [35] revolves around the FAIR principles. These state that "for those wishing to enhance the reusability of their data holdings," those data should be FAIR. In the LotF, the FAIR principles will need to be fully embedded in the lab culture and operating model. Implementing FAIR [36] is very much a change process rather than just introducing new technology. If fully implemented, though, FAIR will make it massively easier for the vast quantities of digital assets generated by organizations to be made much more useful. Data science as a discipline, and data scientists (a role which can be considered currently to equate to that of "informatician"), will grow enormously in importance and size/number. Organizations that are almost purely data driven will thrive, with any lab work they feel the need to do being outsourced via LaaS [37] to flexible, cost-effective LotFs that operate per the REAF process.

Supporting the growth of FAIR requires the data that is generated in these LaaS LotFs to be easily transferable back to the requester/customer in a format which the lab can generate easily, accurately, and reproducibly, and which the customer can import and interpret, again, easily, accurately, and reproducibly. This facile interchange of "interoperable" data will be enabled by the widespread adoption of data standards such as SiLA and Allotrope. We describe these new data standards in more detail in the following section.

Two additional, significant data considerations for the LotF are those of data security and data privacy, just as they are now. The more LotF services that are operated outside the "firewall" of an organization, and the more that future labs are driven by data, the more risks potentially arise from accidental or malicious activities. Making sure that those risks are kept low, through continued diligence and data security, will ensure that the LotF is able to develop and operate to its full capability. Similarly, in labs that work with human-derived samples (blood, tissues, etc.), the advent of regulations such as the General Data Protection Regulations (GDPR) [38, 39], along with the historical stringency surrounding informed consent [40] over what can happen to human samples and the data that arises from their processing, will put even more pressure on the organizations that generate and are accountable for human data to ensure these data are effectively secured. Improved adherence to the FAIR data principles, especially Findability and Accessibility, will ensure that LotFs working with human-derived materials can be responsive to data privacy requests and are not compromised.

Going hand in hand with the data explosion of the past decade has been the evolution of the now ubiquitous, key operational technology of “Cloud Computing.” As explained by one of the originating organizations in this area, “cloud computing is the delivery of computing services – including servers, storage, databases, networking, software, analytics, and intelligence – over the Internet (the cloud) to offer faster innovation, flexible resources, and economies of scale.” [41] In the context of LotF, assuming that the equipment in the lab is fully networked, cloud computing means that all the data generated by the lab can be quickly, fully, and securely captured and stored on remote infrastructure (servers). This book is not the place to describe cloud computing in detail, but it should be sufficient to say that the LotF will not be reliant on IT hardware close to its location (i.e. on-site) but will be highly reliant on speedy, reliable, available networks and efficient, cost-effective cloud computing.

Finally, there is a data and modeling technology, which has been present in industries outside life science for many years, which could play a growing role in the LotF which is more automated and more remote. This is the technology termed “digital twin.” [42, 43] We say more on this exciting new technology in Section 1.2.5.1.

1.2.5 New Technology

In any future-looking article we can only make some best guesses as to the new technologies and science that could be important during the next 5–10 years. In this section we make some suggestions as to what new technologies we feel will impact the LotF, and what new science will be happening in those future labs. In the first part of this section, we focus on new technologies. In the second part, we suggest some scientific areas which we feel will grow in importance and hence might drive the evolution of the LotF and the technology that is adopted in that new lab environment.

New technologies will undoubtedly play a major role in driving the development of the critical components within the LotF, but their introduction and usage need to be appropriate to the type of lab being used. The role of the new technologies must be aligned to the future challenges and needs of the lab environment. These needs include, more specifically:

- Flexibility and agility of the experiment cycles, balancing between prediction (in silico) and physical (in vitro) experiments
- Improved data collection and experiment capture (e.g. “data born FAIR”)

- Reproducibility of the experiment processes
- Enhancements to the scientists' UX and capabilities in the lab.

To emphasize these aspects, we focus on three broad areas in this section:

1. Lab automation integration and interoperability
2. Quantum computing and the LotF
3. Impact of AI and machine learning (ML).

1.2.5.1 Lab Automation Integration and Interoperability

Lab instrument integration and interoperability to support higher levels of lab automation have been and will continue to evolve quickly, driven by the pressure from scientists and lab managers and, above all to have better ways to manage and control their equipment [44–46]. Capabilities as diverse as chemical synthesis [47] and next-generation sequencing (NGS) [48] are seeking to better automate their workflows to improve speed and quality and to align with the growing demands of AI in support of generative and experimental design as well as decision-making [49]. An additional stimulus toward increased automation, integration, and interoperability is that of experiment reproducibility. The reproducibility crisis that exists in science today is desperately in need of resolution [50]. This is manifested not only in terms of being unable to confidently replicate externally published experiments, but also in not being able to reproduce internal experiments – those performed within individual organizations. Poor reproducibility and uncertainty over experimental data will also reduce confidence in the outputs from AI; the mantra "rubbish in, rubbish out" will thus continue to hold true! Having appropriate automation and effective data management can support this vital need for repeatability, for example of biological protocols [51]. This will be especially important to support and justify the lab as a service business model, which we have mentioned previously. It is our belief that the increased reliability and enhanced data-gathering capability offered by increased automation initiatives in the LotF will be one important way to help to address the challenge of reproducibility.

Updated automation will always be coming available as an upgrade/replacement for the existing equipment and workflows; or to enhance and augment current automation; or to scale up more manual or emerging science workflows. When considering new automation, the choices for lab managers and scientists will depend on whether it is a completely new lab environment (a "green-field site") or an existing one (a "brown-field site").

As mentioned previously, the growth of integration protocols such as IoT [52] is expanding the options for equipment and automation to be connected [53]. The vision for how different workflows can be integrated – from single measurements (e.g. balance measurements), via medium-throughput workflows (e.g. plate-based screening), to high data volume processes such as high content screening (HCS) involving images and video – has the potential to be totally reimagined. IoT could enable the interconnectivity of a huge range of lab objects and devices, such as freezers, temperature control units, and fume hoods, which previously would have been more standalone, with minimal physical connectivity. All these devices could be actively connected into expanded data streams and workflows where the measurements they take, for example, temperature, humidity, and air pressure, now become a more integral part of the experiment record. This enhanced set of data collected during experiments in the LotF will be hugely valuable during later analysis to help spot more subtle trends and potential anomalies. Furthermore, these rich datasets could play an increasing role as AI is used more and more for data analysis; small fluctuations in the lab environment do have a significant impact on experimental results and hence reproducibility. As well as this passive sensor monitoring, there is also the potential for these devices to be actively controlled remotely; this opens up options for further automation and interaction between static devices and lab robots, which have been programmed to perform tasks involving these devices. As always, it will be necessary to select appropriate automation based on the lab's needs, the benefits the new automation and workflows can provide, and hence the overall return on investment (ROI).

While the potential for these new systems with regard to improved process efficiency is clear, yet again, though, there is one vital aspect which needs to be considered carefully as part of the whole investment: the data. These LotF automation systems will be capable of generating vast volumes of data. It is critical to have a clear plan of how that data will be annotated and where it will be stored (to make it findable and accessible), in such a way to make it appropriate for use (interoperable), and aligned to the data life cycle that your research requires (reusable). A further vital consideration will also be whether there are any regulatory compliance or validation requirements.

As stated previously, a key consideration with IoT will be the security of the individual items of equipment and the overall interconnected automation [54, 55]. With such a likely explosion in the number of networked devices [56], each one could be vulnerable. Consequently, lab management will need to work closely with colleagues in IT Network and Security to mitigate any security risks. When bringing in new equipment it will be evermore important to validate the credentials of the new equipment and ensure it complies with relevant internal and external security protocols.

While the role of lab scientist and manager will clearly be majorly impacted by these new systems, also significantly affected will be the physical lab itself. Having selected which areas should have more, or more enhanced and integrated, lab automation, it is highly likely that significant physical changes to the lab itself will have to be made, either to accommodate the new systems themselves or to support enhanced networking needs.

In parallel to the lab environment undergoing significant change over the upcoming decades, there will also be new generations of scientists entering the workforce. Their expectations of what makes the LotF efficient and rewarding will be different from previous generations. The UX [57] for these new scientists should be a key consideration when implementing some of the changes mentioned in this book. For example, apps on mobile phones or tablets have transformed peoples' personal lives, but there has been slower development and adoption of apps for the lab. The enhanced usage of automation will very likely need to be managed through apps; they will therefore become a standard part of the LotF. One cultural caveat around the growth of lab apps should be flagged here. With apps enabling much more sophisticated control of automation operating 24/7, via mobile phones, outside "human working hours," there will need to be consideration of the new scientists' work/life balance. If handled sensitively, though, developments such as lab apps could offer much-increased efficiency and safety, as well as reducing experiment and equipment issues.

Voice-activated lab workflows are also an emerging area, just as voice assistants have become popular in the home and in office digital workflows [58]. For the laboratory environment, the current challenges being addressed are how to enrich the vocabulary of the devices with the specific language of the lab, not only basic lab terms but also domain-specific language, whether that is biology, chemistry, physics, or other scientific disciplines. As with IoT, specific pilots could not only help with the assessment of the voice-controlled device or system but also highlight possible integration issues with the rest of the workflow. A lab workflow where the scientist has to use both hands, like a pianist, is a possible use case where voice activation and recording could have benefits. The ability to receive alerts or updates while working on unfamiliar equipment would also help to support better, safer experimentation.

As with voice control, the use of AR and virtual reality (VR) in the lab has shown itself to have value in early pilots and in some production systems [59]. AR is typically deployed via smart glasses, of which there is a wide range now in production. There are a number of use cases already where AR in the lab shows promise, including the ability to support a scientist in learning a new instrument or to guide them through an unfamiliar experiment. These examples will only grow in the LotF. To take another, rather mundane example, pipetting is one of the most familiar activities in the lab. In the LotF where low throughput manual pipetting is still performed, AR overlays could support the process and reduce errors. AR devices will likely supplement and enhance what a scientist can already do and allow them to focus even more productively.

Another area of lab UX being driven by equivalents in consumer devices is how the scientist actually interacts physically with devices other than through simple keyboard and buttons. Technologies such as gesture control and multitouch interfaces will very likely play an increasing role controlling the LotF automation. As with voice activation, these input and control devices will likely evolve to support the whole lab and not just a single instrument. Nevertheless, items such as projected keyboards could have big benefits, making the lab even more digitally and technologically mature.

As mentioned before there is another technology which could play a significant role in enhancing the UX in the LotF; this is the "digital twin." [60] In brief, a digital twin is a representation in silico of a person, a process, or a thing. Its role has been evolving in recent years, such that digital twins can now be seen as virtual replicas of physical environments or objects which managers, data scientists, and business users can use to run simulations, prepare decisions, and manage operations [42, 61].

This technology has the potential to impact the LotF in two primary areas: (i) simulation and (ii) remote control.

Starting with simulation, digital twins, unlike the physical world, which shows you a picture of the present, can review the past and simulate the future. The digital twin can therefore become an environment to test out in pilot mode not only emerging technologies such as voice activation, AR, VR, and multigesture devices but also novel or redesigned workflows without the need for full-scale deployment. Indeed, with increased computational capability (provided by exascale computing and ultimately quantum computing – see Section 1.2.5.2), the processes that operate within the LotF will be simulatable to such a degree of sophistication that a person will be able to see, in silico, a high-resolution representation of the technology, experiment, or process they are looking to perform, in a simulation of the lab in which it will run. This digital twin will allow the operator to check, for example that the novel process is likely to run smoothly and deliver the output that is hoped for. While digital twin technology may be more applicable to the protocol-driven lab, it may also have applicability in the research lab as a means of exploring "what-if" scenarios prior to doing the actual physical experiment.

Turning to digital twin technology and improved remote control, massively improved computational technology combined with advances in AR and VR will allow operators, who might be located nowhere near the lab in which their experiment is being run, to don appropriate AR/VR headsets and walk into an empty space that will "feel" to them like they are right inside the lab or even right inside the experiment itself. The potential for scientists to "walk" into the active site of an enzyme and "manually" dock the molecules they have designed, or for an automation operator to "step into" the reaction vessel running the large-scale manufacturing of, say, a chemical intermediate to check that there are no clumps, or localized issues (e.g. overheating), will revolutionize how the LotF can operate, making it more likely to be more successful and, importantly, safer.

One final, obvious application of digital twin technology is where that LotF is not even on Earth. Running experiments in low or zero gravity can lead to interesting, sometimes unexpected findings [62]. This has led to numerous experiments having been performed on the NASA Space Station [63]. But having a trained astronaut who can effectively run any experiment or protocol, from organic synthesis to genetic manipulation, is asking a great deal. Digital twin technology could make the LotF in zero gravity a much more compelling proposition [64].

Returning to the area of instrument integration and interoperability, a more practical consideration is how different instruments communicate with each other, and how the data they generate is shared.

Within any lab there is and always will be a wide range of different instruments from different manufactures, likely bought over several years to support the business workflows. This "kit diversity" creates a challenge when you want to define a protocol which involves linking two or more instruments together that do not use the same control language. SiLA-2 [65] is a communication standard [66] for lab instruments, such as plate readers, liquid handling devices, and other analytical equipment, to enable interoperability. As indicated throughout this section, the ability to fully connect devices together will enable a more flexible and agile lab environment, making it possible to track, monitor, and remote control automation assets. This will further enable enhanced robotic process automation (RPA) as well as easier transition to scale up and transfer to remote parties. Specific devices connected together for one workflow will be easily repurposable for other tasks without a monolithic communication design and coding.

Data in all its forms will remain the dominant high-value output from lab experiments. As with protocols and communications, there need to be standards to support full data integration and interoperability within and between research communities. Over the years, data standards have evolved to support many aspects of the life science process whether that is for registration of new chemical entities [67], images [68], or macromolecular structures [69] or for describing the experiment data itself. Analytical instrument data (e.g. from nuclear magnetic resonance machines [NMRs], chromatographs, and mass spectrometers) are produced by a myriad of instruments, and the need to analyze and compare data from different machines and support data life cycle access in a retrievable format has driven the creation of the Allotrope data format [70] (ADF). This is a vendor-neutral format, generated initially for liquid chromatography, with plans to expand to other analytical data. These wide community-driven efforts such as those from Allotrope, SLAS, IMI [71], or the Pistoia Alliance [72] highlight the value of research communities coming together in life sciences, as happens elsewhere in industries such as financials and telecoms. Such enhanced efforts of collaboration will be needed even more in future.

In summary, the use of open standards will be critical for the success of the LotF, as the range of devices grows and science drives changes. There will need to be reliable, robust ways for the instruments, workflows, and data to be shared and accessible in order to support flexible, open-access, and cross-disciplinary collaborations, innovation, and knowledge exchange. The automation in the LotF will need to be effective across many different sizes and types of labs – from large, high-throughput labs doing screening or sequencing, to midsize labs with some automation workbenches, to the long tail of labs with a few specialist instruments. In planning for a new lab, creating a holistic vision of the design will be a key first element. That vision will include the future processes that your lab will want to tackle, as well as the potential new technologies to be deployed in the lab, e.g. IoT, AR, or voice control. Additionally, new skills will need to be acquired by those involved to help implement these changes, and an investment in staff and their training remains vital. Furthermore, in future there will likely be an ecosystem of lab environments both local and more disparate to consider; the LotF will be smarter and more efficient but not just through the adoption of a single device.

1.2.5.2 Quantum Computing and the Lab of the Future

The field of quantum computing is moving so fast that any review or update is soon superseded by the next breakthrough [73]. Consequently, this section focuses on introducing some of the concepts of quantum computing and how it might impact the LotF [74] and its workflows going forward especially those in the design (model/predict) and analyze stages.

Quantum computers differ [75] from our current classical computers in that they offer a fundamentally different way of performing calculations; they use the theories of quantum mechanics and entanglement [76, 77] and qubits (multiple simultaneous states) rather than bits (binary states – 0 and 1). This gives them the potential to solve problems and process tasks that would take even the fastest classical computer hundreds if not thousands of years to perform. Such performance will enable the simulation of highly complex systems, such as the behavior of biological molecules and other life science challenges [78]. A key concept in this area is that of the "quantum supremacy" [79] threshold, where quantum computers crossover from being an interesting and pure research-driven project to doing things that no classical computer can. Quantum supremacy is defined as a situation where a quantum computer would have to perform any calculation that, for all practical purposes, a classical computer cannot do because of the time involved. There is much discussion about whether we have reached "quantum supremacy," but it does seem clear that, for the foreseeable future, quantum computers will not be used for everyday activities but for highly specific, truly value-adding and accelerated tasks, much in the same way that exascale supercomputers work today. One further critical step will be needed to ensure that quantum computers are able to operate outside the research domain, that is to create quantum compilers [80] which can make code run efficiently on the new hardware, just as traditional compilers were needed with classical computers.

There are good parallels between quantum computers and the exascale, supercomputers, and clusters of today when thinking about the impact on life science and broader research. There are limited numbers of supercomputers at the moment due to their cost and the skills needed to fully utilize them. Consequently, researchers have to bid for time slots at the regional and national centers which house them. It is likely that the same process will happen with quantum computers, with regional/national [81–83] centers being established to support scientists who use them remotely to process their calculations and model building. Quantum cloud computing [84] and associated services will likely evolve in the same way that existing cloud compute and storage infrastructure and business models have evolved over the past decade.

We now focus on how quantum computing will more directly impact the LotF and the experiments which will run within it. The researchers involved will, at least in the early years, have to balance their "classical" and "quantum" calculation time with their physical experiment effort to help drive their insights and decision-making. Experiments will still be performed on complex systems, but they will be influenced even more by the work done in silico. There will likely be more rapid experiment cycles since the ability to perform quicker calculations will enhance the speed of progress and encourage research in areas that have until now been hard to explore, for example molecular simulations of larger biological entities.

Data will remain a key element of the workflow. Being able to send data to quantum computers and to retrieve the outputs from them quickly will help to influence the next experiment. However, with the rarity of quantum computing, careful planning of the holistic workflow of the data and compute will be needed to ensure best efficiency of location and data pipelines. There will be an even greater need to maintain the large volumes of data necessary for the calculations "close" to the compute power to avoid large delays in moving data around. The timelines for the impact of quantum computing remain uncertain as the jump from research to production ready is hard to judge. Not every LotF will have a quantum compute facility nearby, but in time they will be able to access this accelerator technology more readily to support their key processes. Unarguably, quantum computing will be a very exciting area for life science and will create a whole new era of scientific exploration.

1.2.5.3 Impact of AI and ML

Even with all the hype around it, AI and its subtypes, e.g. ML, will undoubtedly reshape the R&D sector and have a huge impact on the LotF [85, 86]. Many see AI as the competitive edge which will accelerate products to market, or improve patient outcomes and care, and drive cost efficiencies. As a consequence, there now exists a major talent war as organizations seek to attract the best candidates.

With the rise of AI within life sciences and health care, it has become obvious that a key blocker to success is not the maturity of the AI tools and techniques but access to data in sufficient volume and quality for the AI and ML methods to operate meaningfully. The phrase "no data, no AI/ML" is a signature of the current challenge, with much of the accessible data having been created without due care and attention to reproducibility and the FAIR principles, which are only now driving business improvement in data collection and annotation. Depending on the AI/ML model being developed, having access to a broad cohort of data from across the particular domain will be critical to ensure the necessary diversity, edge cases, and breadth. It is this which will make the analyses successful and be broadly applicable.

The LotF will be both the source of new data to drive new insights from the AI predictive workflows and a beneficiary of the AI outputs which can augment the scientists' work. As mentioned earlier, voice activation, AR, and other assisted technologies all use elements of AI to support the user, whether as chatbots or more sophisticated experiment assistants for the scientist. For example, an automated AI assistant needs to be trained on data to enhance its capability. In time it learns from the human interactions, and this helps to improve its responses and output. Even without AI though, the drive for higher quality and more abundant data remains critical.

The role of AI in generating new ideas fits perhaps most cleanly in the in silico predictive, "design" workflows that have always existed in science. However, AI has the potential to produce new ideas not previously explored or considered by humans. For the lab scientist, the role of AI will be multivariate, from supporting the initial idea to be explored, through experimental design and execution, through to finally how the data is captured and the results analyzed. AI will augment the scientists' capability during their time in the lab as well as provide new insights to guide the best outcome from the experiment. For some, the likely benefit will be decreased experiment cycle times, allowing a better outcome in a fixed time period, for others it will be quicker decision-making through linking the virtual with the physical. Complementary to this, using AI and robotics appropriately in the LotF will allow scientists to focus on the practical things that these technologies do not support well. This will make the fewer humans in the LotF more efficient and productive. Other “softer,” less technical factors will also become increasingly important going forward; these include the broader ethics of AI and the possible regulatory implications of using AI for R&D decisions. The clamor to solve these issues will become louder as the potential and positive impact of AI on life science and health care is demonstrated, validated through application of the AI models to real decision-making.

1.2.6 New Science

Any attempt to predict what will be the big new, “hottest” areas of science is fraught with risk. When one overlays, for the purpose of this book, how those “hot new science areas” might impact the experiments and activities going on in the lab of the future, combined with how that LotF might look physically, then the chances of this section being at best, a bit “off” and at worst plain wrong increase rather dramatically! Nevertheless, even with this “caveat emptor,” we feel that in this forward-looking section, it is important to call out a few of the new scientific areas [87] which we personally feel are worth watching for how they might impact the LotF. In keeping with the broad scope of this book we have concentrated more on the likely scientific developments in (i) the health care and (ii) the life sciences domains, but we have also picked out a small number of examples in (iii) other scientific areas.

1.2.6.1 New Science in Health Care

The biggest drive recently in health care, for both diagnosis and treatment, has been the move away from more population-based approaches toward a much more personalized focus. This has been made possible by the huge advancements in gene and genome-based technologies. Advances in gene and whole-genome sequencing will continue to assist better diagnosis, with sequencing times and costs reducing dramatically, and accuracy and quality rising significantly. These advances will make the protocol-driven labs more prevalent, more efficient, and more cost-effective. The development of better treatments based on gene expression manipulation and gene editing (e.g. CRISPR) [4]) as well as pure gene therapy [88] will continue apace. Diseases that will benefit from such developments will include many inheritable conditions such as Huntington’s chorea and cystic fibrosis, as well as many cancers.

On the whole cell front, improvements in chimeric antigen receptor T-cell (CAR-T) [89] treatments to “supercharge” a patient’s own immune system will mushroom. Individual CAR-T therapies to fight cancers more widely, not just leukemia and lymphoma but also more difficult-to-treat infections (e.g. tuberculosis [90] and some viruses), will become more widespread and cost-effective [91].

Other, more traditionally based approaches to the treatment of diseases, such as vaccines to combat certain viruses (e.g. influenza and novel corona viruses) and some cancers (e.g. cervical cancer), as well as stem cell therapy [92] will continue to thrive. New, more effective vaccine approaches to a greater range of cancers and novel viruses will be developed more quickly than before. Better understanding of some long-standing diseases, for example in the cardiovascular arena, will demonstrate infectious components [93], and these too will become susceptible to vaccine approaches.

Building on the infectious agent theme, research into novel approaches to treat bacterial and viral infections will continue, although probably mostly in academic and charitable trust-funded labs. Approaches such as phage-based treatment for bacterial infections will become more of a focus as traditional small molecule-based strategies are met with evermore intractable and resistant bacteria [94]. Supercharged immunological approaches to bacterial infection will also be a focus for research.

The growth of such novel therapeutics as CAR-T, alongside other whole cell-based approaches and non-small molecule agents, will complement the ever-expanding set of large-molecule therapies. The use of these so-called biopharmaceuticals or biologics has become more widespread in the past decade and will continue to grow. Similarly, the research, development, and manufacture of antibodies [95], modified RNA [96], peptides [97], conjugates, proteolysis targeting chimera agents (PROTACS) [98], antisense oligonucleotides, and other therapeutic macromolecules will continue to expand rapidly. While in vitro activity of such agents can often be demonstrated relatively clearly, they present a major challenge when it comes to in vivo efficacy. The development of novel formulation and drug delivery systems to enable effective administration of these twenty-first century therapeutics will become a major area of scientific investigation.

Finally, an area of growing interest, which could be considered the antithesis of antimicrobial research, is that of the microbiome [99]. There is increasing recognition that the commensal bacteria and other microbes which live symbiotically in and on our bodies (mainly mucous membranes in, for example the gut and also on the skin) can play a major role in our acquisition, presentation, and the severity of certain diseases (e.g. irritable bowel syndrome, Crohn's disease, and psoriasis). Research into an individual's microbiome and treatments based on "normalization" of a person's inherent flora will grow and become more mainstream over the next few decades [100].

1.2.6.2 New Science in the Life Sciences Domain

As discussed in several of the earlier parts of this section, there is one critical, global driver which will dominate new science and how it is performed in the LotF; that key driver is climate change and the supporting concept of "sustainability". There will be new research looking specifically into climate change and sustainability as areas of interest in themselves, but the need for the LotF, both the hypothesis- and the protocol-driven lab, to be more sustainable, less dependent on oil and oil-based products, and yet be more efficient, will become paramount in the decades to come. Labs that do "chemistry" will be a primary focus for these developments, but biology-focused labs will not be immune. The pressure to be more environmentally friendly, using fewer reagents and disposable materials, will lead to new research to discover, for example effective replacements for all the lab plastics currently used; greener chemistry (use of less-toxic solvents and reagents); greater use of catalysts; and more use of biological systems to perform complex chemical transformations. None of these examples are exactly new, but their importance and greater use in the LotF will be significant.

Just as the next generation of scientists is exquisitely conscious of the environment, so too is it particularly focused on animal welfare. The ever-growing drive toward minimization of the use of animals in research and product testing, while it can never in truth be completely eliminated, will continue to accelerate. Initiatives such as the "3Rs" [101] looking to replace, reduce, and refine the use of animals in the lab will gain more traction [102]. In vitro approaches to meet the goals of the 3Rs will include developments such as organ-on-a-chip [103] and the increasing use of stem cells. These new methods will become widespread in the LotF.

Finally, there is one lab technique, which has been a mainstay of the lab for hundreds of years, yet is still undergoing significant evolution and is likely to feature significantly in the LotF: microscopy. Advances in traditional imaging revolutionized life sciences over a decade ago, but current developments in microscopy are likely to transform utterly how in the future we perceive "things" both at the molecular and macromolecular levels. There are two specific examples, which we feel are worth mentioning here: firstly, the scanning tunneling microscope (STM) [104] and secondly, the cryo-electron microscope (cryo-EM) [105]. STM and other comparable new microscopy techniques [106] have the potential to take to an even higher level our ability to study cells, solid-state materials, and many other surfaces. STM has clear potential applications in biology, chemistry, surface science, and solid-state physics [107]. The STM, which operates through the principles of quantum tunneling, utilizes the wavelike properties of electrons, allowing them to "tunnel" beyond the surface of a solid into regions of space that are normally forbidden under the rules of classical physics. While the use of STM has been focused mainly on physicochemical and solid-state challenges, increasingly scientists are looking at STM as a means to see more deeply into chemical and biochemical systems, right down to the atomic level [108]. Cryo-EM is the electron microscopic imaging of rapidly frozen molecules and crystals in solution. It demonstrates its main benefits at the macromolecular level, enabling scientists to see the fine structures of proteins, nucleic acids, and other biomolecules, and even to study how they move and change as they perform their functions, but without having to use the intense electron beams and high vacuum conditions used in traditional electron microscopy [109].

1.2.6.3 Other Important New Science Areas

We have asserted throughout this section that the driver of climate change and the push to greater sustainability will dramatically affect how the LotF will look, and what will take place within it. In a final piece of speculation on what new science will be taking place in these future labs, we suggest two research areas, which we believe will occupy a great deal of time and effort in labs over the next 10–20 years. These two areas are carbon (actually carbon dioxide) fixing and sequestration [110], and R&D around new battery technology, particularly new technologies which avoid the use of heavy metals [111]. The scientists working in or near the LotFs will do a great disservice to their descendants and to the planet if they do not research these critical areas.

1.3 Thoughts on LotF Implementation

The lab environment is changing – this is certain. New and existing science demands combined with critical issues of data management and reproducibility will require a strategic direction to be set and then deployed. It will be important for lab managers to identify what they want to achieve by employing the new approaches of AI, quantum computing, and advanced automation technology. Business ambition and needs, and the assessment of the maturity of organizations beyond the lab environment in the context of initiatives such as FAIR data, will need to be investigated as a matter of urgency to help drive lab of the future decision-making. With such a pace of change it will be important to "think big" as well as be practical during implementation. Thinking in expansive terms, organizations must consider all the opportunities on offer within the key areas of technology, data, people, and process to highlight possible future visions and ways of working. They should use scenario planning to explore, influence, plan for, and manage the future. These scenarios will perhaps be most effective when they are personalized to the organization, function, lab, or team's future, rather than to a generic vision. The benefit of running pilots prior to fuller implementation in the LotF cannot be overstated. Small LotF pilots will allow experimentation across the broad themes. These will reveal what works and what needs adjustment based on the key lab environments. The successful use cases can result in new designs, collaborations, future partnering with technology groups, and new predictive models to support experiments in a timely manner. Moving beyond these smaller pilots and the learnings from them will help catalyze organizational change to support a lab environment that can adapt to new science and get the most from data, digital technology, and AI-driven transformations. All these changes will present new business opportunities, the chance for new relationships with vendors, and the need for new business partners. They will also present opportunities for all lab colleagues to take part in the transformation and to take on new roles and skills to support the implementation and future impact.

1.4 Conclusion

In this section we have endeavored to show how the LotF will potentially evolve, using five main areas as a focus for those possible changes and developments: (i) the people and organizational culture aspects; (ii) the process components; (iii) the LotF environment and design; (iv) the data management challenges; and (v) the new technologies and the new science which will take place in those LotFs. In this concluding section, we would like to pick out just a few key messages from each of these areas to highlight the promise and the challenge that “LotF” presents.

From a people and culture perspective, the point we would stress most is the importance of considering the future lab from the perspectives of the different roles working in, around, or in association with the LotF: the scientists – not just the practical hands-on chemists, biologists, biochemists, physicists, etc. but also the new breed of data scientists and engineers – the lab managers and building managers, the technicians and equipment operators, and all the other staff who will make the LotF an exciting, stimulating, and challenging place to work. The LotF will be more “open,” collaborative, and more automated, if rather more sparse of people. Critical to the LotF’s success will be the “UX” of all the people associated with it.

The processes in the LotF will be dominated by flexible automation and robotics, whether that lab is a hypothesis-driven, research lab, or a manufacturing, testing lab operating more in “LaaS” mode. More effective in silico modeling of the lab processes will make the LotF a safer, more productive place to work.

The lab environment, as well as being designed around large amounts of automation and robotics, flexibly configured, and interconnected, will more often than not be remote from the “customers” of the work actually being done. Good data and network interconnectedness of the LotF will be absolutely critical if it is to operate effectively and securely. The LotF will also be a markedly more sustainable and greener environment.

The data generated by the LotF, whether it is the “raw” data coming off the instruments or the “refined” result data derived from the raw data, will continue to be key to the LotF; if anything, the criticality and value of the digital assets generated by LotFs will become even more important in the future. Data-focused technologies and standards such as IoT, FAIR, SiLA, and Allotrope will ensure that the high-value digital assets are well managed and secured. The increasing focus on data privacy, security, and protection will put heavy pressure on LotFs with regard to good governance and compliance.

Finally, when considering new technologies such as AI/ML and quantum computing, and new science such as CRISPR and CAR-T, we feel we cannot overstress that science, technology, research, and development never cease to evolve. New discoveries are being made constantly, and these will without doubt have an impact on the LotF in ways we cannot predict now, in 2021. We can state quite confidently that there will be some technologies or scientific discoveries we have not mentioned here, which will affect significantly what happens in the labs of the future. We have highlighted those we feel now are important to help guide and stimulate you, the reader as you try to understand where and how the LotF is likely to develop. There will be others. In fact during 2020 a number of the themes and directions we have highlighted in this chapter have come to pass as the world has grappled with the momentous events surrounding the SARS-CoV-2 (COVID-19) pandemic. The pace of scientific and medical response to understanding the virus and its treatment has been unparalleled. Global, open and collaborative sharing of data and information on the virus itself, on the epidemiology of the disease, on its acute treatment through, for example, accelerated drug repurposing and the development of an effective vaccines, has allowed enormous progress to be made towards helping the control of the virus [112]. New technology has also enabled safer lab working to cope with COVID-19 restrictions (e.g. equipment booking, lab capacity planning, remote access to instruments supporting home working, and tracking of contacts). Technology and automation have supported the faster establishment of new test facilities, but there have been differences in approach between larger and smaller local labs, and between different countries, e.g. between Germany and UK (in the UK these are known as "Lighthouse Labs" [113]). And new science has played a huge role in the development of the many potential vaccines currently being progressed and trialled in labs and clinics across the world [114]. Nevertheless, despite this explosion of cross-border, cross-research group and company collaboration, there have still been challenges around speed of data sharing, data accuracy and trust in the information being disseminated widely, particularly as that sharing has often happened without or before robust peer review [115]. This tells us that there is still a long road ahead on the LotF journey. Most assuredly though, the lab of the future in say, 2030, will be very different from the lab of 2020; but it will be a fascinating, exhilarating and safer place, not only to work, but also to have your work done, and to do new science.

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